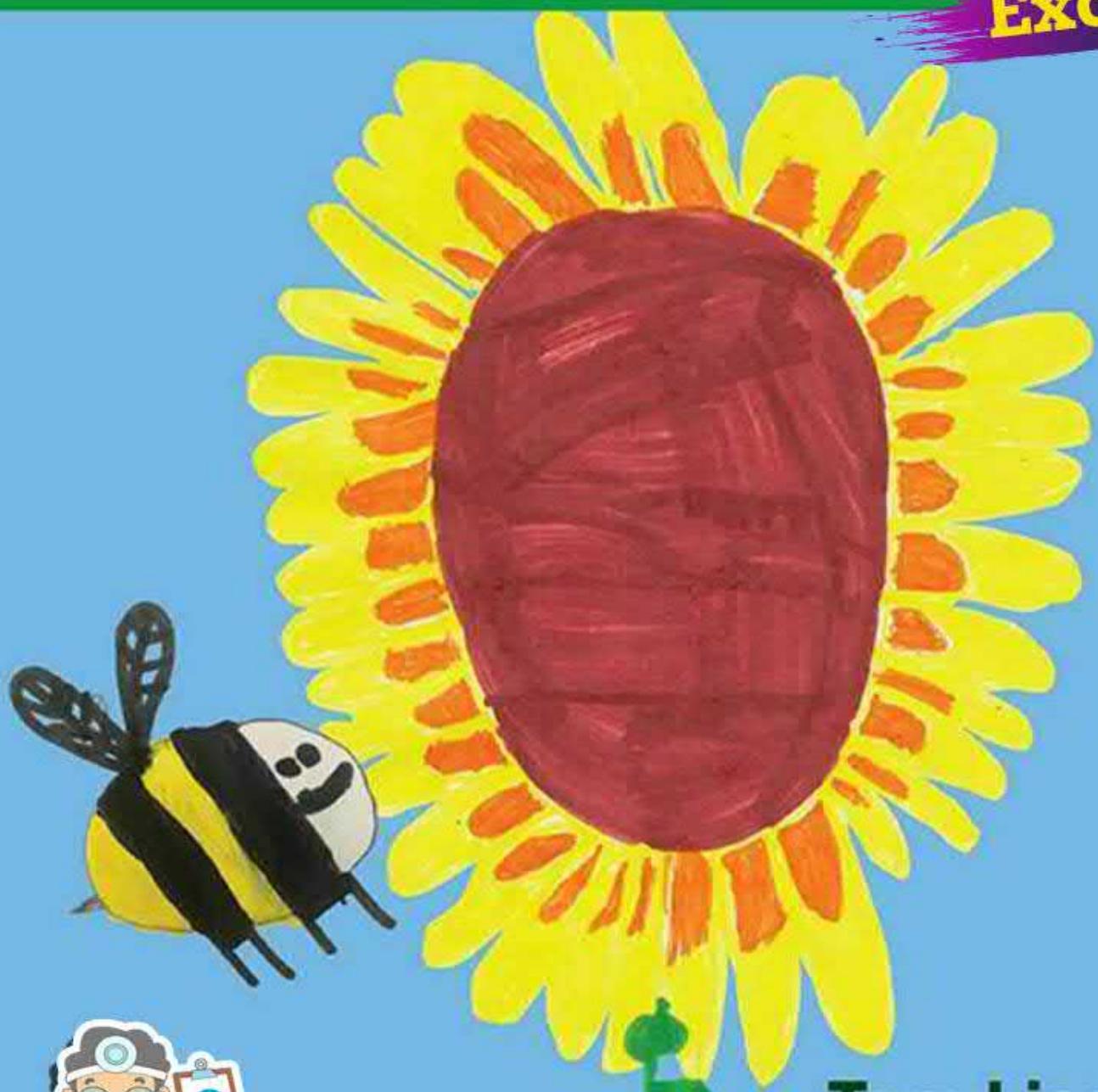


Illustrated Textbook of **PAEDIATRICS**

SIXTH EDITION

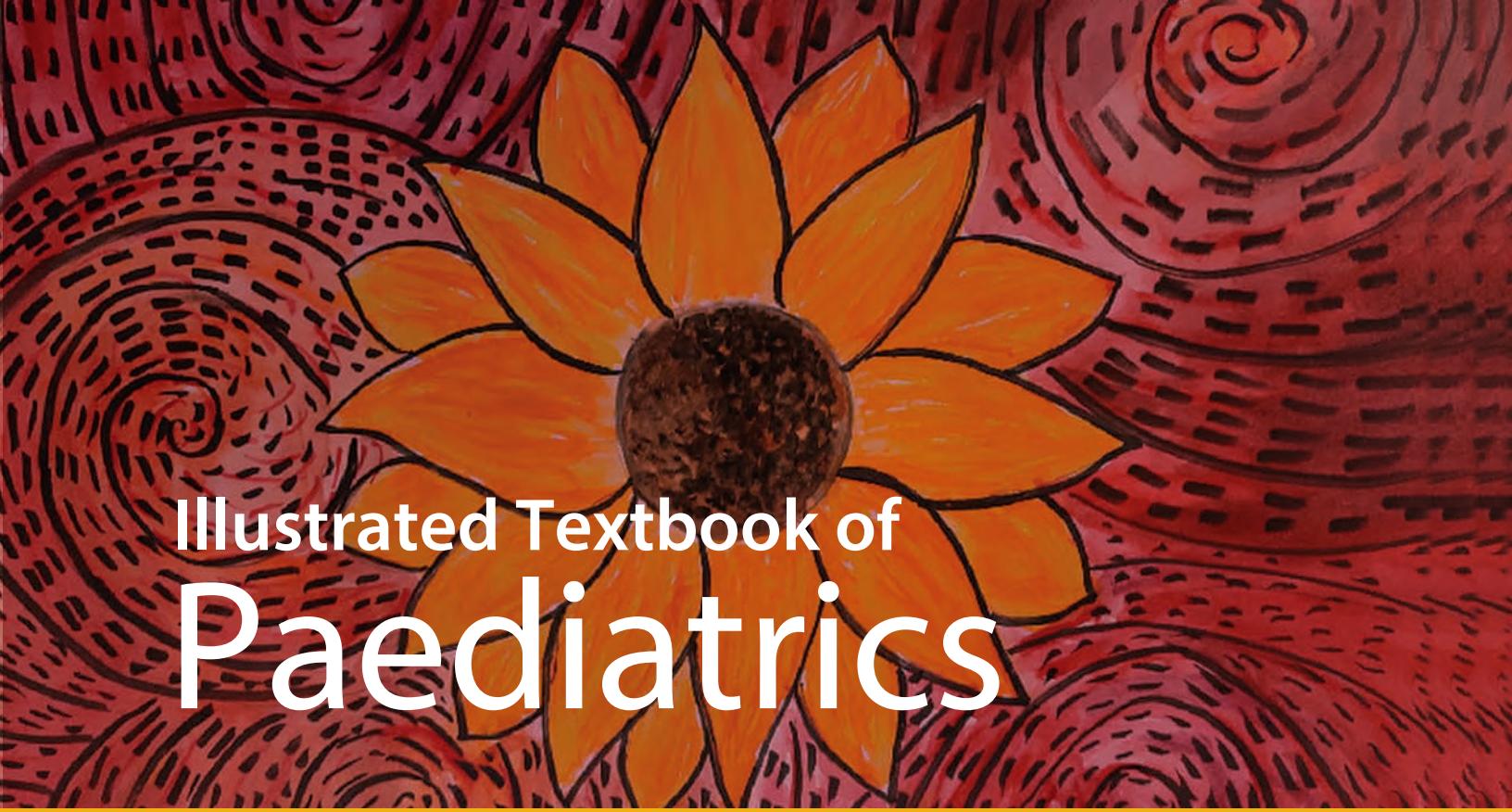
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Pediatrics & Neonatology Journals
[Ahmed Manfy] on **TELEGRAM**

Tom Lissauer
Will Carroll

Illustrated Textbook of
Paediatrics



Illustrated Textbook of Paediatrics

SIXTH EDITION

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Foreword by Dr Ranj Singh



I can still remember how I felt when I started my paediatrics rotation at medical school: terrified. I had no idea about children, especially sick ones. They were a complete mystery to me. A bit like when I first encountered the Krebs Cycle... only a little bit cuter.

However, I wanted to be as prepared as possible. The word on the street was that you had to get yourself a copy of this book. It'll see you through all your exams and beyond, they said. It was this book that got me through that rotation with flying colours.

This wonderful text helped me turn that initial terror into a keen interest in the health and wellbeing of children and young people. Little did I know that one day that same interest would lead to a career that I love and cherish so much.

And those people were right. This book did serve me for a very long time: for my medical school finals, during my elective placement overseas, and even when I was sitting my MRCPCH exams. It covers everything that a medical student, and budding paediatrician, needs to know and does it in a way that is engaging as well as relevant to what you will see in practice. The clear diagrams, pop-out boxes filled with useful information, and the incredible clinical images ensure that you get a detailed insight into so many topics and conditions. It's just so easy to pick up and read... and that comes from someone who gets anxiety at the thought of picking up a textbook.

I still dip into it now and again. Sometimes to find out a key piece of information quickly, and sometimes to remind myself of why I do what I do.

Any doctor will tell you that there are key texts that you will remember and refer to throughout your career. Written by legends from the medical world, and trusted by countless students and professionals across the globe. For me, this is one of them. And it will continue to have pride of place on my bookshelf for a long time to come.



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He appeared as a celebrity dancer on the BBC's
Strictly Come Dancing.

Foreword by Professor Sir Alan Craft



When the late Frank A. Oski wrote the foreword for the first edition of this book in 1997, he gave it generous praise and predicted that it would become a 'standard by which all other medical textbooks will be judged'. He was a great man and a wonderful writer, so his prediction was no doubt welcomed by the editors, Tom Lissauer and Graham Clayden, both well known for their contributions to undergraduate and postgraduate medical education and assessment.

I have a much easier task in writing the foreword for the sixth edition. The mere fact that there is a sixth edition is testimony in itself, but there is also the fact that this book has become the recommended paediatric textbook in countless medical schools throughout the world and has been translated into more than 12 languages. I have travelled the world over the last 20 years and wherever I have been in a paediatric department, the distinctive sunflower cover of *Lissauer's Illustrated Textbook of Paediatrics* has been there with me. Whether it is Hong Kong, Malaysia, Oman, or South Shields, it is there!

It is not surprising that it has won major awards for innovation and excellence at the British Medical Association and Royal Society of Medicine book awards. The book is well established and widely read for the simple reason that it is an excellent book. Medicine is now so complex and information so vast that students are no longer expected to know all there is to know about medicine. What they need are the core principles, and guidance as to where to find out more. This book not only gives the core principles, but it also provides a great deal more for the student who wishes to extend his or her knowledge. It is in a very accessible form and has a style and layout which facilitates learning. There are many diagrams, illustrations and case histories to bring the subject to life and to impart important messages. This new edition includes summaries to help revision and there is also a companion book for self-assessment.

Will Carroll has succeeded Graham Clayden as co-editor; he is also a paediatrician with great expertise in medical education and assessment, and has helped ensure that the book continues to provide the paediatric information medical students need. The editing team has been further strengthened for this edition by Keir Shiels as an Associate Editor. The book has been thoroughly

updated and has many new contributors, all of whom are experts in their field and have been chosen because of their ability to impart the important principles in a non-specialist way. The book continues to focus on the key topics in the undergraduate curriculum, and in keeping with this aim there are new, expanded chapters on child maltreatment, genetics and global child health.

There are now countless doctors throughout the world for whom this textbook has been their introduction to the fascinating and rewarding world of paediatrics.

For students, it is all they need to know and a bit more. For postgraduates, it provides the majority of information needed to get through postgraduate examinations. It stimulates and guides the reader into the world of clinical paediatrics, built on the sound foundation of the knowledge base provided by this book.

The editors are to be congratulated on the continuing success of this book. I can only echo what Frank Oski said in his preface to the first edition: 'I wish I had written this book!'



Professor Sir Alan Craft

Emeritus Professor of Child Health, Newcastle University
Past President of the Royal College of Paediatrics and Child Health

Why paediatrics is such a great speciality



Quotes from Dr Ranj Singh

"Most of us go into medicine to help people. There is no other specialty where you can make a bigger difference to someone's life overall than paediatrics. Even if you can't cure someone (and as doctors we soon learn that we can't fix everything), you can have such a massive impact on a child or young person's life that it helps them for years to come. That's what being a doctor is all about. Plus, working with kids can be so much fun!"

"I could go on about how interesting and varied paediatrics is as a specialty, or how no two days at work are the same, or how there's huge potential to do exciting research. But everyone knows that. That's not what got me interested. Children have this amazing ability to bring you back down to earth, teach you what really matters, and show you how to be a better doctor. Plus, seeing how resilient they are and how much joy they can bring makes going to work so much better. I mean, how many jobs are there where you can blow bubbles and watch Frozen on a ward round?!"

"When a student, I know paediatrics is scary, but just throw yourself in. The more you get involved in things – teaching, ward rounds, sitting in clinic, spending time in A&E – the more you will get out of it. You don't have to know it all – that's our job to teach you. My top tip: show that you care and join in."



Quotes from Professor Sir Alan Craft



"Paediatrics spans tiny premature babies to 2 metre high teenagers; everything from health to serious illness; an opportunity with chronic illness to see a child develop. And it all takes place in a family whom you will get to know well."

"When I started in paediatric oncology, fewer than one in five children could be cured. Now it is over 80% in high-income countries. Adapting treatment to be economically possible and worthwhile for those in low- and middle-income countries has been an exciting and rewarding challenge."

"All doctors, whatever their speciality, need to have an understanding of children's development and illness as well as their place in the life of a family and society. Children are the future, and whatever help you give today will be seen in generations to come."

Preface



This textbook provides the knowledge required for the paediatrics and child health curriculum of most undergraduate medical schools and for the Medical Licensing Assessment (MLA) in the UK. It also covers a high proportion of the knowledge needed to prepare for postgraduate examinations such as the Diploma of Child Health (DCH) and Membership of the Royal College of Paediatrics and Child Health (MRCPCH). We are delighted that our "sunflower book" is widely used in many countries outside the UK, including northern Europe, India, Pakistan, Australia, and South Africa, and that there have been numerous translations. We are also pleased that many nurses, therapists and other health professionals who care for children are using the book.

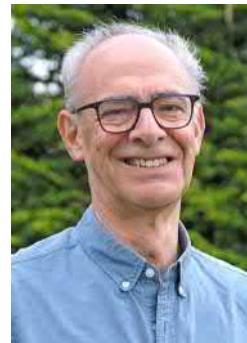
Whilst the real appreciation of why paediatrics is such a great specialty comes from encountering children and young people and their families in clinical practice, this book aims to provide what is required for the 6 to 10 weeks usually allocated to paediatrics and child health in undergraduate training. In recognition of the short time available, we have tried to facilitate learning by using a lecture-note style, by incorporating numerous diagrams and flow charts, and by including illustrations or images to help in the recognition of important signs or clinical features. To make the topics more interesting and memorable, there are key learning points and clinical case histories. Summary boxes of important facts have been provided to help with revision.

The huge amount of positive feedback we have received on the first five editions of the book from medical students, post-graduate doctors, tutors, nurses and allied health professionals in the UK and abroad has spurred us on to produce this new edition. The book has been fully updated, with many sections rewritten, new diagrams created and illustrations redone. There are new, separate or expanded chapters on child maltreatment, genetics and global child health to accommodate their increasing

importance in paediatric practice. There is also a companion book of self-assessment questions.

We would like to thank Graham Clayden, editor for the first four editions, for the inspiration he brought to the book, and all our contributors, both to this and to previous editions, without whom this book could not have been produced. We are also pleased to welcome Keir Shiels as an Associate Editor, who has brought fresh ideas to improve the book. Thanks also to our families – in particular Ann Goldman, Rachel and David and Sam Lissauer, and Lisa Carroll, Daniel, Steven, Natasha, and Belinda Carroll – for their ideas and assistance, and for their understanding of the time taken away in the preparation of this book. We would also like to thank Hannah Lissauer, aged 7 years, for the lovely picture of the sunflower for the cover, helping to maintain its reputation as "the sunflower book".

We welcome feedback on the book.



Tom Lissauer



Will Carroll



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Paediatrics and child health

The child and young person's world
Wellbeing

1
6

Major issues in child health in the UK and high-income countries
Conclusion

7
11

Features of paediatrics and child health:

- The world in which we grow up, in combination with our genes, determines who we are.
- A child's chances of survival is a useful indicator of population health and quality of healthcare services – whereas the infant mortality in the UK is 3.6 per 1000 live births, in Sweden it is 2.2 whilst in Bangladesh it is 25 and in Malawi 35 per 1000 live births.
- Important public health priorities for children and young people in the UK are reduction in: mortality, health inequalities, variations in health outcomes, obesity, adverse childhood events, emotional and behavioural problems, smoking and drug abuse; and improving the safeguarding of vulnerable children.
- Many of the causes and determinants of poor health outcomes in childhood are preventable.

Doctors can play a role by raising society's awareness of how the public health priorities can be achieved and in improving the health systems and healthcare services they provide.

The child and young person's world

Most medical encounters with children involve an individual child presenting to a doctor with a symptom, such as difficulty breathing or diarrhoea. After taking a history, examining the child and performing any necessary investigations, the doctor arrives at a diagnosis or differential diagnosis and makes a management plan. This disease-oriented approach, which is the focus of most of this book, plays an important part in ensuring the immediate and long-term wellbeing of the child. However, the child does not have their illness in isolation, but within the wider context of their environment. Doctors, especially those who work with children, must understand how that context affects their wellbeing throughout childhood and beyond ([Case history 1.1](#)). This is the primary focus of the rest of this chapter. It goes without saying that everyone's unique characteristics – their genes, age, gender – will affect their health status and wellbeing. But health, development and temperament



Case history 1.1

David's asthma attack

David is a 9-year-old boy who has been admitted to hospital with an asthma attack.

He has been admitted three times in the past 6 months. His previous hospital records show that he has missed his last two hospital appointments to review his asthma, and on the last occasion the consultant had recorded that she was worried he was not taking his medications.

On arrival in the Paediatric Emergency Department, he is very short of breath and needs oxygen, nebulized bronchodilators, and intravenous steroids. His condition improves and he is admitted to the children's ward for further treatment.

Next morning he is ready for discharge. A colleague has re-emphasized to David the importance of taking his medicine regularly, rechecked his inhaler technique and arranged another appointment.

Question

Is there anything else that you would like to do before discharge? (Continued later in the chapter.)

are also profoundly influenced by the social, cultural and physical environment, much of which is outside the individual's control. These influences can be felt at many different levels, from their family and immediate social environment, to the local social fabric, all the way to the national and international environment ([Fig. 1.1](#)). Our ability to intervene as clinicians needs to be seen within this context of complex interrelating influences on health.



In order to be a truly effective clinician, the doctor must be able to place the child's clinical problems within the context of the family and of the society in which they live.

The child's immediate social environment

At various ages, different aspects of the social environment (Fig. 1.1) will exert varying degrees of influence over the health and wellbeing of a child:

- Infant or toddler: life mainly determined by the home environment.
- Young child: school and friends, in addition to home environment.
- Young people: physical and emotional changes of adolescence, but also aware of and influenced by events nationally and internationally, e.g. in music, sport, fashion or politics.

Family structure

Although the 'two biological parent family' remains the norm, there are many variations in family structure. In the UK, the family structure has changed markedly over the last 20 years (Fig. 1.2).

Lone-parent households – 22% of children in the UK now live in a lone-parent household (86% of which are headed by a female parent). Whilst many lone parents are excellent parents, being a lone parent is associated with an increased risk of social adversities: a higher level of unemployment, poor housing and financial hardship, with nearly half (47%) of the children living in poverty. These disadvantages may in turn mean lone parents require

greater support in providing for their children, e.g. the provision of a healthy diet, take-up of preventive services such as immunization and developmental screening, vigilance about safety, and coping with an acutely sick child at home. This may in part explain why children raised in a lone-parent family are at higher risk of poor educational and health outcomes, including mental health.

Reconstituted families – The increase in the number of parents who change partners and the accompanying rise in reconstituted families (1 in 10 children live in a step-family) mean that children are having to cope with a range of new and complex parental and sibling relationships. This can lead to greater risk of emotional, behavioural and social difficulties.

Looked-after children – The term 'looked-after children' is generally used to mean those children who are looked after by the State. Most of these children will be in foster care, either living with a kinship (family) carer or with a non-family foster carer. A small number live in children's homes or other supported living accommodation. Children enter care for a number of reasons including physical, sexual or emotional abuse or neglect, or being an unaccompanied asylum-seeking minor. In 2016/17, there were over 96,000 children in care in the UK. They have significantly greater health needs than children and young people from comparable socio-economic backgrounds who have not been 'looked after'. Past experiences, including an often chaotic start in life, removal from family, placement location and transitions mean that these children are often at risk of having poor access to health services, both universal and

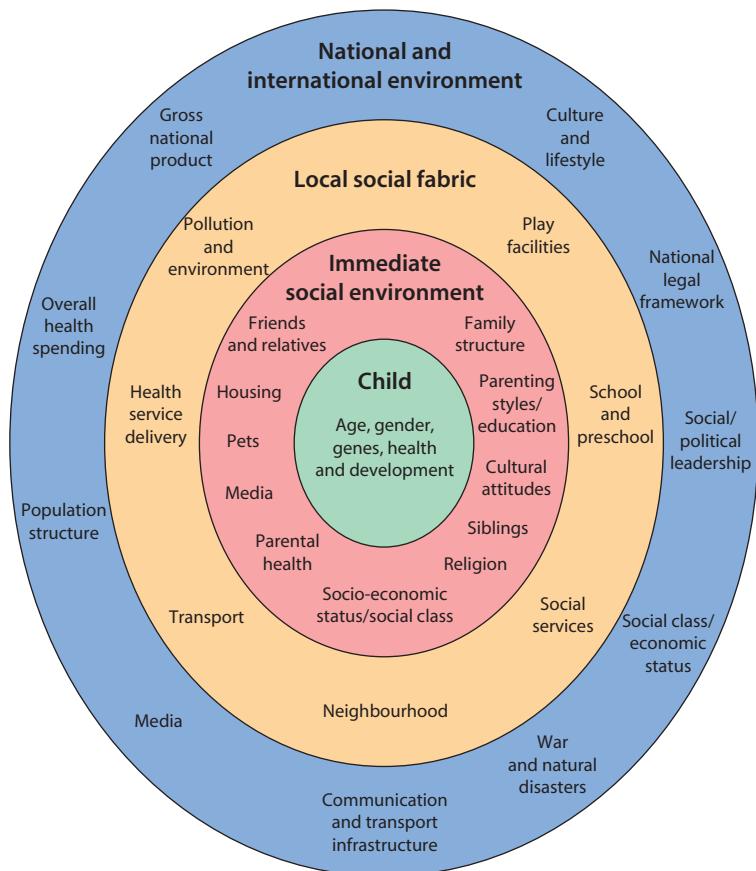


Figure 1.1 A child's world consists of overlapping, interconnected and expanding socio-environmental layers, which influence children's health and development. (After: Bronfenbrenner U: Contexts of child rearing: problems and prospects. American Psychologist 34:844–850, 1979.)

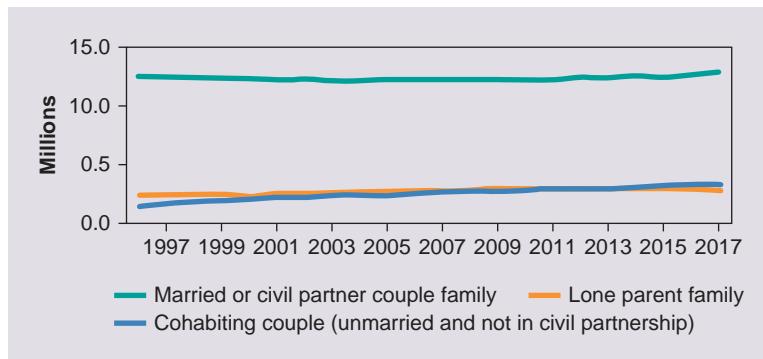


Figure 1.2 Structure of families in the UK, 1995–2017, showing that there are around 1.7 million lone-parent families in the UK, and that this number has been relatively constant over the last 20 years. (From: Labour force survey. Office for National Statistics.)

specialist. For example, they are less likely to have been immunized. They fall short even of their statutory health checks – such as dental and annual medical assessments – with nearly 15% of children missing out. There is increasing evidence that children who experience these ‘adverse childhood experiences’ (ACEs) are more likely to have physical and mental health problems throughout their life (Table 1.1).

Asylum seekers – These are people who have come to the UK to apply for protection as refugees. They are often placed in temporary housing and moved repeatedly into areas unfamiliar to them. In addition to the uncertainty as to whether or not they will be allowed to stay in the country, they face problems as a result of language barrier, poverty, fragmentation of families and racism. Many have lost family members and are uncertain about the safety of friends and family. All of these can have a serious impact on both physical and mental health. Children have particular difficulties as the frequent moves can disrupt continuity of care. It also disrupts childhood friendships, education, and family support networks. As with looked-after children, they are more likely to have been exposed to multiple adverse childhood experiences, which have an inevitable impact on a child’s wellbeing and put them at risk of poor health outcomes.

Parenting styles

Children rely on their parents to provide love, stimulation and security and to nurture them, as well as catering for their physical needs of food, clothing and shelter. Parenting that is warm and receptive to the child, while imposing reasonable and consistent boundaries, will promote the development of an autonomous and self-reliant adult. However, some parents are excessively authoritarian or extremely permissive. Children’s emotional development may also be damaged by parents who neglect or abuse their children. The child’s temperament is also important, especially when there is a mismatch with parenting style; for example, a child with a very energetic temperament may be misperceived in a quiet family as having attention deficit hyperactivity disorder (ADHD).

Siblings and extended family

Siblings clearly have a marked influence on the family dynamics. How siblings affect each other appears to be determined by the emotional quality of their relationship

Table 1.1 Adverse Childhood Experiences (ACE) and their associated outcomes

Examples of Adverse Childhood Experiences	Increased lifetime health risks
History of abuse (physical, emotional and sexual) or neglect	Mortality
Domestic violence	Risk-taking behaviours, e.g. smoking, substance abuse
Parent/family member with alcohol or substance abuse	Mental health problems, e.g. anxiety, depression
Parent/family member with mental illness	Coronary heart disease including stroke
Witnessing or experiencing community violence	Diabetes
Parental separation/divorce	Some cancers

with each other and also with other members of the family, including their parents. Many grandparents play an important role assisting with child care, often to enable parents to go to work, and are also influencing family dynamics.

Cultural attitudes to child-rearing

The way in which children are brought up evolves within a community over generations, and is influenced by culture and religion, affecting both day-to-day issues and fundamental lifestyle choices. For example, in some societies children are given considerable autonomy, from deciding what food they want to eat to their education, and even to participating in major decisions about their medical care. By contrast, in other societies, children are largely excluded from decision-making. Another example of marked differences between societies is the use of physical punishment to discipline children; in England and Northern Ireland it is not illegal for a parent to smack their child to administer ‘reasonable punishment’ as long as it does not leave a mark or harm the child and is not administered with an

instrument, whereas corporal punishment for children is illegal in 46 countries, including Scotland and Wales. The expected roles of males and females both as children and as adults differ widely between cultures.

Peers

Peers exert a major influence on children. Peer relationships and activities provide a 'sense of group belonging' and have potentially long-term benefits for the child. Conversely, they may exert negative pressure through inappropriate role modelling. Relationships can also go wrong, e.g. persistent bullying, which may result in or contribute to psychosomatic symptoms, misery and even, in extreme cases, suicide. The increasing role of mobile technologies and social media has changed the nature of peer relationships and is an area of increasing importance to children and young people's social and mental wellbeing.

Socio-economic status

Poverty is the single greatest threat to the wellbeing of children, as it can affect every area of a child's development – social, educational and personal. Children and young people living in poverty are more likely to be materially deprived, meaning they are unable to afford adequate basic needs such as food and clothing. Deprivation and low socio-economic status are associated with poorer access to food of adequate quantity or nutritional value, substandard housing or homelessness, poor parental education and health, and poor access to healthcare and educational facilities. In the UK, prevalence of the following are increased by poverty:

- low birthweight infants
- injuries (accidental and non-accidental)
- hospital admissions
- poor physical health from long term conditions such as asthma and diabetes
- behavioural problems
- mental health problems
- academic underachievement, special educational needs
- neglect.

The most widely used poverty measure in the UK is 'household income below 60 percent of median income' – so-called 'relative poverty'. Data for 2016–2017 estimate that there are 4.1 million children living in poverty in the UK – a rise of more than 500,000 children since 2011/2012. When the cost of housing is factored in, this equates to 30% of children in the UK living in relative poverty. The proportion of children living in poverty has not declined since 2002 (Fig. 1.3). The groups that are more at risk from poverty include lone parents, large families, families affected by disability, and minority ethnic groups.

Even a few years of poverty can have negative consequences for a child's development and is especially harmful from the ages of birth to 5 years. Research indicates that being poor at both 9 months and 3 years is associated with increased likelihood of poor behavioural, learning and health outcomes at age 5 years (Magnuson, 2013). By the age of 4 years, a development gap of more than 18 months can be seen between the most disadvantaged and the most advantaged children, and this can significantly impact on education and social relationships (Sutton Trust, 2012).

Local social fabric

Neighbourhood

The physical environment in which children live – the quality of housing and public facilities, the level of environmental pollution, and whether they have safe areas for play – will affect children's health. Living in cohesive, supportive communities is a protective factor for positive physical, emotional and social development. Conversely, social adversities, such as gang violence and drugs, will negatively affect the emotional and social development of children, as well as their physical health.

The increasing access that children and young people have to mobile technology and social media means that the boundaries of their social network often far outstrip those of their physical neighbourhood. Social cohesion, community support and the influence of peers among these virtual networks have become as important as those of their immediate physical environment for many children and young people.

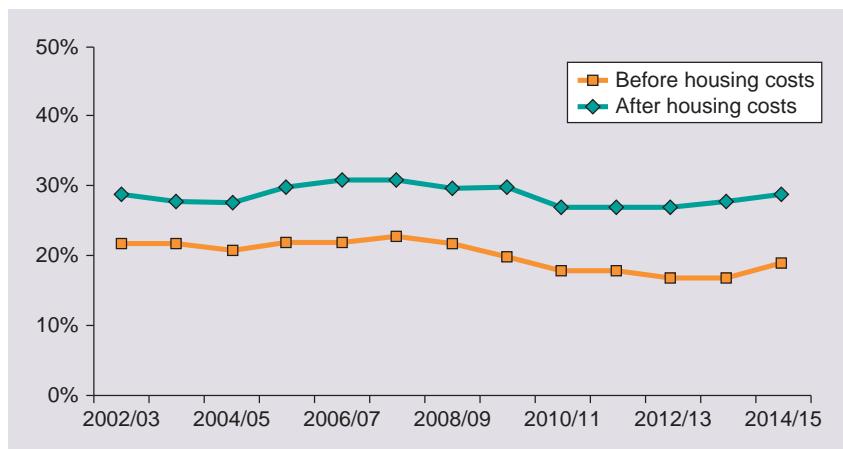


Figure 1.3 Proportion of UK children living in poverty (60% of median income) from 2002/2003 to 2017/2018, shown calculated with or without including housing costs. Households below average income: 1994/1995 to 2017/2018. (From: UK Department for Work and Pensions, 2019.)

Health services

Healthcare for children and young people varies across the globe, as a result of structural, economic and cultural factors, which affect how children, young people and families access healthcare, as well as how healthcare is delivered. This variation is replicated at local level, and impacts on morbidity and mortality in children. It may reflect patient or family preferences, but more often relates to how easy it is to access healthcare; how the quality of services differ depending on the provider; and how health services are set up to balance local needs with more specialist services. An example of how these factors affect health service use is shown in Fig. 1.4, demonstrating a fifteen-fold variation in hospital admission rate for bronchiolitis in England which cannot be explained by differences in patient characteristics and did not correlate with deprivation.

Schools

Schools provide a powerful influence on children's emotional and intellectual development and their subsequent lives. Differences in the quality of schools in different areas can accentuate inequalities already present in society. Schools provide enormous opportunities for influencing healthy behaviour through personal and social education and through the influence of peers and positive role models. They also provide opportunities for monitoring and promoting the health and wellbeing of vulnerable children.

Travel

The increasing ease of travel can broaden children's horizons and opportunities. Especially in rural areas, the ease and availability of transport allow greater access to medical care and other services. However, the increasing use of motor vehicles contributes to the large number of injuries sustained by children from road traffic accidents, mainly as pedestrians. It also decreases physical activity, as shown by the high proportion of children taken to school by car. Whereas 80% of children in the UK went to school by foot or bicycle in 1971, only 47% of children aged 5–16 years did so in 2018.

Air quality

Sustained exposure to air pollution (predominantly in the form of nitrogen dioxide and airborne particulate matter such as dust or soot) is associated with poor respiratory and cardiovascular outcomes, and increases the risk of respiratory deterioration and death in vulnerable children, such as those with asthma or cystic fibrosis. There is emerging evidence that maternal exposure to air pollution is associated with higher risk of premature birth and low birthweight.

Worldwide, 93% of children and young people aged <18 years are exposed to air pollution levels which the WHO deems unsafe. The problem is worst in low- and middle-income countries, but even in the UK nearly a third of children live in areas of poor air quality. Air pollution can be outdoor (ambient pollutants primarily from industrial or transport-related fossil fuel combustion) or within households (from polluting fuels and appliances, and tobacco smoke). Children living in deprived neighbourhoods, particularly in urban areas, are disproportionately affected ([Case history 1.1 \(continued\)](#)). The WHO included air quality and climate change within the top ten global public health threats of 2019.

National and international environment

Economic wealth

In general, a country's economic wealth is positively correlated with the health of its children and young people. The lower the gross national product (a national measure of economic wealth):

- the greater the proportion of the population who are children
- the higher the childhood mortality.

However, as described above, even in countries with a high gross national product, many children live in poverty.

In addition, in all countries, including those with high gross national product, difficult choices need to be made about the allocation of resources. These decisions often favour high users of healthcare such as the

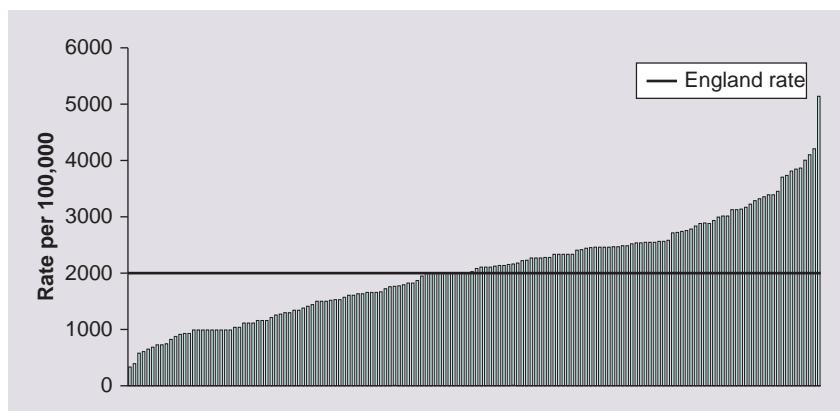


Figure 1.4 Admissions for bronchiolitis in children per 100,000 population aged under 2 years by area of residence in England, showing 15-fold variation in admission rates. (From: Cheung CR, Smith H, Thurland K et al: Population variation in admission rates and duration of inpatient stay for bronchiolitis in England. Arch Dis Child 98:57–59, 2013.)



Case history 1.1 (continued)

David's asthma: looking beyond the disease

Before you discharge David from hospital, you explore further how the asthma is affecting him more broadly. You find that David's school attendance is only 78% over the past school year, and his teacher is concerned that his work is falling behind his peers.

A safeguarding meeting is held, including involvement from social care. David's mother is initially angry at the implication that she is neglectful of his medical needs, but it soon emerges that she is wracked with guilt over David's admission, and recognizes that she has not helped him manage his care as well as she should. She did not realize how unwell one could become with asthma.

Her partner recently left the family, and their changed circumstances meant they had to move to a small one-bedroom property on a busy crossroad, affected by mould

and damp. She had to take on a second evening job to make ends meet. Her 15-year-old son, who had recently started smoking, would often look after his siblings in the evening after school while she worked. She herself had serious health problems requiring hospital care, and had already been warned that taking any more time off work would risk her losing her job, which added more pressure to repeatedly rearrange David's appointments.

The biopsychosocial model of health (Table 1.2) can be used for better understanding the underlying issues (such as the impact of his home and environment) on his asthma control.

Questions

What should be done next?

Which other professionals and services can assist?

Table 1.2 Biopsychosocial model to explore David's asthma

	Biological/development	Psychological	Social
Predisposing	Maternal family history of respiratory problems	Mother's anxiety over her ability to manage David's health	Housing quality
Precipitating	Brother starting smoking	Family relationship breakdown	Financial impact of father leaving home
Perpetuating	Poor adherence to medications; Poor understanding of asthma management	Worry about financial situation at home	Difficulty getting to medical appointments due to work pressures

elderly, despite the evidence that improving the health of children and young people provides a greater return on economic investment. Difficult decisions also have to be faced in deciding the affordability of very expensive procedures, such as heart or liver transplantation, neonatal intensive care for extremely premature infants and certain high-cost or cutting-edge drugs. These choices are increasingly the source of economic and philosophical debate across society, and particularly pertinent for countries like the UK in which healthcare is predominantly state-funded.

Media and technology

The media has a powerful influence on children. The impact of television, computers and mobile technology can be positive and educational. However, there are concerns over adverse effects, such as reduced opportunities for social interaction and active learning, lack of physical exercise and exposure to violence, sex, and cultural stereotypes. The evidence for the overall impact of social media on physical and mental health outcomes in children and young people is still relatively sparse. Self-reported wellbeing does seem to be negatively affected among very high users of internet and social media, although it is not clear whether one is the cause of the other.

An advantage of the internet is that it enables parents and children to become better informed about and gain

support for their children's medical problems. This is especially beneficial for the many rare conditions encountered in paediatrics. A disadvantage is that it may result in the dissemination of information that is incorrect or biased, and may result in requests for inappropriate or untested investigations or treatment.

War and natural disasters

Children are especially vulnerable when there is war, civil unrest or natural disasters. Not only are they at greater risk from infectious diseases and malnutrition but also they may lose their caregivers and other members of their families and are likely to have been exposed to highly traumatic events. Their lives will have been uprooted, socially and culturally, especially if they are forced to flee from their homes and become refugees. Recently, the huge increase in the number of refugee children following war and ethnic violence in parts of the Middle East, South-East Asia and Africa, with families displaced internally or in other countries, often in refugee camps, is resulting in deterioration in even their basic health outcomes.

Wellbeing

The concept of wellbeing encompasses a number of different elements and includes emotional, psychological

and social wellbeing. The wellbeing of children is key to the development of healthy behaviours and educational attainment and impacts on their childhood and life chances and on their families and communities.

Overall, young people in the UK report fairly high levels of wellbeing, with 78% of girls and 80% of boys aged 10–15 years in the UK reporting ‘high’ or ‘very high’ life satisfaction in 2018 (ONS, 2019). But this appears to be declining, with another overall contentment survey (The Children’s Society, 2020) among 10–15 year olds being the lowest in a decade.

There is a gender gap, with girls tending to report lower wellbeing than boys. One of the most important factors in promoting children’s wellbeing appears to be the quality of family relationships and parental behaviours and in particular the availability of emotional support. Children with low wellbeing report to feel there is conflict in the family, that they do not have enough friends and have fewer resources than their friends. They are more likely to have been bullied recently. This increasingly takes place online – in 2014, 10% of boys and 19% of girls aged 15 in England reported having experienced cyberbullying in the preceding 2 months (HSCIC/NHS Digital, 2015).

Interventions which can result in improvement in childhood wellbeing include parenting support programmes, emotional health and wellbeing programmes in schools, access to green spaces and opportunities to be active. Children in the UK do much worse in terms of wellbeing compared with other European countries and across the world.

Major issues in child health in the UK and high-income countries

It is the goal of a successful society to ensure that its children and young people are healthy, safe, enjoy life, make a positive contribution and achieve economic wellbeing (DFES, 2003). This section will focus on some of the major public health issues for the 11 million

children and young people in the UK and those in other high-income countries. The additional issues in low- and middle-income countries are considered in Chapter 31, Global child health.

Child mortality

Mortality is a widely used indicator of population health and quality of healthcare services. In 1900–1902, 146 out of every 1000 children born in England and Wales would die before their first birthday; by 1990–1992 the rate had fallen to 7 deaths per 1000 live births and to 3.9 per 1000 live births in 2017 (Fig. 1.5). This dramatic reduction in childhood mortality over the last century was primarily due to improvements in living conditions such as better sanitation and housing, and access to food and clean water. There has also been a marked reduction in childhood deaths from infectious disease, augmented by the increased range and uptake of immunizations.

Today, around 60% of deaths in childhood in the UK are in infants (under one year old); of those, three quarters occur in neonates (first 4 weeks of life). Prematurity and/or low birthweight contribute considerably to infant mortality. Other factors that influence infant mortality include young maternal age (almost double if under 20 years old), ethnic group and socio-economic deprivation. In 2017, black and Pakistani infants in England had two to three times the mortality rate of their white counterparts (Fig. 1.6).

Comparison with other European countries

Although childhood mortality rates have declined over the past three decades, the UK continues to have a much higher child mortality rate compared with many European countries, and its relative position is deteriorating. In 2018, the under 5 mortality rate for the UK was 4.3 deaths per 1000 live births, compared with 4.0 deaths per 1000 live births in France and 2.7 deaths per 1000 live births in

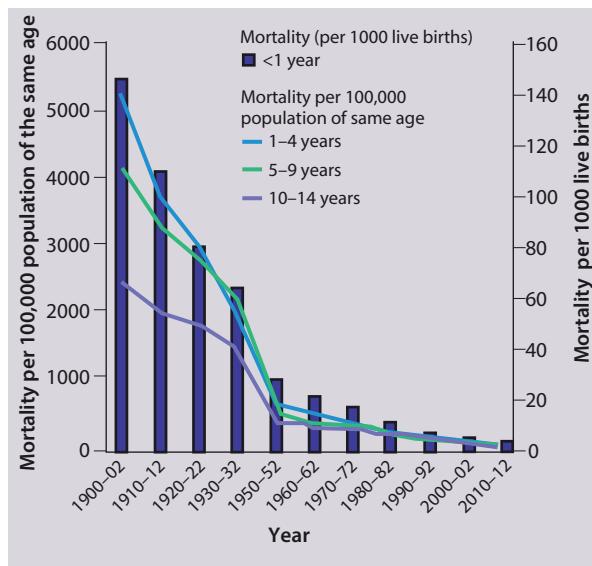


Figure 1.5 Marked reduction in childhood deaths between 1900 and 2012 in the UK. This is shown as deaths by age group per 100,000 population of the same age and infant mortality per 1000 live births. (Source: ONS, 2014.)

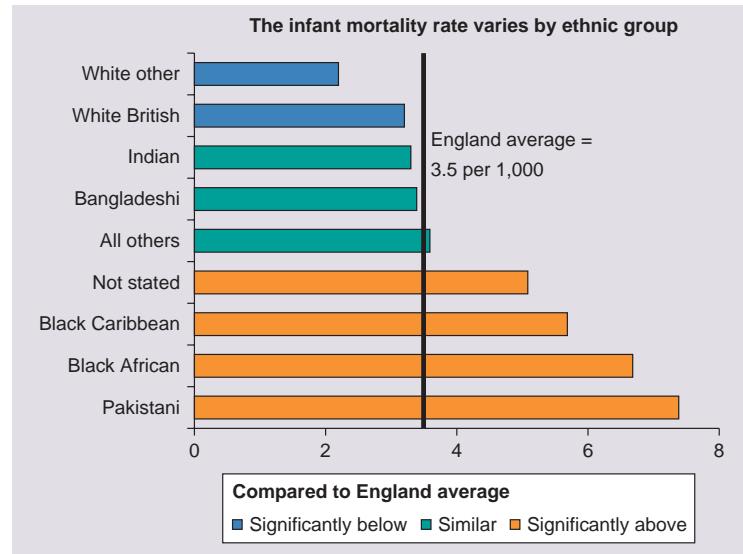


Figure 1.6 Infant mortality rate per 1000 live births by ethnic group in England, 2014. (From: Public Health England. Public Health Outcomes Framework: Health Equity Report. Focus on Ethnicity, 2017.)

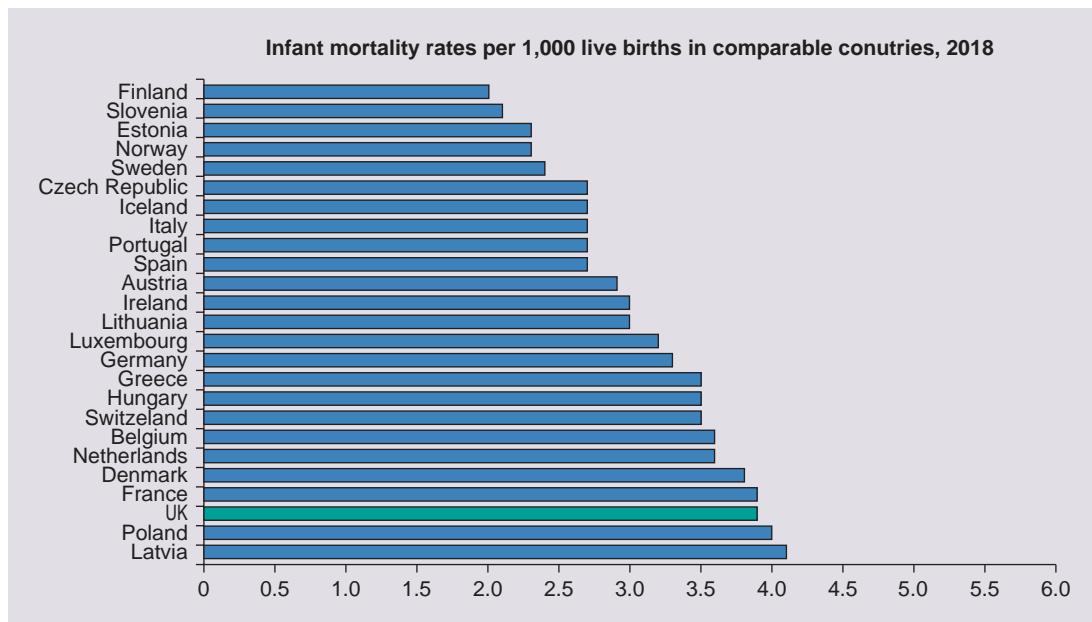


Figure 1.7 Infant mortality rates per 1000 live births in comparable countries, 2018. (From: OECD, 2020, Infant mortality rates: indicator, <http://doi.org/10.1787/83dea506-en>.)

Sweden. The reasons for this are complex, but contributing factors are:

- high rates of low birthweight and preterm rates when compared with some other European countries, both of which have a strong influence on infant mortality (Fig. 1.7).
- the UK has one of the highest rates of child poverty compared with other comparable wealthy countries. Childhood mortality rates are higher in countries with a high proportion of deprived households. The Nordic countries have low levels

of deprivation and also show some of the lowest child mortality rates.

- the UK performs less well in the recognition and management of serious illness in primary and secondary care and in the community.
- outcome measures for chronic illnesses are poorer: for instance, blood glucose control for children and young people with diabetes are much worse than in comparable European countries, as is the mortality rate for asthma. More effective prevention and better medical care of these children could reduce mortality and morbidity.

Inequalities in child health

Inequality pervades all aspects of the health of children across the world. The causes of inequalities in health are complex, as there are so many factors that influence the health of a child. Some of these relate to poverty, while others relate to other aspects of deprivation as described earlier in this chapter, such as environmental factors; family and social support; health literacy and access to health services. Examples of the effect of deprivation on child health, comparing the most with the least deprived, are:

- Infant deaths – a quarter would be avoided if all births had the same level of risk as those with the lowest level of deprivation (Fig. 1.8)

Examples of the effect of deprivation on child health, comparing the most with the least deprived

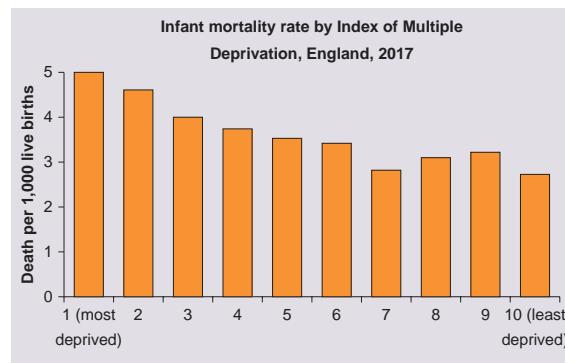


Figure 1.8 Infant mortality rate by index of multiple deprivation, showing highest mortality rate in the most deprived groups. (From: National Statistics Socioeconomic Classification (NS-SEC) for England, 2017.)

- Attendance at an emergency department – more than 50% increase
- Emergency admission rate for asthma – more than doubled (Fig. 1.9)
- Breastfeeding rate – markedly reduced (Fig. 1.10)
- Obesity – prevalence markedly increased (Fig. 1.11).

Approaches to public health have traditionally followed either a universal approach to improve wellbeing across the population (e.g. universal vaccination programmes, Change4Life campaign for healthy lifestyles) or targeted approach to improve the lives of the most vulnerable (e.g. welfare for those no- or low-income families, targeted health promotion programmes such as Family Nurse Partnership, which provides intensive support for vulnerable first-time parents). Increasingly, 'proportional'

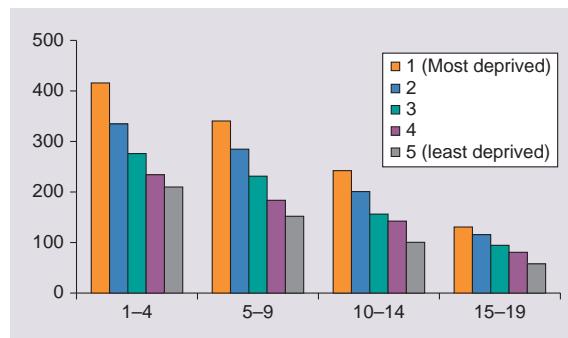


Figure 1.9 Emergency hospital admission for asthma per 100,000 children by age and deprivation quintile (fifth of population), in England 2013/14. (Modified from: Kossarova L, Cheung R, Hargreaves D and Keeble E (2017) Admissions of inequality: Emergency hospital use for children and young people. Briefing, Nuffield Trust. www.nuffieldtrust.org.uk/research/admissions-of-inequality-emergency-hospital-use-for-children-and-young-people.)

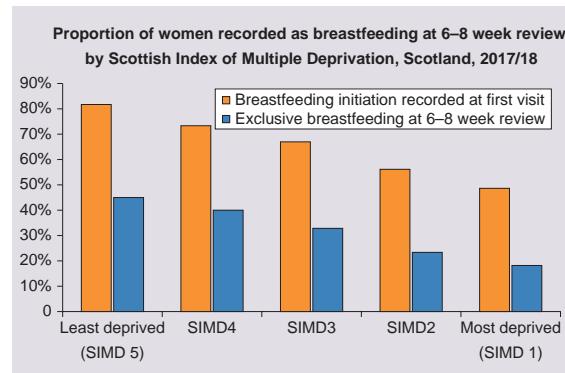


Figure 1.10 Proportion of babies ever breastfed, and still exclusively breastfed at 6–8 weeks of age, Scotland, 2019/2020. (From: Public Health Scotland, with permission.)

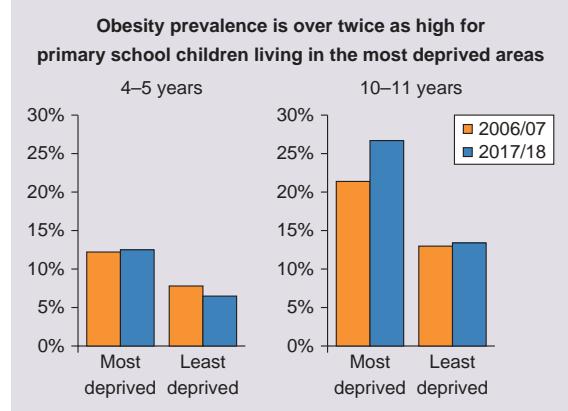


Figure 1.11 Obesity in primary school children at 4–5 years and at 10–11 years, in 2006/2007 and 2018/2019 showing marked increase in incidence between the most and least deprived children. (From: National Childhood Measurement Programme 2018/2019. Public Health England.)



Case history 1.1 (continued)

Keeping David well after discharge

Following the issues raised in the 4p framework (see [Table 1.2](#) above):

- The patient was discharged to his mother's care under a Child in Need plan, so that social care were tasked with supporting his family to ensure that his needs were met.
- His mother received advice on income and disability-related welfare support.
- Applications were made to re-house the family in more appropriate accommodation.
- Social care and health services worked together to enable him to receive his medical care for his asthma.
- His school nurse was tasked to keep track of his medications at school.
- His iron deficiency anaemia was treated, and he and his family received dietary advice tailored to their family circumstances.

This demonstrates how putting these additional (mainly non-healthcare-related) services in place are likely to make a positive impact on his asthma management, compared to just making a follow-up appointment.

'universalism' – a blended approach where services are provided for all, but with extra resource directed at vulnerable or deprived communities – is advocated as the most effective way to reduce health inequalities ([Case history 1.1 continued](#)).

COVID-19 pandemic

Severe illness from the Sars-CoV-2 virus mainly affects older adults. Relatively few infants and young children have become ill, although a small number of older children and young people have developed critical illness from paediatric multisystem inflammatory syndrome (see Chapter 15, Infection and immunity). However, the indirect effects of the global COVID-19 pandemic and its accompanying social restrictions have impacted markedly on the lives of children and young people. These include:

- disruption to schooling and assessments
- reduced social interaction with friends and wider family
- reduced family income in many homes from loss or reduced parental employment
- reduced wellbeing and increased mental health problems.

Many of these problems disproportionately affect those living in the most deprived households. Given the importance for children of their social environment, as described in this chapter, for their wellbeing and mental health, it is no surprise that COVID-19's seismic societal impact will have wide repercussions on the health and wellbeing of children and young people for many years.

Child protection (safeguarding)

This is the process of protecting individual children identified as either suffering, or at risk of significant harm as a result of maltreatment or neglect. In 2018, 61,500 children in the UK were identified as needing protection from maltreatment, about 0.4% of the total child population. (Child protection is considered in detail in [Chapter 8](#), Maltreatment of children and young people.)

Obesity

Obesity in children continues to increase in almost all high-income countries. In 2017/2018, the proportion of children in England who were overweight or obese (BMI >91st centile) was about 23% at school entry (5 years) and 35.7% by the last year of primary school (aged 11 years) – and by this age more than 20% were obese (BMI >95th centile). Furthermore, obesity is disproportionately prevalent in children who live in deprived areas (see [Fig. 1.11](#)). Doctors can help promote healthy eating through supporting breastfeeding in infancy; advising families and young people on healthy lifestyles; monitoring growth parameters and the consequences of obesity; and through advocacy and support for local and national healthy lifestyle programmes. (Further details are described in [Chapter 13](#), Nutrition.)

Emotional and behavioural difficulties

According to a mental health prevalence survey in England in 2019, 11% of children aged 5–15 years suffer from a defined emotional or behavioural problem. Older adolescents aged 15–19 years have a higher prevalence of mental health problems, and this has been rising in this age range in the UK over the past two decades. Some of this rise may relate to better recognition and a welcome reduction in stigma attached to mental health problems, but this is unlikely to be the whole explanation. Suicide is a key indicator of mental health of older adolescents. The rate in the UK has been declining over the last 20 years, though more recently it appears to have risen. (Further details are described in [Chapter 24](#), Child and adolescent mental health.)

Disability

It is estimated that about 7% of children in the UK have a disability. As medical science improves, more children are surviving from what would previously have been fatal conditions. Many of these children survive with disabilities, and their ongoing survival may rely on the availability of new medical technologies (such as long-term home ventilation) which did not previously exist. More than ever, child health professionals need to work closely with children and young people, families, local communities and other services to ensure that the needs of individual children with disabilities are appropriately catered for. This may include outlining a child's health needs in an Education, Health and Care Plan, formulating an individual healthcare plan, and advocating for the resources to implement this. Doctors also provide

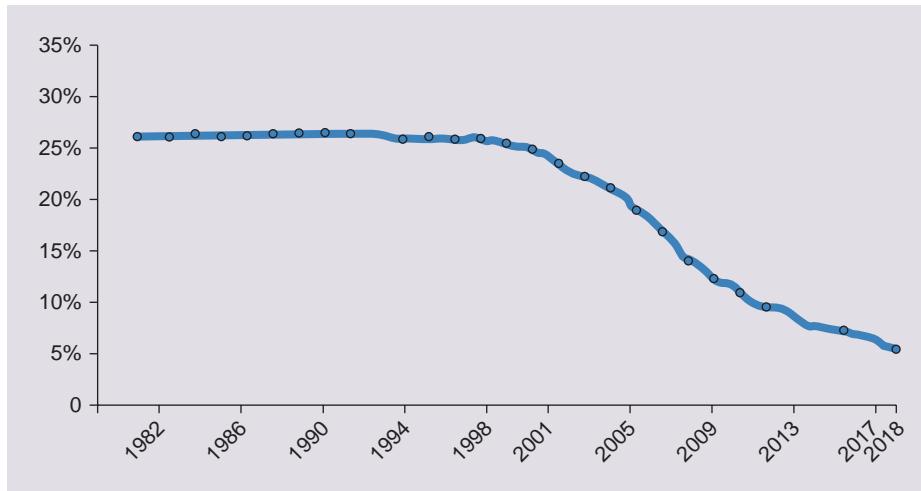


Figure 1.12 Reduction in proportion of females who are regular smokers at age 15 years in England 1982–2018. (From: NHS Digital, 2019. Drinking and Drug Use among Young People in England 2018.)

education and social services with data relating to the levels of need within their own population, in order to ensure resources are allocated appropriately for all disabled children in the local area.

Smoking, alcohol and drugs

In 2016, 3% of 11–15-year-olds surveyed in England smoke regularly (Fig. 1.12); 10% had taken drugs in the past month, and 10% had drunk alcohol in the past week (NHS Digital, 2017). Doctors have been instrumental in campaigning for legislation to protect young people from targeted advertising (and to enforce plain packaging of cigarettes), and to raise awareness of the dangers of smoking, alcohol and drugs. There is evidence that prevalence of all three behaviours are decreasing. The advent of electronic cigarettes ('e-cigarettes' or 'vaping'), with 2% of 11–15-year-olds using them regularly, requires ongoing evaluation.

Conclusion

Children rely on their family and society to care for them and provide an environment where they can grow both physically and emotionally to reach their full potential. Their health is dependent on a nurturing environment and good health services. When doctors treat a child with a specific disease or condition, they must take into consideration the impact that the child's family, social and physical environment has on the disease, the treatment and on the child's overall health and wellbeing. They should help the child and their family to understand this impact, and support them to improve or manage those factors so that the child can thrive, both physically and emotionally.

Doctors can help children by the wider use of their knowledge about child health. This may be through advocacy about children's issues and by providing evidence to inform public debate.

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History and examination

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Features of history and examination in paediatric practice:

- In contrast to adult medicine, the questions asked in the history and the way the examination is conducted need to be adjusted according to the child or young person's age and stage of development.
- Examination may require ingenuity and is opportunistic, e.g. prioritizing auscultation when an infant or young child is quiet, and may require distraction or play.
- The problems children and young people experience are affected not only by biological processes, but also by psychological reactions, social relationships and socio-economic circumstances. Alongside a conventional medical model of diseases, consider what biopsychosocial issues are affecting the situation.
- Parents and children and young people rapidly recognize and appreciate doctors who demonstrate interest, empathy, and skill.

Most diagnoses in paediatrics are made on the basis of the history, astute observation and targeted examination of the child. History-taking and clinical examination therefore continue to be the cornerstone of paediatric clinical practice. This remains the case despite advances in medical technology and the availability of ever more sophisticated investigations.

Common clinical scenarios in paediatric consultations are:

- an acute illness, e.g. respiratory tract infection, a febrile child, exacerbation of asthma, acute abdominal pain
- a chronic problem, e.g. faltering growth, constipation, headaches, musculoskeletal pain
- a newborn infant, e.g. with respiratory distress or jaundice

- problems in development, e.g. delayed walking or speech, autism spectrum disorder
- behavioural problems, e.g. temper tantrums, hyperactivity, eating disorders.

Increasingly, children and young people in paediatric practice have a number of complex problems, e.g. the child with a respiratory tract infection may be an infant born extremely premature and who has been in neonatal intensive care and has underlying lung disease, or may be a young person with Down syndrome who had surgery for congenital heart disease and has attention deficit hyperactivity disorder.

The aims and objectives of clinical consultations are to:

- establish the relevant facts of the history from both the parent's and the child or young person's perspectives; this is usually the most fruitful source of diagnostic information
- elicit all relevant clinical findings
- collate the findings from the history and examination
- formulate a working diagnosis or differential diagnosis
- assemble a problem list and management plan
- communicate this to the child / young person and their family.

Key factors that determine the way the history and examination are conducted are:

- the child's age ([Fig. 2.1](#)) and developmental stage
- the nature of the problem – for example, a complex developmental problem is likely to require a more lengthy and detailed evaluation than a simple rash
- observation of the child's appearance, behaviour, and play, before, during and after the interview as this will provide clues regarding how you approach examining the child as well as to diagnosis and management.

To maximize the value of each consultation, organize the immediate environment so that it is welcoming

Paediatrics is a specialty governed by age and stage of development

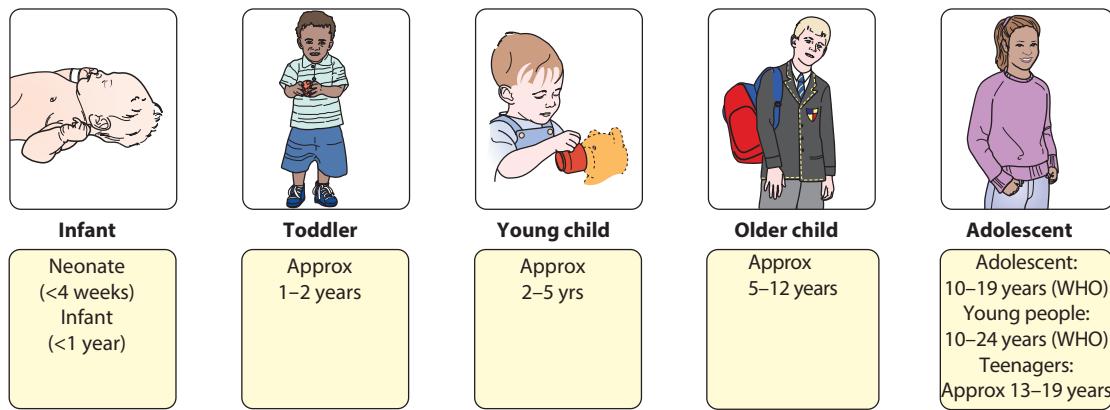


Figure 2.1 Depiction of the wide age range encountered in paediatric practice, and some of the terms used to represent different periods of growth and development.



Paediatrics stretches from newborn infants to adolescents. Whenever you consider a paediatric presentation, whether medical, developmental or behavioural, first consider ‘What is the child’s age?’ Also consider developmental stage, even during adolescence chronological age is a poor indicator of developmental stage.

and unthreatening. Have suitable toys or activities available. Avoid desks or beds between you and the family. Encourage young people to take the seat nearest you.



Parents or carers know their children best – never ignore or dismiss what they say.

Taking a history

Introduction

- Read any referral letter and/or hospital notes before the start of the consultation.
- When you greet the child or young person and family, check that you know the child or young person’s first name and gender. Ask how the child or young person prefers to be addressed.
- Introduce yourself.
- Determine the relationship of the adults to the child or young person.
- Establish eye contact and rapport with the family, but keep a comfortable distance. Infants and some toddlers are most secure in parents’ arms or laps. Young children may initially be wary of the unfamiliar situation.

Involving children and young people

It can be easy to sideline children or young people in a consultation, in favour of their more articulate parents. However, keep the child or young person, depending on age and developmental stage, involved, as they are the topic of the consultation. Strategies include:

- Be patient: young children may need some time to feel at ease.

- Observe how the child plays and interacts with any siblings present.
- Address questions to the child, when appropriate, and always to young people. Involvement with management will vary with age and stage of development.
- Alter your vocabulary to suit the age of a child: a 4-year-old will understand ‘tummy’ but not ‘abdomen’.
- Be authentic. Do not try to be ‘cool’ with adolescents or too much of a clown with school-age children.
- Be aware of different communication methods especially in non-verbal children, such as Makaton – a simple sign and symbol language used by many children.
- There will be occasions when the parents and adolescents should be seen separately. This is usually to avoid embarrassing them while discussing sensitive information. This must be handled tactfully, often by negotiating to talk separately to each in turn. Give an adolescent the opportunity to talk to you alone. This can be introduced as ‘It is my usual practice to...’ See the adolescent after the parents so he/she knows that confidential information is not being disclosed when out of the room (see Ch. 30, Adolescent medicine).

Don’t neglect involving children or young people, but make sure that this doesn’t compromise your history-taking.

Presenting symptom

Full details are required of the presenting symptoms. Start with an open question. Let the parents and child or young person recount the presenting complaints in

their own words and at their own pace. Note onset, duration, severity, previous episodes, what relieves/aggravates them, time course of the problem, if getting worse and any associated symptoms. Has the child or young person or the family's lifestyle been affected? Is the problem the same in different environments, e.g. is the child disruptive at home, but 'good as gold' at school? What has the family done about it? If describing a rash or an event such as a seizure, parents may have a photograph or video on their mobile phone. These can be very helpful, but you may need to ask for them!

Make sure you know:

- what prompted the referral
- what the parents/young people think or fear is the matter.

Have the parents or young people been searching the internet or discussed it with others? They often search online for answers, which can be a source of anxiety; no-one writes a blog about common benign headaches which self-resolved, but there is a multitude of articles online about headaches caused by much rarer brain tumours.

Focus the history

The scope and detail of further history-taking are determined by the nature and severity of the presenting complaint and the child's age and developmental stage. While the comprehensive assessment listed here is sometimes required, usually for a complex, multisystem problem or to become familiar with paediatric history and examination, a selective approach is usually adopted. This is not an excuse for a short, slipshod history, but instead allows one to focus on the areas where a thorough, detailed history is required. For example, in a young child with delayed speech, a detailed birth and neonatal history and details of developmental milestones should be established, but would not be appropriate for a young person with headaches (Fig. 2.2).

Make sure that you and the parent or child mean the same thing when describing a problem. For example, parents may use the word 'wheeze' to describe any respiratory sound. Do not make any assumptions even about non-medical phrases. A baby who is 'refusing his bottle' might be too lethargic to feed, or might be angrily batting it away because a sore throat hurts when he/she swallows.

General enquiry and systems review

Regardless of the presenting complaint, cover some basic indicators:

- general health – how active and lively? When were they last their 'normal' self?
- growth – following their weight and height centiles?
- feeding/appetite – establish what the normal feeding pattern is. Has there been a significant deviation from this pattern?
- sleeping – does the symptom affect their sleep at all? Or might poor sleep explain the symptom?
- any recent change in behaviour or personality?



Figure 2.2 The history must be adapted to the child's / young person's age. The age when a child first walks is highly relevant when taking the history of a toddler or child with a developmental problem but irrelevant for an adolescent in secondary school with headaches.

A screen of other organ systems can be helpful. Be selective to inform an accurate differential diagnosis:

- general – rashes, fever (if measured), recurrent infections
- respiratory – cough, noisy breathing, breathlessness
- ear, nose, throat – earache, throat infections, snoring
- cardiovascular – pallor, cyanosis, exercise tolerance, faints
- gastrointestinal – vomiting, bowel habit, abdominal pain
- genitourinary – dysuria, frequency
- neurological – seizures, headaches, abnormal or impaired movements
- psychological – change in behaviour, low mood, anxiety, any psychosocial stressors (e.g. bullying)
- musculoskeletal – gait, pain, swelling
- pubertal development.



Smartphones are particularly helpful in paediatric practice as parents or young people will often have photographs or videos of what they are concerned about, e.g. a rash or abnormal movements of the limbs or eyes.

Past medical history

Often easiest to follow in chronological order:

- maternal obstetric problems including antenatal scans and screening bloods, delivery
- birthweight and gestation (was the child premature?)
- perinatal problems, such as breathing difficulties or jaundice requiring admission to the neonatal unit.
- immunizations – ideally from the personal child health record (is the child fully immunized?)
- past illnesses, hospital admissions, operations, accidents and injuries.

Medication

Always check:

- past and present medications, both prescribed and 'over the counter'
- whether the child is taking tablets or syrups
- known allergies
- if adolescent, who is responsible for the medication – parent/shared/self-management (Fig. 2.3)?



Parents will often know the dose of syrups in millilitres, not milligrams. Syrups can be available in multiple different concentrations, so be careful not to second-guess or miswrite drug doses.

convenient way to document it. (See [Case history 2.1](#).)

- What are their preferred play or leisure activities? Who is the young person closest to in the family / talks to most?
- In an adolescent it may be appropriate to take a formal psychosocial history (see [Table 30.2](#); use of HEADS acronym).
- What has been the *impact* of this illness on the child / young person and family?
- Are the family/young person claiming all the state financial support/welfare they are entitled to? Are there any housing problems?
- Are there other professionals involved with the family? This may indicate whether the family are known to social care.

Family history

Families share houses, genes, and diseases!

- Have any members of the family or friends had similar problems or any serious disorder? Any neonatal/childhood deaths?
- Draw a family tree (see [Ch. 9, Genetics](#), for details). If there is a positive family history, extend family pedigree over several generations.
- Is there consanguinity?



Beware of conditions that mostly affect adults! A reported family history of 'diabetes' and 'heart disease' may be middle-age-onset lifestyle-associated diseases, which may not be relevant to the paediatric problem.

Social history

Check:

- Relevant information about the family and their community – parental occupation, economic status, housing, relationships, parental smoking, marital stresses. 'Who lives with you at home?' Adding this to the family tree is a

This 'social snapshot' is crucial, since many childhood illnesses or conditions are caused by or affected by adult problems, for example:

- alcohol and drug abuse/misuse
- long-term unemployment/poverty
- poor, damp, cramped housing
- parental mental health disorders
- domestic violence.

Development

This is a prominent and specific aspect of paediatric history and examination. Ask about:

- parental concerns about development, vision, hearing
- key developmental milestones. In infants and young children these are considered in terms of the developmental domains ([Fig. 2.5](#)).

In older children and young people, parents rarely remember ages of developmental milestones in detail; it is better to match abilities against expectations and social functioning:

- concerns or contact with health or education support services
- bladder and bowel control in young children (toilet training)

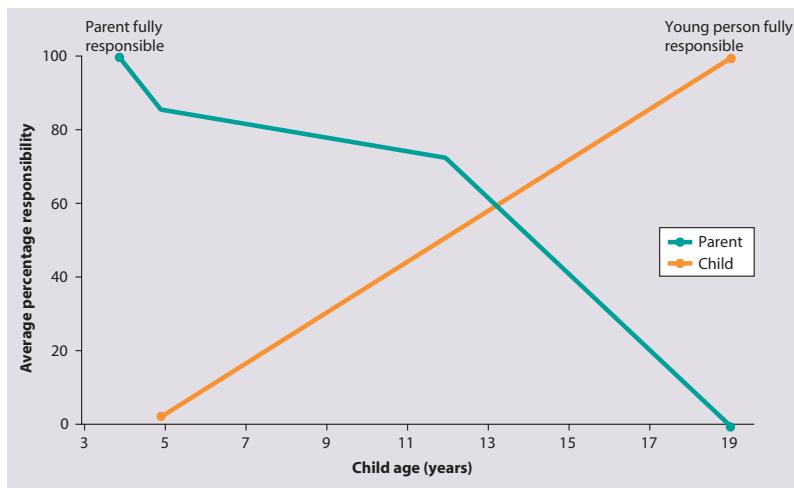


Figure 2.3 Transition of responsibility for asthma treatment by age, showing the transition from complete responsibility by parents in the young child gradually transferring to the adolescent by 19 years. Communication during the consultation needs to reflect this. (Adapted from: Orelle-Valente JK, et al; At what age do children start taking daily asthma medicines on their own? *Pediatrics* 2008; 122:e1186-e1192.)



Case history 2.1

Drawing social arrangements on a family tree

Jade, a 3-year-old girl, presents with faltering growth. She has one 'full' sibling, but her mother has another two older children by a previous partner who gives her no financial support. Her current partner, Simon, is out of work. Chris, his 17-year-old son from a previous

relationship is also living in the house. This can most easily be understood by drawing the family's social arrangements on the family tree (Fig. 2.4). These details could be missed if a full family and social history is not taken.

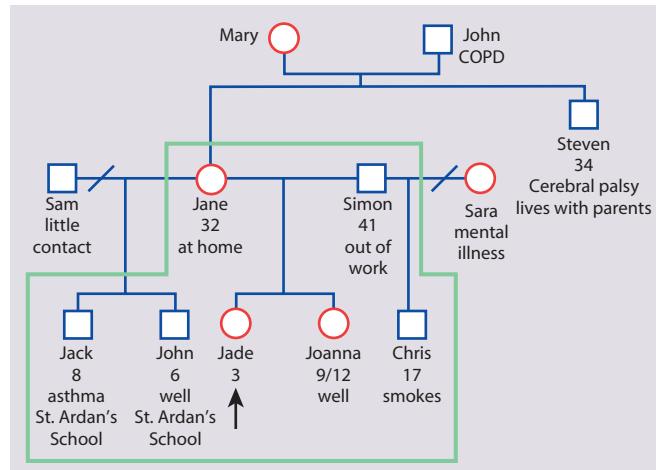


Figure 2.4 Drawing the family's social arrangements on the family tree can be helpful in understanding the child's social environment. The green box shows the members of the family living together in the family home.

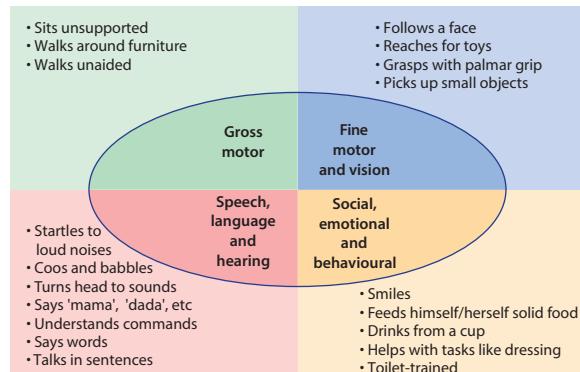


Figure 2.5 Some key developmental milestones in infants and young children. These are considered in detail in [Chapter 3](#) (Normal child development, hearing and vision); adolescent milestones are considered in [Chapter 30](#) (Adolescent medicine).

- child / young person's temperament, behaviour and sleep
- concerns and progress at nursery/school/college
- languages spoken at home (children from multilingual households may have slower progress in one or more languages).

In adolescence, developmental status other than pubertal assessment is primarily determined from the history-taking:

- Sexual maturation and growth – Is the intellectual, pubertal and growth stage appropriate for their chronological age?

- Thinking** – Is the young person using concrete or abstract constructs? Do they have sufficient self-esteem and/or sense of purpose?
- Education** – What education is the young person attending?
- Peers/parents** – How connected is the young person to their peers and parents? Who is responsible for the young person's healthcare decisions?

This is considered further in [Chapter 30](#). (Also, see STEP approach to Adolescent Development: www.e-lfh.org.uk, Adolescent Health Programme module 2_006.)

An approach to examining children or young people

While it may be difficult to examine some toddlers and young children fully, it is possible with resourcefulness and imagination on the doctor's part. Parents are great allies; they can facilitate examination with a combination of distraction, sympathy and gentle restraint.

To perform the examination:

- Babies in the first few months are best examined on an examination couch with a parent next to them.
- A toddler is best initially examined on their parent's lap or occasionally over a parent's shoulder.
- Parents are reassuring for the child and helpful in facilitating the examination if guided as to what to do ([Fig. 2.6](#)).



Figure 2.6 Distracting a toddler with a toy allows auscultation of the heart.

- Preschool children may initially be examined while they are playing.
- Older children and young people are often concerned about privacy. Young people should normally be examined in the presence of a parent or suitable chaperone. Do not assume a young person will want their parent to be their chaperone during physical examination. Be aware of cultural sensitivities in different ethnic groups.

Warm, clean hands

Hands must be washed before (and after) examining a child / young person. Warm smile, warm hands, and a warm stethoscope all help.

Obtaining the child's cooperation

- For young children, get on their level and try and engage in play or conversation. Try to make sure that your eye line is at the same height or lower than theirs if at all possible. It is intimidating to have an adult tower over you!
- Make eye contact and a smile to build trust. Even very young children can judge your facial expression and attitude. Be gentle but confident.
- Be patient – If the child still looks scared don't just press on, but wait, allowing the parent to reassure them.
- Explain what you are about to do and what you want the child to do, in language he or she can understand. Examination is essential, not optional, so do not ask the child for permission – it may be refused!
- When first examining a young child, start at a non-threatening area, such as a knee, or even a teddy bear. Short mock examinations, e.g. auscultating a

teddy or a parent's hand, may allay a young child's fears.

- Leave unpleasant procedures such as ear and throat examinations until last.

Undressing children and young people

Be sensitive to modesty, particularly during adolescence. The area to be examined must be inspected fully but this is best done in stages, redressing the child when each stage has been completed. It is easiest, kindest and helpful to ask a child or parent to do the undressing or get adolescents to do this themselves. Requesting adolescents to bring a pair of shorts and T shirt to change into for examination is often a useful addition to the appointment letter.

Developmental skills of young children

In younger children, a good overview of developmental skills can be obtained by watching the child play. A few simple toys, such as some bricks, a car, doll, ball, pencil and paper, pegboard, miniature toys, and a picture book, are all that is required, as they can be adapted for any age. If developmental assessment is the focus of the examination, it is advisable to assess this before the physical examination, as co-operation may then be lost.

Examination

Initial observations – watch before you examine

Careful observation is usually the key to success in examining children and young people. Observation will provide information on:

- severity of illness
- growth and nutrition
- behaviour and social responsiveness
- level of hygiene and care.

Severity of illness

Is the child or young person sick or well? If sick, how sick? For the acutely ill infant or child, perform the 'rapid clinical assessment: an ABCDE approach' (see Fig. 6.1):

- airway and breathing – respiration rate and effort, presence of stridor or wheeze, cyanosis
- circulation – heart rate, pulse volume, peripheral temperature, capillary refill time
- disability – level of consciousness
- exposure – trauma, rash.

The care of the seriously ill child is described in Chapter 6, Paediatric emergencies.

Measurements

Abnormal growth may be the first manifestation of illness in children. Always measure and plot growth on centile charts for:

- weight, noting previous measurements from personal child health record
- length (in infants, if indicated) or height in older children
- head circumference in infants and young children.

Different growth charts are used depending on the sex of the child and special charts are available for certain conditions (e.g. cerebral palsy, Down Syndrome).

Also, as appropriate:

- temperature
- blood pressure
- oxygen saturation.

Conducting the examination

Examination should be guided by history; it is impossible and unnecessary to perform every examination listed below for every child. Be selective and focused on what clues you wish to pursue.

Examination in younger children needs to be opportunistic; if a baby is quiet you may choose to auscultate the chest before undressing the infant, which may make the infant cry. There is no strict order and there is no 'right place to stand or sit' when examining an individual child, but by the end of the examination a thorough examination needs to have been performed. Some components of the examination, like abdominal examination are easier to do from the child's right hand side if you are using your right hand to palpate for organomegaly.

Whilst it may be necessary to deviate from a strict order when examining a child, it helps to provide the relevant examination findings in a structured order when recording and reporting them. It is usual to report them as: general appearance, respiratory, cardiovascular, gastrointestinal, neurological, musculoskeletal, head and neck findings. For most systems it is helpful to look first (and longest), listen next and then feel or touch last (and least).

General appearance

The face, head, neck, and hands are examined. The general morphological appearance may suggest a genetic syndrome. Is the head large or small? In infants, palpate the fontanelle and sutures. Look for any congenital anomalies. Is the child/young person dehydrated, jaundiced, or anaemic? In older children and adolescents look for signs of self-harm, particularly upper non-dominant arm or thighs, i.e. areas normally hidden from view.

Respiratory system

Peripheral examination

Examine:

- fingernails – for clubbing (Fig. 2.7a)
- colour of hands – pink, pale, blue?
- central cyanosis – best seen under the tongue
- oxygen saturation if available and relevant – cyanosis is late sign of hypoxaemia
- respiratory support or aids – oxygen, non-invasive ventilation; nebulizer, incentive spirometer, mucus clearance aid.

Respiratory rate and increased work (effort) of breathing

- Count respiratory rate over one whole minute (Table 2.1).
- Identify increased work (effort) of breathing (Table 2.2).

Chest appearance

Observe for:

- hyperexpanded chest (Fig. 2.7b)
- pectus excavatum (hollow chest) – fixed sternal depression
- pectus carinatum (pigeon chest)
- Harrison sulcus – permanent groove of ribs, from inward pull at insertion of diaphragm
- scars
- asymmetry of anatomy or chest wall movement, e.g. in pneumothorax
- tracheostomy
- portacath access port.

Chest palpation

- Chest expansion – reduced symmetrical expansion is difficult to detect. Assess distance of the thumbs during deep inhalation (Fig. 2.7c). If in doubt, measure chest expansion with a tape measure
- trachea – palpating it is seldom helpful. Disliked by children. Use selectively when concerned about mediastinal shift
- location of apex beat – to detect mediastinal shift
- tactile vocal fremitus – palpable vibration when speaking, e.g. saying "99", over areas of consolidation. Reduced over an effusion. Rarely useful or informative.

Percussion and auscultation

Percuss over at least six areas of the front and back of the chest. Is the note:

- resonant – a pneumothorax
- dull – localized collapse or consolidation
- stony dull – fluid (effusion or empyema).

Listen to at least six areas front and back (Table 2.3).

Respiratory system



Figure 2.7a Clubbing is associated with chronic suppurative lung disease (e.g. cystic fibrosis, as here), cyanotic congenital heart disease, cirrhosis and inflammatory bowel disease.



Figure 2.7b Hyperexpanded chest from chronic obstructive airways disease. This boy had severe asthma.



Figure 2.7c Assessing chest expansion by palpation. Normal expansion is 3–5 cm.



In infants with pneumonia, tachypnoea may be the only respiratory sign; they may not have any abnormal signs on auscultation.



Tachypnoea is the most sensitive marker of respiratory disease, but is less specific than chest recession.

Table 2.1 Normal respiratory rate and tachypnoea by age group

Normal	Breaths/min	Tachypnoea
Neonate	35–60	>60
Infant	30–40	>50
Young Child	20–30	>40
School-age child	20–25	>30
Adolescent	15–20	>30

Table 2.2 Signs of respiratory distress in children

Clinical sign	Description
Nasal flaring	Nostrils widen during inspiration
Tracheal tug	Thyroid cartilage visibly dips during inspiration
Recession (retraction)	Part of chest wall draws in during inspiration (can be suprasternal, subcostal, intercostal or all three)
See-sawing	Chest moves inwards and abdomen outwards during inspiration (strong diaphragm and weak chest wall)
Grunting	Airway briefly occludes during expiration to create positive end expiratory pressure (PEEP)
Difficulty with feeds/speech	Tachypnoea and effort impede breath holding and control

Table 2.3 Clinical findings on auscultation

Added sound	Interpretation
Cough	Wet (mucus) or dry?
Harsh sounds everywhere	Transmitted sounds from upper airways (e.g. coryza)
Stridor	Low-pitched, inspiratory sound from upper airways obstruction
Normal breath sounds	Soft, low pitched, inspiratory phase longer than expiration
Bronchial breathing	Hollow, high-pitched, short inspiratory phase, followed by pause and long expiration
Wheeze	High-pitched, expiratory sound from distal airway obstruction
Crackles	Discontinuous 'moist' sounds from the opening of bronchioles

Cardiovascular system

Peripheral examination

Observation:

- tongue for cyanosis ([Fig. 2.8a](#))
- facial features suggestive of a syndrome
- finger clubbing ([Fig. 2.7a](#))
- fingernails for splinter haemorrhages in endocarditis
- capillary refill time
- oxygen saturation if monitored
- any respiratory support.

Pulses

Assess:

- rate ([Table 2.4](#))
- rhythm – variation of pulse rate with respiration is normal ('sinus arrhythmia')
- volume and character – small in circulatory insufficiency or aortic stenosis; increased in high-output states (stress, anaemia); collapsing in patent ductus arteriosus, aortic regurgitation
- blood pressure – at end of examination; see below.

Chest inspection

Observe for:

- respiratory rate for tachypnoea
- respiratory distress
- precordial bulge caused by cardiac enlargement
- scars ([Fig. 2.8b](#)) from surgery
- ventricular impulse visible if thin, hyperdynamic circulation or left ventricular hypertrophy.

Palpation

Feel for:

- heave from ventricular hypertrophy, e.g. at lower left sternal edge from right ventricular hypertrophy
- thrill – palpable murmur, on chest and over carotid arteries (aortic stenosis)

- apex beat at 4th to 5th intercostal space, mid-clavicular line – but not palpable in some normal infants, overweight children, or dextrocardia; displaced and increased with left ventricular hypertrophy
- hepatomegaly from congestive cardiac failure
- percussion of the cardiac contour is rarely useful in children; percussion of the liver margins may be useful.

Auscultation

Heart sounds

Listen for:

- splitting of second sound – usually easily heard and is normal ([Fig. 2.8c](#))
- fixed splitting of second heart sound – in atrial septal defects
- third heart sound in mitral area – normal in young children.

Heart murmurs

Note:

- timing: systolic/diastolic/continuous
- duration – mid (ejection) systolic/pansystolic
- third heart sound in mitral area is normal in young children
- loudness ([Table 2.5](#))
- site of maximal intensity.

Listen for radiation:

- to neck in aortic stenosis
- to back in coarctation of the aorta or pulmonary stenosis

For features of innocent and significant murmurs, see [Table 2.6](#). The location and characteristics of common murmurs are shown in ([Fig. 2.8d](#)). Draw your findings (see Ch. 18, Cardiac disorders).

Cardiovascular system



Figure 2.8a Cyanosis is a blueish discolouration best seen under the tongue. It is caused by desaturated haemoglobin. (Courtesy of Don't forget the Bubbles.)

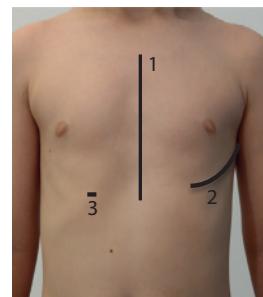


Figure 2.8b Scars to look out for include median (1) and left lateral (2) thoracotomy scars as well as sites of drains (e.g. 3).

Table 2.4 Site to palpate pulse and normal heart rate in children

Normal	Palpate pulse	Beats/min
Neonate	Femoral	100–160
Infant	Femoral or brachial	80–140
Young child	Brachial	80–110
School-age child	Brachial or radial	70–100
Adolescent	Radial	60–90

Table 2.5 Grading of loudness of murmurs

Grade	Description
1	Heard by an expert in quiet room
2	Soft murmur
3	Murmur heard easily
4	Murmur heard easily + thrill
5	Murmur all over precordium + thrill
6	Audible without a stethoscope

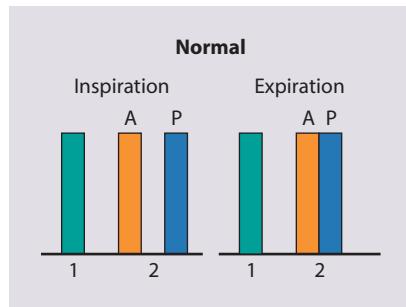


Figure 2.8c The second heart sound is split in inspiration. (A denotes the closing of aortic valve, P closing pulmonary valves).

Table 2.6 Features of murmurs

Innocent murmurs

aSymptomatic
Soft, blowing, murmur
Systolic only
Left Sternal edge
Also: normal heart sounds
No parasternal thrill
No radiation

Significant murmurs

Audible all over precordium
Loud
Thrill (Grade 4 to 6)
Any diastolic murmur
Other abnormal cardiac signs

Cardiovascular system – cont'd

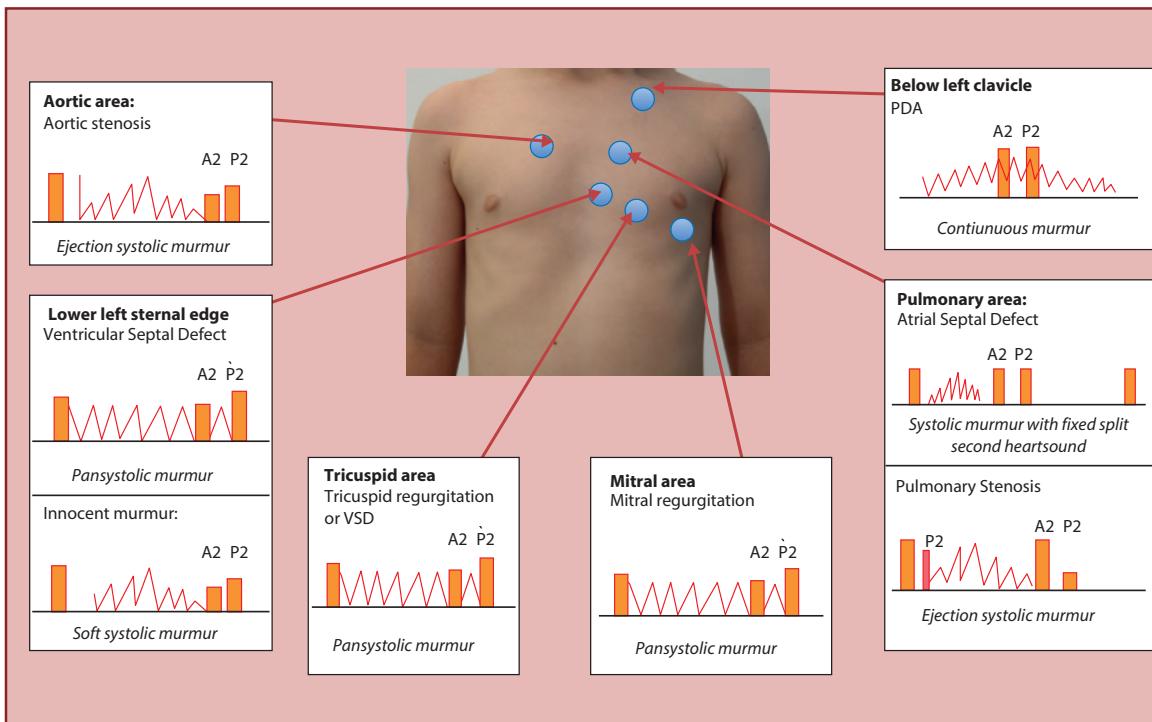


Figure 2.8d Auscultation of heart murmurs: location and characteristics of heart murmurs on different parts of the precordium. (VSD, ventricular septal defect; PDA, patent ductus arteriosus.)



Congenital heart disease is more common in children with other congenital anomalies or genetic disorders, e.g. Down or Turner syndrome.



Features of heart failure in infants include: poor feeding, faltering growth, sweating, tachypnoea, tachycardia, gallop rhythm, cardiomegaly, hepatomegaly.

Gastrointestinal system

Peripheral examination

Observe for:

- fingers for clubbing
- conjunctiva for jaundice and anaemia
- mouth for ulcers (Fig. 2.9a)
- neck, axillae and supraclavicular for lymphadenopathy
- palms for palmar erythema in liver disease
- muscle wasting in coeliac disease or malnutrition
- feeding devices – nasal or percutaneous feeding tubes and pumps.

Abdominal inspection

Observe the abdomen for:

- abdominal shape:
 - protuberance is normal in infants and toddlers
 - distension – may be caused by organomegaly (grossly enlarged liver, spleen or kidney) or a mass or fluid
- signs of pain – is the child still or writhing?
- dilated veins and spider naevi – in liver disease
- abdominal striae
- operative scars (Fig. 2.9b)
- peristalsis – from pyloric stenosis, intestinal obstruction
- hernias (umbilical, inguinal)

Auscultation

Listen for bowel sounds. They may be:

- increased in gastroenteritis or intestinal obstruction
- decreased in ileus or peritonitis.



On examining the abdomen:

- Inspect first, palpate later
- Superficial palpation first, deeper palpation later
- Watch for pain
- Guarding or rebound tenderness – often unimpressive in children

Genital area

Examination of the genital area is routine in infants, but only performed in older children when indicated by the clinical history.

In males:

- Penis and scrotum – check length and for hypospadias and chordee causing curvature of shaft of penis



Figure 2.9a Mouth ulcers are an easily missed sign of Crohn disease.

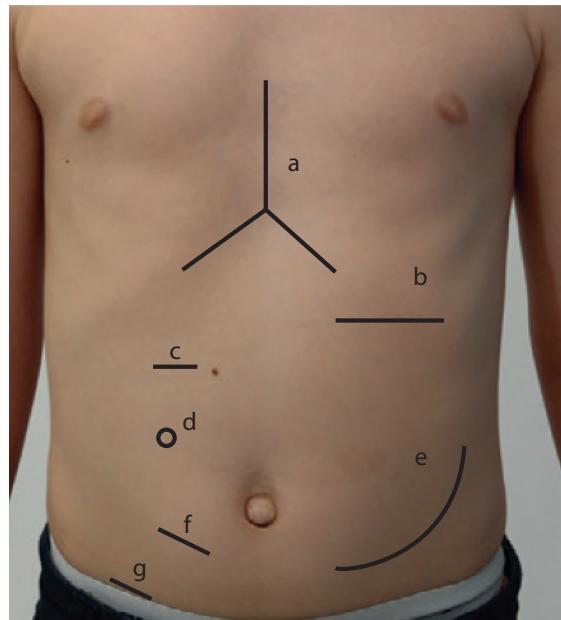


Figure 2.9b Common abdominal scars: The shape and position of scars provides a lot of information about the underlying medical history.

Scars from:

- a – liver transplant
- b – splenectomy
- c – pyloromyotomy
- d – drain or laparoscopy
- e – kidney transplant
- f – appendicectomy
- g – inguinal hernia repair.

- Testes and inguinal area – check testes located in scrotum, scrotal swelling (hydroceles), and for inguinal hernias.

In females:

- Check external genitalia looks normal.

Anus – normal appearance and location. Do not perform digital rectal examination.

Gastrointestinal system – Abdominal palpation and percussion

For successful palpation, the abdominal wall muscles must be relaxed:

- Kneel down so your face is level with the child's face.
- Explain what you're doing, and keep the parent close.
- A young child may become more cooperative if you palpate first with their hand or by putting your hand on top of theirs.
- Ask where it hurts.
- Start away from any painful areas.
- Palpate lightly in each quadrant first, before going deeper to feel for liver, spleen, kidneys and bladder.
- Watch the child's face, not your hand, for signs of pain.

To identify hepatomegaly (Table 2.7):

- Palpate from right iliac fossa.
- Locate edge (green) with tips or side of finger.
- Edge may be soft or firm.
- Unable to get above it.
- Moves with respiration.
- Measure (in cm) extension below costal margin (blue) in mid-clavicular line.
- 1–2 cm palpable edge is normal (Fig. 2.9c).
- Liver tenderness is likely to be due to inflammation from hepatitis.

To identify kidney enlargement:

- Palpate by ballotting bimanually.
- They move on respiration.
- One can 'get above them' (unlike the spleen or liver).
- Tenderness implies inflammation.

Percussion:

- Liver – dullness delineates upper and lower border. Record span.
- Spleen – dullness delineates lower border.
- Ascites – shifting dullness.

To identify ascites – percuss from centre of abdomen towards the flank to determine where percussion becomes dull, noting point. Repeat with child lying on side. Point becomes resonant.

Percuss downwards from the lung to exclude downward displacement of the liver due to lung hyperinflation, e.g. in bronchiolitis.

To identify splenomegaly (Table 2.8):

- Palpate from right iliac fossa.
- Edge (green) is usually soft.
- Unable to get above it.
- Notch is occasionally palpable if markedly enlarged.
- Moves on respiration (ask the child to take a deep breath).
- Measure size (in cm) below costal margin (blue) in mid-clavicular line.
- Palpable spleen tip is normal in infants (Fig. 2.9c).
- If difficult, use bimanual approach.

Identify pain:

- *Tenderness* – localized in appendicitis, hepatitis, pyelonephritis; generalized in mesenteric adenitis, peritonitis.
- *Guarding or rebound tenderness* – often unimpressive on direct palpation in children.

Peritoneal irritation:

- Symptoms – pain on coughing, moving about/walking/bumps during car journey.
- Signs – pain on blowing out the tummy as big as they can, and sucking it in as far as possible; walking with back bent from psoas inflammation in appendicitis; unable to jump on the spot.

Identify any abdominal masses:

- Wilms tumour – renal mass, sometimes visible, does not cross midline.
- Neuroblastoma – irregular firm mass, may cross midline; the child is usually very unwell.
- Faecal masses – mobile, non-tender, indentable, usually in left iliac fossa.
- Intussusception – acutely unwell, mass may be palpable, most often in right upper quadrant.
- Bladder – round, smooth suprapubic mass, which you can feel above, palpable in urinary retention and bladder neck obstruction from constipation.

Table 2.7 Causes of hepatomegaly

Infection	Congenital, infectious mononucleosis (Epstein–Barr virus), hepatitis, malaria
Haematology	Sickle cell disease, thalassaemia
Liver disease	Chronic liver disease, portal hypertension
Oncology	Leukaemia, lymphoma, Wilms' tumour, neuroblastoma, hepatoblastoma
Metabolic	Glycogen and lipid storage disorders, mucopolysaccharidoses
Cardiovascular	Heart failure
Apparent	Lung hyperexpansion (e.g. asthma, bronchiolitis)

Table 2.8 Causes of splenomegaly

Infection	Viruses, especially Epstein–Barr virus, malaria, leishmaniasis, infective endocarditis
Haematology	Haemolytic anaemia, e.g. sickle cell disease, thalassaemia
Malignancy	Leukaemia, lymphoma
Liver disease	Portal hypertension
Other	Systemic juvenile idiopathic arthritis

Neurology examination

A quick neurological and developmental overview should be performed whenever an infant or young child is examined. When doing this:

- Use common sense to avoid unnecessary examination.
- Adapt it to the child's age and developmental stage.
- Take into consideration the parent's account of developmental milestones.

In infants, observe:

- *Posture* – Is it flexed (normal in neonates; Fig. 2.10a)? Is it rigid?
- *Limb movement* – Is it symmetrical and controlled? Hand preference before 18 months of age is abnormal.
- *Tone* – When picked up: the limbs and body may feel normal, stiff, or floppy (hypotonic) (Fig. 2.10b).
- *Head control and movement* – Is there age-appropriate range of movement? Orientation to stimuli? Is there abnormal head lag on pulling to sitting (Fig. 2.10c; see also Fig. 2.10d).
- *Primitive reflexes* – Have they persisted beyond the time they should have resolved (see Fig. 3.4)?

In young children, identify:

- *Communication* – Is speech clear and fluent? Is social interaction and facial expression appropriate?
- *Play* – Are vision, hearing and speech normal? Are manipulative skills like grip and coordination normal?
- *Movement* – Can the child run, walk, climb, hop, skip or dance?



Most children are neurologically normal.
Only perform a full neurological examination to further investigate a neurological or developmental problem.

Detailed neurological examination

Observation of the face and limbs

Some of the neurological abnormalities which may be identified on inspection of the head and face, skin and limbs are shown in [Table 2.9](#).

Tone

Limbs

- Look for increased tone (spasticity) on pronation of the forearms at rest, or in adductors and internal rotators of the hips.
- Take the whole weight of the limb and *feel resistance* and *range of passive movement* of the limbs. Flex the elbows, supinate the wrists, and flex and extend the knees.
- Assess *rigidity and clonus* (rhythmic beating) at the ankles, by rapidly flexing the foot into dorsiflexion – usually from pyramidal dysfunction. This differs from lead-pipe rigidity in extra-pyramidal conditions, which, if accompanied by a tremor, is called 'cog-wheel' rigidity.

Trunk

- Look at posture. In extra-pyramidal tract disorders, the trunk is hypertonic and the head tends to arch backwards (extensor posturing).
- In hypotonia, the child feels floppy (hypotonic) to handle and cannot support the trunk in sitting. This occurs in muscle disease and some central brain disorders.

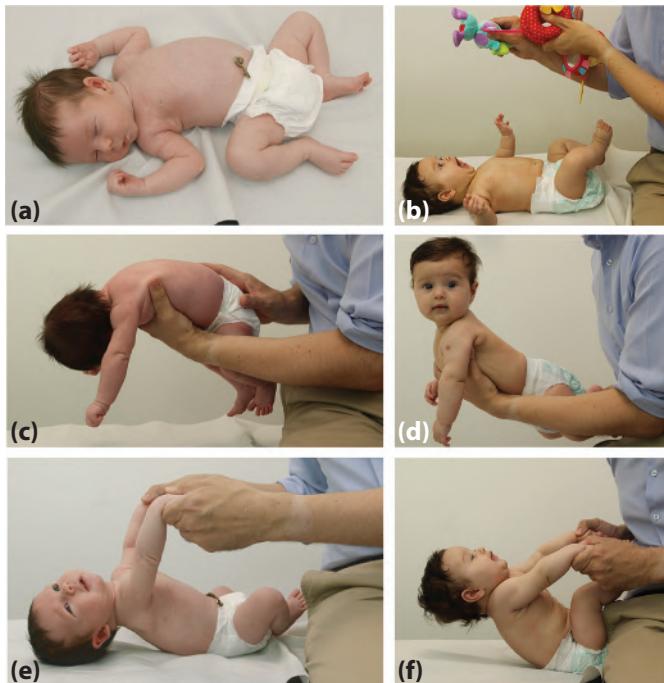


Figure 2.10 (a) Normal relaxed posture is flexed in a neonate. (b) Tone, power, coordination and attention can all be easily assessed for symmetry and control through simple play. (c) A newborn lacks the tone and power to raise their head when held prone, but a 5-month-old can support their head easily, as shown in (d). (e) To assess head lag, pull the infant up slightly by the arms from the supine position. In a 5-day-old infant, head lag is normal. (f) This infant is 5 months old and has no head lag, demonstrating the marked effect of age in neurological assessment.

Neurological abnormalities

Table 2.9 Neurological abnormalities which may be identified on observation

Inspection	Appearance	Example
Head and face		
Genetic disorder or syndrome	Dysmorphic features	Down syndrome, Williams syndrome
Myopathic face	Expressionless face, often with ptosis and drooping of mouth	Neuromuscular disease, e.g. myotonic dystrophy
Reduced head circumference	Microcephaly (Fig. 2.11a)	Cerebral palsy, congenital infections, e.g. cytomegalovirus, Zika virus
Ptosis	Drooping of eyelid	Unilateral ptosis – third nerve palsy Bilateral – myasthenia gravis
Facial asymmetry (Fig. 2.11c)	Are movements of forehead preserved or weak?	Preserved: upper motor neurone lesion Weak: Bell palsy (Fig 2.11b)
Tongue fasciculation	Wriggling of tongue fibres	Spinal muscular atrophy
Skin		
Neurocutaneous skin lesions	Multiple café-au-lait spots Port-wine stain over trigeminal nerve area	Neurofibromatosis Tuberous sclerosis
Limbs		
Muscle wasting	Reduced muscle bulk	Cerebral palsy, meningomyelocele, muscle disorder
Calf muscle hypertrophy	Muscle replaced by fat and connective tissue	Duchenne muscular dystrophy
Contractures	Shortened muscles from increased tone or hypotonia	Immobility, restricted movements <i>in utero</i>
Hypertonic posture	Scissoring, fisting, pronation of arms, extended back and legs	Cerebral palsy
Hypotonic posture	Sitting in frog-like posture of legs	Spinal muscular atrophy
Dystonic posture	Abnormal posturing and extension from fluctuating tone	Dystonic cerebral palsy
Muscle fasciculation	Wriggling of muscle fibres	Lower motor neurone lesions
Asymmetry	Unilateral weakness	Hemiplegia



Figure 2.11 Examples of neurological abnormalities identified on observation. (a) Microcephaly. (b) Asymmetry of the face in Bell palsy. (c) Play being used to test muscles of facial expression.

Limb power

From 6 months, observe the pattern of mobility. When old enough, observe gait and standing up from lying and climbing stairs.

From 4 years, power can be tested formally against gravity and resistance.

- Turn examination into a fun game of strength!

- First test proximal, then distal, muscle power and compare sides.
- Ask the child to hold their arms out straight with palms of hands upwards and close their eyes. Observe for drift or tremor.
- Power can be graded using the Medical Research Council (MRC) power scale (Table 2.10).

Table 2.10 Medical Research Council power scale

Power score	Ability
5	Normal power against resistance
4	Weak active movements against gravity and resistance
3	Movement against gravity but not against resistance
2	Unable to move against gravity
1	Minimal movement/flicker
0	No movement at all

Coordination

Coordination is the use of visual and proprioceptive feedback to make complex patterns of movement. It is governed by the cerebellum.

- Unlike cortical issues, cerebellar problems result in ipsilateral, not contralateral signs.
- Coordination improves with age, so normal young children may have poor coordination.
- Cerebellar signs can be remembered by the acronym "DANISH" (Table 2.11).

Reflexes

With the child in a relaxed position, explain what you are about to do before approaching with a tendon hammer, or demonstrate on a parent or toy first, or place your finger over the tendon and tell the child you are going to strike your finger. A young child may find the tendon hammer scary!

Use a tendon hammer to elicit:

- Brachial and wrist reflexes in the upper limb.
- Knee and ankle reflexes in the lower limb.

Always double check abnormal reflexes:

- brisk reflexes (hyperreflexia) – anxiety in the child or a pyramidal disorder

Table 2.11 Deficits in coordination from cerebellar pathology

'DANISH' deficit	Description
Dysdiadochokinesia	Inability to perform alternating clapping
Ataxic gait	Broad unsteady gait when walking
Nystagmus	Horizontal beating tremor of the eyes
Intention tremor	Past-pointing on finger-to-nose test or cannot rub heel up and down leg
Slurring	Dysarthric speech
Hypotonia	Low muscle tone

- absent reflexes – neuromuscular problem or a lesion within the spinal cord, or inexpert technique.

Plantar responses

Unreliable under 1 year of age. Up-going plantar responses provide additional evidence of pyramidal dysfunction.

Sensation

As a screening test, brush a fine piece of cotton wool systematically over the dermatomes of the limbs.

- Is there a level below which there is no sensation (e.g. transverse myelitis)?
- Ask about perineal and peri-anal numbness (spinal and cauda equina lesions – there may also be a palpable bladder).
- Ask about 'pins and needles' (paraesthesia)
- Where sensory abnormality is likely (e.g. meningo-myelocele), more detailed investigation can be performed with an orange-stick or neuro-tip, as in adults.
- Formal investigation can be carried out with nerve conduction studies if indicated.

Spine

Look at the base of the spine for skin lesions, e.g. birth marks and tufts of hair, suggestive of spina bifida occulta, or a tethered cord.

Look at the curvature of the spine. Is there scoliosis, or abnormal kyphosis or lordosis?

Patterns of movement – gait

Assess standing from prone:

- Children *up to 3 years* of age will turn prone in order to stand because of poor pelvic muscle fixation.
- *Beyond 3 years*, the need to turn prone to rise and subsequently to use their hands to walk up the legs to stand is known as Gowers sign (see Fig. 29.6). It suggests proximal neuromuscular weakness (e.g. Duchenne muscular dystrophy) or low tone, which could be due to a central (brain) cause.

Assess walking and running:

- Incorporate it into a game, for example: 'how fast can you run?', walk on a line on the floor 'as though walking on a tightrope'.
- From age 5, when walking, the foot should strike the floor in a heel-toe pattern (Table 2.12).
- A toe-heel pattern of walking (toe-walkers) – often idiopathic, but may be from pyramidal tract (corticospinal) dysfunction or pelvic girdle neuromuscular weakness.
- Subtle asymmetries in gait – may be revealed by Fogo's test – walking on his/her toes, heels, the outside, and then the inside of his/her feet. Watch for the associated movements in the upper limbs.

 Always ask children to remove their shoes. The pattern of wear on the soles provides clues about abnormal gaits. Equally, an abnormal gait could be caused by ill-fitting footwear!

Table 2.12 Different forms of abnormal gait, and some of their causes

Gait	Appearance on affected side	Sample condition
Antalgic (to minimize pain)	Stance phase is briefer than swing	Musculoskeletal pain
Broad-based	Staggering gait, wide-spread feet	Cerebellar ataxia
Choreoform	Irregular, involuntary jerking	Choreoathetoid cerebral palsy
Circumduction (Sweeping)	Hypertonic leg circumducts a plantarflexed foot.	Hemiplegia
Scissoring	Hypertonic legs drag and cross the midline	Diplegia
Waddling	Dropping of the hip girdle on contralateral side to muscle weakness	Proximal muscle weakness
Foot drop	Leg raised to avoid scraping plantarflexed foot on ground	Peripheral motor neuropathy
Stamping	High stamping steps without weakness	Sensory neuropathy

Table 2.13 Cranial nerve examination

Cranial nerve (CN)	Function	Test
I (Olfactory)	Smell (not routinely tested)	Identify scent of hidden mint/orange/soap
II (Optic)	Pupils, visual fields, visual acuity	Pupil reaction (direct and consensual), visual fields, fundoscopy. Snellen (pictographic for young children) and Ishihara charts
III (Oculomotor), IV (Trochlear), VI (Abducent)	Eye and eyelid movement, pupils	Full eye movements. Is there a <i>squint</i> (see Fig. 4.10) or <i>nystagmus</i> ?
V (Trigeminal)	Motor: muscles of mastication Sensory: facial sensation	Clench teeth and waggle jaw against resistance. Sensation of three branches: ophthalmic (forehead), maxillary (cheek), and mandibular (lower jaw), tested with cotton wool
VII (Facial)	Muscles of facial expression	Raise eyebrows. Close eyes tight, blow out cheeks, smile or show teeth
VIII (Auditory)	Hearing	Identify soft sound when distracted in opposite ear.
IX (Glossopharyngeal)	Motor: pharynx Sensory: taste posterior third of tongue	Test together with Xth cranial nerve
X (Vagus)	Motor: muscles of pharynx and larynx Sensory: larynx	Inspect mouth for uvula deviation to unaffected side and palatal movement on saying 'aah'; difficulty swallowing. Listen for hoarse voice
XI (Accessory)	Trapezius and sternomastoid	Turn head and shrug against resistance
XII (Hypoglossal)	Tongue movements	Stick out tongue. Note deviation or fasciculation

Cranial nerve examination (Table 2.13)

- Test the cranial nerves in order, to help you keep track.
- Visual field testing can be difficult in young children. Use distraction on one side whilst presenting a subtle stimulus on the other.
- In young children, demonstration and play may be required (Fig. 2.11c).
- **When in doubt about visual or hearing loss, seek formal assessment.**

Musculoskeletal examination

The pGALS (paediatric Gait Arms Legs Spine) is a rapid screen to identify musculoskeletal problems and abnormal joints in children and young people. It is similar to the adult GALS assessment with some additional manoeuvres. It is shown in Figure 2.12.

pGALS – musculoskeletal screening for school-age children

(Differences from adult GALS highlighted in bold)

Screening questions

- **Do you (or your child) have any pain or stiffness in your joints, muscles or your back?**
- **Do you (or your child) have any difficulty getting yourself dressed without any help?**
- **Do you (or your child) have any difficulty going up and down stairs?**

Posture and Gait

Observe standing (from front, back and sides)

Observe walking
'Walk on your tip-toes, walk on your heels'

Arms

'Put your hands out straight in front of you'

'Turn your hands over and make a fist'

Arms

'Pinch your index finger and thumb together'

'Squeeze the metacarpophalangeal joints for tenderness'

'Put your hands together palm to palm'

'Put your hands back to back'

'Reach up and touch the sky'

'Look at the ceiling'

Figure 2.12 Musculoskeletal examination: pGALS screening for school-age children. (See www.pmmonline.org for videos and e-modules and pGALS app.)

Continued

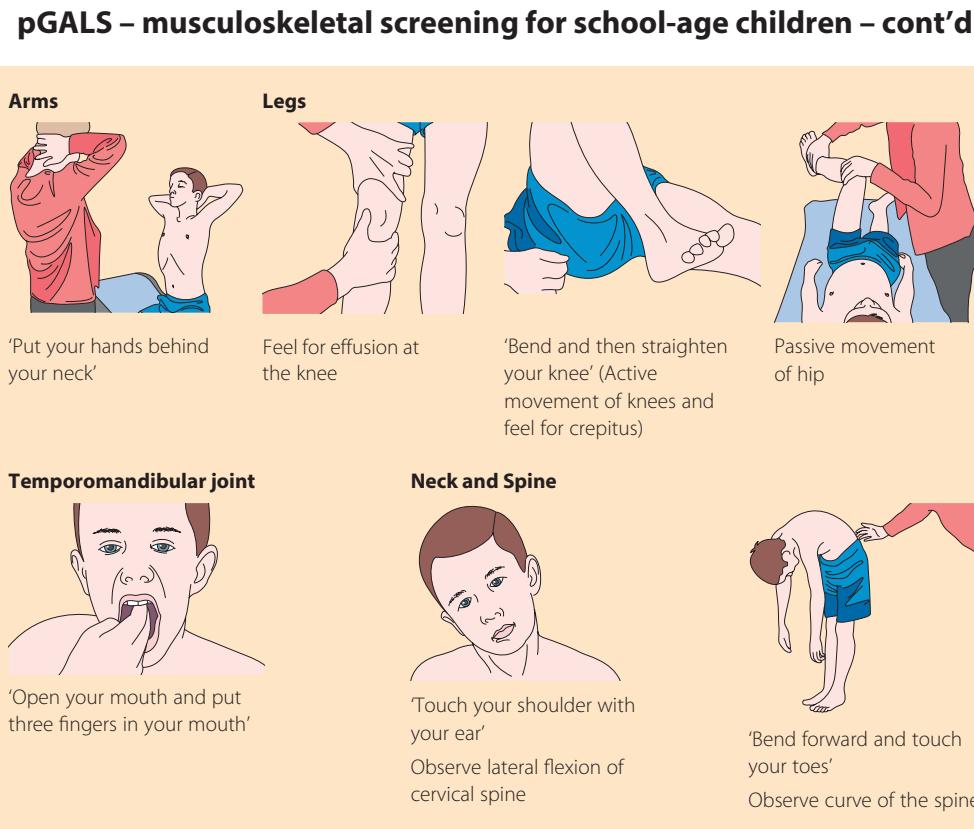


Figure 2.12 Continued

paediatric Regional Examination of the Musculoskeletal System – pREMS

If an abnormality is found, a more detailed regional examination (pREMS) of the affected joint as well as the joint above and below should be performed.

Look:

- For signs of discomfort.
- Skin abnormalities – rashes, scars, bruising, colour, nail abnormalities.
- Limb alignment, leg length, muscle bulk and evidence of symmetry.
- Bony deformity, soft tissue, joint swelling or muscle change.

Feel:

- Each joint, long bones and neighbouring soft tissues.
- Palpate along bones and joint line for tenderness.
- Feel for warmth (infection or inflammation).
- Delineate bony or soft tissue swellings.
- Check for joint effusion, most readily at the knee.

Move:

- For each joint, ask the child to move the joint first (active movement). Observe for discomfort, symmetry and range of movement.
- Passively move the joint, noting range of any restriction of movement (compare sides but note bilateral changes).
- Lateral and rotational movements may be as important as flexion and extension.

Function:

- For lower limb joints – check gait.
- For small joints such as hands – check grip.

Special tests for the knee are:

- The anterior and posterior draw test (cruciate ligaments) ([Fig. 2.13a](#)).
- Varus and valgus strain (lateral collateral ligaments) ([Fig. 2.13b](#)).

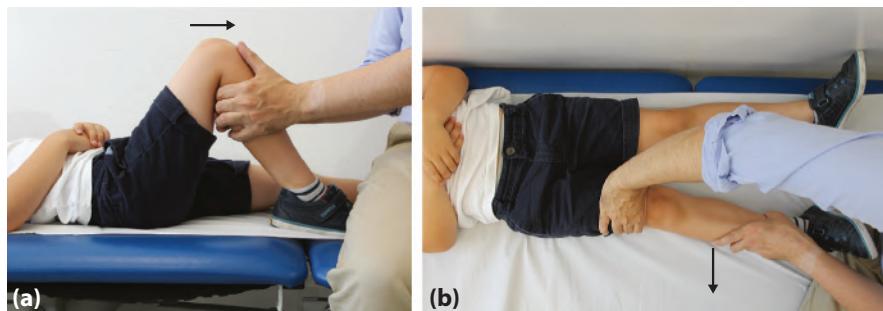


Figure 2.13 (a) The anterior draw test. There should be no laxity in the joint. (b) Valgus and varus strain demonstrates lateral instability of the knee.

Head and neck examination

Swellings

Inspect the head and neck for swellings and note:

- location
- restriction of neck movement (e.g. sternocleidomastoid 'tumour' from muscle fibrosis)
- asymmetry (Fig. 2.14a)
- movement on tongue protrusion (e.g. thyroglossal cyst)
- moves on swallowing (e.g. goitre)

Palpate (Fig. 2.14b) for:

- *pain* – tender or non-tender
- *heat* – warm or normal?
- *colour* – erythema?
- *texture* – fluctuant, firm or rubbery?
- *contour* – smooth or craggy?
- *mobility* – tethered or mobile?



Always listen over a lump with a stethoscope: you may hear the bruit of a vascular malformation.



Figure 2.14a Asymmetry identified on inspection: the left ear is pushed forward by mastoiditis.

Lymph nodes

Children often have multiple, small, easily palpable lymph nodes, particularly in the anterior cervical (Fig. 2.14c), inguinal and axillary regions, and this is a normal finding.

Thyroid

- *Inspect* – swelling uncommon in childhood; occasionally at puberty
- *Palpate* – for swelling, nodule, thrill
- *Movement* on swallowing or tongue protrusion?
- *Listen* – auscultate for bruits if enlarged
- *Look and ask* for clinical features of hypo- and hyperthyroidism (see Ch. 26, Diabetes and endocrinology).

Eye examination

Inspect for:

- *Pupils* – shape, reactivity and symmetry
- *Iris* – complete (coloboma), colour (e.g. pink in albinism)
- *Sclerae* – for inflammation and colour (e.g. blue in osteogenesis imperfecta)
- *Movement* – full and symmetrical? Is there a squint? (see Figs 4.9 and 4.10)
- *Nystagmus* – cerebellar or ocular, but do not test gaze too lateral
- *Epicantic folds* (common in Asian ethnic groups).

Ophthalmoscopy:

- In infants, check *red reflex* (Fig. 2.14d) – partial or complete absence occurs in corneal clouding, cataract, and retinoblastoma
- *Optic fundi* – should be examined in children or young people with headaches, diabetes mellitus or hypertension.
- *Mydriatics* are not usually needed in older children
- *Detailed fundoscopy* – best by ophthalmologist.



Figure 2.14b Palpate from behind. Be careful. Placing your hands near the throat can invoke fear or be ticklish! Either reaction will interfere with your examination.

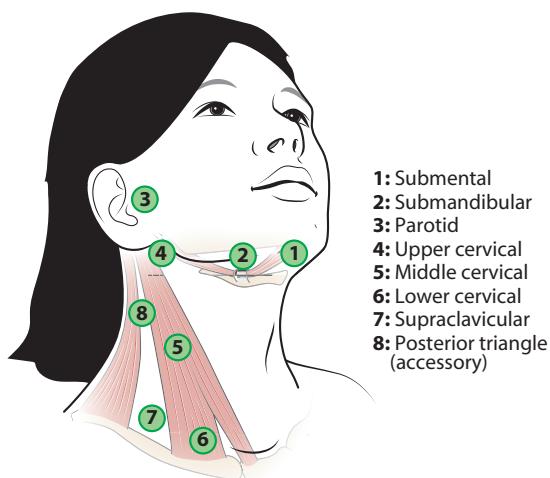


Figure 2.14c The site of normal cervical lymph nodes.

Head and neck examination cont'd



Figure 2.14d Red reflex is best seen from a distance of 20–30 cm.

Ear and throat examination

Examine the ears and throat of all children with upper respiratory infections, unexplained fever, ear pain or discharge or impaired hearing.

Inspect the tympanic membrane (Fig. 2.14e) for:

- swelling
- erythema
- perforation
- dullness
- effusion, fluid level.

Inspect the throat with an otoscope and tongue-depressor (Fig. 2.14f) for:

- *Tonsils* – for swelling and exudate
- *Uvula* – for deviation in quinsy or vagal nerve palsy
- *Pharynx* – red in pharyngitis
- *Palate* – high or arched? (Marfan syndrome), posterior petechiae (Fig. 2.14g) in EBV
- *Dentition* for caries and erupting teeth.



Always leave examination of the ears and throat until last as it can upset a previously cooperative child.

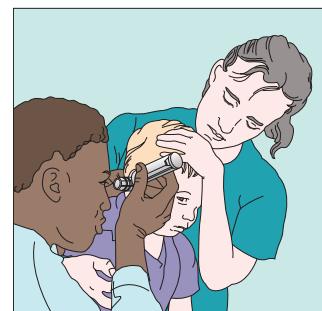


Figure 2.14e Holding a young child correctly is essential for the successful examination of the ear with an auroscope. The parent wraps one arm firmly around the child's arms and the other stabilizes the child's head to avoid injury.



Figure 2.14f Holding a young child to examine the throat. The parent has one hand on the head and the other across the child's arms.



Figure 2.14g Posterior palate petechiae in Epstein–Barr virus (EBV) infection.

Communicating with children and young people

Why should I speak to the child / young person when I can get all the information from parents? You might think that this is a question that we don't need to ask anymore, but the experience of children and young people is still that they are very frequently side-lined in conversations between the adults (Table 2.14).

Reasons it is essential that children and young people's voices are heard in the consultation are:

- To respect and acknowledge their views are important as they are the topic being discussed.
- They may say something to clinicians that they have never said to their parents.
- They may have a different perspective or use different language about a symptom or problem from their parents.

- parents, in a way that is useful diagnostically or in their management.
- If you get to know the child or young person then you can understand better their response to their problem – is the child or young person very anxious? boisterous? do they want to be different from who they are?
 - Anyone who is involved in the decision-making around their treatment is more likely to adhere to it, and children and young people are no exception.
- Some tips on how to talk to children and young people in clinical practice are shown in [Table 2.14](#).

Table 2.14 How to talk to children and young people in clinical practice

- Make your aim not talking to the child or young person, but *with*. This often requires you to wait until they are ready to communicate with you, and make the ‘first move’ either verbally or non-verbally, thus inviting you into a conversation. It is crucial to spot this conversational opening and react to it, even just with a smile.
- At all times, and with all ages, be authentic. If you have to pretend to be interested in talking to children or young people, paediatrics may not be the right specialty for you! Show that you care.
- When talking to the child or young person, consider both age and stage of development. Especially during adolescence, chronological age is a poor indicator of developmental stage.

Preschool child (2–5 years)	School-age child (4–10 years)	Adolescent (10–19 years)
Communication strategies		
Start by finding an ‘in’ with them, often something visual or a toy. Ask them about it once they feel happy to approach you. Figurative play is often key for children of 3 to 4 years, so talking about bodies/ symptoms using teddy bears or dolls can be very helpful.	At this age it’s often appropriate to start the consultation by talking to the child about their life generally, before bringing in the parents. However, be aware that: Direct questions can make children feel pressurized. Try statements (which may be silly), e.g. ‘I think your teacher this year is actually a polar bear’, or starting what would otherwise be a question with ‘I wonder’, for example ‘I wonder if the pain is more sore after dinner.’ Remember that in school, children are encouraged to guess the answer, even if they have not understood the question. Establish that the rules are different here, and agree how they will let you know if they haven’t understood, don’t know or don’t want to answer you.	Here, a respectful attitude is paramount. It may be that the young person just won’t talk to you with their parents in the room, so the facility to talk to them alone is essential. Watch for any sign of interest in the conversation, and ask their opinion regularly. Don’t give any sign, verbal or non-verbal, that you find lack of engagement annoying or rude. Don’t try to be cool or connect with the young person ‘on their level’. It very seldom works. Depersonalize – what would your friends say/think/do? Some young people worry about this – do you ever?

Investigations

There are a number of investigations which may be included as part of a paediatric consultation and which are described here. Other more specific investigations are described throughout the book. In general, investigations are kept to a minimum and are only performed if their results would change management. If possible, non-invasive investigations such as ultrasound are used, and invasive tests such as blood tests or ionizing radiation from X-rays and CT scans kept to a minimum.

Blood pressure

Blood pressure must be measured in acutely unwell children as part of assessing 'Circulation'. It should also form part of the assessment whenever the blood pressure may be abnormal, for example when assessing a child who is overweight or obese or has with renal or cardiac disease, diabetes mellitus, receiving drug therapy that may cause hypertension, e.g. corticosteroids, and some neurological presentations or disorders, e.g. headaches. Hypertension is considered in more detail in [Chapter 19](#) (Kidney and urinary tract disorders).

Blood pressure is measured with a manual or automatic sphygmomanometer:

- Show the child that there is a balloon in the cuff and demonstrate how it is blown up.
- Use largest cuff that fits comfortably, covering at least two-thirds of the length of the upper arm ([Fig. 2.15](#)). An incorrectly sized cuff is the most common cause of abnormal blood pressure readings in children!
- The child / young person must be relaxed and not crying.
- It is conventionally measured in the right arm, level with the heart.
- Systolic pressure is the easiest to determine in young children and clinically the most useful.
- Diastolic pressure is when the sounds disappear. May not be possible to discern in young children.

Measurement

Must be interpreted according to a centile chart for sex, age and height (see Appendix [Table A.1](#) or online at <https://www.mdcalc.com/aap-pediatric-hypertension-guidelines>). Blood pressure is increased by tall stature and

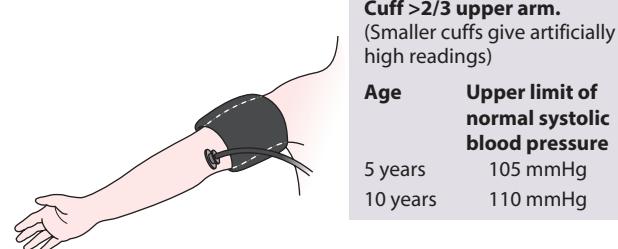


Figure 2.15 Measurement of blood pressure.



Figure 2.16 Measurement of peak flow rate with a peak flow meter.

if overweight or obese. An abnormally high reading must be repeated, with the child relaxed, on at least three separate occasions; the average value is used. An elevated BP is >90th centile, hypertension is ≥95th centile or ≥130/80 (whichever is lower).

Peak flow or lung function tests

Measuring peak flow rate or obtaining spirometry is part of the respiratory examination in school-age children. It can be performed in most children from 5 years. It is most often used to monitor control of asthma ([Fig. 2.16](#) and see Appendix [Fig. A.5](#)).

Urinalysis

Urinalysis using a dipstick is required to identify protein, blood, glucose and ketones in the urine. The presence of leukocytes and nitrites may assist with screening for a urine infection. In infants and young children, obtaining an uncontaminated sample for microscopy, culture, and sensitivity to identify a urinary tract infection can be problematic. This is considered in [Chapter 19](#).

Transcutaneous bilirubin

Jaundice is common in the first few weeks of life, and the severity of the hyperbilirubinaemia can be estimated non-invasively using a transcutaneous bilirubinometer. A light is flashed onto the skin and the device measures the intensity of light of specific wavelengths reflected using optical

spectroscopy. The bilirubin concentration is measured to establish if phototherapy is indicated (see Ch. 11, Neonatal medicine). High bilirubin levels need to be confirmed by serum testing.

Summary and management plan

By the end of the consultation, have you covered the 'ideas, concerns and expectations' (ICE) of the child or young person and parents, not only for the consultation but also about their attitudes to illness in general? It provides a better understanding of where the family is coming from. If you go one step further and incorporate the information into your management plan, you are more likely to be in tune with the family's way of thinking. This might include:

- Ideas – 'What do you think is the matter?'
- Concerns – 'What particular worries or concerns did you have?'
- Expectation – 'And what are you hoping that we might be able to do for you?'

Finally, summarize the key problems:

- Consider the 'four p' biopsychosocial framework:
 - Predisposing factors: e.g. a history or family history of atopy
 - Precipitating factors: e.g. perfume and animals
 - Perpetuating factors: e.g. poor inhaler technique, insufficient prophylaxis, anxiety, effect on sports and exams
 - Protective factors: e.g. salbutamol for asthma, EpiPen for anaphylaxis, family smoking cessation.
- List the diagnoses and if possible differential diagnoses. Draw up a management plan to address the problems, both short and long term. This could be reassurance, a period of observation, performing investigations or therapeutic intervention.
- Provide an explanation to the parents and to the child, if old enough, or young person. Consider providing further information, either written or on the internet.
- If relevant, discuss what to tell other members of the family.
- Consider which other professionals should be informed.
- Record a brief summary in the child's personal child health record.
- Ensure your notes are legible, dated and signed.

Summary

In taking a history and performing a clinical examination

- The child / young person's age and developmental stage are key features – it will determine the nature of the problem, how the consultation is conducted, the likely diagnosis, and its management.
- The interview environment should be welcoming – with suitable toys for young children and privacy assurance for adolescents.
- Involve the child or young person with the consultation, as appropriate to their age and developmental stage.
- Most information is usually obtained from a focused history and observation.
- Consider biopsychosocial issues alongside specific diagnoses.
- Check growth, including charts in personal child health record, and development.
- With young children – be confident but gentle, do not ask their permission to examine them or they may say 'no'.
- Leave unpleasant procedures (ears and throat) until last.



Always consider if there are child protection (safeguarding) issues. Do you have any concerns that this child / young person is not adequately cared for, or at risk? Any concerns must be reported to a senior member of the paediatric team.

Acknowledgements

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Further Reading

- Shiels K, Brugha R: *Pocket tutor paediatric clinical examination*, ed 2, London, 2020, JP Medical Ltd.
Gill D, O'Brien N: *Paediatric clinical examination made easy*, ed 6, Edinburgh, 2017, Elsevier.



Normal child development, hearing and vision

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Features of normal child development, hearing and vision:

- The acquisition of developmental skills in young children follows a similar pattern.
- There are ages by which most children have achieved specific developmental milestones.
- Further assessment is warranted if milestones are not achieved by these ages.
- There is an integrated programme of screening tests, immunization, developmental reviews and health promotion for all children; in England this is called the Healthy Child Programme.
- As part of this programme, all newborn infants have their hearing screened.
- Screening of visual acuity and squint occurs at school entry.

A child's development is an integral part of paediatrics and needs to be considered at every consultation. Child development refers to the sequence of physical, speech and language, cognitive and social, behavioural and emotional changes that occur from birth to adulthood. There are particularly rapid gains in all developmental domains during the first 5 years of life. In the school years, the evidence of developmental progression is predominantly cognitive and the development of abstract thinking, although there is also further maturation of early developmental and social skills.

In the preschool years development is monitored:

- by parents, who are provided with guidance about normal development in their child's Personal Child Health Record
- at regular child health surveillance checks
- whenever a young child is seen by a healthcare professional.

The main objectives of assessing a young child's development are to confirm normal developmental progress or detect delayed development early in order to:

- help the child achieve their maximum potential
- provide treatment or therapy promptly (particularly important for impairment of hearing and vision)
- act as an entry point for the investigation, care and management of the child with special needs.

This chapter covers normal development. Delayed or disordered development and the child with special needs are considered in [Chapter 4](#) (Developmental problems and the child with special needs).

Influence of nature and nurture on development

A child's development represents the interaction of nature (genetic potential) and nurture (environment) on the developing brain. Nature determines the potential of the child, while the care the child receives influences the extent to which that potential is achieved. There is now increasing evidence that, via epigenetics, these influences are not independent, but that our environment influences our genes, and that this can be inter-generational. For optimal development, children require a secure, responsive and loving environment to meet their physical and psychological needs ([Fig. 3.1](#)). This changes with the age and stage of the child:

- Infants are totally dependent on their parents for all physical needs, and require a limited number of carers.

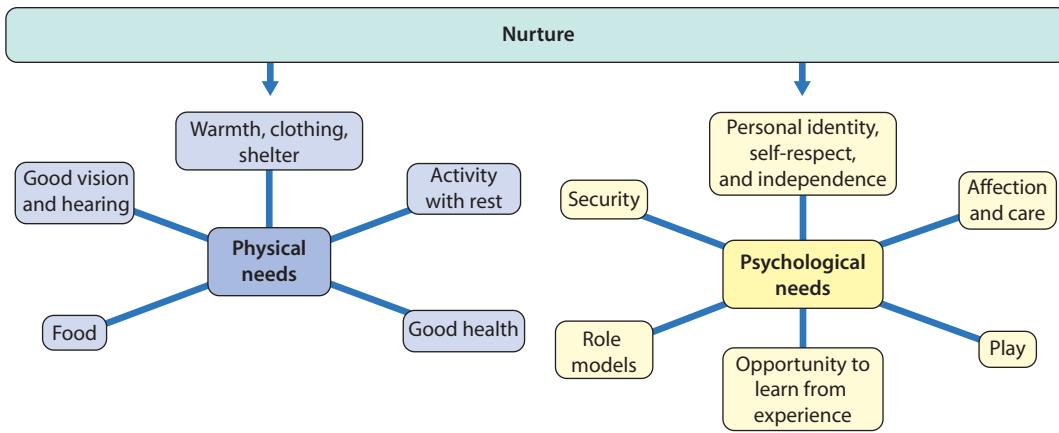


Figure 3.1 Development can be impaired if the child's physical or psychological needs are not met.

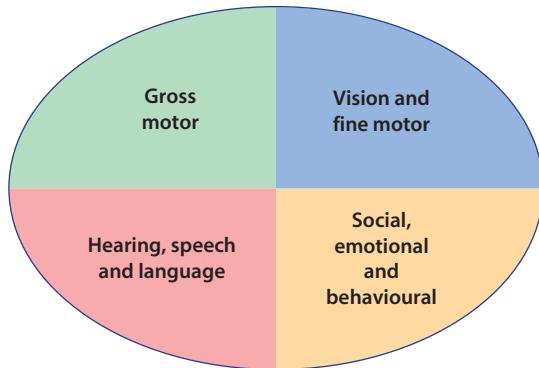


Figure 3.2 The four domains of child development.

- Primary school age children can meet some of their physical needs and cope with many social relationships.
- Young people are able to meet most of their physical needs while experiencing increasingly complex social and emotional needs.

Developmental domains

In development there are four domains to consider whenever a young child is seen (Fig. 3.2):

- gross motor
- vision and fine motor
- hearing, speech and language
- social (including self-care skills), emotional and behavioural.

Gross motor skills are the most obvious initial area of developmental progress. As fine motor skills require good vision, these are grouped together. Similarly, normal speech and language development depend on good hearing and so these are considered together. Social, emotional and behavioural skills are a spectrum of psychological development.

The acquisition of developmental skills for each domain follows a remarkably consistent pattern between children, but does vary in rate. Thus the normal pattern for acquisition of skills:

- is sequentially consistent
- should always be considered longitudinally, relating each stage to what has gone before and what lies ahead
- varies in rate between children.

A delay or disorder in any one skill area can have an impact on other areas. For instance, a hearing impairment may affect a child's social, emotional and behavioural development as well as speech and language development. As a child grows, additional skills become important, such as attention and concentration, and children need to integrate these skills. Neglect or child abuse can affect a child at any age but may have particularly profound impacts on all developmental domains in young children.

Developmental milestones

Chronological age, growth and development usually progress together. Just as there are normal ranges for growth, so there are for development. Important skills are called developmental milestones.

When considering developmental milestones:

- *Median age* is the age when half of a population of children achieve that skill; it serves as a guide to when stages of development are likely to be reached but does not tell us if the child's skills are outside the normal range.
- *Red flag age* is the age by which a developmental milestone should have been achieved. They are more useful as a guide to whether a child's development is normal than the median ages. Failure to meet a red flag age is a prompt for more detailed assessment to determine if investigation or intervention is required.

Median and red flag ages

The difference between median and red flag ages is shown by considering the age range for the developmental milestone of walking unsupported. The percentage of children who take their first steps unsupported is:

- 25% by 11 months
- 50% by 12 months
- 75% by 13 months
- 90% by 15 months
- 97.5% by 18 months.

The median age is 12 months and is a guide to the common pattern to expect, although the age range is wide. The red flag age is 18 months. Of those not achieving the red flag age, many will be normal late walkers, but a proportion will have an underlying problem, such as cerebral palsy, global developmental delay, or a primary muscle disorder. Some may be under-stimulated from neglect. Hence any child who is not walking by 18 months of age should be assessed and examined. Setting the limit age earlier may allow earlier identification of problems, but will also increase the number of children described as delayed who are in fact normal (false positives).

Variation in the pattern of development

Development is sequential. Taking motor development as an example, in the first year, infants develop head control, reach out for objects, transfer objects from one hand to another, start to roll, get into a sitting position and then learn to stay sitting, start to crawl, pull to stand, cruise along furniture, stand alone and then start to walk; a head to toe (cephalocaudal) progression of voluntary motor control. However, there is some variation in the way skills are acquired in otherwise normal children; while most infants (83%) crawl, some bottom-shuffle and others become mobile with their abdomen on the floor, so-called commando crawling or creeping (Fig. 3.3).

The red flag age of 18 months for walking applies to children who crawled as their early mobility pattern. Children who bottom-shuffle tend to walk later than children who crawl, so that within those not walking at 18 months of age there will be some children who demonstrate a gross motor variant pattern, with other aspects of their developmental progress still being normal. Overall, of children who bottom-shuffle, 50% will walk independently by 18 months and 97.5% by 27 months of age. Late-walkers

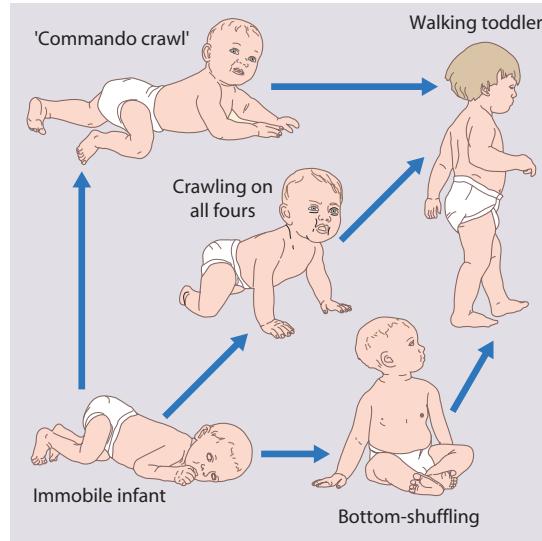


Figure 3.3 Early locomotor patterns. Most children crawl on all fours prior to walking, but some 'bottom-shuffle' and others 'commando crawl' (creep). Bottom-shuffling often runs in families. The late walking that often goes with this locomotor variant needs to be differentiated from an abnormality such as cerebral palsy.

should be assessed to exclude the hyper- or hypotonia of a cerebral palsy, global developmental delay, a primary muscle disorder, joint hypermobility, or developmental dysplasia of the hip.

Infants have a number of primitive reflexes at birth, which gradually disappear, whilst postural reflexes essential for independent sitting and walking emerge (Fig. 3.4). Persistence of primitive reflexes may interfere with normal motor development.

Adjusting for prematurity

As with growth, if a child has been born prematurely, this should be allowed for by calculating developmental age from the expected date of delivery. Thus the anticipated developmental skills of a 9-month-old baby (chronological age) born 3 months early at 28 weeks' gestation are more like those of a 6-month-old baby (corrected age). Correction is not required after 2 years of age when the number of weeks of prematurity no longer represents a significant proportion of the child's life.

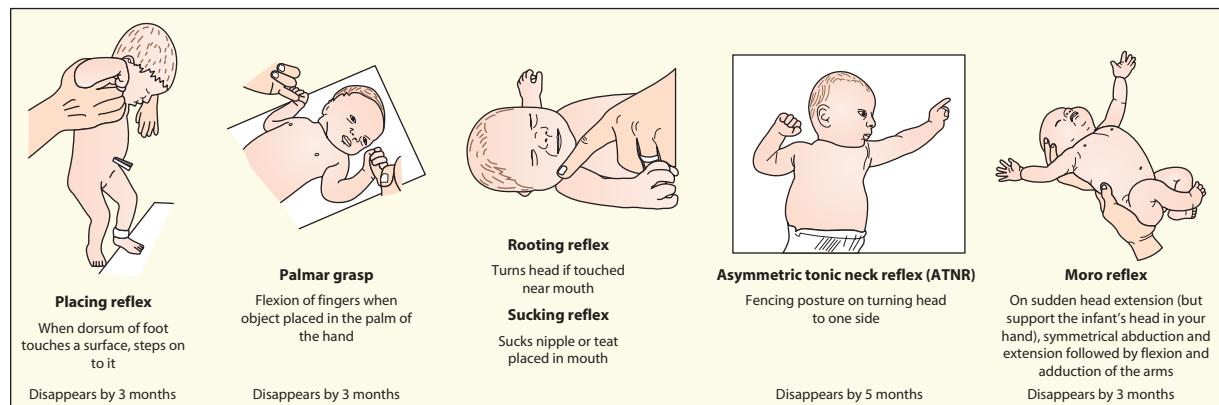


Figure 3.4a Primitive reflexes. The primitive reflexes evident at birth gradually disappear as postural reflexes essential for independent sitting and walking emerge.

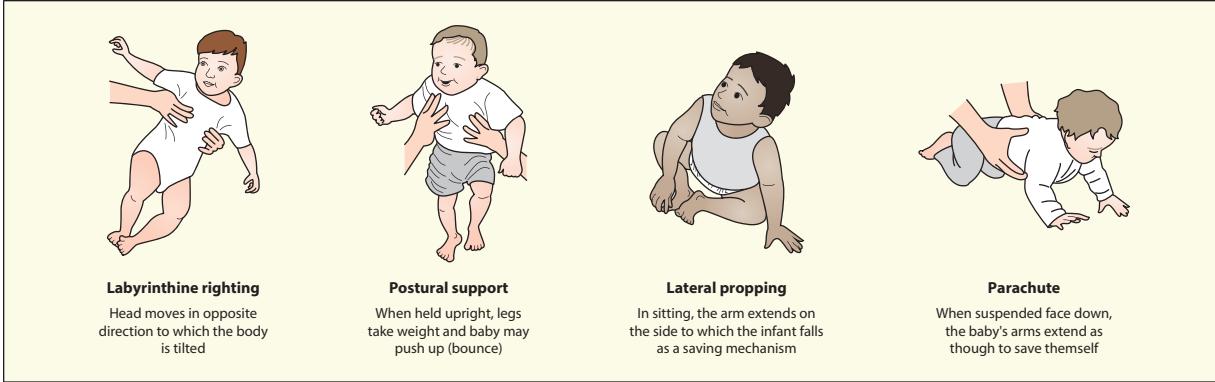


Figure 3.4b Postural reflexes (appear at 4 to 12 months)

Assessing if development is normal

When evaluating a child's developmental progress and considering whether it is normal or not:

- Start with each domain of development (gross motor; vision and fine motor; hearing, speech and language; social, emotional and behavioural) separately.
- Consider the developmental pattern by thinking longitudinally and separately about each developmental domain. Ask about the sequence of skills achieved as well as those skills likely to develop in the near future.
- Determine the level the child has reached for each developmental domain.
- Next relate the progress of each developmental domain to the others. Is the child progressing at a similar rate in each domain, or do some developmental domains lag behind the others?
- Finally relate the child's developmental achievements to age (chronological or corrected).

This will enable you to decide if the child's developmental progress is normal or delayed. Normal development implies steady progress in all four developmental domains with acquisition of skills occurring before red flag ages are reached. If there is developmental delay, does it affect all four developmental domains (global developmental delay), or one developmental domain only (specific developmental delay). As children grow older and acquire further skills, it becomes easier to make a more accurate assessment of their abilities and developmental status.

Summary

Assessing if development is normal

When assessing a young child's development, consider:

- the four developmental domains: gross motor; vision and fine motor; hearing, speech and language; social (including self-care skills), emotional and behavioural
- that the acquisition of developmental abilities follows a similar sequence between children, but may vary in rate and still be normal.

Terms used include:

- developmental milestones: for specific developmental skills
- median age: the age when half the population acquires a skill; serves as a guide to normal pattern of development
- red flag age: the age when a skill should have been acquired by 97.5% of children and so further assessment is indicated if not achieved.

When evaluating a child's development, consider:

- each domain separately
- the sequence of developmental progress
- the stage the child has reached for each domain
- if progress is similar in each domain
- the child's overall developmental profile and how that relates to the child's age.

Pattern of child development

This is shown pictorially for each developmental domain and includes key milestones:

- gross motor development ([Fig. 3.5](#))
- vision and fine motor ([Fig. 3.6](#))
- hearing, speech and language ([Fig. 3.7](#))
- social, emotional and behavioural ([Fig. 3.8](#)).

In order to screen a young child's development, it is only necessary to know a limited number of key developmental milestones and their red flag ages ([Fig. 3.9](#) and [Table 3.1](#)).

Cognitive development

Cognition refers to the process of acquiring knowledge and understanding. This evolves with age. The thoughts of preschool children (pre-operational thought) tend to be that:

- they are the centre of the world
- inanimate objects are alive and have feelings and motives
- events have a magical element
- everything has a purpose.

Gross motor development (median ages)

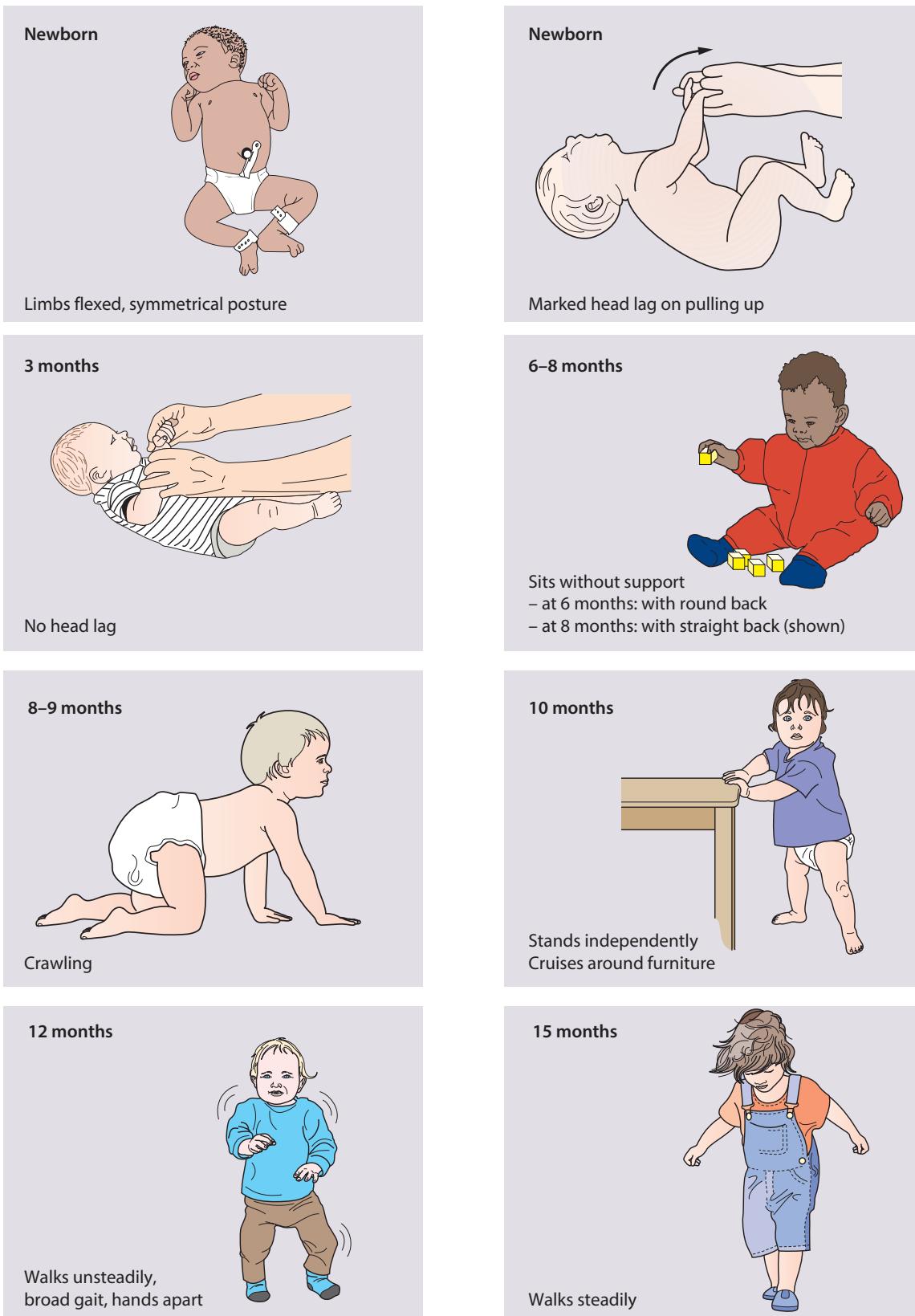
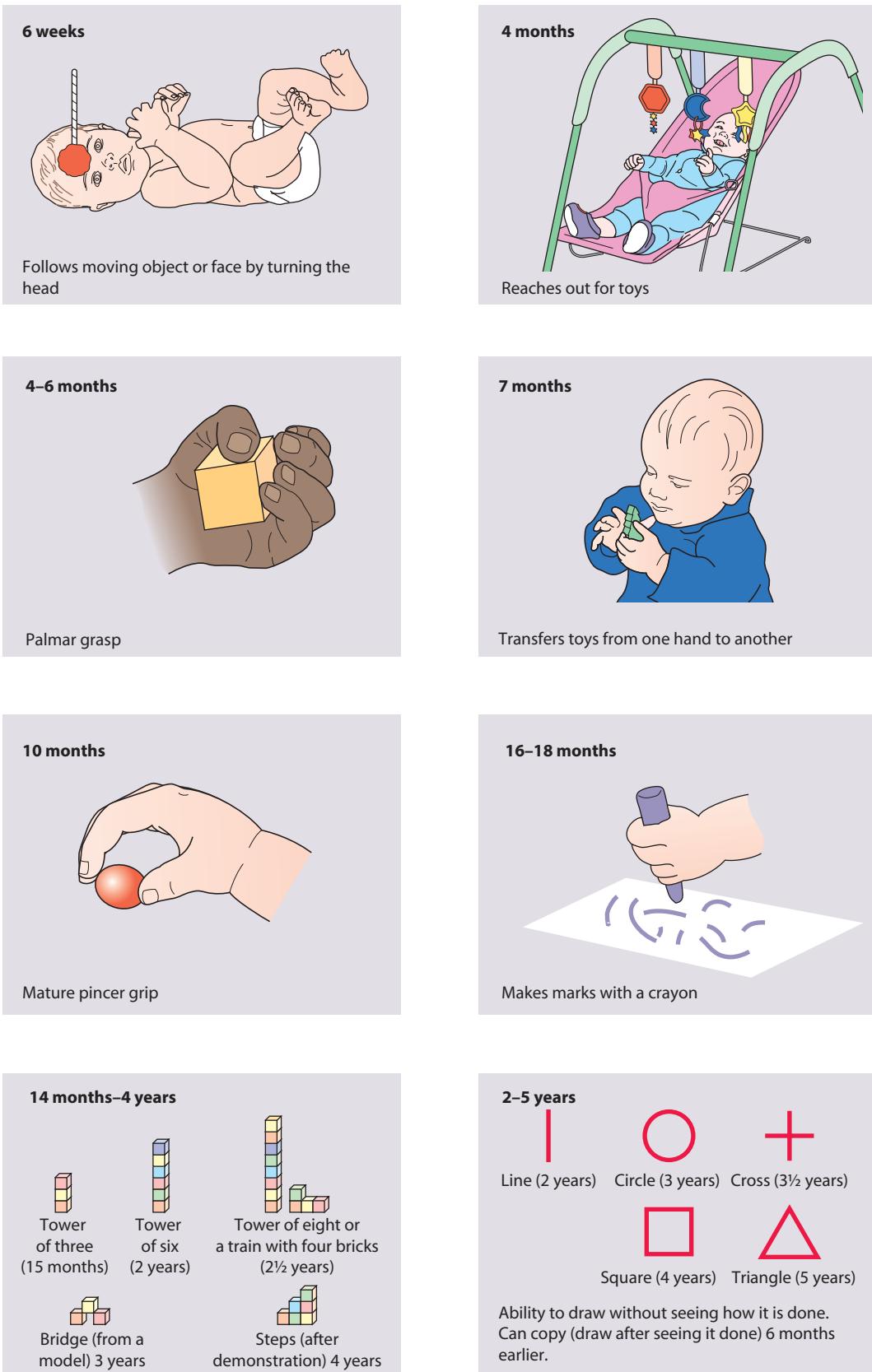


Figure 3.5 Gross motor development (median ages).

Vision and fine motor (median ages)**Figure 3.6** Vision and fine motor skills (median ages).

Hearing, speech and language (median ages)

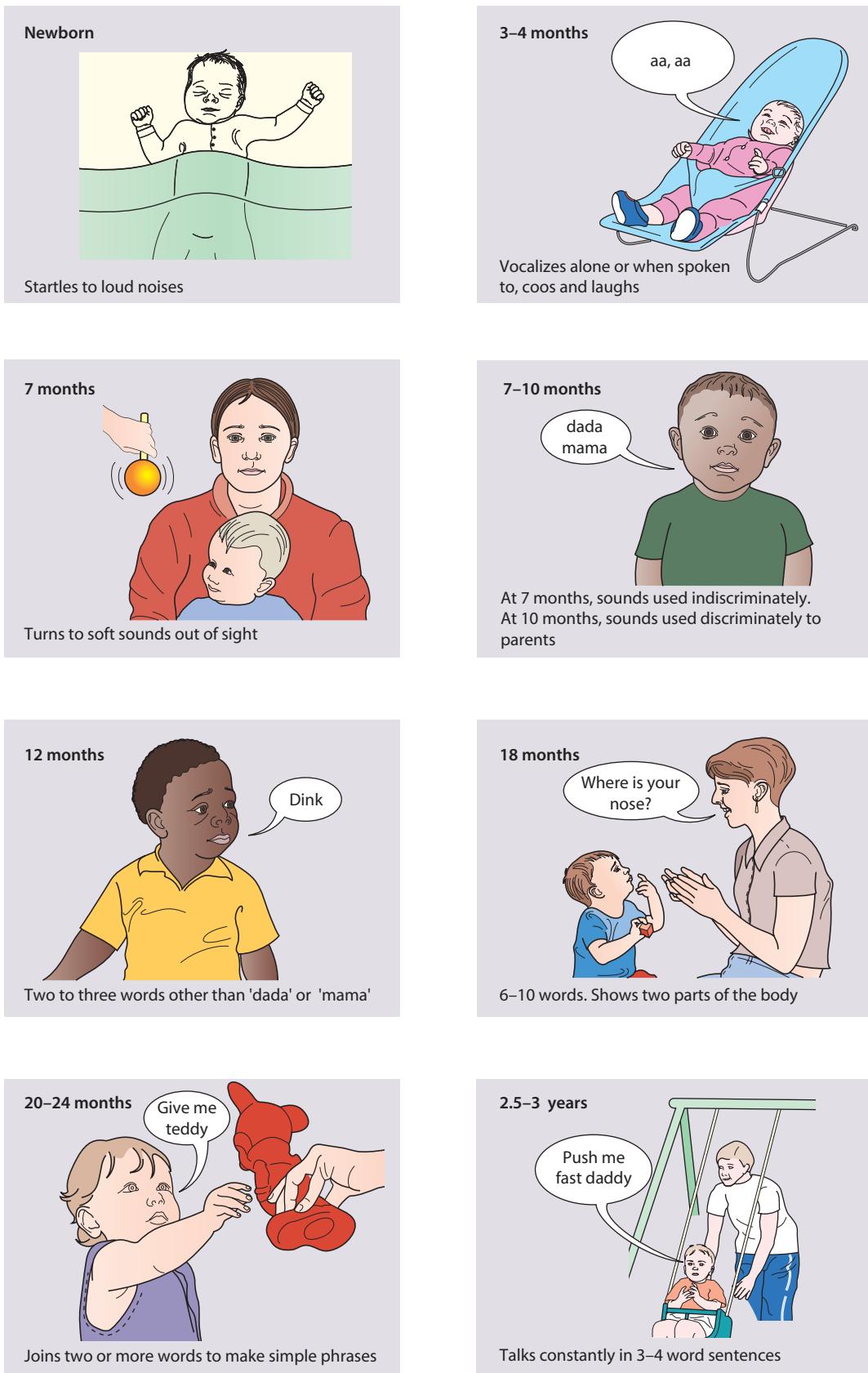
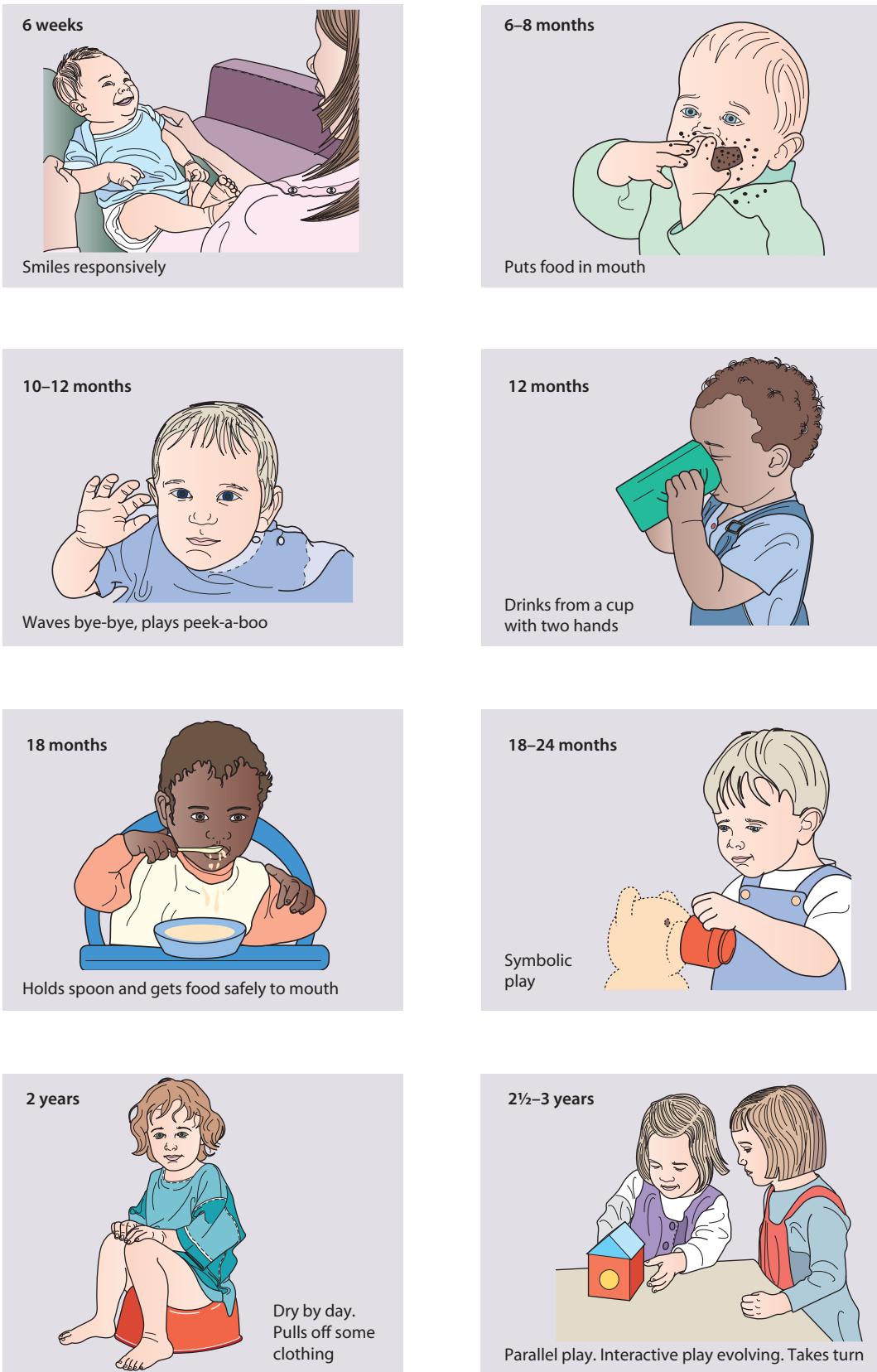


Figure 3.7 Hearing, speech and language (median ages).

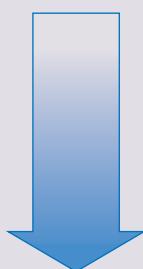
Social, emotional and behavioural development (median ages)**Figure 3.8** Social, emotional and behavioural development (median ages).

Summary

Development domains with red flag ages

Gross motor development

- Acquisition of tone and head control
- Primitive reflexes disappear
- Sitting
- Locomotor patterns
- Standing, walking, running
- Hopping, jumping, peddling



Gross motor

Head control
Sits unsupported
Stands with support
Walks independently

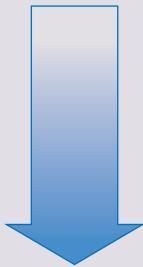
Red flag ages

4 months
9 months
12 months
18 months



Vision and fine motor development

- Visual alertness, fixing and following
- Grasp reflex, hand regard
- Voluntary grasping, pincer, points
- Handles objects with both hands, transfers from hand to hand
- Writing, cutting, dressing



Vision and fine motor

Fixes and follows visually
Reaches for objects
Transfers
Pincer grip

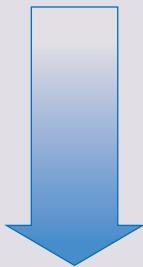
Red flag ages

3 months
6 months
9 months
12 months



Hearing, speech and language development

- Sound recognition, vocalization
- Babbling
- Single words, understands simple requests
- Joining words, phrases
- Simple and complex conversation



Hearing, speech and language

Polysyllabic babble
Consonant babble
Saying 6 words with meaning
Joins words
3-word sentences

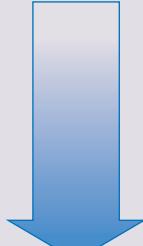
Red flag ages

7 months
10 months
18 months
2 years
2.5 years



Social, emotional, behaviour development

- Smiling, socially responsive
- Separation anxiety
- Self-help skills, feeding, dressing, toileting
- Peer group relationships
- Symbolic play
- Social/communication behaviour



Social behaviour

Smiles
Fear of strangers
Feeds self/spoon
Symbolic play
Interactive play

Red flag ages

8 weeks
10 months
18 months
2–2.5 years
3–3.5 years



Figure 3.9 Development domains with red flag ages.

Summary

Table 3.1 Developmental milestones by median age

Age	Gross motor	Vision and fine motor	Hearing, speech, and language	Social, emotional, and behavioural
Newborn	Flexed posture	Follows face or light by 2 weeks	Stills to voice Startles to loud noise	Smiles by 6 weeks
7 months	Sits without support	Transfers objects from hand to hand	Turns to voice Polysyllabic babble	Finger feeds Fears strangers
1 year	Walks independently	Pincer grip (10 mo) Points	2–3 words Understands name	Drinks from cup Waves
15–18 months	Walks independently and steadily	Immature grip of pencil Random scribble	6–10 words Points to two body parts	Feeds self with spoon Beginning to help with dressing
2½ years	Runs and jumps	Draws	3-word to 4-word sentences Understands two joined commands	Parallel play Clean and dry

Toys and other objects are used in imaginative play as aids to thought to help make sense of experience and social relationships.

In middle-school children, the dominant mode of thought is practical and orderly, tied to immediate circumstances and specific experiences (operational thought).

It is only in adolescence that an adult style of abstract thought (formal operational thought) begins to develop, with the ability for abstract reasoning, testing hypotheses and manipulating abstract concepts.

Checking developmental progress

A focused approach to developmental assessment

So far, development has been considered over time, taking each domain and its progression separately, and then relating the progress in each developmental domain to that occurring in the others, and to chronological age. Detailed questioning and observation is required to assess children with developmental problems, but a swifter approach to screening developmental progress in normal clinical practice is needed.

At different ages, different developmental domains are dominant and this helps guide initial developmental questioning. Thus, for a child aged:

- less than 18 months – start with questions on gross motor abilities, acquisition of vision and hearing skills, followed by questions about hand skills
- 18 months to 2.5 years – start with questions about speech and language and fine motor (hand) skills with only brief questioning about gross motor skills

(such as *age of walking independently*, as it is likely the child would have presented earlier if these were of concern)

- 2.5 to 4 years – initial questions are best focused around speech and language and social, emotional and behavioural development.

Developmental questioning needs to cover all areas of developmental progress but this more focused way of taking a developmental history is time efficient. It directs the assessment to current abilities instead of concentrating on parents trying to remember the age when their child acquired developmental milestones sometime in the past.

Observation during questioning

Observation is a key paediatric skill, and it is important to watch the child throughout any consultation. Not only will this provide an almost immediate guide to where to begin questioning, but it also offers the opportunity for a rapid overview of the child's abilities, behaviour, play skills, peer group and parent-child relationships, all of which will go towards determining the overall picture about the child's developmental skills.

Equipment for developmental testing

Simple basic equipment is all that is needed for most developmental assessments. Equipment is aimed at bringing out the child's skills using play. Cubes, a ball, picture book, doll and miniature toys such as a tea set, crayons and paper allow a quick but useful screen of mobility, hand skills, play and imagination, speech and language, and behaviour. These items allow the child to relax by having fun at the same time as facilitating observer assessment of skills.

Summary

Checking child development

When checking a child's developmental progress:

- consider the child's age and then focus your questions on the areas of likely current developmental progress
- offer the child suitable toys to find out about skills through play
- observe how the child uses the toys and interacts with people.

Summary

Developmental screening and assessment

- Developmental screening – checks of whole populations or groups of children at set ages by trained professionals.
- Developmental assessment – detailed analysis of overall development or specific areas of development.

Formal developmental screening and assessment

Developmental screening (checks of children at set ages by trained professionals) is a formal process within a child health surveillance and promotion programme. The reliability of screening is improved with a questionnaire completed by parents beforehand, and in England this is the Ages and Stages Questionnaire, a standardized questionnaire using 19 age-specific developmental questions starting at 4 months and ending at 60 months of age. It has high specificity and negative predictive values which supports its use in identifying children who are not at risk of developmental delay.

Developmental assessment is a more detailed analysis of development that follows concern at screening that a child's developmental progress may be delayed or disordered in some way. It is part of the diagnostic process and includes investigation, therapy and advice on how to optimize the child's progress. It is performed by a specialist service such as a local multidisciplinary child development service, which is able to offer input by a paediatrician and therapists and other specialists; it is discussed further in [Chapter 4](#).

A range of tools have been developed to assess development in a formal reproducible manner. These include:

- screening tests, e.g. the Schedule of Growing Skills and the Denver Developmental Screening Test
- standardized tests that assess the overall development of infants and young children, e.g. Griffiths and Bailey Infant Development Scales
- standardized tests concentrating on assessing specific aspects of development, e.g. the Reynell Language Scale, the Gross Motor Function Measure, the Autism Diagnostic Interview and the Autism Diagnostic Observation Schedule.

These tests are time-consuming and require training for reliable results. Cognitive function (higher mental function) can be assessed objectively with formal intelligence quotient (IQ) tests. However, IQ tests:

- may be affected by cultural background and linguistic skills
- do not test all skill areas
- do not necessarily reflect an individual child's ultimate outcomes
- may be compromised by specific disabilities, such as cerebral palsy.

Cognitive assessment of school-age children using IQ and other tests is sometimes carried out by clinical or educational psychologists.

Child health surveillance

In most countries there is a programme of child health surveillance. In the UK, the Healthy Child Programme is an evidence-based approach for all children, from pregnancy to 19 years of age, that aims to ensure every child gets the good start they need to lay the foundations for a healthy life ([Table 3.2](#)). It includes:

- screening tests – for early detection of disease
- immunization – for prevention of infectious diseases
- developmental screening reviews – to identify health and wellbeing issues early, so that support and early interventions can be provided in a timely manner
- health promotion – information and guidance to promote good parenting and healthy lifestyle choices, including helping parents develop and sustain a strong bond with their children, reduce childhood obesity by promoting healthy eating and physical activity.

The 0–5 years component of the programme is led by health visiting services, with a focus on ensuring that children are school ready. In addition to universal screening, health visitor support is directed to need, with most input devoted to families with complex needs, called progressive universalism. The 5–19 years component is led by school nursing services, with input from primary care, education and other providers. Increasingly, many developmental problems in young children are identified by early years and nursery staff.

Details of each review are entered into the child's Personal Child Health Record (PCHR or 'the red book') kept by parents and brought whenever the child is seen by a health professional. This record is becoming digital.

Summary

The child health surveillance programme

- Is provided by primary and community care services.
- Includes screening, immunization, developmental review and health promotion.
- Emphasizes the role of parents in the early detection of problems with health, development, hearing and vision.

Table 3.2 Overview of Healthy Child Programme in UK provided by integrated local services (2021)

Age	0–2 years	2–10 years	10–19 years
Screening	Antenatal health promoting visit Newborn infant physical examination (NIPE) <72 hr old Newborn blood spot (biochemical) screening, day 5 Repeat NIPE (newborn infant physical examination) at 6–8 weeks	Preschool vision screening (and hearing in some areas) National Child Measurement Programme (4–5 years)	National Child Measurement Programme (10–11 years)
Immunization	See Childhood Immunization Schedule, Chapter 15	See Childhood Immunization Schedule, Chapter 15	See Childhood Immunization Schedule, Chapter 15
Developmental screening reviews	New baby review (by 14 days) 6–8 week check 7–10 month review	2 years (Ages and Stages Questionnaire) Preschool review	Health review at school entry and age 10–11 years (questionnaire)
Health Promotion	Feeding, weaning, safety at home and in cars, passive smoke, SIDS prevention and safe sleeping Personal child health record	Nutrition, obesity prevention, injury prevention, emotional health, psychological wellbeing	Encourage physical activity, emotional health, psychological wellbeing and mental health, reduction of risk-taking behaviour, sexual health

Note: SIDS, sudden infant death syndrome.

Hearing

By 25–26 weeks' gestation, a fetus responds to noises and voice. At birth, a baby startles to loud sounds, and has a marked preference for voices. Subsequent development of speech and language requires adequate hearing; its progression is shown in Fig. 3.7.

Early detection and amelioration of significant hearing impairment improves the outcome for speech and language and behaviour, which in turn impacts on educational achievement, employment prospects and improves mental health and participation in society. Hearing is improved by using amplification (e.g. hearing aids or cochlear implants), and by providing support and advice to parents to help their child develop effective communication and enhance learning.

Neonatal hearing screening

Two automated, electrophysiological tests are used for universal neonatal hearing screening. These are:

- *Automated Otoacoustic Emission (AOAE)* (Fig. 3.10) – a soft earpiece placed in the ear canal produces a series of clicks, which evokes a faint sound or 'echo' from the outer hair cells of a healthy cochlea which is detected by a microphone. It establishes normal cochlear function
- *Automated Auditory Brain Response (AABR)* (Fig. 3.10) – evokes brainwaves in response to a sound stimulus. It tests both the cochlea and the auditory nerve.

Screening has been introduced in many countries. In the UK, babies are usually offered screening with Automated Otoacoustic Emission (AOAE) before leaving hospital. If abnormal, it is usually checked directly with Automated

Box 3.1 Risk factors for hearing loss

- Family history of hereditary hearing loss
- Genetic syndromes with hearing loss, e.g. Down syndrome
- Craniofacial anomalies of ear (including cleft lip and palate)
- Admission to NICU (>48 h)
- Congenital infection, e.g. CMV (cytomegalovirus), rubella
- Bacterial meningitis

Auditory Brain Response (AABR). Infants who have been in NICU (Neonatal Intensive Care Unit) have a ten-fold increased risk of hearing loss (may have experienced mechanical ventilation, severe hyperbilirubinaemia, ototoxic drugs, e.g. gentamicin, hypoxic-ischaemic encephalopathy, complications of prematurity) and should have both AOAE and AABR tests. Any infant with an abnormal AABR or other risk factors (Box 3.1) are referred directly to audiology.

Behavioural hearing tests in children

Children can be tested with behavioural hearing tests based on their developmental age. Sounds can be presented via air conduction to both ears (sound field), by headphones or ear inserts (ear specific), or by bone conduction on the mastoid process.

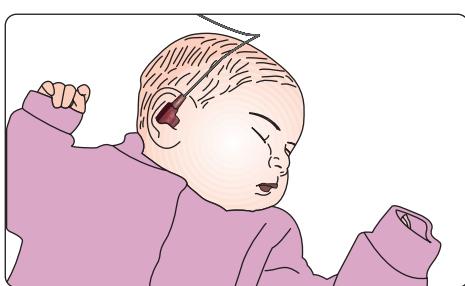
Visual reinforced audiometry

Effective from 6 months to 2½ years (Fig. 3.11). The child is conditioned to turn to look at a visual reward (e.g. animated or illuminated toy) when they hear a sound. Can test both ears together (sound field) or each ear separately (ear specific using soft ear probe or headphones), and both air and bone conduction. One tester distracts the

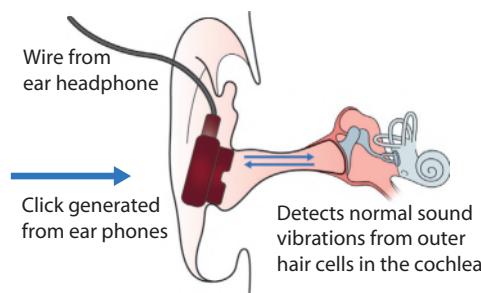
Hearing screening of newborn infants

Hearing screening of newborn infants

(a) Automated otoacoustic emission (AOEA)



Newborn infant having automated otoacoustic emission hearing test



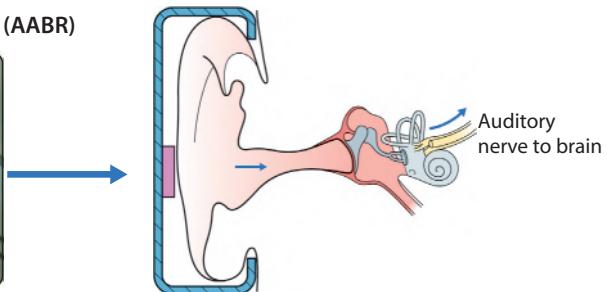
Advantages:

- simple and quick to perform, though is affected by ambient noise
- used to screen all babies

Disadvantages:

- misses auditory neuropathy as function of auditory nerve or brain not tested
- relatively high false-positive rate in first 24 hours after birth as vernix or amniotic fluid are still in ear canal
- not a test of hearing but a test of cochlear function

(b) Automated auditory brainstem response (AABR)



Auditory stimulus via earphones

Signal via ear and auditory nerve to brain

Auditory brainstem waveforms – computerized analysis determines if normal or abnormal



Advantages:

- screens hearing pathway from ear to brainstem
- low false-positive rate
- used if no clear response to AAOE or was on NICU

Disadvantages:

- affected by movement, so infants need to be asleep or very quiet, so time consuming
- complex computerized equipment, but is mobile
- requires electrodes applied to infant's head, which parents may dislike

Figure 3.10 Universal neonatal hearing screening is usually performed using (a) automated otoacoustic emission testing or (b) automated auditory brainstem response audiometry.

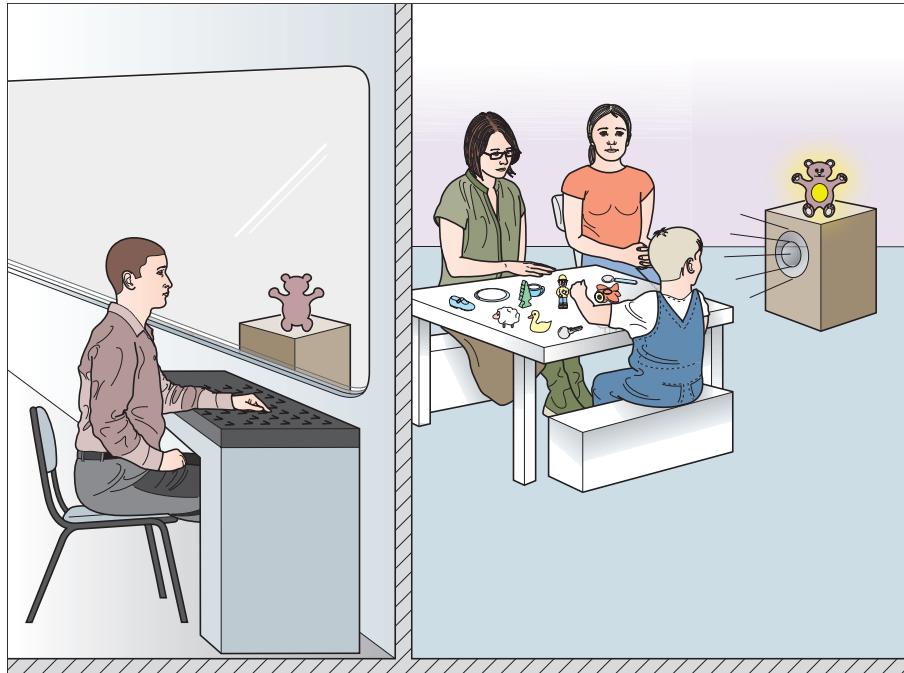


Figure 3.11 Visual reinforced audiometry. While an assistant plays with the child, sounds of a specific frequency are emitted from a speaker. When the child turns to it, the tester lights up a toy by the speaker to reinforce the sound with a visual reward. This test is particularly useful at 10–18 months of age.

child with low level toys whilst the other tester presents specific sounds through a speaker and activates a reward.

Pure tone audiometry (a performance test)

From about 3 years to adult. The child is actively involved – e.g. conditioned to put man in boat or brick in box (up to school entry) or press button when they hear a sound (from around 5 years). Can test both ears together (sound field) or each ear separately (ear specific using headphones). One tester presents specific sounds through a handheld warbler or headphones and activates a reward.

Bone conduction testing

If a child is found to have a hearing loss then bone conduction testing can be used to discriminate between a sensorineural and a conductive hearing loss. This is done by modifying the visual reinforced audiometry or pure tone audiometry by using a small vibrator placed on the mastoid, instead of sound field or ear insert/headphones. The sounds pass directly through the bone to the cochlear. If the cause for the hearing loss is a conduction problem in the outer or middle ear, bone conduction will be normal.

Middle ear testing

If a child has a hearing loss or there are concerns about middle ear fluid then a tympanogram is undertaken (see Ch. 4). This is an objective test of middle ear function and movement of the tympanic membrane. A soft earpiece is placed in the ear canal and a pump produces a small increase in pressure; any movement of the tympanic membrane is detected by the earpiece. It is a test of middle-ear function, allowing discrimination between conductive and sensorineural hearing loss.

Audiology referral

As outlined above, newborn infants should be referred to audiology if they have an abnormal AABR or a neonatal risk factor listed in Table 3.8. In addition, regardless of the result of newborn hearing screening, infants and children should be referred for audiological assessment:

- if any parental or professional concern about hearing
- whenever there is speech and language delay
- in global developmental delay
- after significant head injury or skull fracture, particularly basal skull fracture
- following bacterial meningitis – urgent referral
- if genetic syndrome associated with hearing loss is identified
- if congenital infection, particularly congenital CMV, is diagnosed.

Summary

Hearing

- Early detection and treatment of hearing impairment improves the outcome of speech, language and behaviour.
- Newborn hearing screening is performed for early identification of hearing loss.
- Children can develop hearing loss throughout childhood and adolescence.
- If there are any concerns by parents or others about hearing, the child should be referred for formal audiological assessment.

Table 3.3 Testing vision at different ages

Age	Test
Birth	Aware of light Fixes on a face and begins to follow horizontally contrasting black and white patterned image or dangling coloured ball
6–8 weeks	Face fixation and follows objects to either side
6 months	Fixates on 2.5-cm brick Visually directed reach Responds to preferential looking tests of acuity (e.g. Keeler or Teller cards)
12 months	Fixates 1-mm objects e.g. 'hundreds-and-thousands' cake sprinkle
1–2 years	Preferential looking tests of acuity (e.g. Cardiff cards)
2–3 years	Names or matches pictures in linear array (e.g. Kay pictures or Lea symbols). Distant and near
3 years +	Names or matches letters (e.g. Sonksen logMAR, or logMAR crowded). Distant and near

Note: single letters/pictures should not be used as they overestimate acuity and will miss significant interocular differences (i.e. miss amblyopia). At all ages: observe the child's eyes. Is eye contact established? What is the child looking at? How does the child respond to what is apparently seen?

Vision

At birth, a newborn's visual acuity is poor. Although newborn infants can fix on a face or high contrast objects, they will appear fuzzy. The peripheral retina is well developed but the fovea is immature and the optic nerve is unmyelinated. By 6 weeks of age most babies watch their parent's face closely and track a moving target up to 90° either side of them. They may have a transient squint. By 7 months of age a baby can pick up and transfer toys from one hand to another; by 12 months they can pick up a 1-mm 'hundreds-and-thousands' cake sprinkle. Clarity of vision matures; visual acuity improves from 6/200 at birth to 6/60 at 3 months and 6/6 at 5 years of age.

As well-focused images on the retina are required for the acquisition of visual acuity, any obstruction to this, e.g. from a refractive error or cataract, will interfere with the normal development of the optic pathways and visual cortex unless corrected early in life. This type of visual loss is called amblyopia and can be permanent.

Vision screening

This is performed at:

- birth – for structure of eye and red reflex (cataracts impede a red reflex) – part of Newborn Infant Physical Examination (NIPE)
- 6–8 week check – red reflex for cataracts; fixing and following – part of NIPE
- preschool vision screening by orthoptist – checks visual acuity and eye alignment.

Vision testing

The assessment of vision at different ages is shown in **Table 3.3**. Children rarely complain about having poor vision. Reduced vision can impact on a child's learning and development. If a parent or professional is concerned about a child's vision or their eyes, if they have a short attention span for visual activities, lose their place when reading, avoid reading or other close activities, or have delayed development particularly of fine motor skills, they

should have formal assessment of their vision. Family photographs and videos are useful to detect cataract (loss of red reflex), retinoblastoma (white pupil), squints and eye movement abnormalities.

Summary

Vision

- Visual acuity is poor at birth but gradually improves to normal adult levels by about 5 years of age.
- Babies and toddlers have to learn to track objects, converge their eyes and develop depth perception.
- Cataract screening is conducted at birth and six weeks.
- Vision screening is performed at school entry or in preschool children.
- Children rarely complain about having poor vision.

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Further reading

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Developmental problems and the child with special needs

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Features of developmental problems and the child with special needs:

- Developmental problems may be anticipated antenatally, or identified from birth onwards.
- Cerebral palsy is the commonest cause of motor impairment in children.
- Autism spectrum disorder and attention deficit hyperactivity disorder (ADHD) usually present in preschool or early school years.
- Early detection of severe impairment of hearing or vision minimizes its detrimental effect on development.
- The medical, social, emotional and educational requirements of affected children are complex, often requiring multidisciplinary child development services.

Children with developmental problems may present in several ways:

- parental concern regarding development, behaviour or social skills
- via routine child health surveillance or development screening
- presence of risk factors (family history/affected siblings, prematurity, antenatal screening tests, dysmorphic features, abnormal neurology) leading to targeted assessment

- professionals in early years education settings may recognize delayed or disordered patterns of development
- opportunistic detection at other health contacts, e.g. acute illness.

Definitions

The terminology is imprecise and different terms are used by health and education.

Medical terms:

- The four developmental domains are:
 - gross motor
 - fine motor and vision
 - hearing, speech and language
 - social, emotional and behavioural.
- Delay is used only in the 0–5 age group and describes slow acquisition of skills but in the correct order. It may be global (affecting two or more skill areas) or specific (affecting only one skill area).
- Developmental disorder – the term is used when developmental skills are both delayed and acquired in the incorrect order (disordered).
- Learning/intellectual disability – describes school-aged children with significantly reduced ability to understand new or complex information, learn new skills, and to cope independently with everyday life, impacting most areas of the person's life.

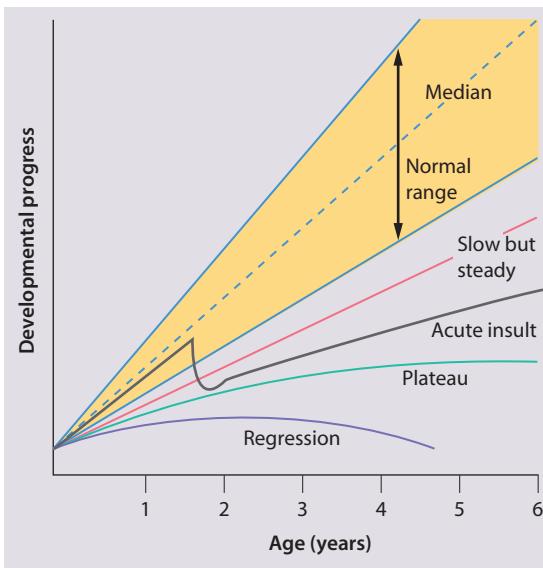


Figure 4.1 Patterns of abnormal development. These may be slow but steady, plateau, regression. They may follow an acute injury.

Education terms:

- Learning difficulty – is typically used in relation to school-age children usually affecting cognitive or specific functional skills.
- Specific learning disorder – developmental skills in one area of development are disordered, e.g. a specific disorder of spelling/reading in dyslexia.

The following are agreed definitions:

- *impairment* – loss or abnormality of physiological function or anatomical structure
- *disability* – any restriction or lack of ability due to the impairment.

Difficulty and disability are often used interchangeably, but difficulty is used particularly in an educational context. Impairment is now generally used instead of disability when describing problems with vision or hearing.

The patterns of abnormal development (Fig. 4.1) can be categorized as:

- slow but steady
- plateau effect
- regression – acute regression following brain injury with subsequent slow recovery but not to normal levels, or slow progressive regression as with neurodegenerative disorders.

The approach to a child with developmental problems and special needs

Any child whose development is delayed or disordered needs assessment to determine the cause and management. Neurodevelopmental problems present at all ages, with an increasing number now recognized antenatally (Table 4.1). Many are identified in the neonatal period

because of abnormal neurology or dysmorphic features. During infancy and early childhood, problems often present at an age when a specific area of development is most rapid and prominent (i.e. motor problems during the first 18 months of age, speech and language problems between 18 months and 3 years, and social and communication disorders between 2 and 4 years of age). Abnormal development may be caused not only by neurodevelopmental disorders (Table 4.2) but also by ill health or if the child's physical or psychological needs are not met.

A detailed history about the child's development is required. The history will also include prenatal, perinatal, and postnatal events, including maternal health during pregnancy. The Personal Child Health Record is often a valuable source of information because it contains additional details of the pregnancy, delivery, condition at birth, Apgar scores, birthweight, birth head circumference, newborn blood spot test, and hearing screen results. A thorough environmental, social and family history is essential, particularly asking about consanguinity and a family history of developmental problems or learning difficulties, which may point to metabolic diseases or genetic conditions.

Developmental assessment

- Observe the child from the first moment seen.
- Make it fun.
- Toys to use are cubes, ball, car, doll, pencil, paper, pegboard, miniature toys and a picture book.
- Ask the parent about the child's abilities as you assess. Start at a level below that ability to retain confidence of the parent and child.
- Assess the child to a level slightly above their apparent ability, to establish their ceiling of skill for each developmental area.
- Observe the child's interaction with and responses to their parent/carer.

Physical examination

A detailed systemic examination is also required. This includes:

- weight, height, head circumference measured and plotted on centile chart – Microcephaly? Macrocephaly?
- dysmorphic features: do they look like other family members? Are there any unusual features? Are body proportions unusual?
- skin abnormalities for neurocutaneous syndromes: café-au-lait patches, axillary freckling in neurofibromatosis or hypopigmented patches (ash-leaf macules) in tuberous sclerosis
- neurological disorder: observation movements/gait/running after a ball for signs of unsteadiness, asymmetry, weakness or spasticity. Check tone/power and reflexes
- child's ability to sit up and to stand up from lying down supine and to clear the floor on jumping from a standing position for muscle weakness, e.g. muscular dystrophy
- observation of eye movements and examination of eyes looking for cataracts, nystagmus/wobbly eye

Table 4.1 Presenting features of potential neurodevelopmental problems by age

Prenatal	Positive family history, e.g. affected siblings or family members; ethnicity, e.g. Tay–Sachs disease in Jewish parents Antenatal screening tests, e.g. ultrasound or blood test or non-invasive prenatal testing (cell-free DNA testing of fetal cells from maternal blood) for Down syndrome; neural tube defects such as spina bifida and hydrocephalus. Amniocentesis for suspected genetic disorders
Perinatal	Following perinatal asphyxia with neonatal hypoxic–ischaemic encephalopathy Preterm infants with intraventricular haemorrhage/periventricular leukomalacia, post-haemorrhagic hydrocephalus Dysmorphic and neurocutaneous features Abnormal neurological behaviour – tone, feeding, movement, seizures, visual inattention
Infancy	Global developmental delay Delayed or asymmetric motor development Neurocutaneous features Dysmorphic features Vision or hearing concerns (parents or post screening)
Preschool	Speech and language delay and/or disorder Abnormal gait, clumsy or poor motor skills Poor social communication skills Unusual behaviour – stereotypical, overactivity, inattention
School age	Problems with balance and coordination Learning difficulties Inattentiveness Hyperactivity Specific learning difficulties, e.g. dyslexia, dyspraxia Social communication difficulties
Any age	Acquired brain injury, e.g. after meningitis, traumatic brain injury Regression with loss of skills

Table 4.2 Conditions that cause abnormal development and learning disability

Prenatal	
Genetic	Chromosome/DNA disorders, e.g. Down syndrome, fragile X syndrome, chromosomal microdeletions or duplications
Structural brain problems	Cerebral dysgenesis, e.g. microcephaly, absent corpus callosum, neuronal migration disorder. Hydrocephalus
Cerebrovascular	Stroke – haemorrhagic or ischaemic
Metabolic	Hypothyroidism, phenylketonuria
Teratogenic	Alcohol or drug abuse
Congenital infection	Rubella, cytomegalovirus, toxoplasmosis, HIV, Zika
Neurocutaneous syndromes	Tuberous sclerosis, neurofibromatosis, Sturge–Weber, Ito syndrome
Perinatal	
Extreme prematurity	Intraventricular haemorrhage/periventricular leukomalacia
Perinatal asphyxia	Hypoxic–ischaemic encephalopathy
Metabolic	Symptomatic hypoglycaemia, hyperbilirubinaemia
Postnatal	
Infection	Meningitis, encephalitis
Anoxia	Suffocation, near drowning, seizures
Trauma	Traumatic brain injury – accidental or non-accidental
Metabolic	Hypoglycaemia, inborn errors of metabolism
Cerebrovascular	Stroke – haemorrhagic or ischaemic
Nutritional deficiency	Malnutrition, vitamin deficiency
Other	Chronic illness, child maltreatment, neglect
No cause identified	About 25%

Note: The site and severity of brain damage influence the clinical outcome, i.e. whether specific or global developmental delay, learning and/or physical disability.

- movements for disorder of vision and underlying neurological condition
- cardiovascular examination – abnormalities are associated with many dysmorphic syndromes
 - abdominal examination for hepatomegaly in a metabolic/storage disorder

At the end of the developmental assessment you should be able to describe what a child can and cannot do in terms of gross motor, vision and fine motor, hearing, speech and language, and social, emotional and behaviour. Are the abilities within normal limits for age and, if not, which developmental fields are outside the normal range?

If indicated, formal tools for developmental assessment include Schedule of Growing Skills, Griffiths and Bayley Scales of Infant and Toddler Development.

Red flags ages for each domain, which suggest that the child's development is significantly delayed and/or disordered and requires prompt referrals and interventions, are listed in [Chapter 3](#) (Normal child development, hearing and vision; see [Fig. 3.9](#)).

Investigations

History and examination often guide the choice of investigations required, e.g. identifying dysmorphic features (facial appearance), neurological abnormalities (e.g. low muscle tone), single or multiple organ malformations and behavioural phenotypes. Conditions such as Down, Prader–Willi, Angelman, fragile X and Williams syndromes require genetic testing as described in [Chapter 9](#) (Genetics).

First-line investigations to be considered are listed in [Table 4.3](#). Hearing and vision should be also be assessed to identify impairment.

Second-line investigations ([Table 4.4](#)) may need to be done in conjunction with specialist services such as clinical genetics, neurology and/or developmental/community paediatrics. Cranial imaging is only recommended in the presence of abnormal neurology.

If a specific diagnosis cannot be made, it is often helpful to see if a pattern emerges over time. Some children who present early with global developmental delay

Table 4.3 First-line investigations to consider for children with developmental delay and/or disorder

Test category	Test
Genetic	Array-based comparative genomic hybridization (aCGH) / microarray Fragile X analysis (in selected cases) Whole genome sequencing (if available) Developmental delay panels
Biochemical	U/E (urea and electrolytes), creatinine TFTs (thyroid function tests – TSH and T4) Creatine kinase Bone chemistry, liver function tests Lead (if risk of environmental exposure/pica) Full blood count, ferritin B_{12} (if dietary restriction)
Metabolic	See Table 27.3

Table 4.4 Second-line investigations to consider for children with developmental delay and/or disorder

Test category	Test	Possible pathology/indications
Imaging	Cranial ultrasound in newborn CT brain MRI brain Skeletal survey	Ventricular dilatation, bleeding, cysts Calcification, structural brain malformations, bleeds Structural brain malformations, bleeds, infarction, neuronal migration disorders Storage disorders
Neurophysiology	EEG Nerve conduction studies EMG	Evidence of seizure disorder or pattern suggestive of neurological impairment, encephalopathy or regression Peripheral nerve lesions/neuropathy myopathy
Metabolic	Second line metabolic investigations to be guided by specialists	

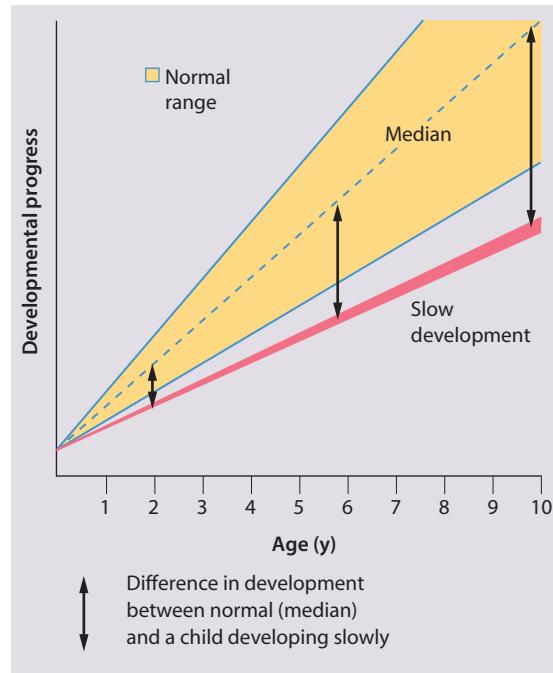


Figure 4.2 For children with abnormal development, the gap between their abilities and what is normal widens with age.

catch up with their peers over time but the majority do not and the gap between them and their peers often widens (Fig. 4.2). As children become older and the clinical picture is clearer, it is more appropriate to describe the individual difficulties such as learning disability or motor disorder rather than using the term global developmental delay.

Management

This may need to be determined by the child development service. Development of secondary disabilities and comorbidities need to be monitored, such as epilepsy, gastro-oesophageal reflux, constipation, postural deformities, scoliosis, dystonia, movement disorders, pain, bladder problems, sensory impairments, osteopenia, dental problems, sleep problems, growth and endocrine disorders.

Abnormal motor development

This may present as a delay in acquisition of motor skills, as problems with balance, an abnormal gait, asymmetry of hand use, involuntary movements or, rarely, loss of motor skills (Fig. 4.3).

Causes of abnormal motor development include:

- central motor deficit, e.g. cerebral palsy
- spinal cord lesions, e.g. spina bifida (see Ch. 29, Neurological disorders)
- neuropathy
- congenital myopathy or primary muscle disease
- global developmental delay; may be associated with a syndrome, or an unidentified cause.

Cerebral palsy (CP)

Cerebral palsy describes a group of permanent disorders of movement and posture causing activity limitation, resulting from non-progressive structural abnormalities in the developing brain. The motor disorders of cerebral palsy are often accompanied by disturbances of cognition, communication, vision, perception, sensation, behaviour, seizure disorders and secondary musculoskeletal problems. Although the causative lesion is non-progressive and damage to the brain is static, clinical manifestations change over time, reflecting the balance between normal and abnormal cerebral maturation. Motor dysfunction is usually evident early, often from birth, when acquisition of motor skill is occurring most rapidly, though more subtle changes may present later.

CP is the most common cause of motor impairment in children, affecting about 2–3.5 per 1000 live births in high-income countries. If the brain injury occurs after the age of 2 years, it is diagnosed as acquired brain injury.

Causes

The causes of cerebral palsy are:

- prenatal – 80%
- perinatal brain injury – 10%
- postnatal – 10%.

Prenatal causes are cortical migration disorders or structural maldevelopment of the brain during gestation and cerebrovascular haemorrhage or ischaemia. Some of these problems are genetic. Other antenatal causes are genetic syndromes and congenital infection.

Perinatal brain injury may be due to hypoxic-ischaemic injury before or during delivery, and this proportion has remained relatively constant over the last decade. Perinatal brain injury may also result from arterial and venous stroke. Preterm infants are especially vulnerable to brain damage from periventricular leukomalacia secondary to ischaemia and/or severe intraventricular haemorrhage and venous infarction. The improved survival of extremely preterm infants has been accompanied by an increase in survivors with CP, although the number of such children is relatively small.

Postnatal causes are meningitis/encephalitis/encephalopathy, head trauma from accidental or non-accidental injury, symptomatic hypoglycaemia, hydrocephalus and hyperbilirubinaemia.

Presentation

Cerebral palsy evolves over time. Many children who develop cerebral palsy will have been identified as being at risk in the neonatal period. Early presentation may be with:

- feeding difficulties, with oromotor incoordination, resulting in slow feeding, difficulties latching on to the breast, gagging and vomiting
- delayed motor milestones – of rolling over, not sitting unsupported by 9 months, not walking by 18 months
- poor head control, limbs floppy or stiff, abnormal movements, asymmetry of hand function / hand preference
- abnormal gait once walking is achieved, e.g. toe-walking
- global developmental delay.

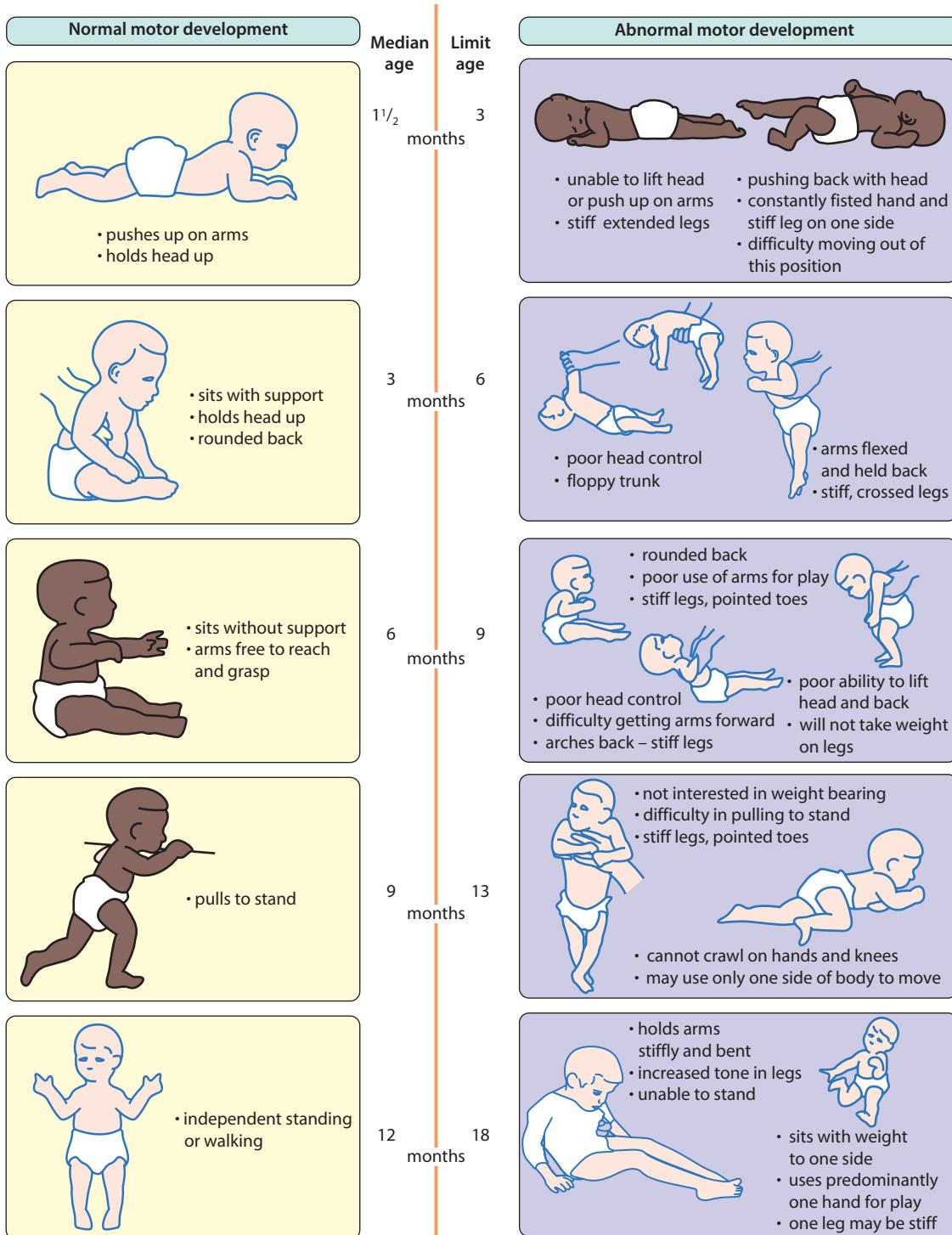


Figure 4.3 Normal motor milestones and patterns of abnormal motor development. Cerebral palsy (hemiplegia or quadriplegia) is the most common cause of developmental problems. (Adapted from: Pathways Awareness Foundation, Chicago, IL; see also [pathways.org.](http://pathways.org/))

Examination

The diagnosis is made by clinical examination, with particular attention to assessment of posture and the pattern of tone in the limbs and trunk, hand function and gait:

- abnormal neurology – reduced central tone
- limbs – reduced or increased tone, increased tendon reflexes (in spastic cerebral palsy), upgoing plantar response
- exaggerated startle response
- persistence of primitive reflexes
- unusual fidgety movements or other abnormalities of movement, including ataxia or unusual writhing movements in athetoid cerebral palsy
- delayed motor milestones
- abnormal gait once walking – toe walking, flexion of arms when running
- slowing of head growth.

The most likely causes can usually be discerned from history and examination. MRI brain scans may assist in identifying the cause of the CP, in directing further investigations, and in supporting explanations to the parents, but are not required to make the diagnosis. Early cranial ultrasound scans in preterm infants or MRI following hypoxic–ischaemic encephalopathy may be helpful. Children with known risk factors should be placed on an enhanced screening programme.

Types of cerebral palsy

The classification of cerebral palsy depends on the predominant motor abnormality:

- spastic, bilateral or unilateral – 80%
- dyskinetic – 6%
- ataxic – 4%
- mixed – 10%

The gross motor function level (functional ability) is described using the Gross Motor Function Classification System ([Table 4.5](#)).

Spastic cerebral palsy

In this type, there is damage to the upper motor neurone (pyramidal or corticospinal tract) pathway. Limb tone is persistently increased (spasticity) with associated brisk deep tendon reflexes and extensor plantar responses. The tone in spasticity is velocity dependent, so the faster the muscle is stretched the greater the resistance will be. This elicits a dynamic catch, which is the hallmark of spasticity. The increased limb tone may suddenly yield under pressure in a ‘clasp knife’ fashion. Limb involvement is described as unilateral or bilateral to acknowledge asymmetrical signs. Spasticity tends to present early and may even be seen in the neonatal period. Sometimes there is initial hypotonia, particularly of the head and trunk. There are three main types of spastic CP:

- unilateral (*hemiplegia*) – unilateral involvement of the arm and leg. The arm is usually affected more than the leg, with the face unaffected. Affected children often present at 4–12 months of age with fisting of the affected hand, thumb adduction, a flexed arm, a pronated forearm, asymmetric reaching, hand function or toe pointing when lifting the child. Subsequently,

Table 4.5 Gross Motor Function Classification System (GMFCS) for children 6–12 years old

Level I	Walks without limitations
Level II	Walks with limitations
Level III	Walks using a handheld mobility device
Level IV	Self-mobility with limitations; may use powered mobility
Level V	Transported in a manual wheelchair

Note: See www.canchild.ca/en/resources/42-gmfcs-e-r for further details.

a tiptoe walk on the affected side may become evident. Affected limbs may initially be flaccid and hypotonic, but increased tone soon emerges as the predominant sign. The medical history may be normal, with an unremarkable birth history and no evidence of hypoxic–ischaemic encephalopathy giving rise to the possibility of a prenatal cause, which is often silent. In some children, the condition is caused by neonatal stroke. More severe vascular insults may cause a hemianopia (loss of half of visual field) of the same side as the affected limbs.

- bilateral (*quadriplegia*) – all four limbs are affected, often severely. The trunk is involved with a tendency to opisthotonus (extensor posturing), poor head control and low central tone ([Fig. 4.4](#)). This more severe form of CP is often associated with seizures, microcephaly and moderate or severe intellectual impairment. Usually from structural brain anomalies or genetic disorders or perinatal hypoxic–ischaemic encephalopathy.
- bilateral (*diplegia*) – all four limbs, but the legs are affected to a much greater degree than the arms, so that hand function may appear to be relatively normal. Motor difficulties in the arms are most apparent with functional use of the hands. Walking is abnormal. Diplegia is one of the patterns associated with preterm birth due to periventricular brain damage seen as periventricular leukomalacia on MRI brain.

Dyskinetic cerebral palsy

Dyskinesia refers to movements that are involuntary, uncontrolled, occasionally stereotyped and often more evident with active movement or stress. Muscle tone is variable and primitive motor reflex patterns predominate. May be described as:

- chorea – irregular, sudden and brief non-repetitive movements



Figure 4.4 An infant with spastic bilateral (quadriplegia) cerebral palsy showing scissoring of the legs from excessive adduction of the hips, and pronated forearms and ‘fisted’ hands.

- athetosis – slow writhing movements occurring more distally such as fanning of the fingers
- dystonia – simultaneous contraction of agonist and antagonist muscles of the trunk and proximal muscles often giving a twisting appearance.

Intellect may be unimpaired. Affected children often present with floppiness, poor trunk control and delayed motor development in infancy. Abnormal movements may only appear towards the end of the first year of life. The signs are due to damage or dysfunction in the basal ganglia or their associated pathways (extra-pyramidal). In the past, the most common cause was hyperbilirubinaemia (kernicterus) due to Rh (rhesus) isoimmunization but it is now hypoxic-ischaemic encephalopathy at term. The MRI brain scan will often show bilateral changes predominantly in the basal ganglia.

Ataxic (hypotonic) cerebral palsy

Most are genetically determined. When due to acquired brain injury (cerebellum or its connections), the signs occur on the same side as the lesion but are usually relatively symmetrical. There is early trunk and limb hypotonia, poor balance and delayed motor development. Incoordinate movements, intention tremor and an ataxic gait may be evident later.

Mixed cerebral palsy

Combination of types; most often spastic and dyskinetic, characterized by involuntary movements and athetosis.

The different types of CP are summarized in Fig. 4.5. The following are red flags that abnormal motor development is not cerebral palsy, and which should prompt further assessment and investigations:

- absence of risk factors
- family history of a progressive neurological disorder
- loss of cognitive or developmental abilities
- development of focal neurological signs
- atypical features such as dysmorphism
- MRI findings not in keeping with clinical signs or diagnosis of cerebral palsy.

Management

Parents should be given details of the diagnosis as early as possible, but prognosis is difficult during infancy until the severity and pattern of evolving signs and the child's developmental progress have become clearer over several months or years of life. Children with CP are likely to have a wide range of associated medical, psychological and social problems, making it essential to adopt a multidisciplinary approach to assessment and management. The use of integrated care pathways is important as this clarifies actions and interventions at key points. Good communication with parents/carers and young people, and empowering them to ensure they are well informed about care plans and interventions is vital.

Medications, such as baclofen (a skeletal muscle relaxant) and diazepam, can be used in conjunction with orthoses for spasticity. These serve to reduce muscle tone and relax muscles. Anticholinergic drugs, such as trihexyphenidyl, can be used for dyskinetic CP and dystonia. Other treatments for treating hypertonia in CP include

botulinum toxin injections to muscles followed by serial casting, selective dorsal rhizotomy (a proportion of the nerve roots in the spinal cord are selectively cut to reduce spasticity), intrathecal baclofen and deep brain stimulation of the basal ganglia.

Prognosis

Factors affecting prognosis include the type of cerebral palsy, comorbidities, and the degree of developmental delay. Children with hemiplegic CP with no other deficit almost always walk by 2 years of age, while 50% of those with spastic diplegia walk by the age of 3 years.

Of children with spastic quadriplegia, 25% need help with care and all activities of daily living, and only 33% eventually walk. The more severe the child's physical, functional or cognitive impairment, the greater the possibility of difficulties with walking. A child's motor ability at 2 years of age can be used as a rough guide to future ambulation:

- If a child can sit – it is likely they will be able to walk unaided by age 6.
- If a child cannot sit but can roll over – there is a possibility that they may be able to walk unaided by age 6.
- If a child cannot sit or roll over – unlikely to be able to walk unaided.

Summary

Cerebral palsy

- Has many causes. Only about 10% follow hypoxic-ischaemic encephalopathy.
- Usually presents in infancy with abnormal tone and posture, delayed motor milestones and feeding difficulties.
- May be spastic, dyskinetic, ataxic, or a mixed pattern.

Speech, language and communication needs

Language is divided into receptive language (understanding) and expressive language (speech). Children have more advanced receptive language than expressive.

Speech and language delay

This is a common developmental problem. The pattern and sequence is usually normal, but delayed.

It may be due to:

- hearing impairment
- global developmental delay
- environmental deprivation / lack of opportunity for social interaction.

Summary

Type of cerebral palsy	Aetiology	Clinical features
Unilateral cerebral palsy (hemiplegia) Spastic or dystonic	Often due to perinatal stroke (middle cerebral artery infarct)	 <ul style="list-style-type: none"> • Spastic or dystonic tone, one side of body affected (opposite to the side of the brain lesion) • Arm often more affected than leg • Often presents at 4–12 months with asymmetric hand function • May have visual field defect on side of hemiplegia • Risk of learning difficulties and seizures • Often GMFCS level 1 and 2
Bilateral spastic cerebral palsy (diplegia)	<p>Damage to the periventricular areas of developing brain, often associated with prematurity</p> <p>Leg motor fibres from the homunculus are closest to the ventricles, so legs more affected than arms.</p>	 <p>Young child – pattern with walking on their toes with scissoring of the legs</p>  <p>Older child – crouch gait pattern is typical when the child gets heavier and cannot remain on their toes.</p> <ul style="list-style-type: none"> • Predominantly affects legs • Arms may be subtly affected (supination, fine motor control) • Spasticity is main motor type • Usually no feeding or communication difficulties and good cognition • Often associated with squints • Frequently GMFCS level 1–3
Bilateral spastic cerebral palsy (quadriplegia, 4 limb pattern)	Extensive damage to the periventricular areas of the developing brain, including cortex, usually from structural brain anomalies or genetic disorders; may be due to perinatal asphyxia.	 <ul style="list-style-type: none"> • Both arm and leg involvement – predominantly spastic but dystonia often also present • Extensor posturing (opisthotonus of trunk) • Associated with learning difficulty, feeding difficulties, problems with speech, vision and hearing • Seizures common • At increased risk of hip subluxation and dislocation • Usually dependent on others for activities of daily living • Powered mobility a common requirement • Often GMFCS levels 4 and 5
Dyskinetic cerebral palsy (dystonia, athetosis, chorea)	Perinatal asphyxia – particularly affecting the basal ganglia. Also kernicterus, but this is now rare.	 <ul style="list-style-type: none"> • Mixture of motor patterns including dystonia, athetosis and chorea • Cognition may be preserved but feeding difficulties are common • Risk of hip deformity and scoliosis • Many are dependent on others for activities of daily living due to their severe movement difficulties even if cognitively normal • Usually GMFCS level 4–5
Ataxic (hypotonic) cerebral palsy	Most genetic	<ul style="list-style-type: none"> • Early – trunk and limb hypotonia, poor balance and delayed motor development • Later – incoordinate movements, intention tremor and an ataxic gait

Figure 4.5 The different types of cerebral palsy.

Developmental language disorder

This is a specific language disorder where the child has difficulty producing or understanding language. The speech and language development is not following the usual pattern or sequence.

Language development in young children is crucial to literacy skills and is a key indicator of children's educational success and life chances. To acquire good communication, young children learn speech and language through direct personal interaction by talking, playing and reading. Poor communication skills under the age of five are a key indicator of children's educational success and life chances. This is a major public health issue. In the UK, in some areas more than 50% of children start school with a speech, language and communication need, and in 10% it is long term.

The aim is to recognize and intervene early. Children usually present following parental concern or identification via child health surveillance or early years education settings. A hearing test and assessment by a speech and language therapist may be the initial steps. If delay is marked or there are features of a developmental language disorder, a full developmental assessment is required.

Autism spectrum disorders

Up to 1% of the UK child population have an autism spectrum disorder. An estimate of the worldwide prevalence is similar. It needs to be considered in any child presenting with delayed or disordered speech, language and communication. Children can present at any age, but often in the preschool years between 2 and 4 years when language and social skills emerge and develop rapidly. The core features of autism are:

- persistent impairments in social communication
- persistent impairments in social interaction
- restricted and repetitive patterns of behaviours, interests and activities including sensory sensitivities (Box 4.1).

These features must be pervasive, i.e. present in all settings and cause functional impairment. Comorbidities are common (Box 4.2).

Assessment for autism spectrum disorders is complex and usually requires a multidisciplinary team. A detailed medical and developmental assessment needs to be considered in the context of the child's current functioning at home and other social settings. In nursery or school-age children, screening questionnaires are useful, and information from the child's nursery or school setting is required. Formal standardized parental interviews are available, including 3Di (Developmental, Dimensional and Diagnostic interview), ADI-R (Autism Diagnostic Interview – Revised), and DISCO (Diagnostic Interview for Social COmmunication disorders). Standardized observational assessment is available; the most widely used is the ADOS-2 (Autism Diagnostic Observation Schedule – 2), which has four age-related modules so it can be used to assess a child from toddler age to adulthood and at any level of language from pre-verbal to fluent.

Asperger syndrome was previously recognized as a separate diagnostic entity for those with social impairments of an autism spectrum disorder but at the milder

Box 4.1 Features of autism spectrum disorders

Impaired social communication and interaction

- Unusual eye contact – usually reduced or avoidant, but might be too intense and unbroken
- Does not seek comfort, share pleasure; reduced bringing and showing behaviours
- Reduced peer interaction and awareness, prefers own company
- Reduced joint attention with another person by gesture or eye contact
- Lack of appreciation of social cues
- Behaviour can be self-directed and socially and emotionally inappropriate
- Delayed and disordered speech and language skills
 - echolalia – immediate or delayed repetition of a word or phrase beyond 36 months of age
 - use of jargon or invented words with no meaning (neologisms)
 - unusual intonation, volume or rate of speech, unusual accent and stereotypical use of language (using words or phrases they have heard others use or from the TV/internet)
 - difficulties using pronouns correctly, referring to self by own name or as 'you'
- Impaired comprehension, over-literal interpretation of language
- Lack of or reduced non-verbal communication skills – use of gestures and directed facial expressions

Restricted, repetitive patterns of behaviour, interests, or activities

- Imposition of routines on self and others with extreme emotional response (temper tantrums, self-injurious behaviour) if not followed
- Non-functional rituals
- Highly restricted, fixated interests that are abnormal in intensity or focus, e.g. lining or sorting object by type, size or colour, unusually interested in parts of toys/objects, e.g. wheels of a toy car
- Lack of imaginative play
- Unusual or stereotypical movements such as hand flapping, tiptoe walking with stiffening and posturing
- Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of environment, e.g. covering ears to certain sounds, smelling or licking non-food items, aversive reactions to certain fabrics or textures

Box 4.2 Comorbidities of autism spectrum disorders

- General learning and attention difficulties (about two-thirds)
- Seizures
- Affective disorders – anxiety, sleep disturbance
- Mental health issues in up to 70% (particularly in adolescent years)
- Gastrointestinal symptoms, eating problems
- Behaviours that challenge

end and near normal speech development and normal intellect, typically characterized by a stilted way of speaking and narrow, unusual and often intense interests. It has been removed as a diagnostic entity in current classification systems but those with a pre-existing diagnosis, such as the climate change campaigner Greta Thunberg, may continue to use this term.

In most cases of autism spectrum disorder, no specific cause is identified, but any comorbid neurodevelopmental and medical conditions need to be identified. The aetiology is probably multifactorial, with a genetic component in some children.

Management

Autism spectrum disorder usually has lifelong consequences of varying degrees. Behavioural and educational interventions are often required. Parental education and support needs to be provided.



Autism spectrum disorder:

- Usually presents at 2–4 years of age.
- Main features are persistently impaired social communication and social interaction, and restricted and repetitive patterns of behaviours, activities or interests.

Learning disability

Learning or intellectual disability is the medical term used when school-age children have significantly reduced ability to understand new or complex information and to learn new skills, and reduced ability to cope independently with everyday life. It impacts most areas of their life. The degree of learning disability can be classified as mild, moderate or severe based on functional assessment of communication and adaptive functioning. It can also be described according to intelligence quotients (IQ) based on formal assessments by educational psychologists, but these are not done routinely.

Most children with a moderate or more severe learning disability present in preschool years with global developmental delay. Those with mild learning disability may present later. Assessment and investigations are the same as for global developmental delay. Vision and hearing should be checked and any associated diagnoses such as autism spectrum disorder, attention deficit hyperactivity disorder and developmental coordination disorder identified.

Specific learning difficulties

These have an impact on a specific area of the child or young person's life/skills, and assessment is usually the remit of educational psychologists or other professionals.

These include:

- dyslexia – difficulties with reading
- dyscalculia – difficulties in learning and comprehending numbers
- dysgraphia – difficulties with writing skills.

Developmental coordination disorder

Developmental coordination disorder (known as dyspraxia) is a common neurodevelopmental disorder affecting motor execution and/or planning with no significant findings on standard neurological examinations. It is a disorder of higher cortical processes, and there may be associated problems of perception (how the child interprets what he/she sees and hears), use of language and putting thoughts together. Children may present with difficulties with:

- handwriting – which is typically awkward, messy, slow, irregular and poorly spaced
- self-care skills such as dressing – difficulties with collars, buttons, zips, laces
- feeding – unable to cut up food at age appropriate level
- riding a bicycle
- ball skills – catching, kicking, throwing
- swimming as well as other recreational and educational activities.

Messy eating from difficulty in coordinating biting, chewing and swallowing, and dribbling of saliva, may be a feature; this is called oromotor dyspraxia. Specific difficulties related to speech production may be present.

Although the problems are usually recognized preschool, diagnosis is often made only after starting school. It affects approximately 6% of 5–12 year-olds and is more common in boys, with a male to female ratio of 3:1. Formal diagnosis is made using standardized assessment tools of the child's motor ability, such as the Movement Assessment Battery for Children (Movement ABC) by an occupational therapist.

The medical role is to exclude an underlying neurological condition and identify comorbidity (attention deficit hyperactivity disorder, autism spectrum disorders, dyslexia and tics, low self-esteem, social difficulties and mental health issues). With therapy (including an emphasis on sensory integration, sequencing, executive planning, and speech and language therapy when needed) and maturity the condition usually improves, but difficulties can persist into adult life.

Problems with concentration and attention

Attention deficit hyperactivity disorder (ADHD)

Children are naturally energetic, lively, loud and inquisitive. They like to run, jump and climb. However, children with ADHD present with difficulties with attention, hyperactivity and impulsivity which adversely affect their social and academic or occupational functioning and are evident in all aspects of their lives; at home, at school and in their social lives. Their difficulty with attention means they cannot sustain attention and are easily distracted as they cannot ignore distractions in the environment. They fail to persist with tasks such as household duties or homework, are disorganized and have poor concentration. They lose things and are messy in their work.

Their hyperactivity manifests as excessive movement or motor restlessness, fidgetiness, difficulty remaining

seated and still. Their impulsivity is evident in their being thrill seekers, and failing to think through the consequences of their actions. They struggle with emotional regulation and turn-taking and can be socially disinhibited. These difficulties adversely affect all aspects of their lives including school performance and social functioning.

Low self-esteem, poor peer relations, poor mental health and poor school performance are often associated with ADHD. These children are at risk of exclusion from schooling and antisocial behaviour. They are over-represented in the youth offending population. In ADHD there is both inattention and hyperactivity, but there are subtypes: inattentive when this is the cardinal feature or hyperactive–impulsive when these predominate in the absence of inattention.

The worldwide prevalence of ADHD in children aged 4–17 years is estimated at approximately 7%. It is three times more common in males than females. ADHD has a higher prevalence in extremely premature infants, children in care, those with mental health disorders, epilepsy, acquired brain injury or other neurodevelopmental disorder such as autism.

Children may be referred due to parents or school raising concerns. This necessitates psychosocial and mental health assessments and observer reports. Use of standardized rating scales – completed by parent, teacher and young person – can be valuable.

First-line management in preschool and school-age children with mild to moderately severe disorder is the active promotion of behavioural and educational progress. Parental and teacher information and advice, and parenting programmes along with psychosocial treatments, are helpful. If insufficient, pharmacological management can be considered, usually only in those over 6 years. Stimulant medication in the form of methylphenidate is recommended as first-line management. Close medical monitoring is needed to identify side effects (particularly anxiety, weight loss and hypertension), and to titrate dosage to response. It may be necessary to continue medical treatment for many years, even into adulthood, with periodic trials off medication to reassess the need. Close liaison with school is required, and the involvement of educational psychology can be beneficial.

Summary

Attention deficit hyperactivity disorder

- Affects males more than females.
- Clinical features: inattention, hyperactivity, impulsivity; often socially disinhibited, poor at relationships, prone to temper tantrums, poor school performance.
- Management: behavioural programmes in school, parenting intervention, medication if necessary.

Hearing impairment

Any concern about hearing should be taken seriously. Any child with delayed speech or language, learning difficulties or behavioural problems should have their hearing formally tested, as hearing impairment may be

the underlying cause. A unilateral hearing loss can cause hearing difficulties when the unaffected ear has an infection or chronic secretory otitis media (glue ear). It can also cause difficulty localizing sounds.

The types of a hearing impairment are:

- sensorineural – caused by a lesion in the hair cells of the cochlea or auditory nerve
- conductive – from problems in the transmission of sound through the outer or middle ear to the cochlea. This may be from abnormalities of the external auditory canal (such as atresia), the tympanic membrane (such as a perforation) or conduction of the sound by the three ossicles in the middle ear (most often from chronic secretory otitis media)
- mixed hearing loss when both a sensorineural and conductive element are present
- central auditory dysfunction resulting from damage or dysfunction to the auditory nerve, auditory brain stem or cerebral cortex.

The causes, natural history and management of hearing loss are listed in [Table 4.6](#).

Hearing tests are described in [Chapter 3](#). The typical audiogram in sensorineural and conductive hearing loss is shown in [Fig. 4.6](#).

Sensorineural hearing loss

This type of hearing impairment is uncommon. It is irreversible, of any severity, including profound. In the UK, the incidence of permanent childhood hearing impairment (PCHI) is 0.9 per 1000 live births and is predominantly sensorineural, with unilateral PCHI adding a further 0.7 per 1000 live births. Although neonatal hearing screen programmes are designed to identify these children as early as possible, some sensorineural hearing impairment is progressive and another 0.7 per 1000 children acquire this form of hearing loss by the age of 10 years. Treatment of congenital hearing loss from congenital cytomegalovirus infection with anti-viral medication is being evaluated.

The child with severe bilateral sensorineural hearing impairment will need early amplification with hearing aids for optimal speech and language development. Hearing aid use requires close supervision, beginning in the home together with the parents and continuing into school. Children may resist wearing hearing aids because background noise can be amplified unpleasantly. Cochlear implants may be required where hearing aids give insufficient amplification ([Fig. 4.7](#)).

Many children with moderate hearing impairment can be educated within the mainstream school or in hearing impairment units attached to mainstream schools. These children should be placed in the front of the classroom so that they can readily see the teacher. Gesture, visual context and lip movement will also allow children to develop language concepts. Speech may be delayed, but with appropriate therapy can be of good quality. Modified and simplified signing such as Makaton can be helpful for children who are both hearing-impaired and learning-disabled. Peripatetic teachers for children with hearing impairment provide support for these children in preschool and school years. Children who communicate through signing (e.g. Makaton, British Sign Language or sign-supported English) may need to attend special school for children who are deaf.

Table 4.6 Causes, natural history and management of hearing loss

	Sensorineural	Conductive
Causes	Genetic – causes 80% of congenital hearing loss in high-income countries Antenatal and perinatal causes: <ul style="list-style-type: none"> congenital infection (e.g. congenital cytomegalovirus) prematurity hyperbilirubinaemia Postnatal: <ul style="list-style-type: none"> meningitis/encephalitis head injury drugs (e.g. aminoglycosides and frusemide) neurodegenerative disorders 	Chronic secretory otitis media – the most common cause Eustachian tube dysfunction – causes include: <ul style="list-style-type: none"> Down syndrome cleft palate Pierre Robin sequence mid-facial hypoplasia Hypoplasia of the external auditory canal and, rarely, wax in the external auditory canal Perforation of tympanic membrane
Hearing loss	Unilateral or bilateral, at some or all frequencies. Can be profound (>95 dB) hearing loss Air and bone conduction are both reduced and the tympanogram is normal	Unilateral or bilateral, usually low to mid frequencies, mild or moderate (<60 dB hearing loss) Bone conduction is normal and the tympanogram is abnormal (flat or negative)
Natural history	Does not improve and may progress	Self-limiting, may recur or fluctuate. Permanent if caused by malformation of outer or middle ear.
Management	Amplification using air conduction hearing aids or cochlear implantation; rarely provide aid for unilateral losses in children	Conservative, nasal inflation balloons, amplification with bone conduction hearing aid or surgery for tympanostomy tube (grommet) and adenoidectomy (if preventing discharge of effusion from the Eustachian tube)

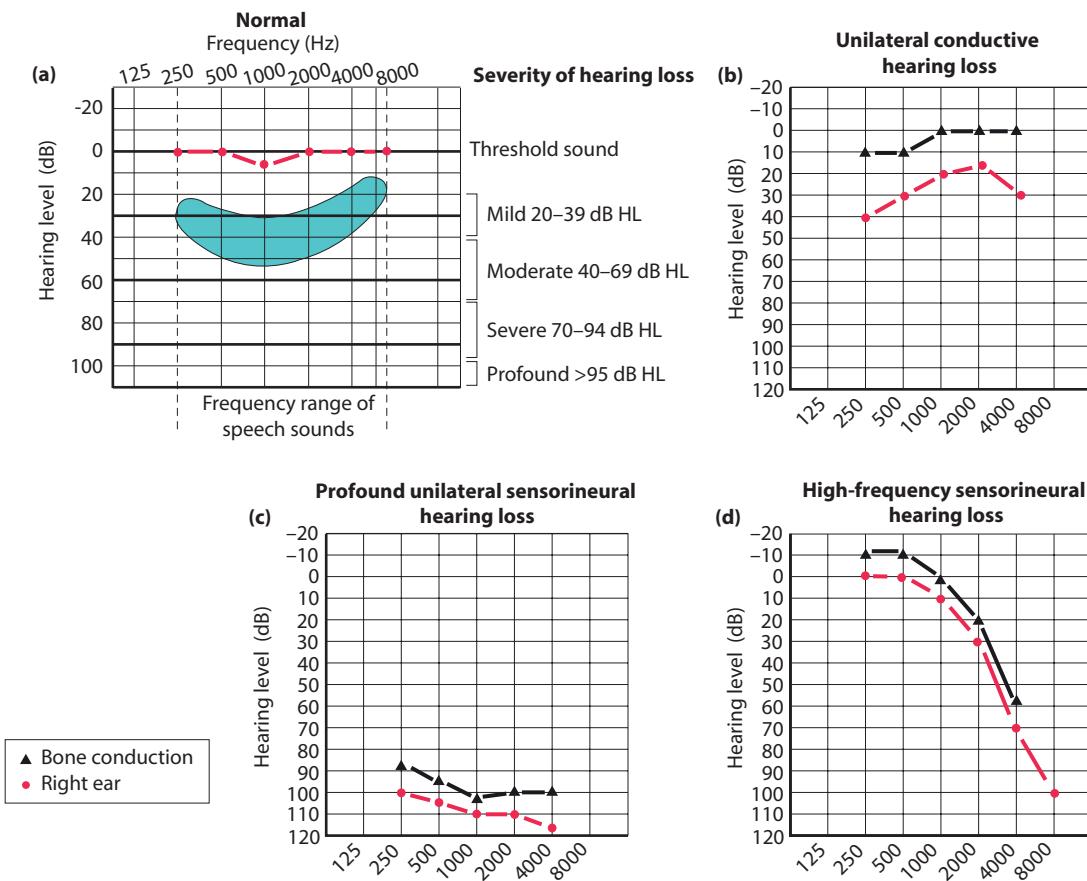


Figure 4.6 (a) Audiogram showing normal hearing and the loudness of normal speech (blue area). The consonants are high-frequency sounds, whereas the vowels are low-frequency sounds. (b) Audiogram showing unilateral conductive hearing loss of the right ear. There is a 30-dB to 40-dB hearing loss. (c) Audiogram showing unilateral profound sensorineural hearing loss. (d) Audiogram showing unilateral high-frequency sensorineural hearing loss.

Conductive hearing loss

Conductive hearing loss is usually mild or moderate but may require treatment. It is much more common than sensorineural hearing loss. In association with upper respiratory tract infections, many children have episodes of hearing loss, which are usually self-limiting. In some cases of chronic secretory otitis media, the hearing loss may last many months or years. Tympanography, which measures the air pressure within the middle ear and the compliance of the tympanic membrane, assists in deciding if the middle ear is functioning normally (Fig. 4.8). If the condition does not improve spontaneously, nasal inflation balloons (opening the eustachian tube by breathing out of the nose to inflate a balloon) can be tried though children usually



Figure 4.7 Cochlear implant. There is a microphone to detect sound, a speech processor, and a transmitter and receiver/stimulator. It converts speech into electric impulses, which are conveyed to the auditory nerve, bypassing the ear. It provides a deaf person with a representation of sounds.

need to be school-aged before they can use the device. Bone conduction hearing aids can be used whilst awaiting natural resolution. If that fails, surgery may be considered, with insertion of tympanostomy tubes (grommets) with or without the removal of adenoids. The decision whether to intervene surgically should be based on the degree of functional disability rather than on absolute hearing loss.



Any child with poor or delayed speech or language must have his/her hearing formally assessed.

Summary

Hearing impairment

- Sensorineural hearing loss
 - This is usually present at birth and is irreversible.
 - In neonates, may be identified by newborn hearing screening.
 - Early amplification with hearing aids or cochlear implants for optimal speech and language development is needed for severe hearing impairment.
 - Peripatetic teachers of the deaf support children with significant hearing impairment.
- Conductive hearing loss
 - This is usually due to middle ear disease, often chronic secretory otitis media.
 - This is usually mild or moderate and transient.
 - Consider nasal inflation balloons, bone conduction hearing aid or insertion of tympanostomy tubes (grommets) with or without the removal of adenoids if it does not resolve.

Visual impairment

Normal visual development and tests of vision are described in [Chapter 3](#). Visual impairment may present in

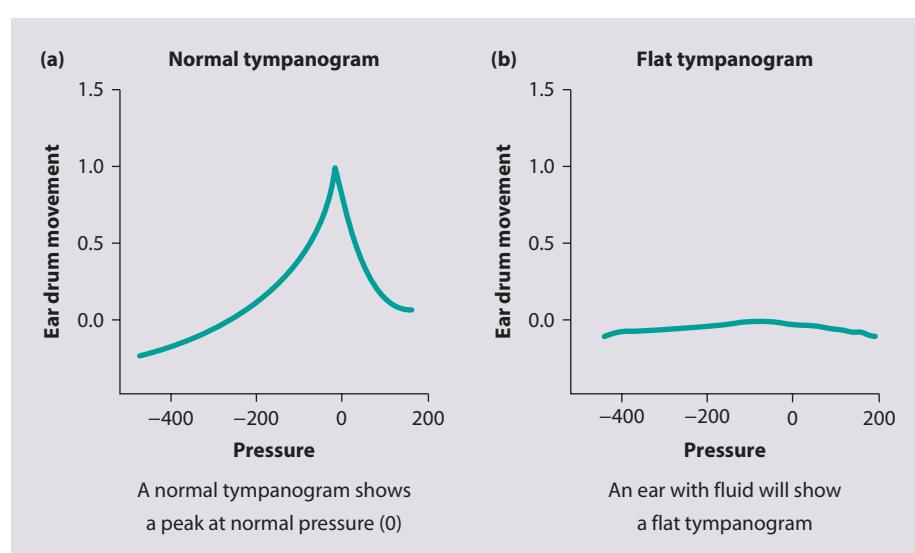


Figure 4.8 Tympanogram, in which variable air pressure in the ear canal tests middle ear function. (a) Normal. (b) Middle ear fluid.

an infant or young child in various ways including:

- obvious ocular malformation (e.g. anophthalmia)
- absent red reflex or a white reflex (leukocoria) due to opacification of intraocular structures (cataract), corneal abnormalities or an intraocular tumour (retinoblastoma)
- not smiling responsively by 6 weeks post-term
- concerns about poor visual responses, including poor eye contact
- roving eye movements
- nystagmus
- squint.

Any infant presenting with an ocular abnormality needs prompt referral to an ophthalmologist as some underlying conditions are sight-threatening, and retinoblastoma is life-threatening.

Nystagmus

This is a repetitive, involuntary, rhythmical eye movement. It is usually horizontal but can be vertical. It is associated with a structural eye problem (sensory defect nystagmus), but can also be a consequence of a problem at the cortical level. Nystagmus, which is a manifestation of an eye problem, may improve over time. If no structural eye or brain problem is found, a diagnosis of idiopathic nystagmus is made.

Squint (strabismus)

In this common condition there is misalignment of the visual axes. Squint should be assessed in order for the underlying cause to be identified and treated where possible. There may be a family history. Transient misalignment is common up to 3 months of age. Marked epicanthic folds may suggest a squint when one is not present. Any infant with a squint should have red reflexes checked. Squints persisting beyond 3 months of age should be referred for a specialist ophthalmological opinion. The most common underlying cause is a refractive error, but cataracts, retinoblastoma and other intraocular causes must be excluded.

Squints are commonly divided into:

- *concomitant* (non-paralytic, common) – usually due to a refractive error in one or both eyes. Correction of the refractive error with glasses often corrects the squint. The squinting eye most often turns inwards (convergent), but there can be outward (divergent) or, rarely, vertical deviation
- *paralytic* (rare) – varies with gaze direction due to paralysis of the orbital muscle nerves (III, IV and VI). This can be serious because of the possibility of an underlying space-occupying lesion such as a brain tumour.

Corneal light reflex test

Non-specialists can use this test to detect squints (Fig. 4.9). A pen torch (flashlight) is held at a distance to produce reflections on both corneas simultaneously. If the light reflection does not appear in the same position in the two

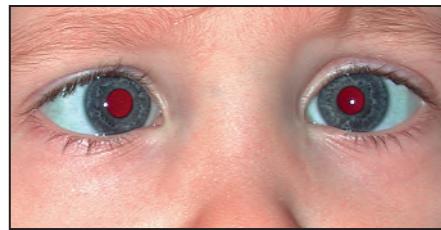


Figure 4.9 Corneal light reflex (reflection) test to detect a squint. The reflection is in a different position in the two eyes because of a small convergent squint of the right eye.

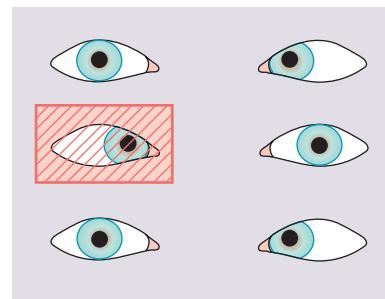


Figure 4.10 The cover test is used to identify a squint. If the fixing eye is covered, the squinting eye moves to take up fixation. This diagram shows a left convergent squint.

pupils, a squint is present. However, a minor squint may be difficult to detect.

Cover test

The child is encouraged to look at a toy/light. If the fixing eye is covered, the squinting eye will move to take up fixation; this movement identifies the squint (Fig. 4.10). The test should be performed with near (33 cm) and distant (at least 6 m) objects, as certain squints are present only at one distance. These tests are difficult to perform and reliable results are best obtained by an orthoptist or ophthalmologist.

Refractive errors

Hypermetropia (long sightedness)

Mild hypermetropia is common in early childhood and is overcome through the process of accommodation – changing the shape of the lens in the eye. If treatment is needed, hypermetropia can be corrected with convex (plus) lenses which make the eye look bigger.

Myopia (short sightedness)

This is relatively uncommon in young children, presenting usually in adolescence. However, in children born preterm it is the most common refractive error and may present at a younger age. Myopia can be corrected with concave (minus) lenses which make the eye look smaller.

Astigmatism (abnormal corneal curvature in two planes)

Astigmatism means that the eye is shaped more like a rugby ball than a football. Minor degrees of astigmatism are common and may not cause problems or require correction. However, unilateral astigmatism can result in amblyopia.

Amblyopia

This is a potentially permanent reduction of visual acuity from an eye that has not received a clear image. It affects 2%–3% of children. It is usually unilateral but can be bilateral. The most common causes of amblyopia are squint, refractive errors or an obstruction to the visual pathway, e.g. cataract. Amblyopia may occur in squint when the brain is unable to combine the differing images from each eye; this leads to the brain ignoring visual data from the squinting eye to avoid double vision. Treatment is focused on the underlying condition, together with patching of the healthy eye for specific periods of the day to encourage the other eye to work, and therefore develop better vision. Early treatment is essential, as after 7 years of age improvement is unlikely. Considerable encouragement and support should be given often, to both the child and parents, as young children usually dislike having their good eye patched. Amblyopia may be asymptomatic, and its identification is the primary purpose of preschool vision screening in the UK.

Severe visual impairment

This occurs in 1 in 1000 live births in the UK, but is higher in low-income countries. The main causes are listed in [Table 4.7](#).

Recent epidemiological studies suggest that in the UK up to 50% of children with severe visual impairment have a cerebral pathology as the underlying cause; about one third are hereditary, affecting eye structures. In low-income countries, acquired causes such as infection are more prevalent.

Investigations may include an electroretinogram, which assesses the retinal function, or visual evoked potentials, which assess the visual pathways from the eye to the brain. When visual impairment is of cortical origin, examination of the eye, including the pupillary responses, may be normal.

Although few causes of severe visual impairment can be cured, early detection allows certain elements to be treated, and timely advice can be given on supporting developmental progress. In the UK, this advice is usually provided by peripatetic teachers for children with visual

Summary

Visual impairment

- Abnormal eye movements in an infant, absence of responsive smiling by 6 weeks post-term, or parental concern about vision at any age – consider visual impairment and refer for an ophthalmological opinion.
- Refer for an ophthalmological opinion any infant with:
 - an absent red reflex
 - a white reflex
 - a squint persisting after 3 months of age.
- Testing for squints – corneal light reflex (reflection) test for the non-specialist, cover test for the specialist.
- Amblyopia may be asymptomatic; treatment often includes patching of the 'good' eye for short periods each day.
- Visual impairment and ocular abnormalities including refractive errors are more common in children with neurodevelopmental problems.

impairment, who work with families from the time of diagnosis, irrespective of the child's age. Input from a paediatrician and other members of the child development service may also be required. Partially sighted children may benefit from provision of low vision aids, high-powered magnifiers, small telescopic devices and computers. Although many severely visually impaired children have a visual disability alone, at least half have additional neurodevelopmental problems.

Multidisciplinary approach – child development services

Disability impacts all areas of a child's life including education, social life and family life, hence a multidisciplinary and multiagency joined-up approach is required. Child development services are designed to provide holistic care and may involve paediatricians, occupational therapists, clinical psychologists, speech and language therapists, nursery nurses, dieticians and physiotherapists, with close links to educational and social care services. Access to specialist neurodisability services, orthopaedic surgery and tertiary neurology is required for complex needs ([Case history 4.1](#)).

Table 4.7 Causes of visual impairment

Genetic	Antenatal and perinatal	Postnatal
Cataract	Congenital infection	Trauma
Albinism, including ocular albinism	Retinopathy of prematurity	Infection
Retinal dystrophy	Hypoxic-ischaemic encephalopathy	Juvenile idiopathic arthritis
Retinoblastoma	Cerebral dysgenesis or damage	
	Optic nerve hypoplasia	



Case history 4.1

Complex neurodisability

Lucy, the second-born child, was born at term by normal delivery. Her mother had been in good health throughout the pregnancy apart from a minor flu-like illness at about seventeen weeks gestation. Shortly after birth, Lucy was noted to be excessively irritable, her feeding was poor and she had microcephaly. She failed her newborn hearing screening test and was referred to a paediatrician. An MRI brain revealed extensive bilateral abnormalities. Congenital cytomegalovirus was diagnosed and she had profound bilateral sensorineural hearing loss.

Her complex neurodisability was managed by the child development and allied services. The common medical problems and the services provided are shown in (Fig. 4.11). Over subsequent months she had growth faltering, developed clinical features of cerebral palsy, global developmental delay and subsequently developed epilepsy. She required a gastrostomy and bilateral cochlear implants.

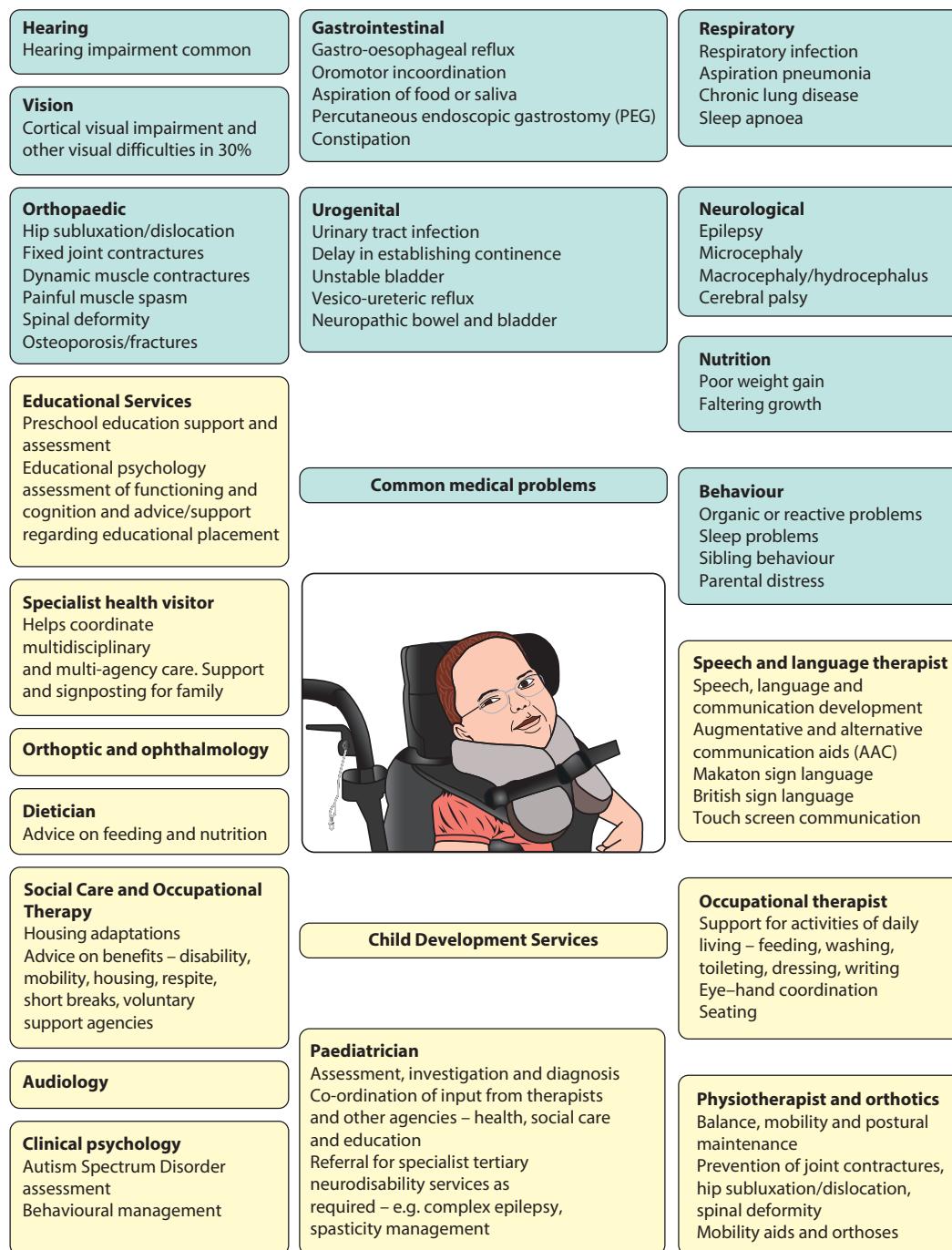


Figure 4.11 Common medical conditions and the many professionals in the child development services involved in the care of children with developmental problems.

Education

Many children with developmental problems have additional educational needs. As early intervention is important, timely communication from health to education about their additional needs is required. Assessment and support for development and learning needs may come from specialist preschool teachers and educational psychologists.

Children with special educational needs should receive educational input according to their requirements, including integration into mainstream schooling, whenever possible; this is referred to as inclusion. Specialist schooling may be available for those with more complex needs or disability, with therapists on site, and with access to specialist teachers and resources. The balance of inclusive education and specialist provision varies in different countries.

The biopsychosocial model of disability, disability rights and advocacy

In the past, disability began where health ended; once disabled, a child was in a separate 'disabled' category. Now, health and functioning, rather than disability, are rightly stressed. It is now acknowledged that everyone can experience a reduction in health and therefore experience some disability. A biopsychosocial model of disability is embraced to integrate the medical and social models with their different perspectives on health into three functional tiers; the level of body part, the whole person, and the whole person in a social context. Disability therefore involves dysfunction at one or more of these levels – impairments, activity limitations or participation restrictions (Fig. 4.12).

Technological advances to improve communication (Fig. 4.13) and mobility (Fig. 4.14) help to enable people with disability to better achieve their full potential, rather than being held back by their disability. However, this requires skilled assistance and adequate resources. Prominent public figures who function effectively despite disabilities help to make the public appreciate what can be achieved and serve as an inspiration to those with disabilities.

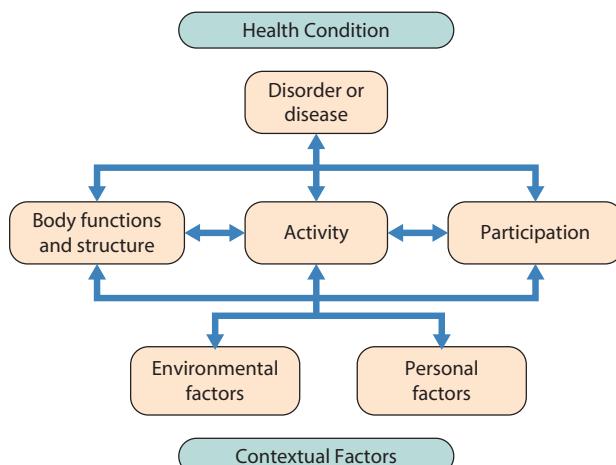


Figure 4.12 International Classification of Functioning, Disability and Health (ICF) biopsychosocial model of disability (WHO).



Figure 4.13 An example of a touchscreen speaking communication aid to assist children who may have speaking and movement difficulties.



(a)



(b)

Figure 4.14 (a) A boy with spastic cerebral palsy is able to walk with the help of a frame. (b) A motorized wheelchair that enables this young person with cerebral palsy to be mobile.

Irrespective of their disability, the aspirations and rights of children, as affirmed by the United Nations Convention on the Rights of the Child, need to be respected. Paediatricians and other health professionals have an important role in advocating for the rights of disabled children and young people. By shifting the focus away from the disability to inclusion, participation, empowerment and enablement, children and young people with disabilities will be valued contributors and participants in their communities and society.

Transition

Transition is a purposeful, planned process that addresses the medical, psychosocial and educational/vocational needs of adolescents and young adults with chronic physical and medical conditions as they move from paediatric to adult services/care. It is called 'preparing for adulthood' in education and social care. A biopsychosocial approach is needed with the young person at the centre and input from a variety of agencies. This is described in [Chapter 30](#) (Adolescent medicine).

Transition is a particular challenge for the young person with complex disabilities, as an adult equivalent of the community or neurodisability paediatrician may not exist, and services are less developed.

Acknowledgements

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Further reading

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Emond A, editor: *Health for all children*, ed 5, 2019, Oxford University Press.

Websites

Council for Disabled Children: councilfordisabledchildren.org.uk.

UK Down Syndrome Medical Interest Group (DSMIG): www.dsmitg.org.uk.

Unique: www.rarechromo.org. *Understanding rare chromosome and gene disorders*.

National Metabolic Biochemistry Network: www.metbio.net.

Disability Matters: www.disabilitymatters.org.uk.

National Autistic Society: www.autism.org.uk.

National Attention Deficit Disorder Information and support service: www.addiss.co.uk.



Care of the ill child and young person

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When children or young people become ill:

- The provision and organization of their medical care differs markedly from that of adults
- The care provided should be holistic and take into account both the wishes and expectations of the family and child or young person.
- Their differing physical, intellectual, emotional and social stage of development impacts on all aspects of the delivery of healthcare, including pain management, prescribing, communication, ethics, and palliative and end-of-life care.

Medical care

Most medical care for children and young people is initially provided by general practitioners ("family doctors") or in some settings by primary care paediatricians, in conjunction with other healthcare professionals, such as health visitors, midwives and pharmacists. In the UK, they also deliver the Healthy Child Programme for all children, which includes immunization, developmental reviews, and health promotion (see Ch. 3, Normal child development, hearing and vision).

Most acute illness in children is mild and transient (e.g. upper respiratory tract infection, gastroenteritis) or readily treatable (e.g. mild exacerbation of asthma) and care is provided by parents and family themselves at home (Fig. 5.1). On average, in the UK, parents consult their general practitioner six times a year for acute illness for children under 4 years old. Advice is also available by telephone (e.g. NHS 111 in England) or via the internet. More serious acute illness – e.g. a young infant with a high fever or not feeding, difficulty breathing, seizures, lethargy – is likely to need assessment and treatment in an Emergency Department.

General practitioners will also care for children and young people with serious, long-term or complex paediatric illnesses (e.g. cystic fibrosis, diabetes mellitus) or disability (e.g. cerebral palsy) or child and adolescent mental

health problems. Each affected child or young person and family are likely to require considerable support from the whole of the primary care team to ensure optimal care. Close communication with specialist services is required.

Urgent and emergency care

Of the 23 million annual attendances at Emergency Departments in the United Kingdom, one in four are children and young people. The rates of attendance are highest for preschool children and are only exceeded by those over 80 years of age. Specially trained staff and facilities designed for children and young people are recognized to be best for their urgent assessment and management, as listed in Box 5.1. Children and young people should be kept separate from the often inappropriate environment of adult Emergency Departments. As a result, the number of dedicated, separate Paediatric Emergency Departments is increasing.

Hospital admission rates

Children represent around 12% of the total number of hospital admissions. Most paediatric admissions are of infants and young children under 4 years of age and are emergencies, such as respiratory infections, whereas surgical admissions, one-third of which are elective, peak at 5 years of age. The most common reasons for medical admission are shown in Table 5.1.

The hospital admission rate has continued to rise over the last 15 years (Fig. 5.2). The reasons for this are unclear, but probably include:

- lower threshold for admission accompanying increasingly risk-averse nature of medical practice
- rapid discharge of newborns from maternity resulting in reattendance with feeding difficulties and jaundice
- increased mental health emergency attendance
- lack of ready access to older family members, e.g. grandparents, with experience of ill children who provide reassurance and assistance

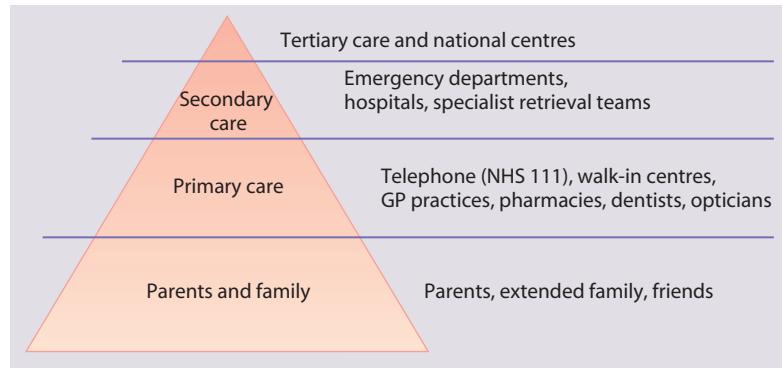


Figure 5.1 Schematic representation of provision of medical care for sick children in the UK. Most is by the family with medical support from primary care. Relatively few need secondary care, and only a very small number require sub-specialist (tertiary) care or national centres.

Box 5.1 Services that should be available for children attending an emergency department

Environment	Staff	Medical care
<p>Initial clinical assessment occurs within 15 min of arrival to determine priority, pain score and vital signs</p> <p>Separate area from adults, designed around needs of children and parents/carers: separate waiting area, play facilities, child-friendly treatment and recovery areas</p> <p>Access for parents to examination, X-ray and anaesthetic rooms</p> <p>Access to play specialist</p>	<p>Medical and nursing staff trained and experienced in the care and treatment of children and young people, including mental health</p> <p>Non-paediatric staff trained in communicating with children and families</p> <p>Effective communication with other health professionals</p> <p>Prepared for major incidents</p>	<p>Resuscitation and monitoring of high-dependency children available</p> <p>Children given priority for prompt treatment as condition may deteriorate rapidly</p> <p>Special priority arrangement for children with complex medical needs – check if have an emergency care plan</p> <p>If off-site intensive or specialist care required, dedicated transport services available within regional critical care or specialist networks</p> <p>Child protection training provided for staff; advice available from experienced paediatrician</p> <p>Procedures and counselling in place following the sudden death of a child</p> <p>Paediatric mental health practitioner available for advice and assessment</p>

(Adapted from: Facing the Future: Standards for children in emergency care settings, RCPCH, 2018.)

Table 5.1 Reasons for emergency admission of children under 15 years of age to hospital

System	Specific disorders
Respiratory 25%	Respiratory infections 20% Asthma 3%
Injuries and poisoning 17%	Head injury 5% Poisoning 1%
Gastroenterological 13%	Gastroenteritis 5%
Infection 6%	Viral infection 5%
Urogenital 3%	Urinary tract infection 2%
Neurological 2%	Seizures 1%
Endocrine and metabolic 2%	Diabetes mellitus 1%
Skin 2%	
Musculoskeletal 2%	
Other 28%	

(Data based on 58,061 admissions, 2009–2010. ISD Scotland.)

Emergency admissions by age

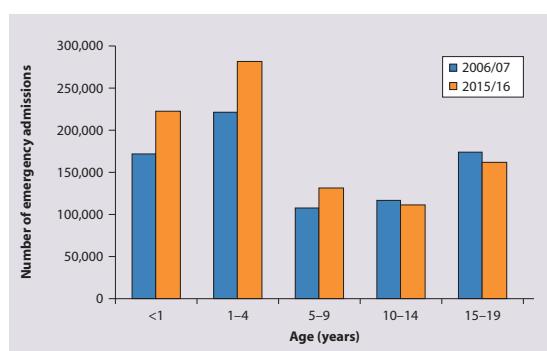


Figure 5.2 Emergency hospital admission of children and young people by age in the UK, comparing 2006/2007 and 2015/2016, showing increase in admissions of infants and young children. (Data from: Nuffield Trust at www.nuffieldtrust.org.uk.)

- an increasing number of children and young people with long-term conditions and/or complex needs, e.g. extremely preterm infants, children with cerebral palsy, malignant disease or organ failure, who require repeated admissions.

Although the number of admissions has risen, the average duration of admissions has decreased, creating a very high turnover of patients. In 1996 just over half of all admissions were less than 24 hours, and by 2016 it had risen to three quarters. Other statistics relating to admission of children to hospital are listed in the summary box.

Strenuous efforts have been made to reduce the rate and length of hospitalization:

- Paediatric emergency medicine, with paediatric emergency medicine consultants, has been developed into a subspecialty to provide care for all acutely ill children, with an aim of preventing admission whenever possible by facilitating early review by a senior paediatrician.
- Dedicated children's short stay paediatric 'clinical decision' units within or alongside the emergency department are increasingly available to allow children and young people to be treated or observed for a number of hours and discharged home directly, avoiding the need for admission to the ward.
- Day-case surgery is now standard for most elective operations, and day units are used for complex investigations and procedures instead of inpatient wards.
- 'Home-care' or 'ambulatory' teams provide specialist care in the child's home, e.g. for treating diabetes and asthma or giving intravenous medication, home oxygen therapy, parenteral nutrition or palliative care (Fig. 5.3).
- Children's hospices provide respite and palliative care for children with life-threatening conditions such as neurodegenerative and malignant disorders
- Some teams provide a 'hospital-at-home' service for children who are acutely ill.

Clinical networks have been developed to co-ordinate these services.



- Hospital admission of children and young people:**
- should be avoided whenever possible
 - most medical admissions are infants and young children; surgical admissions occur throughout childhood.



Figure 5.3 Providing palliative care in a child's home. Although this child required a subcutaneous morphine infusion to control her pain from malignant disease, she was able to remain at home and enjoyed playing with her pet rabbit. (By kind permission of the child's parents and Dr Ann Goldman.)

Summary

Secondary and tertiary care for children in the UK

Each year:

- Up to half of infants aged under 12 months and one quarter of older children attend emergency departments.
- 1 in 11 children are referred to a hospital outpatient clinic.
- 1 in 10 children are admitted to hospital.
- 1 in 1000 children require intensive care.
- 1 in 8 newborn babies are admitted to a neonatal unit. Of those, about 1%–3% need intensive care.

Children in hospital

Children should only be admitted to hospital if effective and safe care cannot be provided at home. Removing young children from their familiar environment to a strange hospital ward is stressful and frightening for the child, parents and family. As a result, some ill or injured children may regress in their behaviour and development. Hospitals place the child at risk of nosocomial infections and iatrogenic harm through medical errors, e.g. prescribing errors. Admissions disrupt family routines, not only of the child in hospital but also of siblings who still need to be looked after at home and transported to and from nursery or school. If a child has to be admitted, the facilities and care required are outlined in Fig. 5.4.

Subspecialist care and networks

The number of children requiring subspecialist (tertiary) care is relatively small, so it is concentrated in specialist centres, often in children's hospitals. This care includes neonatal and paediatric intensive care and organ-specific specialties such as cardiology and nephrology. Specialist children's hospitals have the advantage of having a wide range of medical, surgical, nursing and other healthcare professional staff, and diagnostic and other services to deliver expertise in the investigation and treatment of complex or uncommon conditions. For critically ill neonates, children and young people, specialist retrieval teams have been developed to provide transport to the subspecialist centre. Some rare and complex disorders (e.g. immune deficiency disorders and inborn errors of metabolism) and complex treatments (e.g. organ transplantation and craniofacial surgery) are managed at relatively few national centres so that the skills required to achieve the best outcomes can be further concentrated. A disadvantage is that they are often some distance from the child or young person's home, and hospital stays may be prolonged, e.g. following a bone marrow transplant. Accommodation for families should be provided. To minimize the need for the child or young person to travel to subspecialist centres, shared-care networks have been established between specialist centres and local hospitals. For example, a child with leukaemia will attend the specialist centre for a diagnostic assessment and initial treatment, and subsequently for specialized treatment and periodic review, but much of the maintenance therapy is provided

Care of children in hospital

Putting the family and child at the centre of care

- Child-centred and family-centred care – holistic, including emotional, spiritual, educational and social needs
- Parent of young children can stay with their child over night
- Mutually agreed plan of responsibilities with parents for their child's care – neither pressurized to accept responsibilities they are not confident about nor brushed aside and undervalued. e.g. many parents rapidly learn some procedures, such as nasogastric tube feeding



Environment

- Children's ward – appropriate for child's physical and emotional maturity and needs
- Adolescents – with others of their own age and ward arrangements, e.g. bed-time not designed for babies
- Child or adolescent friendly
- Education and play facilities
- Access to prayer rooms and specific dietary requirements, such as kosher and halal foods



Communication

Parents know best about their child's usual behaviour and habits – due attention needs to be paid to their worries or comments, particularly in recognizing acute deterioration

Multidisciplinary care

- Coordinated, multidisciplinary team
- All children and young people under care of paediatrician or paediatric surgeon

Skilled staff

- All medical, nursing and other healthcare professionals trained in the care of children and young people
- Non-professional staff trained in communicating with children and families
- Surgeons and anaesthetists must treat a sufficient number of children to maintain their skills
- Dedicated children's physiotherapists and occupational therapists, dieticians and pharmacists should be available
- Play specialists – essential part of the team to help children of all ages understand their illness and its treatment



Information

- Given personally and preferably also written and in the parents' first language
- Elective admissions - advance visit offered and details of treatment explained to both parents and child or young person



Figure 5.4 Provision of care required for children and young people admitted to hospital. (a) The child/young person and family are at the centre of care (b) Mother nasogastric tube feeding her baby. (c) Music therapy. (d) Distraction to reduce pain of establishing intravenous access. (e) Staff explaining an operation to a young child using a doll. (Photos courtesy of: (a, c, e) University Hospital of the North Midlands; (b) Lissauer T, Fanaroff A, Miali L, Fanaroff J; Neonatology at a glance, ed 4, Wiley-Blackwell, 2020; (d) Baxter A, Pediatric Clinics of North America 60(5):1163–1183, 2013. Courtesy of Heidi Giese, Saint Joseph's Children's Hospital, Marshfield Clinic Children's Hospital, Marshfield, WI, USA.)

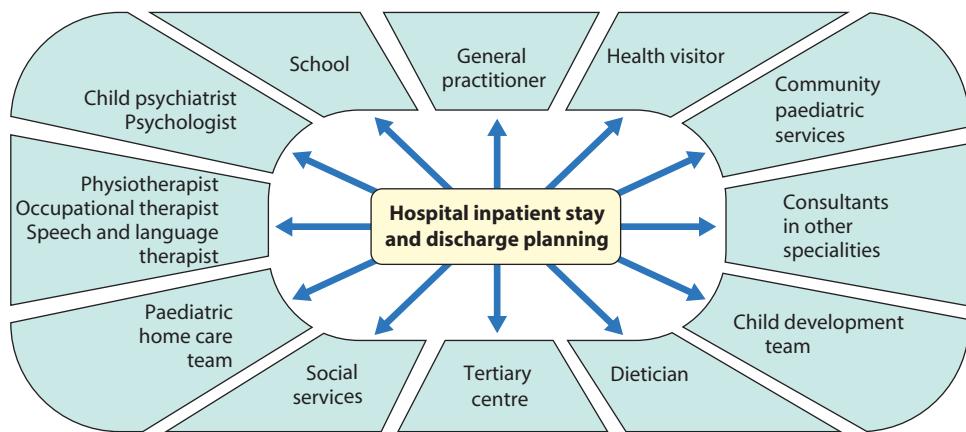


Figure 5.5 Some of the professionals who may need to be informed about the admission or discharge of a child admitted to a hospital.

by the local hospital together with monitoring of their health and regular blood and other tests performed by a specialist nurse at home. Specialists from the subspecialist centre may also hold periodic clinics at the shared-care centre. Such shared-care networks rely on mutual respect and excellent communication between all the health professionals involved.

Discharge from hospital

Children and young people should be discharged from hospital as soon as clinically and socially appropriate. Although there is increasing pressure to reduce the length of hospital stay to a minimum, this must not allow discharge planning to be neglected. Before discharge from hospital, parents and children should understand:

- the reason for admission and any implications for the future
- details of medication and other treatment
- any clinical features that should prompt them to seek medical advice, and how this should be obtained
- problems or questions likely to be asked by other family members or in the community. These should be anticipated by the team and discussed. For instance, what does the nursery or school, babysitters or friends need to know? What about sports, etc.?
- plans for follow-up (if required).

In addition, consider:

- suitability of home circumstances
- social support that may need to be arranged, especially in relation to child protection
- what medical information should be added to the child's personal child health record
- which professionals should be informed about the admission and what information it is relevant for them to receive.

This must be done before or at the time of discharge. The aim is to provide a seamless service of care, treatment and support with the family and ensure that all the professionals are fully informed (Fig. 5.5).

Summary

What should be provided for children and young people in hospital

- Family-centred care: holistic approach to family, parent of young children able to stay and provide parental care.
- Age-oriented environment: appropriate for child or young person's age, together with education and play facilities.
- Information and psychosocial support: verbal and written information for both parents and child.
- The opportunity for children and families to express their views and fears and be listened to.
- Skilled staff, specially trained to care for children.
- Multidisciplinary care.
- Access to subspecialist care, with shared-care arrangements with local hospital and primary care.

Pain in children

Pain is a major concern for children and parents across all specialties. Whilst it is easy to ignore or underestimate pain in children, it should ideally be anticipated and prevented, and always taken seriously.

Acute pain

This may be caused by:

- musculoskeletal tissue or organ damage, e.g. trauma, burns or fractures
- inflammatory processes – from local infection, e.g. skin, respiratory or urinary tract, joint, bone, peritonitis, meningitis
- obstruction – e.g. intussusception, renal colic, hydrocephalus
- vaso-occlusive disease, e.g. sickle cell crisis
- medical intervention, i.e. investigations e.g. venepuncture or lumbar puncture or procedures such as change of wound dressings
- surgery.

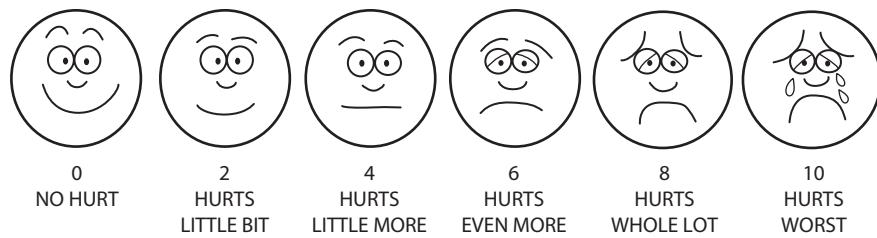


Figure 5.6 An example of a scoring system for pain assessment in children. Wong Baker Faces scale. (From: Wong DL, Winkelstein ML, Schwartz P, et al.: Wong's essentials of pediatric nursing, St Louis, MO, 2001, Mosby, with permission.)

Chronic pain

In children, chronic severe pain sometimes occurs as a result of disorders such as malignant disease, juvenile idiopathic arthritis or persistent unexplained physical symptoms. Intermittent pain of mild or moderate severity, e.g. headache or recurrent abdominal pain, is more common and can be distressing for children and their families.

Management

Pain management should be approached by recognizing, responding and reassessing.

Recognition of pain

Older children, like adults, can describe the nature and severity of the pain they are experiencing. In younger children and those with impaired communication, assessing pain can be more difficult. Observation and parental impression are commonly used, and a number of assessment tools have been designed for infants and young children (Fig. 5.6). Observation of behaviour is a key component of pain assessment in children; the child who is extremely quiet, especially after trauma, may be in significant discomfort.

Responding to pain

A multimodal approach to pain management is described in Box 5.2. This should allow pain to be prevented or kept to a minimum. Explanation should be given when possible, and the approach should be reassuring and age appropriate; however, it is imperative not to lie to children, otherwise they will lose trust in what they are told in the future.

For minor medical procedures, e.g. venepuncture or inserting an intravenous cannula, pain can be alleviated by explanation and the use of a topical anaesthetic such as lidocaine cream or cold-spray. Additional and appropriate use of inhalation agents such as nitrous oxide or the adjunctive use of mild sedatives (midazolam) or hypnotics (ketamine) alongside pain relief can be helpful for more painful procedures such as suturing a wound. Distraction techniques such as blowing bubbles, telling stories, holding familiar toys, or playing computer games, as well as the involvement of play specialists, can be highly successful in ameliorating procedural pain. Some children develop particular preferences for a particular venepuncture site or distraction technique, and this should be accommodated as far as possible. For more invasive procedures, e.g. bronchoscopy, a general anaesthetic should be given.

Postoperative pain can be markedly reduced by local infiltration of the wound, nerve blocks and postoperative

Box 5.2 Approaches to pain management

Non-pharmacological

- Psychological – explanation and reassurance by the parent, doctor, nurse or play specialist
- Behavioural – positioning
- Distraction
- Hypnosis

Pharmacological

- Local: anaesthetic cream, local anaesthetic infiltration, nerve blocks, warmth or cold, physiotherapy, transcutaneous electrical nerve stimulation
- Analgesics:
 - mild/moderate – paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs)
 - strong – morphine
- Sedatives and anaesthetic agents:
 - ketamine, midazolam, nitrous oxide, general anaesthetic
- Antiepileptic and antidepressant drugs for neuropathic pain

Consider the route for analgesics – oral if possible, otherwise intravenous, subcutaneous or rectal. Intranasal administration is becoming increasingly widely used in children as it is well tolerated.

analgesics. Severe pain, especially from fractures and surgical procedures, should be adequately treated with opioid analgesics. In the past, there was reluctance to use morphine in children for fear of depressing breathing, but this should not occur when morphine is given in appropriate dosage under nursing supervision to children with a normal respiratory drive. Intravenous morphine can be given using a patient-controlled delivery system in older children or a nurse-controlled system in young children. Acutely, intranasal opiate agents (e.g. diamorphine) can be given, which are highly effective as they are absorbed rapidly from a child's nasal mucosa. Codeine should not be prescribed in children <12 years old. Most of its analgesic effect is due to conversion to morphine by the cytochrome P450 mixed function oxidase system, CYP2D6. There is marked variability in the activity of this enzyme between individuals, leading to risks of toxicity or lack of effect.

Reassessment

This is a vital part of pain management in children, to determine whether analgesia has been effective, is wearing off,

or whether further intervention is required. Although children often have parents and carers as advocates, the child themselves should be regularly reviewed.



Pain should be anticipated and prevented as well as being treated promptly.

Prescribing medicines for children

There are marked differences in the absorption, biology, clearance and distribution (ABCD) of drugs between children and adults. A basic understanding of the pharmacology of the commonly encountered medicines in paediatrics is helpful when prescribing – i.e. how it is absorbed in different age groups, how it works (its biology), how it is cleared (and how quickly), and how it is distributed.

The child's age also affects drug formulation used and choice:

- Young children find it difficult to take tablets and thus a liquid formulation is required. However, children as young as 4 years old can be taught to swallow solid formulations.
- Persuading children to take medicines is often a problem, especially if the preparation has an unpleasant taste, though experience and imagination can help to overcome reluctance.
- Avoiding unpleasant-tasting medicines when possible may improve adherence (compliance).
- Adherence is also improved when medicines are only required once or twice a day and if regimens are kept simple.

Absorption

- In neonates and infants, the intake of oral liquid formulations cannot be guaranteed and absorption may be unpredictable as it is affected by gastric emptying and acidity, gut motility, and the effects of milk in the stomach. In acutely ill neonates and infants, drugs are therefore given intravenously to ensure reliable and adequate blood and tissue concentrations. In older children and young people, the oral route is often reliable, provided they are well enough to tolerate the medication.
- Intramuscular injections should be avoided in children where possible as there is little muscle bulk available for injection, absorption is variable, and they are painful.
- Rectal administration can be used for some drugs; although absorption may be more reliable than oral administration, this route is not popular in the UK.
- Significant systemic absorption can occur across the skin, particularly in preterm infants. This is a potential cause of toxicity, e.g. alcohol and iodine absorption from cleansing solutions applied to the skin for procedures, unless removed afterwards.

Biology

- The precise mechanism of action can vary considerably between adults and children and within children of different ages for the same drug. For instance, paracetamol is metabolized by a different and slower mechanism in neonates compared with older children and adults; this may increase the risk of overdose.
- Some medicines should be avoided in children as they may cause idiosyncratic adverse reactions (e.g. aspirin should be avoided in children <16 years of age as it is associated with a risk of Reye syndrome, causing encephalopathy and liver failure).
- Certain medicines should be used with caution due to their potential effect on growth and development (e.g. corticosteroids may affect growth and some tetracyclines irreversibly stain teeth).

Clearance

- In neonates, drug biotransformation is reduced, as microsomal enzymes in the liver are immature. This leads to a prolonged half-life of drugs metabolized in the liver, e.g. theophylline.
- The glomerular filtration rate increases over the first year of life from 20–30 ml/min/1.73 m² at birth to adult levels (80–120 ml/min/1.73 m²) by one year of age. As a result, clearance is reduced of renally excreted drugs resulting in a need for increased dosing intervals (e.g. penicillins in the neonatal period).
- Therapeutic drug monitoring is required for a number of drugs, typically those with a narrow therapeutic window ([Fig. 5.7](#)), or where a particular plasma concentration is required for effect, e.g. aminoglycoside antibiotics; phenytoin for seizures.

Distribution

- Water comprises a larger percentage of the body in the neonate (80%) than in older children and adults (60%). As a result, water-soluble drugs will require a larger dose relative to body weight in young infants than in adults.
- For drugs with a high margin of safety (wide therapeutic window), drug dosages are expressed per kilogram body weight or based on age, with the assumption that the child is of average size.
- For drugs with a narrow therapeutic window, as extracellular fluid correlates with body surface area, this is often used to guide dosing, e.g. cytotoxic agents
- Weight-based dosages cannot simply be extrapolated to older children, as the dosage will be excessively large – safe prescribing needs consideration of maximum daily dose (usually the adult dose).
- In the first few months of life, plasma protein concentration is low and some drugs may be partially unbound and remain pharmacologically active. In jaundiced babies, for example, bilirubin may compete with some drugs, e.g. sulphonamides, for albumin binding sites, making such drugs unsuitable for use in this situation.

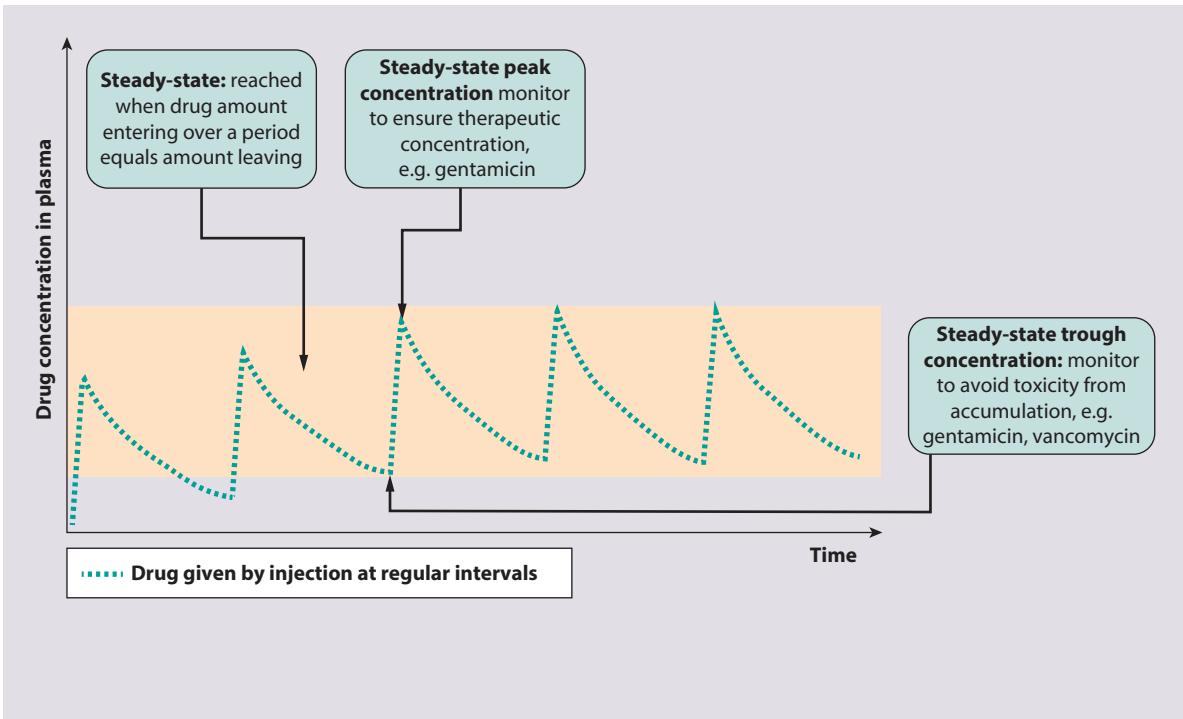


Figure 5.7 Therapeutic drug monitoring.

Prescribing errors

Unfortunately, prescribing errors are common on paediatric wards. An analysis of prescriptions over a number of hospitals identified that 13% of all prescriptions contained errors. The five main reasons are:

- *Doses need to be individualized; they have to be calculated and change over time* – A common source of error is the need to make calculations, usually based on weight, but also on surface area. Misplacement of decimal points leading to tenfold dosing errors, obesity resulting in exceeding maximum drug dosage, and inaccurate or lack of recent weight were other sources of error. Long-term prescriptions, such as antiepileptic drugs, require regular dose increases with growth. Intravenous drug formulations are manufactured with adult dosing in mind; as a result paediatric infusions often need to be diluted, a common source of error.
- *Off-licence prescribing is common* – Most medicines in common paediatric use are licensed for children but a number of drugs developed for adults are not licensed for use in children (off-licence). This can result in lack of clear dosing information and cause confusion, especially between hospitals, general practitioners and community pharmacies. It also results in a paucity of child-specific adverse effect information.
- *Liquid formulations* – Liquid formulations cause errors because of conversion from millilitres to milligrams and vice versa. They may also be produced in different concentrations (e.g. paracetamol, or amoxicillin 5 mls of syrup may

contain a wide concentration range). If a repeat prescription is issued with a different medication concentration from that initially prescribed, overdosing or underdosing can occur with consequent side effects.

- *Communication issues* – Parents may give incomplete, misleading or incorrect information about their child's medication, and doctors may provide inadequate information about prescribing decisions and doses. Dosing regimens can be complicated, particularly when medications are being introduced (e.g. antiepileptics) or withdrawn (e.g. steroids in nephrotic syndrome). Even basic medications can cause confusion without appropriate instructions. Doctors should prescribe drug doses by weight (or in some cases international units), and pharmacists need to be vigilant to translate this into correct dose volumes for parents to administer when a liquid formulation is used. Clear, written, step-by-step information should be provided for parents and caregivers to assist with dosing changes.
- *Experience working with children* – Paediatric trainees have been shown to make fewer errors than doctors from other specialties, though all doctors make errors. This highlights the need for specific training for prescribing for children.

Avoiding errors

Always consult a formulary (British National Formulary for Children) to double-check up-to-date dosing, however experienced you are. In addition, get another person to double-check calculations, though this cannot be relied on. Computer calculation improves accuracy compared to manually calculated doses. Checking by paediatric pharmacists is invaluable.

Summary

Medicines for children

- Oral formulations need to be given as liquids in infants and young children.
- Medicines are usually prescribed per kilogram of body weight, but check the maximum dose.
- Intravenous drug dosages can easily be miscalculated as they vary widely in children because of their different size, and drugs often need to be diluted; all dosages and dilutions must be checked independently by two trained members of staff.
- To improve compliance, use formulations requiring the least number of doses per day and consider its flavouring in young children.
- Always check drug dosage in the *British National Formulary for Children* and/or with the paediatric pharmacist.

Communicating serious problems

Doctors often face the task of imparting serious issues to parents and children. In paediatric practice, examples include:

- the identification of a serious problem at birth, e.g. chromosomal disorder, hypoxic-ischaemic encephalopathy or complications of extreme prematurity
- the diagnosis of a disabling condition, e.g. cerebral palsy or neurodegenerative disorder
- the diagnosis of a serious illness, e.g. meningitis or malignant disease
- the sudden unexpected death of a child, e.g. sudden unexplained death in infancy (SUDI).

Communicating about a serious or life-threatening condition with a family is always daunting and upsetting for everyone involved. Increasingly, children and young people are being involved in discussions about their illness. This enables them to understand what is happening and improve their cooperation. It may also enable them and their family to obtain the care most appropriate for their needs. Sensitive communication matters greatly to the child or young person and their family; they will often recall it vividly for many years. In the past, information about serious or life-threatening illness was often withheld from children or young people to protect them from distress, and this is often parents' natural instinct, or they feel their child is too young to understand. While it is important to take this into account, it is increasingly recognized that children as young as 5 years old are often able to understand the concept of serious illness and personal mortality. Communication between health-care professionals and parents or caregivers needs to take into account the cognitive, emotional and psychological development of the child or young person as well as the family's cultural and religious beliefs. Age itself is a poor guide to developmental capacity and wish for involvement in communication; some older children and young

Box 5.3 Factors to consider when communicating with a child or young person about a serious or life-threatening problem

Child or young person

- Age
- Developmental capacity
- Previous experience of serious illness – personal or in the family
- Beliefs and values

Parents

- Degree of understanding about the problem or diagnosis
- Previous experience of serious illness
- Prediction of child or young person's reaction
- Emotional wellbeing
- Beliefs and values
- Level of education
- Communication style within the family

Healthcare professional

- Knowledge and experience
- Beliefs and values

people want minimal involvement, others wish to be deeply involved.

Parents will be dealing with their own emotional distress, but they know their child best and should be fully engaged in the process. They will be able to tell you about what their child already knows and how to make the information appropriate to their level of understanding; they will also understand their child's coping strategies. They may wish to break the news first; but this involves planning and negotiating the best way forward. A 'one size fits all' approach is clearly inappropriate. An important factor is also the communication style within the family, particularly whether children are involved or excluded from decision-making within the family. **Box 5.3** lists some of the factors to take into account.

Palliative and end-of-life care

Palliative care should begin from the time of diagnosis of a life-limiting illness and may continue for many years. It includes pain and symptom management for the child, psychosocial support for the child and family, attention to practical needs, and spiritual care. It may also include respite care and bereavement support for the family after the child has died. End-of-life care is used specifically to describe the period of care when death is imminent.

Care plan

An Advanced Care Plan (ACP) should be completed between families and professionals for children with a life-threatening illness. This should involve the child or young person whenever feasible. It needs to address symptom care and medical and emotional support, clarify the roles

of the clinical teams involved, and make management plans for potential crises. It needs regular review as the illness evolves.

The Child and Young Person's Advance Care Plan Collaborative (cypacp.uk) provides a systematic proforma for bespoke care plans and is recognized nationally within the UK.

End-of-life care

Families should be involved in the child's end-of-life care and care after death, according to their wishes. Their individual cultural and religious beliefs and rituals should be accommodated whenever possible. Some families may wish to take their child to their home or to a hospice. If care is provided at home, it is essential that the family has support and information about whom to contact for routine and emergency problems, including medications, and what to expect when the child dies and afterwards. The needs of the child are paramount, but all family members including siblings must be considered. Many will not have encountered death before. Some families will have specific religious or cultural requirements about burial and its timing. Families are encouraged to hold their child before and afterwards, if they wish to do so. The family should be provided with written information about registering a death and making funeral arrangements. Some families create memory boxes with mementos of the child. All health professionals involved should be informed when the child has died. Grief following death is normal and intense and may continue to affect families for years. The family should be informed about support that is available.

Caring for staff

Staff may be distressed especially if they have known the child for a long time. If the death was sudden and unexpected, there may be feelings of failure. Open discussion or a 'debrief' is often helpful by clarifying the events and allowing staff to express their feelings and concerns. There is increasing recognition that providing psychological support for staff in times of distress helps to prevent burn-out and facilitates improvement in mental health.

Ethics

The complexity of modern medicine presents clinicians with an increasing number of clinical situations which raise difficult ethical issues. Paediatric practice is no exception, with the added issue of patients who are usually unable to express their own choice and the need for others to make decisions for them. A number of ethical principles can be applied to provide a structured approach to assist decision-making:

- *Autonomy* – This encompasses the right to self-determination, allowing an individual to make an independent decision, based on a full understanding of the implications, treatments and outcome of their medical condition, to allow informed consent. This understanding is limited for most children and young

people, and they rely upon others to make decisions on their behalf.

- *Beneficence, and its obverse, non-maleficence* – These principles comprise ensuring that decisions and actions are in the best interests of the patient and will not cause them harm. However, assessing and defining a child's best interests may be problematic.
- *Justice/social responsibility* – This is the principle of ensuring that healthcare resource is distributed sensibly and fairly.
- *Respect for the truth* – Lying to patients or their families is never justified; however, parents may wish not to overwhelm their child with information they consider they are not ready for or cause distress – but withholding information requires working out ways with families to reveal information gradually with integrity; this can be challenging.
- *Respect for confidentiality/fidelity* – Children and their family entrust healthcare professionals with sensitive information about their health and other matters in confidence, with an expectation that this information will not be disclosed for reasons other than healthcare without their express consent. It is a legal obligation, but there are situations in paediatric practice where it may be appropriate to disclose information without consent, for example where the child or young person is at risk of physical or sexual maltreatment.

Consent

Valid consent is required for all complex or high-risk procedures or treatments and for all surgical procedures other than emergencies or when urgent intervention is necessary to prevent serious risk of present or future harm. It provides the ethical and legal authority for action, which would otherwise be a common assault, or interfere with the right of individuals to decide what should be done to them (autonomous choice). To be valid, consent must be sufficiently informed and freely given by a person who is competent to do so. Clinicians have a duty to provide sufficient information to enable a reasonable person to make the decision and must answer all questions honestly. Information has to be given in language that is clear and understandable. Documentation about the communication with the parents and the explanation given about the benefits and risks of the procedure or treatment need to be recorded, including a signature on a consent form. Consent for a surgical procedure must be obtained by someone familiar with and capable of performing the procedure, or who has been trained to take consent for the procedure. It is impractical to obtain detailed consent from parents for every routine procedure performed during a hospital admission, but parents and the child or young person should be given an overview about the care and the range of procedures to be performed, both verbally and in an information leaflet.

In UK law, the legal age of consent to medical treatment is 16 years. The right of children below this age to give consent depends on their competence rather than their age. They may consent to medical examination and treatment provided they can demonstrate that they have the maturity and judgement to understand and appraise the nature and implications of the proposed treatment, including the risks and alternative courses of action.

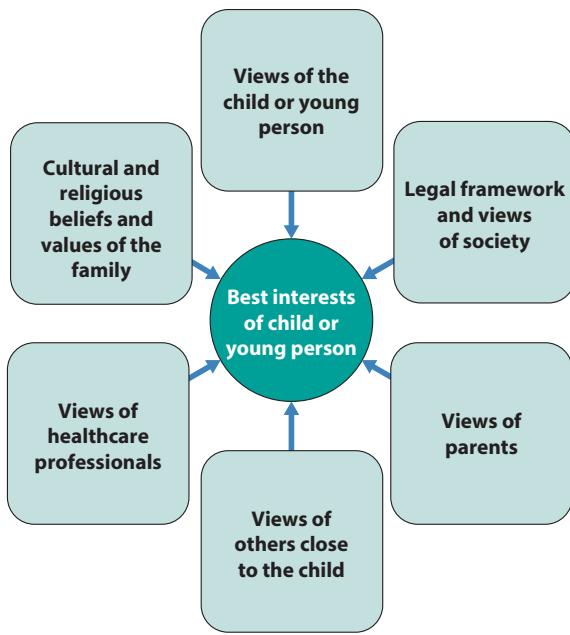


Figure 5.8 Views to consider in the evaluation of best interests of a child.

When a child lacks the maturity and judgement to give consent, this capacity is given to a person having parental responsibility – usually a natural parent – or to a court. In practice, problems occur only when there is disagreement between the parents and clinicians over management, or, rarely, between the young person and their parents and clinicians.

Despite including children's views in consent, legal judgements have not supported young people who refuse treatment which parents and clinicians feel to be in their best interests, especially if its purpose is to save life or prevent serious harm, e.g. heart transplantation for acute cardiomyopathy in an intelligent 15-year-old patient. Where disputes cannot be resolved by negotiation or mediation, or where there is doubt over the legality of what is proposed, legal advice should be sought. Whatever the outcome, children and young people should have their views heard and be given reasons as to why they are being overridden.

Best interests

It is a general ethical and legal maxim that the best interests of the child or young person are paramount (Fig. 5.8). Doctors therefore have a duty to save life, restore health and prevent disease by treatments that confer maximum benefit and minimal harm and which respect the autonomy of the child or young person as far as possible. Parents have the ethical and legal duty to make decisions on behalf of their child, provided that they act in their best interests. Usually parents and their child and healthcare professionals agree over the best course of management. However, disagreements can occur between parents and healthcare professionals over the best interests of the child or young person especially when the withholding or withdrawing of life-sustaining treatment is involved. Under these circumstances, a structured, stepwise approach to resolving the disagreements may be helpful:

- open discussion with efforts to identify common goals, with separation of fact-based from value-based issues to help each side understand the other's concerns

- discussion with the wider clinical team
- an internal second opinion
- ethics committee involvement
- mediation
- external second opinion, explore transfer to another hospital
- legal consultation
- court decision.

Courts have been supportive of the position that in some circumstances the burden to the child of providing life-sustaining treatment outweighs its benefits.

[Case histories 5.1 and 5.2](#) demonstrate some of the ethical problems encountered in paediatrics.

Summary

Ethics in paediatrics

- Both clinicians and parents aim to do what is in the child's best interests.
- Conflicting views can usually be resolved by good communication.
- If not resolved, help may be sought from further, wider communication or mediation, from a second, truly independent opinion, or sometimes from a hospital ethical committee. Rarely, it may go to court.
- In young people who understand the issues and have strong views as to what should or should not be done to them, there is increasing ethical and legal support for them to exercise as much autonomy as they are capable of.

Evidence-based practice

Evidence-based practice provides a systematic approach to enable clinicians to use the best available evidence, usually from research, to help them solve their clinical problems. The difference between this approach and old-style intuitive clinical practice is that clinicians need to know how to turn their clinical problems into questions. As clinical problems are often complex, the different elements (aetiology, diagnosis, therapy, prognosis) need to be tackled as separate questions. A search of the research literature for the evidence needs to be conducted and appraised, and the evidence incorporated into clinical or policy decisions.

To what extent is paediatric practice based on sound evidence?

There are two paediatric specialities in which there is a considerable body of reliable, high-quality evidence underpinning clinical practice, namely paediatric oncology and, to a lesser extent, neonatology. Virtually all children with malignant disease are enrolled into multicentre trials designed to identify improvements in treatment.



Case history 5.1

Acute lymphatic leukaemia, truth telling and stopping treatment

Millie, aged 10 years, has acute lymphoblastic leukaemia, which was diagnosed four years ago. She has relapsed, with early involvement of the central nervous system. She is well known to the staff of her local children's ward as she has had four relapses of her leukaemia and a previous bone marrow transplant. It is the opinion of her paediatric oncology team that no further medical treatment is likely to be curative. Millie asks one of the junior paediatric doctors why her parents had been so upset following a recent discussion with the consultant, at which she had not been present. The parents had made it very clear to all the staff that they did not want Millie to be informed of the poor prognosis as they did not want her to be upset, nor would they tell her why she was not having further chemotherapy.

The parents have heard of a new drug that is claimed, in some reports on the internet, to help such children. However, it is very expensive, there is evidence that it does not cross the blood-brain barrier, and the doctors consider it highly unlikely to be of benefit. The parents insist on a trial of the drug.

Ethical issues to consider are:

- *Autonomy* – the parents claim the right to control the information reaching their child on the grounds that it is in her best interests as judged by them.
- *Truth telling* – the staff feel that it would be wrong to reassure her falsely.
- *Non-maleficence* – the parents wish to avoid the shock of the news and the loss of hope in their daughter.

- *Beneficence* – the staff wish to support the child effectively, which would be difficult if she were to be isolated by ignorance of what is upsetting her family and carers.
- *Justice* – should scarce resources be used on this new drug? Because her parents are desperate, should Millie be given a drug which, in the specialist team's opinion, will not benefit her?
- *Best interests* – what are Millie's best interests and who should decide them? What weight should be given to Millie's own views based on her experience of her illness?

In such situations, further discussion between the parents and staff whom they trust is usually the key to resolving the situation. The parents will need to understand the mutual benefits of adopting as open a pattern of communication as possible. They may be helped by a member of staff being present or helping them talk or listen to the child, who will usually understand more than the parents suspect.

Parents almost always wish to do the best for their child. Detailed explanation is likely to help them see that the child's best interests may not be to seek further cure but to accept a change of focus towards palliative care. A second opinion from an independent specialist may be helpful, as may a specific ethical review. If, despite all efforts to reach agreement, the parents reject the doctor's advice, it may be appropriate to let a court of law decide whether or not to accept the parents' demands.



Case history 5.2

Issues of quality of life

Jack, a 2-year-old boy, has chronic lung disease and severe four-limb cerebral palsy and cerebral impairment, having been born at 24 weeks' gestation. He is admitted to hospital with a chest infection. Despite treatment with intravenous antibiotics and high-flow humidified oxygen therapy, his condition deteriorates. He is referred to paediatric intensive care and is intubated and mechanically ventilated. After several unsuccessful attempts to extubate Jack, the treating doctors explain to his parents that the paediatric intensive care team consider continued mechanical ventilation is not in his best interests and further escalation of care is not appropriate. In their view, the suffering that would be caused by more medical intervention would outweigh the slim chance of survival; in addition they expressed the opinion that his premorbid disability had already significantly limited his quality of life. Jack's parents, however, saw him as a valued part of their family; he responds to their voices and touch, and they want everything that could be done to help him survive. They are aware of other children who had received tracheostomies and home ventilation in similar circumstances.

The issue of autonomy is difficult – the responsibility for determining what care should be given no longer lies with the patient, but is handed to his parents, who must be supported in their decision-making through detailed and informed discussion with healthcare professionals. All care is aimed at achieving 'quality of life', but this can be very subjective. The culture, religion and values not only of the family themselves and their community, but also of the healthcare professionals and of the wider society have a significant impact in its determination. While ethically wrong to withhold treatment purely on the basis of disability, both over- and undertreatment of disabled children is wrong. The principle of justice is also important: in an ideal world, all treatments would be available to all individuals irrespective of pre-existing disease; however, high-dependency, technology-dependent care, such as home ventilation, is very expensive and supply is limited, leading to a need for decision-making that is fair and ethical, with defined inclusion and exclusion criteria. This case highlights some of the difficulties in determining what management options are in Jack's best interests, and how views about it may differ.

The trials are national or, increasingly, international, and include short-term and long-term follow-up. In general, the ability to apply evidence-based practice in paediatrics is poorer than in adult medicine, as the research literature is more limited. However, evidence-based medicine is not cookbook medicine. Incontrovertible evidence is rare, and clinical decisions are complex, which is why clinical care is provided by skilled and experienced clinicians. Evidence-based healthcare cannot change this, but it is an essential tool to help clinicians make rational, informed decisions together with their patients. It also provides a way for clinicians to articulate their priorities for research and thereby set research agendas that are relevant to service needs.

Summary

Evidence-based paediatrics

- Should be adopted whenever possible. However, clinical decisions are complex and the evidence base usually informs rather than determines clinical decision-making.

Research

Health professionals want to provide the best possible care for their patients, which, when possible, should be evidence-based. This can only be achieved when evidence is available from properly conducted research. It is therefore unethical for properly conducted research on children and young people *not* to be performed.

Practical difficulties in conducting research in children and young people

The number of trials and other forms of research is much less than in adult medicine. As this paucity of research is highly detrimental to improving care, great effort is being made to increase research conducted in paediatrics. Recently, there has been a marked increase in research involving children and young people.

Practical difficulties include:

- The number of children and young people with a specific problem or condition is often small and interventional trials often need to be multicentre, which adds to their complexity and cost. In addition, as outcomes improve, adverse outcomes become uncommon, so larger studies are needed to show efficacy for new approaches. Trial development and delivery is facilitated by networks working co-operatively.
- The regulatory requirements for trials, particularly those concerning drugs, have become increasingly stringent, making it expensive and onerous to set up and conduct such trials.
- Pharmaceutical companies have been reluctant to conduct drug trials in children, as market and commercial gain is small, but are increasingly required to do so.

- Consent is often required during a time of parental distress, e.g. after the birth of a preterm infant or after the acute onset of a serious illness in their child, making it more difficult to approach them.
- As children cannot give consent themselves, it may not be possible to justify performing additional investigations or other tests, especially if they are painful or not of direct benefit to the child.
- If required, repeated follow-up may be intrusive into family or school life.
- In young people, concordance with therapy and follow-up may be problematic.
- There is less of a culture of research in paediatrics compared with adult medicine.

Clearly, all research must be peer-reviewed, have ethics approval, and all large multicentre trials must have a Data Safety and Monitoring Committee.

Why is research so important?

There are many examples from the past where, through lack or failure to disseminate results of properly conducted research, clinicians have inadvertently harmed children, for example:

- *Blindness from retinopathy of prematurity.* In the 1950s, following anecdotal reports, many neonatal units started nursing all premature infants in additional ambient oxygen, irrespective of need. This reduced mortality, but no properly conducted trials were performed of this new therapy, and it took several years for it to be realized that oxygen therapy was also responsible for many thousands of babies becoming blind from retinopathy of prematurity.
- *Advice that babies should sleep lying on their front (prone), which increases the risk of SUDI (sudden unexplained death in infancy).* Medical advice given during the 1970s and 1980s to put babies to sleep prone appears to have been based on physiological studies in preterm babies, which showed better oxygenation when nursed prone. Furthermore, autopsies on some infants who died of SUDI showed milk in the trachea, which was assumed to have been aspirated and this was thought to be more likely if they were lying on their back. However, an accumulation of more valid evidence from cohort and case-control studies showed that placing term infants prone was associated with an *increased* risk of SUDI.
- Research in 1972 identified that antenatal steroids reduced the incidence of respiratory distress syndrome and death in preterm infants, but it was not until the 1990s that it was adopted into standard clinical practice. High quality peer review and subsequent dissemination of important research is vital for patients to benefit from it.

Acknowledgements

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Paediatric emergencies

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Features of paediatric emergencies:

- The primary assessment is a rapid initial clinical assessment of the seriously ill child or young person and should be conducted with an ABCDE approach.
- Key to management of the seriously ill child or young person is early recognition and intervention to prevent respiratory or circulatory failure; once present they are difficult to reverse.
- The management of cardiopulmonary resuscitation in children and young people is different from adults but follows the same principles.
- There are management guidelines for status epilepticus and anaphylaxis.
- Public health education strategies have markedly reduced the number of sudden unexpected infant deaths.

There are few situations that provoke greater anxiety than being called to see a child who is seriously ill. This chapter outlines the recognition and emergency management of the seriously ill child.

Identification of the seriously ill child needs to be at the point of first contact with healthcare services. 'Triage' is the process of determining the urgency in which patients need to be assessed and treated according to their illness severity rather than their order of attendance. This may begin with telephone or online consultation to a national centre, or via primary care or ambulance service. In an emergency department, it is based on a brief history and measurement of vital signs (temperature, respiratory and heart rate) ([Table 6.1](#)) and oxygen saturation.

For children admitted to hospital, paediatric early warning scores (PEWS) are now widely used to assist in identifying clinical deterioration (see Appendix Fig. A.3). Physiological measurements, such as heart rate, respiratory rate, level of consciousness, oxygen saturation, temperature and blood pressure, are ascribed a score dependent upon the extent of their deviation from expected normal

ranges for age. This is used to generate a composite overall score; higher scores are used to trigger a graduated response and need for reassessment with a view to possible intervention to prevent or reverse deterioration.

Assessment, resuscitation, stabilization and management of the seriously ill or injured child requires well coordinated, experienced, multidisciplinary teamwork working in a time-pressured situation on complex problems. Training in paediatric life support plays a vital role in achieving this, and is mainly achieved with simulation. Regular training is required to maintain skills.

Table 6.1 Normal vital signs

Age group	Heart rate (bpm)	Respiratory rate (bpm)	Systolic blood pressure
Newborn (0 to 1 month)	100–160	35–60	50–70
Infant (1 to 12 months)	80–140	30–40	70–100
Toddler (1 to 3 years)	80–130	20–30	70–110
Preschool (3 to 6 years)	80–110	20–30	80–110
School age (6 to 12 years)	70–100	20–25	80–120
Adolescents (12+ years)	60–90	15–20	100–120

(Adapted from: Advanced Life Support Group. 2016. *Advanced Paediatric Life Support*. The Practical Approach, ed 6, Blackwell BMJ Books.)

Structured clinical assessment of the seriously ill child

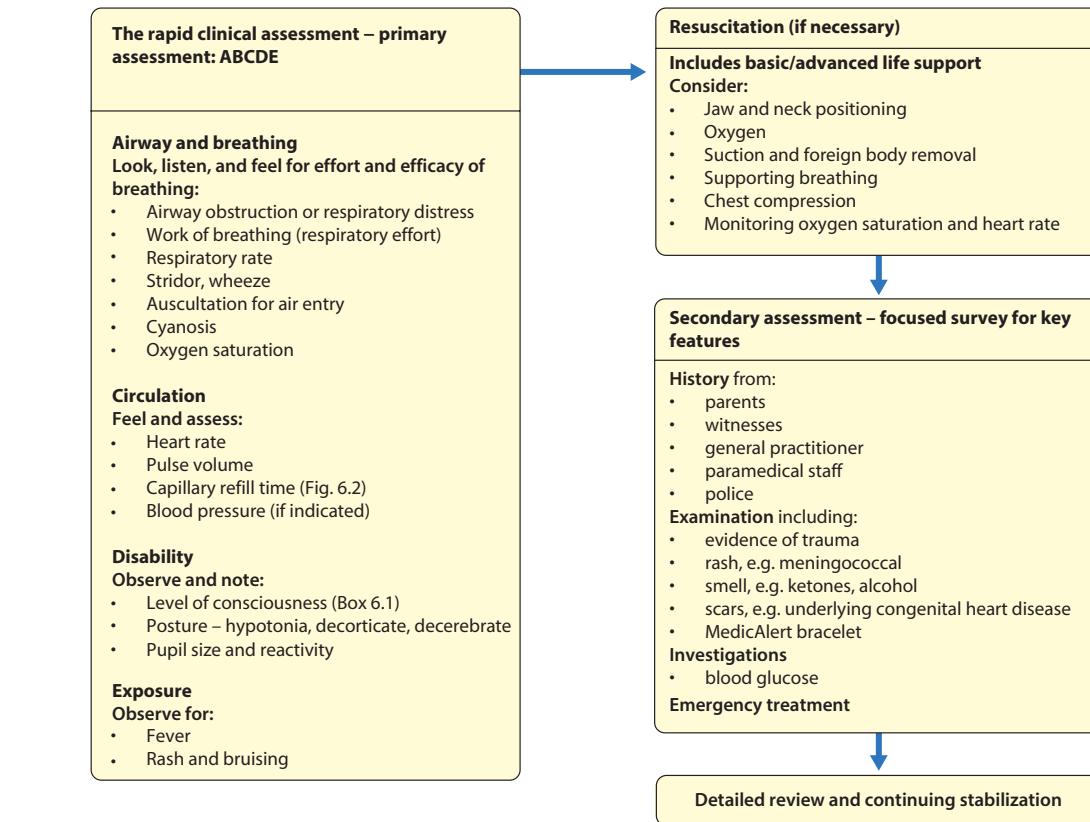


Figure 6.1 Structured clinical assessment of the seriously ill child. (Adapted from: Advanced paediatric life support, ALSG, ed 6. 2016. Wiley-Blackwell.)

Box 6.1 Rapid assessment of level of consciousness (AVPU)

A	ALERT
V	Responds to VOICE
P	Responds to PAIN
U	UNRESPONSIVE

A score of P means that the child's airway is at risk and will need to be maintained by a manoeuvre or adjunct.

More detailed evaluation is with the Glasgow Coma Scale.

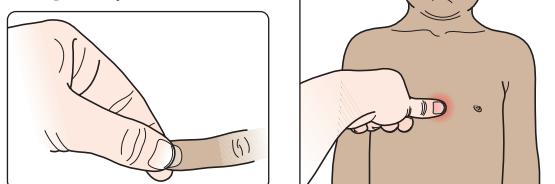
The seriously ill child

The initial rapid clinical assessment of the seriously ill child, the primary survey, aims to identify respiratory, circulatory or neurological failure (Fig. 6.1). Resuscitation is given immediately, if necessary, followed by secondary assessment when a focused history and examination will identify most emergency interventions required. The modes of presentation of the seriously ill child and their main causes are listed in Fig. 6.3.

In common with adult resuscitation, paediatric life support is structured according to an ABCDE approach:

- Airway (oral cavity, larynx and trachea)
- Breathing (lungs and conducting airways)
- Circulation (heart, blood vessels, blood)
- Disability (central and peripheral nervous systems)
- Exposure (skin, major organs and temperature control).

Capillary refill time



Press on the skin of the sternum or a digit at the level of the heart
Apply blanching pressure for 5 s
Measure time for blush to return
Prolonged capillary refill if >2 s

Figure 6.2 Capillary refill time.

Capillary refill time is affected by body exposure to a cold environment.

Presentation and causes of serious illness in children and young people

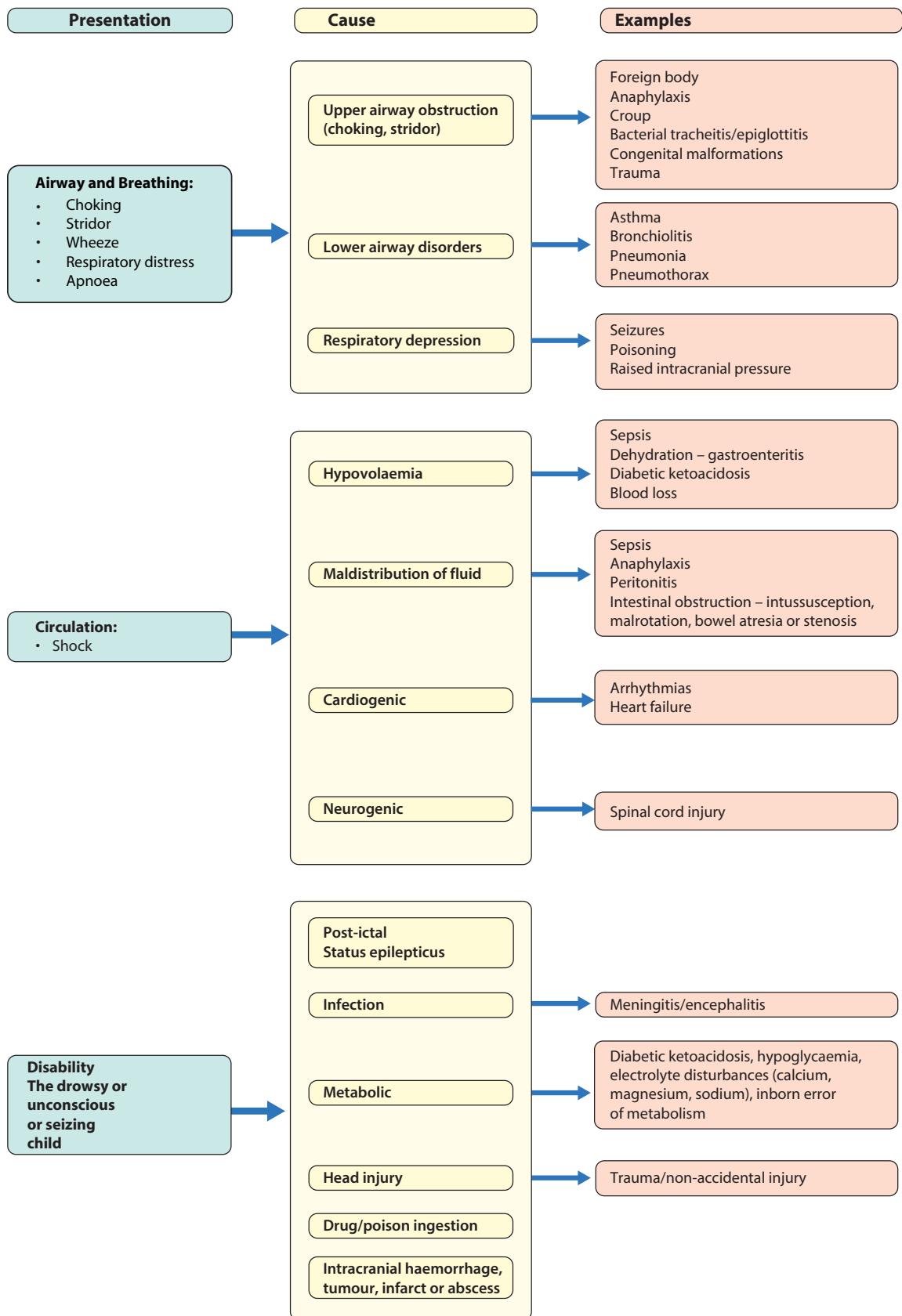


Figure 6.3 The main modes of presentation of serious illness in children and young people and their causes.

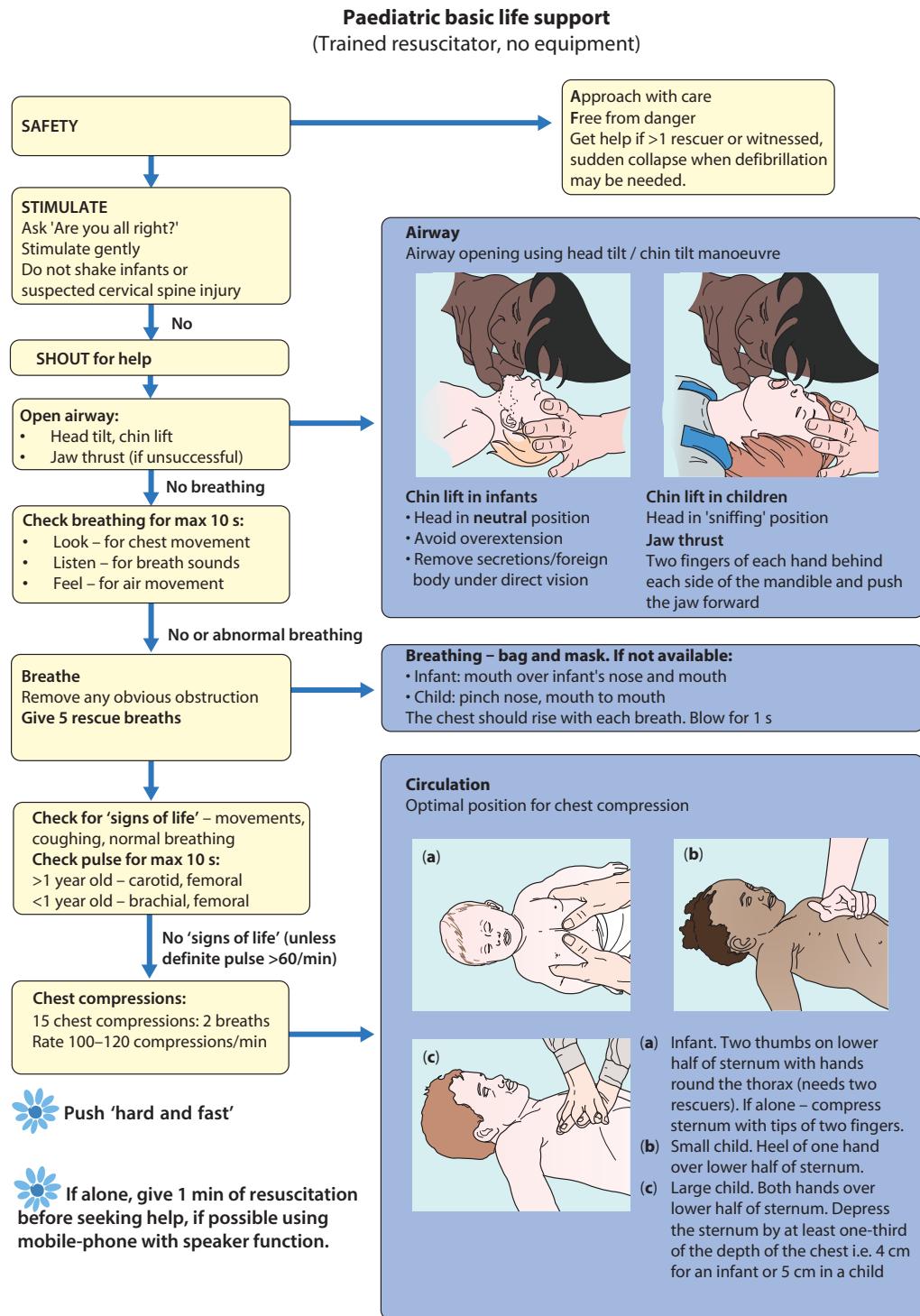


Figure 6.4 Paediatric basic life support. (Adapted from: Resuscitation Council (UK): Guidelines on paediatric life support, London, 2021, Resuscitation Council.)

Summary

Regarding the seriously ill child

- Triage and paediatric early warning scores are used to help identify urgency of medical treatment.
- Primary assessment is performed to recognize impending respiratory, circulatory or central neurological failure.

Resuscitation – Basic and Advanced Paediatric Life Support

In adults, cardiopulmonary arrest is often cardiac in origin, secondary to ischaemic heart disease. By contrast, in previously well children with healthy hearts, cardiopulmonary arrest is usually secondary to hypoxia from respiratory or neurological failure or shock. Paediatric Basic Life Support is resuscitation that takes place without access to any medical equipment (Fig. 6.4).

Paediatric Advanced Life Support (Fig. 6.5, Table 6.2) requires access to resuscitation equipment – means of

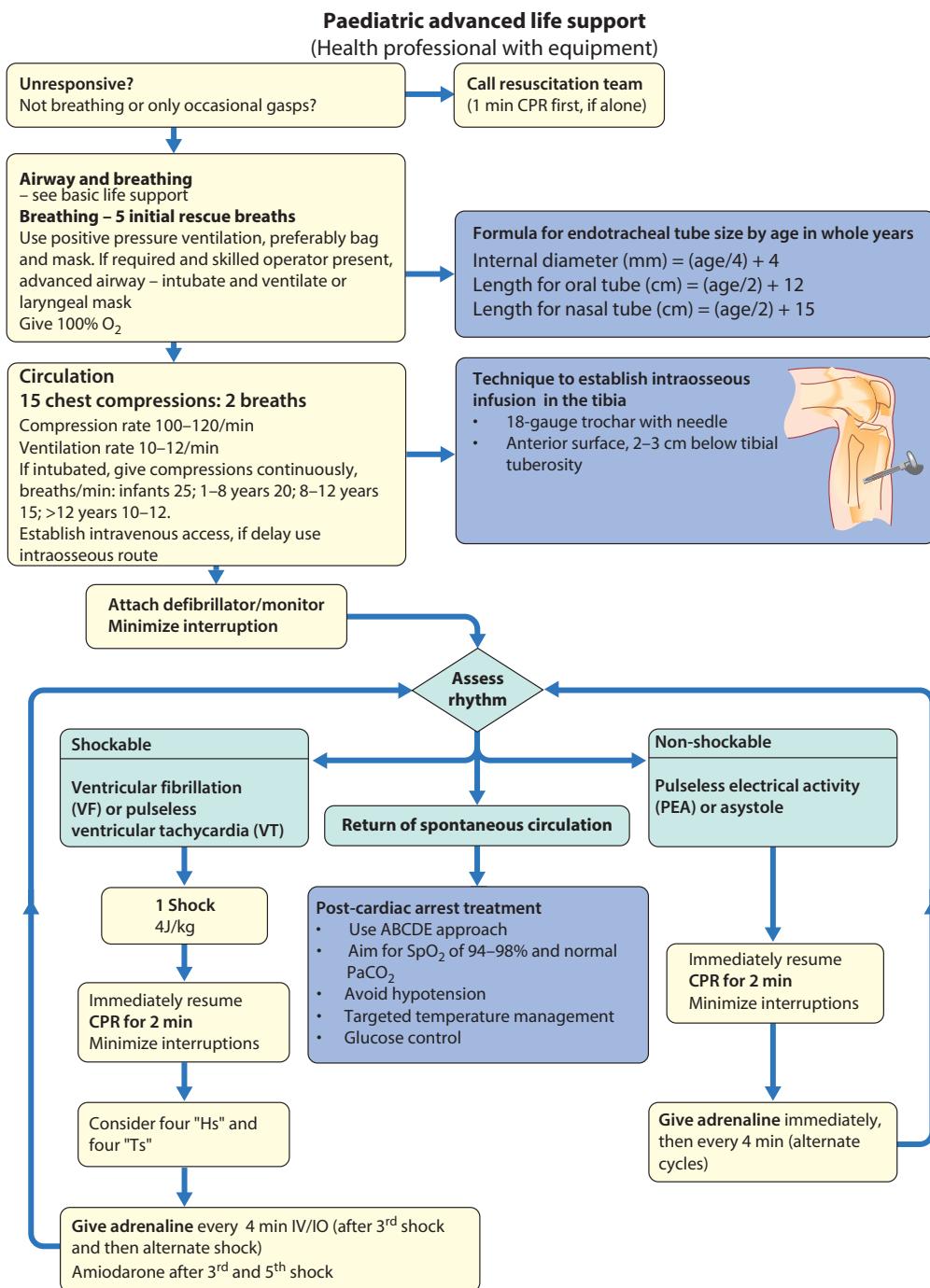


Figure 6.5 Paediatric advanced life support. (Adapted from Resuscitation Council (UK): Guidelines on paediatric life support, London, 2021, Resuscitation Council.)

Table 6.2 Reversible causes – the four ‘H’s and the four ‘T’s

Four ‘H’s		Four ‘T’s	
Pathology	Treatment	Pathology	Treatment
Hypoxia	Oxygen during ventilation	Tension pneumothorax	Needle thoracocentesis
Hypovolaemia	Intravenous saline or blood	Tamponade of the heart	Needle pericardiocentesis
Hypothermia	Warming with blankets and warm intravenous fluids	Toxins	Reversal agents if available (e.g. naloxone for opiates)
Hypokalaemia/ Hyperkalaemia	Intravenous potassium / intravenous salbutamol, insulin and dextrose	Thrombus	Thrombolysis/anticoagulation



Figure 6.6 A public-access defibrillator in a specially converted UK telephone box.

respiratory support, a defibrillator, intravenous or intraosseous access, and drugs such as adrenaline. Automated External Defibrillators (AEDs) in public places (Fig. 6.6) have proliferated and improve survival of out-of-hospital cardiac arrests in adults. In children, where primary cardiac events are rare causes of collapse, they are rarely required. However, there are case reports of positive outcomes, even in young children.

Resuscitation and management of the seriously injured child is considered in Chapter 7 (Accidents and poisoning).

Unlike adult resuscitation, the equipment size and medication doses vary widely according to the child's size – a 3-kg baby obviously cannot be intubated with the same size endotracheal tube as a 60-kg adolescent. With seriously ill patients, however, it is rarely possible to ascertain an accurate weight before starting resuscitation. The 'WETFLAG' acronym (see Appendix Table A.5) provides a prompt for the estimation of the weight of a child, based on age, and calculations of what equipment and medication doses are required. This can be used immediately in an emergency or in preparation of the arrival of a seriously ill patient by ambulance.



Regular life support training should be undertaken by all healthcare professionals to maintain skills.



Doctors should be able to provide life support for children of all ages, from newborn to adolescents.

Airway obstruction

Unconscious children will typically obstruct their airway and will require airway-opening manoeuvres or adjuncts (oral or nasopharyngeal airway) to hold their airway open.

Box 6.2 Clinical features of respiratory distress in infants

Moderate

- Tachycardia
- Respiratory rate >50 bpm
- Nasal flaring, grunting
- Use of accessory muscles
- Intercostal and subcostal recession
- Head retraction
- Unable to feed

Severe

- Cyanosis
- Exhaustion
- Reduced conscious level
- Saturation <92% despite oxygen therapy
- Rising partial pressure of carbon dioxide (pCO_2)

Any foreign matter should be removed under direct vision; a blind finger sweep is not advised. Conscious children with partially obstructed airways such as from croup or epiglottitis will naturally adopt a posture that maximizes air entry and comfort; interfering with this position (for examination purposes, for example) may jeopardize their ability to maintain their airway. A calm approach is essential: increasing anxiety often worsens obstruction.

Breathing – respiratory failure

Respiratory failure, when the lungs cannot maintain adequate gas exchange, may be due to any combination of alveolar hypoventilation, diffusion impairment, intrapulmonary shunting, or ventilation–perfusion mismatch. It may lead to hypoxaemia, which causes tissue hypoxia, or hypercarbia, or both. Prompt recognition and treatment is crucial to maintain gas exchange and prevent subsequent organ damage.

Assessment

Assessment of the child with respiratory failure follows the standard ABCDE approach, with an emphasis on the effort of breathing and the effects of hypoxaemia on other organ systems, particularly the heart and brain (Box 6.2). Specific conditions causing respiratory failure are listed in Fig. 6.3 and their treatment is discussed in Chapter 17 (Respiratory disorders).

Supportive therapy

Supportive therapy can be escalated from administration of supplementary oxygen (via face mask or nasal cannula) through non-invasive ventilation to endotracheal intubation and mechanical ventilation.

Supplementary oxygen

If the oxygen saturation (SpO_2) is less than 92%, supplementary oxygen should be administered to achieve normal saturations. The maximum fraction of inspired

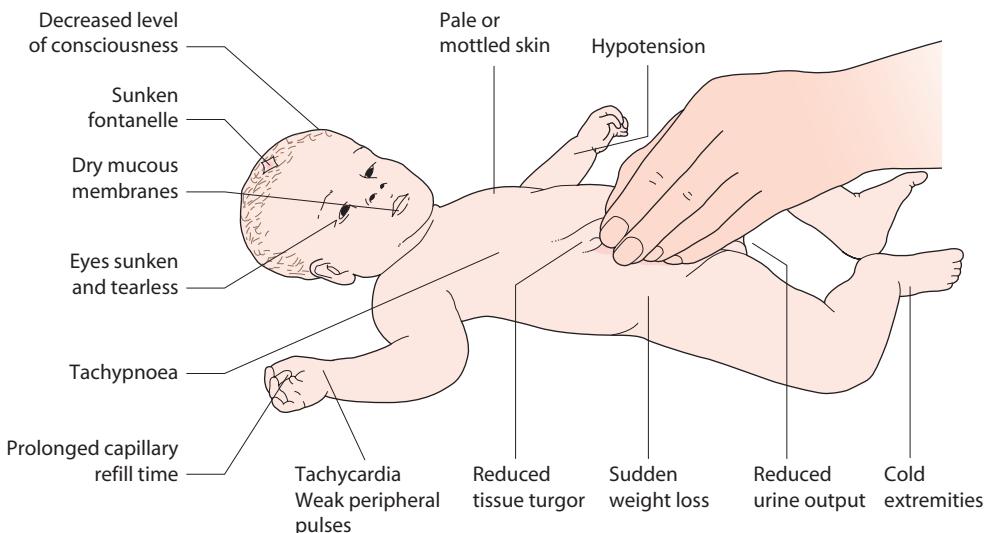


Figure 6.7 Clinical features of shock in an infant.

oxygen (FiO_2) delivered varies according to the device used, the rate of oxygen flow and the respiratory rate and tidal volume of the child. Typically, the maximum FiO_2 delivered by facemask is 0.60 unless a non-rebreather mask with a reservoir bag is used.

Respiratory support

Non-invasive respiratory support (without endotracheal intubation) includes high-flow nasal cannula therapy which delivers high-flow humidified oxygen, continuous positive airways pressure (CPAP), and biphasic positive airways pressure (BiPAP) via face mask or nasal mask. These can all be delivered outside a paediatric intensive care unit but require the recipient to be able to protect their own airway.

Mechanical ventilation should be considered in any child with impending or severe respiratory failure, or where they are unable to protect their airway. Worsening hypoxaemia or hypercarbia may help evaluate the need for mechanical ventilation, but the decision to start mechanical ventilation is based on the child's clinical condition.

Circulatory failure – shock

Shock is present when the circulation is inadequate to meet the metabolic demands of the tissues. This is common in critically ill children although the reasons are varied. The causes can be categorized as:

- hypovolaemia
- maldistribution of fluid (e.g. sepsis, anaphylaxis)
- cardiogenic (e.g. arrhythmias, heart failure)
- neurogenic (e.g. spinal cord injury).

Clinical features

The clinical features of shock are shown in Fig. 6.7. They are manifestations of compensatory physiological mechanisms to maintain the circulation and the direct effects of poor perfusion of tissues and organs (Box 6.3).

Box 6.3 Clinical signs of shock

Early (compensated)	Late (decompensated)
Tachypnoea	Acidotic (Kussmaul) breathing
Tachycardia	Bradycardia
Decreased skin turgor	Confusion/depressed cerebral state
Sunken eyes and fontanelle	Blue peripheries
Delayed capillary refill (>2 s)	Absent urine output
Mottled, pale, cold skin	Hypotension
Core-peripheral temperature gap (>4°C)	
Decreased urinary output	

In early, compensated shock, blood pressure is maintained by increased heart and respiratory rates, redistribution of blood from venous reserve volume, and diversion of blood flow to essential organs such as the brain and heart from non-essential tissues such as the skin in the peripheries, which become cold. Low blood pressure is a late feature of paediatric shock and signifies that compensatory responses are failing.

It is important to recognize early compensated shock, as it is reversible, in contrast to decompensated shock, which may be irreversible.

Dehydration

The prevention of shock from dehydration relies on its early recognition and treatment. Dehydration is most often from gastroenteritis (see Ch. 14, Gastroenterology), but also from burns, sepsis, diabetic ketoacidosis, diabetes insipidus, and nephrotic syndrome. Even relatively benign problems such as sore throats and fever can contribute to dehydration in young children as they will refuse to drink fluids if swallowing is painful.

Table 6.3 Clinical assessment of dehydration

	No clinical dehydration	Clinical dehydration	Shock
General appearance	Appears well	Appears unwell or deteriorating 	Appears unwell
Conscious level	Alert and responsive	Altered responsiveness, e.g. irritable, lethargic 	Decreased level of consciousness
Urine output	Normal	Decreased	Decreased
Skin colour	Normal	Normal	Pale or mottled
Extremities	Warm	Warm	Cold
Eyes	Normal	Sunken 	Grossly sunken
Mucous membranes	Moist	Dry	Dry
Heart rate	Normal	Tachycardia 	Tachycardia
Breathing	Normal	Tachypnoea 	Tachypnoea
Peripheral pulses	Normal	Normal	Weak
Capillary refill time	Normal	Normal	Prolonged (>2s)
Skin turgor	Normal	Reduced 	Reduced
Blood pressure	Normal	Normal	Hypotension (indicates decompensated)

The more numerous and more pronounced the symptoms and signs, the greater the severity of dehydration.

 'Red flag' sign – helps to identify children at risk of progression to shock.

(Adapted from: *Diarrhoea and vomiting caused by gastroenteritis in under 5s: diagnosis and management*, London, 2009, NICE. Available from www.nice.org.uk/guidance/cg84.)

Infants are at particular risk of dehydration because they have higher body water content, higher metabolic rate and increased surface area-to-body mass ratio than older children or adults, resulting in their high maintenance fluid requirements of 100–120 ml/kg per day, i.e. 10%–12% of body weight.

Clinical assessment of dehydration is difficult (Table 6.3, Fig. 6.7). The most accurate measure of dehydration is the degree of weight loss during the period of illness. Ideally, weights should be measured on the same scales, in the same state of dress, but this information is seldom available. The history and examination are used to classify the degree of dehydration as:

- no clinically detectable dehydration (usually <5% loss of body weight)
- clinical dehydration – 5%–9% loss of body weight
- shock – ≥ 10% loss of body weight.

Fluid resuscitation

Fluid resuscitation refers to the initial rapid re-expansion of intravascular volume using intravenous fluids for shock (Fig. 6.8). This will usually be through the administration of boluses of 10 ml/kg bodyweight of balanced isotonic crystalloids such as Plasma-lyte or Hartmann's solution, or else 0.9% NaCl. In trauma, where blood loss, rather than maldistribution is the likely cause of shock, replacement of circulating volume is with blood and blood products and given in volumes of 5–10 ml/kg. Reassessment of

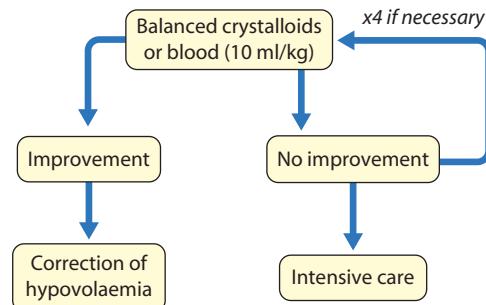


Figure 6.8 Initial fluid resuscitation in shock.

 Children who require more than 40 ml/kg of resuscitation fluid are likely to require mechanical ventilation. A healthcare professional with advanced airway skills should be called for help if multiple fluid boluses are required.

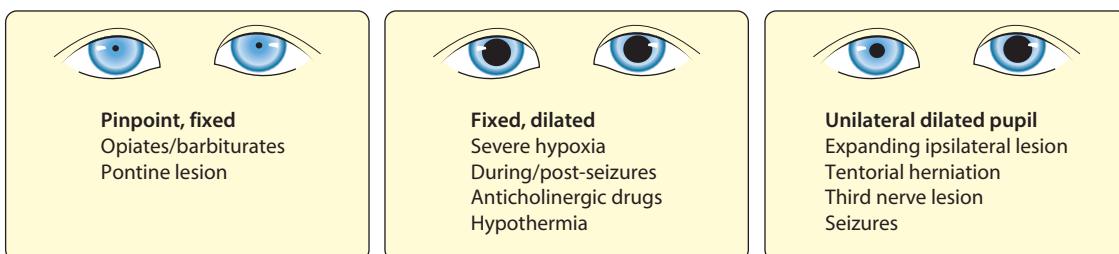
circulatory adequacy following each resuscitation bolus is essential to determine if further boluses are required to avoid the risk of fluid overload. Infants and children with a febrile illness should not be given fluid boluses unless they have clinical signs of shock.

If there is no improvement following initial fluid resuscitation or there is progression of shock and respiratory failure, the child may need mechanical ventilation and intensive care.

Table 6.4 Glasgow Coma Scale, incorporating Children's Coma Scale

	Glasgow Coma Scale	Children's Coma Scale (<4 years)	
	Response	Response	Score
Eye opening	Spontaneous	Spontaneous	4
	To sound	To sound	3
	To pressure	To pain	2
	None	No response	1
Best verbal response	Oriented	Talks normally, interacts	5
	Confused	Words	4
	Words	Vocal sounds	3
	Sounds	Cries	2
	None	None	1
Best motor response	Obeys commands	Obeys commands	6
	Localizing	Localizes pain	5
	Normal flexion	Flexion to pain	4
	Abnormal flexion	Abnormal flexion (decorticate posture)	3
	Extension	Abnormal extension (decerebrate posture)	2
	None	No response	1

A score of <8 out of 15 means that the child's airway is at risk and will need to be maintained.

**Figure 6.9** Pupillary signs in coma.

Fluid management

Following fluid resuscitation, children in shock will require intravenous fluids calculated to correct for dehydration as well as maintenance fluids and ongoing losses and other clinical circumstances. This is explained in [Fig. A.7](#) in the Appendix, together with a clinical example ([Case History A.1](#)). Intravenous fluids are only indicated for shock, severe burns, inability to take fluids enterically or persistent vomiting. Otherwise, rehydration should be enterically.



Falling systolic blood pressure is a late sign of decompensated shock in children; tachycardia is an earlier indicator than hypotension.

- level of consciousness – done rapidly with the AVPU Scale (see [Box 6.1](#) above) or the Glasgow Coma Scale, which has also been adapted for young children ([Table 6.4](#))
- posture – for hypotonia, decorticate or decerebrate
- pupil size and reactivity ([Fig. 6.9](#)).

The causes of coma are listed in [Fig. 6.3](#). It is essential not to omit assessment of neurological status during primary assessment, as reduced consciousness itself may cause airway instability. Also, some causes of coma are reversible, such as hypoglycaemia and opiate toxicity. Seizures, sepsis, meningitis and herpes simplex encephalitis need to be identified and treated.

Raised intracranial pressure will require neuroprotective strategies to reduce secondary brain injury ([Box 6.4](#)).

Disability – disordered consciousness

During primary assessment, disability or neurological status is determined by observing:

Sepsis

In bacteraemia, where bacteria disseminate and proliferate in the bloodstream, the host response includes

Box 6.4 Neuroprotective strategies for raised intracranial pressure to reduce secondary brain injury

- Head positioned midline and tilted up 20° to 30°
- Avoid hypoxia
- Fluid restriction with isotonic fluids
- Intubation and ventilation if Glasgow Coma Scale (GCS) <9
- Maintain normothermia
- Osmotic diuretics (e.g. mannitol) to reduce raised intracranial pressure (ICP)
- Optimize blood pressure to maintain cerebral perfusion
- If intubated, maintain normocapnia (paCO_2 4.5–5.3 kPa)

Box 6.5 Clinical features of sepsis

History	Examination
Fever	Fever or hypothermia
Poor feeding	Tachycardia, tachypnoea, low blood pressure
Miserable, irritable, lethargy	Purpuric rash (meningococcal septicaemia)
History of focal infection, e.g. meningitis, osteomyelitis, gastroenteritis, cellulitis	Shock
Predisposing conditions, e.g. sickle cell disease, immunodeficiency	Multiorgan failure

a release of inflammatory cytokines and activation of endothelial cells. The physiological derangement caused by dysregulation of this response leads to the clinical syndrome of sepsis.

If not identified and treated quickly, sepsis can rapidly result in septic shock, with multiorgan failure and death.

The most common organisms identified from blood culture in children in the UK are *Staphylococcus aureus*, non-pyogenic streptococci, and *Streptococcus pneumoniae* (pneumococcus). The Gram-negative organisms *Neisseria meningitidis* (meningococcus) and *Escherichia coli* are also still prevalent. Sepsis related to *Haemophilus influenzae* type B, meningococcus and pneumococcus have all declined since inclusion of vaccines against them in the immunization schedule.

In neonates, early-onset sepsis is most commonly caused by group B streptococcus and *E. coli*, whereas in late-onset sepsis *coagulase-negative staphylococcus* (*CoNS*) predominates. Whilst *CoNS* is often isolated from blood culture in older children, it is almost always a contaminant from the skin and not a true infection.

Children with underlying health conditions, indwelling catheters and immunodeficiency are at higher risk of infection progressing to sepsis.

Clinical features

See Box 6.5.

Management priorities

Children with septic shock need to be rapidly stabilized and may require transfer to a paediatric intensive care unit.

Antibiotics

Antibiotic therapy must be started without delay. The choice depends on the child's age, the likely pathogen, and any predisposition to infection. Beyond the neonatal period, a broad-spectrum antibiotic such as ceftriaxone is used in most cases, but patients with risk factors for more aggressive or resistant infections (neutropenia,

cystic fibrosis) will require extended-spectrum coverage based on local policies and specialist advice.

Fluids

Severe hypovolaemia is often present in sepsis, caused by maldistribution of intravascular proteins and fluid, due to 'capillary leak'. This occurs as a result of endothelial cell dysfunction secondary to vasoactive mediators as part of the inflammatory response. Urinary catheterization and central venous pressure monitoring may be required to guide the assessment of fluid balance. Capillary leak into the lungs causes pulmonary oedema, which may lead to respiratory failure, necessitating mechanical ventilation.

Circulatory support

Myocardial dysfunction occurs as inflammatory cytokines and circulating toxins depress myocardial contractility. Inotropic support may be required.

Disseminated intravascular coagulation

Widespread inflammation causes microvascular thrombosis throughout the body which consumes both platelets and clotting factors. This can result in subcutaneous bleeding and hence a non-blanching rash. Clotting derangement should be corrected with fresh frozen plasma, cryoprecipitate and platelet transfusions under the guidance of a haematologist or paediatric intensivist.

Summary

Sepsis

- Early recognition, antibiotic therapy and fluid resuscitation for shock are life-saving.
- In septic shock, the child may need admission to paediatric intensive care for management of multiorgan failure.

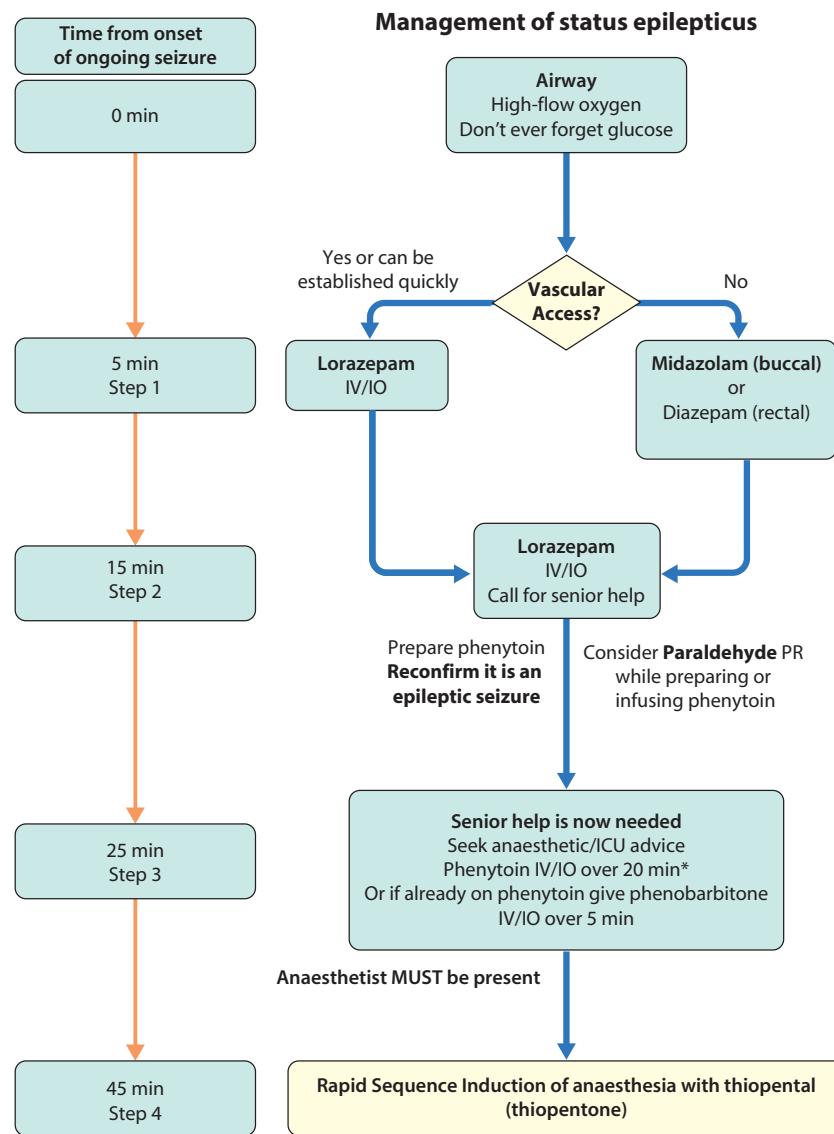


Figure 6.10 Management of status epilepticus. (*Levetiracetam is used in some centres as an alternative to phenytoin). (Adapted from: Advanced Life Support Group. 2016. Advanced paediatric life support: The practical approach, ed 6, Blackwell BMJ Books.)

Status epilepticus

Status epilepticus is defined as a continuous seizure lasting more than 30 minutes, or intermittent clinical or electroencephalographic seizures lasting more than 30 minutes without full recovery of consciousness between seizures.

Early termination of seizures is crucial because those of longer duration are associated with a poorer outcome and can be more resistant to treatment. Therefore, after immediate primary assessment and resuscitation (ABCDE), the priority is to escalate treatment according to guidelines, as in Fig. 6.10. Ensure to treat any reversible causes such as hypoglycaemia or electrolyte disturbance. The aim is to prevent any seizure which is 'prolonged', i.e. lasts 5 minutes or longer, from developing into status epilepticus.

Anaphylaxis

Anaphylaxis is a severe, life-threatening, sudden-onset systemic allergic reaction. Although most reactions do

not result in severe outcomes, in about 1 in 1000 cases it is fatal. Minutes to several hours after exposure to a likely allergen, there is acute onset of one or more of the life-threatening problems listed in Fig. 6.11. There is usually, but not always, acute involvement of the skin and mucosal tissue with generalized urticaria, swollen lips and tongue and uvula. In children, approximately two thirds of anaphylaxis is caused by food allergy. Other triggers such as insect stings or medication are much less common than in adults. Most paediatric anaphylaxis occurs in children under 5 years of age, but the majority of fatalities occur in adolescents with allergy to milk followed by peanut and tree nuts. Asthma is an additional risk factor. No trigger is identified in about 20%. The acute management of anaphylaxis relies on early administration of intramuscular adrenaline. Prevention of future events is considered in Chapter 16 (Allergy). Elevated serum mast cell tryptases may assist in confirming anaphylaxis where the diagnosis is unclear, but a negative test does not rule out anaphylaxis.

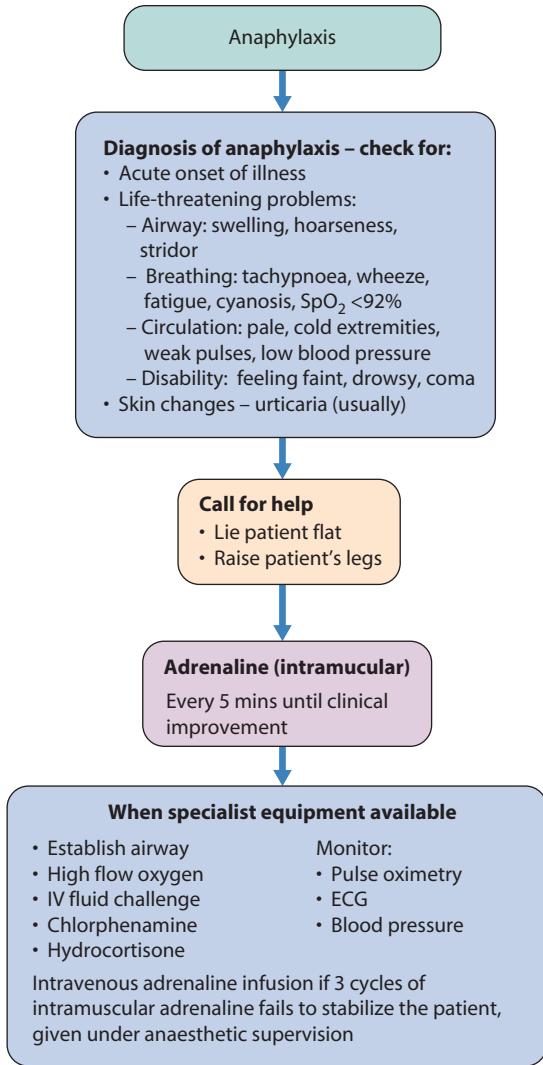


Figure 6.11 Algorithm for acute management of anaphylaxis. (Adapted from: Anagnostou K, Turner PJ. Myths, facts and controversies in the diagnosis and management of anaphylaxis. Arch Dis Child 2019; 104:83–90.)

Summary

Anaphylaxis in children/adolescents

- Reaction is mainly to food – about 1 in 1000 episodes is fatal.
- Acute management is ABCDE and early administration of intramuscular adrenaline.

Brief resolved unexplained events (BRUE)

This term is used to describe a sudden, transient (less than one minute) episode consisting of one or more of the following:

- cyanosis or pallor
- absent, decreased or irregular breathing
- change in tone (increased or decreased)
- altered level of responsiveness.

Box 6.6 Criteria for a low-risk BRUE

- Age >60 days
- Born at 32 weeks' gestation or above
- First BRUE
- Event <1 minute
- No CPR given by a trained medical provider
- No concerning features in the history or examination

In addition, the episode must have resolved completely, and cannot be explained by a thorough history and physical examination.

Many of these episodes were previously called 'apparent life-threatening events' (ALTEs), but this terminology has changed to reflect the fact that the BRUE label is based on the clinician's assessment of the event, rather than the caregiver's perception that an event was life-threatening.

Low-risk BRUEs (Box 6.6) require no more than a period of observation and monitoring of vital signs. Parents or caregivers will need a detailed explanation about the nature of these events and basic life support training offered. An ECG, a pernasal swab for pertussis and a period of continuous pulse oximetry may be considered. Other laboratory and imaging studies are unlikely to be helpful and should not be performed. Infants who have experienced higher risk BRUEs (i.e. do not meet low-risk criteria) require more detailed observation and investigation, as they may represent a serious underlying cause.

Sudden unexpected death in infancy

Deaths that occur suddenly and unexpectedly in infants are termed sudden unexpected death in infancy (SUDI). In some, a previously undiagnosed congenital abnormality, e.g. congenital heart disease, will be found at autopsy or another condition, e.g. inborn error of metabolism, is identified. However, in most instances of sudden death in a previously well infant, no cause is identified even after a detailed autopsy, and the death is classified as sudden infant death syndrome (SIDS). There were 200 such deaths in the UK in 2018 (0.3 per 1000 live births). The peak age is 2–4 months, but it occurs throughout the first year; 55% are boys, and the risk is increased in those who were low birthweight (fivefold) and with mothers under 20 years old (fivefold greater than all other age groups). The vast majority of such deaths, even when occurring more than once in the same family, are due to natural but unexplained causes. Rarely, the death may be due to suffocation, particularly due to unintentional overlying while bed sharing, or from non-accidental injury.

The incidence of SIDS has fallen dramatically in the UK since the national 'Back to Sleep' campaign advising parents to place their infants on their backs to sleep rather than previous widely given advice to lay them prone (Fig. 6.12). Further epidemiological studies have identified additional risk factors, and advice to parents to minimize risk of SIDS is summarized in Fig. 6.13. The management following the death of an infant from Sudden Infant Death Syndrome is outlined in Case History 6.1.

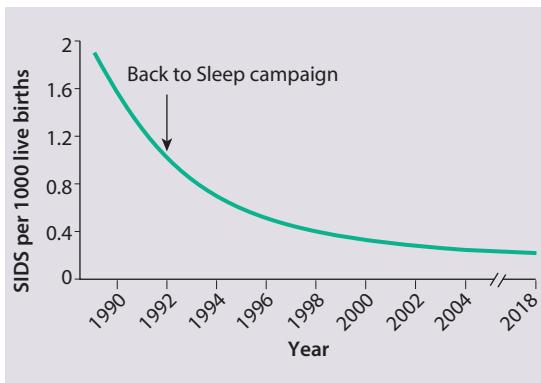


Figure 6.12 Decline in the number of deaths from SIDS in the UK from 1.9/1000 live births in 1989 to 0.3/1000 live births in 2018.



Following a sudden unexpected death in infancy:

- A detailed history and thorough physical examination should be performed by a paediatrician. Postmortem blood and urine samples should be taken according to local policies.
- Good communication between relevant agencies (police, social care, primary healthcare) is essential.
- Parents should be made aware that the Coroner is likely to decide that a postmortem examination will be necessary.
- Parents and family should be offered the opportunity to see and hold the baby and take photographs and gather mementoes.
- Bereavement support should be offered and follow-up arranged.



Figure 6.13 Advice to parents to reduce the risk of SIDS. (Adapted from: Lullaby Trust. www.lullabytrust.org.uk/wp-content/uploads/Safer-sleep-saving-lives-a-guide-for-professionals-web.pdf.)



Case history 6.1

Sudden infant death syndrome

Max, a previously well 9-week-old baby, is found to be still and lifeless by his mother when trying to wake him for a feed in the morning. The previous night he had fed well at midnight although he had coryzal symptoms the previous day. An ambulance is called and Max is rushed to hospital. Basic life support is initiated by the paramedic ambulance crew at the scene.

The team in the children's emergency department is prepared for his arrival. A member of the nursing team is assigned to accompany his mother to a separate room. After 20 minutes of cardiopulmonary resuscitation, he still has no signs of life, and resuscitation attempts are halted.

Max's father had been called to come directly to the hospital. The paediatrician records a comprehensive account of the resuscitation, the history from the

paramedics and findings on complete physical examination, including the absence of signs of external injury. An unexpected death occasions police involvement and a member of the police child protection team accompanies the paediatrician who explains to the parents what has happened and takes a detailed history from each of them.

The parents are offered the opportunity to see and hold their baby and to take photographs and gather mementoes. They are reassured that involvement of the police and social services is standard practice. The local coroner is informed and a multiagency information sharing meeting is convened to discuss the death. A postmortem is performed by a paediatric pathologist, which does not identify a definitive cause of death and a label of SIDS is applied. Follow-up with a paediatrician and bereavement support is arranged.

Summary

Sudden infant death syndrome

- SIDS is the most common cause of death in children aged 1 month to 1 year.
- The peak age for the occurrence of SIDS is 2–4 months.
- SIDS has been dramatically reduced by advice on safe sleeping, particularly lying babies on their back to sleep.

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Further reading

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Resuscitation Council (UK): Guidelines on paediatric life support, London, 2015, Resuscitation Council.

Royal College of Pathologists: Sudden unexpected death in infancy: Multi-agency guidelines for care and investigation, 2016. Available at: www.rcpath.org/uploads/assets/874ae50e-c754-4933-995a804e0ef728a4/Sudden-unexpected-death-in-infancy-and-childhood-2e.pdf.

Websites

Anaphylaxis: <http://www.anaphylaxis.org.uk>. Provides information and support for families affected by anaphylaxis.

Resuscitation Council (UK): www.resus.org.uk.

The Lullaby Trust: <http://www.lullabytrust.org.uk/safer-sleep-advice/what-is-sids>. Provides information about SIDS (Sudden Infant Death Syndrome) and emotional support for bereaved families.

Accidents and poisoning

Accidents 99

Poisoning 107

Features of accidents and poisoning in children and young people:

- Accidental injury is the most common reason for children and young people to seek emergency healthcare.
- Poisoning in young children is usually accidental, in contrast to the deliberate self harm of young people and adults.

Accidents and poisoning are classified as external causes of morbidity and mortality as they are entirely dependent on the presence of an extrinsic environmental factor; for example, a motor vehicle or a swimming pool. Although external causes are the leading cause of death in 1-year-old to 15-year-old children worldwide, they have declined sufficiently in the UK now to be the second most frequent cause, after malignant diseases (Fig. 7.1). However, external factors remain the most common cause of death of 15- to 19-year-olds in the UK.

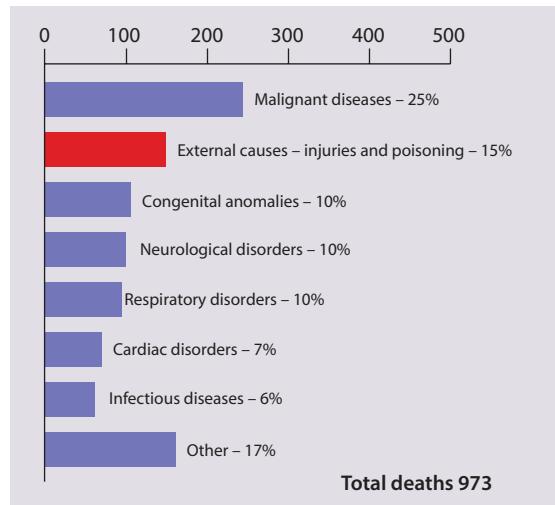


Figure 7.1 Cause of death in children aged 1 year to 15 years in England and Wales in 2018. (Data from: Office of National Statistics, 2020.)

Accidents

Approximately 2 million children and young people attend an emergency department with an accidental injury each year in the UK. Fortunately, the majority suffer only minor and temporary damage; however, a small proportion sustain significant injuries with life-changing consequences from disability, disfigurement and psychological harm, and for a few it is fatal (Fig. 7.2).

Different types of accident are prevalent at different ages, relating to the child's development. Accidental injuries to preschool children most commonly occur in the home, as a result of their natural inquisitiveness, poor stability and lack of awareness of risk. Typical injuries include falls down steps and trapping fingers in doors. By school age, accidents are more likely to occur outside the home; in particular, injuries from road traffic collisions are the leading cause of serious injury, accounting for over half of accidental deaths in children aged 5–14 years. The

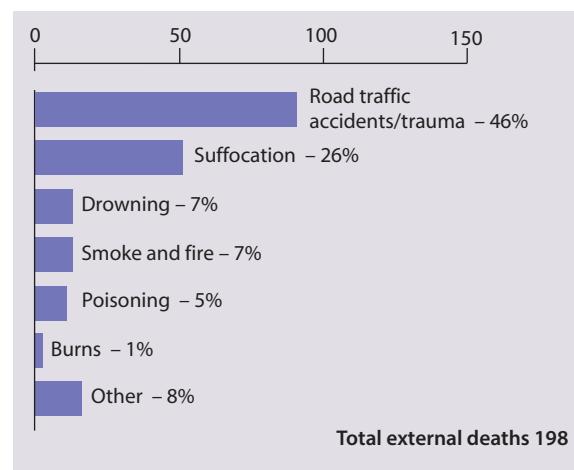


Figure 7.2 External causes of death in children aged 1 to 14 years in England and Wales in 2015. (Data from: Office of National Statistics, 2018.)

majority of these children are as pedestrians or cyclists. Older children and young people may indulge in risk-taking behaviour and underestimate the magnitude of any associated danger.



Accidents are the second most common cause of death in children 1 to 15 years of age in England and Wales, but the commonest cause worldwide.

Accident prevention

Accident prevention is an important public health issue. Primary prevention strategies relate to the avoidance of the event causing the injury in the first place. Secondary prevention strategies relate to injury control after an event and include the provision of appropriate healthcare services for the treatment of the injured child – for example, specialized trauma and burn services, with subsequent tailored rehabilitation.

Primary accident prevention strategies typically tackle three main factors:

- modification of product design, e.g. for road traffic accidents, vehicle child restraint design, and legislation change
- alteration of the environment, e.g. reduction in speed limits or road layout design
- education of children and their carers, e.g. school safety campaigns.

Specific examples of these are shown in **Figure 7.3**. Healthcare professionals are well placed to deliver anticipatory guidance as well as to identify and publicize risk factors. Implementation is usually more successful when

supported by legislative and environmental change, rather than education alone. For example, Norway and Sweden have both implemented 'Vision Zero', a safety project that aims to eliminate fatalities and serious injuries involving road traffic. After instigating multiple interventions since 2001, Oslo achieved zero pedestrian and cyclist deaths in 2019.



The number of deaths of children in the UK due to accidental injury has declined steadily over the last 25 years.

The seriously injured child

A structured approach to major trauma ensures that life-threatening injuries are identified and managed during the 'primary survey'. In trauma, catastrophic haemorrhage should be dealt with immediately, before the usual ABCDE approach (**Fig. 7.4**).

Life-threatening injuries that need to be identified during the primary survey include:

- Airway obstruction
- Tension pneumothorax
- Open pneumothorax
- Massive internal or external haemorrhage
- Flail chest
- Cardiac tamponade.

Cervical spine injury should be assumed; the preferred method of immobilization is manual in-line stabilization (holding the neck in a midline neutral position) followed by head blocks and straps if necessary. Application of cervical collars is no longer recommended, as children often wriggle around in them, which puts their neck at risk.

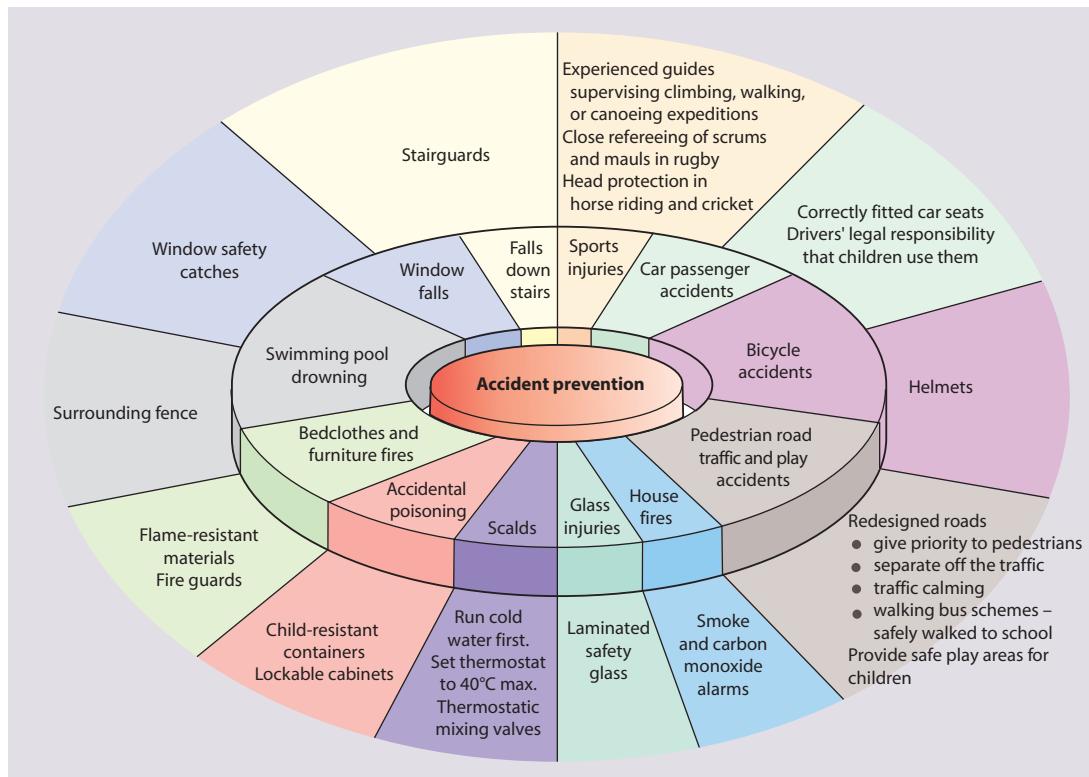


Figure 7.3 Examples of accident prevention.

Management of the seriously injured child

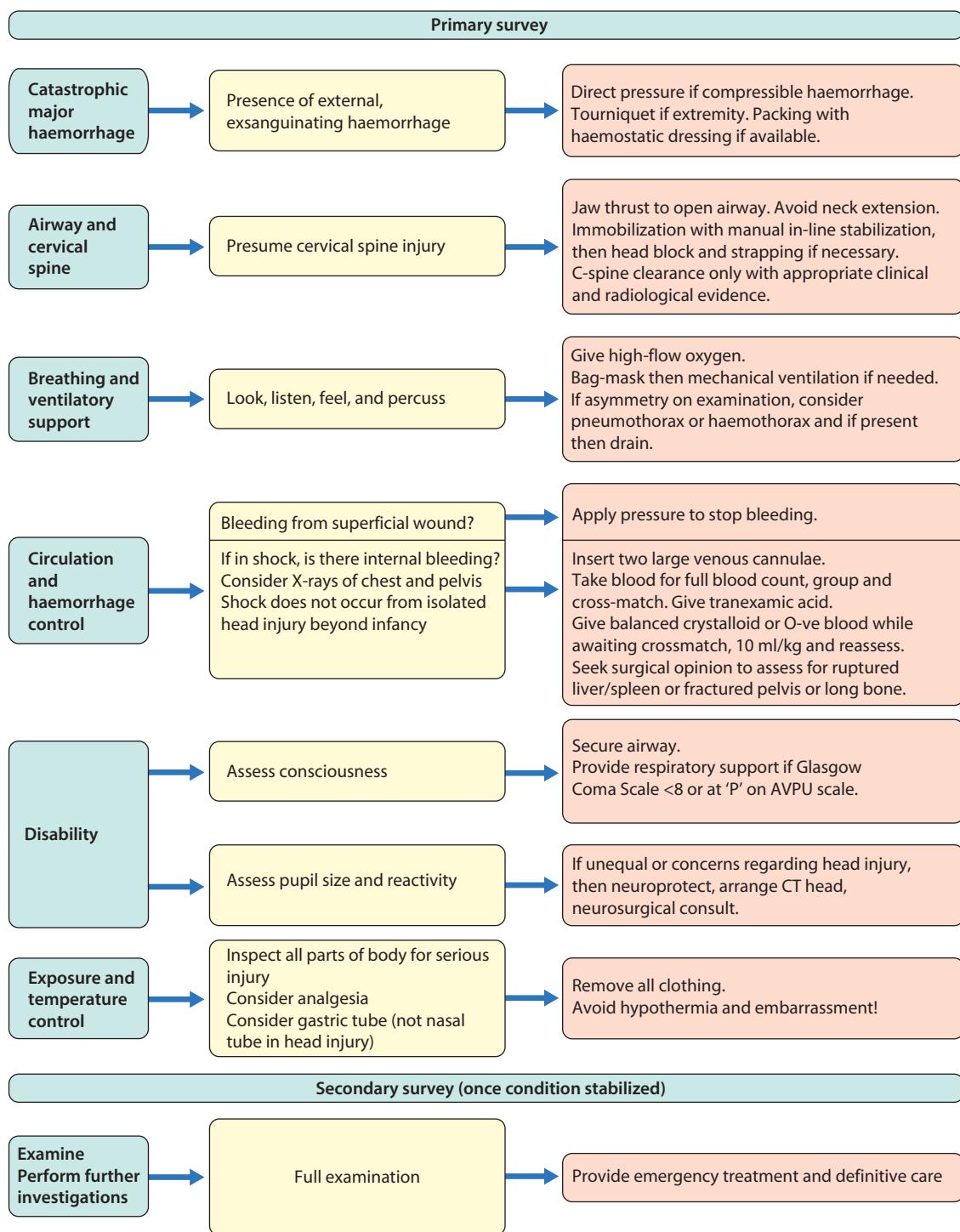


Figure 7.4 Management of the seriously injured child.

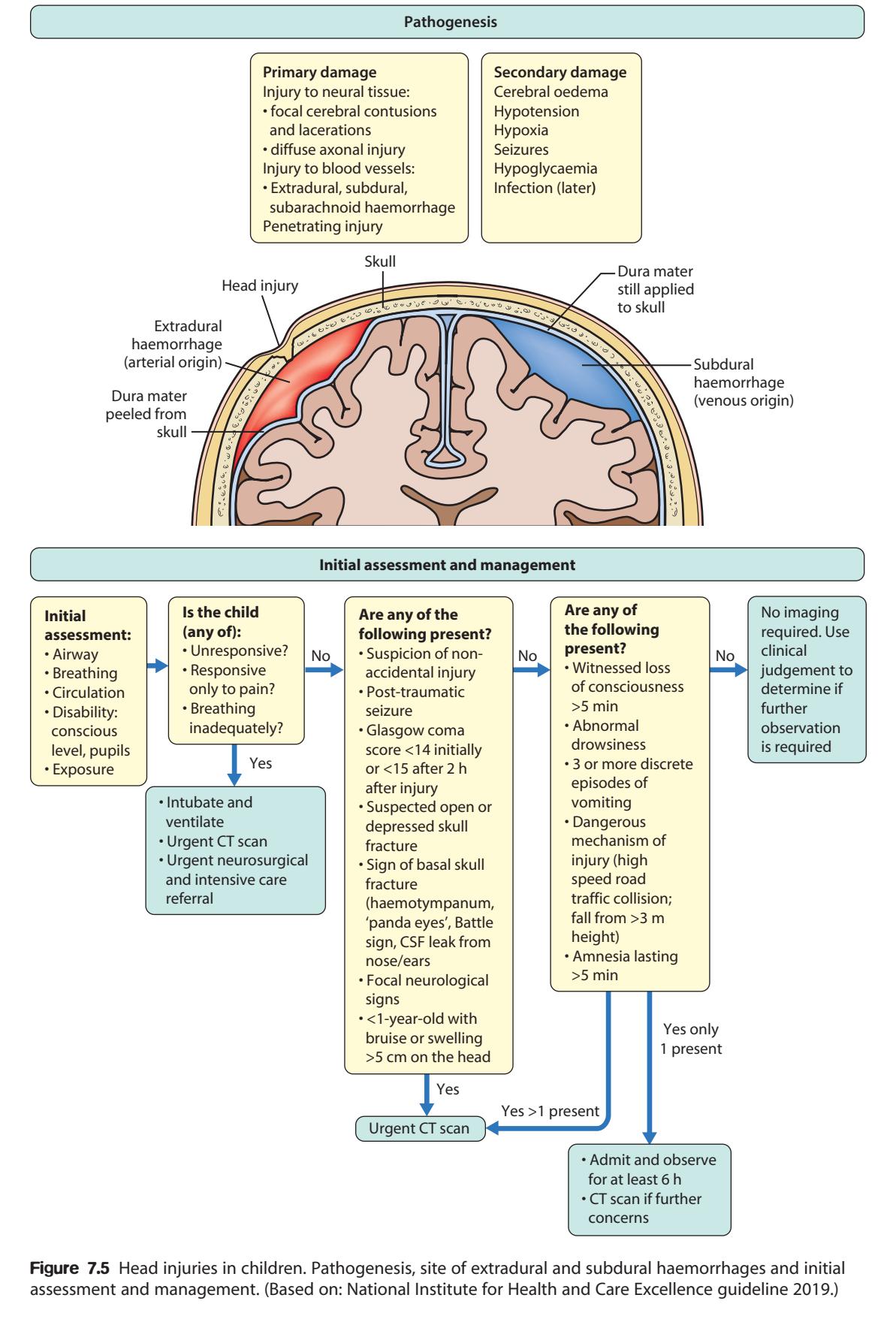
A 'secondary survey' of all injuries is performed once the patient is stabilized. This will include minor injuries, lacerations and less obvious fractures.

Head and neck injuries

Head injury is common in children. Fortunately, in the vast majority it is only minor and a full recovery with no long-term adverse effects can be expected. However, it is also the most frequent cause of death and serious

morbidity in children who have been injured. Initial assessment is therefore directed at identifying the small proportion of children who are likely to have sustained an intracranial injury, and thus need neuroimaging. This assessment is based on the history and neurological condition of the patient. Various clinical guidelines have been developed to help determine which children need brain imaging (Fig. 7.5 and Case history 7.1). These decisions tend to be highly sensitive but not highly specific, resulting in many normal CT scans for every scan that identifies a significant injury.

Head injuries in children





Case history 7.1

Head injury

Tom, a 3-year-old boy, is being carried on his uncle's shoulders when he falls two metres to the ground, banging his head on the concrete floor. He cries immediately but does not lose consciousness. He is taken to the emergency department where he vomits once. Clinical examination is normal apart from a 4-cm diameter firm swelling over his left temple. After a period of observation, Tom is discharged home with advice to return if he:

- vomits repeatedly
- complains of a worsening headache
- becomes abnormally sleepy
- behaves abnormally
- develops weakness of one side of his body.

Tom remains well overnight but the following morning begins to vomit again and becomes lethargic. He is brought back to the emergency department where a CT brain scan reveals an extradural haematoma (Fig. 7.6). Tom's haematoma is evacuated by the neurosurgeons, and he makes an uneventful recovery.

This illustrates how children with a significant head injury may appear normal at initial presentation. It is essential to provide parents and caregivers with safety net advice to ensure they know to return should symptoms evolve.

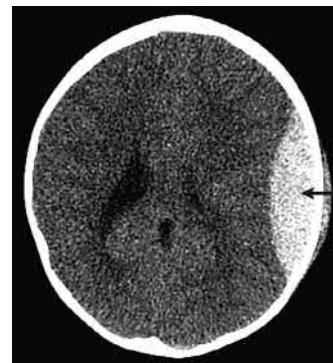


Figure 7.6 CT scan of head showing a left extradural haemorrhage (arrow).

Management

Once an intracranial injury is identified, the aim of management is to avoid secondary damage to the brain by maintaining its blood supply and minimizing the damage from raised intracranial pressure. This may include:

- tranexamic acid to reduce bleeding
- intravenous mannitol or hypertonic saline to reduce intracranial pressure
- surgical evacuation of intracranial haemorrhage
- intubation and ventilation to allow control of blood pressure and blood carbon dioxide levels, both of which affect cerebral perfusion.

In infants with skull sutures that have not yet fused, marked bleeding into the brain and surrounding space may lead to shock before any neurological symptoms and signs appear. Unexplained head injury in young infants must always lead to consideration of the possibility of non-accidental injury.

Children with severe traumatic brain injury can make a good physical recovery, though the period of rehabilitation may be long. Cognitive, behavioural, and mental health problems are common in these children, however, and specialist follow-up is required.

Neck injury resulting in spinal cord damage is rare in children and usually only associated with high impact trauma such as high-speed road traffic collisions. The most common neck injury is fracture of the upper two cervical vertebrae. The elasticity of the cervical spine can also allow damage to the spinal cord to occur without injury to the bony structures, termed 'SCIWORA' (spinal cord injury without radiologic abnormality).

Summary

Head injury management

- No symptoms or signs and benign mechanism of injury – discharge home with written advice.
- Minor symptoms or dangerous mechanism of injury – monitor for evolution of symptoms.
- Significant or progressive symptoms and signs – resuscitate (if necessary), CT scan, and surgical/neurosurgical referral as appropriate.

Internal injuries

Internal injuries in children are usually associated with high impact trauma due to road traffic collisions and falls from significant heights. In particular, young children have less fat and a more elastic skeleton protecting tightly packed internal organs. This means that impact force is distributed widely through the body, resulting in a greater possibility of multisystem trauma compared with adolescents or adults.

Abdominal injuries are typically caused by blunt trauma due to seat belt restraints or bicycle handlebars. Liver and spleen rupture may occur and become apparent rapidly, while bowel and pancreatic injuries may take longer to become evident. Close observation and imaging are necessary.

There is a very limited evidence base for focused abdominal sonography in trauma (FAST) scan in a child presenting with trauma; it is operator-dependent and only available in some centres. CT imaging is more sensitive

and specific and should be performed if there is a suspicion of internal organ injury based on the mechanism of injury or clinical signs. Bruising of the abdominal wall is highly suggestive of internal injury.

Contained splenic and hepatic haematomas can be managed conservatively but rapid access to paediatric surgery must be available immediately in the event of clinical deterioration.

Chest injuries, including pneumothorax and haemopericardium, are also typically due to blunt trauma. The pliable rib cage in children may allow significant injury to underlying organs with little external evidence; additionally, rib fractures may perforate internal organs. There must be a high index of suspicion for these injuries in the event of a significant mechanism of injury.



Assessment of circulation ('C') in trauma includes abdominal examination, assessment for pelvic bony injury, and identification of any suspected long bone fractures (and intracranial injuries in infants), as large volumes of blood can be lost into these body cavities.

Choking, suffocation and strangulation

Young children are prone to choking. Toddlers have a natural tendency to put objects in their mouths, and their airway diameter is small and hence more readily occluded. Food is the most common cause of non-fatal choking, followed by toys. The emergency management of the choking child is outlined in [Figures 7.7 and 7.8](#).

The choking child

Management of the choking child

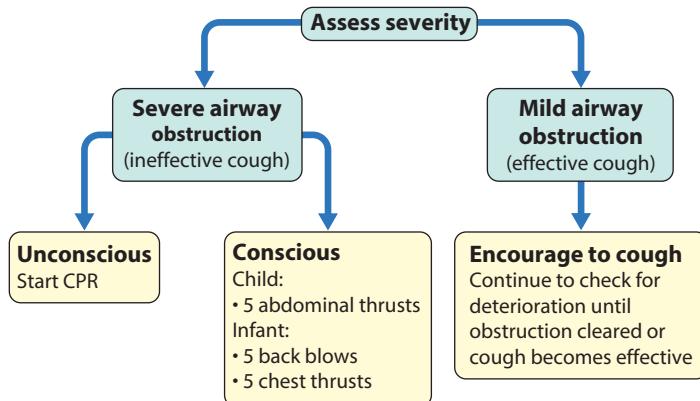


Figure 7.7 Management of the choking child from a foreign body airway obstruction (FBAO).

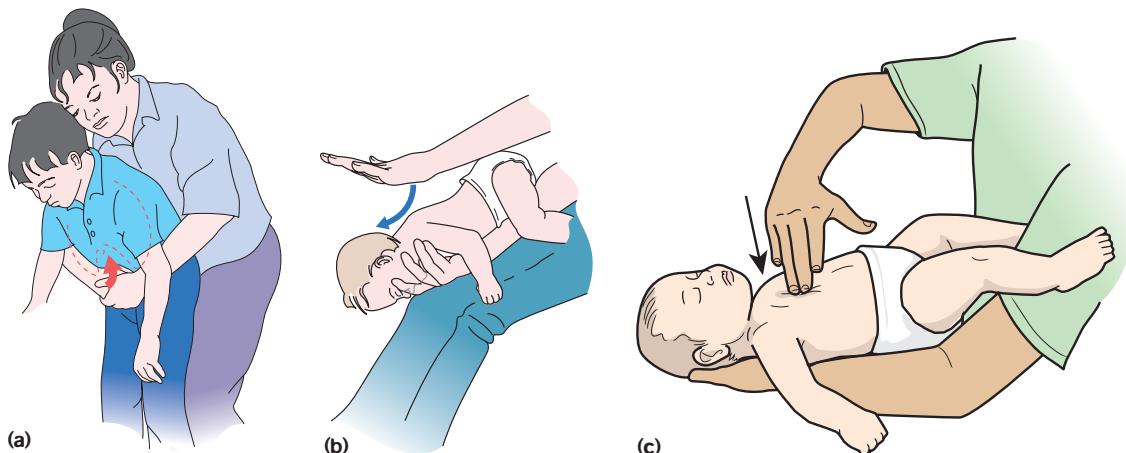


Figure 7.8 (a) Abdominal thrusts (Heimlich manoeuvre) in older children – place a fist against the child's upper abdomen in the midline and grasp with the other hand. Pull backwards and upwards to expel air from the lungs. In infants, back blows (b) and chest thrusts (c) are recommended, avoiding abdominal thrusts due to the risk of injury to the liver and spleen.

Accidental suffocation can occur as a result of playing with plastic bags or packaging. Young children may strangle themselves accidentally when clothes or bedding gets caught on furniture. Product safety initiatives and public education campaigns aim to eliminate these tragic accidents. Strangulation can also be a form of non-accidental injury. In adolescents, it is also a method of attempting suicide. Survivors of strangulation may exhibit dysphonia (hoarseness), difficulty swallowing, facial petechiae and neck oedema. Depending on the duration of the asphyxia, hypoxic brain damage may occur.

Drowning

Drowning, the respiratory impairment produced by submersion or immersion in liquid, causes a number of accidental deaths in children each year. Babies and toddlers tend to drown in domestic situations: baths, paddling pools, or garden ponds. Older children get into difficulty away from home: in canals, lakes, and the sea. Once submerged, asphyxiation occurs with or without aspiration of water. Up to 30% of fatalities can be avoided by skilled on-scene resuscitation. If the water is cold, the resulting hypothermia can have a protective effect and, even in the presence of fixed dilated pupils, resuscitation should continue until the child is warmed up to a normal body temperature, as recovery may still be possible.

Burns and scalds

Burns and scalds are relatively common in children and young people, owing to the natural inquisitiveness and lack of sense of danger in young children, and the risk-taking behaviour of adolescents. Most burns in children and young people are minor. Major burns are a significant cause of death worldwide (although typically deaths in house fires are due to asphyxiation). Inhalation of superheated smoke or steam may cause significant airway swelling. Injuries from house fires may also be complicated by serious injury as a result of, for example, falls from a height during escape. For all burns, the possibility of non-accidental injury must be considered (see Ch. 8, Child protection).

Burn first aid

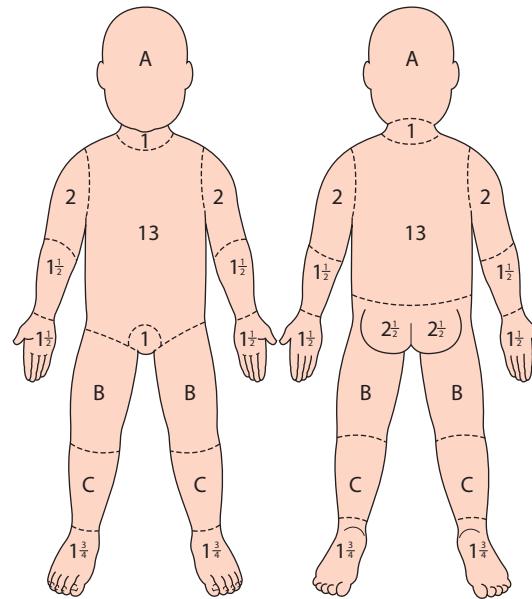
This comprises:

- Pain relief to be provided immediately; intranasal opiates are very useful, as they work quickly and do not require venous access.
- Cool the area with running water for 20 minutes but avoid hypothermia (which causes vasoconstriction and may worsen the burn injury).
- Cool running water is still effective up to four hours post burn, so if the child presents to the emergency department having had the burn placed under running water for 5 minutes at home, ensure to make up the remaining 15 minutes.
- Plastic (cling film) wraps can be used after cooling to limit evaporation from the burnt area and provide pain relief.
- Chemical burns should be copiously irrigated.

Estimation of burn surface area

The percentage body surface area which is burned is the best guide to severity and management:

- A burn diagram should be used (such as the Lund and Browder chart (Fig. 7.9), or an app that allows the user to calculate surface area by colouring in a body map on a mobile device or tablet computer).
- As a rough measure, an area the size of the child's palm and outstretched fingers represents 1% of that child's body surface area.
- The 'rule of nines' can be used to estimate surface area when a map is not available (Table 7.1).



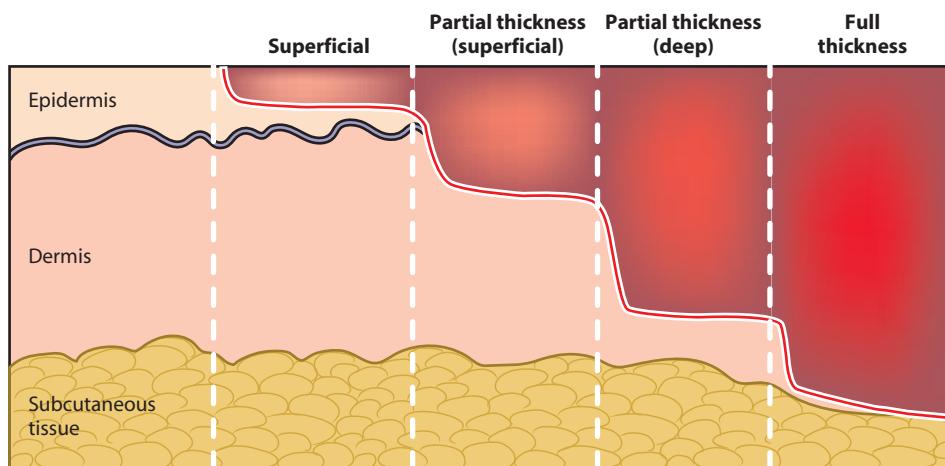
Area indicated	Surface area at			
	1 year	5 years	10 years	15 years
A	8.5	6.5	5.5	4.5
B	3.25	4.0	4.5	4.5
C	2.5	2.75	3.0	3.25

Figure 7.9 Lund and Browder chart for accurate assessment of body surface area.

Table 7.1 Rule of nines for body surface area estimation.

Body Area	Body Surface Area
Whole limb	9%
Face	9%
Back of head	9%
Chest (front and back)	18%
Abdomen (front and back)	18%
Genitalia	1%

The depth of burns



Depth	Superficial – limited to epidermis	Partial thickness (superficial)	Partial thickness (deep)	Full thickness
Possible cause	Sunburn, minor scald	Scald	Scald, brief contact with flame	Significant flame contact
Appearance	Dry and erythematous	Moist, erythematous, blistered	Moist with white slough, erythematous, mottled	Dry, charred, white
Pain sensation	Painful	Painful	Painful or painless	Painless
Healing	Rapid – 1 week	1–3 weeks	3–4 weeks – often requires grafting	Needs skin grafting to heal

Figure 7.10 Burn depth assessment.

- Areas which are only erythematous (i.e. superficial epidermal burns) are NOT included in the body surface area calculation.
- Burns affecting over 10% body surface area require admission (usually to a specialist centre) and careful intravenous fluid management.

Burn depth assessment

This should also be carried out (Fig. 7.10) but will need to be repeated as the burn injury can evolve and initial assessment can over- or underestimate the extent of the burn. Laser Doppler Imaging (LDI) is a sensitive and specific tool to allow non-invasive assessment of burn depth.

Major burns

Immediate assessment of major burns comprises:

- airway and breathing – in particular, check for evidence of airway burns:
 - soot in the nasal and oral cavities
 - cough, hoarseness, or stridor
 - coughing up black sputum
 - breathing and/or swallowing difficulty
 - blistering around or in the mouth
 - scorched eyebrows or hair

- early intubation if there is evolving airway swelling; intubation may become impossible with progressive obstruction of the airway
- circulation:
 - early circulatory compromise is rarely due to the burn injury and other sources of fluid loss should be sought (e.g. major haemorrhage)
 - in electrical burns, an ECG should be obtained
 - maintain circulation – additional intravenous fluids are required if over 10% of the body surface area is affected (calculated by the ‘Parkland formula’; see [Appendix](#))
 - monitor urine output to best assess the adequacy of fluid replacement.

Further management

This should be directed at:

- relieving pain – assess with pain score; intravenous analgesia such as morphine or ketamine is often required on an ongoing basis
- provision of wound care:
 - superficial burns with erythema only are treated with simple exposure

- small, superficial partial-thickness burns can be cleaned, debrided and dressed with a non-adherent dressing. Antibiotics should not be started prophylactically. Superficial partial thickness burns should heal spontaneously, but require review
- signs of infection should be monitored, as there is a risk of invasive infection and toxic shock syndrome (see Ch. 15, Infection and immunity) even with small burns. A child who has had a burn and develops signs such as fever, vomiting, diarrhoea, rash, or lethargy, needs urgent medical assessment
- psychological support should be provided if required, as psychological sequelae of severe burns are often marked and long-lasting.

Burns that require specialist burns service review

These are:

- partial-thickness burns covering 5% or more of the body surface area
- deeper partial-thickness burns, and full-thickness burns (deeper burns will often require debridement and skin grafting to ensure a good cosmetic outcome)
- all burns (of any size or depth) to the face, ears, eyes, hands, feet, genitalia, perineum, nipples, or a major joint.

Summary

Burns management

- Provide prompt and effective analgesia.
- Cool the burn for a total of 20 minutes, within 4 hours of injury.
- Estimate body surface area and depth of burns.
- Refer to specialist burns services if deep and/or extensive burns or burns to sites where scarring would be particularly troublesome or disfiguring.
- Additional fluid replacement is required for major burns.
- Consider the possibility of non-accidental injury.
- Do not start prophylactic antibiotics.

Poisoning

Poisoning in children may be:

- accidental – common in young children
- due to deliberate self-harm or experimentation with recreational substances – by adolescents
- iatrogenic – as a result of drug errors occasionally made by health professionals
- intentional – by parents or carers, though this is rare.

Accidental poisoning usually occurs when young children are found by parents or carers either playing with tablets or household or garden substances or with some in their mouths. The peak age is 30 months, and typically exposure occurs in the child's home. Serious harm is uncommon as many common household substances

and medications are of low toxicity, and children usually ingest only small amounts. A small number of medicines (including antihypertensives and antidepressants commonly prescribed to adults) are potentially fatal to young children even in small doses. The most common causative agents vary from country to country due to differing availability of medications over the counter, and a variation in rural and urban lifestyles, e.g. lamp oil ingestion is a frequent cause of childhood poisoning in some rural areas where electricity supply is limited. The relative toxicity of some common medicines and household and garden substances is shown in Table 7.2.

Accidental ingestion of button batteries also has the potential to cause serious harm, as they can discharge a small electrical current and erode through gastric tissue causing bleeding and strictures. Small magnets run the risk of clamping together with bowel wall trapped between them, causing ischaemic damage and perforation. If more than one magnet is swallowed, urgent surgical referral is required.

There has been a marked reduction in the incidence of severe poisoning from accidental ingestion by young children. Reasons for this include:

- the introduction of child-resistant containers for many medicines and household products and use of blister packs for medicines
- reduction in the number of tablets available per pack in analgesics bought over the counter.

Adolescents attempting self-harm typically ingest medications commonly found in their environment – most often paracetamol and ibuprofen. However, they are likely to have ingested much larger quantities of tablets than young children and are therefore more likely to suffer significant toxicological effects. Some adolescents experiment with toxic substances which may or may not be illegal to purchase. Recreational drugs vary greatly in their potency and effects: even the most careful experimentation can go wrong. Wherever possible, perform a HEADS assessment (see Ch. 30, Adolescent medicine) to determine whether alterations in consciousness, appetite, and behaviour could be related to recent use of drugs such as cannabis products.

Investigation and management

An approach to the investigation and management of the potentially poisoned patient is outlined in Figure 7.11. Details of some of the more commonly ingested poisons with their specific management are detailed in Table 7.3. Usually, the identity of the ingested substance is known. Use of a poisons information service will assist in guiding assessment and management ('ToxBase' in the UK). Occasionally, poisoning is suspected but the substance is unknown; clinical signs may then help to identify the class of causative agent (Table 7.4). Following paracetamol and salicylate poisoning, blood levels can help to guide management (Case history 7.2).

Young children who have been exposed to agents of low toxicity and are asymptomatic can usually be discharged with advice to return if symptoms develop. The circumstances surrounding the exposure need to be considered to determine if there are social issues such as inadequate supervision that need to be addressed.

All older children and young people who have attempted to deliberately harm themselves must be

Table 7.2 Relative toxicity following ingestion of some common medicines and household and garden substances

Toxicity	Medicines	Household products	In the garden
Low	Oral contraceptives, most antibiotics, topical hydrocortisone	Liquid soap, lipstick, washing-up liquid, fish food, water-based glue and paint	Animal faeces, slugs, geraniums, compost
High	Opioids, beta-blockers, tricyclic antidepressants, oral hypoglycaemics, paracetamol, digoxin, iron, salicylates	Strong bleach, concentrated oven cleaner, liquid nicotine (e.g. for e-cigarettes), ethylene glycol (antifreeze), petroleum distillates	Laburnum, death cap mushroom, yew, foxglove, organophosphorus pesticides, kerosene

Management of a poisoned child or young person

Outline of management

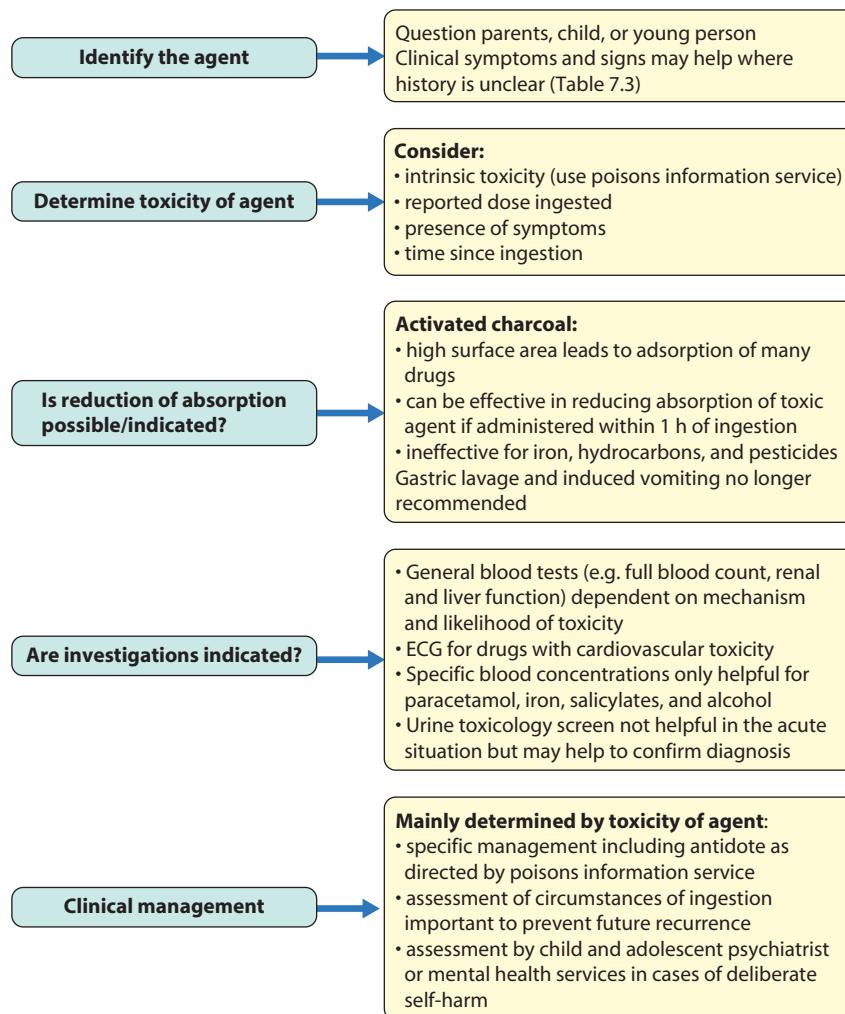
**Figure 7.11** Outline of management of poisoning.

Table 7.3 Some poisons and their treatment

Agent	Clinical symptoms	Mechanism	Management
Paracetamol	Early: <ul style="list-style-type: none">• abdominal pain, vomiting Later (12 h to 24 h): <ul style="list-style-type: none">• liver failure	Initial gastric irritation Toxic metabolite (NAPQI) produced by saturation of liver metabolism	Risk assessed by measuring plasma paracetamol concentration Treat with intravenous acetylcysteine if concentration is high or liver function abnormal
Button batteries	Abdominal pain Gut perforation and stricture formation	Corrosion of gut wall due to electrical circuit production of caustic hydroxide	X-ray of chest and abdomen to confirm ingestion and identify position Endoscopic removal is recommended if in the oesophagus, the object fails to pass, or symptoms are present (e.g. abdominal pain or melaena)
Carbon monoxide	Early: <ul style="list-style-type: none">• headache, nausea Later: <ul style="list-style-type: none">• confusion, drowsiness leading to coma	Binds to haemoglobin causing tissue hypoxia	High-flow oxygen to hasten dissociation of carbon monoxide The role of hyperbaric oxygen therapy is unclear
Salicylates (e.g. aspirin, oil of wintergreen)	Early: <ul style="list-style-type: none">• vomiting, tinnitus Later: <ul style="list-style-type: none">• respiratory alkalosis followed by metabolic acidosis	Direct stimulation of respiratory centre Uncouples oxidative phosphorylation leading to metabolic acidosis and hypoglycaemia	Plasma salicylate concentration 2–4 h after ingestion helps to estimate toxicity Alkalization of urine increases excretion of salicylates Haemodialysis also effectively removes salicylate
Tricyclic antidepressants	Early: <ul style="list-style-type: none">• tachycardia, drowsiness, dry mouth Later: <ul style="list-style-type: none">• arrhythmias, seizures	Anti-cholinergic effects, interference with cardiac conduction pathways	Treatment of arrhythmias with sodium bicarbonate Support breathing
Ethylene glycol (anti-freeze)	Early: <ul style="list-style-type: none">• intoxication Later: <ul style="list-style-type: none">• tachycardia, metabolic acidosis leading to renal failure	Production of toxic metabolites that interfere with intracellular energy production	Fomepizole inhibits the production of toxic metabolites; alcohol may also be used but has more adverse effects Haemodialysis to remove toxic metabolites in severe cases
Alcohol (accidental or experimenting by older children)	Hypoglycaemia Coma Respiratory failure	Direct inhibitory effect on glycolysis in the liver and neurotransmission in the brain	Monitor blood glucose and correct if necessary. Support ventilation if required Blood alcohol levels may help to predict severity
Iron	Initial: vomiting, diarrhoea, haematemesis, melaena, acute gastric ulceration Latent period of improvement 6–12 h later: drowsiness, coma, shock, liver failure with hypoglycaemia, and convulsions Long term: gut strictures	Local corrosive effect on gut mucosa Disruption of oxidative phosphorylation in mitochondria leads to free radical production, lipid peroxidation, and metabolic acidosis	Serious toxicity if >75 mg/kg elemental iron ingested Serum iron level 4 h after ingestion is the best laboratory measure of severity Intravenous deferoxamine chelates iron and should be administered in cases of moderate-to-severe toxicity

Continued

Table 7.3 Some poisons and their treatment (*continued*)

Agent	Clinical symptoms	Mechanism	Management
Hydrocarbons (e.g. paraffin, kerosene)	Pneumonitis Coma	Low viscosity and high volatility facilitates aspiration, resulting in direct lung toxicity Direct inhibitory effect on neurotransmission in the brain	No specific antidote – supportive treatment only
Organophosphorus pesticides	Cholinergic effects: <ul style="list-style-type: none">• salivation, lacrimation, urination, diarrhoea and vomiting, muscle weakness, cramps and paralysis, bradycardia and hypotension Central nervous system effects: <ul style="list-style-type: none">• seizures and coma	Inhibition of acetylcholinesterase resulting in accumulation of acetylcholine throughout the nervous system	Supportive care Atropine (often in large doses) as an anticholinergic agent Pralidoxime to reactivate acetylcholinesterase

NAPQI, *N*-acetyl-*p*-benzoquinone imine.**Table 7.4** Physical findings that may help identify different classes of drugs in overdose

Type of effect	Heart rate and blood pressure	Respiratory rate	Temperature	Pupils	Sweating
Anticholinergic (e.g. tricyclic antidepressants, antihistamines)	Increased	No effect	Increased	Dilated	Reduced
Opioid (e.g. morphine, codeine)	Reduced	Reduced	Reduced	Constricted	Reduced
Sympathomimetic (e.g. cocaine, amphetamines)	Increased	Increased	Increased	Dilated	Increased
Sedative-hypnotic (e.g. anticonvulsants, benzodiazepines)	Reduced	Reduced	Reduced	No effect	Reduced



Case history 7.2

A 3-year-old girl with paracetamol overdose

Amira a 3-year-old girl, is brought to the emergency department by her mother. Amira's 5-year-old brother had complained of tummy ache and their mother had administered some liquid paracetamol. When her mother's back was turned, Amira had drunk an unknown quantity directly from the bottle – her mother knows that the bottle was full originally, but not how much was ingested, as there was syrup around Amira's mouth, and some spillage. However, the maximum possible dose received is estimated to be potentially toxic.

Four hours after the ingestion, blood tests were sent for liver function, INR and a serum paracetamol concentration. The serum paracetamol concentration was plotted on a nomogram (Fig. 7.12). Amira's concentration plots below the treatment line indicating no treatment is required.

Health visitors were contacted to provide an accident risk assessment in the home and offer Amira's mother health promotion advice in relation to safe storage of medication.

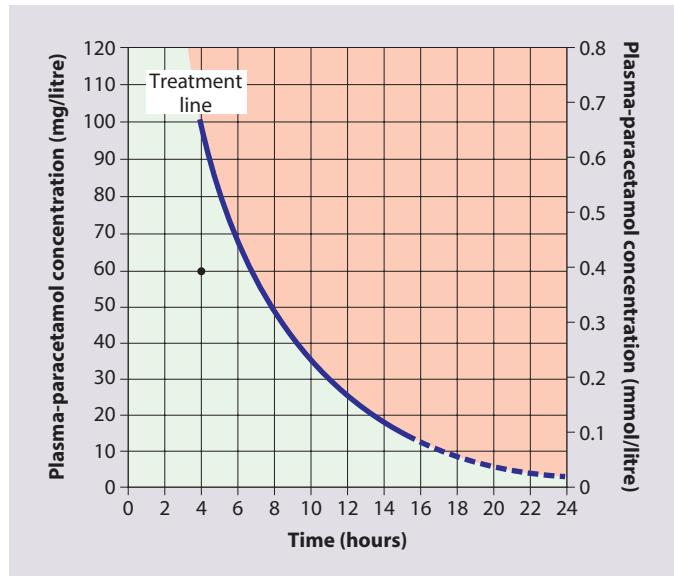


Figure 7.12 Paracetamol overdose nomogram. If the paracetamol level is on or above the line, *N*-acetyl cysteine treatment should be started. (Reproduced courtesy of Medicines and Healthcare Products Regulatory Agency, British National Formulary for Children.)

assessed for risk of a repeated attempt, irrespective of the toxicity of the ingested substance. Liaison with Child and Adolescent Mental Health services is essential. The risk of recurrence is increased by a number of factors, including ongoing thoughts of self-harm or suicide, a lack of regret, evidence of planning, e.g. leaving a note, and a lack of protective social factors. The social circumstances of young people who inadvertently poison themselves as a result of experimentation with illicit drugs or alcohol should also be explored, with onward referral to substance misuse services, and gang-violence intervention services, where appropriate.

Chronic environmental poisoning

Young children are a high risk group for chronic environmental poisoning, because exposure potentially occurs when they are most physiologically susceptible. Their engagement in frequent hand-to-mouth activities during play and meals leads to ingestion of more contaminants in dust and dirt than adults. Their small body size makes them more susceptible to doses that would not harm an adult, and their developing brains are at greater risk of permanent damage due to neurotoxic effects of exposure.

Lead is one of the most important chronic environmental toxins affecting children worldwide. Although it is now uncommon in the UK and other high-income countries, in some low- and middle-income countries contamination of water supplies and the home environment by mining processes and factories remains a significant problem. The symptoms of chronic lead exposure are non-specific but include:

- behavioural changes
- hyperactivity or decreased activity
- developmental delay or loss of developmental milestones
- chronic lead nephropathy.

More significant exposure may result in:

- abdominal pain, vomiting, constipation
- headache and ataxia
- lethargy, seizures, and coma.

The most important treatment is to prevent further exposure to lead. Chelation therapy can be effective in reversing acute symptoms such as encephalopathy but treatment is complex, particularly as lead is deposited in bone and therefore has a long half-life.

Although acute exposure to organophosphate and carbamate pesticides results in well-known acute syndromes, there is growing evidence that chronic exposure to these agents in early life can have adverse effects on neurodevelopment and behaviour. In addition, there is evidence associating some pesticides with an increased incidence of leukaemia and brain tumours.

Summary

Accidental poisoning in children

- Common in toddlers and young children; older children may ingest potentially harmful substances as a form of self-harm or as part of risk-taking behaviour.
- Most substances do not cause serious harm.
- When an ingestion has occurred, identify the agent and assess its toxicity to plan management.
- Poisons potentially harmful in children include alcohol, acids and alkalis, bleach, digoxin, batteries, iron, paracetamol, petroleum distillates, salicylates, and tricyclic antidepressants.
- Assess the social circumstances behind why it happened.

Acknowledgements

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Further reading

Advanced Life Support Group: Advanced paediatric life support: A practical approach to emergencies, ed 6, 2016, Wiley Blackwell.

Websites

Child Accident Prevention Trust (CAPT): www.capt.org.uk.

Making the Link: Working together for safer children: www.makingthelink.net.

Paediatric Trauma Manual of the Royal Children's Hospital Melbourne: Available at: www.rch.org.au/trauma-service/manual.

Toxbase: www.toxbase.org (requires password).



Maltreatment of children and young people

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Maltreatment of children and young people:

- Includes physical and sexual abuse, neglect, emotional abuse, sexual exploitation, fabricated and induced illness, witnessing domestic violence and also harm that comes from outside the home such as bullying and community violence.
- Health professionals have an important role in identifying and responding to children and young people who may have been maltreated, and advocating for better preventive measures.
- Health professionals work together with colleagues in children's social care services and law enforcement in response to concerns about maltreatment.
- Is a public health issue with immediate and lifelong consequences for children and young people and society.

In order to flourish and reach their full potential, children and young people require parents or carers to love and look after them, provide shelter, ensure that their health, wellbeing and education needs are met, and protect them from harm. The parents and carers also need a society that will support them to nurture their children.

Unfortunately, not all children and young people grow up in a safe, supportive, responsive environment. Emotional, physical and sexual abuse and neglect of children and young people by parents, carers and others and/or damaging conditions in wider society continue to impair the lives of children and young people, as they have throughout history. The health and societal cost of child maltreatment is huge.

The UN Convention on the Rights of the Child (UN CRC) specifically refers to the rights of children to be protected from maltreatment, both physical and mental ([Box 8.1](#)). It gives governments the responsibility to ensure that children are properly cared for and protected from violence, exploitation, abuse, and neglect. Most countries have a legislative framework that aims to protect and support children in line with the UN convention. Health professionals have statutory responsibilities in relation to child maltreatment and a key role in advocating for the well-being of the children in their society.

Box 8.1 Summary of the United Nations Convention on the Rights of the Child (1989)

1 Survival rights

The child's right to life and to the most basic needs – food, shelter, and access to healthcare.

2 Developmental rights

To achieve their full potential – education, play, freedom of thought, conscience, and religion. Those with disabilities to receive special services.

3 Protection rights

Against all forms of abuse, neglect, exploitation, and discrimination.

4 Participation rights

To take an active role in their communities and nations.

Adverse effects of maltreatment

Love and nurture in infancy is critical for brain growth and developing the basis for sound attachment. Observational studies of infants raised in conditions of extreme neglect and emotional deprivation, now supported by physiological and biomolecular studies, have shown that there are numerous adverse effects on the nervous, endocrine, and immune systems at this time of rapid development which result in impairment in cognitive, social, and emotional functioning ([Fig. 8.1](#)).

The term adverse childhood experiences (ACEs) is used to describe a wide range of stressful or traumatic experiences that infants, children and young people can be exposed to while growing up. The main ACEs in the home environment identified from surveys are shown in [Figure 8.2](#).

Experiences in children and young people's broader environment outside the home which have been shown to have an adverse effect on long term health and well-being are summarized in [Figure 8.3](#). This is often referred to as 'contextual safeguarding'. With age and maturity,

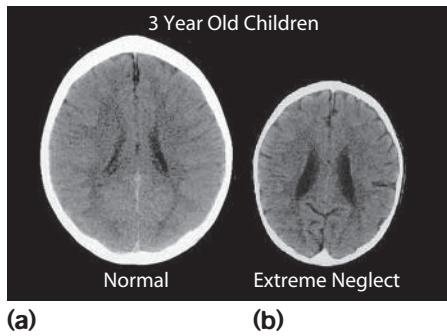


Figure 8.1 These images illustrate the negative impact severe neglect may have on the developing brain. (a) CT scan from a healthy 3-year-old with an average head size (50th centile). (b) Scan from a 3-year-old suffering from severe sensory-deprivation neglect, showing the brain is much smaller (3rd centile) and has enlarged ventricles and cortical atrophy. (Source: Perry BD. Childhood experience and the expression of genetic potential: what childhood neglect tells us about nature and nurture. *Brain and Mind*, 2002;3:79–100.)

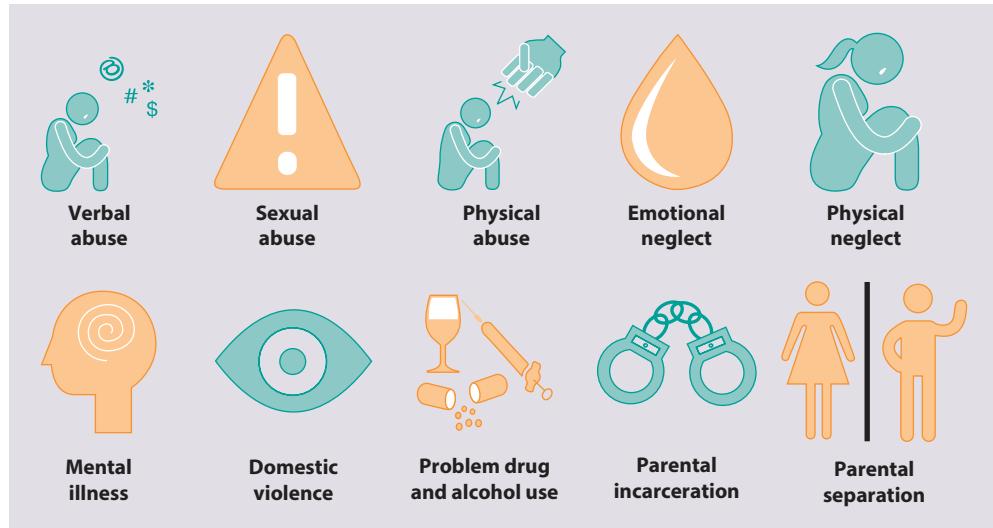


Figure 8.2 The 10 sentinel markers of adverse childhood experiences within the home. (Based on figure from: Adverse childhood experiences, resilience and trauma informed care: a public health approach to understanding and responding to adversity. The annual report of the Director of Public Health, NHS Highland, 2018. Copyright Noun Project Inc. Figure source: Felitti V et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) study. *Am J Prev Med* 1998; 14:245–258.)

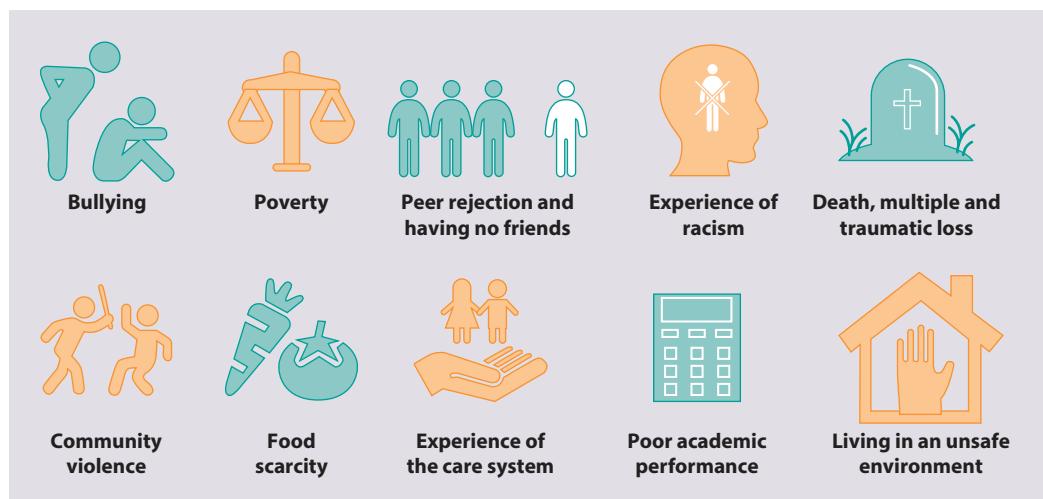


Figure 8.3 Adverse childhood experiences in the child's broader environment. (Based on figure from: Adverse childhood experiences, resilience and trauma informed care: a public health approach to understanding and responding to adversity. The annual report of the Director of Public Health, NHS Highland, 2018. Copyright Noun Project Inc. Figure source: Smith M. Capability and adversity: reframing the "causes of the causes" for mental health. *Nature* 2018; 4:13.)

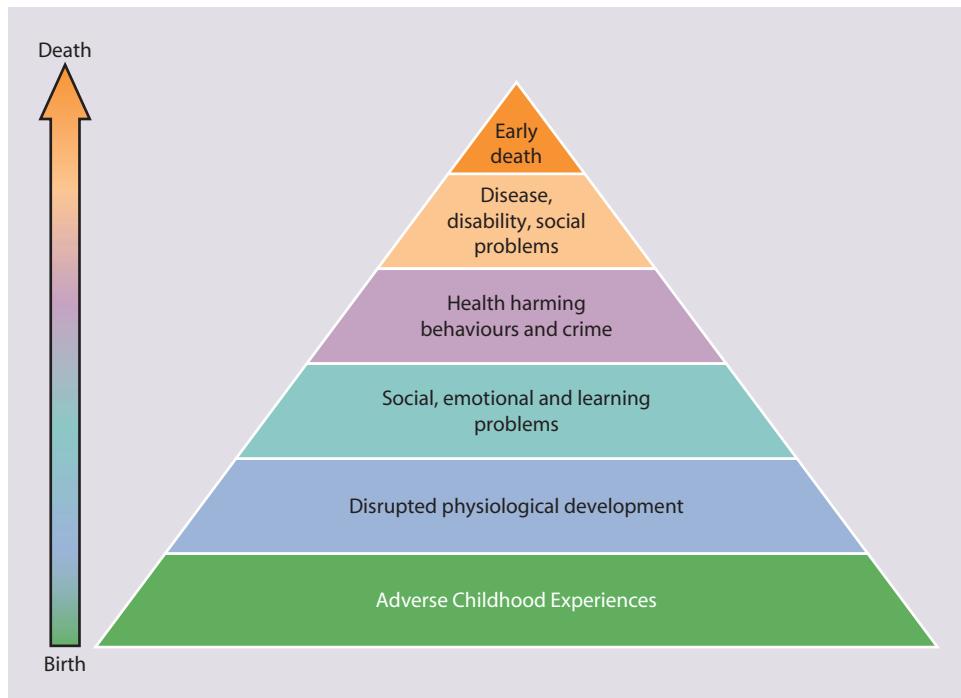


Figure 8.4 Influence of adverse childhood experiences on life course. (Adapted from: Felitti VJ, Anda RF, Nordenberg D et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) study. *Am J Prev Med* 1998; 14:245–58.)

young people spend increasing amounts of time socializing with peers. The extent to which they encounter protection or abuse depends on the nature of their schools and neighbourhoods, and the relationships that they form. Young people can encounter significant harm in settings away from their family, where parents and carers have little influence. Examples are robbery on public transport, sexual violence in parks and gang-related violence on streets, through to online bullying and harassment from school-based peers and abuse within their intimate relationships. If young people socialize in safe and protective schools and community settings, they will be supported to form safe and protective peer relationships. However, if they form friendships in contexts characterized by violence and harm, then these relationships may be antisocial and unsafe, and likely to promote problematic behaviour as a way of surviving in those environments.

Effects of multiple ACEs across the life course

Adverse experiences often cluster in children and young people's lives. Children who are exposed to one type of maltreatment are at high risk of suffering from other types and of repeated exposure over time, making maltreatment a chronic condition, not an isolated event. The greater the number of ACEs, the greater the likelihood of negative outcomes in terms of health and wellbeing including a range of poor educational, social, physical and mental health outcomes across the life course (Fig. 8.4). The cost to the individual, the family and to society is huge.

The behavioural, physical and mental health problems that maltreated children and young people are at increased risk of as adults include:

- perpetrating or being a victim of violence
- depression
- smoking
- obesity
- high-risk sexual behaviours
- unintended pregnancy
- alcohol and drug misuse.

A high number of ACEs is also associated with an increased incidence of cancer and cardiovascular disease in later life.

Resilience

Resilience is the ability to cope with, and adapt and recover from adversity. Identifying and responding to concerns about child maltreatment can help to promote protective factors that will balance the negative effects of adverse experiences and support the development of resilience in the child, the child's family and within the wider community.

As a general practitioner or doctor in nearly any specialty you will encounter situations where you will be concerned that a child or young person is being maltreated. Sometimes the concern will be immediately obvious. Not infrequently, the possible maltreatment will be less obvious when you first encounter the child or young person and you will need to work with others to gather more information according to your local child protection procedures. This chapter provides an understanding of what to look for and how to respond when you are concerned.

Summary

- Throughout childhood, a nurturing, safe environment allows children and young people to reach their potential and eventually make their own contribution to society.
- Maltreatment and other adverse childhood experiences impair development, with immediate and long-term adverse effects not only for the child but their family and wider society. The effect is cumulative and the cost to society is huge.
- Resilience can be promoted and allows children to overcome some of the negative effects of adverse experiences – the earlier the intervention, the better.
- Healthcare professionals have an important role in identifying and responding to children where there are concerns about maltreatment.

Types of maltreatment

Various terms are used for child maltreatment including child abuse and neglect and violence against children. In this chapter we use child maltreatment to encompass the forms of harm that are damaging to children and young people during development with potentially lifelong consequences for health and wellbeing. Systems to prevent and respond to child maltreatment are called Child Protection Services, Social Services and, in the UK, Safeguarding Children services.

The WHO defines child maltreatment as 'the abuse and neglect that occurs to children under 18 years of age. It includes all types of physical and/or emotional ill-treatment, sexual abuse, neglect, negligence and commercial or other exploitation, which results in actual or potential harm to the child's health, survival, development or dignity in the context of a relationship of responsibility, trust or power' (www.who.int/news-room/fact-sheets/detail/child-maltreatment).

Child maltreatment encompasses both inflicting harm and failing to act to prevent harm. Children may be maltreated in a family at home, or in an institution or community. They may be abused by one or more adults, both male and female, or another child or other children.

Conventionally, child maltreatment is categorized into:

- physical abuse
- emotional abuse
- sexual abuse, including sexual exploitation
- neglect.

Physical abuse

Physical abuse may involve hitting, shaking, throwing, poisoning, burning or scalding, drowning, suffocating, or otherwise causing physical harm to a child or failing to protect a child from that harm. Physical harm may also be caused when a parent or carer fabricates the symptoms of, or deliberately induces, illness in a child. In adolescents, intimate partners, including other adolescents, may inflict the physical abuse.

Emotional abuse

Emotional abuse is the persistent emotional maltreatment of a child resulting in severe and persistent adverse effects on the child's emotional development. It may involve conveying to a child or young person that they are worthless or unloved, inadequate, or valued only insofar as they meet the needs of another person, who may be an adult parent, carer or other significant adult in the child's life or an adolescent intimate partner. It may feature developmentally inappropriate expectations being imposed on children. These may include interactions that are beyond the child's developmental capability, as well as overprotection and abnormal social interaction. It may involve seeing or hearing the ill treatment of another child or person. It may also involve serious bullying that causes children to feel frightened or in danger, or the exploitation or corruption of children. Some level of emotional abuse is involved in all types of maltreatment of a child, although it may occur alone.

Sexual abuse and sexual exploitation

Sexual abuse involves forcing or enticing a child or young person to take part in sexual activities, including prostitution, whether or not the child is aware of what is happening. The activities may involve physical contact, including penetrative acts such as rape, anal sex or oral sex, and/or non-contact activities, such as involving children in looking at or producing pornographic material or watching sexual activities, or encouraging children to behave in sexually inappropriate ways. Both men and women sexually abuse children and indeed children can also be perpetrators of sexual abuse.

Sexual exploitation is a type of sexual abuse in which children, both girls and boys, are sexually exploited for money, power, or status. Children or young people may be tricked into believing they are in a loving, consensual relationship. They might be invited to parties and given drugs and alcohol. They may also be groomed online. Some children and young people are trafficked into other countries or within their own country for the purpose of sexual exploitation. Sexual exploitation can also happen to young people in gangs.

Neglect

Neglect is the persistent failure to meet a child's basic physical and/or psychological needs, likely to result in the serious impairment of the child's health or development. It may involve a parent or carer failing to provide:

- adequate food and clothing
- shelter, including exclusion from home or abandonment
- protection from physical and emotional harm or danger
- adequate supervision, including the use of inadequate caregivers or parental failure to ensure safety for an adolescent in the community
- access to appropriate medical care or treatment.

It may also include neglect or unresponsiveness to a child's basic emotional needs.

Fabricated or induced illness

This is a form of physical abuse. It is a broad term to describe a group of behaviours by parents (or carers), but usually the mother (>80%), which cause harm to children. It fulfils the parent's (or carer's) own needs.

It may consist of a parent, usually in isolation, fabricating (i.e. inventing) symptoms and signs in the child, telling a false story to healthcare professionals, leading them to believe the child is ill and requires investigation and treatment. In community settings, the false stories may lead to medication, special diets, and a restricted lifestyle or special schools.

It may also lead to induction of illness by a variety of means including:

- suffocation of the child, which may present as an acute life-threatening event
- administration of noxious substances or poisons
- excessive or unnecessary administration of ordinary substances (e.g. excess salt)
- excess or unnecessary use of medication (prescribed for the child or others)
- the use of medically provided portals of entry (such as gastrostomy buttons, central lines).

Organic illness may coexist with fabricated or induced illness in a child, thus making the fabrication more difficult to identify.

Intimate partner violence

Observing violence between adults who are, or have been, intimate partners or family members, irrespective of sex or sexuality, is a form of emotional abuse. Threatening behaviour, violence, and abuse (psychological, physical, sexual, financial, or emotional) are recognized to contribute to poor short-term and long-term outcomes for children and young people.

Experiencing partner violence can be a feature of adolescent intimate partnerships.

Bullying

Bullying may be defined as deliberately hurtful behaviour, usually repeated over a period of time, where it is difficult for those bullied to defend themselves. It can take many forms, but the three main types are physical (e.g. hitting, kicking, theft), verbal (e.g. racist or homophobic remarks, threats, name calling) and emotional (e.g. isolating an

individual from the activities and social acceptance of their peer group). Additionally, cyber-bullying can occur. This involves online chastisement both directly and indirectly. The damage inflicted by bullying can easily be underestimated. It can cause considerable distress to children and young people to the extent that it affects their health and development or, at the extreme, cause them significant harm (including self-harm). All settings in which children are provided with services or are living away from home should have in place rigorously enforced antibullying strategies.

Other forms

In some countries, there are other child maltreatment considerations, e.g. child labour, child soldiers, child marriage, child trafficking, forced marriage, as well as female genital mutilation.

Prevalence

Estimating the prevalence and magnitude of child maltreatment is difficult. There are two main sources of information:

- Official statistics from agencies that work with children, investigating reports of child abuse, e.g. social services, the police, the courts, numbers of children in care. Accurate data is not available in all countries or regions.
- Self-reports of abuse in childhood from young people and adults – these usually reveal much higher numbers than from services that work with children. It is thought that many children do not tell anyone about the abuse at the time because they fear the consequences or because they are unsure who to tell or how to tell someone. Children also worry about an investigation from the authorities or the effect on their family. However, even with the anonymity of research, there are some people who never disclose what happened to them.

Within these limitations, **Table 8.1** is a guide to the prevalence of the various forms of child abuse in high-income countries. As noted already, many children suffer from more than one type of abuse and/or are subject to abuse in various forms throughout childhood.

Table 8.1 Cumulative prevalence of abuse from self-reports (0–18 years) in high-income countries, from official statistics and self-reported abuse in high-income countries

Type of abuse	Physical	Sexual (all forms)	Emotional	Neglect	Witnessing intimate partner violence
Cumulative prevalence	5%–35%	15%–30% for girls 5%–15% for boys	4%–9%	6%–12%	8%–25%

(Source: Gilbert R, Widom CS, Browne K, et al. *Lancet* 2009;373(9657):68–81.)

Safeguarding

As mentioned above, safeguarding is the term used in child protection processes and procedures in the UK. It means that not only should we intervene when there is concern about child maltreatment, but also that there should be early recognition and response to vulnerabilities. As well as parents and carers, key professionals involved are health professionals, teachers, social workers and the police. Keeping the wider community safe for children and young people involves other agencies, services and legislation, e.g. housing, licensing of sale of tobacco and alcohol, ensuring a framework of processes of safeguarding in religious and sporting organizations. Providing early help is more effective in promoting the welfare of children than reacting to maltreatment. The key principles of safeguarding children are:

- Safeguarding is everyone's responsibility – for services to be effective each professional and organization should play their full part.
- Child-centred approach – for services to be effective they should be based on a clear understanding of the needs and views of children and young people.

Risk factors

Maltreatment of children and young people occurs across socio-economic, religious, cultural, racial, and ethnic groups. Although no specific causes have been definitively identified that lead a parent or other caregiver to abuse or neglect a child or young person, research has recognized a number of risk factors associated with maltreatment (Table 8.2). It must be emphasized, however, that although certain factors are over-represented among families where maltreatment occurs, this does not mean that the presence of these factors will always result in child abuse and neglect. For example, there is a relationship between poverty and maltreatment, yet most people living in poverty do not harm their children.

Presentation

Child abuse may present with one or more of:

- physical symptoms and signs
- psychological symptoms and signs
- a concerning interaction observed between the child and the parent or carer
- the child may tell someone about the abuse
- the abuse may be observed.

Identification of child abuse in children with disabilities may be more difficult; disability is also a risk factor for child abuse.

In order to diagnose child abuse or neglect, a detailed history and thorough examination are crucial. In most

Table 8.2 Risk factors for maltreatment of children and young people

In the child	Failure to meet parental expectations and aspirations, e.g. disabled, 'wrong' gender, 'difficult' child
In the parent/carer	Born after forced, coercive, or commercial sex Mental health problems Parental indifference, intolerance, or over-anxiousness Alcohol, drug abuse
In the family	Step-parents Domestic violence Multiple / closely spaced births Social isolation or lack of social support Young parental age
In the environment	Poverty Poor housing

instances where child abuse is considered, seeking advice from colleagues, e.g. more experienced members of the team, paediatric radiologists, and paediatric or orthopaedic surgeons is essential.

Physical abuse

Factors to consider in the presentation of a physical injury are:

- the child's age and stage of development
- the history given by the child (if they can communicate) or young person
- the plausibility and/or reasonableness of the explanation for the injury ([Case history 8.1](#))
- any background, e.g. previous child protection concerns; multiple attendances to emergency department or general practitioner
- unreasonable delay in reporting the injury
- significant inconsistent histories from caregivers
- inappropriate reaction of parents or caregivers who are vague, evasive, unconcerned, or excessively distressed or aggressive.

It is sometimes not clear whether an injury is inflicted or non-inflicted. [Table 8.3](#) gives examples of injuries and a guide as to the likelihood that it is due to an inflicted injury. The context and one's observations of the family are very important in evaluating injuries that may be inflicted.

Physical injuries that can be caused by child abuse



Case history 8.1

Severe physical abuse

A 2-month-old boy was brought into the emergency department by ambulance, with sudden loss of consciousness. His mother accompanying him appeared to have learning difficulties and could not explain what had happened. His father arrived soon after and said that he had been changing the child's nappy on the floor when suddenly he 'went all floppy and asleep'.

The child was unresponsive (U on AVPU) and had shallow breathing. His pupils were dilated. He appeared well nourished and was dressed only in a nappy. There were no obvious injuries seen.

Medical management was rapidly instituted. CT head scan showed subdural haemorrhages (Fig. 8.5). A chest X-ray obtained following intubation showed old posterior rib fractures (Fig. 8.6). Subsequent ophthalmological examination showed bilateral retinal haemorrhages (Fig. 8.7).

The child was transferred to an intensive care unit, where he died. A postmortem skeletal survey showed metaphyseal fractures (Fig. 8.8).

The parents maintained their story, despite the compelling evidence of inflicted head injury and shaking. The case went to the criminal court and both were sentenced on a number of charges.

Severe physical child abuse resulting in death gains considerable attention from the media but is rare, estimated at about 1 child per week in the UK. Many more children suffer permanent injury after serious physical abuse. Most have been seen previously by health professionals. Early recognition and response to child protection concerns could prevent severe injury.

Fracture lines with no healing
(difficult to see)

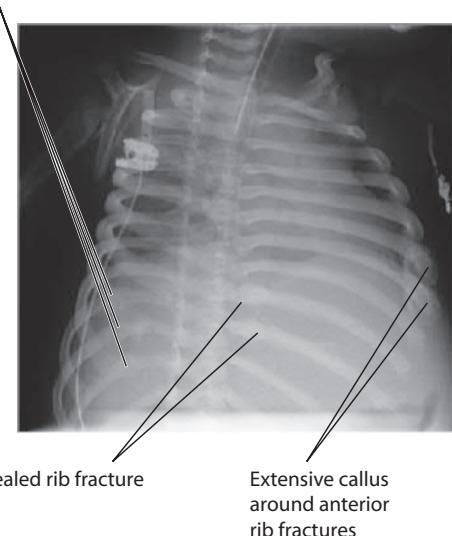


Figure 8.6 Multiple rib fractures of different ages.

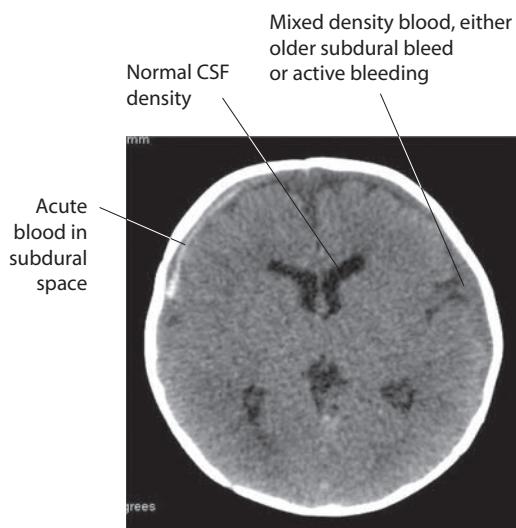


Figure 8.5 Subdural haemorrhage. CSF, cerebrospinal fluid.



Figure 8.7 Retinal haemorrhages from trauma to the head. (Courtesy of Clare Roberts.)



Figure 8.8 Metaphyseal fracture of distal humerus.

Table 8.3 Examples of injuries and a guide as to how likely it is due to an inflicted injury

Injury	More likely to be inflicted	May be inflicted, accidental or due to an underlying disorder	Less likely or unlikely to be inflicted
Fractures	Any fracture in a non-mobile child (excluding fragile bones) Rib fractures Multiple fractures (unless significant accidental trauma, e.g. road traffic accident) Multiple fractures of different ages	Skull fracture in young child Long bone fractures in a young but mobile child	Fracture in school-age child with witnessed trauma, e.g. fall from swing
Bruises	Bruising in the shape of a hand (Fig. 8.9a) or object Bruises on the neck that look like attempted strangulation Bruises around the wrists or ankles that look like ligature marks Bruise to the buttocks in a child less than 2 years or any age without a good explanation	Bruising to the trunk with a vague history	Bruises on the shins of a mobile child
Burns	Any burn in a child who is not mobile. A burn in the shape of an implement – cigarette, iron A ‘glove or stocking’ burn consistent with forced immersion (Fig. 8.9b)		A burn to mobile toddler with splash marks, a history of pulling drink onto himself – but may indicate neglect in the form of poor supervision
Bites	Bruising in the shape of a bite thought unlikely to have been caused by a young child (Fig. 8.9c)		A witnessed biting of one toddler by another



(a)



(b)



(c)

Figure 8.9 (a) Bruising from finger trauma to a baby's head. (b) Scald with stocking distribution including the soles from forced immersion in hot water. (c) A bite mark on an infant's leg. Adult bite marks may be seen in abuse, but bites from other children are not uncommon.



Key features of bruising:

- The age of a bruise cannot be accurately estimated.
- Bruising is hard to detect on children with dark skin.
- Congenital dermal melanocytosis (Mongolian blue spots) can be mistaken for bruises, as they may still be present at several years of age (see [Fig. 10.15d](#)).

- lacks needed medical or dental care or immunizations
- seems ravenously hungry
- is dirty
- is wearing inadequate clothing in cold weather
- is abusing alcohol or other drugs
- says there is no one at home to provide care.

Consider the possibility of neglect when the parent or other adult caregiver:

- appears to be indifferent to the child
- seems apathetic or depressed
- behaves irrationally or in a bizarre manner
- is abusing alcohol or other drugs.

Neglect

Consider the possibility of neglect when the child or young person:

- consistently misses important medical appointments

Emotional abuse

This damaging form of abuse can be difficult to identify in a single brief healthcare interaction with a child and carer ([Case history 8.2](#)) but may be apparent when the observation period recurs or is longer, e.g. an inpatient or neonatal unit setting. Some clues may be found by



Case history 8.2

Is there emotional abuse or neglect?

A general paediatrician sees a 6-year-old boy for recurrent abdominal pain resulting in missing 20% of school this year.

The boy and his mother are accompanied by his 3-month-old sister. The boy is all over the clinic room – climbing onto the examination couch, turning the ophthalmoscope on and off, crawling under the desk, trying to get hold of the computer keyboard and turning the water tap of the hand-basin on and off. The baby is crying, but her mother is holding her at arm's length and not comforting her or taking any notice of her son's behaviour.

With the help of the clinic nurse, the boy is shown some toys, settles down and shows good ability to put a simple jigsaw puzzle together. The baby keeps crying until the mother eventually gives her a bottle of formula from her bag. The mother's affect is very flat and is vague about the history of abdominal pain and why so much school has been missed.

Examination shows that he is on the 50th centile for weight and height. His mother says she has lost his personal child health record. He is in school uniform and is clean but his hair is not brushed. He has dental caries but mother cannot remember when he last saw the dentist. The boy says that he cleans his teeth twice a day. He has some bruising to the shins but examination is otherwise normal.

From this description, what are the concerning features? What are the positive features ([Table 8.4](#))?

What else do you need to know?

- Who else is at home – partner, other children, others?
- What other support is available – family, friends?

noting how the parent or caregiver perceives the child. Is the child:

- the 'wrong' gender,
- born at a time of parental separation or violence, or
- seen as unduly 'difficult'?

Table 8.4 Concerning and positive features relating to the family

Concerning features	Positive features
6-year-old boy Has missed 20% of school Very active, risky or inappropriate behaviour in clinic – does he have attention deficit hyperactivity disorder? Hair is not brushed Has dental caries	Shows good concentration Is in a school uniform and is clean Says that he cleans his teeth twice a day Growth is satisfactory
Baby Crying most of the time	
Mother Affect seems very flat Not intervening to stop inappropriate behaviour Holding her baby at arm's length and not comforting her Cannot remember when her son last saw the dentist Has lost the personal child health record	Has thought to bring along a bottle of formula for the baby Has dressed the 6-year-old in a clean uniform

There may be clues from the behaviour of the child. This depends on the child's age:

- babies:
 - apathetic, delayed development, non-demanding
 - described by the mother as 'spoiled, attention-seeking, in control, not loving her'
- toddlers and preschool children:
 - violent, apathetic, fearful
- school children:
 - wetting, soiling, relationship difficulties, non-attendance, antisocial behaviour
- adolescents:
 - self-harm, depression, oppositional, aggressive behaviour.

Sexual abuse

Recognition

The child or young person may:

- tell someone about the abuse. It is important to take the child's disclosure seriously and take action ([Case history 8.3](#)).
- be identified in pornographic material
- be pregnant (by legal definition this is an offence for a girl under the age of 13)
- have a sexually transmitted infection with no clear explanation (but some sexually transmitted infections can be passed from the mother to the baby during pregnancy or birth or through autoinoculation of e.g. warts).

Physical symptoms

- Vaginal bleeding in pre-menarche, itching, discharge – though these symptoms may be due to other causes, e.g. bleeding from tumours, worms causing itching, vulvovaginitis causing discharge and/or bleeding.
- Rectal bleeding – again the cause may be related to other causes, e.g. constipation.

Behavioural symptoms

- Any of the symptoms outlined for emotional abuse in the previous section.
- Unexpected awareness or acting out of sexualized behaviour beyond what would be expected for age.
- Soiling, secondary enuresis.
- Self-harm, aggressive or sexualized behaviours, regression, poor school performance, persistent unexplained physical symptoms (PUS).

Signs

There are few definitive diagnostic signs of sexual abuse on examination and nearly all examinations after suspected sexual abuse show no positive findings. This is because sexual abuse of children often comprises touching or kissing or other activities that do not involve significant physical force or contact. Furthermore, the genital area heals very quickly in young children, so signs may be absent even a few days after significant trauma. Forensic material also decays rapidly. Examination of children suspected of having been sexually abused requires doctors and services with specific expertise and training, facilities for photographic documentation, sexually transmitted infection screening and management and, where indicated, forensic testing. Forensic testing of swabs from the child or his/her clothing/bedding may reveal DNA from a body fluid of the perpetrator.



Case history 8.3

Sexual abuse

A 14-year-old girl is brought to the paediatric emergency department at 6 a.m. as she has told her mother that she has been sexually abused. The girl met the perpetrator online four months previously and arranged to meet him in the park the previous day for the first time. Online he told the girl he was 16 years old. When they met he was considerably older. He took her to a nightclub and bought her drinks and then took her back to his apartment where there were several other men. He then had penetrative vaginal sex with her. The girl managed to get out of the apartment and home where she immediately told her mother.

Children's social care services and the police were immediately informed. The girl had a full physical examination in the department to ensure she was medically fit. She was advised to remain in her current clothing and not to wash. Arrangements were made for her to go straight to a special facility for a forensic sexual assault examination.

This case history demonstrates:

- Sexual exploitation of children and young people is often initiated by online grooming.
- Perpetrators of childhood exploitation often buy gifts, drinks and drugs for their victims.

Investigation

In physical abuse, fractures in young children may not be detectable clinically and only revealed on X-rays or other forms of imaging. A full radiographic skeletal survey including oblique views of the ribs should be performed in all children under 2 years of age with suspected physical abuse. Some lesions may be inconspicuous initially but, if indicated, become evident on X-rays repeated 1–2 weeks later. CT head scans may also be indicated. Guidelines for skeletal surveys exist in many countries, and it is important to discuss the case and review the findings with a consultant paediatric radiologist.

Other medical conditions that need to be considered and excluded in suspected child abuse are:

- bruising – coagulation disorders ([Fig. 8.10](#)), Congenital dermal melanocytosis (Mongolian blue spots) that can occur almost anywhere on the body
- fractures – osteogenesis imperfecta (OI), commonly referred to as brittle bone disease. The type commonly involved with unexplained fractures is type I, which is an autosomal dominant disorder, so there may be a family history. Blue sclerae (see [Fig. 28.25b](#)) are a clinical finding, and there may be generalized osteoporosis and/or Wormian bones in the skull (extra bones within skull sutures) on skeletal survey. Confirming the diagnosis of osteogenesis imperfecta requires considerable specialist expertise
- scalds and cigarette burns – may be misinterpreted in children with bullous impetigo or scalded skin syndrome.



Figure 8.10 A thorough medical assessment is required in all children when non-accidental injury is suspected. This girl's large bruise followed what was said to be a minor bump. Non-accidental injury was suspected, but examination showed multiple bruises and petechiae. She had immune thrombocytopenic purpura.

Where brain injury is suspected all children require:

- an immediate CT head scan followed later by an MRI head and spine
- a skeletal survey to exclude fractures
- an expert ophthalmological examination to ascertain the presence of retinal haemorrhages
- a coagulation screen.

Management

Maltreated children and young people may present to doctors in the hospital or to medical or nursing staff in the community. They may also be brought for a medical opinion by social services or the police. Concerns are often picked up by teachers in school-age children. In all cases, the procedures of the local safeguarding children partnership or local child protection protocols should be followed. For children and young people who are able to talk it is good practice to use a chaperone and speak to children without parents present. The medical consultation should be the same as for any medical condition, with a detailed history and full examination. It is usually most productive when this is conducted in a sensitive and concerned way without being accusatory or condemning. Any injuries or medical findings should be carefully noted, measured, recorded, and drawn on a body map and photographed (with consent). The height, weight and head circumference (where appropriate) should be recorded and plotted on a centile chart. The interaction between the child and parents should be noted. All notes must be meticulous, dated, timed, and signed on each page. Treatment of specific injuries should be instigated, and any blood tests and X-rays undertaken.

If abuse is suspected or confirmed, a decision needs to be made as to whether the child needs immediate protection from further harm. If medical treatment is not necessary, but it is felt to be unsafe for the child to return home, a placement may be found with foster carers, other family members or the alleged perpetrator moving out of the home.

If medical treatment is needed, admission to hospital is required. If sympathetically handled, most parents are willing to accept medical advice for hospital admission for investigation. Occasionally, this is not possible and legal enforcement is required.

When dealing with any child suspected of having been abused, the safety of any other siblings or children at home must be considered. The police and/or social services should be alerted to any concerns.

In addition to a detailed medical assessment, evaluation by social workers and other health professionals will be required. A strategy meeting and later a child protection conference may be convened in accordance with local procedures. Members may include social workers, health visitors, police, general practitioner, paediatricians, teachers, lawyers and other professionals who know the child and family. Parents attend all or part of the case conference. Details of the incident or concerns leading to the conference and the family background will be discussed. Good communication and a trusting working relationship between the professionals are vital, as it can be extremely difficult to evaluate the likelihood that injuries were inflicted deliberately and the possible outcome of legal proceedings. The conference will decide:

- whether the child should be provided with a child protection plan ([Case history 8.4](#))
- whether there should be an application to the Court to protect the child
- what follow-up is needed.



Safeguarding can be difficult as:

- it goes against the assumption that parents have their children's best interests at heart
- can involve confronting parents who may be manipulative or aggressive
- requires detailed evaluation of the history and examination to identify inconsistencies and interpret subtle findings
- depends on good multi-professional teamwork and respect of colleagues.

Summary

Maltreatment of children and young people

- Takes various forms – physical abuse, emotional abuse, sexual abuse, neglect, fabricated or induced illness, bullying, witnessing intimate partner violence. Community and environmental factors may contribute.
- All doctors have a responsibility to be aware of and alert to symptoms and signs of child maltreatment. They need to know the local procedures for seeking help in responding to concerns.
- Concerns about child maltreatment must not be avoided or ignored because they raise difficult issues.
- The interests of the child should be kept uppermost to ensure protection from harm.
- In many instances it is initially not clear whether or not the problem is one of child maltreatment. Good communication with parents, children and other involved professionals – e.g. social workers and police – is vital.



Case history 8.4

Possible child abuse

Parents brought their 8-month-old daughter into the children's emergency department. They were worried that she had not been moving her right arm for that day. The family remembered that at the evening meal two evenings before, her father was bringing dishes for the family meal to a low corner coffee table in the sitting room. Mother was sitting with baby on her knee, next to the table, trying to control the older siblings, when father had accidentally dropped a heavy serving bowl of food. Mother automatically reached out to try to catch it, dropping the baby in doing so and, in the confusion, the serving bowl hit the baby's arm. The baby cried very loudly for about 10 minutes or so but then seemed to settle. The next day she did not use the right arm but the family thought this was explained by the injury causing a 'strain' as they could not see any bruising on the arm. An X-ray showed a fracture of the right radius and ulna (Fig. 8.11).

Child protection concerns

- Baby under 1 year with fracture.
- Delayed presentation.

Positive features

- Plausible, consistent story.
- Good parent-child interaction observed by medical and nursing staff.
- Well-nourished, well-cared-for appearance of baby.
- No other injuries on full examination.
- Skeletal survey showed no other fractures.
- Personal child health record showed regularly weighed, thriving baby up to date with immunizations.



In child protection, conclusive evidence is often not available.

Acknowledgements

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Further reading

HM Government: Working together to safeguard children: A guide to interagency working to safeguard and promote the welfare of children, London, 2018, HM Government. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/942454/Working_together_to_safeguard_children_inter_agency_guidance.pdf



Figure 8.11 X-ray of right arm showing fracture of the radius and ulna.

- No general practitioner or home visit concerns about the family.
- Not previously known to local children's social services.

Outcome

- Strategy meeting – no additional concerns identified.
- Decision – increased health visitor contact and parents received advice about safety in the home.

Lancet Series: Child maltreatment, 2008. Available at: www.thelancet.com/series/child-maltreatment.

National Institute for Health and Care Excellence: Child maltreatment: When to suspect maltreatment in under 18s, Clinical guideline [CG89], London, 2009, NICE. Available at: www.nice.org.uk/guidance/cg89.

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Genetics

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Features of the genetic basis of diseases:

- It is now estimated that the human genome contains 20,000–25,000 genes, although the function of many of them remains unknown. Great diversity and complexity at the protein level is achieved by alternative messenger RNA splicing and post-translational modification of gene products.
- Microarray techniques and high-throughput sequencing are increasing the volume and speed of genetic investigations and reducing their cost, leading to a greater understanding of the impact of genetics on health and disease.
- Access to genome browser databases containing DNA sequence and protein structure has greatly enhanced progress in scientific research and the interpretation of clinical test results (Fig. 9.1).

- Genetic databases are available on thousands of multiple congenital anomaly syndromes, on chromosomal variations and disease phenotypes, and on all Mendelian disorders.
- Clinical application of these advances is available to families through specialist genetic centres that offer investigation, diagnosis, counselling and antenatal diagnosis for an ever-widening range of disorders.
- Gene-based knowledge is entering mainstream medical and paediatric practice, especially in diagnosis and therapeutic guidance, such as for the treatment of malignancies.

Genetic disorders are:

- common, with 2% of live-born babies having a significant congenital anomaly and about 5% a genetic disorder

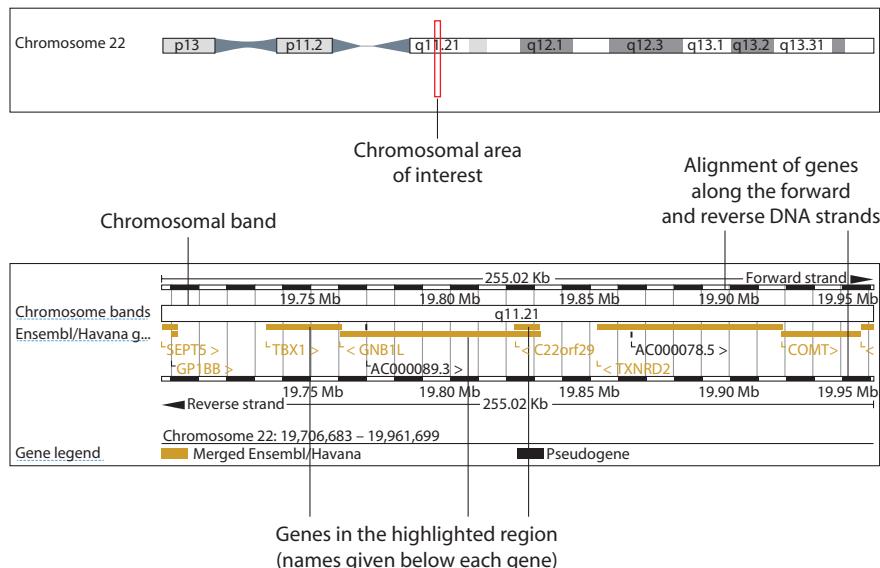


Figure 9.1 Ensembl genome browser. The image shows part of chromosome region 22q11, involved in 22q11 deletion syndrome (DiGeorge syndrome). Although only part of the commonly deleted region is shown, the image shows several genes that are deleted in 22q11 deletion syndrome. The online Ensembl browser can be used to 'zoom in' on specific areas, showing the genes present in different chromosome regions, and can also be used to show the gene sequence itself.

- burdensome to the affected individual, family, and society, as many are associated with severe and permanent disability.

Genetically determined diseases include those resulting from:

- chromosomal abnormalities
- the action of a single gene (Mendelian disorders)
- unusual genetic mechanisms, such as imprinting
- interaction of genetic and environmental factors (polygenic, multifactorial, or complex disorders), which include epigenetic influences on gene expression from early in life.

Chromosomal abnormalities

Genes are composed of DNA that is wound around a core of histone proteins and packaged into a succession of supercoils to form chromosomes. The human

chromosome complement was confirmed as 46 in 1956. The chromosomal abnormalities in Down, Klinefelter, and Turner syndromes were recognized in 1959, and thousands of chromosome defects have now been described.

Chromosomal abnormalities are either numerical or structural. They occur in approximately 10% of spermatozoa and 25% of mature oocytes and are a common cause of early spontaneous miscarriage. The estimated incidence of chromosomal abnormalities in live-born infants is about 1 in 150. They often cause multiple congenital anomalies and cognitive difficulties. Acquired chromosomal changes play a significant role in carcinogenesis and tumour progression.

Disorders of chromosome number

Down syndrome (trisomy 21)

This is the most common autosomal trisomy and the most common genetic cause of severe learning difficulties (Fig. 9.2a–c, Box 9.1). The incidence (without antenatal screening) in live-born infants is about 1 in 650. The incidence increases with maternal age.

Down syndrome



Figure 9.2a Characteristic facies seen in Down syndrome. The girl's posture is due to hypotonia.



Figure 9.2b Single palmar crease.



Figure 9.2c Pronounced 'sandal' gap with wide space and often a deep fissure between the big toe and second toe.

Box 9.1 Characteristic clinical manifestations of Down syndrome

Typical craniofacial appearance

- round face and flat nasal bridge, short neck
- upslanted palpebral fissures
- epicanthic folds (a fold of skin running across the inner edge of the palpebral fissure)
- Brushfield spots in iris (pigmented spots)
- small mouth and protruding tongue
- small ears
- flat occiput and third fontanelle

Other anomalies

- single palmar creases, incurved and short fifth finger, and wide 'sandal' gap between first and second toes
- hypotonia
- congenital heart defects (in 40%)
- duodenal atresia (or other intestinal atresias)
- Hirschsprung disease (<1%)

Later medical problems

- delayed motor milestones
- learning difficulties – severity is variable, usually mild to moderate but may be severe
- short stature (special growth chart for children with Down Syndrome)
- increased susceptibility to infections
- hearing impairment from secretory otitis media (75%)
- visual impairment from cataracts (15%), squints, myopia (50%)
- increased risk of hypothyroidism (15%)
- increased risk of leukaemia and solid tumours (<1%)
- increased risk of coeliac disease
- acquired hip dislocation and atlantoaxial instability
- obstructive sleep apnoea (50% to 75%)
- epilepsy
- early-onset Alzheimer disease

Clinical features

If not diagnosed antenatally, Down syndrome is usually suspected at birth because of the baby's facial appearance. Most affected infants are hypotonic and other characteristic clinical signs include a flat occiput, single palmar creases, incurved fifth finger, and wide 'sandal' gap between the big and second toes. The diagnosis can be difficult to make when relying on clinical signs alone and a suspected diagnosis should be confirmed by a senior paediatrician. Before blood is sent for analysis, parents should be informed that a test for Down syndrome is being performed. The results may take 1–2 days, using real-time PCR (rtPCR) or rapid fluorescence in situ hybridization (FISH) techniques. Parents need information about the short-term and long-term implications of the diagnosis. They are also likely, at some stage, to appreciate the opportunity to discuss how and why the condition has arisen, the risk of recurrence, and antenatal diagnosis in future pregnancies.

It is difficult to give a precise long-term prognosis in the neonatal period. Congenital heart disease is present in about 40% and is a major cause of early mortality, particularly atrioventricular canal defects. Duodenal atresia is another problem in the newborn period. Over 85% of infants with trisomy 21 survive to 1 year of age. In the UK, at least 50% of affected individuals live longer than 50 years.

Child development services will provide or coordinate care. This will include regular review of the child's development and health. Children with Down syndrome should be screened periodically for impairment of vision and hearing, hypothyroidism, coeliac disease, and atlantoaxial instability.

Cytogenetics

The extra chromosome 21 may result from meiotic nondisjunction (Fig. 9.3), translocation (Fig. 9.4), or mosaicism.

Meiotic nondisjunction (94%)

In nondisjunction trisomy 21:

- Most result from an error at meiosis.
- The chromosome 21 pair fails to separate, so that one gamete has two chromosome 21s and one has none.
- Fertilization of the gamete with two chromosome 21s gives rise to a zygote with trisomy 21.
- Parental chromosomes do not need to be examined.

The incidence of trisomy 21 due to nondisjunction is related to maternal age (Table 9.1). However, as the proportion of pregnancies in older mothers is small, most affected babies are born to younger mothers. Furthermore, meiotic nondisjunction can occur in spermatogenesis so that the extra copy of chromosome 21 can be of paternal origin. All pregnant women are now

Table 9.1 Risk of Down syndrome (live births) with maternal age at delivery, prior to screening in pregnancy

Maternal age (years)	Risk of Down syndrome
All ages	1 in 650
20	1 in 1530
30	1 in 900
35	1 in 385
37	1 in 240
40	1 in 110
44	1 in 37

Inheritance of Down syndrome

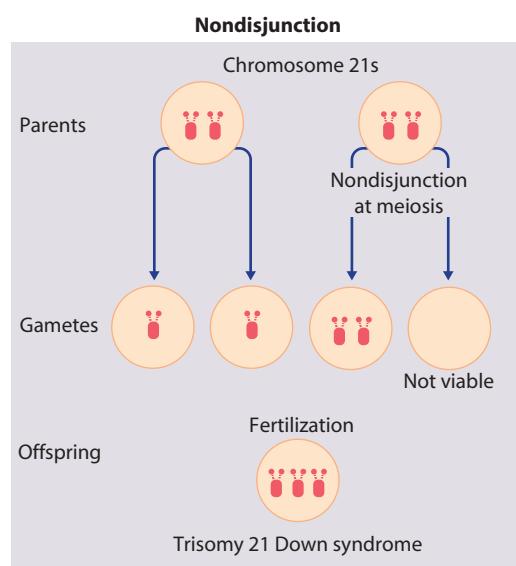


Figure 9.3 Nondisjunction Down syndrome.

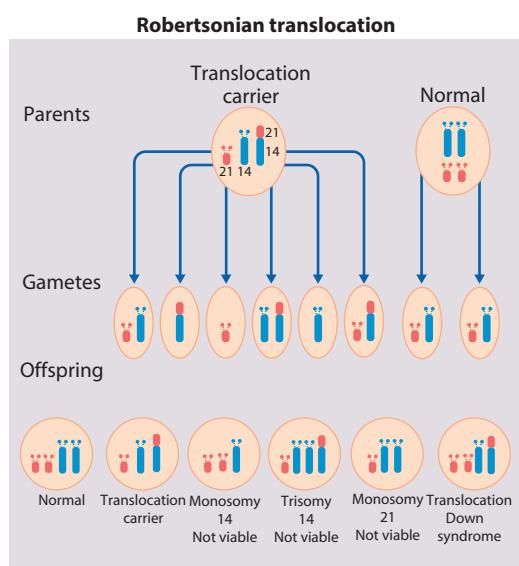


Figure 9.4 Translocation Down syndrome. There is a Robertsonian translocation involving chromosomes 21 and 14, which has been inherited from a parent.

offered screening tests measuring biochemical markers in blood samples and nuchal thickening on ultrasound (thickening of the soft tissues at the back of the neck) to identify an increased risk of Down syndrome in the fetus. Non-invasive prenatal testing (NIPT) is now possible, in which cell-free DNA is analyzed from maternal blood; this has a positive predictive value of ~80% as a primary screen of all mothers or ~90% as a secondary test, when the primary screen indicates an increased risk. This leads to fewer amniocenteses being performed to check the fetal karyotype. After having one child with trisomy 21 due to nondisjunction, the risk of recurrence of Down syndrome is given as 1 in 200 for mothers under the age of 35 years, but remains similar to their age-related population risk for those over the age of 35 years.

Translocation (5%)

When the extra chromosome 21 has fused with another chromosome (usually chromosome 14, but occasionally chromosome 15, 22, or 21), this is known as a Robertsonian translocation. This may be present in a phenotypically normal carrier with 45 chromosomes (two being 'joined together') or in someone with Down syndrome and a set of 46 chromosomes but with three copies of chromosome 21 material. In this situation, parental chromosome analysis is recommended, because one of the parents may well carry the translocation in balanced form (in 25% of cases;).

In translocation Down syndrome:

- The risk of recurrence is 10%–15% if the mother is the translocation carrier and about 2.5% if the father is the carrier.
- If a parent carries the rare 21:21 translocation, all the offspring will have Down syndrome.
- If neither parent carries a translocation (75% of cases), the risk of recurrence is less than 1%.

Mosaicism (1%)

In mosaicism, some of the cells are normal and some have trisomy 21. This usually arises after the formation

Summary

Down syndrome (trisomy 21)

- Natural incidence – about 1.5 per 1000 infants.
- Cytogenetics – nondisjunction (most common, related to maternal age), translocation (one parent may carry a balanced translocation), or mosaicism (rare).
- Presentation – antenatal screening, prenatal diagnosis, or clinical presentation; confirmed on chromosome analysis.
- Immediate medical complications – increased risk of duodenal atresia, congenital heart disease.
- Clinical manifestations – see **Box 9.1**.

of the chromosomally normal zygote by nondisjunction at mitosis but can arise by later mitotic nondisjunction in a trisomy 21 conception. The phenotype is sometimes milder in Down syndrome mosaicism.

Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13)

Although rarer than Down syndrome (1 in 8000 and 1 in 14,000 live births, respectively), particular constellations of severe multiple abnormalities suggest these diagnoses at birth; most affected babies die in infancy (**Fig. 9.5**, **Boxes 9.2** and **9.3**) but extended survival is possible. The diagnosis is confirmed by chromosome analysis. Many affected fetuses are detected by ultrasound scan during the second trimester of pregnancy and diagnosis can be confirmed antenatally by amniocentesis and chromosome analysis. Can also be diagnosed on non-invasive prenatal testing (NIPT). Recurrence risk is low, except when the trisomy is due to a balanced chromosome rearrangement in one of the parents.

Edwards syndrome and Patau syndrome

Box 9.2 Clinical features of Edwards syndrome (trisomy 18)

- Low birthweight
- Prominent occiput
- Small mouth and chin
- Short sternum
- Flexed, overlapping fingers (**Fig. 9.5**)
- 'Rocker-bottom' feet
- Cardiac and renal malformations



Figure 9.5 Overlapping of the fingers in Edwards syndrome.

Box 9.3 Clinical features of Patau syndrome (trisomy 13)

- Structural defect of brain
- Scalp defects
- Small eyes (microphthalmia) and other eye defects
- Cleft lip and palate
- Polydactyly
- Cardiac and renal malformations

Turner syndrome



Figure 9.6 Turner syndrome. The woman on the left has marked short stature but no other clinical features; the adolescent female on the right has neck webbing and has received growth hormone and is 150 cm in height.

Box 9.4 Clinical features of Turner syndrome

- Lymphoedema of hands and feet in neonate, which may persist
- Spoon-shaped nails
- Short stature – a cardinal feature
- Neck webbing or thick neck
- Wide carrying angle (cubitus valgus)
- Widely spaced nipples
- Congenital heart defects (particularly coarctation of the aorta)
- Delayed puberty
- Ovarian dysgenesis resulting in infertility, although pregnancy may be possible with *in vitro* fertilization using donated ova
- Hypothyroidism
- Renal anomalies
- Pigmented moles
- Recurrent otitis media
- Normal intellectual function in most cases

Turner syndrome

Turner syndrome usually results in early miscarriage (>95%) and is increasingly detected by ultrasound antenatally when oedema of the neck, hands, or feet or a cystic hygroma may be identified. In live-born females, the incidence is about 1 in 2500. Fig. 9.6 and Box 9.4 show the clinical features of Turner syndrome, although short stature may be the only clinical abnormality in children.

Treatment is with:

- growth hormone therapy
- oestrogen replacement for development of secondary sexual characteristics at the time of puberty (but infertility persists).

In about 50% of girls with Turner syndrome, there are 45 chromosomes, with only one X chromosome. The other cases have a deletion of the short arm of one X chromosome, an isochromosome that has two long arms but no short arm, or a variety of other structural defects of one of the X chromosomes. The presence of a Y chromosome sequence may increase the risk of gonadoblastoma. The incidence does not increase with maternal age, and risk of recurrence is very low.

Klinefelter syndrome (47, XXY)

This disorder occurs in about 1–2 per 1000 live-born males. For clinical features, see Box 9.5. Recurrence risk is very low.

Box 9.5 Clinical features of Klinefelter syndrome

- Infertility – most common presentation
- Hypogonadism with small testes
- Pubertal development may appear normal (some males benefit from testosterone therapy)
- Gynaecomastia in adolescence
- Tall stature
- Intelligence usually in the normal range, but some have educational and psychological problems

Disorders of chromosome structure

Deletions

Deletions involve loss of part of a chromosome and usually result in physical abnormalities and cognitive impairment. It is now possible to specify the genes involved in chromosomal deletions as molecular methods are replacing standard cytogenetic investigations. A variety of micro-deletion syndromes are described below and in Table 9.2.

Duplications

Gain of structural material can also lead to congenital malformations and intellectual impairment. Duplications are often better tolerated – and less likely to cause clinically important changes – than deletions. Duplications and deletions are also described as gene copy number variation (CNV).

Table 9.2 Examples of microdeletion syndromes

5p microdeletion	Cri du Chat syndrome	High pitched cry in infancy Hypotonia Microcephaly Intellectual disability Severity variable depending on size of deletion
22q11.2 microdeletion	DiGeorge syndrome (velocardiofacial syndrome)	Abnormal facies Cleft palate (posterior, may be submucosal) Cardiac anomalies Hypoplasia of thymus gland Immune dysfunction (see Fig. 15.28) Intellectual disability Autism/ADHD
7q11 microdeletion including the elastin gene	Williams syndrome	Characteristic facies Transient neonatal hypercalcaemia (occasionally) Supravalvular aortic stenosis Mild-to-moderate learning difficulties Short stature

An example of a duplication syndrome is partial trisomy of 17p. The duplication can range from being submicroscopic to being large enough to be visible on a karyotype. If it involves duplication of the *PMP22* gene at 17p12, then the patient will have (or develop) the type IA form of Charcot–Marie–Tooth disease (peripheral neuropathy) in addition to other features resulting from the abnormality.

Translocations

An exchange of material between two different chromosomes is called a translocation. When this exchange involves no loss or gain of chromosomal material, the translocation is ‘balanced’ and usually has no phenotypic effect. Balanced reciprocal translocations are relatively common, occurring in 1 in 500 of the general population. A translocation that appears balanced on conventional chromosome analysis may still involve the loss of a few genes or the disruption of a single gene at one of the chromosomal break points, resulting in an abnormal phenotype. Studying the break points in individuals with balanced translocations has been one way of identifying the location and function of specific genes.

Unbalanced reciprocal translocations involve a loss or gain of the overall amount of chromosomal material and often impair both physical and cognitive development, leading to dysmorphic features, congenital malformations, developmental delay, and learning difficulties. When recognized in a newborn baby, the prognosis is difficult to predict but the effect is usually severe. The parents’ chromosomes should be checked to determine whether the abnormality has arisen *de novo*, or as a consequence of a parental rearrangement. Finding a balanced translocation in one parent indicates a recurrence risk for future pregnancies, so that antenatal diagnosis by chorionic villus sampling or amniocentesis should be offered as well as testing relatives who might be carriers.

Patterns of inheritance

Mendelian inheritance

Mendelian inheritance, described by Mendel in 1866 from work on garden peas, is the transmission of inherited traits or diseases caused by variation in a single gene in a characteristic pattern. These Mendelian traits or disorders are individually rare but collectively numerous and important: over 6000 have been described so far. For many disorders, the Mendelian pattern of inheritance is known. If the diagnosis of a condition is uncertain, its pattern of inheritance may be evident on drawing a family tree (pedigree), which is an essential part of genetic evaluation (Fig. 9.7).

Autosomal dominant inheritance

This is the most common mode of Mendelian inheritance (Box 9.6). Autosomal dominant conditions are caused by alterations in only one copy of a gene pair, i.e. the condition occurs in the heterozygous state despite the presence of an intact copy of the relevant gene. Autosomal dominant genes are located on the autosomes (chromosomes 1–22), and so males and females are equally affected. Each child from an affected parent has a 1 in 2 (50%) chance of inheriting the abnormal gene (see Fig. 9.8a,b). This appears to be straightforward, but complicating factors include the following factors.

Homozygosity

In the rare situation where both parents are affected by the same autosomal dominant disorder, there is a 1 in 4 risk that a child will be homozygous for the altered gene. This is usually associated with a more severe phenotype, for example in achondroplasia.

Variation in expression

Within a family, some affected individuals may have different phenotypes, with some manifesting the disorder

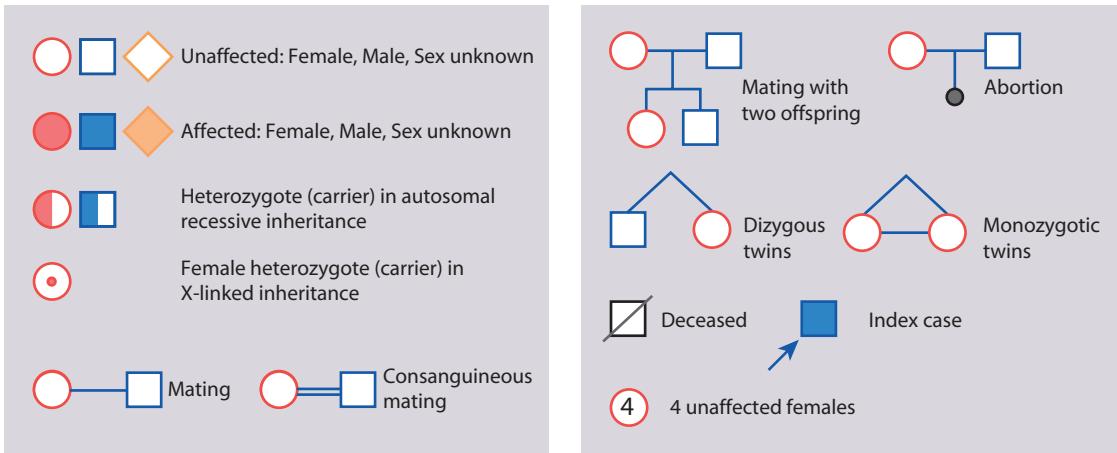


Figure 9.7 Examples of pedigree symbols.

Autosomal dominant inheritance

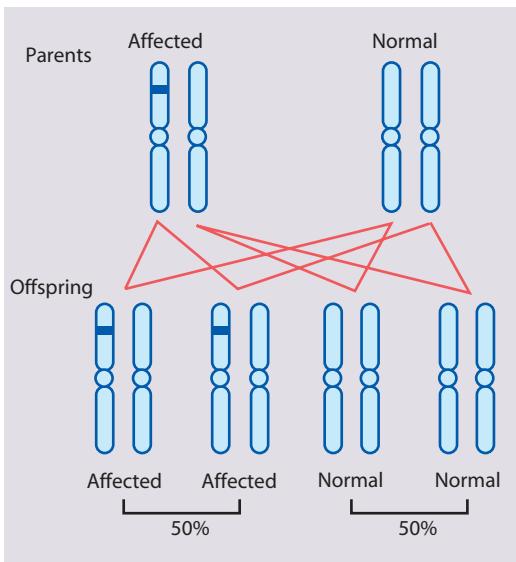


Figure 9.8a Autosomal dominant inheritance.

Box 9.6 Examples of autosomal dominant disorders

- Achondroplasia
- Familial hypercholesterolaemia (almost all cases)
- Huntington disease
- Marfan syndrome
- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta (most forms)
- Otosclerosis
- Polyposis coli
- Tuberous sclerosis

Summary

Autosomal dominant inheritance

- Most common mode of Mendelian inheritance.
- Affected individual carries the abnormal gene on one of a pair of autosomes.
- There is 1 in 2 chance of inheriting the abnormal gene from affected parent, but there may be variation in expression, non-penetrance, no family history (new mutation, parental mosaicism, non-paternity), or homozygosity (rare).

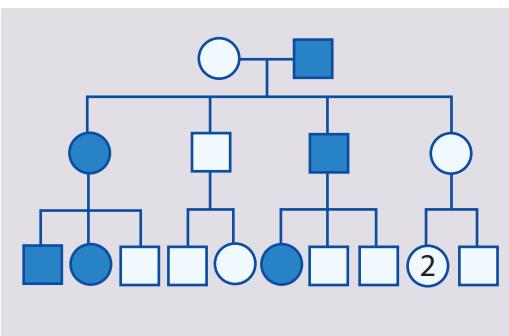


Figure 9.8b Typical pedigree of an autosomal dominant disorder.

mildly, if at all, and others more severely. This may be the result of variation at other genes, environmental effects, or sheer chance.

Non-penetrance

Refers to the lack of clinical signs and symptoms in an individual who has inherited the abnormal gene. An example of this is otosclerosis, in which only about 40% of gene carriers develop deafness (Fig. 9.9).

De novo mutation

A mutation is classed as *de novo* if it does not affect either parent. It may be due to:

- a new mutation in one of the gametes leading to the conception of the affected person. This is the most common reason for absence of a family history in autosomal dominant disorders, e.g. about 80% of individuals with achondroplasia have unaffected parents. The risk of such new mutations increases with paternal age
- mosaicism in a parent – very occasionally a healthy parent carries the disease-causing mutation in only some of their cells, e.g. in their gonads or in their soma and their gonads. This can account for recurrences of autosomal dominant disorders in siblings born to apparently unaffected parents. It has been described in congenital lethal osteogenesis imperfecta
- non-paternity – if the apparent father is not the biological father.

Knudson two-hit hypothesis

Some autosomal dominant conditions related to cancer susceptibility follow Knudson's two-hit hypothesis. Both copies of the gene need to be mutated for a malignancy to occur. If a person is born with only one working copy of the gene in every cell in his/her body, then only one further mutation event needs to occur for both copies of the gene to be inactivated, meaning cancer susceptibility occurs. The chance of this happening is much greater than the chance of two successive mutations occurring in someone who starts life with two functional copies of the gene. The susceptibility to cancer is therefore inherited in a dominant fashion but the development of cancer within a cell can be thought of as a local, recessive event within

the individual, so that not every person who inherits the susceptibility will necessarily develop a malignancy.

An example in paediatrics is mutation in the retinoblastoma (*Rb*) gene. If a child inherits the susceptibility, i.e. a mutation in one copy of the *Rb* gene, then a tumour will occur if a second hit occurs on the working copy in a cell of the relevant type, so that the child inheriting a mutation will often have a tumour in both eyes, but approximately 10% will escape with neither eye affected.

Autosomal recessive inheritance

An affected individual is homozygous for the mutant allele in the gene. Sometimes, there is a different mutation on each copy of the gene, for example cystic fibrosis, and the affected individual is a compound heterozygote. In either situation, they will have inherited an abnormal allele from each parent, both of whom will usually be unaffected heterozygous carriers (Box 9.7). For a couple who are both carriers, the risk of any child being affected, male or female, is 1 in 4 (25%; Fig. 9.10a,b). All offspring of an affected individual will carry the condition. If an affected individual has children with an unaffected carrier, then each has a 50% chance of being affected.

Consanguinity

It is thought that we all carry six to eight abnormal recessive genes. Fortunately, our partners usually carry different ones. Marrying a cousin or another relative increases the chance of both partners carrying the same autosomal recessive gene mutation. Cousins who marry have a modest increase in the risk of having a child with a serious recessive disorder. Raising this for discussion with families must be done in a sensitive way, as discussion may trigger feelings of guilt, blame, and intercultural disrespect.

The frequencies of disease alleles at recessive gene loci vary between population groups. When the gene occurs sufficiently often and the gene or its effects can be detected, population-based carrier screening can be performed and population-based risk screening can be offered for high-risk pregnancies where both parents are carriers. Disorders that have been screened for in this way for many years include sickle cell disease in black Africans, black Caribbeans and African Americans, the thalassaemias in those from Mediterranean or Asian populations, and Tay–Sachs disease in Ashkenazi Jews. With developments in DNA-sequencing technologies, it is becoming possible for the range of disorders being screened to increase dramatically. In places where consanguineous marriage is customary, these technologies can be used to help prevent affected pregnancies by identifying carrier status. This information may inform the selection of partners, or inform reproductive decision-making.

X-linked inheritance

X-linked conditions are caused by alterations in genes found on the X chromosome. These may be inherited as X-linked recessive or X-linked dominant traits but the distinction between these is much less clear than in autosomal traits because of the variable pattern of X chromosome inactivation in females.

In X-linked recessive inheritance (Box 9.8, Fig. 9.11a,b):

- Males are affected.
- Female carriers are usually healthy, though occasionally a female carrier shows features of the disease.

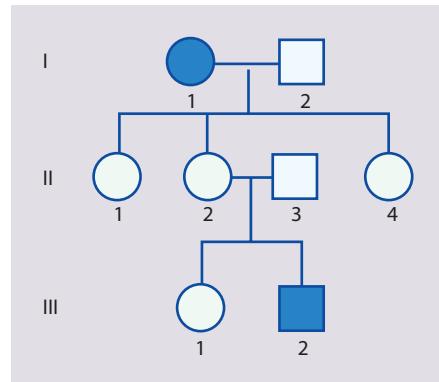


Figure 9.9 Example of non-penetrance. I1 and III2 have otosclerosis. II2 has normal hearing but must have the gene (a new mutation event is most unlikely to arise independently for a second time in the family). The gene is non-penetrant in II2.

Autosomal recessive inheritance

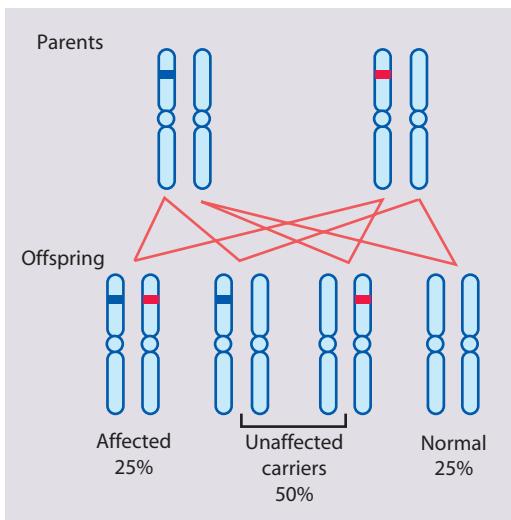


Figure 9.10a Autosomal recessive inheritance.

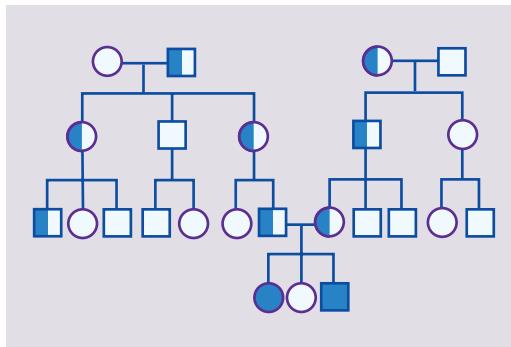


Figure 9.10b Pedigree to show autosomal recessive inheritance.

- Each son of a female carrier has a 1 in 2 (50%) risk of being affected.
- Each daughter of a female carrier has a 1 in 2 (50%) risk of being a carrier.
- All daughters of affected males will all be carriers.
- Sons of affected males will not be affected, because a man passes a Y chromosome to his sons.

The family history may be negative, because new mutations and (gonadal) mosaicism are fairly common in some conditions. Identification of carrier females in a family requires interpretation of the pedigree, the search for mild clinical manifestations, and the identification of carriers using specific biochemical or molecular tests. Identifying carriers is important because a female carrier has a 50% risk of having an affected son (regardless of who her partner is) and X-linked recessive disorders can be very severe.

Box 9.7 Examples of autosomal recessive disorders

- Congenital adrenal hyperplasia
- Cystic fibrosis
- Friedreich ataxia
- Galactosaemia
- Glycogen storage diseases
- Hurler syndrome
- Oculocutaneous albinism
- Phenylketonuria
- Sickle cell disease
- Tay–Sachs disease
- Thalassaemia
- Werdnig–Hoffmann disease (SMA1)

Summary

Autosomal recessive inheritance

- Affected individuals are usually homozygous for the abnormal gene; each unaffected parent will be a heterozygous carrier.
- Two carrier parents have a 1 in 4 risk of having an affected child.
- Risk of these disorders varies between populations and is increased by consanguinity.
- Mutation in the gene for an enzyme in a metabolic pathway will often be inherited as an autosomal recessive disorder, while mutation in genes for structural proteins that function as large, multimeric protein assemblies (e.g. collagen molecules) are often inherited in an autosomal dominant manner.

Summary

X-linked recessive inheritance

- Males are affected; females can be carriers but are usually healthy or have mild disease.
- Family history may be negative – many arise from new mutations or gonadal mosaicism.
- Identifying female carriers is important to be able to provide genetic counselling.
- All the female offspring of affected males will be carriers, but none of the male offspring can inherit the mutation.
- Half of the male offspring of a female carrier will be affected and half of the female offspring will be carriers.

X-linked recessive inheritance

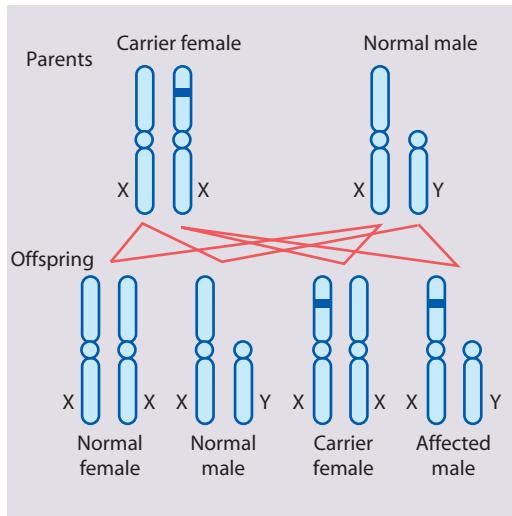
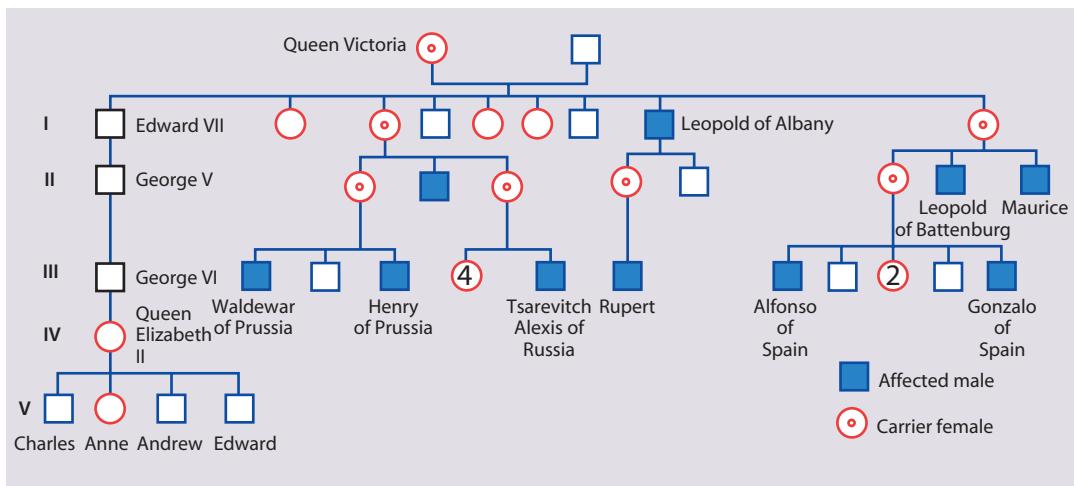


Figure 9.11a X-linked (recessive) inheritance.

Box 9.8 Examples of X-linked recessive disorders

- Colour blindness (red-green)
- Duchenne and Becker muscular dystrophies
- Fragile X syndrome
- Glucose-6-phosphate dehydrogenase deficiency
- Haemophilia A and B
- Hunter syndrome (mucopolysaccharidosis II)

Figure 9.11b Typical pedigree for X-linked (recessive) inheritance, showing Queen Victoria, a carrier for haemophilia A, and her family. It shows affected males in several generations, related through females, and that affected males do not have affected sons (contrast with autosomal dominant inheritance).



X-linked dominant disorders, where both males and females are affected, are unusual. An example is hypophosphataemic (vitamin D-resistant) rickets. In some other X-linked dominant disorders, a female carrying the mutation will be affected while the mutation-carrying males have an even more serious condition. Thus, a mutation that causes Rett syndrome (a neurodegenerative disorder) in a girl will cause a lethal, neonatal-onset encephalopathy in males. Another reason why a sex-linked condition may predominantly affect females is because it usually arises through mutations at spermatogenesis (e.g. Rett syndrome). As male offspring must inherit a Y chromosome from their father, they will not inherit any mutations on the X chromosome that arise during spermatogenesis.

Y-linked inheritance

Y-linked traits are extremely rare. Y-linked inheritance would result in only males being affected, with transmission from an affected father to all his sons. Y-linked genes determine sexual differentiation and spermatogenesis, and mutations are associated with infertility and so are rarely transmitted.

Unusual genetic mechanisms

Trinucleotide repeat expansion mutations

This is a class of unstable mutations that consist of expansions of trinucleotide repeat sequences. Fragile X syndrome, myotonic dystrophy, and Huntington disease are among the best known of these disorders. They share certain unusual properties due to the nature of the underlying mutation. Trinucleotide repeat disorders exhibit a phenomenon known as anticipation. The triplet repeat mutation is unstable and can expand between subsequent generations. In general, a larger expansion causes a more severe form of the disease. This means that these conditions become more severe in successive generations of the same family.

There are two major categories of triplet repeat disorder, depending on whether or not the triplet repeat is in the coding sequence of the gene. When the triplet repeat expansion is in the coding sequence, as in Huntington disease (and in a number of other neurodegenerative disorders), proteins containing an excess of the amino acid, glutamine, are produced. These polyglutamine

Fragile X



Figure 9.12 A child with fragile X syndrome. At this age, the main physical feature is often the prominent ears.

expansions are toxic, damaging the cells in the central nervous system through a gain-of-function mechanism and leading to neurodegeneration. When the triplet repeat expansion is in other regions of the gene, reduced quantities of the protein are produced. In these cases, the reduction in the amount of the available protein leads to the symptoms of the condition. One such example is myotonic dystrophy, which is described further in [Chapter 29](#) (Neurological disorders).

Most of the triplet repeat disorders are autosomal dominant, but there is one autosomal recessive disorder, Friedreich ataxia, and one which is X linked, fragile X syndrome.

Fragile X syndrome

The prevalence of significant learning difficulties in males due to fragile X syndrome is about 1 in 4000 ([Fig. 9.12](#) and [Box 9.9](#)). This condition was initially diagnosed on the basis of the cytogenetic appearance of a 'fragile site', (a local failure of chromatin condensation), in the distal part of the long arm of the X chromosome. Diagnosis is now achieved by molecular analysis of the trinucleotide repeat expansion in the gene (FMR1).

Although it is inherited as an X-linked disorder, some 40% to 50% of female carriers have learning difficulties (usually mild to moderate).

Males can be unaffected but transmit the condition through their daughters to their grandsons. This is not possible in haemophilia or Becker muscular dystrophy, for example, where a male cannot inherit the condition from his family and transmit the condition to his children without himself being affected. This can occur in fragile X because the triplet repeat expansion varies in its nature with its size. The normal range of repeat numbers is up to about 45 repeats; when larger than that, the block of repeats becomes increasingly unstable but continues to permit fragile X gene expression until a 'full mutation' is reached at about 200 repeats. From 55 repeats to 200 repeats is known as the 'premutation' range. A male can inherit a premutation and transmit it to his daughters (who will all be carriers) while being intellectually normal and without the physical features of fragile X.

Box 9.9 Clinical findings in males in fragile X syndrome

- Moderate–severe learning difficulty (IQ 20–80, mean 50)
- Macrocephaly
- Macroorchidism – postpubertal
- Characteristic facies – long face, large everted ears, prominent mandible, and broad forehead, most evident in affected adults
- Other features – mitral valve prolapse, joint laxity, scoliosis, autism, hyperactivity

Because these full mutations always arise from expansion of premutations, and never directly from normal genes, the mothers of affected males have to be carriers of a premutation or full mutation. Offering referral for genetic counselling is therefore appropriate for all fragile X families, especially as there can be associated disorders for premutation carriers in adult life, a neurodegenerative condition especially in males and premature ovarian failure in females.



Fragile X syndrome is one of the commonest causes of severe learning difficulties.

Mitochondrial or cytoplasmic inheritance

Mitochondria are cytoplasmic organelles that function as a cellular compartment within which many different metabolic pathways are located, including the production of energy by oxidative phosphorylation. They contain their own DNA (mtDNA), but most of the proteins involved in mitochondrial metabolic reactions are encoded in the nuclear genome. The mtDNA encodes proteins involved in oxidative phosphorylation together with the RNA and proteins necessary for mitochondrial protein synthesis.

Each cell contains thousands of copies of the mitochondrial genome. Inherited disorders of mitochondrial function may result from mutations in the nuclear genome or, less often, from mutations in the mitochondrial genome (mtDNA). Diseases caused by mutations in mtDNA show only maternal transmission, because only the egg contributes mitochondria to the zygote.

In disorders of the mtDNA, the mutation may be present in all or only some of the mitochondria, so that the tissues affected and the severity of the condition can be highly variable. Mutations in mtDNA cause overlapping clusters of disease phenotypes, with tissues with high energy requirements such as muscle, brain, the heart, and the retina being more often affected (e.g. Leber hereditary optic neuropathy and various mitochondrial myopathies and encephalopathies, such as Kearns–Sayre, MERRF, MELAS, and NARP). These conditions are described in more detail in [Chapter 27](#) (Inborn errors of metabolism).

Imprinting and uniparental disomy

The expression of some genes is influenced by the sex of the parent who transmitted it. This phenomenon is called 'imprinting'. If one copy of a gene is said to be imprinted, that copy is switched off, at least in some tissues.

An example involves Prader–Willi syndrome (Fig. 9.13 and Box 9.10). The PWS chromosomal region is found at 15q11–13 (i.e. at bands 11 to 13 on the long arm of chromosome 15). Both the paternal and the maternal copies of this chromosomal region must function for normal development. In the absence of a (functioning) paternal copy of this region, a child will develop PWS, as some genes are maternally imprinted. By contrast, the failure to inherit a (functioning) maternal copy of this chromosomal region results in an entirely different condition, Angelman syndrome, leading to severe cognitive impairment, a



Figure 9.13 Prader–Willi syndrome.

characteristic facial appearance, ataxia, and epilepsy. This is due to a lack of expression of the *UBE3A* gene and the paternal copy being imprinted.

There are several ways a child can develop one or other condition:

- deletion *de novo* (Fig. 9.14) – parental chromosomes are normal, and a deletion occurs as a new mutation in the child. If the deletion occurs on the paternal chromosome 15, the child has PWS. If the deletion affects the maternal chromosome 15, the child has Angelman syndrome
- uniparental disomy (Fig. 9.15) – this is when a child inherits two copies of a chromosome from one parent and none from the other parent. In PWS the affected child has no paternal (but two maternal) copies of chromosome 15q11–13. In Angelman syndrome the affected child has no maternal (but two paternal) copies of chromosome 15q11–13. This can be detected with DNA analysis
- point mutation within the *UBE3A* gene also causes Angelman syndrome

There are other, less common mechanisms that can lead to these conditions.

Box 9.10 Clinical features of Prader–Willi syndrome

- Characteristic facies
- Hypotonia
- Hypogonadism
- Neonatal feeding difficulties
- Faltering growth in infancy
- Hyperphagia and obesity in later childhood
- Developmental delay
- Learning difficulties

Imprinting

Imprinting from a deletion

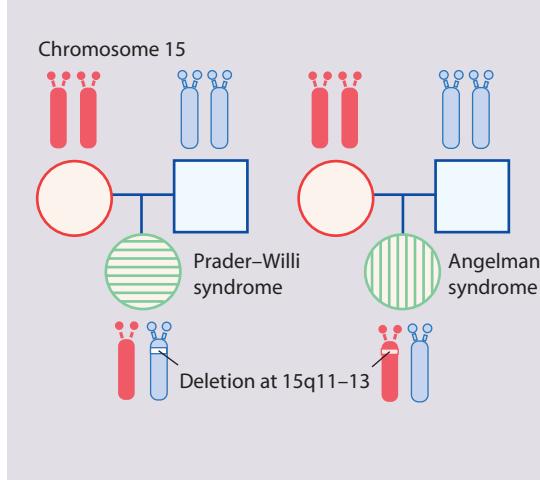


Figure 9.14 Genetic disorder resulting from deletion of an imprinted gene. If the deletion occurs on chromosome 15 inherited from the father, the child has Prader–Willi syndrome. If the deletion occurs on chromosome 15 from the mother, the child has Angelman syndrome.

Imprinting from a uniparental disomy

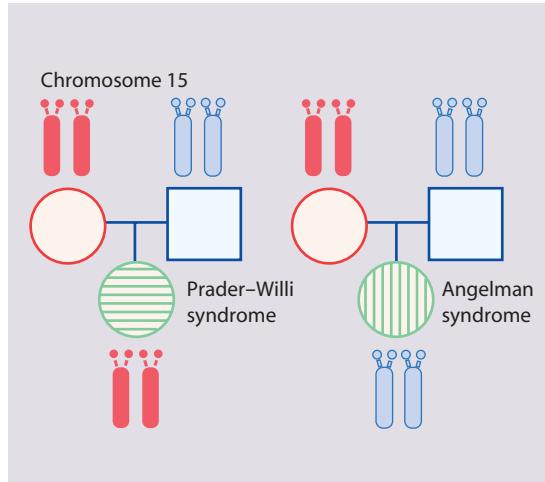


Figure 9.15 Genetic disorder resulting from uniparental disomy affecting imprinted chromosome region. A child who inherits two maternal chromosome 15s will have Prader–Willi syndrome. A child who inherits two paternal chromosome 15s will have Angelman syndrome.

Multifactorial and polygenic inheritance

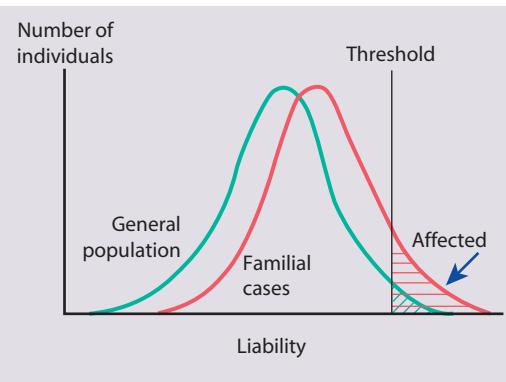


Figure 9.16 Diagram showing the increased liability to a multifactorial disorder in relatives of an affected person.

Box 9.11 Conditions often associated with multifactorial (polygenic) inheritance

Congenital malformations (in their non-syndromic forms)

- neural tube defects (anencephaly and spina bifida)
- congenital heart disease
- cleft lip and palate
- pyloric stenosis
- developmental dysplasia of the hip (DDH)
- talipes equinovarus
- hypospadias

Childhood

- atopy (especially asthma and eczema)
- epilepsy
- diabetes mellitus type 1 (insulin-dependent diabetes)

Adult life

- atherosclerosis and coronary artery disease
- diabetes mellitus type 2
- Alzheimer disease
- malignancy (especially the common cancers, e.g. breast and colorectal cancer)
- hypertension
- cerebrovascular disease (especially stroke)



Imprinting is the unusual property of some genes that express only the copy derived from the parent of a given sex.

Multifactorial and polygenic inheritance

There is a spectrum in the aetiology of disease, from environmental factors (e.g. trauma) at one end to purely genetic causes (e.g. Mendelian disorders) at the other. Between these two extremes are many disorders that result from the interacting effects of several genes (polygenic) with or without the influence of environmental or other unknown factors, including chance (multifactorial or complex) (Box 9.11).

Variation in quantitative traits, such as height and intelligence, results from complex interactions between environmental factors and multiple genetic influences. The environmental factors include early life (including intrauterine) experiences. These parameters are thought to show a Gaussian (normal) distribution in the population. Similarly, the liability of an individual to develop a disease of multifactorial or polygenic aetiology has a Gaussian distribution. The condition occurs when a certain threshold level of liability is exceeded. Relatives of an affected person show an increased liability due to inheritance of genes conferring susceptibility, and so a greater proportion of them than in the general population will fall beyond the threshold and will manifest the disorder (Fig. 9.16). The risk of

recurrence of a polygenic disorder in a family is usually low and is most significant for first-degree relatives. Empirical recurrence risk data are used for genetic counselling. They are derived from family studies that have reported the frequencies at which various family members are affected. Factors that increase the risk to relatives are:

- having a more severe form of the disorder, e.g. the risk of recurrence to siblings is greater in bilateral cleft lip and palate than in unilateral cleft lip alone
- close relationship to the affected person, e.g. overall risk to siblings or children is greater than to more distant relatives
- multiple affected family members, e.g. the more siblings already affected, the greater the risk of recurrence
- sex difference in prevalence, with the recurrence risk greater in the more commonly affected sex and if the affected individual is of the less commonly affected sex.

The phenotype (clinical picture) of a disorder may have a heterogeneous (mixed) basis in different families, e.g. hyperlipidaemia leading to atherosclerosis and coronary heart disease can be due to a single gene disorder such as autosomal dominant familial hypercholesterolaemia, but some forms of hyperlipidaemia are polygenic and result from an interaction of the effect of several genes and dietary factors.

In some complex disorders, such as Hirschsprung disease, the molecular genetic basis and the important contribution of new mutations are becoming clear. In many multifactorial disorders, however, the 'environmental factors' remain obscure. Clear exceptions include dietary fat intake and smoking in atherosclerosis, and viral infection in insulin-dependent diabetes mellitus. For neural tube defects, the risk of recurrence to siblings is lowered from about 4% to 1% or less in future pregnancies if the mother takes folic acid before conception and in the early weeks of pregnancy.

Epigenetic factors

Epigenetics describes the biological processes that connect the genotype of a cell or multicellular organism with the phenotype: the mechanisms or switches capable of turning genes on and off, or altering their expression. The result is functionally relevant changes that are not caused by alterations in the DNA sequence.

The prenatal, neonatal and early childhood periods are when epigenetic DNA imprinting is most active. The role of epigenetic regulation before and after birth will be critical in understanding how the perinatal and early childhood periods relate to disease susceptibility in later life, for example the association between low birthweight and both cardiovascular disease and type II diabetes mellitus.

Dysmorphology

The term 'dysmorphology' literally means 'the study of abnormal form'. It refers to the assessment of birth defects and unusual physical features that have their origin during embryogenesis.

Pathogenic mechanisms

Malformation

A primary structural defect occurring during the development of a tissue or organ, e.g. spina bifida, cleft lip, and palate.

Deformation

Implies an abnormal intrauterine mechanical force that distorts a normally formed structure, e.g. joint contractures or pulmonary hypoplasia caused by severe oligohydramnios.

Disruption

Involves disruption to the structure of a part that initially formed normally, e.g. vascular accidents, or amniotic bands that may cause limb reduction defects. Maternal medications such as phenytoin, warfarin, or thalidomide can cause teratogenic effects. Intrauterine virus exposure, such as rubella or cytomegalovirus, may damage the normally formed embryo or fetus.

Dysplasia

Refers to abnormal cellular organization or function of specific tissue types, e.g. skeletal dysplasias, dysplastic kidney disease.

Clinical classification of birth defects

Single-system defects

These include single congenital malformations, such as spina bifida, which are often multifactorial in nature with fairly low recurrence risks.

Sequence

Refers to a pattern of multiple abnormalities occurring after one initiating defect. 'Potter syndrome' (fetal compression and pulmonary hypoplasia) is an example of a sequence in which all abnormalities may be traced to one original malformation causing failure of fetal urine excretion from renal agenesis or posterior urethral valves.

Association

A group of malformations that occur together more often than expected by chance, but in different combinations from case to case, e.g. vertebral anomalies, anal atresia, cardiac defects, tracheo-oesophageal fistula, renal anomalies, limb defects (VACTERL) association.

Syndrome

When a particular set of multiple anomalies occurs repeatedly in a consistent pattern and there is known or thought to be a common underlying causal mechanism, this is called a 'syndrome'. Multiple malformation syndromes are often associated with moderate or severe cognitive impairment and may be due to:

- chromosomal defects
- a single gene defect (dominant, recessive, or sex linked)
- exposure to teratogens such as alcohol, drugs (especially anticonvulsants such as valproate, carbamazepine, and phenytoin), or infection (especially viral) during pregnancy
- unknown cause.

Syndrome diagnosis

Although most syndromes are individually rare, recognition of a dysmorphic syndrome is worthwhile as it may give information regarding:

- prognosis
- risk of recurrence, with potential impact on reproduction for both the proband and parents
- likely complications, which can be sought and perhaps treated successfully if detected early
- the avoidance of unnecessary investigations
- experience and information, which parents can share with other affected families through family support groups.

Examples of syndromes recognizable by facial appearance are Noonan syndrome (Fig. 9.17 and Box 9.12), Williams syndrome (Fig. 9.18) and Prader–Willi syndrome (Fig. 9.13 and Box 9.10 above). The importance and impact of syndrome diagnosis is demonstrated in Case history 9.1. Databases are available to assist with the recognition of thousands of multiple congenital anomaly syndromes (e.g. London Dysmorphology Database).



Figure 9.17 Noonan syndrome affects both males and females. There are some similarities to the phenotype in Turner syndrome, but it is caused by mutation in an autosomal dominant gene and the karyotype is normal.

Box 9.12 Clinical features of Noonan syndrome

- Characteristic facies
- Short webbed neck with trident hair line
- Pectus excavatum
- Congenital heart disease (especially pulmonary stenosis, atrial septal defect)
- Short stature
- Occasional mild learning difficulties



Figure 9.18 Williams syndrome is usually sporadic.



Case History 9.1

Syndrome diagnosis

Sean, the second child of healthy parents, was born at term by emergency caesarean section for fetal distress. The pregnancy had been uneventful and no abnormalities were detected on antenatal ultrasound scan. He developed respiratory distress and investigation triggered by a cardiac murmur revealed an interrupted aortic arch and ventricular septal defect that required surgical correction in the neonatal period.

The parents asked about recurrence risk for congenital heart disease and were referred to the genetic clinic. At that time, Sean was thriving and early developmental progress appeared normal. On examination, there were minor dysmorphic features, including a short philtrum, thin upper lip, and prominent ears (Fig. 9.19). There was no family history of congenital heart disease or other significant problems, and no abnormalities were detected on examination of the parents.

Because of an association between outflow tract abnormalities of the heart and deletions of chromosome 22, cytogenetic analysis was performed. This was by chromosomal microarray (Fig. 9.20), but can also be identified by FISH (fluorescence in situ hybridization) (Fig. 9.21) or Ensembl genomic

database (see Fig. 9.1 above). A submicroscopic deletion of the long arm of one chromosome 22 (band 22q11) was detected, DiGeorge syndrome. Other features of the syndrome (hypocalcaemia and T-cell deficiency), which occurs with the same chromosome deletion, were excluded but could have been important in Sean's medical management.

Parental chromosome analysis showed no deletion at chromosome 22q11 in either parent, indicating a low recurrence risk for future pregnancies because gonadal mosaicism for this deletion is very rare. The older sibling was also normal on testing. Because the parents had normal karyotypes, their own brothers and sisters were not required to be tested.

Identification of a 22q11 deletion indicated that other associated problems were likely, particularly developmental delay. Subsequently, this required assessment by a multidisciplinary child development team, which led to: the formal assessment of his educational needs and the recommendation for placement in an appropriate school for children with learning difficulties; input from a clinical psychologist when behavioural problems appeared (ritualistic behaviour and obsessional tendencies); input from speech therapist and plastic surgeon (indistinct speech due to velopharyngeal incompetence); and audiology review (conductive hearing loss due to recurrent otitis media).

The impact of the diagnosis and its implications was considerable for the family, and the parents needed support from a variety of professionals while coming to terms with the various problems as they became apparent. Written information and details of the 22q11 support group were given to the parents. Medical care was coordinated by the paediatrician.

There was the additional worry for the family about a subsequent pregnancy. Fetal echocardiography showed no evidence of congenital heart disease, and the offer of invasive tests for cytogenetic analysis was declined because of the low chance of recurrence and the risk of miscarriage from the test. The baby was born unaffected, with chromosome studies performed on a cord blood sample revealing no abnormality.



Figure 9.19 Sean's facial appearance showing the short philtrum (vertical groove in the upper lip), thin upper lip, and prominent ears.

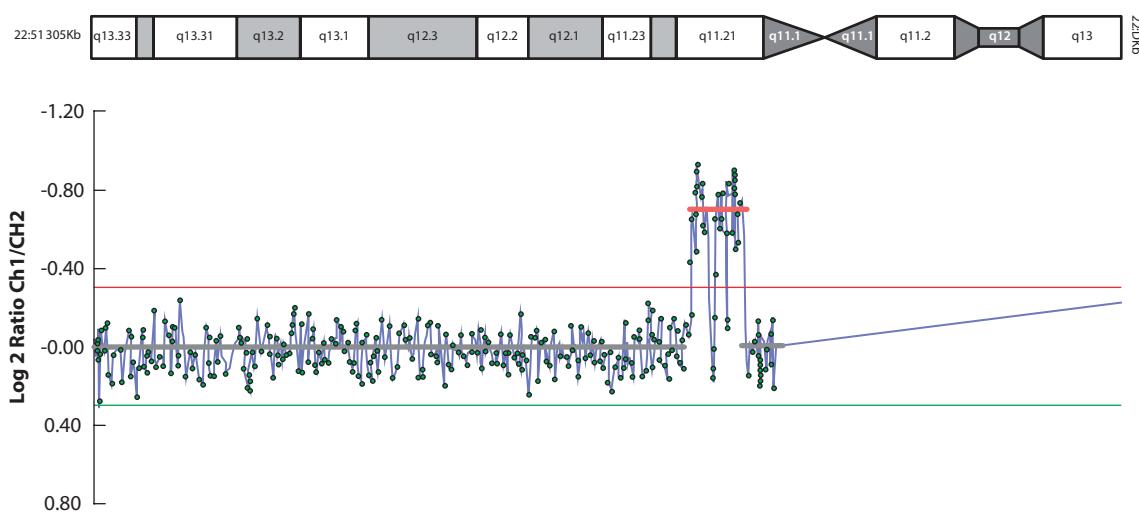


Figure 9.20 Array comparative genomic hybridization (microarray) result for a patient with 22q11 deletion. There is a reduction in the ratio of patient:control sequences from within band 22q11 on the long arm of chromosome 22.

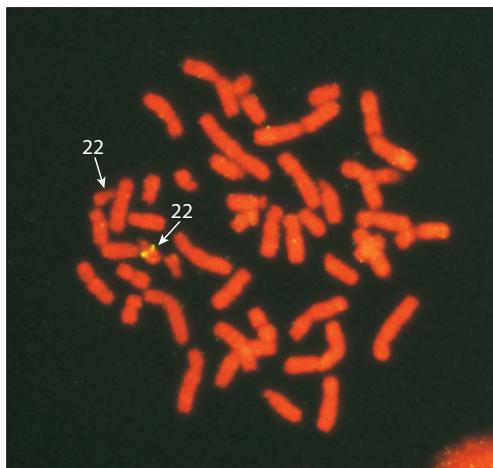


Figure 9.21 Fluorescence in situ hybridization (FISH) demonstrating a microdeletion on chromosome 22 associated with DiGeorge syndrome. Hybridization signals are seen on one chromosome 22 but not on the other because of the presence of a deletion. (Courtesy of L. Gaunt, St Mary's Hospital, Manchester, UK.)

Summary

Dysmorphology

- Comprises birth defects and abnormal clinical features originating during embryogenesis.
- May be a malformation, deformation, disruption, or dysplasia.
- May be classified as a single-system defect, sequence, association, or syndrome.
- Syndromes can be recognized by 'Gestalt', which may be aided by dysmorphology databases.

Rare diseases

Rare diseases are defined as a disease that affects less than 1 in 2000 of the general population. In the UK, a single rare

disease may affect up to about 30,000 people, with the vast majority of rare diseases affecting far fewer than this. There are over 6000 known rare diseases, and around 80% have a genetic component.

These disorders are often associated with significant morbidity and mortality, can be challenging to diagnose and have few treatment options. Sequencing technologies play an important role in the diagnosis of rare disease. Diagnosis often enables access to information, support and co-ordination of care, in addition to access to treatment, participation in research and peer support networks.

Genetic investigations

For many years, genetic investigation relied on determining the karyotype by visualization of the chromosomes with light microscopy. This has been transformed by the tremendous advances in molecular testing, which are summarized in [Table 9.3](#).

Cytogenetic analysis

- Karyotype:** Chromosomes are stained and visualized under a microscope. Detects alterations in chromosome number and structural rearrangements; this method is being replaced by molecular methods such as comparative genomic hybridization, except when looking for chromosomal rearrangements.
- Microarray comparative genomic hybridization:** Detects chromosomal imbalances (see [Fig. 9.20](#)) using thousands of DNA probes to investigate a whole genome with much greater sensitivity than cytogenetic methods. No specific target is required for the test to be effective. Microarrays only provide quantitative data, and cannot be used to check for structural rearrangements, e.g. balanced translocations or inversions.
- Molecular cytogenetic analysis – fluorescence in situ hybridization (FISH):** Fluorescent-labelled DNA probes to detect the presence, number, and

Table 9.3 Different forms of genetic testing and their indications

	Dosage methods			Sequencing methods	
Scope of Test	<i>Genome wide</i>	<i>Large target region</i>	<i>Short target sequence</i> ¹	<i>Genome wide</i>	<i>Exons of multiple genes</i> ²
Testing Method	Karyotyping aCGH	FISH QF-PCR	MLPA QF-PCR	Whole exome sequencing; whole genome sequencing: always using NGS	Gene Panel Testing. NGS increasingly used for this.
Able to identify	Changes in amount of genetic material – gene copy number variation (CNV) including duplications (increased copy number) and deletions (decreased copy number)	Changes in ‘amount’ of genetic material at a specific chromosomal location	Changes in copy number of selected sequences. Test result gives information about number of copies of clinically important sequences	Order or sequence of base pairs across the whole genome or the exons (protein coding part of the genome)	Order or sequence of base pairs at particular loci known to account for a given phenotype
Use	Investigate broad/complex phenotype	To answer a specific clinical question	To answer a specific clinical question	Formerly used mostly in research to identify candidate genes for particular phenotypes but now increasingly applied as a diagnostic method	Investigate a particular phenotype with multiple candidate genes
Clinical question	Is there a chromosomal copy number variation which can account for this phenotype? For karyotype only: is there a chromosomal rearrangement?	Can this phenotype be explained by a dosage change of this specific chromosome or sub-chromosomal region?	Can this phenotype be explained by a dosage change at this specific location?	Can we identify new candidate genes that account for this phenotype?	Does a change in any of these known genes account for this phenotype?

¹May give information about large regions or whole chromosomes if multiple reactions are used.²Multiple genes that are associated with a shared function or phenotype.

aCGH – array comparative genomic hybridization; FISH – fluorescence in-situ hybridization; MLPA – multiplex ligation-dependent probe amplification; QF-PCR – quantitative fluorescent polymerase chain reaction; NGS – next generation sequencing.

chromosomal location of specific chromosomal sequences. Useful for microdeletion syndromes (see Fig. 9.21).

- **PCR:** Amplification of a specific target site within the genome, which then permits the conventional sequencing of the amplified DNA.

Next-generation sequencing

It is now possible to generate large volumes of DNA sequence data in a rapid and cost-effective fashion. These techniques of high-throughput sequencing are used to enable:

- gene panel testing – where a specific set of genes is sequenced, for example all the genes known to be relevant to a specific disease presentation (e.g. retinal degeneration, cardiomyopathy, infantile-onset epilepsy)
- whole exome sequencing (WES) – the exome is the protein coding part of the genome. WES involves

sequencing the coding regions of the genome to determine variants, which are then analyzed to interpret the findings

- whole genome sequencing (WGS) – the whole genome is sequenced, including noncoding regions. Development in this field is rapid and whole genome sequencing has technical advantages over whole exome sequencing, so that the current use of whole exome sequencing is likely to be replaced by WGS over the next few years.

In a diagnostics laboratory, the sequencing step of a genomic analysis may be performed by WGS while the interpretation of variants may be restricted to those in the exome or in a panel of genes relevant to the patient’s phenotype. ‘Trio’ sampling involves comparing the sequence data for a proband with those of the unaffected biological parents, allowing the rapid identification of *de novo* variants which are more likely to account for disease.

Recent studies have focused on implementation of next-generation sequencing in clinical practice ([Case history 9.2](#)). The Deciphering Developmental Disorders study utilized exome sequencing in a large cohort of undiagnosed patients with developmental delay and their parents. The results have been (and still are being) entered into a database (DECIPHER) of genotypes and related phenotypes. In the UK, the 100,000 Genomes Project (100KGP) is utilizing WGS to study a wide range of clinical conditions in adults and children (see Further reading).

Genetic services

In the UK, all health regions have a clinical genetics centre where specialist genetic services are provided by consultants, genetic counsellors, and laboratory scientists. Specialist clinical genetic assessment and genetic counselling are provided at the centre and in a network of clinics. Genetic investigations can be accessed through these clinical services as well as directly through primary and secondary care, where many commonly used genetic tests are being 'mainstreamed' into the practice of other specialties. Increased recognition of disorders antenatally has necessitated expansion of prenatal genetic services working alongside fetal medicine.



Case History 9.2

Diagnosing the cause of developmental delay

Archie, an 8-month-old boy, is referred to tertiary neurology services with concerns regarding his gross motor development. He was born by spontaneous vaginal delivery at term following an IVF pregnancy. On examination he has reduced central tone and distal rigidity. Reflexes are normal. Biochemical analysis of blood and CSF did not reveal any evidence of sepsis or inflammation, and MRI scan of the brain and spine was normal. Chromosomal microarray was normal, and trio whole exome sequencing was undertaken to look for inherited autosomal recessive causes.

This revealed a compound heterozygous variation in the *TH* gene. Biallelic variants in this gene are known to cause Segawa syndrome, also known as tyrosine hydroxylase deficiency. This disorder has a broad phenotypic spectrum, but includes hypotonia, delay and some dystonia and movement problems. Severity is often linked to age of onset. This variant of uncertain significance guided metabolic testing which was able to support the diagnosis. This allowed reclassification of the variant from one of uncertain significance to one of likely pathogenicity.

This case history demonstrates how rapid whole exome sequencing provides a clinically useful adjunct to the investigation and diagnosis of complex paediatric presentations. Establishing a diagnosis curtailed the 'diagnostic Odyssey' frequently encountered with complex or rare diseases and reduced the need for repeated investigations, for example further imaging under sedation. A diagnosis enabled effective genetic counselling, including future reproductive risk, and access to treatment of his enzyme deficiency with symptomatic improvement.

Genetic counselling

Genetic counselling aims to support and provide information for individuals, couples, and families:

- to understand their situation
- to make their own decisions about managing a particular disease or risk of disease, including decisions about genetic testing and reproduction
- to adjust to their situation of being affected by or at risk of the genetic condition
- to consider the implications of a disease or risk of disease for other family members.

A primary goal of genetic counselling is to provide information to allow for greater autonomy and choice in reproductive decisions and other areas of personal life. Avoiding additional cases of genetic disease in a family may be a consequence of genetic counselling but is not the primary aim. The elements of genetic counselling include:

- listening to the questions and concerns of the patient, or family
- establishing the correct diagnosis – this involves detailed history, examination, and appropriate investigations that may include chromosome or molecular genetic analysis, biochemical tests, X-rays, and clinical photographs. Despite extensive investigation, including searching databases, the diagnosis may remain unknown, e.g. in children with learning disability and normal appearance or only mild and non-specific dysmorphic features
- risk estimation – this requires both diagnostic and pedigree information. Drawing a pedigree of at least three generations is an essential part of a clinical genetic assessment. The mode of inheritance may be apparent from the pedigree even when the precise diagnosis is not known. In some cases it may not be possible to define a precise recurrence risk and uncertainty may remain, e.g. conditions that only affect one member of a family and are known to follow autosomal dominant inheritance in some families and autosomal recessive inheritance in others (genetic heterogeneity)
- communication – information must be presented in an understandable and unbiased way. Families often find written information helpful to refer back to, and diagrams are often used to explain patterns of inheritance. The impact of saying 'the recurrence risk is 5% or 1 in 20' may be different from saying 'the chance of an unaffected child is 95% or 19 out of 20', and so both should be presented
- discussing options for management and prevention – if there appears to be a risk to offspring, all reproductive options should be discussed. These include not having (any more) children, reducing intended family size, taking the risk and proceeding with pregnancy or having antenatal diagnosis, with the selective termination of an affected fetus. For some couples, donor insemination or ovum donation may be appropriate and, for others, achieving a pregnancy through *in vitro* fertilization and preimplantation genetic diagnosis may be possible
- putting parents in touch with appropriate sources of support, which provides support for families affected by rare chromosomal imbalances.

Counselling should be non-directive, but should also assist in the decision-making process (Box 9.13). Information from lay support groups may also be helpful.

 **Genetic counselling aims to allow parents greater autonomy and choice in reproductive decisions.**

Presymptomatic (predictive) testing

Children may be referred because they are at increased risk of developing a genetic disorder in childhood or adult life.

If the condition is likely to manifest in childhood (e.g. Duchenne muscular dystrophy) or if there are useful medical interventions available in childhood (e.g. screening by colonoscopy for colorectal tumours in children at risk of familial adenomatous polyposis coli), then genetic testing is appropriate in childhood.

If the child is at risk of a late-onset and untreatable disorder (e.g. Huntington disease), then deferring genetic testing until the child becomes an adult, or at least sufficiently mature to be actively involved in seeking the test and can make the decision for himself/herself, is usually preferred.

If the child is not at risk of developing the condition but may be a carrier at risk of transmitting the disorder to their future children, then there is also a good case for deferring testing until the young person can participate actively in the decision. There may be less at stake with these reproductive carrier tests than with predictive tests for untreatable disorders, but there are still good grounds for caution and for careful discussion before proceeding with such tests.

These difficult issues are often best handled through a process of genetic counselling supporting open and sustained communication within the family and especially between parents and children.

 **Presymptomatic testing of disorders which manifest in adult life should not be performed until the individual can consent on their own behalf unless there is clear clinical benefit from testing earlier.**

Gene-based therapies

The treatment of most genetic disorders is based on conventional therapeutic approaches. Gene therapy is an umbrella term for a number of techniques aimed at treating or preventing genetic disease. The mechanisms of gene-based therapies include:

- replacing the mutated copy of a gene with a functional copy, restoring protein function
- inactivating a mutated gene that has impaired function ('knocking out')
- introduction of a new gene for the production of a beneficial protein.

Vectors are genetically engineered to allow the introduction of the new gene. Particular viruses can be modified to introduce the new gene through infection of the cell. Different viral vectors act in different ways, for example, retroviruses integrate their own genetic

Box 9.13 Influences on decisions regarding options for genetic counselling

- Magnitude of risk
- Perceived severity of disorder
- Availability of treatment
- Person's experience of the disorder
- Family size
- Availability of a safe and reliable prenatal diagnostic test
- Parental cultural, religious, or ethical values

material, including the new gene, into the chromosome in the human cell, whereas adenovirus introduces DNA into the nucleus without chromosomal integration.

There are still many technical and safety issues to be resolved. Gene therapy has been initiated in adenosine deaminase deficiency (a rare recessive immune disorder), malignant melanoma, cystic fibrosis and some retinal disorders. Early gene therapy was limited to somatic cells, and germline gene therapy remains controversial. While germline gene therapy could prevent disease in future generations, it might also affect the fetus in unknown ways, or have long-term consequences which are as yet unknown.

An increasing understanding of the molecular mechanisms underlying the pathophysiology of many genetic conditions has also led to new targeted drug treatments in several conditions, including enzyme replacement therapy for certain inborn errors of metabolism and mTOR inhibitor therapy in tuberous sclerosis.

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- Strachan T, Read AP, editors: Human molecular genetics, ed 5, London, 2019, Garland.
- Turnpenny P, Ellard S: Emery's elements of medical genetics, ed 15, Edinburgh, 2017, Churchill Livingstone.

Websites

Genome browsers

Decipher: Available at: decipher.sanger.ac.uk.

Ensembl: Available at: www.ensembl.org.

Online resources

Contact – for families with disabled children: www.cafamily.org.uk. UK family support group alliance.

Unique: the rare chromosome disorder support group (includes printable information sheets about many chromosomal disorders): www.rarechromo.co.uk. Resource for families with disabled children.

GeneReviews: www.ncbi.nlm.nih.gov/books/NBK1116. Resource for clinicians, with information on many rare genetic diseases.

Genomics England: www.genomicsengland.co.uk. The 100,000 Genome Project.

London Medical Databases: www.face2gene.com/lmd-library-london-medical-database-dysmorphology. Database of genetic conditions, with photographs.

Online Mendelian Inheritance in Man (OMIM): www.ncbi.nlm.nih.gov/omim.

Orphanet: www.orpha.net.

Health Education England: www.genomicseducation.hee.nhs.uk. Genomics Education Programme and the course 'Genomics 101'.



Perinatal medicine

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Features of perinatal medicine:

- Good maternal health and care optimize not only obstetric but also neonatal outcomes.
- Antenatal screening identifies a wide range of congenital anomalies.
- All doctors, nurses and midwives who care for newborn infants should be able to perform newborn resuscitation.
- All babies should have a newborn infant physical examination within 72 hours of birth.

Box 10.1 Some definitions used in perinatal medicine

Commonly used terms in perinatal medicine in the UK

- stillbirth – infant born with no signs of life ≥ 24 weeks of pregnancy
- perinatal mortality rate – stillbirths + deaths within the first week after birth per 1000 live births and stillbirths
- neonatal mortality rate – deaths of live-born infants within the first 4 weeks after birth per 1000 live births
- neonate – infant ≤ 28 days old
- preterm – gestation < 37 weeks of pregnancy
- term – 37–41 weeks of pregnancy
- post-term – gestation ≥ 42 weeks of pregnancy
- low birthweight – < 2500 g
- very low birthweight – < 1500 g
- extremely low birthweight – < 1000 g
- small for gestational age – birthweight $< 10^{\text{th}}$ centile for gestational age
- large for gestational age – birthweight $> 90^{\text{th}}$ centile for gestational age

The term 'perinatal medicine' refers to medical care of the fetus and infant, particularly those with complex problems, before, during and after birth, acknowledging the continuity of fetal and neonatal life. Using modern technology, such as high-resolution ultrasound, magnetic resonance imaging and DNA analysis, detailed information about the fetus can now be obtained for a large and increasing number of conditions. Close cooperation is important between the professionals involved in the care of the pregnant mother and her fetus and those caring for the newborn infant.

Some definitions used in perinatal medicine are listed in **Box 10.1**.

Pre-pregnancy care

The better a mother's state of health and nutrition and the higher her socio-economic living standard and the quality of healthcare she receives, the greater the likelihood of a successful outcome of her pregnancy.

Couples planning to have a baby often ask what they should do to optimize their chances of having a healthy child. They can be informed that for the mother:

- *smoking* reduces birthweight, which may be of critical importance if born preterm. On average, the babies of smokers weigh 200 g less than those of non-smokers, but the reduction in birthweight is related to the number of cigarettes smoked per day. Smoking is also associated with an increased risk of miscarriage, abruption and stillbirth. The infant has a greater risk of sudden infant death syndrome.
- *folic acid* supplements taken pre-pregnancy and continued until 12 weeks reduce the risk of neural tube defects (anencephaly and spina bifida) in the fetus. Low-dose folic acid supplementation is recommended for all women planning a pregnancy. A higher dose is recommended for women at increased risk of neural

- tube defects (if they have a personal or family history, a previously affected pregnancy, are obese, have diabetes or are taking certain anticonvulsants).
- with any medical conditions, such as diabetes, epilepsy or hypertension, should be offered to have their management reviewed to consider the implications of pregnancy.
- certain medications* such as retinoids, warfarin, and sodium valproate should be avoided because of teratogenic effects.
- alcohol* ingestion and *drug use* (opiates, cocaine) may damage the fetus and should be avoided.
- exposure to toxoplasmosis* should be minimized by avoiding eating undercooked meat, by wearing gloves when handling cat litter and when gardening.
- listeria infection* can be acquired from eating unpasteurized dairy products, soft ripened cheeses, e.g. brie, camembert and blue veined varieties, pâté and ready-to-eat poultry, unless thoroughly reheated.
- eating liver* during pregnancy is best avoided as it contains a high concentration of vitamin A which can be teratogenic.
- it is best to avoid eating swordfish and to limit tuna because of high levels of mercury. Limit oily fish intake as may contain pollutants.

Any obstetric risk factors for complications of pregnancy or delivery (e.g. recurrent miscarriage or previous preterm delivery) should be identified and treated or monitored.

Maternal obesity is associated with an increased risk of miscarriage, gestational diabetes and pre-eclampsia. Babies of obese mothers are at an increased risk of stillbirth, congenital anomalies, macrosomia and neonatal mortality. In addition, the children of obese mothers are more likely to be obese themselves. It is therefore advisable for women to bring their weight into the normal range before planning to conceive.

Couples at increased risk of inherited disorders should receive genetic counselling before pregnancy. They can then be fully informed, decide whether or not to proceed and consider antenatal diagnosis if available. Pregnancies at increased risk of fetal abnormality include those in which:

- the mother is older (if she is >40 years old, the risk of Down syndrome is 1 in 110 although screening is now offered to all pregnant women)
- there is a previous congenital anomaly
- there is a family history of an inherited disorder
- the parents are identified as carriers of an autosomal recessive disorder, e.g. thalassaemia
- a parent carries a chromosomal rearrangement
- parents are close blood relatives (consanguinity).



Pre-pregnancy folic acid supplements reduce the risk of neural tube defects in the fetus.

Antenatal diagnosis

Antenatal diagnosis has become available for an increasing number of disorders. Screening tests performed on maternal blood and ultrasound of the fetus are listed in **Box 10.2**. The main diagnostic techniques for antenatal diagnosis are maternal serum screening and detailed ultrasound scanning. More specialized techniques are chorionic villus sampling, amniocentesis, non-invasive

prenatal testing and fetal blood sampling (**Fig. 10.1**). In some rare conditions, preimplantation genetic diagnosis allows genetic analysis of cells from a developing embryo created through IVF (in-vitro fertilization) before transfer to the uterus. The structural anomalies and other lesions that can be identified on ultrasound are listed in **Box 10.3**, with an example in **Figure 10.2**.

Antenatal screening for disorders affecting the mother or fetus allows:

- reassurance where disorders are not detected
- optimal obstetric management of the mother and fetus
- interventions for a limited number of fetal conditions, such as draining pleural effusions to improve perinatal outcome
- counselling and planning delivery at centres with appropriate neonatal and sub-specialty care if a problem is identified
- the option of termination of pregnancy for severe disorders affecting the fetus (**Case history 10.1**) or compromising maternal health.

Parents require accurate medical advice and counselling to help them with these difficult decisions. Many transient or minor structural disorders of the fetus are also detected, which may cause considerable anxiety.



Antenatal diagnosis allows many congenital anomalies which used to be diagnosed at birth or during infancy to be identified before birth.

Fetal medicine

Fetal medicine, a sub-specialty of obstetrics, deals with the diagnosis and management of conditions before birth. Examples where the mother is given medical care to treat her infant include:

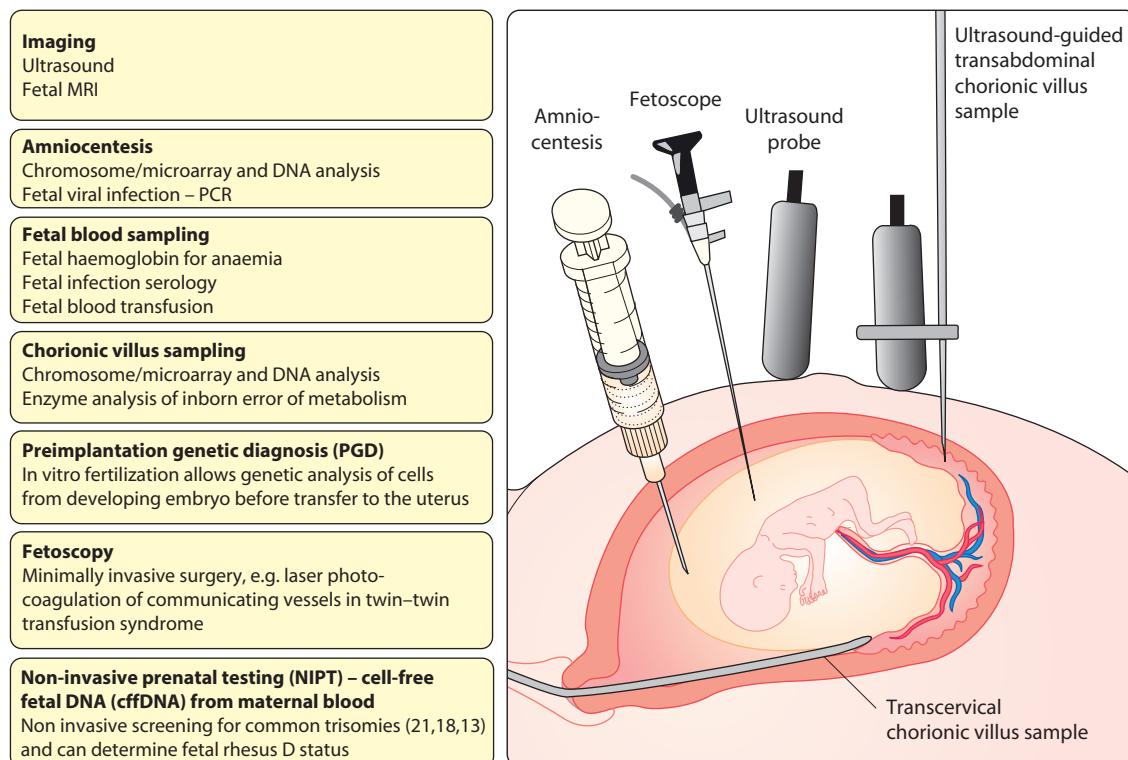
- glucocorticoid therapy* before preterm delivery accelerates lung maturity and surfactant production. This has been tested in over 15 randomized trials and markedly reduces the incidence of respiratory distress syndrome (relative risk 0.66), intraventricular haemorrhage (relative risk 0.54) and neonatal mortality (relative risk 0.69) in preterm infants. For optimal effect, a completed course needs to be given at least 24 hours before delivery and within 1–7 days before birth.
- digoxin or flecainide* can be given to the mother to treat fetal supraventricular tachycardia.

There are a few conditions in which therapy can be given to the fetus directly:

- Rh (rhesus) isoimmunization* (see **Ch. 11**) – severely affected fetuses become anaemic and may develop *hydrops fetalis*, with oedema and ascites. Fetuses at risk are identified by maternal antibody screening. Regular ultrasound of the fetus is performed to detect fetal anaemia non-invasively using Doppler velocimetry of the fetal middle cerebral artery. Fetal blood transfusion via the umbilical vein may be required regularly from about 20 weeks' gestation. The incidence of Rh haemolytic disease has fallen markedly since anti-D immunization of mothers was introduced but hydrops fetalis is still seen due to other red blood cell antibodies such as c and Kell.

Box 10.2 Screening tests for antenatal diagnosis

Maternal blood	Blood group and antibodies – for Rh and other red cell incompatibilities Hepatitis B Syphilis HIV infection Neural tube defects – raised maternal serum alphafetoprotein with spina bifida or anencephaly, but ultrasound alone increasingly used Down syndrome (trisomy 21), Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) – risk estimate calculated from maternal age and maternal and fetoplacental hormones. This is combined with ultrasound screening of nuchal translucency (fluid at the back of neck) and confirmed with amniocentesis or chorionic villous sampling. Detects 90% with Down syndrome, but 3%–5% false-positive rate and 1% risk of fetal loss. Alternatively, screening by non-invasive prenatal testing (NIPT) is increasingly available and scheduled as routine screening test in UK
Ultrasound screening	Gestational age – calculated at 11–13 weeks but can be estimated later in pregnancy. Multiple pregnancies – including chorionicity Structural malformation – up to 50%–98%, depending on type, of major congenital malformations can be detected. If a significant abnormality is suspected, a more detailed scan by a specialist is indicated Fetal growth – can be estimated by measuring head circumference, abdominal circumference, femur length, and monitored with serial scans. Fetal wellbeing can be assessed by Doppler ultrasound of the umbilical artery and other vessels. Amniotic fluid volume (oligohydramnios) – may result from reduced fetal urine production (because of dysplastic or absent kidneys, or obstructive uropathy), from preterm prelabour rupture of the membranes (PPROM), or may be associated with severe intrauterine growth restriction. It may cause pulmonary hypoplasia and limb and facial deformities from pressure on the fetus (Potter sequence) Amniotic fluid increased (polyhydramnios) – this is associated with maternal diabetes and structural gastrointestinal abnormalities, e.g. oesophageal atresia in the fetus

**Figure 10.1** Some of the techniques used for antenatal diagnosis.

Box 10.3 Main structural malformations and other lesions detectable by ultrasound

Central nervous system	Neural tube defects – anencephaly, spina bifida, encephalocele Ventriculomegaly, hydrocephalus Microcephaly
Cardiac	About 50% of severe malformations detected on ‘routine’ screening, over 90% at specialist centres
Intrathoracic	Congenital diaphragmatic hernia, congenital pulmonary airway malformation (CPAM) oesophageal atresia
Facial	Cleft lip, micrognathia
Gastrointestinal	Bowel obstruction, e.g. duodenal atresia Abdominal wall defects – exomphalos and gastroschisis
Genitourinary	Dysplastic or cystic kidneys Obstructive disorders of kidneys or urinary tract (hydronephrosis, distended bladder)
Skeletal	Skeletal dysplasias, e.g. achondroplasia and limb reduction deformities
Hydrops	Oedema of the skin, pleural effusions, and ascites
Chromosomal	Common trisomies (Down, Edwards, Patau) may be suspected from screening, from structural anomalies and/or growth impairment, and may be confirmed from an invasive test. Other chromosomal disorders – from identifying multiple abnormalities

Example of antenatal diagnosis – gastroschisis

(a)



(b)

Figure 10.2 Gastroschisis on antenatal ultrasound showing free loops of small bowel outside the fetal abdomen, in the amniotic fluid (a) and following delivery (b). Antenatal diagnosis allowed the baby to be delivered at a paediatric surgical unit and the parents to be counselled antenatally by a paediatric surgeon. Satisfactory surgical repair was achieved. (Courtesy of Karl Murphy.)

**Case history 10.1****Antenatal diagnosis**

A routine ultrasound scan at 18 weeks’ gestation identified an abnormal ‘lemon-shaped’ skull (Fig. 10.3). This, together with an abnormal appearance of the cerebellum, is the Arnold–Chiari malformation, which is associated with spina bifida. An extensive spinal defect was confirmed on ultrasound. Dilatation of the cerebral ventricles and talipes equinovarus already present in this fetus suggested a severe spinal lesion. After counselling, the parents decided to terminate the pregnancy.



Figure 10.3 Transverse section showing a ‘lemon-shaped’ skull on ultrasound instead of the normal oval shape. This is associated with spina bifida. (Courtesy of Guy Thorpe-Beeston.)

- *neonatal alloimmune thrombocytopenia* – this condition is analogous to Rh isoimmunization but involves maternal antiplatelet antibodies crossing the placenta. It is rare, affecting about 1 in 5000 births. Intracranial haemorrhage secondary to fetal thrombocytopenia occurs in up to 20% of cases. Maternal intravenous immunoglobulin should be offered in subsequent pregnancies to reduce the risk of recurrence.



Maternal glucocorticoid therapy before preterm delivery markedly reduces morbidity and mortality in the neonate.

Fetal surgery

Fetal surgery is a relatively new development with varying results. Procedures that have been performed include:

- *catheter shunts inserted under ultrasound guidance* – to drain fetal pleural effusions (pleuro-amniotic shunts), often from a chylothorax (lymphatic fluid). One end of a looped catheter lies in the chest, the other end in the amniotic cavity. Procedure works well; outcome depends on underlying problem.
- *laser therapy for twin-twin transfusion syndrome* – to ablate placental anastomoses in affected monozygotic twin pregnancies.
- *open fetal surgery for myelomeningocele (uterus opened at 23–25 weeks' gestation)* – May reduce the need for ventricular shunting and result in some improvement in motor outcomes, but results in uterine scarring and increased risk of preterm birth. Surgery can now sometimes be performed by fetoscopy.

Careful case selection and follow-up are required to ensure that these novel forms of treatment are of long-term benefit.

Obstetric conditions affecting the fetus

Pre-eclampsia

Mothers with pre-eclampsia may require preterm delivery because of the maternal risks of eclampsia and cerebrovascular accident or the fetal risk of stillbirth associated with placental insufficiency and growth restriction. Determining the optimal time for preterm delivery requires an evaluation of the risk to the mother and fetus of allowing the pregnancy to continue compared with the neonatal complications associated with preterm birth.

Placental insufficiency and intrauterine growth restriction (IUGR)

Fetal growth may be progressively restricted because of placental insufficiency. Transfer of oxygen and nutrients is reduced. The growth-restricted fetus will need to be monitored closely to prevent intrauterine death. This is done by measuring growth parameters, the amniotic fluid volume and Doppler blood flow assessment

(umbilical, middle cerebral arteries and ductus venosus). Absence or reversal of flow velocity in the umbilical artery during diastole carries an increased risk of morbidity from hypoxic damage to the gut or brain, or of intrauterine death. These measurements assist in deciding the optimal time for delivery of a growth-restricted fetus.

Preterm delivery

In the UK, 7.7% of births are preterm (before 37+0 weeks). However, only 5.9% of births in Sweden and Japan are preterm, but 10% in the USA. Estimates of the global burden of mortality from prematurity are shown in [Figure 10.4](#).

Neonates may be born preterm following:

- spontaneous labour with intact membranes (40%–50%)
- preterm premature rupture of the membranes (25%–30%)
- labour induction or caesarean delivery for maternal or fetal indications (35%–40%).

The main causes are shown in [Figure 10.5](#).

There are many epidemiological risk factors presumably responsible for the wide inter-country variation in prematurity rate, but they are poorly understood. Factors that increase the risk of preterm delivery include previous preterm infant, a short inter-pregnancy interval (<6 months), maternal age (<20 or >35 years), previous caesarean section, maternal undernutrition or obesity, ethnicity (e.g. higher in Black mothers), multiple births (influenced by assisted reproduction practices), maternal infection, smoking and substance misuse, socio-economic deprivation and maternal psychological or social stress.

The management of preterm labour may involve:

- antenatal corticosteroids as they reduce rates of respiratory distress syndrome, intraventricular haemorrhage and neonatal death (see above)
- antibiotics to reduce risk of chorioamnionitis and neonatal infection for preterm premature rupture of the membranes
- progesterone – prophylactically to reduce risk of preterm birth in those at high risk of preterm labor
- tocolysis – to suppress uterine contractions to try and suppress labour and allow completion of the course of antenatal steroids and transfer to a centre with the appropriate neonatal services.
- magnesium sulphate – studies show it reduces the incidence of cerebral palsy; however, its mode of action is unknown
- *in utero* transfer to a centre appropriate for level of care likely to be required by the preterm baby.

The aim is to prolong pregnancy for as long as possible whilst ensuring that the condition of the mother and fetus is not compromised. The mode of delivery needs to be planned, and arrangements made for the infant to receive the required level of care. The care of preterm infants is described in [Chapter 11](#) (Neonatal medicine).

Multiple births

Twins occur naturally in the UK in about 1 in 90, triplets in about 1 in 8000 (1 in 90²), and quadruplets in

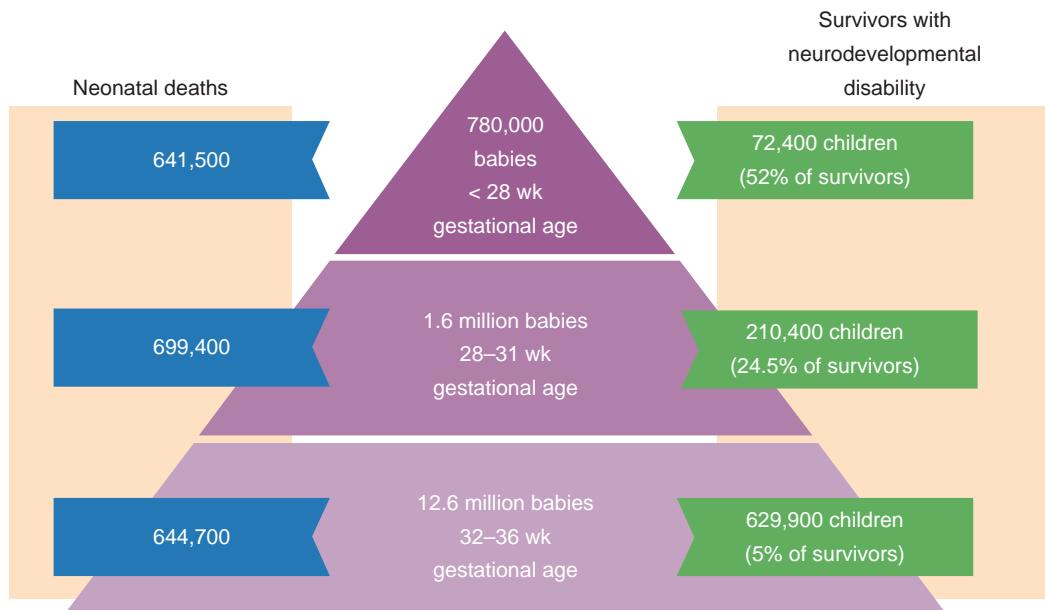


Figure 10.4 Global mortality and morbidity of preterm births. Estimates of global burden of mortality and morbidity for the 15 million preterm infants born in 2010 (11% of all 135 million births). (Adapted: from Blencowe H, Lee ACC, Cousens S, et al: Preterm birth-associated neurodevelopmental impairment estimates at regional and global levels for 2010. Beyond newborn survival. *Pediatric Research* 2013;74 (Supplement 1):17–34, 2013.)

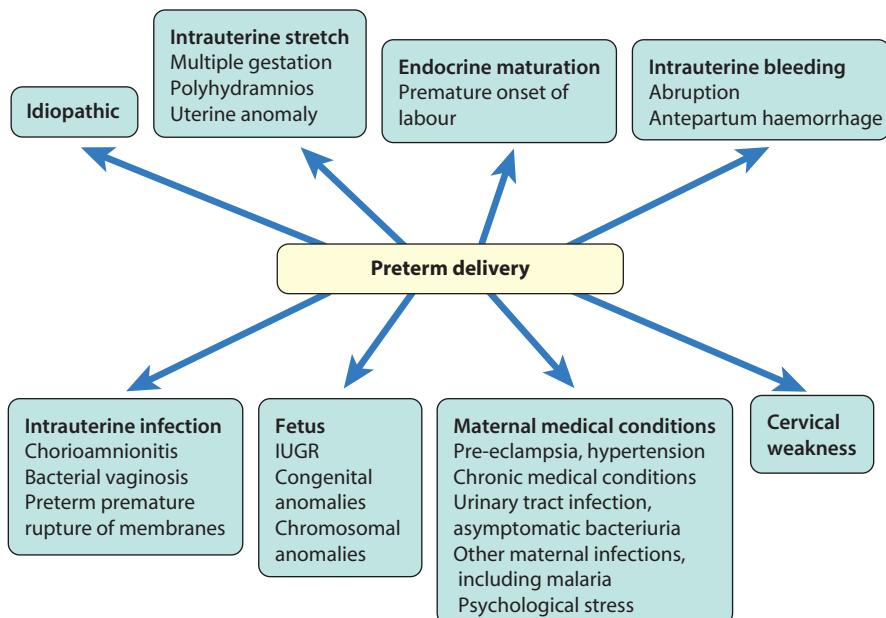


Figure 10.5 Causes of prematurity. IUGR, intrauterine growth restriction. (From: Lissauer T, Fanaroff A, Miall L, et al: *Neonatology at a glance*, ed 4. Oxford, 2020, Wiley Blackwell, with permission.)

about 1 in 700,000 (1 in 90³) deliveries. In recent years, the number of triplets and higher-order births has more than doubled, mainly from assisted reproduction programmes and advancing maternal age; 1 in 64 births is now a multiple birth, although the number of triplets and higher order births has recently declined in the UK mainly as a result of implementing single embryo transfer during IVF cycles.

The main problems for the infant associated with multiple births are:

- preterm labour – the preterm delivery rate for twins is about 60%, with 11% before 32 weeks. Preterm delivery is the most important cause of the greater perinatal mortality of multiple births, especially for triplets and higher-order pregnancies.

- intrauterine growth restriction (IUGR) – fetal growth in one or more fetuses may deteriorate and regular growth monitoring is required
- congenital abnormalities – there is a 4% risk in dichorionic and 8% risk in monochorionic (compared with singleton 2% risk)
- twin–twin transfusion syndrome (TTTS) – occurs in approximately 10%–15% of monochorionic twin pregnancies due to placental arteriovenous anastomoses. The ‘donor’ twin has low perfusion pressures, causing oliguria and oligohydramnios and is often growth restricted. The ‘recipient’ twin experiences hypervolemia, with polyuria and polyhydramnios, which may result in high output cardiac failure. *In utero* treatment with fetoscopic laser therapy to divide the placental blood vessels is sometimes indicated, or preterm delivery by caesarean section. Survival of TTTS varies from 60%–90%.
- complicated deliveries – e.g. due to malpresentation of the second twin at vaginal delivery.
- conjoined twins – if twinning of monozygotic twins occurs very late (>14th day) they may be conjoined, with fused skin or organs. Very rare (only 1 per 100,000 pregnancies), but conjoined twins attract considerable media attention.

In the UK, delivery in uncomplicated monochorionic twin pregnancies is offered at 36 weeks, in dichorionic twin pregnancies at 37 weeks, and triplet pregnancies at 35 weeks to optimize fetal outcome.

Although multiple births may look endearing, the families may need additional assistance and support:

- feeding – often possible to breastfeed twins, usually not possible for higher-order births
- practical – with their care and housework (requires about 200 hours/week for triplets in infancy) and going out
- emotional and physical exhaustion
- loss of privacy as a couple; increased rate of separation and divorce
- additional financial costs
- increased behavioural problems in the infants and their siblings. While being a multiple birth may provide companionship, affection, and stimulation between each other, it may also engender domination, dependency, and jealousy
- although low, the rate of disability is increased, mainly related to prematurity.

There are local and national support groups for parents of multiple births.

Summary

Multiple births

- Have markedly increased over the last 20 years.
- Are associated with an increased risk of prematurity, IUGR, congenital malformations, and twin–twin transfusion syndrome (in monochorionic twins).
- Are responsible for 30% of very low birthweight infants (<1.5 kg birthweight).
- Provide many additional demands on their parents to care for them.

Maternal conditions affecting the fetus

Diabetes mellitus

Women with pre-existing (type 1DM and type 2DM) diabetes find it more difficult to maintain good diabetic control during pregnancy. There is an increasing number of women with type 2 diabetes, associated with the increase in obesity in the population. Poorly controlled diabetes is associated with polyhydramnios and pre-eclampsia, increased rate of early fetal loss, congenital anomalies, and late unexplained intrauterine death. Ketoacidosis (in type 1DM) carries a high fetal mortality rate. With meticulous attention to diabetic control, the perinatal mortality rate is now only slightly greater than in non-diabetics. The National Institute for Health and Care Excellence (NICE) has produced guidance on the management of diabetes and its complications from preconception to the postnatal period. The emphasis is on aiming for good control of blood glucose.

Fetal problems associated with maternal diabetes are:

- *congenital malformations* – overall, there is a 6% risk of congenital malformations, a four-fold increase compared with the non-diabetic population. The range of anomalies is similar to that for the general population, apart from an increased incidence of cardiac malformations, sacral agenesis (caudal regression syndrome) and hypoplastic left colon, although the latter two conditions are rare. Studies show that good diabetic control periconceptionally reduces the risk of congenital malformations.
- *IUGR* – there is a three-fold increase in growth restriction in mothers with long-standing microvascular disease
- *macrosomia* (Fig. 10.6) – maternal hyperglycaemia causes fetal hyperglycaemia as glucose crosses the placenta. As insulin does not cross the placenta, the fetus responds with increased secretion of insulin, which promotes growth by increasing both cell number and size. About 25% of infants of diabetic mothers are macrosomic, i.e. have a birthweight greater than 4 kg compared with 8% of non-diabetics. The macrosomia predisposes to cephalopelvic disproportion, birth asphyxia, shoulder dystocia and brachial plexus injury.



Figure 10.6 Infant of a diabetic mother showing macrosomia and plethora. Born vaginally at 36 weeks' gestation, she weighed 5.5 kg and suffered a right-sided brachial plexus injury.

Neonatal problems include:

- *hypoglycaemia* – transient hypoglycaemia is common during the 1st day of life from fetal hyperinsulinism, but can often be prevented by early feeding. The infant's blood glucose should be closely monitored during the first 24 hours and hypoglycaemia treated.
- *respiratory distress syndrome* – more common as surfactant maturation is delayed.
- *hypertrophic cardiomyopathy* – hypertrophy of the cardiac septum occurs in some infants. It regresses over several weeks but may cause heart failure from reduced left ventricular function.
- *polycythaemia* (venous haematocrit >0.65) – makes the infant look plethoric. Treatment with partial exchange transfusion to reduce the haematocrit and normalize viscosity may rarely be required if symptomatic.

Gestational diabetes is when carbohydrate intolerance occurs only during pregnancy. It is more common in women who are obese and in those of Black and Asian ethnicity and with a positive family history. The incidence of macrosomia and its complications is similar to that of the insulin-dependent diabetic mother, but the incidence of congenital malformations is only marginally increased.

Summary

Maternal diabetes

- Meticulous control preconceptually and during pregnancy markedly reduces fetal and neonatal morbidity and mortality.
- The fetus may be macrosomic because of exposure to maternal hyperglycaemia resulting in hyperinsulinism, or growth restricted secondary to maternal microvascular disease; the fetus is also at increased risk of congenital malformations.
- The macrosomic infant is at an increased risk of birth asphyxia and birth injuries from obstructed labour or delivery.
- The newborn infant is prone to hypoglycaemia and polycythaemia.

Maternal thyroid disease

Maternal hyperthyroidism

If the mother is controlled on treatment, the fetus and infant are usually unaffected. However, 1%–2% of newborn infants of mothers who have or have had Graves disease are hyperthyroid. This is due to circulating thyroid-stimulating immunoglobulin (also called TSH receptor antibody, TRab), which crosses the placenta and binds to TSH receptors, stimulating fetal thyroid hormone production. Hyperthyroidism in the fetus is suggested by fetal tachycardia on the CTG (cardiotocography) trace, and fetal goitre may be evident on ultrasound. In the neonate it is suggested by tachycardia, heart failure, vomiting, diarrhoea and poor weight gain (despite good

intake), jitteriness, goitre and exophthalmos in the first 2 weeks of life. Treatment with anti-thyroid drugs may be necessary for several months until the maternal antibodies are cleared from the baby, when the condition resolves.

Maternal hypothyroidism

If mothers are on treatment with thyroxine, neonatal problems are rare. Worldwide, the commonest cause is iodine deficiency, an important cause of congenital hypothyroidism, leading to short stature and severe learning difficulties. Rarely seen in Europe or North America as iodine deficiency is rare and congenital hypothyroidism is identified on newborn biochemical screening.

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) with antiphospholipid syndrome is associated with recurrent miscarriage, IUGR, pre-eclampsia, placental abruption and preterm delivery. Some of the infants born to mothers with antibodies to the Ro (SS-A) or La (SS-B) antigens develop neonatal lupus syndrome, in which there is a self-limiting rash and, rarely, heart block.

Immune thrombocytopenia

In maternal immune thrombocytopenia (ITP), the fetus may become thrombocytopenic because maternal IgG antibodies cross the placenta and damage fetal platelets. Severe fetal thrombocytopenia places the fetus at risk of intracranial haemorrhage following birth trauma. Infants with severe thrombocytopenia or petechiae at birth should be given intravenous immunoglobulin. Platelet transfusions may be required to reduce the risk of intracranial haemorrhage or if there is acute bleeding.

Maternal drugs affecting the fetus

Relatively few drugs are known definitely to damage the fetus (Table 10.1), but it is clearly advisable for pregnant women to avoid taking medicines unless it is essential. While the teratogenicity of a drug may be recognized if it causes severe and distinctive malformations, as with limb shortening following thalidomide ingestion, milder and less distinctive abnormalities may go unrecognized. Selective serotonin reuptake inhibitors (SSRIs) are an example of this; they have been found to be associated with an increased risk of persistent pulmonary hypertension of the newborn (see Ch. 11, Neonatal medicine). Caution must be taken with all new drugs; studies on pregnant women may be limited, and the recognition or emergence of teratogenic effects may be delayed.



Valproate should not be prescribed to females of child-bearing age as it is associated with congenital anomalies in 10% and developmental delay in 30%–40%. Thalidomide and isotretinoin (for acne) are contraindicated

Table 10.1 Maternal medication that may adversely affect the fetus

Medication	Adverse effect on fetus
Antiepileptic drugs: valproate, carbamazepine, or hydantoins (phenytoin)	Fetal valproate/carbamazepine/hydantoin syndrome – midfacial hypoplasia, CNS, limb and cardiac malformations, and developmental delay
Cytotoxic agents	Congenital malformations
Radioactive iodine	Hypothyroidism
Lithium	Congenital heart disease
Selective serotonin reuptake inhibitors (SSRIs)	Persistent pulmonary hypertension of the newborn
Tetracycline	Enamel hypoplasia of the teeth, yellow-brown staining
Thalidomide	Limb shortening (phocomelia)
Vitamin A and retinoids	Increased spontaneous abortions, abnormal facies
Warfarin	Interferes with cartilage formation (nasal hypoplasia and epiphyseal stippling); ocular, skeletal abnormalities

Alcohol and smoking

Antenatal exposure to alcohol may result in fetal alcohol spectrum disorder (FASD), a continuum of cognitive, behavioural and social impairments. It is now recognized that fetal alcohol syndrome (FAS), characterized by intrauterine growth restriction, reduced head circumference, and typical craniofacial features (Fig. 10.7), represents only the most severe form of the disorder. FASD is under-recognized and underdiagnosed because of poor reliability of self-reported maternal drinking history, social stigma, lack of reliable biomarkers and difficulty in clinical diagnosis. Alcohol consumption in women of child-bearing age varies markedly between countries and within societies. A national survey in Scotland found that 60%–70% of women of child-bearing age were moderate drinkers (consuming up to 14 units per week) and 13%–24% were severe drinkers (14 units per week), with a higher consumption among highest income compared with lowest income households. The UK recommendation is for abstinence from alcohol consumption during pregnancy, but some women drink heavily before they realize they are pregnant, and others continue to drink through their pregnancy. Although a few affected infants are recognized in the neonatal period, most present in childhood. Studies suggest a prevalence of 2%–5% in Europe and North America, but the condition is often unrecognized in older children.

Maternal cigarette smoking is associated with an increased risk of miscarriage, abruption and stillbirth, a reduction in birthweight, and IUGR and can be associated



Figure 10.7 Characteristic facial features of fetal alcohol syndrome with: a smooth philtrum, with flattening of the groove between the nose and upper lip; a thin upper lip (vermilion); small palpebral fissures. Other features are growth restriction and CNS damage, structural or functional. This child also has a strawberry naevus below the right nostril, unrelated to fetal alcohol syndrome).

with fetal anomaly (see pre-pregnancy care, earlier in this chapter).

Substance misuse

Substance misuse is a problem worldwide, exacerbated by rising use of opioid-containing pain relievers. Neonatal abstinence syndrome (NAS) is the range of neonatal clinical features from withdrawal usually following prolonged exposure to maternal opioid use. The fetus may be exposed to other substances, including new psychoactive substances (particularly synthetic cannabinoids), or polysubstance use. NAS usually presents in the first few days of life with:

- neurological excitability – tremor, irritability, high-pitched cry, disturbed sleep-wake cycles and seizures
- gastrointestinal dysfunction – feeding difficulties, vomiting, diarrhoea, inadequate weight gain or weight loss
- autonomic signs – fever or temperature instability, sweating, nasal stuffiness, yawning and sneezing.

The severity of NAS is monitored by regular observation of a range of these signs using a scoring chart. Outcomes are improved if opioid-dependent mothers and their babies remain together from birth and neonatal unit admission is avoided. Environmental measures to reduce stimulation of the baby have been shown to reduce signs of NAS. These include skin-to-skin care, gentle swaddling, soft music, low lighting and massage. Breastfeeding should be encouraged to improve maternal–infant bonding and may reduce clinical features of withdrawal. Pharmacological treatment may be with oral morphine, methadone or buprenorphine. If insufficient, adjuvant therapy is with clonidine or phenobarbitone. A multidisciplinary team, including maternal management during pregnancy and continuing during the hospital stay and post discharge, is required to manage the mothers and their babies and their often complex psychosocial circumstances. This support enables most

babies to be managed without admission to the neonatal unit. With good community support and careful discharge planning, many of the babies can be discharged whilst still receiving pharmacological therapy.



Maternal substance use may be unrecognized until the infant develops signs of neonatal abstinence syndrome (NAS).

Congenital infections

Congenital infections are transplacental infections acquired *in utero*. The infection is usually from maternal primary infection. Those that can damage the fetus are:

- rubella
- cytomegalovirus (CMV)
- *Toxoplasma gondii*
- parvovirus
- varicella zoster
- syphilis.

Congenital infections



Figure 10.8a Cataract from congenital rubella. Congenital heart disease and deafness are the other common defects.

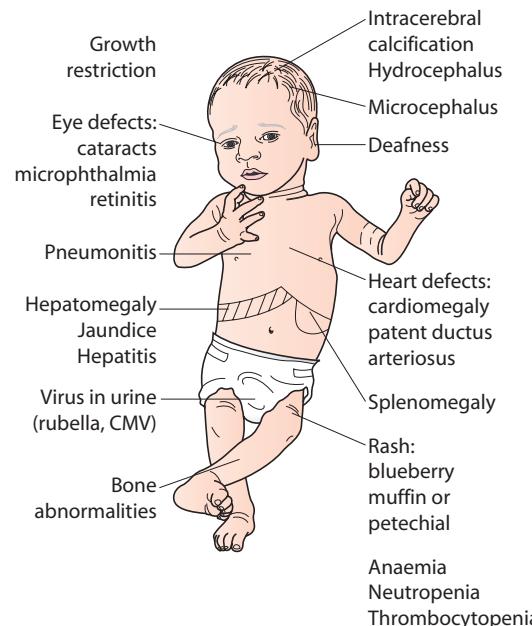


Figure 10.8b Clinical features of congenital rubella, cytomegalovirus, toxoplasmosis, and syphilis.

Rubella

The diagnosis of maternal infection must be confirmed serologically as clinical diagnosis is unreliable. The risk and extent of fetal damage are mainly determined by the gestational age at the onset of maternal infection. Infection before 8 weeks' gestation causes deafness, congenital heart disease, and cataracts in over 80% of cases (Fig. 10.8a). About 30% of fetuses of mothers infected at 13–16 weeks' gestation have impaired hearing; beyond 18 weeks' gestation, the risk to the fetus is minimal. Viraemia after birth continues to damage the infant. Tests used to confirm the diagnosis are shown in Box 10.4. The range of clinical features characteristic of congenital infections is shown in Figure 10.8b.

Congenital rubella is preventable. In the UK, it has become extremely rare since the measles/mumps/rubella vaccine was introduced into the childhood immunization programme, but this is dependent on the maintenance of a high vaccine uptake rate.

Cytomegalovirus

CMV is the most common congenital infection, affecting 0.5/1000 to 1/1000 live births in the UK. In Europe, 50% of pregnant women are susceptible to CMV. About 1% of susceptible women will have a primary infection during pregnancy, and in about 40% of them the infant becomes infected. The infant may also become infected following an episode of recurrent infection in the mother, but maternal to infant transmission rate is lower. When an infant is infected:

- 90% are normal at birth and develop normally
- 5% have clinical features at birth, such as hepatosplenomegaly and petechiae (see Fig. 10.8b), most of whom will have neurodevelopmental disabilities such as sensorineural hearing loss, cerebral palsy, epilepsy and cognitive impairment
- 5% develop problems later in life, mainly sensorineural hearing loss. It is the most common non-genetic cause of sensorineural hearing loss.

Infection in the pregnant woman is usually asymptomatic or causes a mild non-specific illness. There is no CMV vaccine,

Box 10.4 Confirmation of diagnosis of congenital rubella, cytomegalovirus, *Toxoplasma* infection and syphilis

Mother	Seroconversion on screening serology
Fetus	Amniocentesis or chorionic villus sample, polymerase chain reaction (PCR)
Placenta	Microscopy for syphilis, PCR
Urine from infant	Rubella, CMV – PCR
Blood, cerebrospinal fluid, and other samples from infant	PCR
Blood serology	Rubella-specific IgM, CMV-specific IgM, <i>Toxoplasma</i> -specific IgM and persistently raised <i>Toxoplasma</i> IgG

and pregnant women are not screened for CMV. Early treatment with antiviral therapy with oral valganciclovir for infants with sensorineural hearing loss or central nervous system involvement can reduce the adverse impact on sensorineural hearing loss and long-term neurodevelopment.

Toxoplasmosis

Acute infection with *T. gondii*, a protozoan parasite, may result from the consumption of raw or undercooked meat and from contact with the faeces of recently infected cats. In the UK, fewer than 20% of pregnant women have had past infection, in contrast to 80% in France and Austria. Transplacental infection may occur during the parasitaemia of a primary infection, and about 40% of fetuses become infected. In the UK, the incidence of congenital infection is only about 0.1/1000 live births. Most infected infants are asymptomatic. About 10% have clinical manifestations (see Fig. 10.8b), of which the most common are:

- retinopathy, an acute fundal chorioretinitis, which sometimes interferes with vision
- cerebral calcification
- hydrocephalus.

These infants usually have long-term neurological disabilities. Infected newborn infants are usually treated (pyrimethamine and sulfadiazine) for 1 year. Asymptomatic infants remain at risk of developing chorioretinitis into adulthood.

Congenital parvovirus B19

Up to 75% of women are immune to parvovirus B19. Infection in susceptible women is rare and usually uneventful. Rarely, it can lead to severe fetal anaemia (aplastic anaemia), causing fetal hydrops (oedema and ascites from heart failure) and intrauterine death. If infection is identified, serial ultrasound monitoring enables detection of fetal anaemia and need for intrauterine transfusion.

Varicella zoster

A total of 15% of pregnant women are susceptible to varicella (chickenpox). Usually, the fetus is unaffected but will be at risk if the mother develops chickenpox:

- in the first half of pregnancy (<20 weeks), when there is a less than 2% risk of the fetus developing fetal varicella syndrome, which is severe scarring of the skin and possibly ocular and neurological damage and digital dysplasia
- in the last 4 weeks of pregnancy, 7 days before or 7 days after delivery, when the fetus is unprotected by maternal antibodies and the viral dose is high. About 25% develop a vesicular rash. The illness has a mortality as high as 30%. This is known as varicella infection of the newborn.

Exposed susceptible mothers can be protected with varicella zoster immune globulin and treated with aciclovir. Infants born in the high-risk period should also receive zoster immune globulin and are closely monitored and given aciclovir if any signs of infection develop.



If a mother develops chickenpox shortly before or after delivery, the infant needs protection from infection.

Syphilis

Congenital syphilis is rare in the UK. The clinical features are shown in Figure 10.8b. Those specific to congenital syphilis include a characteristic rash on the soles of the feet and hands and bone lesions. If mothers with syphilis identified on antenatal screening are fully treated 1 month or more before delivery, the infant does not require treatment and has an excellent prognosis. If there is any doubt about the adequacy of maternal treatment, the infant should be treated with penicillin.

Adaptation to extrauterine life

In the fetus, the lungs are filled with fluid. The fetus therefore relies on the delivery of nutrients and oxygen from the placenta in blood which travels through the umbilical vein via the ductus venosus to the inferior vena cava to the right atrium (Fig. 10.9). Most of this oxygenated blood flows directly from the right to the left atrium via the foramen ovale. This ensures that the most oxygenated blood goes to the heart and brain. Deoxygenated blood returning from the head and upper body via superior vena cava mainly flows into the right ventricle and then to the pulmonary artery. As the blood vessels that supply and drain the lungs are constricted (providing high pulmonary vascular resistance), most of this deoxygenated blood from the pulmonary artery bypasses the lungs and flows through the ductus arteriosus into the lower aorta and to the placenta via the umbilical arteries. As a consequence of the fetal circulation, fetal oxygen saturations are about 65% (upper body) to 35% (lower body). To compensate for the low oxygen saturations, oxygen delivery to the tissues is enhanced by the high haemoglobin concentration (typically 160 g/L at term), along with the shift to the left of the oxygen dissociation curve of fetal haemoglobin compared with adult haemoglobin (see Fig. 23.1).

Shortly before and during labour, lung liquid production is reduced. Multiple stimuli, including thermal (cold), tactile and hormonal (with a particularly dramatic increase in catecholamine levels), initiate breathing. The high catecholamine levels also stimulate reabsorption of alveolar fluid. During descent through the birth canal, the infant's chest is also squeezed and some lung liquid drained. On average, the first breath occurs a few seconds after birth. The mean time to establish regular breathing is 30 seconds. Once the infant breathes, the majority of the remaining lung fluid is absorbed into the lymphatic and pulmonary circulation. Pulmonary expansion at birth is associated with a rise in oxygen tension, and with falling pulmonary vascular resistance the pulmonary blood flow increases. Increased left atrial filling results in a rise in the left atrial pressure with closure of the foramen ovale. The flow of oxygenated blood through the ductus arteriosus causes physiological and eventual anatomical ductal closure.

Delivery

After a normal delivery, term infants can be placed directly skin-to-skin on the mother's chest, dried and covered with a blanket and hat to keep warm, provided consent is given. The baby's breathing is observed to check it is regular and the baby's skin is pink. It has become normal practice to delay cord clamping after 1 to 3 minutes, as this allows

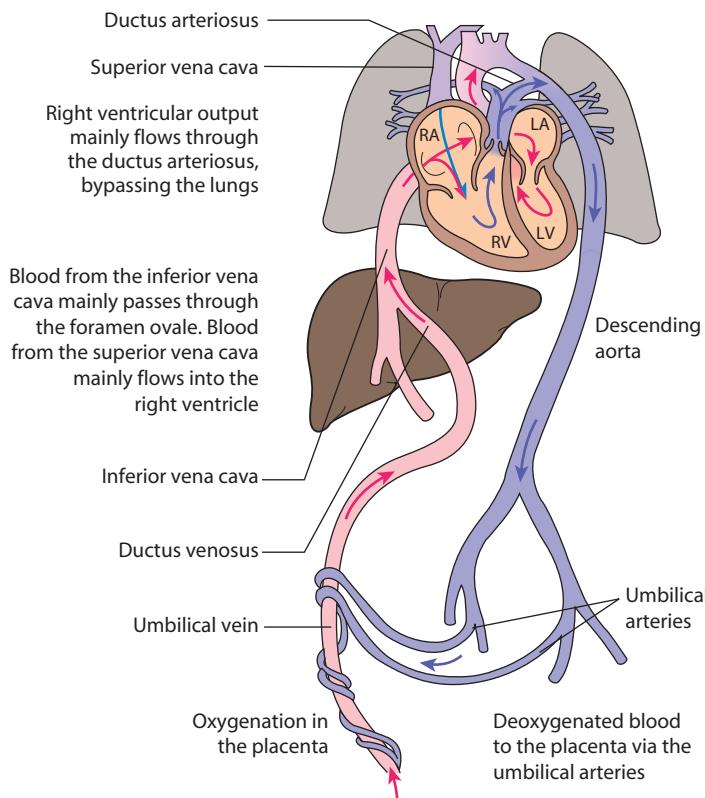


Figure 10.9 The fetal circulation.

continued placental blood transfusion which allows more gradual transition to extrauterine life, preventing sudden changes in venous return to the heart as well as increasing the circulating blood volume by about 30% and reducing later anaemia. The infant rapidly becomes alert, with open eyes and is active, and will feed from the breast. This time enhances mother–infant bonding, and should be disturbed as little as possible.

After an elective caesarean section, when the mother has not been in labour, it may take several hours for the lung fluid to be completely absorbed, causing rapid, laboured breathing (transient tachypnoea of the newborn, or TTN, see Ch. 11). The delay in absorption of lung liquid is mainly because of the absence of the surge in maternal catecholamines during labour and delivery, which stimulates reabsorption of alveolar fluid. In addition, the infant's chest is not squeezed as it does not pass through the birth canal.

A small proportion of infants do not breathe at birth. During normal labour, contractions interrupting blood flow to the fetus may result in relative hypoxia and hypoperfusion, but the fetus recovers fully from these hypoxic-ischaemic events. If the interruption of blood flow is prolonged or severe during labour or delivery the normal adaptive mechanisms are exhausted, and the fetus or infant will attempt to breathe, often described as gasping, but if this is unsuccessful (as it will be if still *in utero*), it will then become apnoeic (primary apnoea), during which time the heart rate is maintained. If oxygen deprivation continues, primary apnoea is followed by irregular gasping and then a second period of apnoea (secondary apnoea), when the heart rate and blood pressure fall. If delivered at this stage, the infant will only recover if resuscitation with lung expansion is provided, e.g. by positive pressure ventilation using a face mask or directly to the lungs via a tracheal tube (Fig. 10.10).

The human fetus rarely experiences a continuous and severe asphyxial insult, except after placental abruption,

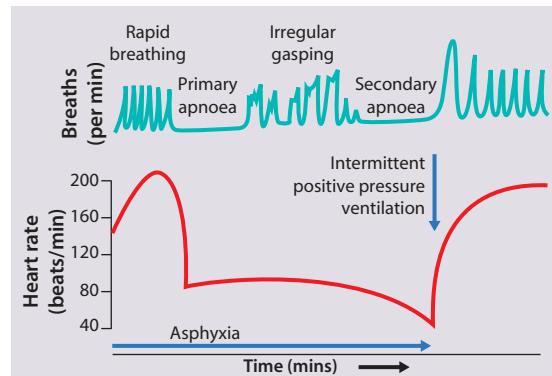


Figure 10.10 Changes in respiration and heart rate with continuous asphyxia. Once the infant has stopped gasping in secondary apnoea, resuscitation with lung expansion is required to establish regular respiration and restore the circulation.

uterine rupture or complete occlusion of umbilical blood flow in a cord prolapse. More commonly, asphyxia which occurs during labour and delivery is intermittent, but the fetus becomes compromised from hypoxia-ischaemia from severe or frequent uterine contractions and prolonged labour and/or the fetus has increased susceptibility as growth restricted or preterm. Although birth asphyxia is the most important cause of failure to establish breathing and the requirement of resuscitation at birth, there are other causes, including birth trauma, maternal analgesic or anaesthetic agents, retained lung fluid, prematurity or a congenital anomaly which interferes with the airway. In some babies, failure to establish breathing immediately after birth is from delay in adaptation to extrauterine life, and breathing is established after gentle stimulation, aided if necessary by airway positioning.

Table 10.2 The Apgar score

	Score		
	0	1	2
Heart rate	Absent	<100 beats/min	≥100 beats/min
Respiratory effort	Absent	Gasping or irregular	Regular, strong cry
Muscle tone	Flaccid	Some flexion of limbs	Well flexed, active
Reflex irritability	None	Grimace	Cry, cough
Colour	Pale/blue	Body pink, extremities blue	Pink

Apgar score

The Apgar score is used to describe a baby's condition at 1 minute and 5 minutes after delivery (Table 10.2). It is also measured at 5-minute intervals thereafter if the infant's condition remains poor. The most important components are the heart rate and respiration.

Neonatal resuscitation

Most infants do not require any resuscitation. As described above, shortly after birth, the baby will take a breath or cry, establish regular breathing and become pink and can be placed directly skin-to-skin on his or her mother's chest, dried, and covered to maintain a normal body temperature (36.5–37.5°C). Cord clamping should be delayed for 1 to 3 minutes. The need for resuscitation can usually be anticipated, and preparations made before delivery (Fig. 10.11a). Any newborn infant who does not establish normal respiration directly requires Newborn Life Support (Fig. 10.11b,c). The infant will need to be transferred to a resuscitaire for further assessment. There should be an overhead radiant heater and the infant should be dried and partially covered and kept warm. Resuscitation takes priority over delay in cord clamping, but in some centres special resuscitaires adjacent to the mother allow stabilisation with the intact cord, and is the subject of ongoing research. Suction of the mouth and nose is usually unnecessary; vigorous suction of the back of the throat may provoke bradycardia from vagal stimulation and should be avoided. If the infant's breathing in the first minute of life is irregular or shallow, management of airway and breathing should be started (Fig. 10.11d). If the heart rate is satisfactory (>100 beats/min), breathing is encouraged with airway opening manoeuvres.

If the infant does not start to breathe, or if the heart rate drops below 100 beats/minute, airway positioning and lung inflation by mask ventilation should be started (Fig. 10.11e–h). If the baby's condition does not improve promptly, or if the infant is clearly in very poor condition:

- Assistance should be summoned immediately while continuing to maintain ventilation.
- Oxygen saturation should be monitored and ECG considered.

- Consider using two-person airway control (Fig. 10.11i).
- Tracheal intubation may need to be performed (Fig. 10.11j).

A rapid rise in heart rate and breathing should be established. If this is not the case, the reasons listed in Box 10.5 should be considered.

If the heart rate drops below 60 beats/minute after five effective inflation breaths and 30 seconds of effective ventilation, chest compressions should be given (Fig. 10.11k). If the response to ventilation and chest compression (Fig. 10.11l–n) remains inadequate, drugs should be given, but are rarely required (Fig. 10.11o,p). Evidence for their efficacy is very poor.



Providing effective lung aeration, shown by improvement in heart rate and good chest wall movement, is the key to successful neonatal resuscitation.

Meconium aspiration

The passage of meconium becomes increasingly common the greater the infant's gestational age, particularly when post-term. Infants who become hypoxaemic may inhale thick meconium and develop meconium aspiration syndrome. Attempting to aspirate meconium from the nose and mouth while the infant's head is on the perineum is not recommended, as it is ineffective. If the infant cries at birth and establishes regular respiration, no resuscitation is required. If respiration is not established, initiating lung inflation within the first minute of life is the priority. If the baby is floppy and was born through thick meconium, it is reasonable to briefly inspect the oropharynx rapidly and remove any thick meconium by suctioning with a large-bore suction catheter, but positive pressure ventilation to aerate the lungs is the priority despite the presence of meconium.

Stabilization of the preterm infant

Cord clamping should be delayed for preterm infants not requiring immediate resuscitation. There is better physiological transition if the lungs are aerated before the cord is clamped. Other benefits include increased peak haemoglobin, reduction in need for blood transfusion, reduced necrotizing enterocolitis and intraventricular haemorrhage.

Most preterm infants are born in a good condition and require assistance in transition to extra-uterine life rather than stabilization. Preterm infants are particularly liable to hypothermia, and every effort must be made to keep them warm during resuscitation and stabilization. Infants of less than 32 weeks' gestation should, with the exception of the face, be placed into a plastic bag or wrapped in clear plastic sheeting without drying to allow the plastic to cling to the skin, and act almost like another layer of skin by avoiding evaporative heat loss. A radiant heat source from the resuscitation table and/or thermal mattress can then warm the baby in the bag.wrap. Using warmed humidified respiratory gases may also help. Excessive tissue oxygenation may cause tissue damage to the brain, lungs and eyes from oxygen free radicals. Whereas air is used for initial resuscitation in term infants, a low concentration (21%–30%) should be used for preterm infants. An air/oxygen blender should be used and any additional oxygen given should be titrated against oxygen saturation, thus avoiding exceeding a preductal saturation of 95%. Preterm infants less than 32 weeks' gestation may benefit from non-invasive respiratory support in the form

(a) Newborn Life Support – Preparation

- All health professionals dealing with newborn infants should be proficient in basic resuscitation i.e. Airway, Breathing with mask ventilation, Circulation with cardiac compressions.
- Additional skilled assistance is needed if the baby does not respond rapidly and should be called without delay.
- The need for resuscitation can usually be anticipated - intrapartum evidence of significant fetal compromise, < 35 weeks' gestation, breech, maternal infection, multiple pregnancies, caesarean delivery (not elective).
- A person proficient in advanced resuscitation or the resuscitation team should attend high-risk deliveries.
- Simulation training helps ensure efficient resuscitation and stabilization.
- A clock should be started at birth for accurate timing of changes in the infant's condition.
- Resuscitation should be performed under a radiant warmer.
- The aim is to maintain the baby's temperature at 36.5°C to 37.5°C, unless a decision to start therapeutic hypothermia is made.
- A pulse oximeter can give a continuous heart rate and oximetry reading.
- ECG is the most accurate way to obtain a rapid and continuous heart rate reading but does not give an indication of cardiac output.
- If preterm and <32 weeks' gestation, to avoid heat loss, place the infant directly into a plastic bag (wrap) without drying but under a radiant warmer.
- Leave the head exposed and cover with a hat.
- Thermal mattress and heated humidified respiratory gases can also be used to avoid hypothermia.
- Delivery room temperature should be 26°C for very preterm infants.
- Is the infant crying, good tone and colour? If that is the case, infant can be placed directly on the mother's chest, if desired, and covered to keep warm.
- Cord clamping is delayed.
- If breathing is not established, dry the baby, remove wet towel and replace with dry one. This will also provide stimulation.
- Assess breathing, heart rate (if >100 beats/min, best assessed with stethoscope) and muscle tone.
- If gasping or not breathing, commence neonatal resuscitation.

(b) Newborn life support – overview

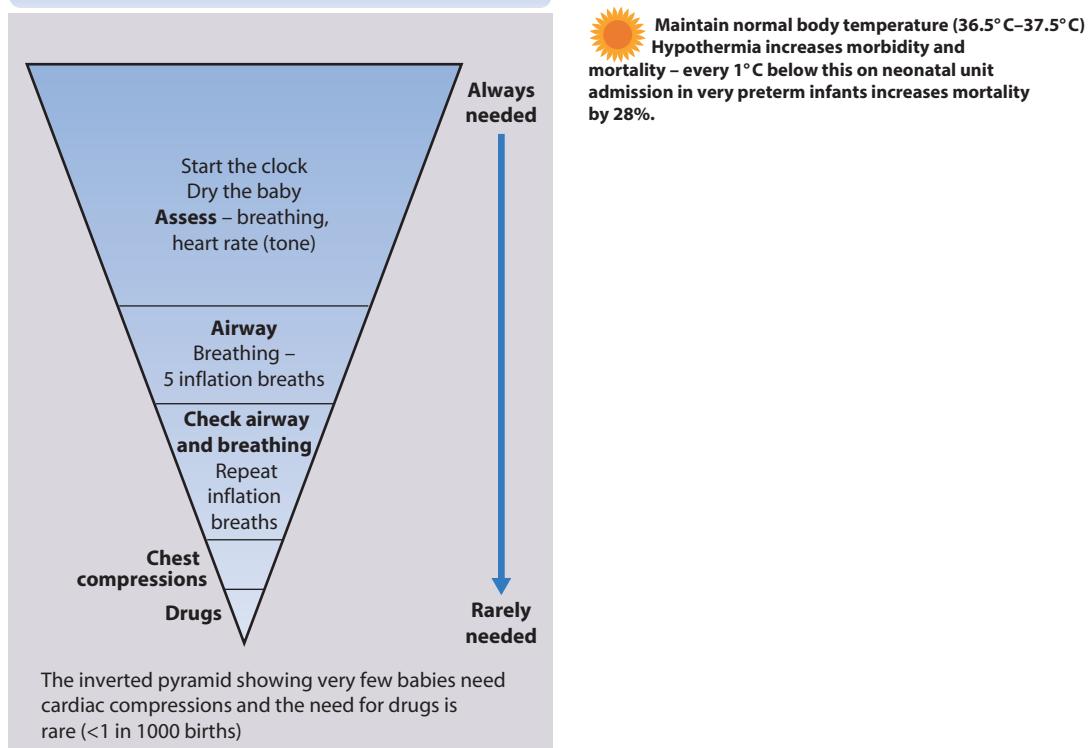


Figure 10.11 Neonatal resuscitation. (From: Newborn Life Support, 2015. Reproduced with the kind permission of Resuscitation Council UK.)

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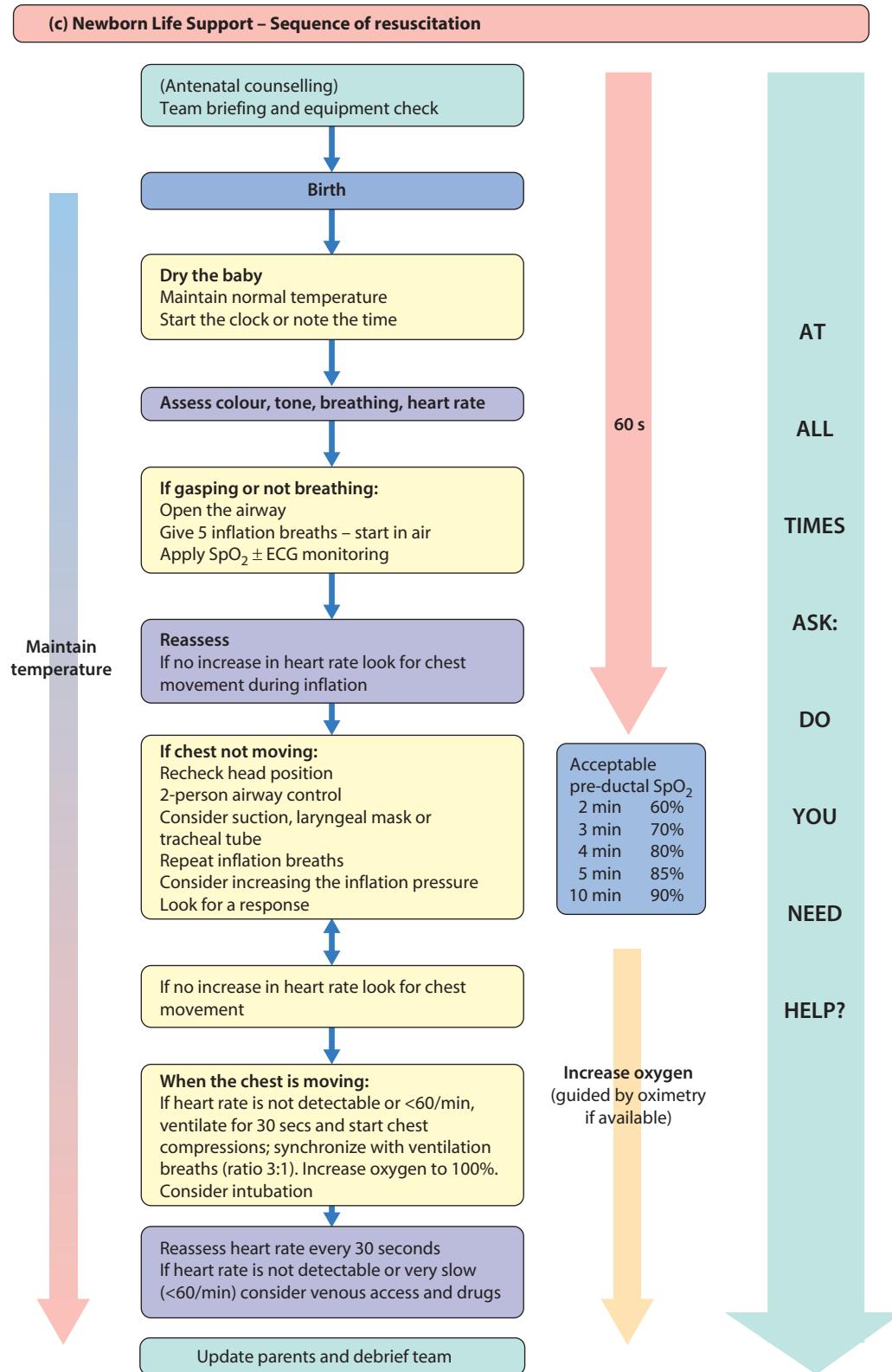


Figure 10.11 Continued

(d) Newborn Life Support – Airway and Breathing

Airway

- Opened by placing the infant's head in a neutral position (e). Place some support under shoulders if necessary
 - Provide chin lift or jaw thrust if necessary (f)
 - Suction any blood or secretions under direct vision if blocking airway

Breathing – mask ventilation

- If not breathing adequately, start mask ventilation. Call for help
 - Mask is placed over mouth and nose (**g**) and connected to flow-controlled pressure-limited circuit (e.g. mechanical ventilator or Neopuff) or self-inflating bag (**h**)
 - Give 5 inflation breaths, inflation time 2–3 seconds at inspiratory pressure of 30 cmH₂O in term infants (25 cmH₂O if preterm) to expand lungs
 - Monitor heart rate with ECG and oxygen saturation with pre-ductal (right hand) pulse oximeter if indicated
 - If heart rate increases, but breathing does not start, continue with peak inspiratory pressure adjusted to achieve chest wall movement (15–25 cmH₂O, 1 second inflation time) and rate of 30 breaths/min
 - Begin ventilatory resuscitation in air to avoid excessive tissue oxygenation if >32 weeks gestation, 21%–30% if 28–31 weeks; 30% if <28 weeks. Titrate additional oxygen with oxygen saturation
 - Reassess every 30 seconds. If heart rate not responding, ensure adequate chest movement. Consider using two-person airway control (**i**)

Intubation

- Intubation and mechanical ventilation (**j**) are indicated if: mask ventilation is ineffective, tracheal suction needed to clear an obstructed airway or congenital upper airway abnormality. Intubation may also be performed to give surfactant to extremely preterm infants
 - Limit intubation attempts to 20–30 seconds. Video laryngoscopy, if available, facilitates intubation by improved visualization of the upper airway

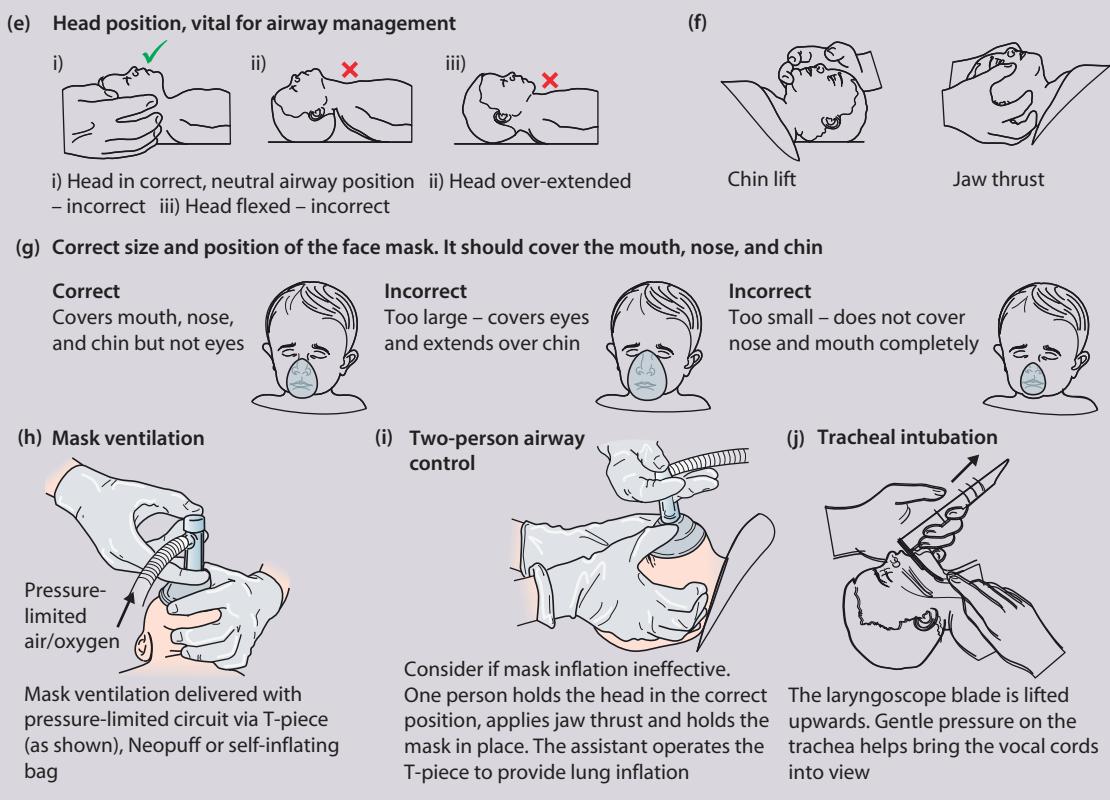


Figure 10.11 Continued

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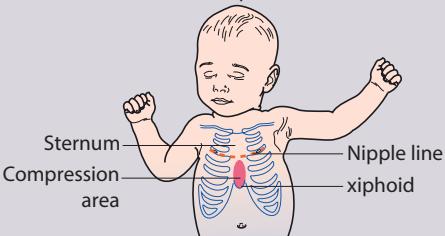
(k) Circulation

Chest compression (l, m and n)

- Start if heart rate <60 beats/min in spite of effective lung inflation. Increase inspired oxygen to 100%
- Ratio of compression: lung inflation of 3:1, rate of 90 compressions: 30 breaths/min (120 events/min) – avoid compressing chest during a ventilation breath
- Recheck heart rate every 30 seconds; stop when heart rate >60 beats/min
- Check oxygenation with pulse oximeter

(l) Chest compression

Landmarks for chest compression



Apply pressure to lower third of sternum, just below imaginary line joining the nipples. Depress to reduce antero-posterior diameter by one-third (1–1.5 cm).

(m)



Thumb technique, with hands encircling the chest. In larger infants thumbs can be placed side by side.

(n)



Two-finger technique – less effective but easier if alone.

(o) Volume and drugs

Consider drugs (p) if heart rate <60 beats/min in spite of adequate ventilation and chest compression, though evidence for their efficacy is lacking and they are rarely needed.

Drugs should ideally be given centrally via an umbilical venous catheter, or, if not possible, via an intraosseous needle.

If hypovolaemic, 0.9% sodium chloride or other isotonic crystalloids or blood transfusion with Group O Rh negative blood may be required; there may be a history of antepartum haemorrhage or acute twin-to-twin transfusion.

(p) Drugs used in neonatal resuscitation

Drug	Concentration	Route/dosage	Indications
Epinephrine (adrenaline)	1:10,000	IV: 0.2 ml/kg (20 µg/kg), then 0.2 ml/kg (10–30 µg/kg) ET: 1ml/kg (100 µg/kg), i.e. 10 times the IV dose, if IV access cannot be obtained	Heart rate <60 beats/min in spite of adequate ventilation and external cardiac compression
Sodium bicarbonate	4.2%	2–4 ml/kg (1–2 mmol/kg)	Severe lactic acidosis
Dextrose	10%	2.5 ml/kg (250 mg/kg)	Hypoglycaemia
Volume expander Isotonic crystalloid Blood		10 ml/kg, repeat if necessary	Blood loss

Figure 10.11 Continued

Box 10.5 Conditions to consider if, after tracheal intubation, the heart rate does not increase and good chest movement is not achieved

For this purpose, the mnemonic 'DOPE' may be used:

- d**isplaced tube: often in the oesophagus or right main bronchus; is exhaled CO₂ detectable? If no CO₂ detected, assume tube is not in the correct position.
- o**bstucted tube: especially meconium
- p**atient:
 - tracheal obstruction
 - lung disorders: lung immaturity or respiratory distress syndrome, pneumothorax, diaphragmatic hernia, lung hypoplasia, pleural effusion

- shock from blood loss
- perinatal asphyxia or trauma
- equipment failure: gas supply exhausted or disconnected

If there is any uncertainty about the adequacy of ventilation in an intubated baby, remove the tracheal tube, give mask ventilation, and then re-intubate if necessary

of CPAP (continuous positive airways pressure), to maintain lung aeration and avoid the need for intubation. Very premature infants may develop respiratory distress syndrome, and early administration of artificial surfactant into the trachea may be indicated. Management of infants at 20+0 to 22+6 weeks' gestation raises particularly difficult ethical issues. An experienced paediatrician should be responsible for counsellng the parents before delivery and agree on whether to provide active (survival focused) or comfort care, and lead the management of the baby after birth.

Post-resuscitation care

If, following resuscitation, the baby is significantly preterm or ill, the infant will need to be stabilized before transfer to the neonatal unit (see Ch. 11). Particular attention needs to be paid to provide adequate respiratory support and to the prevention of hypothermia and hypoglycaemia.

Failure to respond to resuscitation

The decision to stop resuscitation is always difficult and should be made by a senior paediatrician. The longer it takes a baby to respond to resuscitation, the less likely is survival. If there is no breathing or cardiac output after 10 minutes of effective resuscitation, further efforts are likely to be unproductive and consideration should be given to stop resuscitation. If prolonged resuscitation has been required, the infant should be transferred to the neonatal unit for assessment and monitoring.

Size at birth

An infant's gestation and birthweight influence the nature of the medical problems likely to be encountered in the neonatal period. In the UK, 7% of babies are of low birthweight (<2.5 kg). However, they account for approximately 70% of neonatal deaths.

Definitions

Babies with a birthweight below the 10th centile for their gestational age are called small-for-gestational-age (Fig. 10.12). The further the birthweight falls below the mean, the higher the incidence of a pathological cause and neonatal problems. Therefore, some authorities restrict the term to those whose birthweight falls below the second centile (approximately two standard deviations below the mean).

Small-for-gestational-age infants may have grown normally but are small, or they may have experienced intrauterine growth restriction (IUGR), i.e. they have failed to reach their full genetically determined growth potential and appear thin and malnourished. Babies with a birthweight above the 10th centile may also be malnourished, e.g. a fetus growing along the 80th centile that develops growth failure and whose weight falls to the 20th centile. An infant's birthweight may also be low because of preterm birth, or because the infant is both preterm and small for gestational age.

Patterns of growth restriction

Growth restriction in both the fetus and infant has traditionally been classified as symmetrical or asymmetrical.

In the more common asymmetrical growth restriction, the weight or abdominal circumference lies on a lower centile than that of the head. This occurs when the placenta fails to provide adequate nutrition late in pregnancy but brain growth is relatively spared at the expense of liver glycogen and skin fat (Fig. 10.13). This form of growth restriction is associated with uteroplacental dysfunction secondary to maternal pre-eclampsia, maternal smoking or it may be idiopathic. These infants exhibit catch up growth during childhood. This along with early life programming by the in-utero environment predisposes to the development of the metabolic syndrome in later life: the Developmental Origins of Health and Disease (DOHaD) hypothesis.

In symmetrical growth restriction, the head circumference is equally reduced. It suggests a prolonged period of poor intrauterine growth starting in early pregnancy (or that the infant is more premature than their estimated gestational age). It is usually due to a small but normal fetus, but may be due to a fetal genetic disorder or syndrome, a congenital infection, maternal drug and alcohol misuse, a maternal chronic medical condition or malnutrition. These infants are more likely to remain small permanently.

In practice, distinction between asymmetrical and symmetrical growth restriction often cannot be made.

Monitoring the growth-restricted fetus

The fetus with IUGR is at risk from:

- intrauterine hypoxia and intrauterine death
- asphyxia during labour and delivery.

The growth-restricted fetus will need to be monitored closely to determine the optimal time for delivery. Progressive uteroplacental failure results in:

- reduced growth in femur length and abdominal circumference
- oligohydramnios from reduced fetal urine production
- abnormal umbilical artery Doppler waveforms – absent or reversed end-diastolic flow velocity, due to increased placental impedance
- redistribution of blood flow in the fetus – increased flow to the brain, reduced flow to the gastrointestinal tract, liver, skin and kidneys
- abnormal ductus venosus Doppler waveform from cardiac dysfunction
- reduced fetal breathing and movements
- abnormal fetal heart rate trace.

Summary

Size at birth

- Small for gestational age – birthweight <10th centile.
- IUGR – fails to reach genetically determined growth potential.
- IUGR is associated with increased risk of intrauterine hypoxia, intrauterine death, asphyxia during labour and delivery and neonatal hypothermia, hypoglycaemia, and polycythaemia.

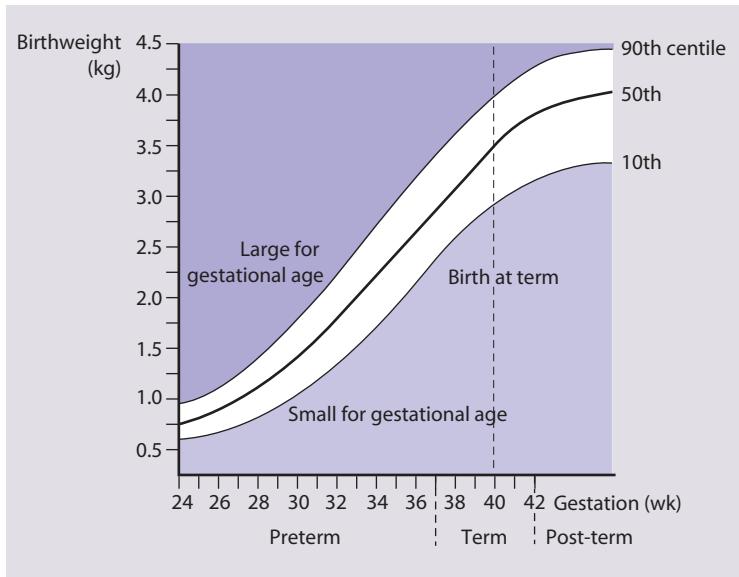


Figure 10.12 The birthweight of small-for-gestational-age infants is below the 10th centile for their gestation. Small-for-gestational-age infants may be preterm, term, or post-term.



Figure 10.13 Severe intrauterine growth restriction in the twin on the right.

The growth-restricted infant

After birth, these infants are liable to:

- hypothermia because of their relatively large surface area (especially their head)
- hypoglycaemia from poor fat and glycogen stores
- hypocalcaemia
- polycythaemia (venous haematocrit >0.65).

Large-for-gestational-age infants

Large-for-gestational-age (LGA) infants are those above the 90th weight centile for their gestation. Most are healthy, large infants, but it is a feature of infants of

mothers with diabetes or a baby with certain genetic syndromes (e.g. Beckwith–Wiedemann syndrome). The problems associated with being large for gestational age are:

- birth trauma, especially from shoulder dystocia at delivery (difficulty delivering the shoulders from impaction behind maternal symphysis pubis) which can result in birth injuries, e.g. brachial plexus nerve injury or fractures
- birth asphyxia from a difficult delivery which may cause hypoxic brain injury or death
- hypoglycaemia due to hyperinsulinism
- polycythaemia
- breathing difficulty from an enlarged tongue in Beckwith–Wiedemann syndrome.

Newborn infant physical examination (NIPE)

Immediately after a baby is born, parents are naturally anxious to know if their baby is alright and appears normal. When the baby's condition is stable following delivery, the midwife (or the paediatrician) will briefly check again that the baby is pink and breathing normally, and also that there are no major abnormalities. If a significant problem is identified, a paediatrician needs to explain the situation to the parents. If the baby is markedly preterm, small or ill, admission to a neonatal unit will be required. Should there be any uncertainty about the child's sex, it is important not to guess but to explain to the parents that further evaluation is necessary. Babies are given vitamin K at birth to prevent haemorrhagic disease of the newborn (now more commonly known as vitamin K deficiency bleeding or VKDB) unless parents do not give consent.

Within 72 hours of birth every baby should have a full and thorough examination, the 'newborn infant physical examination' (NIPE). Its purpose is to:

- detect congenital abnormalities not already identified at birth, e.g. eye abnormalities, congenital heart disease, undescended testes or developmental dysplasia of the hip (DDH)
- check for potential problems arising from maternal disease or familial disorders
- provide an opportunity for the parents to discuss any questions about their baby.

Before approaching the mother and baby, the obstetric and neonatal notes must be checked to identify relevant

information. The examination (Box 10.6) should be performed with the mother or ideally both parents present. Many findings in the newborn resolve spontaneously (Box 10.7). Common significant abnormalities detectable at birth are listed in Box 10.8. A serious congenital anomaly is present at birth in about 10/1000–15/1000 live births (Table 10.3). In addition, many congenital anomalies, especially of the heart, present clinically at a later age. In the UK, the newborn infant physical examination (NIPE) is repeated at 6–8 weeks of age, usually by the general practitioner.

Newborn infant physical examination

Box 10.6 Newborn infant physical examination (NIPE)

Birthweight, gestational age, and birthweight centile are noted (Fig. 10.14).

General observation of the baby's appearance, posture, and movements provides valuable information about many abnormalities. The baby must be fully undressed during the examination.

The head circumference is measured with a paper tape measure and its centile noted. Maximum of 3 measurements is recorded. This is a surrogate measure of brain size.

The fontanelles and sutures are palpated. The anterior fontanelle size is very variable. The sagittal suture is often separated and the coronal sutures may be overriding. A tense fontanelle when the baby is not crying may be due to raised intracranial pressure and cranial ultrasound should be performed to check for hydrocephalus.

The face is observed. If abnormal, this may represent a syndrome, particularly if other anomalies are present. Down syndrome is the most common, but there are hundreds of syndromes. When the diagnosis is uncertain, a book or a computer database may be consulted and advice should be sought from a senior paediatrician or clinical geneticist.

If plethoric or pale, the haematocrit should be checked to identify polycythaemia or anaemia. Central cyanosis, which always needs urgent assessment, is best seen on the tongue.

Jaundice within 24 hours of birth requires further evaluation.

The eyes are checked for red reflex with an ophthalmoscope. If absent, may be from cataracts (see Case History 10.2), retinoblastoma and corneal opacity. This reflex can be hard to illicit in darker-skinned infants but the retinal vessels can be visualized.

The palate needs to be visually inspected, including posteriorly to exclude a posterior cleft palate, and

palpated to detect an indentation of the posterior palate from a submucous cleft.

Breathing and chest wall movement are observed for signs of respiratory distress.

On auscultating the heart, the normal rate is 110–160 beats/minute in term babies, but may drop to 85 beats/minute during sleep.

On palpating the abdomen, the liver normally extends 1 cm to 2 cm below the costal margin, the spleen tip may be palpable, as may the kidney on the left side. Any intra-abdominal masses, which are usually renal in origin, need further investigation.

The femoral pulses are palpated. Their pulse pressure is:

- reduced in coarctation of the aorta. This can be confirmed by measuring the blood pressure in the arms and legs
- increased if there is a patent ductus arteriosus.

The genitalia and anus are inspected on removing the nappy. Patency of the anus is confirmed. In boys, the presence of testes in the scrotum is checked by palpation.

Muscle tone – observe for normal, symmetrical movements of all limbs; feel that it is normal when handling the baby; when held prone term babies lift their head to horizontal position.

If abnormal or asymmetrical, **primitive reflexes** may be checked (Fig. 3.4). For the Moro reflex, the head is allowed to extend suddenly, but supported in the examiner's hand. The arms spread in abduction and extension, followed by flexion and adduction. Some parents find it upsetting, and it does not provide additional information if full range of limb movements has been observed.

The whole of the back and spine is observed, looking for any midline defects of the skin.

The hips are checked for DDH. This is left until last as the procedure is uncomfortable.



Figure 10.14 Term newborn.

Conditions in newborn infants that resolve spontaneously

Box 10.7 Lesions in newborn infants that resolve spontaneously

Peripheral cyanosis of the hands and feet –

common in the first day.

Traumatic cyanosis from a cord around the baby's neck or from a face or brow presentation – causes blue discolouration of the skin, petechiae over the head and neck or affected part but not the tongue.

Swollen eyelids and distortion of shape of the head from the delivery.

Subconjunctival haemorrhages – occur during delivery but should be documented to avoid confusion with non-accidental injury when older.

Small white pearls along the midline of the palate (Epstein pearls).

Cysts of the gums (epulis) or floor of the mouth (ranula).

Breast enlargement – may occur in newborn babies of either sex (Fig. 10.15a). A small amount of milk may be discharged.

White vaginal discharge or small withdrawal bleed in girls. There may be a prolapse of a ring of vaginal mucosa.

Capillary haemangioma or 'stork bites' – pink macules on the upper eyelids, midforehead, and nape of the neck are common and arise from distension of the dermal capillaries. Those on the eyelids gradually fade over the first year; those on the neck become covered with hair.

Erythema toxicum – a common rash appearing

at 2–3 days of age, consisting of white pinpoint papules at the centre of an erythematous base (Fig. 10.15b). The fluid contains eosinophils. The lesions are concentrated on the trunk; they come and go at different sites.

Milia – white papules on the nose and cheeks, from retention of keratin and sebaceous material in the pilosebaceous follicles (Fig. 10.15c).

Congenital dermal melanocytosis (Mongolian blue spots) – blue-grey macular discolouration at the base of the spine and on the buttocks (Fig. 10.15d); occasionally occur on the legs and other parts of the body. Usually but not invariably in dark-skinned infants. They fade slowly over the first few years. They are of no significance unless misdiagnosed as bruises.

Umbilical hernia – common, particularly in black infants. No treatment is indicated as it usually resolves within the first 2–3 years.

Positional talipes – the feet often remain in their *in utero* position. Unlike true talipes equinovarus, the foot can be fully dorsiflexed to touch the front of the lower leg (Figs. 10.15e and 10.15f).

Caput succedaneum (see Fig. 11.25) and **cephalhaematoma** (Fig. 11.25 and Fig. 11.26).



Figure 10.15a Breast enlargement in a newborn infant.



Figure 10.15b Erythema toxicum often has a raised pale centre. (Courtesy of Nim Subhedar.)



Figure 10.15c Milia. (Courtesy of Rodney Rivers.)



Figure 10.15d
Congenital dermal melanocytosis (Mongolian blue spots)

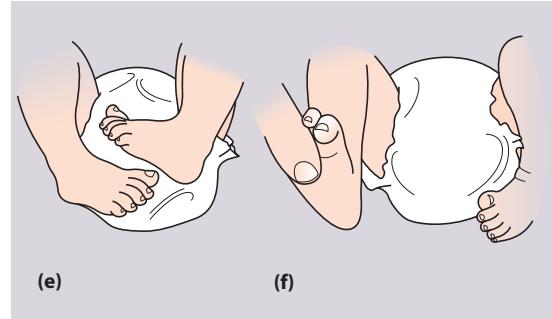


Figure 10.15 (e) Positional talipes. Appearance at birth.
(f) The foot can be fully dorsiflexed to touch the front of the lower leg. In true talipes equinovarus this is not possible.

Some significant abnormalities detected on routine examination

Box 10.8 Some significant abnormalities detected on routine examination

Port-wine stain (naevus flammeus). Present from birth and usually grows with the infant (Fig. 10.16a). It is due to a vascular malformation of the capillaries in the dermis. Rarely, if along the distribution of the trigeminal nerve, it may be associated with intracranial vascular anomalies (Sturge–Weber syndrome), or severe lesions on the limbs with bone hypertrophy (Klippel–Trenaunay syndrome). Disfiguring lesions can now be improved with laser therapy.

Strawberry naevus (infantile haemangioma). Usually not present at birth, but appear in the first month of life and may be multiple (Fig. 10.16b). They are more common in preterm infants. Increase in size until 3–15 months of age, then gradually regress. No treatment is indicated for small lesions, but topical timolol, a beta-blocker used in eye drops, may speed regression. Large lesions or if interferes with vision or the airway are treated with oral propranolol. Ulceration or haemorrhage may occur.

Natal teeth consisting of the front lower incisors – may be present at birth. If loose, they should be removed to avoid the risk of aspiration.

Extra digits – are sometimes connected by a thin skin tag but may be completely attached containing bone (Fig. 10.16c) and should be removed by a plastic surgeon. Otherwise, they are

tied off at its base. Skin tags anterior to the ear and accessory auricles should be removed by a plastic surgeon.

Heart murmur – poses a difficult problem, as most murmurs audible in the first few days of life resolve shortly afterwards. However, some are caused by congenital heart disease. If there are any features of a significant murmur (see Ch. 18, Cardiac disorders), upper and lower limb blood pressures, and pre-ductal and post-ductal pulse oximetry should be checked followed by an echocardiogram. Otherwise, a follow-up examination is arranged and the parents warned to seek medical assistance if their baby feeds poorly, develops laboured breathing, or becomes cyanosed.

Midline abnormality over the spine or skull – such as a tuft of hair, swelling, or naevus – requires further evaluation as it may indicate an underlying abnormality of the vertebrae, spinal cord, or brain.

Palpable and large bladder – if there is urinary outflow obstruction, particularly in boys with posterior urethral valves. Requires prompt evaluation with ultrasound. Usually diagnosed on antenatal ultrasound.

Talipes equinovarus – cannot be corrected as in positional talipes (see Figs. 10.15e and 10.15f).



Figure 10.16a Port-wine stain in an infant.



Figure 10.16b Strawberry naevus.



Figure 10.16c Extra digits.

Red reflex to identify eye abnormalities

See Case history 10.2 for a case study on red reflex.

Detection of undescended testes in boys

Usually detected on newborn examination. It is described in Chapter 20 (Genital disorders).

Checking for developmental dysplasia of the hip (DDH)

To check for DDH (previously called congenital dislocation of the hip), the infant needs to be relaxed, as kicking or crying results in tightening of the muscles around the hip and prevents satisfactory examination. The pelvis is stabilized with one hand. With the other hand, the examiner's middle finger is placed over the greater trochanter and



Case history 10.2

Congenital cataract

On checking for red reflexes (Fig. 10.17) during the routine newborn examination, bilateral absent red reflexes were noted in a male term baby (see Fig. 10.8a earlier in the chapter). The remainder of the examination was normal. Urgent ophthalmology review confirmed bilateral congenital cataracts (presumed idiopathic, but many are

genetic). These occur in about 3–4/10,000 live births and is responsible for about 10% of blindness in children worldwide. Early surgical treatment in the first few weeks of life improves long-term visual function. Other eye abnormalities that may be detected are congenital glaucoma (Fig. 10.18a) and coloboma (Fig. 10.18b).



Figure 10.17 Checking for red reflex. Done by examining the eyes through a direct ophthalmoscope 15–20 cm from the eyes.



(a)



(b)

Figure 10.18 Eye abnormalities on newborn examination. (a) Congenital glaucoma of right eye. And (b) iris coloboma. Keyhole-shaped pupil due to defect of the iris inferiorly. (a, Courtesy of Alistair Fielder; b, Courtesy of Louise Allen.)

Table 10.3 Prevalence of serious congenital anomalies per 1000 live births (England and Wales)

Anomaly	Prevalence
Congenital heart disease	6–8 (0.8 on the 1st day of life)
DDH	1.5 (but about 6/1000 have an abnormal initial clinical examination)
Talipes	1.0
Down syndrome	1.0
Cleft lip and palate	0.8
Urogenital (hypospadias, undescended testes)	1.2
Spina bifida/anencephaly	0.1

the thumb around the distal medial femur. In the Barlow manoeuvre, the hip is held flexed and the femoral head is gently adducted and pushed downwards. If the hip is dislocatable, the femoral head will be pushed posteriorly out of the acetabulum (Fig. 10.19a).

The next part of the examination is the Ortolani manoeuvre to see if the hip can be returned from its dislocated position back into the acetabulum. While gently abducting the hip, upward leverage is applied (Fig. 10.19b). A dislocated hip will return with a ‘clunk’ into the acetabulum. Ligamentous clicks without any movement of the head of femur are of no significance. It should also be possible to abduct the hips fully, but this may be restricted if the hip is dislocated. Clinical examination does not identify some infants who have hip dysplasia from lack of development of the acetabular shelf. DDH is more common in girls (six-fold increase), if there is a positive family history (20% of affected infants), if the birth is a breech presentation (30% of affected infants) or if the infant has a neuromuscular disorder.

Early recognition of DDH is important as early splintage in abduction reduces long-term morbidity. A specialist orthopaedic opinion should be sought in the management of this condition. Ultrasound examination of the hip joint is performed increasingly in many hospitals, either following an abnormal hip examination, the presence of neuromuscular disorder in the lower legs or talipes equinovarus, or to screen babies at increased risk (breech presentation or positive family history). Ultrasound examination can be performed to screen all babies, but is not currently recommended in the UK as it is expensive, requires considerable expertise, and there are many false positives. It will, however, identify some babies missed on clinical examination.

Checking for developmental dysplasia of the hip (DDH)

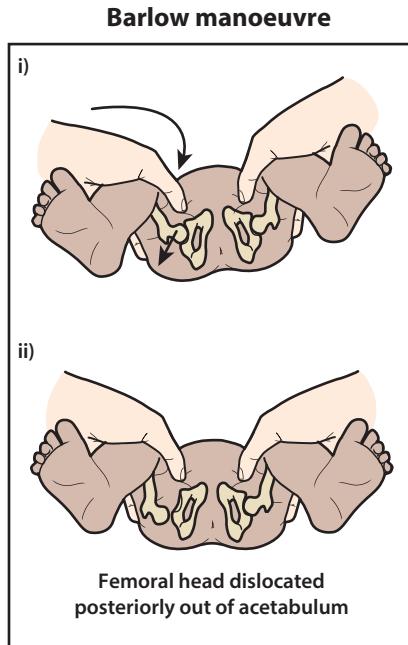


Figure 10.19a In the Barlow manoeuvre, the femoral head is adducted and gently pushed downwards. In DDH the femoral head moves posteriorly out of the acetabulum.

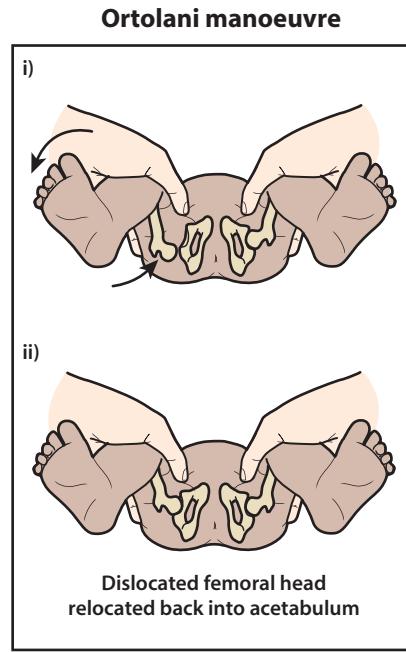


Figure 10.19b In the Ortolani manoeuvre, while abducting the hip, gentle upward leverage is applied. In DDH a dislocated hip will be relocated into the acetabulum with a 'clunk'.

Vitamin K

Vitamin K deficiency may result in vitamin K deficiency bleeding (haemorrhagic disease of the newborn), a rare condition with an incidence of 0.6/100,000 births. This disorder can occur early, during the first week of life, or late, from 1–8 weeks of age. In most affected infants, the haemorrhage is mild, such as bruising, haematemesis and melaena, or prolonged bleeding of the umbilical stump or after circumcision. However, some suffer from intracranial haemorrhage, half of whom are permanently disabled or die.

Breast milk, which has many benefits to both the mother and her baby, is a poor source of vitamin K, whereas infant formula milk has much higher vitamin K content. Vitamin K deficient bleeding may occur in infants who are wholly breastfed but not if fed with an infant formula. Infants of mothers taking anticonvulsants, which impair the synthesis of vitamin K-dependent clotting factors, are at increased risk of bleeding, both during delivery and soon after birth. Infants with liver disease are also at increased risk.

The disease can be prevented if vitamin K is given by intramuscular injection, and in the UK it is recommended for all newborn infants and given shortly after birth. Some parents prefer an oral preparation to the intramuscular injection. As absorption via the oral route is variable, three doses are needed over the first 4 weeks of life to achieve adequate liver storage. Mothers on anticonvulsant therapy should receive oral prophylaxis from 36 weeks' gestation and the baby should be given intramuscular vitamin K.



Vitamin K should be given to all newborn infants to prevent vitamin K deficiency bleeding.

Newborn hearing screening

Universal screening has been introduced in the UK to detect severe hearing impairment in newborn infants. Early detection and intervention improves speech and language. Automated otoacoustic emission (AOAE) testing, in which an earphone is placed over the ear and a sound is emitted, which evokes an echo or emission from the ear if cochlear function is normal, is used as the initial screening test. If a normal test result is not achieved, referral is made to a paediatric audiologist. Testing with automated auditory brain-stem response (AABR) audiology, using computer analysis of electroencephalogram waveforms evoked in response to a series of clicks, may be performed (see Ch. 3, Normal child development, hearing and vision, for further details) if the baby does not pass the initial screening test or if the baby has received neonatal intensive care.



Newborn hearing screening is performed on all infants to detect severe hearing impairment.

Oxygen saturation screening for critical congenital heart disease

Oxygen saturation screening of all newborn infants can be performed in the first 24 hours of life to identify duct-dependent congenital heart disease since early diagnosis and treatment can prevent collapse when the duct closes at 24–48 hours after birth. A low post-ductal oxygen

saturation (left hand or feet) or an abnormally large difference between pre-ductal (right hand) and post-ductal measurement prompts medical review and echocardiography. A low oxygen saturation may also occur with respiratory disease or sepsis. Universal screening has not been approved in the UK, but is performed in some hospitals. It has been introduced in some countries.

Newborn blood spot screening

Newborn blood spot screening (previously called the Guthrie test) is performed on every baby. A blood sample, usually a heel prick, is taken when feeding has been established on day 5. In the UK, all infants are screened for a range of disorders where early identification and treatment can lead to improved outcomes:

- congenital hypothyroidism
- haemoglobinopathies (sickle cell and thalassaemia)
- cystic fibrosis
- six inherited metabolic diseases:
 - phenylketonuria
 - MCAD (medium-chain acyl-coenzyme A dehydrogenase deficiency)
 - maple syrup urine disease
 - isovaleric aciduria
 - glutaric aciduria type 1
 - homocystinuria.

Details about the inborn errors of metabolism are described in [Chapter 27](#) (Inborn errors of metabolism). Screening for cystic fibrosis is performed by measuring the serum immunoreactive trypsin, which is raised if there is pancreatic duct obstruction. If raised, DNA analysis is also performed to reduce the false-positive rate (see [Ch. 17](#), Respiratory disorders). Some countries screen for many more conditions.



In the UK, newborn blood spot screening is performed on all babies to identify congenital hypothyroidism, haemoglobinopathies, cystic fibrosis and six inborn errors of metabolism.

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Neonatal medicine

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Features of neonatal medicine:

- The survival rate of premature infants has increased markedly, even when born at very early gestations (23–28 weeks), but they are at risk of many short- and long-term problems.
- Jaundice is common in newborn infants; the aim of its management is to prevent high levels of bilirubin which may cause brain damage from kernicterus.
- Newborn infants with respiratory distress require urgent assessment of their need for respiratory support.
- Newborn infants are particularly susceptible to infection.

- Hypoxic-ischaemic encephalopathy is a major cause of death and neurodevelopmental disability worldwide.

The dramatic reduction in neonatal mortality throughout the world has accompanied improved care of newborn infants together with improvements in maternal health and obstetric care, public health, maternal education and better living conditions accompanying improving socio-economic circumstances. With neonatal intensive care, in high-income countries, the mortality of extremely premature infants has fallen markedly (Fig. 11.1).

Neonatal survival and neonatal unit admissions and length of stay, by gestational age

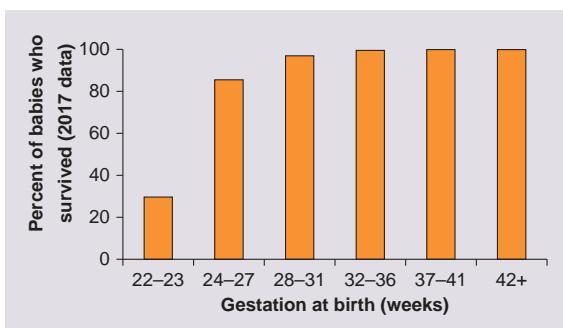


Figure 11.1 Survival by gestational age in the UK, showing the high survival of infants from 24 weeks' gestational age. (Data from: MBRACE-UK. 2019 report on 2017 data. Perinatal mortality surveillance report. Retrieved from: <https://www.npeu.ox.ac.uk/assets/downloads/mbrace-uk/reports/MBRACE-UK%20Perinatal%20Mortality%20Surveillance%20Report%20for%20Births%20in%202017%20-%20FINAL%20Revised.pdf>)

Table 11.1 Number of babies admitted to neonatal units and length of stay by gestation in the UK

Gestation at birth	Number of babies	% of total admitted	Approx length of stay (days)
<25 weeks	1189	1.2	106
26–32 weeks	10,283	10.2	44
33–36 weeks	26,758	26.6	12
>37 weeks	62,427	62	4
Total	100,657	100	

(From: Neonatal Data Analysis Unit, Imperial College, for 2016.)

Most babies do not require any additional medical care after birth and are nursed alongside their mothers in the maternity unit. Some babies require transitional care, where some additional monitoring or care is required, and this is usually provided with the baby nursed alongside his/her mother on the postnatal ward in the maternity unit. About 14% of babies born in the UK are admitted to a neonatal unit for special medical and nursing care, although whenever possible separating mothers from their babies should be avoided. Although the number of extremely preterm infants admitted to neonatal units is relatively small, their length of stay is long and they require long periods of intensive care (Table 11.1). The majority of admissions are term infants (admitted for respiratory disorders (25% of admissions), infection (18%), hypoglycaemia (12%), jaundice (6%) and hypoxic–ischaemic encephalopathy (2.5%). In the UK, neonatal units are organized as networks, with units providing either:

- special care (level 1)
- high dependency and short-term intensive care (level 2, local neonatal units)
- long-term neonatal intensive care (level 3, neonatal intensive care units (NICUs), usually linked to specialist fetal and obstetric care to form a specialist tertiary perinatal centre. About 1%–3% of babies require intensive care. Some NICUs also provide regional specialist neonatal services, e.g. neonatal surgery, paediatric cardiology; ideally co-located with other paediatric specialist services.

Modern technology allows even tiny preterm infants to benefit from the full range of intensive care, anaesthesia, and surgery. If it is anticipated during pregnancy that the infant is likely to require long-term intensive care or surgery or specialist services, it is preferable for the transfer to the tertiary centre to be made *in utero*. When a baby requires transfer postnatally, transport should be by an experienced team of doctors and nurses; this is often organized to serve a number of neonatal units in a regional network.

Admission to a neonatal unit

Neonatal units are a daunting environment for parents. Instead of the joyful occasion of the birth of their newborn infant, they find their baby separated from them because of a serious medical problem. Their newborn baby is likely to be in an incubator, attached to numerous monitors and intravenous infusions and probably receiving respiratory support. They are surrounded by experienced nursing and medical staff who are confidently handling their baby, whereas they are frightened to do so. Every effort needs to be made to help parents overcome their anxieties, and feel at home in the unit.

Neonatal units strive to provide infant- and family-centred developmental care, making the baby and parents the focus of care, rather than the baby's medical problems (Fig. 11.2). It ensures that parents are welcomed as partners in their baby's care, are encouraged to come to the unit at all times and to bond with their baby by touching and then providing skin-to-skin contact with their baby, as soon as their condition is sufficiently stable. Mothers are encouraged to provide breast milk, which will probably need to be given via a nasogastric tube; in time parents may be able to do this themselves. Infant- and family-centred developmental care ensures that attention is paid to the needs of the baby: can the baby be made comfortable, is the baby experiencing pain and how can this be minimized, can the baby be disturbed as little as possible to protect sleep, can procedures wait until the baby is awake and be paced and spaced so that they do not overwhelm the baby? Attention is also paid to the environment – avoiding stressors such as intense lighting and loud or jarring noises, and ensuring that there are facilities for siblings and close family to visit. As premature babies may be on the unit for many weeks, facilities are needed for parents to stay on the unit to allow them to assume their parental role. This can be best achieved with family rooms for the parents and baby when the baby is stable enough; a few units are able to also provide this within the intensive care unit itself.

Infant and family-centred developmental care

Baby's comfort:

- Avoid bright light
- Avoid loud noises

Nursery environment

Always made welcome:

- Facilities for parents on neonatal unit and to stay
- Facilities for family to visit
- Kept informed

Parents and family

Increased role of parents

Parent assists with:

- Establishing breast feeding
- Giving care, e.g. tube feeding
- Skin-to-skin/Kangaroo mother care

Talking and comforting their baby

Getting to know their baby

Adapting care to the baby

When disturbing baby (vital signs, changing) or performing procedures (blood tests, eye exams, etc):

- Do together, but pace them
- Avoid disturbing sleep
- Consider pain

Figure 11.2 Infant- and family-centred developmental care (IFCD), highlighting the need to focus care on the infant and family. (Photo courtesy of Lawrence Miall.)

Stabilizing the preterm or sick infant

After birth, preterm infants of less than 34 weeks' gestation or newborn infants who become seriously ill,

infants will need to be stabilized and monitored following resuscitation, if required (Fig. 11.3). Many of them will need respiratory, circulatory and nutritional support.

Stabilizing preterm or sick infants

Airway and breathing

Check for:

- respiratory distress – tachypnoea, laboured breathing with chest wall recession, nasal flaring, expiratory grunting, cyanosis
- apnoea.

Management, as required:

- clear the airway
- oxygen
- respiratory support with continuous positive airway pressure (CPAP) or high-flow nasal cannula therapy or surfactant therapy or mechanical ventilation.

Monitoring

- oxygen saturation (maintain at 91%–95% if preterm, >95% if term)
- heart rate
- respiratory rate
- temperature
- blood pressure
- blood glucose
- blood urea and electrolytes, blood gases
- weight

Temperature control

- place in plastic bag (wrap) at birth to keep warm if extremely preterm
- perform stabilization under a radiant warmer with or without a heated mattress or in a humidified incubator to avoid hypothermia.

Venous and arterial lines

Peripheral intravenous line

- required for intravenous fluids, antibiotics, and other drugs.



Figure 11.3 Stabilizing preterm or sick infants is important to prevent complications. This preterm infant has leads on his chest for monitoring heart rate and respiratory rate, and temperature and an oxygen saturation monitor on his foot. There are umbilical arterial and venous catheters, an intravenous cannula, and an endotracheal tube for mechanical ventilation.

Umbilical venous catheter:

- may be used for intravenous access at resuscitation, in extremely preterm infants for the first few days or to administer high osmolality fluids (e.g. parenteral nutrition, high-concentration dextrose) or medications needing central delivery (e.g. inotropes).

Arterial line:

- inserted if frequent blood gas analysis, blood tests, and continuous blood pressure monitoring are required. Usually umbilical artery catheter, sometimes peripheral cannula if for short period or no umbilical artery catheter possible.
- the arterial oxygen tension is maintained at 8–12 kPa (60–90 mmHg) and the CO₂ tension at 4.5–6.5 kPa (35–50 mmHg).

Peripherally inserted central catheter (PICC) for parenteral nutrition, if indicated:

- inserted when infant is stable.

Chest X-ray with or without abdominal X-ray

- Assists in the diagnosis of respiratory disorders and to confirm the position of the tracheal tube, central lines and gastric tube.

Initial investigations

- haemoglobin, neutrophil count, platelet count
- blood urea, creatinine, electrolytes, and lactate
- culture – blood±cerebrospinal fluid±urine
- blood glucose (regular)
- C-reactive protein/acute phase reactant
- coagulation screen if indicated.

Antibiotics

- Empirical antibiotics are given, if indicated.

Minimal handling

- All procedures, especially painful ones, adversely affect oxygenation and the circulation. Handling the infant is kept to a minimum and done as gently, rapidly and efficiently as possible. Analgesics and non-pharmacological measures should be provided to prevent pain as necessary.

Parents

- Although medical and nursing staff are usually fully occupied whilst stabilizing the baby, time must be found for parents to allow them to see and touch their baby and to be kept fully informed.

Box 11.1 Potential medical problems of preterm infants

- Need for resuscitation and stabilization at birth
- Respiratory:
 - respiratory distress syndrome
 - pneumothorax
 - apnoea and bradycardia
- Hypotension
- Patent ductus arteriosus
- Temperature control
- Metabolic:
 - hypoglycaemia
 - hypocalcaemia
 - electrolyte imbalance
 - osteopenia of prematurity
- Nutrition:
 - Difficulty establishing feeding
 - Extra-uterine growth impairment
- Infection
- Jaundice
- Intraventricular haemorrhage/periventricular leukomalacia
- Necrotizing enterocolitis
- Retinopathy of prematurity
- Anaemia of prematurity
- Bronchopulmonary dysplasia (BPD)
- Inguinal hernias

The preterm infant

The appearance, the likely clinical course, chances of survival, and long-term prognosis depend on the gestational age at birth. The appearance and maturational changes of very preterm infants are described in [Table 11.2](#) (also see [Fig. 11.4](#)) and the importance of parental involvement is shown in [Figs. 11.5 and 11.6](#). Gestational age is most accurately determined from the early antenatal ultrasound scan. The external appearance and neurological findings can also be scored to provide an estimate of an infant's gestational age if not known from ultrasound scanning, but is less accurate (see [Appendix](#)).

The frequency and severity of problems associated with prematurity decline markedly with increasing gestation. Infants born at 23–25 weeks' gestation encounter many problems ([Box 11.1](#)), require many weeks of intensive and special care in hospital, and have increased mortality.

Respiratory distress syndrome

In respiratory distress syndrome (RDS, also called hyaline membrane disease), there is a deficiency of surfactant, which lowers surface tension. Surfactant is a mixture of phospholipids and proteins excreted by the type II pneumocytes of the alveolar epithelium. Surfactant deficiency leads to widespread alveolar collapse and inadequate gas exchange. The more preterm the infant, the higher the incidence of RDS. It is very common in infants born before 28 weeks' gestation and tends to be more severe in boys than girls. Surfactant deficiency is rare at term but may occur in infants of diabetic mothers and very rarely from genetic mutations in the surfactant genes. A proteinaceous exudate (forming a hyaline membrane) may be seen in the airways on histology. Glucocorticoids, given antenatally to the mother, stimulate fetal surfactant production and are

given if preterm delivery is anticipated (see [Ch. 10](#), Perinatal medicine). The evidence of their benefit is substantial; it significantly reduces RDS, the lung damage of bronchopulmonary dysplasia, intraventricular haemorrhage (IVH) and other causes of neonatal mortality.

At delivery or within 4 hours of birth, babies with RDS develop clinical signs of:

- tachypnoea over 60 breaths/minute
- increased work of breathing, with chest wall recession (particularly sternal and subcostal indrawing) and nasal flaring
- expiratory grunting in order to try to create positive airway pressure during expiration and maintain functional residual capacity
- cyanosis if severe.

The characteristic chest X-ray appearance is shown in [Figure 11.7](#). Management is initially with supplemental oxygen ([Box 11.2](#)) and non-invasive respiratory support (continuous positive airway pressure (CPAP) or high-flow nasal cannula therapy). Surfactant therapy may be required. It is given by instilling surfactant directly into the lungs via a tracheal tube or a fine catheter inserted directly between the vocal cords into the trachea. Mechanical ventilation is initiated if there is inadequate response. Non-invasive respiratory support is used in preference to mechanical ventilation whenever possible as it has fewer complications.



Surfactant therapy reduces morbidity and mortality of preterm infants with respiratory distress syndrome.

Pneumothorax

In RDS, air from the overdistended alveoli may track into the interstitium, resulting in pulmonary interstitial emphysema. In up to 10% of infants ventilated for RDS,

The preterm infant: maturational changes in appearance and development

Figure 11.4 (a) Preterm infant at 23–27 weeks. (b) Term infant.



Table 11.2 The extremely preterm infant compared with the term infant

Gestation	Extremely preterm (23–27 weeks)	Term (37–42 weeks)
Birthweight (50th centile)	At 24 weeks – male 700g, female 620g	At 40 weeks – male 3.55kg, female 3.4kg
Skin	Very thin (Fig. 11.4a) Dark red colour all over body	Thick skin (Fig. 11.4b) Pale pink colour
Ears	Pinna soft, no recoil	Pinna firm, cartilage to edge, immediate recoil
Breast tissue	No breast tissue palpable	One or both nodules >1 cm
Genitalia	Male – scrotum smooth, no testes in scrotum Female – prominent clitoris, labia majora widely separated, labia minora protruding	Male – scrotum has rugae, testes in scrotum Female – labia minora and clitoris covered
Breathing	Needs respiratory support. Apnoea common	Rarely needs respiratory support. Apnoea rare
Sucking and swallowing	No coordinated sucking	Coordinated (from 34–35 weeks)
Feeding	Parenteral nutrition and tube feeding	Cries when hungry. Feeds on demand
Cry	Faint	Loud
Vision, interaction	Eyelids may be fused. Infrequent eye movements. Not available for interaction	Makes eye contact, alert wakefulness
Hearing	Startles to loud noise	Responds to sound
Posture	Limbs extended, jerky movements	Flexed posture, smooth movements



Figure 11.5 Parental involvement in neonatal care. Skin-to-skin contact between infant and parent (kangaroo care) promotes bonding.

Figure 11.6 Parental involvement in neonatal care. Mother giving her baby expressed breast milk (in syringe) via nasogastric tube, allowing close eye and skin contact between mother and baby.

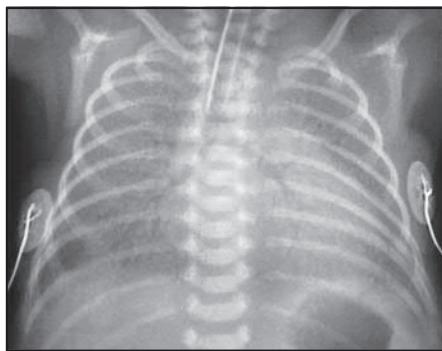


Figure 11.7 Chest X-ray in respiratory distress syndrome showing a diffuse granular or 'ground glass' appearance of the lungs and an air bronchogram, where the larger airways are outlined. The heart border is indistinct. A tracheal tube is present. (From: Lissauer T, Fanaroff AA, Moll L, et al: *Neonatology at a Glance*, ed 3. Oxford, 2015, Wiley Blackwell, with permission.)

Box 11.2 Oxygen therapy in preterm infants

Oxygen therapy should be provided to correct hypoxaemia. However:

- excess oxygen leading to hyperoxia is damaging to the lungs and brain and other organs from excess free radicals
- for neonatal resuscitation, it is now recommended to start with 21%–30% oxygen in preterm infants, avoiding oxygen saturation over 95%; in term infants air should be used
- in preterm infants avoid low saturations (<91%) – increased risk of necrotizing enterocolitis and death, and avoid high saturation (>95%) – increased risk of retinopathy of prematurity

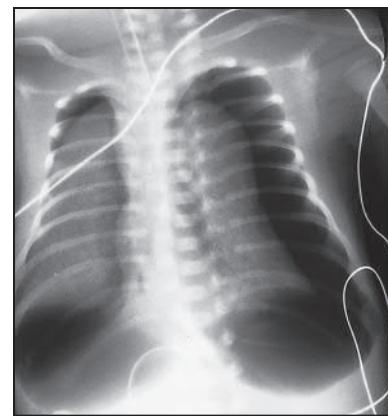


Figure 11.8 Chest X-ray showing bilateral pneumothoraces in a preterm infant with respiratory distress syndrome.

32 weeks' gestational age. Bradycardia may occur, either when an infant stops breathing for over 20–30 seconds, or when breathing continues but against a closed glottis. An underlying cause (hypoxia, infection, anaemia, electrolyte disturbance, hypoglycaemia, seizures, heart failure or aspiration due to gastro-oesophageal reflux) needs to be excluded, but in many instances the cause is immaturity of central respiratory control. Breathing will usually start again after gentle physical stimulation. Treatment with the respiratory stimulant caffeine often helps and has been demonstrated to improve outcomes. CPAP or mechanical ventilation may be necessary if apnoeic episodes are frequent.

Temperature control

Hypothermia causes increased energy consumption and may result in hypoxia and hypoglycaemia, or failure to gain weight. Hypothermia is an independent risk factor for mortality soon after birth. Preterm infants are particularly vulnerable to hypothermia, as:

- they have a large surface area relative to their mass, so there is greater heat loss (related to surface area) than heat generation (related to mass)
- their skin is thin and heat permeable, so transepidermal water loss is significant in the first week
- they have little subcutaneous fat for insulation
- they are often nursed naked and cannot conserve heat by curling up or generate heat by shivering.

There is a neutral temperature range in which an infant's energy consumption is at a minimum level. In the very immature baby, this neutral temperature is highest during the first few days of life and subsequently declines. The temperature of these small babies is maintained using incubators (Fig. 11.9) or initially with overhead radiant heaters. Incubators also allow ambient humidity to be provided, which reduces transepidermal heat loss.

air leaks into the pleural cavity and causes a pneumothorax. When this occurs, the infant's oxygen requirement usually increases and the breath sounds and chest movement on the affected side are reduced, although this can be difficult to detect clinically. A pneumothorax may be demonstrated by transillumination with a bright fibre-optic light source applied to the chest wall point of care lung ultrasound, or on a chest X-ray (Fig. 11.8). A tension pneumothorax is treated urgently with decompression by needle aspiration and subsequent insertion of a chest drain. In order to try and prevent pneumothoraces, infants are ventilated with the lowest pressures that provide adequate chest movement and satisfactory blood gases.

Apnoea and bradycardia and desaturation

Episodes of apnoea and bradycardia and desaturation are common in preterm infants until they reach about

Temperature control

Prevention of heat loss in newborn infants

1. Convection

- raise temperature of ambient air in incubator
- clothe, including covering head
- avoid draughts.

2. Radiation

- cover baby
- double walls for incubators.

3. Evaporation

- dry and wrap at birth; if extremely preterm, place baby's body directly into plastic bag at birth without drying
- humidify incubator.

4. Conduction

- nurse on heated mattress.

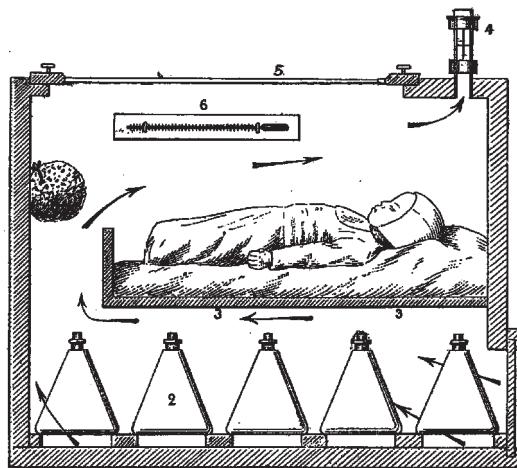


Figure 11.9 The importance of avoiding hypothermia in newborn infants has long been recognized. This incubator was used in the late nineteenth century to keep newborn infants warm by circulating hot air. The sponge is to increase ambient humidity.

Patent ductus arteriosus

The ductus arteriosus remains patent in many preterm infants for several weeks but only becomes a problem in extremely preterm or ill infants. Shunting of blood across the ductus, from the left to the right side of the circulation, is most common in infants with RDS. It may produce no symptoms or it may cause apnoea and bradycardia, increased oxygen requirement, need for respiratory support or difficulty in weaning the infant from mechanical ventilation. The pulses are 'bounding' from an increased pulse pressure, the precordial impulse becomes prominent, and a systolic murmur may be audible. With increasing circulatory overload, signs of heart failure may develop. More accurate assessment of the infant's circulation can be obtained on echocardiography. If the duct is considered haemodynamically significant, pharmacological closure with a prostaglandin synthetase inhibitor, ibuprofen or paracetamol, is used. If these measures fail to close a symptomatic duct, surgical ligation or insertion of an occlusive device by catheterization will be required.

Fluid balance

A preterm infant's fluid requirements will vary with gestational and chronological age. It is adjusted according to the infant's clinical condition, plasma electrolytes, urine output, and weight change. On the first day, about 60–90 ml/kg is usually required, which increases by 20–30 ml/kg per day to 150–180 ml/kg per day by about day 5.

Nutrition

Preterm infants have a high nutritional requirement because of their rapid growth. Preterm infants at 28

weeks' gestation double their birthweight in 6 weeks and treble it in 12 weeks, whereas term babies double their weight in only 5 months and treble it in a year.

Infants of 35–36 weeks' gestational age are mature enough to suck and swallow milk. Less mature infants usually need to be fed via a nasogastric or orogastric tube. Even in very preterm infants, colostrum should be given as mouth care or via the nasogastric tube within the first few hours after birth, and enteral feeds, preferably breast milk, introduced as soon as possible. In some neonatal units, extremely preterm infants are initially fed on donor breast milk if sufficient maternal breast milk is not available. Breast milk may need to be supplemented with additional protein, phosphate, electrolytes and calories, most readily provided by giving breast milk fortifier. If formula feeding is required, special infant formulas are available, which are designed to meet the increased nutritional requirements of preterm infants but, in contrast to breast milk, do not provide protection against infection or other benefits of breast milk. In the very immature or sick infant (typically <1 kg birthweight), parenteral nutrition is often required. This is usually given through a peripherally inserted central catheter (PICC or long line), or an umbilical venous catheter. Central lines carry a significant risk of septicaemia, so staff need to pay strict attention to aseptic technique both during insertion and when lines are accessed. Parenteral nutrition may sometimes be given via a peripheral vein, but extravasation may cause skin damage with scarring. Because of the infection risk associated with parenteral nutrition and the increased risk of necrotizing enterocolitis (see below) with formula, mothers should be encouraged and supported to provide breast milk.

Poor bone mineralization (osteopenia of prematurity) was previously common but is prevented by provision of adequate phosphate, calcium and vitamin D. Because iron

is mostly transferred to the fetus during the last trimester, preterm babies have low iron stores and are at a risk of iron deficiency. This is in addition to loss of blood from sampling and an inadequate erythropoietin response. Iron supplements are started at several weeks of age and continued after discharge home.

Infection

Preterm infants are at an increased risk of infection, as IgG is mostly transferred across the placenta in the last trimester and no IgA or IgM is transferred. In addition, infection in or around the cervix is often a reason for preterm labour and may cause infection in the infant shortly after birth. Preterm infants are also at particular risk of nosocomial (hospital-derived) infection, often associated with indwelling catheters or mechanical ventilation. Infection is considered in more detail later in this chapter.



Infection in preterm infants is a major cause of death and contributes to bronchopulmonary dysplasia, brain injury and later disability.

Necrotizing enterocolitis

Necrotizing enterocolitis is a serious illness and one of the major challenges facing neonatal medicine. The incidence is inversely proportional to gestational age. It is

typically seen in the first few weeks of life. The aetiology of necrotizing enterocolitis is poorly understood, but is thought to be due to ischaemic injury and bacterial invasion of the bowel wall and altered gut microbiome, which is improved with breast milk and possibly prebiotics and probiotics, and adversely affected by formula feeds, unduly rapid increase in enteral feeds and antibiotics. Risk factors are intrauterine growth restriction, especially if accompanied by antenatal reversed end diastolic flow on Doppler studies and perinatal asphyxia.

Early signs of necrotizing enterocolitis include feed intolerance and vomiting, which may be bile stained. The abdomen becomes distended (*Fig. 11.10a*) and the stool sometimes contains fresh blood. The infant may rapidly become shocked and require mechanical ventilation because of abdominal distension and pain. The characteristic X-ray features are distended loops of bowel and thickening of the bowel wall with intramural gas, and there may be gas in the portal venous tract (*Fig. 11.10b*). The disease may progress to bowel perforation.

Treatment is to stop oral feeding and give broad-spectrum antibiotics to cover both aerobic and anaerobic organisms. Parenteral nutrition is needed and mechanical ventilation and circulatory support are often required. Surgery is performed for bowel perforation, difficulty with mechanical ventilation, or a failure to respond to medical management. The disease has significant morbidity and a mortality of about 20%. Long-term sequelae include the development of bowel strictures and malabsorption if extensive bowel resection has been necessary, as well as a greater risk of a poor neurodevelopmental outcome.

Necrotizing enterocolitis



Figure 11.10a Necrotizing enterocolitis showing gross abdominal distension and tense and shiny skin with discolouration over the abdomen. There is also blood on the nappy. (Copyright Nic Alexander.)

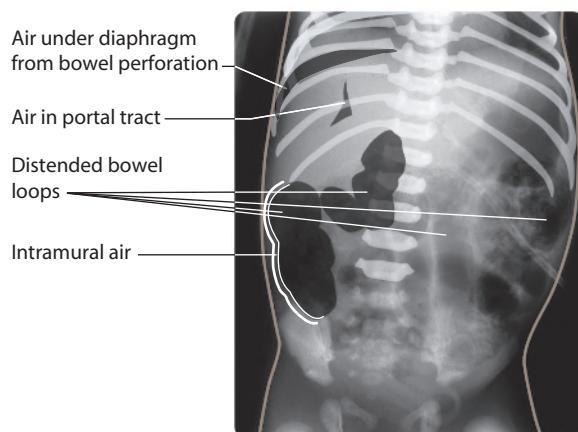


Figure 11.10b Diagram of characteristic features of necrotizing enterocolitis on abdominal X-ray.

Preterm brain injury

Cranial ultrasound is performed to identify a range of brain lesions to which preterm infants are predisposed. Haemorrhages in the brain occur in 25% of very-low-birthweight infants and are easily recognized on cranial ultrasound scans (Fig. 11.11a). Typically, they occur in the germinal matrix above the caudate nucleus, which contains a fragile network of blood vessels. Most intraventricular haemorrhages (IVHs) occur within the first 72 hours of life. They are more common following perinatal asphyxia and in infants with severe RDS. Pneumothorax is a significant risk factor. Antenatal glucocorticoids prior

to preterm delivery is associated with a reduction in the incidence and severity of RDS, and therefore of IVH.

Small haemorrhages are confined to the germinal matrix, but larger haemorrhages may extend into the ventricles. The most severe haemorrhage is unilateral haemorrhagic infarction involving the parenchyma of the brain; this usually results in hemiplegia (Fig. 11.11b).

A large IVH may impair the drainage and reabsorption of cerebrospinal fluid (CSF), thus allowing CSF to build up under pressure. This dilatation (Fig. 11.11c) may resolve spontaneously or progress to hydrocephalus, which may cause the cranial sutures to separate, the head circumference to increase rapidly, and the anterior fontanelle to

Cranial ultrasound in preterm infants

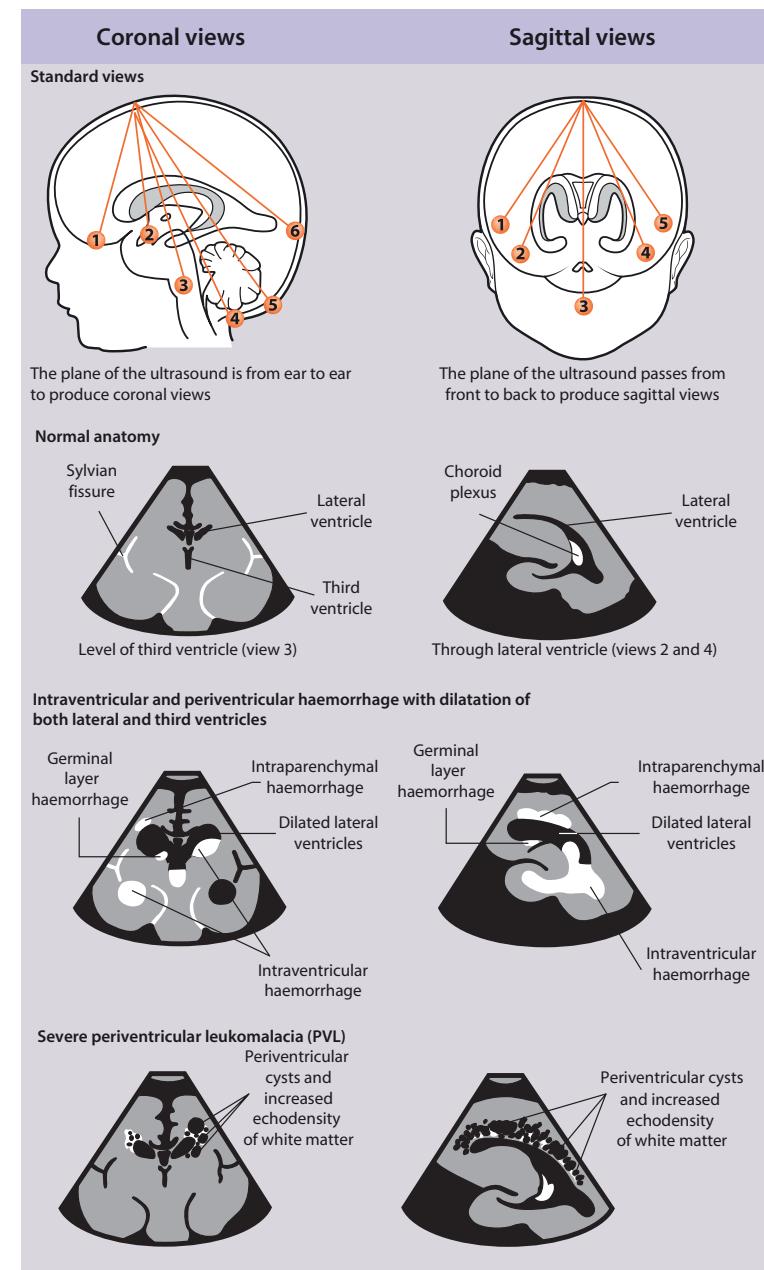


Figure 11.11a Cranial ultrasound in preterm infants.

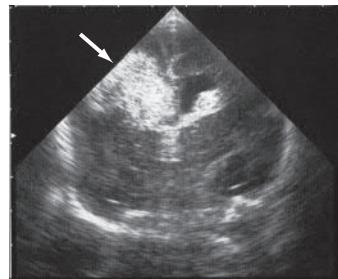


Figure 11.11b Large intraventricular haemorrhage with parenchymal haemorrhagic infarct on the right (arrow).



Figure 11.11c Dilatation of lateral ventricles following intraventricular haemorrhage.



Figure 11.11d Widespread cysts in periventricular leukomalacia.

become tense. A ventriculoperitoneal or subgaleal shunt may be required, but initially symptomatic relief may be provided by removal of CSF by lumbar puncture. About half of infants with progressive post-haemorrhagic ventricular dilatation have cerebral palsy, a higher proportion if parenchymal infarction is also present.

Preterm infants are susceptible to white matter injury and abnormal cerebral development following ischaemia and inflammation even in the absence of haemorrhage. It may result in cystic white matter lesions visible on cranial ultrasound. Bilateral multiple cysts, called periventricular leukomalacia (PVL), have an 80%–90% risk of spastic diplegia, often with cognitive impairment, if posteriorly sited (Fig. 11.11d). This has become uncommon. More common is damage to neural pathways, which increases the risk of neurocognitive impairment.

Both IVH and periventricular leukomalacia may occur in the absence of abnormal clinical signs.

Retinopathy of prematurity

Retinopathy of prematurity affects developing blood vessels at the junction of the vascularized and non-vascularized retina. There is vascular proliferation, which may progress to retinal detachment, fibrosis and blindness. It was initially recognized that the risk is increased by uncontrolled use of high concentrations of oxygen. Now, even with careful monitoring of the infant's oxygenation, retinopathy of prematurity is still identified in about 35% of all very-low-birthweight infants, with severe disease requiring treatment in 5%. The eyes of susceptible preterm infants (≤ 1500 g birthweight or < 32 weeks' gestation) are screened by an ophthalmologist. Laser therapy reduces visual impairment, and intravitreal anti-VEGF (anti-vascular endothelial growth factor) therapy is being investigated. Severe bilateral visual impairment occurs in about 1% of very-low-birthweight infants, mostly in infants < 28 weeks' gestation.

Bronchopulmonary dysplasia

Infants who still have an oxygen requirement at a post-menstrual age of 36 weeks are described as having bronchopulmonary dysplasia (BPD) (also called chronic lung disease). The lung damage is now thought to be mainly from delay in lung maturation, but may also be from pressure and volume trauma from artificial ventilation, oxygen toxicity and infection. The chest X-ray characteristically shows widespread areas of opacification, sometimes with cystic changes (Fig. 11.12). Some infants need prolonged artificial ventilation, but most are weaned onto CPAP or high-flow nasal cannula therapy followed by supplemental oxygen, sometimes over several months. Corticosteroid therapy may facilitate earlier weaning from the ventilator and often reduces the infant's oxygen requirements in the short term, but concern about increased risk of abnormal neurodevelopment including cerebral palsy limits use to those at highest risk and only short, low-dose courses are given. Some babies go home while still receiving additional oxygen. A few infants with severe disease may die of intercurrent infection or pulmonary

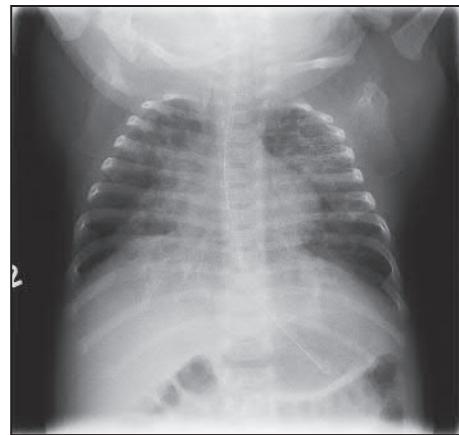


Figure 11.12 Chest X-ray of bronchopulmonary dysplasia (BPD) showing fibrosis and lung collapse, cystic changes and over-distension of the lungs.

hypertension. Subsequent pertussis and respiratory viral infection (e.g. respiratory syncytial virus or rhinovirus) may cause respiratory failure necessitating intensive care.

Problems following discharge

Some of the medical problems likely to be encountered on discharge from hospital are summarized in [Case history 11.1](#).

About 5%–10% of very-low-birthweight infants develop cerebral palsy, but the most common impairment is learning difficulties. The prevalence of cognitive impairment and of other associated difficulties increases with decreasing gestational age at birth, and is greatest if born at very early gestational age (< 26 weeks' gestation; Fig. 11.14). It becomes increasingly evident when the individual child is compared with their peers at nursery or school. In addition, preterm infants are susceptible to difficulties with:

- fine motor skills, e.g. threading beads
- concentration, with short attention span
- behaviour, especially attention deficit disorders
- abstract reasoning, e.g. mathematics
- processing several tasks simultaneously.

A small proportion also have hearing impairment, with 1%–2% requiring amplification, or visual impairment, with 1% blind in both eyes. A greater proportion have refraction errors and squints, and therefore require glasses.

Follow-up studies of very preterm infants who are now adults indicate that whilst many are content and have a good quality of life, overall they are less socially engaged, are poorer in communication, and more easily become worried compared with their peers. This impacts adversely on relationships and careers.

 During infancy, extremely preterm infants, especially those who had bronchopulmonary dysplasia, are at increased risk of respiratory failure from bronchiolitis and other lower respiratory tract infections.



Case history 11.1

The ex-preterm infant going home

Mohammed was born at 24 weeks' gestation. The care pathway showing the potential problems and their timing for an infant born at this gestation is shown in Fig. 11.13. He is about to be discharged from the neonatal unit at 41 weeks' gestational age. His discharge planning meeting identified his needs when going home, which included:

- Home oxygen for his bronchopulmonary dysplasia – he will have respiratory reviews to allow him to wean safely off his oxygen with growth.
- Respiratory syncytial virus prophylaxis during the winter months – to reduce the risk of readmission and need for respiratory support.

- He has already had two sets of primary immunizations at the normal time and this course needs completing.
- He is at a greater risk of inguinal hernias.
- Ophthalmology review – will monitor his early retinopathy of prematurity and decide if any treatment is required.
- Low threshold for hospital readmission – rate increased four-fold, mainly for respiratory disorders.

In addition to the healthy child programme for all children, his growth and neurodevelopment will be monitored, especially during the early years of life.

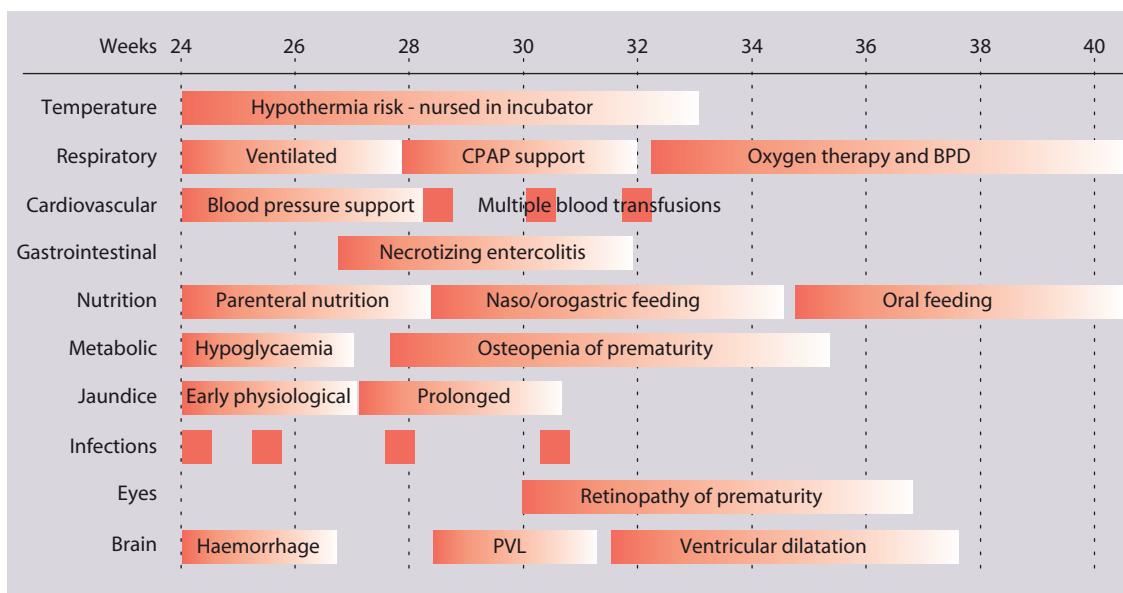


Figure 11.13 Typical care pathway for a 24-week gestation infant showing potential complications and their timing. (RDS, respiratory distress syndrome; CPAP, continuous positive airway pressure; BPD, bronchopulmonary dysplasia; PVL, periventricular leukomalacia.)



Figure 11.14 Outcome data at 3 years of age, a population-based study of all preterm infants <26 weeks' gestation born in England in 2006 (EPICure 2). Compared with babies born in 1995 (EPICure study), there have been improvements in survival but disability remains similar. (Data from: Moore T, Hennessy EM, Myles J, Johnson SJ, Draper ES, et al: Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. *British Medical Journal* 345:e7961, 2012.)

Summary**Summary of problems of very low birthweight infants (<1.5 kg)****Respiratory****Respiratory distress syndrome (surfactant deficiency) (74%)**

- respiratory distress within 4 hours of birth
- antenatal corticosteroids and surfactant therapy reduce morbidity and mortality
- oxygen therapy, but excess may damage the retina
- nasal CPAP (continuous positive airway pressure) (86%) and mechanical ventilation (64%) – often required to expand lungs and prevent lung collapse; high-flow nasal cannula therapy may also be used (75%)

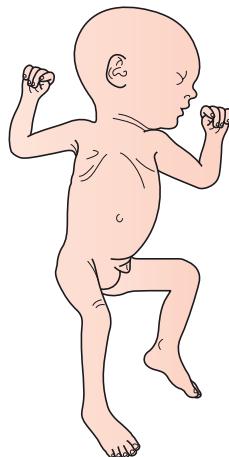
Pneumothorax (4%)**Apnoea and bradycardia and desaturations**

Bronchopulmonary dysplasia (BPD) – oxygen requirement at 36 weeks post-menstrual age (25%)

Circulation

Hypotension – may require volume support, inotropes or corticosteroids

Patent ductus arteriosus – needing medical treatment (12%) or surgical ligation (3%)

**Temperature control**

Avoid hypothermia
Nurse in neutral thermal environment
Nurse in incubator or under radiant warmer
Clothe if possible
Humidity reduces evaporative heat loss

Nutrition

Nasogastric tube feeding – until 35–36 weeks post-menstrual age

Feeding intolerance - PN (parenteral nutrition) often required

Jaundice – common, low treatment threshold

Infection

Common and potentially serious (2% early-onset and 11% late-onset infection)
Increased risk of early-onset infection
– group B streptococcus
Main problem is nosocomial infection
– mainly coagulase-negative staphylococcus, also other infections

Metabolic

Hypoglycaemia – common

Electrolyte disturbances

Osteopenia of prematurity from phosphate deficiency

Anaemia

Often need blood transfusions

Hearing

Checked before discharge

Eyes

Retinopathy of prematurity – may need laser therapy (5%)

Brain injury

Haemorrhage (25%, severe grade III/IV 8%)

– germinal layer, intraventricular, parenchymal

Ventricular dilatation – may need ventriculo-peritoneal shunt

Periventricular leukomalacia (3%)
– ischaemic white matter injury

Following discharge

Specialist community nursing support helpful, if available

Increased risk of respiratory infection and wheezing – especially from bronchiolitis (caused by respiratory syncytial virus, RSV) and pertussis; may need intensive care

Give routine immunizations according to chronological age

Consider prophylaxis against RSV infection

Increased rehospitalization – respiratory disorders, inguinal hernias

Monitor growth, development (for learning disorders, co-ordination, cerebral palsy), behaviour, attention, vision, hearing – increased risk of impairment, according to corrected age until 2 years old

Jaundice

Over 50% of all newborn infants become visibly jaundiced (Fig. 11.15). This is because:

- there is marked physiological release of haemoglobin from the breakdown of red cells because of the high haemoglobin concentration at birth
- the red cell lifespan of newborn infants (70 days) is markedly shorter than that of adults (120 days)
- hepatic bilirubin metabolism is less efficient in the first few days of life.

Neonatal jaundice is important as:

- it may be a sign of another disorder, e.g. haemolytic anaemia, infection, inborn error of metabolism, liver disease
- unconjugated bilirubin can be deposited in the brain, particularly in the basal ganglia, causing brain damage from kernicterus.

Kernicterus

This is the encephalopathy resulting from the deposition of unconjugated bilirubin in the basal ganglia and brainstem nuclei (Fig. 11.16). It may occur when the level

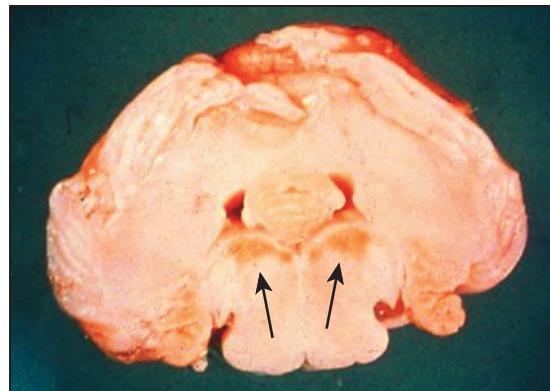


Figure 11.16 Postmortem of brainstem and cerebellum showing kernicterus with yellow bilirubin staining of brainstem nuclei (arrows).

of unconjugated bilirubin exceeds the albumin-binding capacity of bilirubin of the blood. As this free bilirubin is fat soluble, it can cross the blood–brain barrier. The neurotoxic effects vary in severity from transient disturbance to severe damage and death. Acute manifestations are lethargy and poor feeding. In severe cases, there is irritability, increased muscle tone causing the baby to lie with an arched back (opisthotonus), seizures and coma. Infants who survive may develop choreoathetoid cerebral palsy

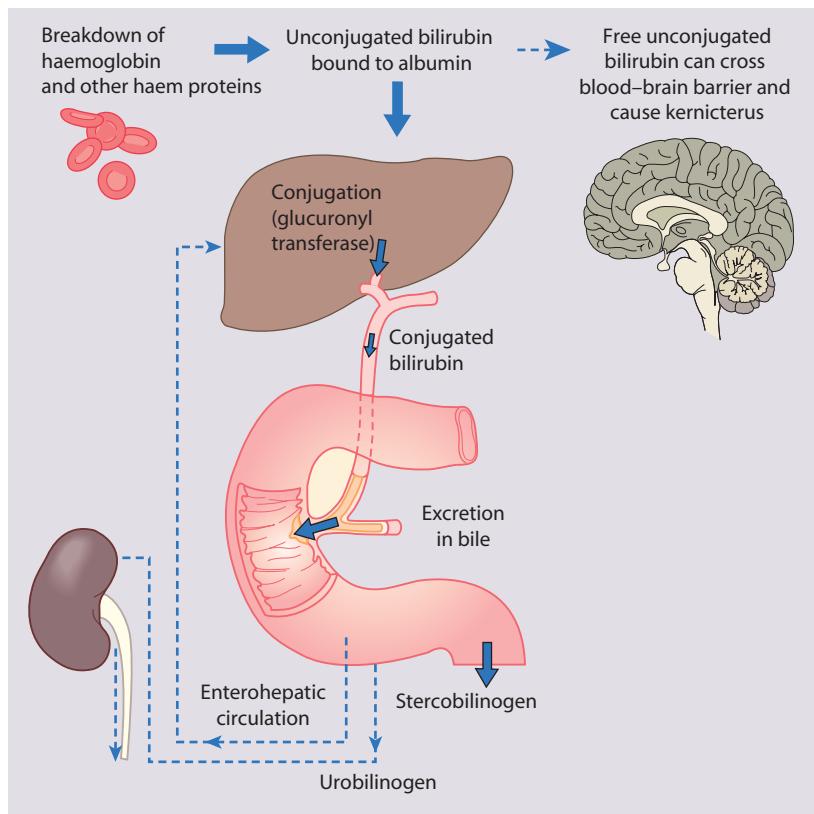


Figure 11.15 The breakdown product of haemoglobin is unconjugated bilirubin (indirect bilirubin), which is insoluble in water but soluble in lipids. It is carried in the blood bound to albumin. When the albumin binding is saturated, free unconjugated bilirubin can cross the blood–brain barrier, as it is lipid soluble. Unconjugated bilirubin bound to albumin is taken up by the liver and conjugated by glucuronyl transferase to conjugated bilirubin (direct bilirubin), which is water soluble and excreted in bile into the gut and then as sterobilinogen and urobilinogen. Some bilirubin in the gut is converted to unconjugated bilirubin and reabsorbed via the enterohepatic circulation and metabolized in the liver.

(due to damage to the basal ganglia), learning difficulties and sensorineural deafness. Kernicterus used to be an important cause of brain damage in infants with severe rhesus haemolytic disease, but has become rare because of the introduction of prophylactic anti-D immunoglobulin for Rh-negative (rhesus-negative) mothers. However, a few cases of kernicterus continue to occur, especially in slightly preterm infants (35–37 weeks) and dark-skin-toned infants in whom jaundice is more difficult to detect; this has led the National Institute for Health and Care Excellence (NICE) to issue guidelines on the management of neonatal jaundice.

Clinical evaluation

Babies become clinically jaundiced when the bilirubin level reaches about $80 \mu\text{mol/l}$. Management varies according to the infant's gestational age, age at onset, bilirubin level and rate of rise, and the overall clinical condition.

Age at onset

The age of onset is a useful guide to the likely cause of the jaundice (Table 11.3).

Jaundice <24 hours of age

Jaundice starting within 24 hours of birth usually results from haemolysis. This is particularly important to identify as the bilirubin is unconjugated and can rise very rapidly and reach extremely high levels.

Table 11.3 Causes of neonatal jaundice

Jaundice starting at <24 h of age	Haemolytic disorders: Rh (rhesus) incompatibility ABO incompatibility G6PD deficiency Spherocytosis, pyruvate kinase deficiency Congenital infection
Jaundice at 24 h to 2 weeks of age	Physiological jaundice Breast milk jaundice Infection, e.g. urinary tract infection Haemolysis, e.g. G6PD deficiency, ABO incompatibility Bruising Polycythaemia Crigler–Najjar syndrome
Jaundice at >2 weeks of age	Unconjugated: Physiological or breast milk jaundice Infection (particularly urinary tract) Hypothyroidism Haemolytic anaemia, e.g. G6PD deficiency High gastrointestinal obstruction, e.g. pyloric stenosis Conjugated (>25 $\mu\text{mol/l}$): Bile duct obstruction Neonatal hepatitis

 **Jaundice at <24 hours of age needs urgent investigation and close monitoring.**

Haemolytic disorders

Rh (rhesus) haemolytic disease

Affected infants are usually identified antenatally and monitored and treated if necessary (see Ch. 10 Perinatal medicine). The birth of a severely affected infant, with anaemia, hydrops and hepatosplenomegaly with rapidly developing severe jaundice, has become rare. Antibodies may develop to rhesus antigens other than D and to the Kell and Duffy blood groups, but haemolysis is usually less severe.

ABO incompatibility

This is now more common than rhesus haemolytic disease. Most ABO antibodies are IgM and do not cross the placenta, but some group O women have an IgG anti-A haemolysin in their blood, which can cross the placenta and haemolyse the red cells of a group A infant. Occasionally, group B infants are affected by anti-B haemolysins. Haemolysis can cause severe jaundice but it is usually less severe than in rhesus disease. The infant's haemoglobin level is usually normal or only slightly reduced and, in contrast to rhesus disease, hepatosplenomegaly is absent. The direct antibody test (Coombs test), which demonstrates antibody on the surface of red cells, is positive. The jaundice usually peaks in the first 12 hours to 72 hours.

G6PD (glucose-6-phosphate dehydrogenase) deficiency (see Ch. 23, Haematological disorders)

Mainly in people originating in the Mediterranean, Middle-East and Far East or in Africa. Mainly affects male infants, but some females develop significant jaundice. Parents of affected infants should be given a list of drugs to be avoided, as they may precipitate haemolysis.

Spherocytosis

This is considerably less common than G6PD deficiency (see Ch. 23). There is often, but not always, a family history. The disorder can be identified by recognizing spherocytes on the blood film.

Congenital infection

Jaundice at birth can also be from congenital infection. In this case, the bilirubin is conjugated and the infants have other abnormal clinical signs, such as growth restriction, hepatosplenomegaly and thrombocytopenic purpura.

 **Jaundice in first 24 hours is usually haemolytic and needs urgent assessment and monitoring.**

Jaundice at 2 days–2 weeks of age

Physiological jaundice

Most babies who become mildly or moderately jaundiced during this period have no underlying cause and the bilirubin has risen as the infant is adapting to the transition from fetal life. The term 'physiological jaundice' can only be used after other causes have been considered.

Breast milk jaundice

Jaundice is more common and more prolonged in breast-fed infants. The hyperbilirubinaemia is unconjugated. The

cause is multifactorial but may involve increased enterohepatic circulation of bilirubin. The condition is benign and the jaundice may last up to 12 weeks.

Dehydration

In some infants, the jaundice is exacerbated if milk intake is poor from a delay in establishing breastfeeding and the infant becomes dehydrated (>10% weight loss from birthweight). Breastfeeding should be continued; feeding may be improved with advice and support. In some infants, nasogastric fluids are needed to correct dehydration.

Infection

An infected baby may develop an unconjugated hyperbilirubinaemia from poor fluid intake, haemolysis, reduced hepatic function and an increase in the enterohepatic circulation. If infection is suspected, appropriate investigations and treatment should be instigated. In particular, urinary tract infection may present in this way.

Other causes

Although jaundice from haemolysis usually presents in the 1st day of life, it may occur during the 1st week. Bruising following delivery and polycythaemia (venous haematocrit is >0.65) will exacerbate the infant's jaundice. The very rare Crigler–Najjar syndrome, in which glucuronyl transferase is deficient or absent, may result in extremely high levels of unconjugated bilirubin.

The causes and management of jaundice at over 2 weeks (term infants) or over 3 weeks (preterm infants) of age (persistent or prolonged neonatal jaundice) are different and are considered separately below.

Severity of jaundice

Jaundice can be observed most easily by blanching the skin with one's finger. The jaundice tends to start on the head and face and then spreads down the trunk and limbs. If the baby is clinically jaundiced, the bilirubin should be checked with a transcutaneous bilirubin meter or blood sample. It is easy to underestimate in dark-skin-toned and preterm babies, and a low threshold should be adopted for measuring the bilirubin of these infants. A high transcutaneous bilirubin level must be checked with a blood laboratory measurement. It is now recommended in the UK that all babies should be checked clinically for jaundice in the first 72 hours of life, whether at hospital or home, and if clinically jaundiced a transcutaneous measurement should be obtained.

Rate of change

The rate of rise tends to be linear until a plateau is reached, so serial measurements can be plotted on a chart and used to anticipate the need for treatment before it rises to a dangerous level.

Gestation

Preterm infants are more susceptible to neurological damage from raised bilirubin, so the intervention threshold is lower and gestation-specific treatment charts should be used.

Clinical condition

Infants who experience severe hypoxia, hypothermia or any serious illness may be more susceptible to damage from severe jaundice. Drugs that may displace bilirubin from albumin, e.g. sulphonamides and diazepam, are avoided in newborn infants.

Management

Phototherapy is the most widely used therapy, with exchange transfusion for severe cases.

Phototherapy

Light (wavelength 450 nm) from the blue–green band of the visible spectrum converts unconjugated bilirubin into a harmless water-soluble pigment excreted predominantly in the urine. It is delivered with an overhead light source placed at an optimal distance above the infant to achieve high irradiance. Although no long-term sequelae of phototherapy from overhead light have been reported, it is disruptive to normal care of the infant and should not be used indiscriminately. The infant's eyes are covered, as bright light is uncomfortable. Phototherapy can result in temperature instability as the infant is undressed, a macular rash, and bronze discolouration of the skin if the jaundice is conjugated.

Continuous multiple (intensive) phototherapy is given if the bilirubin is rising rapidly or has reached a high level ([Case history 11.2](#)).

Exchange transfusion

Exchange transfusion is required if the bilirubin rises to levels that are considered potentially dangerous. Blood is removed from the baby in small aliquots (usually from an arterial line or the umbilical vein) and replaced with donor blood (via peripheral or umbilical vein). Usually, twice the infant's blood volume ($2 \times 90 \text{ ml/kg}$) is exchanged. Donor blood should be as fresh as possible and screened to exclude cytomegalovirus, hepatitis B and C, and HIV infections. The procedure does carry some risk of morbidity and mortality.

Phototherapy has been very successful in reducing the need for exchange transfusion. In infants with Rh haemolytic disease or ABO incompatibility unresponsive to intensive phototherapy, intravenous immunoglobulin (Ig) reduces the need for exchange transfusion.

There is no bilirubin level known to be safe or which will definitely cause kernicterus. In rhesus haemolytic disease, it was found that kernicterus could be prevented if the bilirubin was kept below $340 \mu\text{mol/l}$ (20 mg/dl). As there is no consensus among paediatricians on the bilirubin levels for phototherapy and exchange transfusion, guidelines have been published by NICE to ensure uniform practice in the UK.

Jaundice at >2 weeks of age

Jaundice in babies >2 weeks old (3 weeks if preterm) is called persistent or prolonged neonatal jaundice, and needs to be evaluated differently from jaundice at an earlier age. The key feature is that it may be caused by biliary atresia, and it is important to diagnose biliary atresia



Case history 11.2

Jaundice needing phototherapy

A term male infant was noted to be markedly jaundiced at 10 hours of age. His bilirubin was 170 µmol/l, direct antibody test positive, maternal blood group O rhesus positive, and his blood group was A rhesus positive. A diagnosis of ABO incompatibility was made. He was started on intensive

phototherapy and his bilirubin closely monitored and plotted on a bilirubin chart for term infants (Fig. 11.17). His bilirubin resolved with phototherapy, so immunoglobulin (Ig) therapy and exchange transfusion were not required.

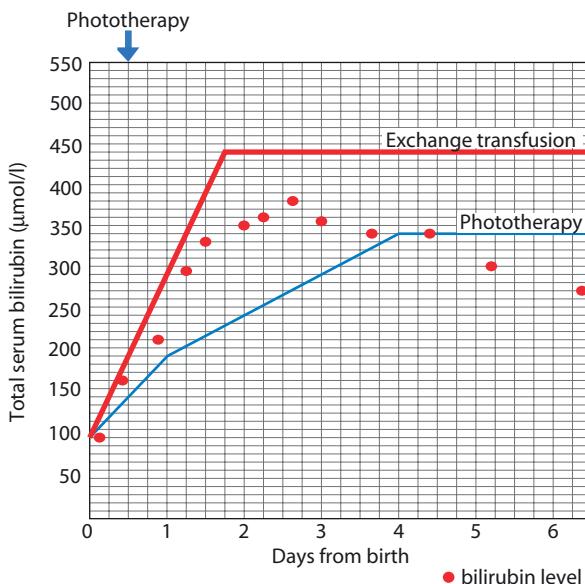


Figure 11.17 Bilirubin chart of bilirubin level and time from birth. It also shows the threshold for starting phototherapy and need to perform an exchange transfusion. Charts vary with gestational age; this is for infants ≥ 38 weeks gestational age. Plotting the bilirubin values, as shown for this infant with ABO incompatibility, allows the rate of rise to be readily determined and if preparation needs to be made for an exchange transfusion. (Adapted from: NICE: National Institute for Health and Care Excellence guideline: Jaundice in newborn babies under 28 days. 2016. Available at: www.nice.org.uk/guidance/cg98.)

promptly, as delay in surgical treatment adversely affects outcome (see Ch. 21, Liver disorders, for further details).

However, in most infants with persistent neonatal jaundice, the hyperbilirubinaemia is unconjugated, but this needs to be confirmed on laboratory testing.

In prolonged unconjugated hyperbilirubinaemia:

- 'breast milk jaundice' is the most common cause, affecting up to 15% of healthy breastfed infants; the jaundice gradually fades and disappears by 12 weeks of age
- infection, particularly of the urinary tract, needs to be considered if the infant is unwell
- congenital hypothyroidism may cause prolonged jaundice before the clinical features of coarse facies, dry skin, hypotonia and constipation become evident. Affected infants should be identified on routine neonatal biochemical screening (Guthrie test).

Conjugated hyperbilirubinaemia (>25 µmol/l) is suggested by the baby passing dark urine and unpigmented pale stools. Hepatomegaly and poor weight gain are other clinical signs that may be present. Its causes include neonatal hepatitis syndrome and biliary atresia, with improved

prognosis of biliary atresia with early diagnosis (see Ch. 21 for further details).

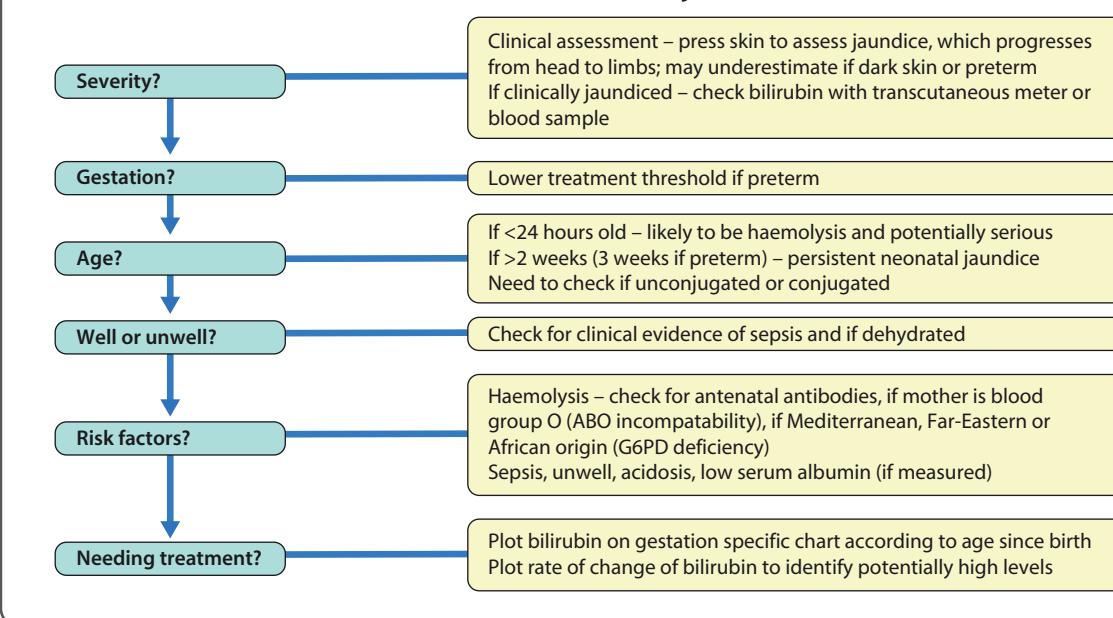
Respiratory distress in term infants

Newborn infants with respiratory problems develop the following signs of respiratory distress:

- tachypnoea (>60 breaths/min)
- increased work of breathing, with chest wall recession (particularly sternal and subcostal indrawing) and nasal flaring
- expiratory grunting
- cyanosis if severe.

The causes in term infants are listed in Table 11.4.

Affected infants should be admitted to the neonatal unit for monitoring of heart and respiratory rates, oxygen saturation and circulation. A chest X-ray will be required to help identify the cause, especially the causes that may need immediate treatment, e.g. pneumothorax or

Summary**Assessment of neonatal jaundice****Table 11.4** Causes of respiratory distress in term infants

Pulmonary	
Common	Transient tachypnoea of the newborn
Less common	Meconium aspiration Pneumonia Respiratory distress syndrome Pneumothorax Persistent pulmonary hypertension of the newborn
Rare	Diaphragmatic hernia Tracheo-oesophageal fistula Pulmonary hypoplasia Milk aspiration Airways obstruction, e.g. choanal atresia Pulmonary haemorrhage
Non-pulmonary	
	Congenital heart disease Hypoxic-ischaemic/neonatal encephalopathy Severe anaemia Metabolic acidosis Sepsis

diaphragmatic hernia. Additional ambient oxygen, respiratory support which may be non-invasive, e.g. CPAP or high-flow nasal cannula therapy, or else mechanical ventilation and circulatory support are given as required.

If infection is considered to be a cause, investigations will need to be performed and empiric antibiotics started and continued until the results of the infection screen are available.

Transient tachypnoea of the newborn

This is by far the most common cause of respiratory distress in term infants. It is caused by delay in the resorption of lung liquid and is more common after birth by caesarean section. The chest X-ray may show fluid in the horizontal fissure. Supplemental oxygen may be required in addition to feeding support with nasogastric feeds or IV fluids if the neonate is unable to feed normally. The condition usually settles within the first day of life but can take several days to resolve completely. This is a diagnosis made after consideration and exclusion of other causes such as infection.

Meconium aspiration

Meconium is passed before birth by 8%–20% of babies. It is rarely passed by preterm infants, and occurs increasingly the greater the gestational age, affecting 20%–25% of deliveries by 42 weeks. It may be passed in response to fetal hypoxia. Asphyxiated infants may start gasping and aspirate meconium before or at delivery. Meconium is a lung irritant and results in both mechanical obstruction and a chemical pneumonitis, as well as predisposing to infection. In meconium aspiration the lungs are over-inflated, accompanied by patches of collapse and consolidation. There is a high incidence of air leak, leading to pneumothorax and pneumomediastinum. Mechanical ventilation is often required. Infants with meconium

aspiration may develop persistent pulmonary hypertension of the newborn, which may make it difficult to achieve adequate oxygenation despite high-pressure ventilation (see the following section for management). Severe meconium aspiration is associated with significant morbidity and mortality. There is no evidence that aspiration of meconium from an infant's oropharynx immediately after delivery of the head or removal of meconium by intubation and tracheal suctioning of the infant after birth reduces the incidence or severity of meconium aspiration.

Pneumonia

Prolonged rupture of the membranes, chorioamnionitis and low birthweight are risk factors for pneumonia.

Pneumothorax

A pneumothorax may occur spontaneously in up to 2% of deliveries. It is usually asymptomatic but may cause respiratory distress. Pneumothoraces also occur secondary to meconium aspiration, respiratory distress syndrome or as a complication of mechanical ventilation. (Management is described earlier in this chapter.)

Milk aspiration

This occurs more frequently in preterm infants and those with respiratory distress or neurodisability. Babies with bronchopulmonary dysplasia often have gastro-oesophageal reflux, which predisposes to aspiration. Infants with a cleft palate are prone to aspirate respiratory secretions or milk.

Persistent pulmonary hypertension of the newborn

This life-threatening condition is usually associated with hypoxic-ischaemic encephalopathy, meconium aspiration, septicaemia or RDS. It sometimes occurs as a primary disorder. As a result of the high pulmonary vascular resistance, there is right-to-left shunting within the lungs and at atrial and ductal levels. Cyanosis occurs soon after birth. Heart murmurs and signs of heart failure are often absent. A chest X-ray shows that the heart is of normal size and there may be pulmonary oligaemia. An urgent echocardiogram is required to exclude congenital heart disease and identify the signs of pulmonary hypertension such as raised pulmonary pressures and tricuspid regurgitation.

Most infants require mechanical ventilation and circulatory support in order to achieve adequate oxygenation. Inhaled nitric oxide, a potent vasodilator, is often beneficial. Another vasodilator, sildenafil (Viagra), is occasionally used. High-frequency or oscillatory ventilation is sometimes helpful. Extracorporeal membrane oxygenation (ECMO), where the infant is placed on heart and lung bypass for several days, is indicated for severe but reversible cases, but is only performed in a few specialist centres.

Diaphragmatic hernia

This occurs in about 1 in 4000 births. Many are now diagnosed on antenatal ultrasound screening. In the newborn



Figure 11.18 Chest X-ray of diaphragmatic hernia showing loops of bowel in the left chest and displacement of the mediastinum.

period, it usually presents with failure to respond to resuscitation or with severe respiratory distress. In most cases, there is left-sided herniation of abdominal contents through the posterolateral foramen of the diaphragm. The apex beat and heart sounds will then be displaced to the right side of the chest, with poor air entry in the left chest. Vigorous resuscitation may cause a pneumothorax in the normal lung, thereby aggravating the situation. The diagnosis is confirmed by X-ray of the chest and abdomen (Fig. 11.18). Once the diagnosis is suspected, a large nasogastric tube is passed and suction is applied to prevent distension of the intrathoracic bowel. Initial management is focused on stabilizing the infant's ventilation. The main problem is pulmonary hypoplasia, as compression by the herniated viscera throughout pregnancy has prevented development of the lung in the fetus. This is often compounded by pulmonary hypertension. Subsequently, the diaphragmatic hernia is repaired surgically. If the lungs are hypoplastic, mortality is high.

Other causes

Other causes of respiratory distress are listed in Table 11.4. When due to heart failure, abnormal heart sounds and/or heart murmurs may be present on auscultation. An enlarged liver from venous congestion is a helpful sign. The femoral arteries must be palpated in all infants with respiratory distress, as coarctation of the aorta and interrupted aortic arch are important causes of heart failure in newborn infants.

Infection

The range of organisms that cause infection in the newborn is shown in Figure 11.19. The neonatal period is the time of highest risk in childhood for acquiring a serious invasive bacterial infection. Neonatal infections in the first few weeks of life are often categorized as early-onset and late-onset sepsis.

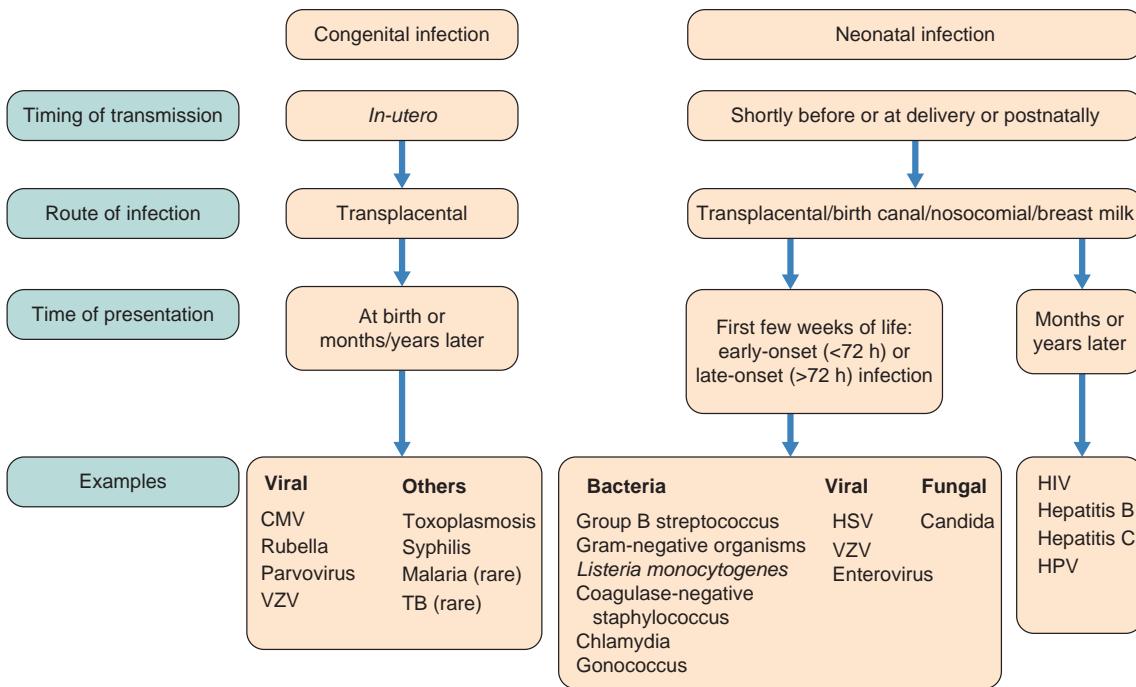


Figure 11.19 Congenital and neonatal infections, showing timing of transmission, route of infection, time of presentations and pathogens. (CMV, cytomegalovirus; VZV, varicella-zoster virus; HSV, herpes simplex virus; HPV, human papilloma virus.)

Early-onset infection

Early-onset sepsis (<72 hours after birth) results from vertical exposure either from ascending infection or exposure to high bacterial load during birth, after rupture of the membranes. The most common organisms are group B streptococcus and Gram-negative organisms (*E. coli*, *Klebsiella*, *Pseudomonas*). *Listeria monocytogenes* is a rare cause.

Presentation may be with respiratory distress, temperature instability and the other clinical features of sepsis (Box 11.3). A septic screen and chest X-ray are performed. A full blood count analysis is performed to detect neutropenia, as well as blood cultures. An acute-phase reactant (C-reactive protein) is helpful but takes 12–24 hours to rise, so one normal result does not exclude infection, but two consecutive normal values are strong evidence against infection. Antibiotics are started immediately without waiting for culture results. Intravenous antibiotics are given to cover group B streptococci and *L. monocytogenes* and other Gram-positive organisms (usually benzylpenicillin or ampicillin), combined with cover for Gram-negative organisms (usually an aminoglycoside such as gentamicin). If cultures and C-reactive protein are negative and the infant has no clinical indicators of infection, antibiotics should be stopped after 36–48 hours. If the blood culture is positive or if there are neurological or generalized signs, CSF must be examined and cultured.

Late-onset infection

In late-onset infection (>72 hours after birth), the source of infection is usually the infant's environment, either the hospital, when it should be viewed as preventable, or community. The presentation is usually non-specific (Box 11.3). Nosocomially acquired infections are an inherent risk in a neonatal unit, and all staff must adhere strictly to

effective hand hygiene measures to prevent cross-infection. In neonatal intensive care, other sources of infection are indwelling central venous catheters for parenteral nutrition, invasive procedures that break the protective barrier of the skin, and tracheal tubes. Coagulase-negative staphylococcus (CONS) is the most common pathogen, but the range of organisms is broad, and includes Gram-positive bacteria (*Staphylococcus aureus* and *Enterococcus faecalis*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas*, *Klebsiella*, and *Serratia* species). Initial therapy (e.g. with flucloxacillin and gentamicin) is aimed to cover most staphylococci and Gram-negative bacilli. If the organism is resistant to these antibiotics or the infant's condition does not improve, specific antibiotics (e.g. vancomycin for coagulase-negative staphylococci or enterococci) or broad-spectrum antibiotics (e.g. meropenem) may be indicated. Use of prolonged or broad-spectrum antibiotics predisposes to invasive fungal infections (e.g. *Candida albicans*) in premature babies. Serial measurements of an acute-phase reactant (C-reactive protein) are useful to monitor response to therapy.

Neonatal meningitis, although uncommon, has a high mortality, with survivors at risk of serious sequelae. Presentation is non-specific (Box 11.3); a bulging fontanelle and hyperextension of neck and back (opisthotonus) are late signs and are rarely seen in newborn infants. If meningitis is thought likely, ampicillin or penicillin and a third-generation cephalosporin (e.g. cefotaxime, which has CSF penetration) are given. Complications include cerebral abscess, ventriculitis, hydrocephalus, hearing loss and neurodevelopmental impairment.

Some specific infections

Group B streptococcal (GBS) infection

The organism causes early-onset and late-onset sepsis. Around 15%–40% of pregnant women have rectal or

Box 11.3 Clinical features of neonatal sepsis

- Respiratory distress
 - Fever or temperature instability or hypothermia
 - Poor feeding
 - Vomiting
 - Apnoea and bradycardia
 - Abdominal distension
 - Jaundice
 - Neutropenia
 - Hypoglycaemia/hyperglycaemia
 - Shock
 - Irritability
 - Seizures
 - Lethargy, drowsiness
- In meningitis:
- tense or bulging fontanelle
 - head retraction (opisthotonus)

vaginal colonization of group B streptococci; about 50% of these infants become colonized and 1%–2% of the colonized infants develop early-onset infection. In the UK, approximately 0.5–1/1000 infants develop early-onset infection. Risk factors are:

- preterm, especially preterm prolonged rupture of the membranes
- prolonged (>18 hours) or prelabour rupture of the membranes
- intrapartum fever >38°C or chorioamnionitis
- previous child with GBS infection
- GBS bacteriuria during pregnancy.

In early-onset sepsis, the infant usually presents within 24 hours of birth with respiratory distress; most have sepsis without a focus, pneumonia and meningitis are present in 5%–10%. Mortality is 2% to 4%, higher in preterm infants.

Two approaches to reducing the risk of the infant developing GBS infection are used. In the UK, Netherlands and several other countries, a risk-based approach is adopted. If GBS is detected during the pregnancy or the mother has any of the risk factors listed above, prophylactic intrapartum antibiotics are offered. In the USA, Australia and many European countries, routine screening is performed at 35–37 weeks, and intrapartum prophylactic antibiotics are offered to those who are GBS positive or have risk factors.

Late-onset disease may present up to 3 months of age. It usually causes sepsis without a focus, but may cause pneumonia, meningitis or occasionally osteomyelitis or septic arthritis.



Group B streptococcal infection is a serious bacterial infection in term as well as preterm infants, from birth to 3 months.

***L. monocytogenes* infection**

Fetal or newborn *Listeria* infection is uncommon but serious. The organism is transmitted to the mother in food, such as unpasteurized milk, soft cheeses and undercooked poultry. It causes bacteraemia, often with mild, influenza-like illness in the mother and passage to the fetus via the placenta. Maternal infection may cause

spontaneous abortion, preterm delivery or fetal/neonatal sepsis. Characteristic features are meconium staining of the amniotic liquor in preterm infants, which is unusual, a widespread rash, septicaemia, pneumonia and meningitis. It has a high mortality.

Gram-negative infections

Early-onset infection is acquired from the mother, late-onset infection from the hospital or community environment, or from the infant's gut microbiome.

Conjunctivitis

Sticky eyes are common in the neonatal period, starting on the third or fourth day of life. Cleaning with saline or water is all that is required and the condition resolves spontaneously. A more troublesome discharge with redness of the eye may be due to staphylococcal or streptococcal infection and can be treated with a topical antibiotic eye ointment, e.g. chloramphenicol or neomycin.

Purulent discharge with conjunctival injection and swelling of the eyelids within the first 48 hours of life may be due to gonococcal infection. The discharge should be Gram-stained urgently, as well as cultured, and treatment started immediately, as permanent loss of vision can occur. In countries such as the UK and the USA where penicillin resistance is a problem, a third-generation cephalosporin is given intravenously. The eye needs to be cleansed frequently.

Chlamydia trachomatis eye infection usually presents with a purulent discharge, together with swelling of the eyelids (Fig. 11.20), at 1–2 weeks of age, but may also present shortly after birth. The organism can be identified with NAAT (nucleic acid amplification) testing or immunofluorescent staining. Treatment is with oral erythromycin for 2 weeks. The mother and partner also need to be checked and treated.

In many countries (excluding the UK) prophylaxis against neonatal conjunctivitis is provided by instilling erythromycin eye drops to all babies shortly after birth.

Umbilical infection

The umbilicus dries and separates during the first few days of life. If the skin surrounding the umbilicus becomes inflamed, systemic antibiotics are indicated. Sometimes



Figure 11.20 Purulent discharge, together with swollen eyelids, in an 8-day-old infant. This is the characteristic presentation of conjunctivitis from *Chlamydia trachomatis*. *Neisseria gonorrhoeae* was absent.

the umbilicus continues to be sticky, as it is prevented from involuting by an umbilical granuloma. This can be removed by applying silver nitrate while protecting the surrounding skin to avoid chemical burns, or by applying a ligature around the base of the exposed stump if unsuccessful. Application of a small amount of table salt and covering the umbilicus with a gauze swab has recently been reported to be a successful and safer alternative treatment.

Herpes simplex virus infections

Neonatal herpes simplex virus (HSV) infection is uncommon, occurring in about 2/100,000 live births. HSV infection is usually transmitted during passage through an infected birth canal or by ascending infection. The risk to an infant born to a mother with a primary genital infection is high, about 50%, whereas the risk from recurrent maternal infection is less than 3%. In most infants who develop HSV infection, the condition is unexpected as the mother does not know that she is infected (asymptomatic or non-specific illness).

Infection is more common in preterm infants. Presentation is at any time up to 4 weeks of age, with localized herpetic lesions on the skin or eye, or with encephalitis or disseminated disease. Mortality due to localized disease is low, but, even with aciclovir treatment, disseminated disease has a high mortality with considerable morbidity after encephalitis. If the mother is recognized as having primary disease or develops genital herpetic lesions at the time of delivery, elective caesarean section is indicated. Women with a history of recurrent genital infection can be delivered vaginally as the risk of neonatal infection is low and maternal treatment before delivery minimizes the presence of virus at delivery. Aciclovir can be given empirically to the baby after birth until evidence of infection is ruled out.

Hepatitis B

Infants of mothers who are hepatitis B surface antigen (HBsAg)-positive should receive hepatitis B vaccination shortly after birth to prevent vertical transmission, rather than waiting until 8 weeks old for routine immunization. An augmented vaccination course needs to be completed during infancy and antibody response checked. Babies are at highest risk of becoming chronic carriers when their mothers are 'e' antigen-positive but have no 'e' antibodies. Infants of 'e' antigen-positive mothers should also be given passive immunization with hepatitis B Ig soon after birth and definitely within 24 hours of birth.



Infants of HBsAg-positive mothers should be vaccinated against hepatitis B, the course starting shortly after birth.

Hypoglycaemia

Hypoglycaemia is particularly likely in the first 24 hours of life in babies with intrauterine growth restriction, who are preterm, born to mothers with diabetes mellitus, are large-for-dates, hypothermic, polycythaemic, or ill for any reason. Growth-restricted and preterm infants have poor glycogen stores, whereas the infants of a diabetic mother have sufficient glycogen stores, but hyperplasia of the islet cells in the pancreas from exposure to elevated maternal glucose causes increased insulin levels. Symptoms are jitteriness, irritability, apnoea, lethargy, drowsiness and seizures.

There is no agreed definition of hypoglycaemia in the newborn. Many babies tolerate low blood glucose levels in the first few days of life. Some studies suggest that blood glucose levels above 2.6 mmol/l are desirable for optimal neurodevelopmental outcome, although during the first 24 hours after birth many asymptomatic infants transiently have blood glucose levels below this level. There is good evidence that prolonged, symptomatic hypoglycaemia can cause permanent neurological disability.

Hypoglycaemia can usually be prevented by early and frequent milk feeding. In infants at increased risk of hypoglycaemia, blood glucose is regularly monitored prefeeds at the bedside. Management guidelines differ; UK guidelines (British Association of Perinatal Medicine, 2017) recommend that if the blood glucose concentration is 2–2.6 mmol/L, the level is rechecked until satisfactory (at least 3 prefeed levels >2 mmol/L), whereas if the level is <2 mmol/L the infant is given dextrose gel to the mouth and the level checked (after 30 mins). If the infant has a very low blood glucose (<1.0 mmol/L) or <2.0 mmol/L and clinical signs or has not responded adequately to two doses of glucose gel, hypoglycaemia should be corrected immediately with an intravenous infusion of dextrose. Abnormal blood glucose results should be confirmed in the laboratory. A hypoglycaemia screen for other causes should be performed under these circumstances. The concentration of the intravenous dextrose may need to be increased from 10% to 15% or even 20%. High-concentration intravenous infusions of glucose should be given via a central venous catheter to avoid extravasation into the tissues, which may cause skin necrosis and reactive hypoglycaemia. If there is difficulty or delay in starting the infusion, or a satisfactory response is not achieved, glucagon can be given.

Hypoxic-ischaemic encephalopathy

In perinatal asphyxia, gas exchange, either placental or pulmonary, is compromised or ceases altogether, resulting in cardiorespiratory depression. Hypoxia, hypercarbia and metabolic acidosis follow. Compromised cardiac output diminishes tissue perfusion, causing hypoxic-ischaemic injury to the brain and other organs (Fig. 11.21). The neonatal condition is called hypoxic-ischaemic encephalopathy (HIE). It remains an important cause of brain damage, resulting in disability or death, and its prevention is one of the key aims of modern obstetric care. In high-income countries, approximately 0.5–3/1000 live-born term infants develop HIE and 0.3/1000 have significant neurodisability. The incidence is higher in low- and middle-income countries.

HIE usually follows a significant hypoxic event immediately before or during labour or delivery, especially if the fetus or infant has increased susceptibility. HIE may occur if there is:

- failure of gas exchange across the placenta – excessive or prolonged uterine contractions, placental abruption, ruptured uterus
- interruption of umbilical blood flow – cord compression including shoulder dystocia, cord prolapse
- inadequate maternal placental perfusion – maternal hypotension or hypertension
- compromised fetus – intrauterine growth restriction, anaemia

- failure of cardiorespiratory adaptation at birth – failure to breathe.

The clinical manifestations start immediately or up to 48 hours afterwards, and can be graded:

- mild (grade 1) – the infant is irritable, responds excessively to stimulation, may have staring of the eyes, and hyperventilation
- moderate (grade 2) – the infant shows marked abnormalities of movement, is hypotonic, cannot feed as cannot suck, may have brief apnoeas and may have seizures
- severe (grade 3) – there are no normal spontaneous movements or response to pain; tone in the limbs is hypotonic; seizures are prolonged and often refractory to treatment; multi-organ failure is present.

The neuronal damage may be immediate from primary neuronal death or may be delayed from reperfusion injury causing secondary neuronal death from secondary energy failure. This delay offers the opportunity for neuroprotection with mild therapeutic hypothermia. Recording of amplitude-integrated electroencephalogram (aEEG, cerebral function monitor) may be used to detect abnormal background brain activity to confirm early encephalopathy. It is also used to identify seizures.

Management

Skilled resuscitation and stabilization will minimize neuronal damage.

Infants with HIE may need (Fig. 11.21):

- respiratory support
- treatment of clinical seizures with anticonvulsants
- fluid restriction because of transient renal impairment and syndrome of inappropriate ADH secretion
- treatment of hypotension by volume and inotrope support
- monitoring and treatment of hypoglycaemia and electrolyte imbalance, especially hypocalaemia.

Randomized clinical trials have shown that mild hypothermia (cooling to a rectal temperature of 33°C to 34°C for 72 hours by wrapping the infant in a cooling jacket) for infants 36 weeks' gestation and over with moderate or severe HIE reduces brain damage if started within 6

hours of birth (Fig. 11.22). Analysis of these trials has demonstrated that for every eight babies cooled, one extra baby will survive without disability. The use of therapeutic hypothermia for mild HIE and in late preterm infants is increasing, but evidence of its efficacy is awaited. Whilst cooling has become the standard therapy in the UK and many high-income countries, it requires neonatal intensive care facilities and is not available in most low- and middle-income countries. Figure 11.23 presents the outcomes of therapeutic hypothermia trials compared with standard care for the management of term/near-term babies with hypoxic-ischaemic encephalopathy.

Prognosis

When HIE is mild, complete recovery can usually be expected. Infants with moderate HIE who have recovered fully on clinical neurological examination and are feeding normally by 2 weeks of age have a good long-term prognosis, but if clinical abnormalities persist beyond that time, full recovery is unlikely. Severe HIE has a mortality of 30%–40%, and, of survivors without cooling, over 80% have neurodevelopmental disabilities, particularly cerebral palsy. Even with cooling, mortality and long-term neurodevelopmental disability rates are high. If magnetic resonance imaging (MRI) of the brain at 5–14 days in a term infant shows significant abnormalities, there is a high risk of later cerebral palsy (Fig. 11.24).

Although hypoxic-ischaemic injury causing encephalopathy usually occurs antenatally or during labour or delivery, or sometimes postnatally, the encephalopathy may sometimes be caused by another neonatal condition, e.g. inborn error of metabolism or kernicterus. The term 'birth asphyxia' has potentially serious medicolegal implications as it identifies that the insult occurred during birth and is best avoided.

Summary

Hypoxic-ischaemic encephalopathy

- Is an important cause of morbidity and mortality worldwide.
- Causes encephalopathy and multi-organ dysfunction.
- Therapeutic hypothermia has become standard therapy in the UK and many high-income countries if clinical grade is moderate or severe.

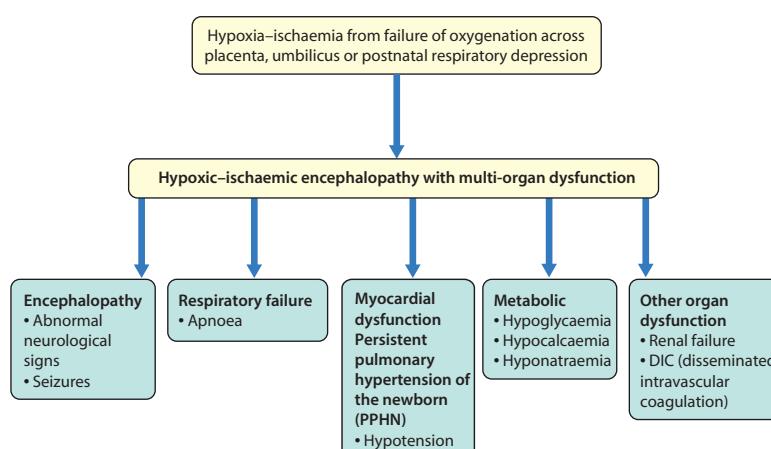


Figure 11.21 Pathogenesis and clinical features of hypoxic-ischaemic encephalopathy.

Hypoxic-ischaemic encephalopathy

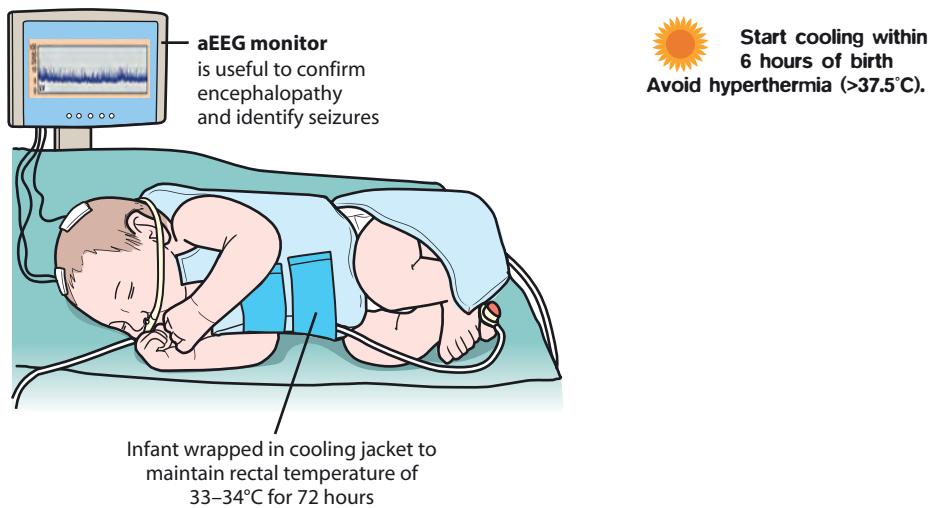


Figure 11.22 Therapeutic hypothermia for moderate or severe hypoxic-ischaemic encephalopathy.

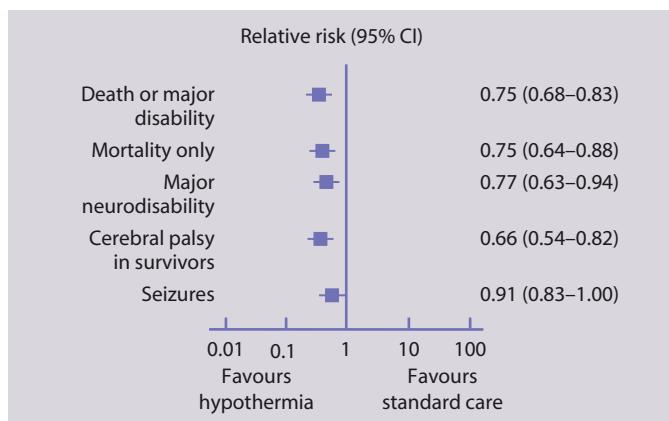


Figure 11.23 Outcomes of therapeutic hypothermia trials compared with standard care for the treatment of term/near-term babies with hypoxic-ischaemic encephalopathy. The figure shows reduction of death or major disability. Reduction in seizures is not demonstrated. (CI, confidence interval.) (Data from: Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, et al: Cooling for newborns with hypoxic-ischaemic encephalopathy. *The Cochrane Database of Systemic Reviews* CD003311, 2013.)

Mild hypothermia for moderate and severe HIE reduces death and severe disability and increases the likelihood of survival with normal neurological function.

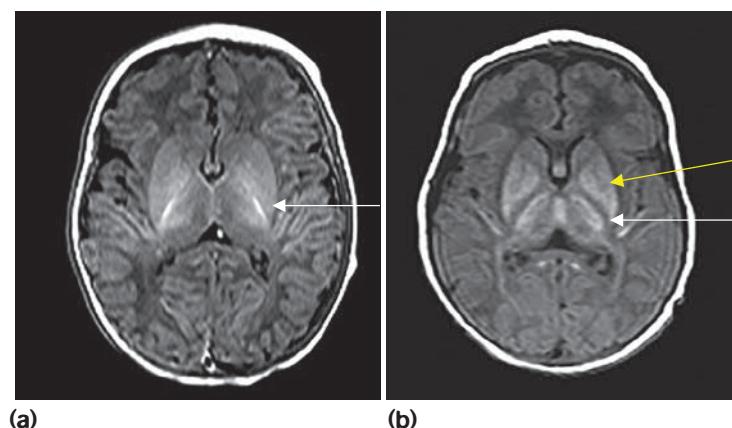


Figure 11.24 Magnetic resonance image (T1 in axial view) of the brain at 14 days in a term infant. (a) Normal scan for comparison, showing high signal in the posterior limb of the internal capsule (PLIC) (arrow). (b) Following severe HIE, showing loss of the normal high signal from myelin in the internal capsule (PLIC) (white arrow) and abnormal high signal in the adjacent basal ganglia and thalamus (yellow arrow). These findings would be associated with a severe motor impairment in the form of cerebral palsy, poor head growth, persistent feeding difficulties, seizures and marked cognitive impairment. (Courtesy of Professor Mary Rutherford.)

Birth injuries

Infants may be injured at birth, particularly if they are malpositioned or too large for the pelvic outlet. Injuries may also occur during manual manoeuvres, from forceps blades or at ventouse (vacuum) deliveries. Fortunately, now that caesarean section is available in every maternity unit, heroic attempts to achieve a vaginal delivery with resultant severe injuries to the infant have become extremely rare.

Soft-tissue injuries

These include:

- **caput succedaneum** (Fig. 11.25) – bruising and oedema of the presenting part extending beyond the margins of the skull bones; resolves in a few days.
- **cephalhaematoma** (Figs. 11.25, 11.26) – haematoma from bleeding below the periosteum, confined within the margins of the skull sutures. It usually involves the parietal bone. The centre of the haematoma feels soft. It resolves over several weeks.
- **chignon** (Fig. 11.27) – oedema and bruising from ventouse delivery.
- bruising to the face after a face presentation and to the genitalia and buttocks after breech delivery. Preterm infants bruise readily from even mild trauma.
- abrasions to the skin from scalp electrodes applied during labour or from accidental scalpel incision at caesarean section.
- forceps marks to face from pressure of blades – transient.
- **subaponeurotic haemorrhage** (Fig. 11.25; very uncommon) – diffuse, boggy swelling of scalp on examination. Blood loss may be severe and can lead to hypovolaemic shock and coagulopathy.

Nerve palsies

Brachial nerve palsy results from traction to the brachial plexus nerve roots. They may occur at breech deliveries or with shoulder dystocia. Upper nerve root (C5 and C6) injury results in an Erb palsy (Fig. 11.28). It may be accompanied by phrenic nerve palsy causing an elevated diaphragm. Erb palsy usually resolves completely, but should be referred to an orthopaedic or plastic surgeon if not resolved by 2–3 months. Most recover by 2 years. A facial nerve palsy may result from compression of the facial nerve against the mother's ischial spine or pressure from forceps. It is unilateral, and there is facial weakness on crying but the eye remains open. It is usually transient, but methylcellulose drops may be needed for the eye. Rarely, nerve palsies may be from damage to the cervical spine, when there is lack of movement below the level of the lesion.

Fractures

Clavicle

Usually from shoulder dystocia. A snap may be heard at delivery or the infant may have reduced arm movement on the affected side, or a lump from callus formation

may be noticed over the clavicle at several weeks of age. The prognosis is excellent and no specific treatment is required.

Humerus/femur

Usually midshaft, occurring at breech deliveries, or fracture of the humerus at shoulder dystocia. There is deformity, reduced movement of the limb and pain on movement. They heal rapidly with immobilization.

Neonatal seizures

Many babies startle or have tremors when stimulated or make strange jerks during active sleep. By contrast, seizures are unstimulated. Typically, there are repetitive, rhythmic (clonic) movements of the limbs that persist despite restraint and are often accompanied by eye movements and changes in respiration. However, they can be difficult to recognize with certainty as the signs can be subtle. Many neonatal units now use continuous single-channel electroencephalogram (amplified-integrated electroencephalogram, aEEG, also called a cerebral function monitor) to be able to confirm changes in electrical discharges in the brain, and some also use continuous EEG with video. The causes of seizures are listed in Box 11.4.

Whenever seizures are observed, hypoglycaemia and meningitis need to be excluded or treated urgently. A cerebral ultrasound is performed to identify haemorrhage or cerebral anomaly. Identification of some cerebral ischaemic lesions or cerebral anomalies will require MRI scans of the brain. Treatment is directed at the cause, whenever possible. Ongoing or repeated seizures are treated with an anticonvulsant, e.g. phenobarbitone, although their efficacy in suppressing seizures is much poorer than in older children. The prognosis depends on the underlying cause.

Perinatal stroke

These result from cerebral vascular injury in the fetus or neonate. The commonest cause is neonatal arterial ischaemic stroke (NAIS), most often affecting the middle cerebral artery. Other causes are haemorrhage or venous thrombosis in the dural venous sinuses. They present with seizures at 12–48 hours in a term infant, but may be asymptomatic in the neonatal period. The seizures may be focal or generalized. In contrast to infants with HIE, there are no other abnormal clinical features. The diagnosis is confirmed by MRI (Fig. 11.29). The mechanism of perinatal arterial ischaemic strokes is thought to be thromboembolism from placental vessels in the fetus. Nearly 50% develop motor disability, usually a hemiplegia of the contralateral side presenting in infancy or childhood, and some cognitive dysfunction. Large lesions may result in epilepsy.

Craniofacial disorders

Cleft lip and palate

A cleft lip may be unilateral or bilateral (Fig. 11.30). It results from failure of fusion of the frontonasal and maxillary

Birth injuries

Soft-tissue injuries:

- caput succedaneum, cephalhaematoma, chignon, bruises, and abrasions
- subaponeurotic haemorrhage

Nerve palsies:

- brachial plexus – Erb palsy
- facial nerve palsy

Fractures:

- clavicle, humerus, femur

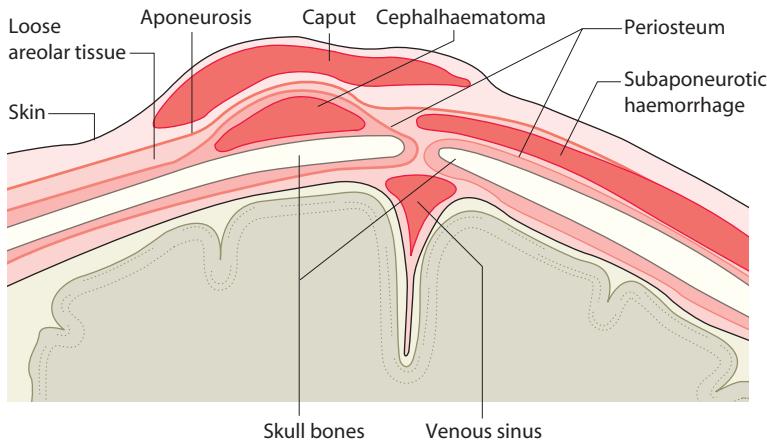


Figure 11.25 Location of extracranial haemorrhages.



Figure 11.26 A large cephalhaematoma.



Figure 11.27 Chignon.



Figure 11.28 Erb palsy. The affected arm lies straight, is limp, and with the hand pronated and the fingers flexed (waiter's tip position).

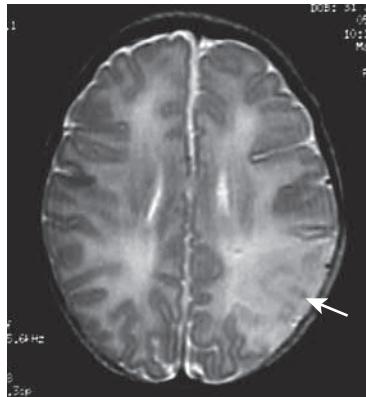
processes. In bilateral cases, the premaxilla is anteverted. Cleft palate results from failure of fusion of the palatine processes and the nasal septum. Cleft lip and palate affect about 0.8 per 1000 infants. Most are inherited polygenically, but they may be part of a syndrome of multiple abnormalities, e.g. chromosomal disorders. Some may be associated with maternal anticonvulsant therapy. They are increasingly identified on antenatal ultrasound scanning,

which allows counselling of the parents and family before birth. Showing parents photographs is often helpful to minimize the shock at birth, as the defect is unsightly. Photos of infants before and after surgery provide reassurance that defects can be corrected with good cosmetic results (Fig. 11.30a, b).

Surgical repair of the lip usually takes place at about 3 months of age. The palate is usually repaired at

Box 11.4 Causes of neonatal seizures

- Hypoxic-ischaemic encephalopathy
- Intracranial haemorrhage
- Cerebral anomalies
- Infection: septicaemia, meningitis, encephalitis, congenital infection
- Metabolic:
 - hypoglycaemia
 - hyponatraemia/hypernatraemia
 - hypocalcaemia
 - inborn errors of metabolism
- Drugs: neonatal abstinence syndrome
- Kernicterus
- Other: pyridoxine dependency, genetic epilepsy syndrome

**Figure 11.31** Micrognathia in Pierre Robin sequence.**Figure 11.29** Magnetic resonance imaging scan showing infarction in the territory of a branch of the left middle cerebral artery (arrow).

6–12 months of age. A cleft palate may make feeding more difficult, but affected infants may still be breastfed successfully. In bottle-fed infants, if milk is observed to enter the nose and cause coughing and choking, special teats and feeding devices may be helpful. Orthodontic advice and a dental prosthesis may help with feeding. Secretory otitis media is relatively common and should be sought on follow-up. Infants are also prone to acute otitis media. Adenoidectomy is best avoided, as the resultant gap between the abnormal palate and nasopharynx will exacerbate feeding problems and the nasal quality of speech. A multidisciplinary team approach is required, involving craniofacial surgeons, paediatrician, orthodontist, audiologist and speech therapist. Parent support groups (e.g. Cleft Lip and Palate Association) can provide valuable support and advice for families.



(a)



(b)

Figure 11.30 Before (a) and after (b) operation for cleft lip. Photographs showing the impressive results of surgery help many patients cope with the initial distress at having an affected infant. (Courtesy of Mr N. Waterhouse.)**Pierre Robin sequence**

The Pierre Robin sequence is an association of micrognathia (Fig. 11.31), posterior displacement of the tongue (glossotaxis) and midline cleft of the soft palate. There may be difficulty feeding and, as the tongue falls back, there is obstruction to the upper airways, which may result in cyanotic episodes. The infant is at risk of growth faltering during the first few months. If there is upper airways obstruction, the infant may need to lie prone, allowing the tongue and small mandible to fall forward. Persistent obstruction can be treated using a nasopharyngeal airway. Eventually, the mandible grows and these problems resolve. The cleft palate can then be repaired.

Gastrointestinal disorders**Oesophageal atresia**

Oesophageal atresia is usually associated with a tracheo-oesophageal fistula (Fig. 11.32). It occurs in 1 in 3500 live births and is associated with polyhydramnios during pregnancy or an absent stomach bubble on antenatal

ultrasound screening. If suspected, a wide-calibre feeding tube is passed after birth and checked by X-ray to see if it reaches the stomach. If not suspected before birth, clinical presentation is with persistent salivation and drooling from the mouth. If the diagnosis is not made at this stage, the infant will cough and choke when fed, and have cyanotic episodes. There may be aspiration into the lungs of saliva (or milk) from the upper airways and acid secretions from the stomach. Almost half of the babies have other congenital malformations, e.g. as part of the vertebral, anorectal, cardiac, tracheo-oesophageal, renal, and radial /limb anomalies (VACTERL) association. Continuous suction is applied to a tube passed into the oesophageal pouch to reduce aspiration of saliva and secretions pending transfer to a neonatal surgical unit for correction. Following surgery, later complications include gastro-oesophageal reflux, chronic cough, and sometimes oesophageal dilation is required in infancy or childhood.

Small bowel obstruction

This may be recognized antenatally on ultrasound scanning. Otherwise, small bowel obstruction presents with persistent vomiting, which is bile stained unless the obstruction is above the ampulla of Vater. Meconium may initially be passed, but subsequently its passage is usually delayed or absent with no transition to normal stool. Abdominal distension becomes increasingly prominent the more distal the bowel obstruction. High lesions will present soon after birth, but lower obstruction may not present for some days.

Small bowel obstruction may be caused by:

- atresia or stenosis of the duodenum (Fig. 11.33) – one-third have Down syndrome and it is also associated with other congenital malformations
- atresia or stenosis of the jejunum or ileum – there may be multiple atretic segments of bowel
- malrotation with volvulus – a dangerous condition as it may lead to infarction of the entire midgut
- meconium ileus – thick inspissated meconium, of putty-like consistency, becomes impacted in the

lower ileum; almost all affected neonates have cystic fibrosis.

The diagnosis is made on clinical features and abdominal X-ray showing intestinal obstruction. Atresia or stenosis of the bowel and malrotation are treated surgically, after correction of fluid and electrolyte depletion. Meconium ileus may be dislodged using Gastrografin contrast medium but otherwise will require surgery.

Large bowel obstruction

This may be caused by:

- meconium plug – a plug of inspissated meconium causes lower intestinal obstruction. Will usually pass spontaneously.

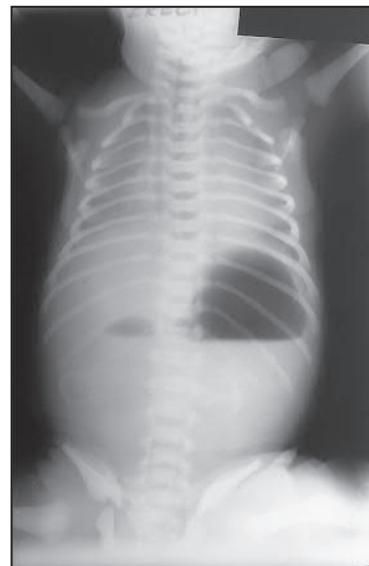


Figure 11.33 Abdominal X-ray in duodenal atresia showing a 'double bubble' from distension of the stomach and duodenal cap. There is absence of air distally.

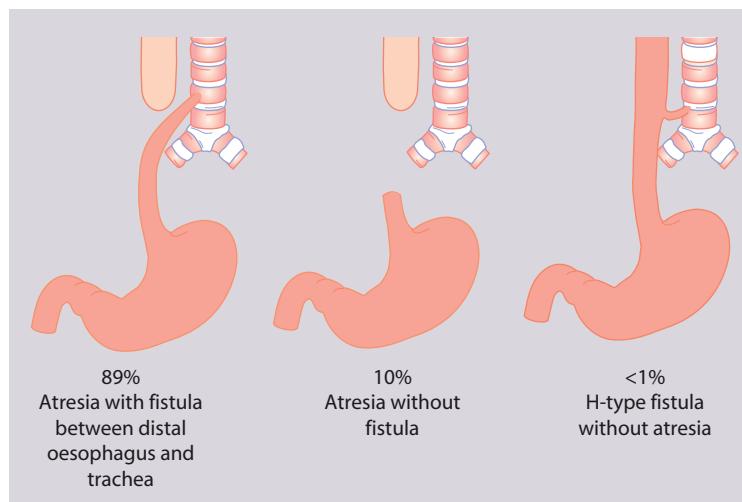


Figure 11.32 Oesophageal atresia and tracheo-oesophageal fistula.

- Hirschsprung disease – absence of the myenteric nerve plexus in the rectum, which may extend along the colon. It is more common in boys and in infants with Down syndrome. The baby often does not pass meconium within 48 hours of birth and subsequently the abdomen distends. About 15% present as an acute enterocolitis.
- anorectal malformation – imperforate anus. Complex anatomy requiring surgery; initially to form a colostomy, followed by delayed reconstruction when the infant is older.



Bile-stained vomiting is from intestinal obstruction until proven otherwise and is a surgical emergency.

Exomphalos and gastroschisis

These lesions are often diagnosed antenatally (see Ch. 10 Perinatal medicine). In exomphalos (also called omphalocele), the abdominal contents protrude through the umbilical ring, covered with a transparent sac formed by the amniotic membrane and peritoneum (Fig. 11.34). It is often associated with other major congenital abnormalities and genetic testing should be undertaken. In gastroschisis, the bowel protrudes through a defect in the anterior abdominal wall adjacent to the umbilicus, and there is no covering sac (see Fig. 10.2). It is not associated with other congenital abnormalities.

Gastroschisis carries a much greater risk of dehydration and protein loss, so the abdomen of affected infants should be covered with a clear occlusive wrap to minimize fluid and heat loss. A nasogastric tube is passed and aspirated frequently and intravenous fluids given. Replacement of fluid loss is often required early on to prevent hypovolaemia. Many lesions can be repaired by primary closure of the abdomen. With large lesions, the intestine is enclosed in a silastic sac sutured to the edges of the abdominal wall and the contents gradually returned into the peritoneal cavity.



Figure 11.34 Small exomphalos with loops of bowel confined to the umbilicus. Care needs to be taken not to put a cord clamp across these lesions.

Safeguarding and the newborn

Already during pregnancy there is a need to consider if there are any safeguarding issues that may arise when the baby is born. This may be because the mother is misusing alcohol or drugs, or due to maternal mental health problems or where the family background, e.g. of violence or previous safeguarding problems, could compromise the health and wellbeing of the newborn. Premature infants may be especially difficult to manage at home after discharge and are at an increased risk of non-accidental injury.

To avoid potential safeguarding concerns later in childhood in normal infants, any abnormalities found during the routine examination of the newborn must be fully described and documented, e.g. dermal melanocytosis (Mongolian blue spots) as they may be mistaken for bruising, and subconjunctival haemorrhages following delivery, which may be mistaken for non-accidental injury.

Acknowledgements

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Further reading

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Rennie JM: *Robertson's textbook of neonatology*, ed 4, Edinburgh, 2011, Elsevier/Churchill Livingstone. *Comprehensive textbook*.

Websites

BLISS: www.bliss.org.uk. For parents of infants born too early, too small or too sick.

Population screening programme UK: www.gov.uk/topic/population-screening-programmes.

Sands: www.sands.org.uk. Stillbirth and neonatal death charity.

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Growth and puberty

Normal growth	198	Tall stature	207
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Puberty	201	Early puberty	210
Short stature	203	Delayed puberty	211

Features of growth and puberty:

- Growth is a key element of child health, and should be considered whenever children are seen.
- The growth of all children should be monitored regularly, especially during the first months of life, and recorded on the growth charts in the parent-held personal child health record.
- An understanding of normal growth and pubertal development is required to recognize deviation from normal.
- Deviation of growth from expected centiles on a growth chart or the normal sequence of pubertal development requires further assessment.

Normal growth

There are four phases of normal human growth ([Fig. 12.1](#)).

Fetal

This is the fastest period of growth, accounting for about 30% of eventual height. Fetal growth is determined by the fetus's genetic growth potential, maternal nutrition and the health of the fetus, placenta and mother. It is stimulated by raised maternal glucose resulting in raised glucose and increased levels of IGF-1 (insulin-like growth factor -1) in the fetus, and restricted by pre-existing or pregnancy-related maternal disease, maternal drugs, smoking or starvation or uteroplacental insufficiency and congenital infection and other disorders of the fetus.

Infantile phase

Growth during infancy is largely dependent on adequate nutrition, good health and normal hormone levels, especially thyroid hormones. This phase is characterized by a

rapid but decelerating growth rate, and accounts for about 15% of eventual height. By the end of this phase, children have progressed from their fetal length (affected by the uterine environment) to their genetically determined growth pattern. An inadequate rate of weight gain during this period is called 'faltering growth' (see [Ch. 13, Nutrition](#)).

Childhood phase

This is a steady but prolonged period of growth to puberty that contributes 40% of final height. Pituitary growth hormone (GH) secretion acting to produce IGF-1 at the epiphyses of the bones is the main determinant of a child's rate of growth, provided there is adequate nutrition and good health. Thyroid hormone, vitamin D, and steroids also affect cartilage cell division and bone formation.

Pubertal growth spurt

Sex hormones, mainly testosterone and oestradiol, cause height acceleration and an increase in spontaneous GH secretion. This adds 15% to final height. The same sex steroids cause fusion of the epiphyseal growth plates and a cessation of growth.

Measurement

Growth parameters should be measured whenever a child is seen clinically as the growth pattern is helpful in assessing their health and in formulating a diagnosis, and it is essential for accurate prescribing (see [Ch. 5, Care of the sick child and young person](#)). All children in the UK also have height and weight measured as part of the National Child Measurement Programme at age 4–5 years and 10–11 years at primary school. This is primarily to monitor trends in obesity in children, but also provides data on their height growth.

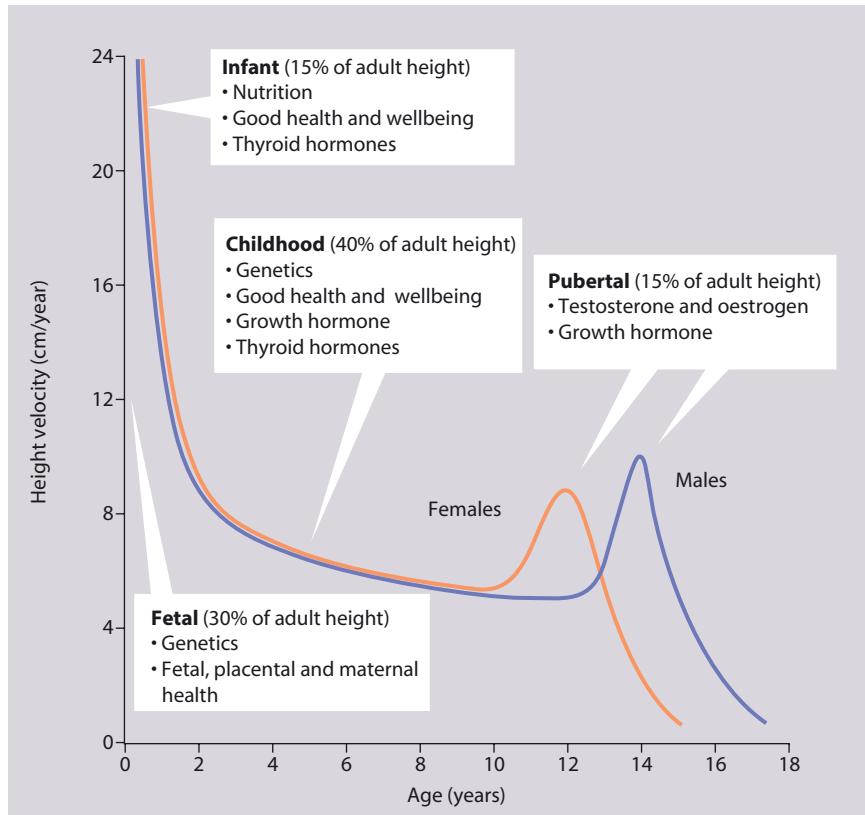


Figure 12.1 Determinants of childhood growth. Male and female height velocity charts (50th percentile) reflecting rate of growth (cm/year) showing the main phases of childhood growth (fetal, infant, childhood and pubertal) and the main factors determining them. Adult males are taller than females as they have a longer childhood growth phase before puberty, their peak pubertal height velocity is higher, and they continue to grow for longer.

Growth must be measured reliably; this requires well-maintained and calibrated equipment, trained staff using the correct technique, and the data to be plotted accurately on a growth chart, manually or electronically. Regarding growth measurement:

- weight – is readily determined with electronic scales. The infant must be naked or the child dressed only in underclothing as an infant might gain an entire month from a wet nappy while a child will gain a year if in jeans.
- height – in children over 2 years of age, the standing height is measured using the technique illustrated in Fig. 12.2. Length in children under 2 years is measured by two people with the child lying horizontally (Fig. 12.3). Accurate length measurement in infants is more difficult to obtain, as the legs need to be held straight and infants often dislike being held still.
- head circumference – the occipitofrontal circumference is a measure of head and hence brain growth. Plot the maximum of three measurements. It is of particular importance in children with developmental delay or suspected hydrocephalus.
- body mass index – calculated using height in square metres / weight in kilograms and plotted on a gender-specific body mass index centile chart to assess if underweight or overweight.

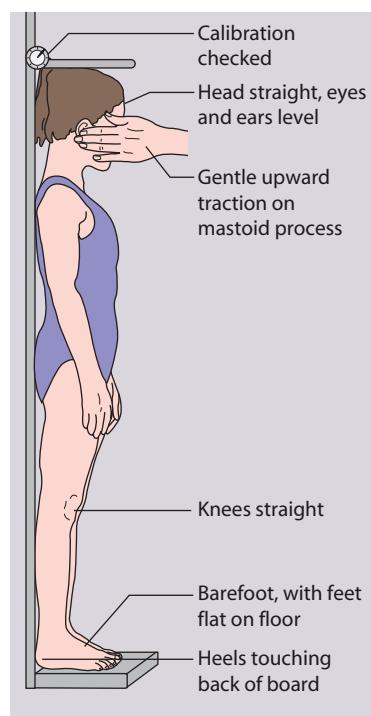


Figure 12.2 Measuring height in children.

Growth charts

Measurements should be plotted as a simple dot on an appropriate growth centile chart for age and biological gender. There are specific charts available for some conditions, e.g. Down and Turner syndrome.

The UK has adopted the World Health Organization (WHO) Global Child Growth Standards for infants and children (0–4 years old, see Appendix Fig. A1). These are based on the optimal growth of healthy children exclusively breastfed up to the age of 6 months. These charts allow for the lower weight of exclusively breastfed infants and therefore reduce the number of breastfed babies labelled as underweight. They also allow earlier identification of formula-fed babies gaining weight too rapidly.

Height in a population is normally distributed and the deviation from the mean can be measured as a centile or standard deviation (SD; Fig. 12.4). The bands on the growth reference charts have been chosen to be two-thirds of an SD apart and correspond approximately to the 25th, 9th, 2nd, and 0.4th centiles below the mean, and the 75th, 91st, 98th, and 99.6th centiles above the mean. The further these centiles lie from the mean, the more likely it is that a child has a pathological cause for his/her short or tall stature. For instance, values below the 0.4th or above the 99.6th centile will occur by chance in

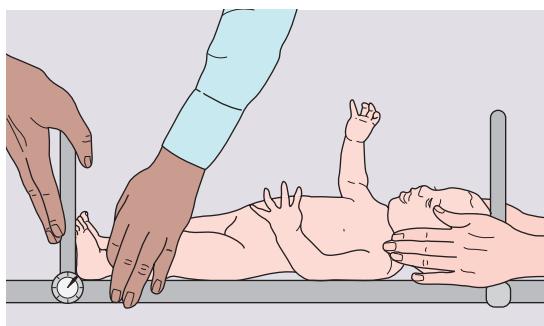


Figure 12.3 Measuring length in infants and young children. An assistant is required to hold the legs straight.

only 4 per 1000 children and can be used as a criterion for referral from primary to specialist care. A single growth parameter should not be assessed in isolation from the other growth parameters, e.g. a child's low weight may be in proportion to the height if short, but abnormal if tall. Serial measurements are used to show the pattern of growth. This is helpful in diagnosing or monitoring many paediatric conditions.

Mid-parental centile (MPC)

The child's growth is assessed in the context of his/her family. Heights from both biological parents should be used to calculate the MPC and the child's current centile can be compared to this. There are two main methods:

- Plotting mother's and father's height on a parent height comparator which are included on growth charts (Fig. 12.5), with a line drawn between the two points, crossing the MPC line.
- Calculating the mean of the father's and mother's height, with 7 cm added to the mid-parental height for a boy and 7 cm subtracted for a girl. Then the centile closest to this on the child's growth chart at age 18 years is identified to give the MPC. Details are described on growth charts.

Most children have a height centile within two centile spaces of the MPC and the further the child is away from the MPC, the more likely they are to have a pathological explanation for their growth pattern.

Correction for gestational age

Specific growth charts are available for preterm infants born less than 32 weeks' gestational age to allow for close monitoring. Their measurements should be plotted at their actual age, but then corrected for the number of weeks the infant was preterm, as shown in Fig. 12.6. This correction is typically continued for the first year of life, but in extremely preterm infants, it is useful to continue until 2 years of age.

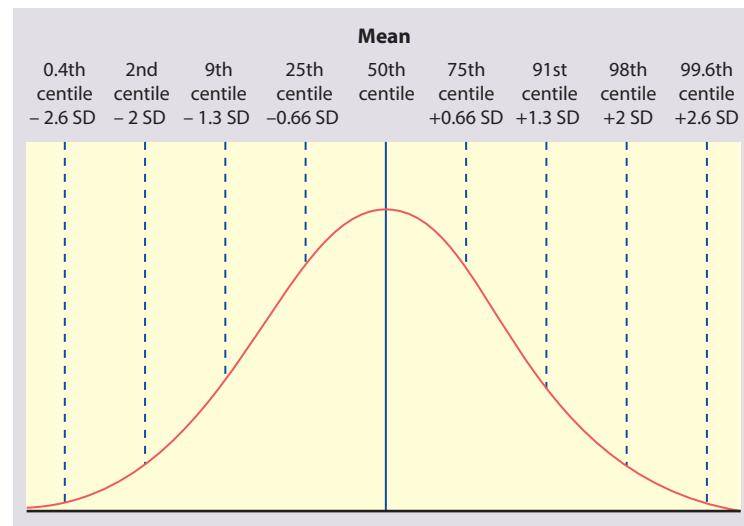


Figure 12.4 Interpretation of the UK growth reference charts. The lines show the mean and centile lines, which are two-thirds of a standard deviation (SD) apart. The centiles are shown in the diagram.

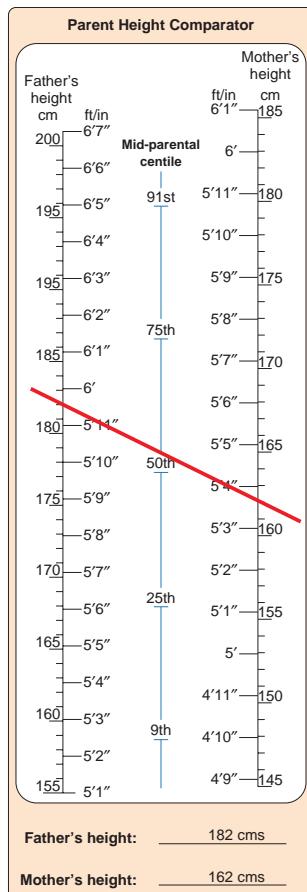


Figure 12.5 An example of parent height comparator which are included on growth charts. In this boy, the father's height is 182 cm, the mother's 162 cm, so the mid-parental height is the 50th centile. Their child's expected height is within 2 centile lines of the 50th centile, i.e. between the 9th and 91st centile.

Summary

Monitoring growth in children

- Measurements must be reliable to provide meaningful monitoring of growth.
- Growth parameters should be plotted on charts to compare to the normal range.
- Patterns of growth which would cause concern are:
 - measurements below the 0.4th or above the 99.6th centiles or distant from the mid-parental centile
 - if height or length centile is markedly discrepant from weight centile
 - if serial measurements cross growth centile lines
- The pattern of growth is essential information when assessing the health of a child; consider genetics, nutrition, general health, and hormones as potential causes of abnormal growth.

Puberty

Puberty follows a well-defined sequence of changes that may be assigned stages, as shown in Fig. 12.7. In the last two decades, girls have started entering puberty at an earlier mean age. However, the age at which menarche occurs has remained stable.

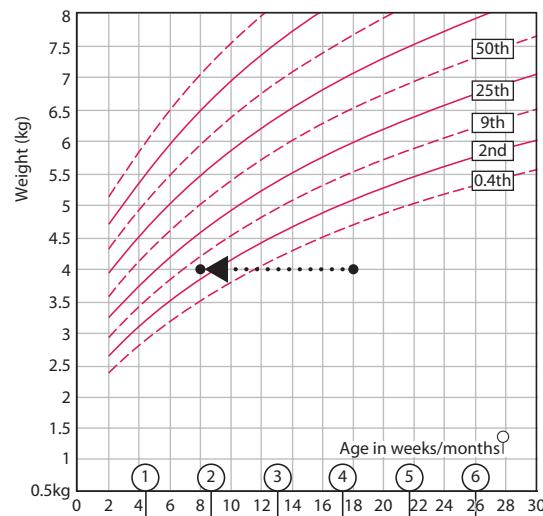


Figure 12.6 Correcting for gestational age. In this example, weight is plotted at actual age (4 kg at 18 weeks of age), which appears to be well below the 0.4th centile. But the child was born at 30 weeks, i.e. 10 weeks early, so her weight plot is moved 10 weeks earlier, as shown. After allowing for her prematurity, her weight is between the 2nd and 9th centile.

In *girls*, normal puberty starts between the age of 8 and 13 years. The features of puberty are:

- breast development – a palpable breast bud is the first sign
- pubic hair growth and accelerated height growth – occur soon after breast development
- menarche – occurs on average 2.5 years after the onset of puberty and signals that growth is coming to an end, with only around 5 cm height gain remaining
- Menstruation has a wide range of normal variation. The normal cycle length varies between 21 days and 45 days.

In *boys*, normal puberty starts between the age of 9 and 14 years. The features of puberty are:

- testicular enlargement to over >4 ml volume, measured using an orchidometer (Fig. 12.8)
- pubic hair growth – follows testicular enlargement
- enlargement of the scrotum
- increase in length and then breadth of the penis
- accelerated height growth – when the testicular volume is 12–15 ml, typically 18 months after the onset of puberty.

The growth spurt in boys occurs later and is of greater magnitude than in girls, accounting for the greater final average height of men compared to women. In both sexes, there will be development of acne, axillary hair, body odour, and mood changes.

Summary

Puberty

- The first sign of female puberty is a palpable breast bud; the first sign of male puberty is testicular volume >4 ml.
- In females, height acceleration starts shortly after breast development; in males, it starts almost 18 months after the first signs of puberty.

Stages of puberty

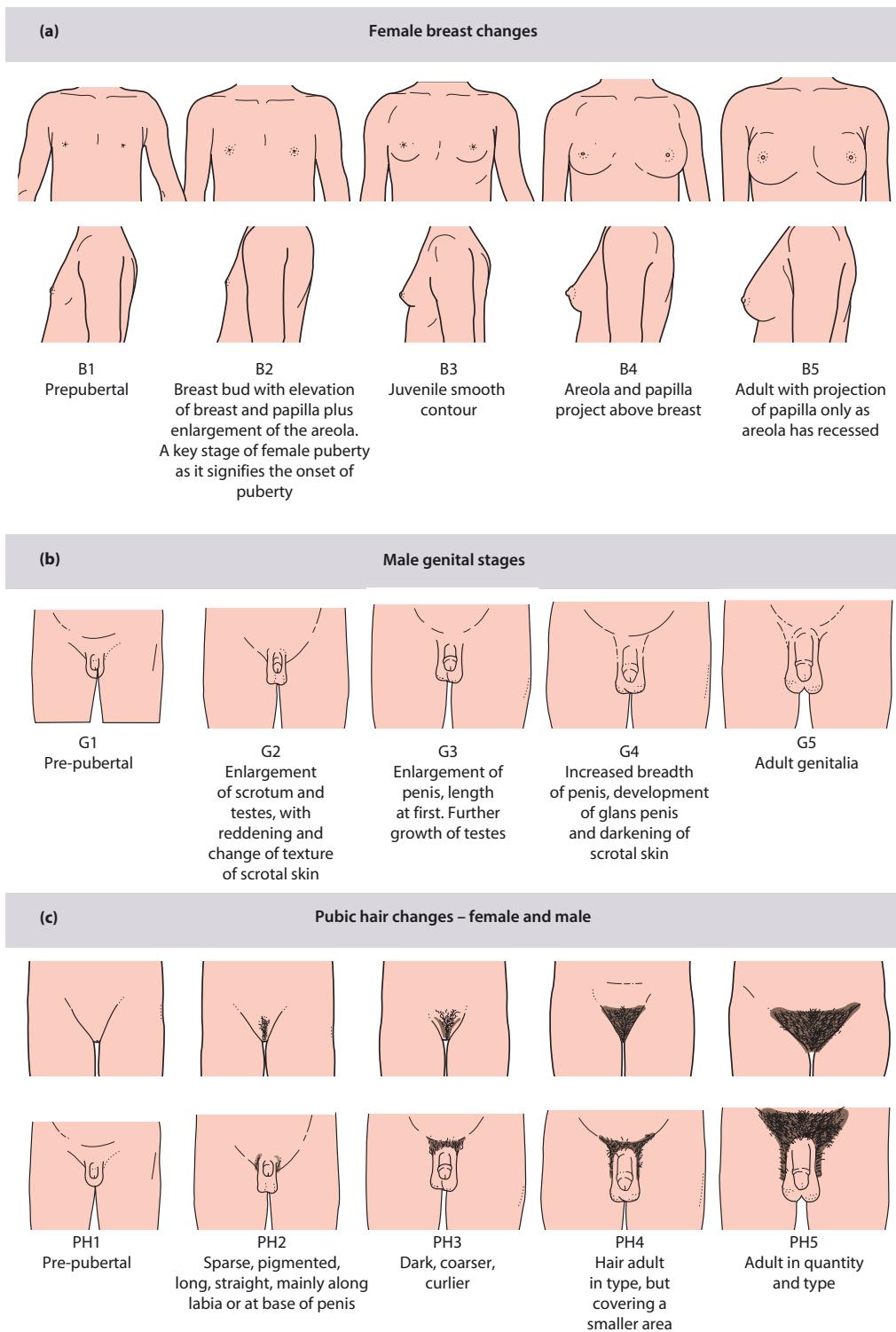


Figure 12.7 Schematic drawings of male and female stages of puberty. Pubertal changes are shown according to the Tanner stages of puberty.

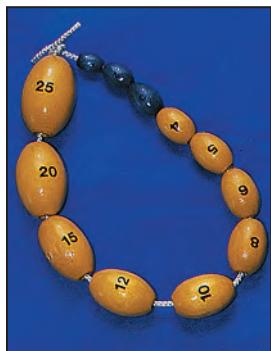


Figure 12.8 Orchidometer to assess testicular volume (in ml). (From: Wales JK, Rogol AD, Wit JM: *Pediatric Endocrinology and Growth*. London, 2003, Saunders, with permission.)

Short stature

Short stature is usually defined as a height below the second centile (i.e. 2 SDs below the mean). Most of these 1 in 50 children will be normal children of short parents. However, the further the child is below these centiles, the more likely it is that there will be a pathological cause. Only 1 in 250 (4 in 1000) children are shorter than the 0.4th centile (-2.6 SD) and these should be assessed for a cause.

The height centile of a child must be compared with the weight centile and an estimate of his/her genetic expected height calculated from the height of his/her parents.

Short children may be psychologically well adjusted to their size. However, there may be problems from being teased or bullied at school, with poor self-esteem, and they may be at a disadvantage in competitive sport. They are also assumed to be younger than their true age and may be treated inappropriately as a result.

When assessing a child with short stature, the history and examination of the child and their growth chart (Fig. 12.9) directs one to the likely cause. Familial, constitutional delay of growth and puberty, genetic disorders, nutritional, general health and endocrine causes need to be considered.

Familial

Most short children have short parents and fall within the target centile range allowing for mid-parental height.

Constitutional delay of growth and puberty

Constitutional delay of growth and puberty is a variation of normal growth, more common in boys, which presents with short stature in teenage years because of a delay in the onset of puberty. Growth during childhood is usually within the lower limits of normal, onset of puberty is delayed but final height is normal for family size. Always ask for a history of delayed growth and puberty in the family, for example age of maternal menarche and age of parents' completing growth (see Case history 12.4 below).

Genetic disorders

Many genetic disorders are associated with short stature. Down syndrome is usually diagnosed at birth, but Turner (see Fig. 12.11 and see Ch. 9, Genetics), Noonan (see Ch. 9, Fig. 9.17), and Russell–Silver (see Fig. 12.9) syndromes may present with short stature and minimal symptoms. Turner syndrome (Case history 12.1) may be particularly difficult to diagnose clinically and should be considered in all short girls.

Other inherited growth disorders are secondary to single gene disorders. Children with skeletal dysplasias, e.g. achondroplasia, have short stature associated with skeletal disproportion. This can be identified by measuring sitting height and comparing this to leg length by subtracting from total height. Charts are available to assess body proportions.

Abnormalities of a gene called short stature homeobox (*SHOX*) located on the X chromosome lead to severe short stature with skeletal abnormalities. In Turner syndrome, absence of one *SHOX* gene is thought to be the cause of short stature (and additional copies in Klinefelter syndrome are responsible for their tall stature).

Nutrition

Nutrition is a major factor affecting growth both antenatally and in the first year of life. About 10% of children born with intrauterine growth restriction or who were extremely premature remain short.

Later in childhood, inadequate nutrition may be due to insufficient food supply or a restricted diet, but whilst it will affect weight it has less impact on height.

General health

Long-term or recurrent health conditions have a significant impact on the growth of a child, usually causing them to be short and underweight, i.e. their weight is on a lower centile than their height. Growth may be affected by:

- poor appetite associated with a long-term illness
- the increased nutritional requirement from a raised metabolic rate, e.g. with increased work of breathing, recurrent infections
- malabsorption of nutrients
- electrolyte imbalance.

Long-term illnesses that may be associated with short stature include:

- coeliac disease, which can present at any age and although there may be gastrointestinal symptoms, slow growth may be the only feature
- inflammatory bowel disease, especially Crohn disease
- chronic kidney disease – may be present in the absence of a history of a renal disorder
- cystic fibrosis – malabsorption, recurrent infections, increased work of breathing, and reduced appetite
- congenital heart disease – increased work of breathing
- juvenile idiopathic arthritis – chronic inflammation.

Children subjected to emotional deprivation may be short and underweight with delayed puberty. Deprivation affects hypothalamic–pituitary function, causing reduced growth hormone secretion. This condition can be difficult to identify, but affected children show an improved growth rate if placed in a nurturing environment.

Endocrine

Hypothyroidism, GH deficiency, IGF-1 deficiency, and steroid excess are uncommon causes of short stature. They are associated with children being overweight relative to their height. By contrast, children with nutritional obesity tend to be relatively tall compared to their mid-parental centile (see Ch. 26, Diabetes and endocrinology).

Investigations for short stature

If a child is short (<0.4th centile), short for mid-parental height, growing at a slow rate (drifting down centiles) or has symptoms suggestive of an underlying illness, investigation should be considered (Table 12.1). The

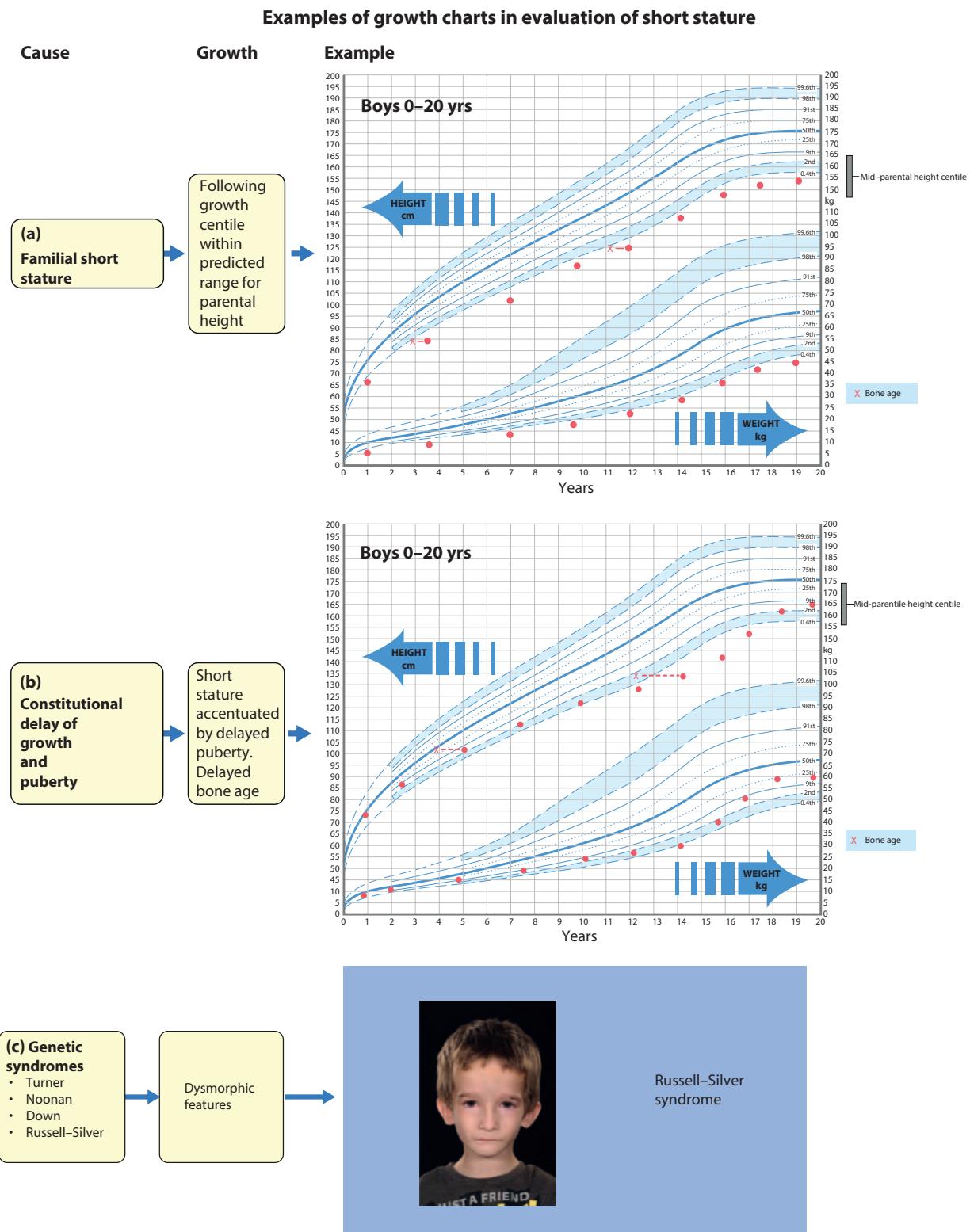


Figure 12.9 Causes of short stature. Plotting bone age with chronological age provides a more accurate estimation of growth potential. (Growth charts reproduced with kind permission of the © Child Growth Foundation.)

Continued

Examples of growth charts in evaluation of short stature

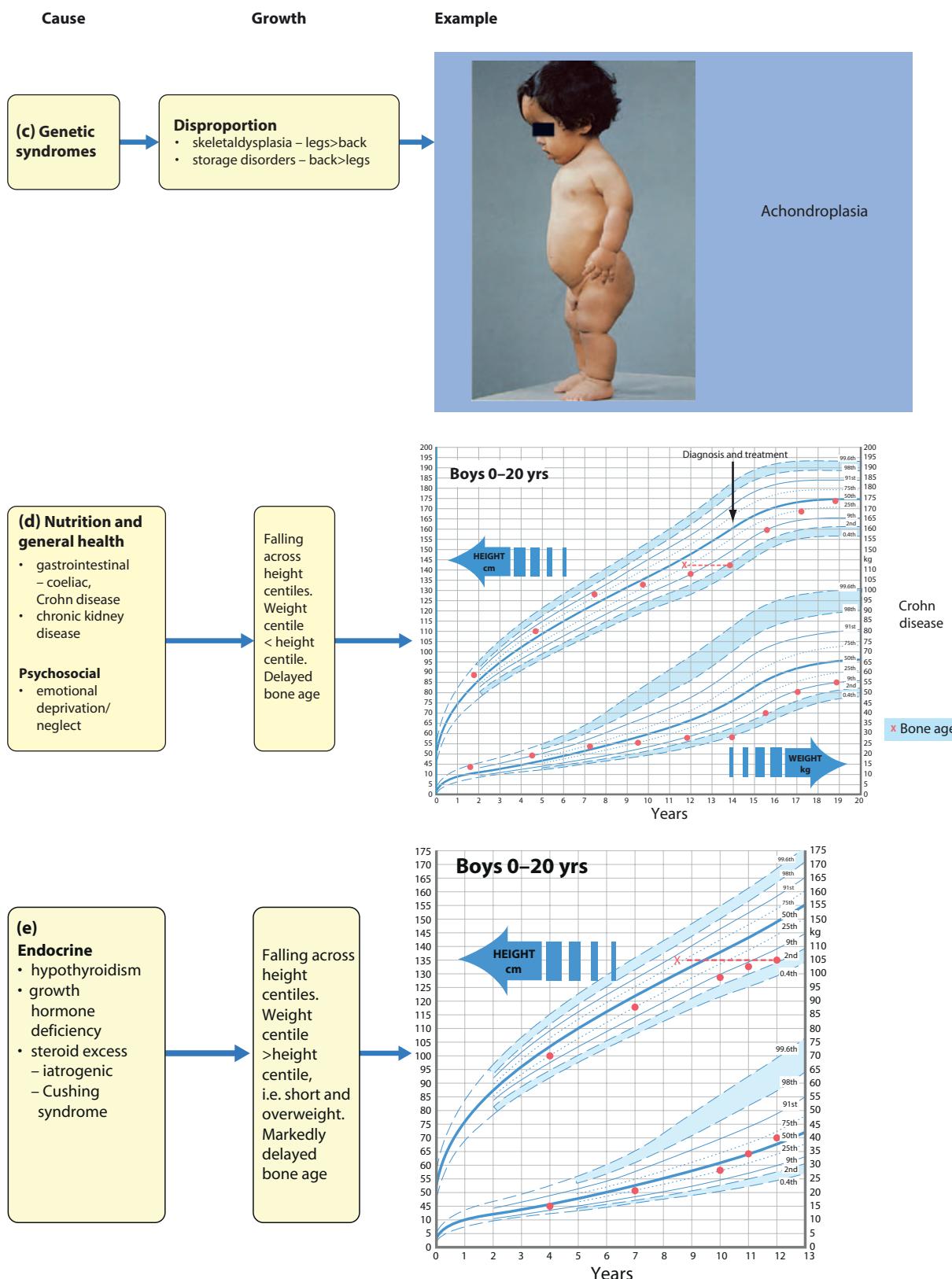


Figure 12.9 Continued

Table 12.1 Investigations for short stature.

Standard investigations for all	Notes
Full blood count	Anaemia may indicate nutritional deficiency, coeliac or Crohn disease
Creatinine, electrolytes and liver function tests	Look for evidence of renal or hepatic dysfunction as there may be few symptoms present
Thyroid stimulating hormone	Acquired hypothyroidism is the most common endocrine cause of short stature and may have few symptoms
Anti-tissue transglutaminase (anti-TTGa) immunoglobulin A antibodies	Coeliac disease is common and symptoms are variable, so this is important to exclude
Karyotype or microarray	Check in all girls, looking for Turner syndrome (45,XO) as dysmorphic features may be subtle
IGF-1	This is a useful screening test for growth hormone deficiency
X-ray of the left hand and wrist for bone age to determine skeletal maturation (Fig. 12.10)	Mild delay in constitutional delay of growth and puberty. Marked delay for hypothyroidism or growth hormone deficiency
Specialist investigations	Notes
C-reactive protein (acute-phase reactant) and erythrocyte sedimentation rate	Check if symptoms suggestive of inflammatory conditions, for example Crohn disease
Calcium, phosphate, alkaline phosphatase, Vitamin D	Consider if renal dysfunction present and check for suspected bone disorders if bone deformity, such as bowing of the legs noted on examination
Limited skeletal survey	If evidence of disproportion, aiming to find skeletal dysplasia. Scoliosis may also cause short stature.
Growth hormone provocation tests (using insulin, glucagon, clonidine, or arginine in specialist centres)	Consider if growth rate is slow and IGF1 low to diagnose growth hormone deficiency
MRI brain scan	If child has headache or neurological signs to rule out intracranial tumour, e.g. craniopharyngioma
Immunoglobulins and functional antibodies	If child has recurrent infections, to rule out immunodeficiency

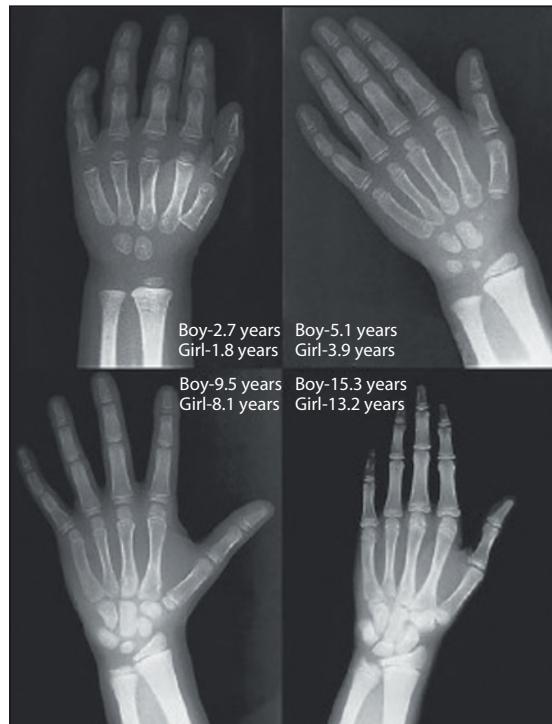


Figure 12.10 X-rays of the left hand and wrist to determine bone age. This technique allows assessment of skeletal maturation from the time of appearance of the epiphyseal centres, using a standardized rating system. The child's height can be compared with skeletal maturation and an adult height prediction made. The ages shown are the bone age of each X-ray.



Case history 12.1

Turner syndrome

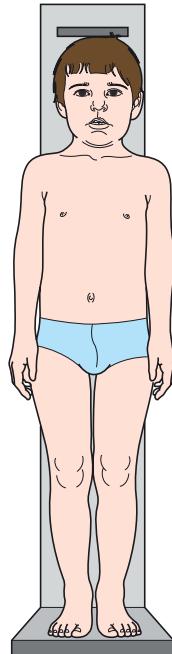
This girl (Fig. 12.11) presented when 10 years old with short stature. She had a history of recurrent ear infections, but was otherwise well. She had always been very short, and her height of 126.4 cm was well below the 0.4th centile on the standard growth chart. Her chromosomes confirmed Turner syndrome 45,XO. She was started on growth hormone injections followed by ethinyl oestradiol (oestrogens) for pubertal induction at 14 years of age. At 15 years of age her height was 150 cm (2nd centile).



Figure 12.11 At 15 years, this girl has few clinical features of Turner syndrome, demonstrating the need to check the karyotype of females with marked short stature.

Summary

Assessment of a child with short stature



History

- Pregnancy: maternal health, alcohol, smoking
- Measurements at birth: Birthweight, gestational age, intrauterine growth restriction
- Feeding history
- General health: long-term illness
- Medication, e.g. corticosteroids
- Family history of growth or pubertal delay
- Emotional health

Examination

- General examination: dysmorphic features, skeletal disproportion
- Nutritional status
- Long-term illness, e.g. coeliac disease, cystic fibrosis, Crohn disease, chronic kidney disease
- Endocrine disorder: hypothyroidism, Cushing syndrome
- Pubertal stage

Growth chart:

- Which centile? Is height below 0.4th centile? Is it discrepant from weight centile?
- How does height centile compare to MPC (mid-parental centile)?
- Is growth pattern following or crossing centiles?

Tall stature

Bone age may be helpful, as it is markedly delayed in some endocrine disorders, e.g. hypothyroidism and GH deficiency, and can be used to estimate adult height potential. Management of endocrine conditions causing short stature are described in [Chapter 26](#).

This is a less common presenting complaint than short stature, as many parents are proud that their child is tall. However, some adolescents become concerned about excessive height during their pubertal growth spurt. Tall

Table 12.2 Causes of excessive growth or tall stature

Genetic	Familial – most common cause Klinefelter syndrome (47,XXY karyotype) Marfan syndrome Homocystinuria Beckwith Wiedeman syndrome Sotos syndrome – associated with large head, characteristic facial features, and learning difficulties
Nutritional	Antenatal – maternal diabetes mellitus Obesity – puberty is advanced, so final height centile is less than in childhood
Hormonal	Hyperthyroidism Excess sex steroids – precocious puberty Excess adrenal androgen steroids – congenital adrenal hyperplasia Excess growth hormone secretion

children may be disadvantaged by being treated as older than their chronological age. The causes are presented in [Table 12.2](#).

Genetic

Most tall stature is inherited from tall parents – compare the child's height centile to MPC. Marfan (a disorder of loose connective tissue, see [Ch. 28](#), Musculoskeletal disorders) and Klinefelter (XXY – an excess of SHOX dose, see [Ch. 9](#)) syndromes both cause long-legged tall stature.

Nutrition

Obesity 'fuels' early growth and may result in tall stature in childhood; however, because puberty is usually earlier than average, it does not increase final height.

Endocrine

Tall stature may be associated with precocious puberty, but there will be early epiphyseal fusion so that final adult height is not excessive. Adrenal, thyroid and growth hormone excess may all cause tall stature (see [Ch. 26](#)).

Most children with tall stature need no treatment for their growth once the cause is established. However, the diagnosis is important so that the child is screened for complications, e.g. aortic root dilatation in Marfan syndrome. Endocrine conditions will need treatment to reduce hormonal excess (see [Ch. 26](#)).

Abnormal head growth

Most head growth occurs in the first 2 years of life and 80% of adult head size is achieved before the age of 5 years. This largely reflects brain growth, but small or large heads may be familial, so comparison with measurements of parents'



Figure 12.12 This boy has microcephaly. He has cerebral palsy. (Courtesy of Dr Gabby Chow.)

heads should be made. At birth, the sutures and fontanelle are open. The posterior fontanelle normally closes by 8 weeks, and the anterior fontanelle by 12 months to 18 months. If there is a rapid increase in head circumference, raised intracranial pressure should be excluded.

Microcephaly

Microcephaly, a head circumference below the 2nd centile ([Fig. 12.12](#)), may be:

- familial – when it is present from birth and development is usually normal
- caused by genetic disorders, syndromes, cerebral anomalies, craniosynostosis
- caused by a congenital infection, fetal alcohol spectrum disorder
- acquired after an insult to the developing brain, e.g. perinatal asphyxia, hypoglycaemia, or meningitis, when it is often accompanied by cerebral palsy, cognitive impairment and seizures.

Macrocephaly

Macrocephaly is a head circumference above the 98th centile. The causes of a large head are listed in [Box 12.1](#). Most are familial and the child is developing normally. A rapidly increasing head circumference suggests raised intracranial pressure and may be due to hydrocephalus, subdural haematoma, or a brain tumour. It must be investigated promptly by cranial ultrasound if the anterior

Box 12.1 Causes of a large head

- Familial macrocephaly
- Raised intracranial pressure (in an infant):
 - chronic subdural haematoma
 - brain tumour
 - neurofibromatosis
- Cerebral gigantism (Sotos syndrome)
- Central nervous system storage disorders, e.g. mucopolysaccharidosis (Hurler syndrome)

Abnormal head shape

Box 12.2 Forms of craniosynostosis

Localized

- Sagittal suture – long narrow skull
- Coronal suture – asymmetrical skull
- Lambdoid suture – flattening of skull

Generalized

- Multiple sutures resulting in microcephaly and developmental delay
- Genetic syndromes, e.g. with syndactyly in Apert syndrome, with exophthalmos in Crouzon syndrome



Figure 12.13 Long flat head of a preterm infant. This can be avoided by lying preterm infants on a soft surface and regularly changing their head position.

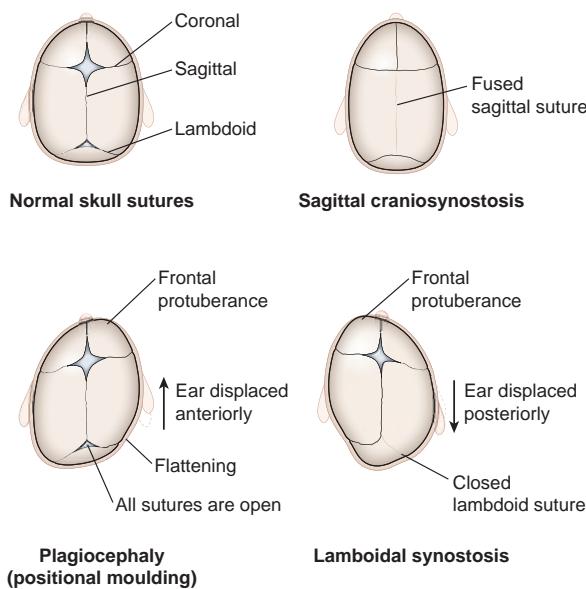


Figure 12.14 Differentiating craniosynostosis from plagiocephaly.



Figure 12.15 Crouzon syndrome showing the typical shallow orbits and exophthalmos. Craniofacial reconstructive surgery is required to prevent visual loss and cerebral damage from raised intracranial pressure and for cosmetic appearance.

fontanelle is still open, otherwise by computed tomography (CT) or magnetic resonance imaging (MRI) scan.



If an infant's head circumference is enlarging and crossing centile lines, consider cranial ultrasound or CT head scan to rule out hydrocephalus.

Asymmetric heads

Skull asymmetry may result from an imbalance of the growth rate at the coronal, sagittal, or lambdoid sutures, although the head circumference increases normally. Occipital plagiocephaly (a parallelogram-shaped head with flattening of the back of the skull) and brachycephaly (flattening of the back of the skull) are common since the advice to parents that babies should sleep lying on their back to reduce the risk of sudden infant death syndrome. It improves with time as the infant becomes more

mobile. Plagiocephaly is also seen in infants with hypotonia. Preterm infants may develop long, flat heads from lying on their sides for long periods on the hard surface of incubators. This can be moderated by providing the infant with a soft surface to lie on and changing their head position frequently (Fig. 12.13).

Craniosynostosis

The sutures of the skull bones normally start to fuse during infancy but do not finally fuse until late childhood. Premature fusion of one or more sutures (craniosynostosis) may lead to distortion of the head shape. Craniosynostosis is usually localized (Box 12.2). It most often affects the sagittal suture, when it results in a long narrow skull (Fig. 12.14).

Craniosynostosis may be generalized (Box 12.2), when it may be a feature of a syndrome (Fig. 12.15). The fused suture may be felt or seen as a palpable ridge and

confirmed on skull X-ray or cranial computed tomography scan. The condition can be treated surgically in specialist centres for craniofacial reconstructive surgery if there is raised intracranial pressure, or for cosmetic reasons.

Early puberty

The development of puberty before 8 years of age in girls and 9 years of age in boys is defined as outside the normal range in the UK. There are several recognized patterns of premature sexual development:

- thelarche – premature breast development
- adrenarche (also known as pubarche) – pubic hair development
- gonadotrophin-dependent precocious puberty
- isolated premature menarche.

Premature breast development (thelarche)

This usually affects girls between 6 months and 2 years of age. The breast enlargement may be asymmetrical and fluctuate in size, rarely progressing beyond stage 3 of puberty. It is differentiated from gonadotrophin-dependent precocious puberty by the absence of other features of puberty or significant acceleration in growth. It is non-progressive and self-limiting. Investigations are not usually required ([Case history 12.2](#)).

High maternal levels of prolactin can cause newborn babies to be born with breast buds and even to lactate. These self-resolve in days.

Adrenarche

This occurs when pubic hair develops before 8 years of age in girls and before 9 years in boys but with no other signs of pubertal development or significant growth acceleration. It is caused by sensitivity to androgen production by the adrenal gland between the age of 6 years and 8 years. There may be a slight increase in growth rate and bone age. It is usually self-limiting. Girls who develop premature adrenarche are at an increased risk of developing polycystic ovarian syndrome in later life.

If the child is growing rapidly, or there is significant virilization, excess production of adrenal hormones should be excluded (see [Ch. 26](#)).

Precocious puberty (PP)

May be categorized ([Fig. 12.17](#)) as:

- gonadotrophin dependent (central, 'true' precocious puberty) from premature activation of the hypothalamic–pituitary–gonadal axis with follicle stimulating hormone and luteinizing hormone secretion. The sequence of pubertal development would be normal, described as 'consonant'.
- gonadotrophin independent – from excess sex steroids produced outside the pituitary gland. The sequence of pubertal development would be abnormal, described as 'dissonant'.



Case history 12.2

Premature thelarche

This 18-month-old female developed enlargement of both breasts ([Fig. 12.16](#)). There were no other features of puberty and she was growing normally. Her bone age was only mildly advanced (21 months). Her subsequent growth rate was normal. A diagnosis of premature thelarche was made.

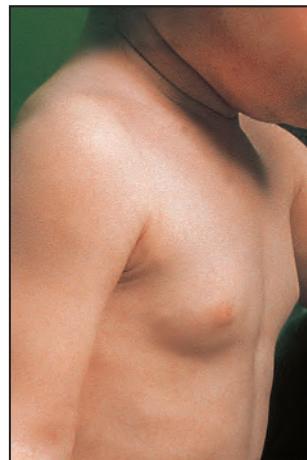


Figure 12.16 Premature breast development in an 18-month-old girl. The absence of a growth spurt and axillary and pubic hair differentiates it from gonadotrophin dependent precocious puberty. It is self-limiting and usually resolves. (From: Wales JK, Rogol AD, Wit JM: Pediatric endocrinology and growth. London, 2003, Saunders, with permission.)

Girls

Gonadotrophins are secreted from the anterior pituitary gland in a pulsatile fashion, with increasing amplitude of those pulses in later childhood. The ovaries are very sensitive to secretion of gonadotrophins from the pituitary gland, so gonadotrophin-dependent precocious puberty is fairly common in girls. Pathological causes of precocious puberty in girls are rare and can be secondary to either:

- gonadotrophin-dependent causes due to a change in the structure of the pituitary gland, e.g. secondary to brain injury, associated with cerebral palsy or a pituitary adenoma. Pubertal development will be consonant.
- gonadotrophin-independent causes such as excess androgens from congenital adrenal hyperplasia or adrenal tumours, presenting with pubic and axillary hair, adult body odour, acne, and virilization of the genitalia before breast development (see [Ch. 26](#)).

Ultrasound examination of the ovaries and uterus is helpful in assessing the progress of puberty. The uterus will change from an infantile 'tubular' shape to 'pear' shape with the progression of puberty and the endometrial lining can be identified close to menarche.

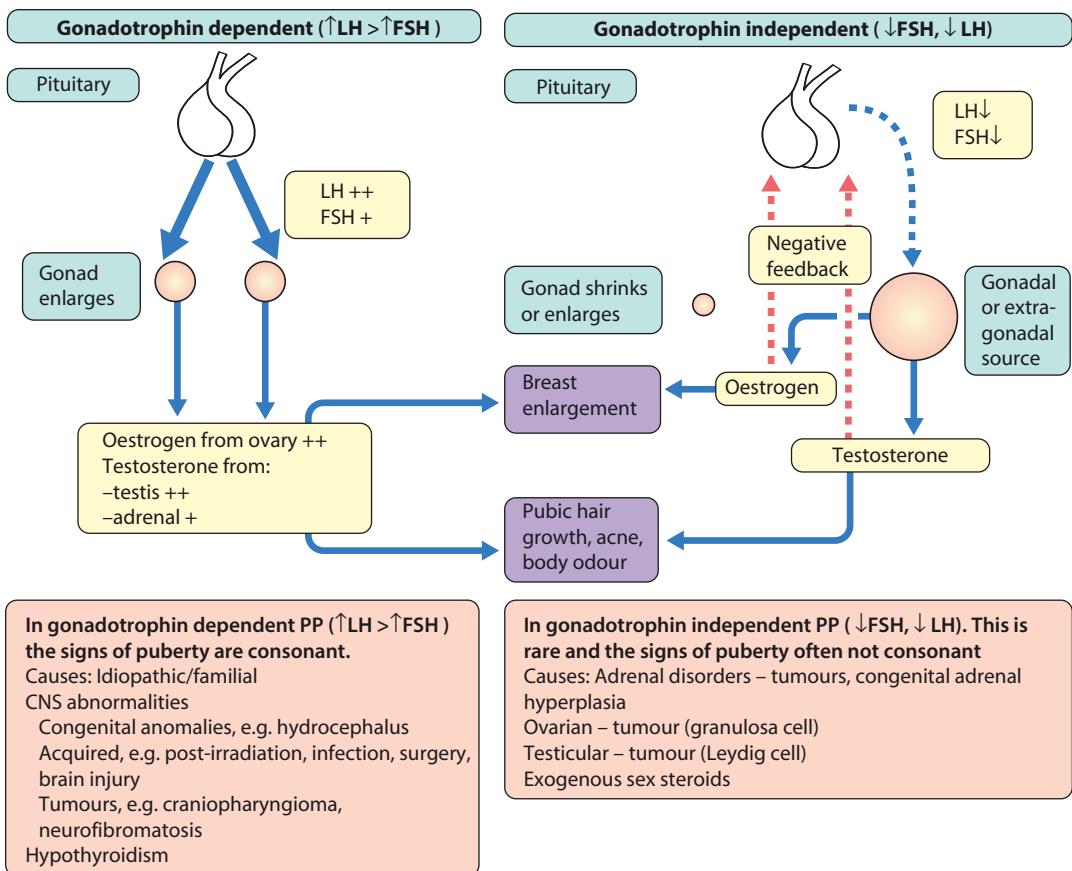


Figure 12.17 Causes of precocious puberty. (Courtesy of Emma Rhodes.)

Boys

The testes are relatively insensitive to secretion of gonadotrophins from the pituitary gland, so gonadotrophin-dependent precocious puberty is uncommon in boys (Case history 12.3). It is important to exclude a pathological cause. Examination of the testes is important:

- bilateral enlargement of the testes, with testicular volumes greater than or equal to 4ml, suggests gonadotrophin-dependent PP. This can be caused by a change in the structure of the pituitary gland, e.g. an intracranial tumour.
- prepubertal testes suggest a gonadotrophin-independent cause, e.g. adrenal pathology.
- a unilateral enlarged testis suggests a gonadal tumour.



Precocious puberty in girls is common and usually due to the premature onset of normal puberty. Precocious puberty in boys is rare and a pathological cause must be excluded.

Management

The management of precocious puberty is directed towards:

- detection and treatment of any underlying pathology, e.g. using MRI scan to identify an intracranial tumour, particularly in boys.

- reducing the rate of skeletal maturation, which is assessed by bone age. An early growth spurt may result in early cessation of growth and a reduction in adult height.
- addressing psychological/behavioural difficulties associated with early progression through puberty.
- delaying the onset of menarche in girls.

It is possible to delay gonadotrophin-dependent puberty using gonadotrophin-releasing hormone analogues.

Delayed puberty

Delayed puberty is defined as the absence of pubertal development by 13 years of age in girls and 14 years in boys. The causes of delayed puberty are listed in Box 12.3.

Boys

In contrast to precocious puberty, delayed puberty is much more common in boys due to the relative insensitivity of the testes to gonadotrophin secretion. Most commonly, this is constitutional delay of growth and puberty, often with a family history of delayed puberty (Case history 12.4). It is a variation of the normal timing of puberty rather than a pathological condition. Most boys referred to clinic have noticed a marked contrast to their peer group – especially as girls of their age may have completed pubertal development – and



Case history 12.3

Gonadotrophin-dependent precocious puberty in a boy

This 6-year-old boy presented with precocious puberty (Fig. 12.18a,b). He was noted to have multiple café-au-lait spots consistent with a diagnosis of neurofibromatosis type 1. An MRI scan showed a mass in the hypothalamus, which proved to be an optic glioma. He was treated with radiotherapy, although full remission was not possible to achieve. The site of injection of gonadotrophin releasing hormone analogue treatment to suppress his sexual development is covered by the plaster.



(a)



(b)

Figure 12.18 (a) Multiple café-au-lait spots. Neurofibromatosis type 1 was diagnosed. (b) Genitalia showing stage 3 genitalia and pubic hair with 12-ml testicles bilaterally. He also had adult body odour. (From: Wales JKH, Rogol AD, Wit JM: Pediatric endocrinology and growth. London, 2003, Saunders, with permission.)

Box 12.3 Causes of delayed puberty

Constitutional delay of growth and puberty/familial

- By far the most common in boys

Low gonadotrophin secretion (hypogonadotropic hypogonadism)

- Systemic disorders:
 - cystic fibrosis, severe asthma, Crohn disease, organ dysfunction, anorexia nervosa, starvation, excess physical training
- Hypothalamo-pituitary disorders:
 - pituitary dysfunction
 - isolated gonadotrophin or growth hormone deficiency
 - intracranial tumours (including craniopharyngioma)
 - Kallmann syndrome (luteinizing hormone-releasing hormone deficiency associated with absent sense of smell)
- Acquired hypothyroidism

High gonadotrophin secretion (hypergonadotropic hypogonadism)

- Chromosomal abnormalities:
 - Klinefelter syndrome (47,XXY)
 - Turner syndrome (45,XO)
- Acquired gonadal damage:
 - After surgery, chemotherapy, radiotherapy, trauma, torsion of the testis, autoimmune disorder



Case history 12.4

Constitutional delay in growth and puberty

A 14-year-old boy is concerned that he is short. He is well, but gets teased at school about his height. His mother had menarche at 13 years of age and his father recalls that he was still growing when he left school at the age of 16 years. Examination reveals a generally well boy, with stage 1 pubic hair and testicular volumes of 4 ml bilaterally. His bone age is delayed by 20 months. So, his short stature is secondary to a lack of height acceleration during puberty. As his mood has been significantly affected by his delayed puberty, he is treated with testosterone for 6 months with good effect on his growth rate and confidence. He then continues to make pubertal progress independently and reaches a final adult height of 166 cm (2nd to 9th centile) (see Fig. 12.9c).

it may adversely affect their self-esteem. An affected child will have delayed bone age and will reach an adult height within the target centile range as growth will continue for longer than in their peers.

Treatment can be offered to induce puberty in boys after 14 years of age, usually using low-dose intramuscular testosterone injections, which will accelerate growth as well as inducing secondary sexual characteristics.

Girls

In girls, as the ovaries are sensitive to gonadotrophins, delayed puberty is less common and a pathological cause should be excluded. Consider the possibility of an eating disorder. Karyotyping should be performed for Turner syndrome, and thyroid and sex steroid hormones should be measured. Pituitary pathology should be excluded by an MRI scan. The aims of management are to:

- identify and treat any underlying pathology
- ensure normal psychological adaptation to puberty and adulthood
- accelerate growth and induce puberty if necessary.

Girls may be treated with oestradiol for several months to induce puberty.



Delayed puberty is common in boys and is usually due to constitutional delay of growth and puberty. Delayed puberty is uncommon in girls and a cause should be sought.

Acknowledgements

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Further reading

Donaldson MDC, Gregory JW, Van Vilet G, Wolfsdorf JI: Practical endocrinology and diabetes in children, ed 4, Oxford, 2019, Wiley Blackwell.

Websites

Treatment of delayed puberty in boys: www.bsped.org.uk/media/1375/testosteronereplacementguideline.pdf.

Pubertal induction in girls: www.bsped.org.uk/media/1378/hormonesupplementationforpubertalinductioningirls.pdf.

Nutrition

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Features of nutrition in children:

- Children are particularly vulnerable to the effects of poor nutrition, because of their additional requirements for growth and development.
- Nutrition of the fetus and early years of childhood affects the risk of developing a range of adult diseases.
- Breastfeeding is the optimal form of feeding, yet breastfeeding rates in the UK continue to lag behind many countries.
- Nutrition can be provided for children unable to eat normally via enteral tubes and parenteral nutrition.
- Vitamin D deficiency continues to be a clinical problem in high-income countries.
- Worldwide, malnutrition is responsible directly or indirectly for more than one-third of all deaths of children under 5 years of age.
- Over one-third of 10- and 11-year-olds in the UK are now overweight or obese.
- Early childhood caries is the commonest reason for primary school-age children to be admitted to hospital.

The nutritional vulnerability of infants and children

Infants and children are more likely to suffer adverse consequences from poor nutrition than adults. This is shown most starkly with severe food shortage, such as from famine or conflict, when babies and young children are the first to become ill and die. What makes them so vulnerable?

High nutritional requirements

Infants have very high energy requirements as they not only need to maintain nutrition but also to sustain their rapid growth (Table 13.1). A term newborn, after the first week of life, requires an intake of 150 ml/kg of milk per day,

i.e. 15% of body weight per day. Even a small reduction of milk volume or quality will rapidly affect the infant's hydration, nutrition and growth. The energy requirements of infants relative to body weight is approximately double that of adults. As children get older, an increasing proportion of their nutrition is from food, making them less reliant on a high fluid intake.

The proportion of dietary energy intake used for growth in infancy is 35%, compared with 5% at 1 year of age, and around 2% until mid-adolescence. A term infant doubles their weight by 5 months and trebles it by 1 year, highlighting the vulnerability of infants to nutritional deficiency during this time.

Low nutritional stores

Newborn infants, particularly those born prematurely or who have experienced poor fetal growth (intrauterine growth restriction), have low stores of fat and protein

Table 13.1 Reference values for energy and protein requirements

Age	Energy (kcal/kg per 24 h)	Protein (g/kg per 24 h)
0–6 months	115	2.2
6–12 months	95	2.0
1–3 years	95	1.8
4–6 years	90	1.5
7–10 years	75	1.2
Adolescence	(male/female)	
11–14 years	65/55	1.0
15–18 years	60/40	0.8

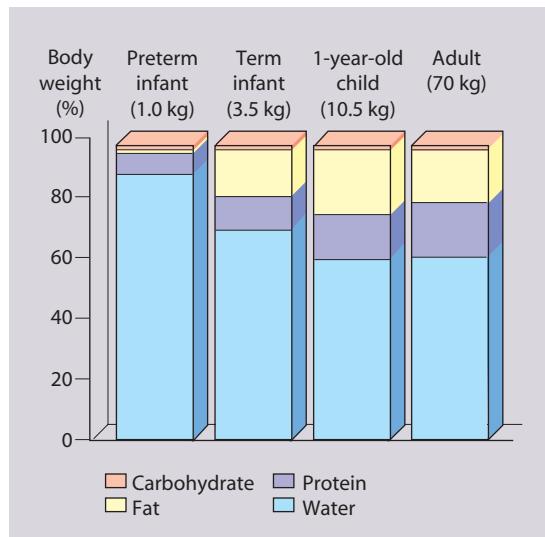


Figure 13.1 Body composition of preterm and term infants, children, and adults. Newborn infants, particularly the preterm, have poor stores of fat and protein.

compared with older children or adults (Fig. 13.1). The lower the calorie reserves, the less able the child will be able to withstand starvation. If the enteral route of feeding is contraindicated in these infants, then parenteral nutrition must be initiated quickly.

Rapid brain growth and development

The brain grows rapidly during the last trimester of pregnancy and throughout the first two years of life. The complexity of interneuronal connections also increases substantially during this time, as evidenced by rapid acquisition of developmental skills. This is why the brain accounts for approximately two-thirds of basal metabolic rate in a baby at term, and for about 50% at 1 year of age (Fig. 13.2). Even modest energy deprivation during this period of rapid brain growth and differentiation is associated with an increased risk of neurodevelopmental impairment.

Illness or surgery

During an acute illness or following surgery, infants and children may not be able to feed or eat. Recurrent infections are common in infancy, causing reduced intake while increasing nutritional demands. Whereas nasal congestion is a minor symptom in older children, it can prevent babies from breathing when feeding on the breast or bottle, so feeding becomes impaired. Poor feeding can become a 'vicious cycle' that is hard to break, as it can lead to lethargy, hypoglycaemia and ketosis; and a lethargic or hypoglycaemic infant lacks the energy to feed. Although infants rapidly lose weight with acute illness, this is only transient. In children with chronic illness, such as cystic fibrosis and Crohn disease, higher metabolic requirements place them at a greater risk of undernutrition compared to healthy children of a similar age.

Following complicated surgery or severe acute illness in an infant, the energy deficit may be so large that they

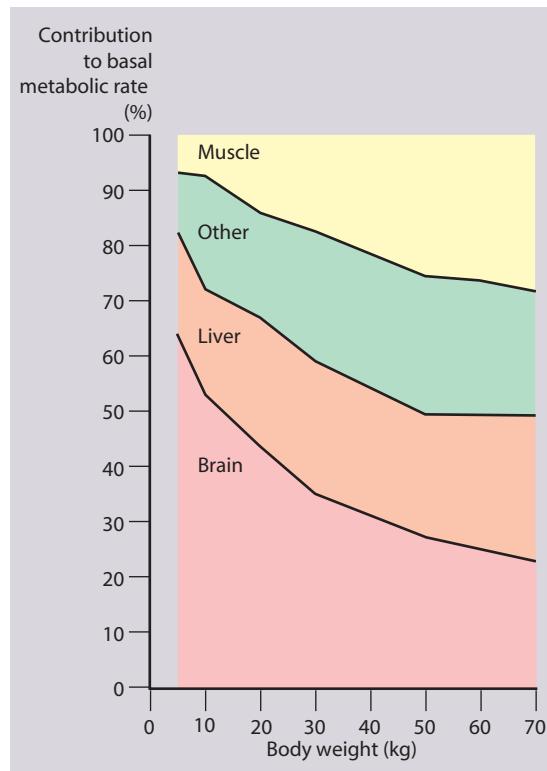


Figure 13.2 The relative contribution to basal metabolic rate derived from brain, liver, and muscle changes with growth. The brain accounts for two-thirds of the basal metabolic rate at birth, but this falls to 25% in adults. (Data from: Holliday MA: Metabolic rate and organ size during growth from infancy to maturity and during late gestation and early infancy. *Pediatrics* 47:169,1971.)

may require an energy intake as high as 150–200 kcal/kg per day (compared with normal of 95–115 kcal/kg per day) to allow catch-up growth to occur. Parenteral nutrition (not simply fluids containing dextrose) must be considered early in these children.

Long-term outcome of early nutritional deficiency

Linear growth of populations

Growth and nutrition are closely related, such that the mean height of a population reflects its nutritional status, health during childhood and genetics. As living conditions have improved in high-income countries, people have become taller. In the Netherlands, the tallest population in the world, for example, average male height has increased by 20 cm over the last 150 years to 182.5 cm; for females to 168.7 cm. However, this increase in height in high-income countries across Europe has stabilized; it has been postulated that the maximum mean population height has been reached, or it is related to choices in nutrition and lifestyle.

Disease in adult life

There is considerable epidemiological evidence suggesting nutrition in the first 1000 days of life, from conception to the age of 2 years, has long-term effects on later health and risk of illness, in particular an increased risk of

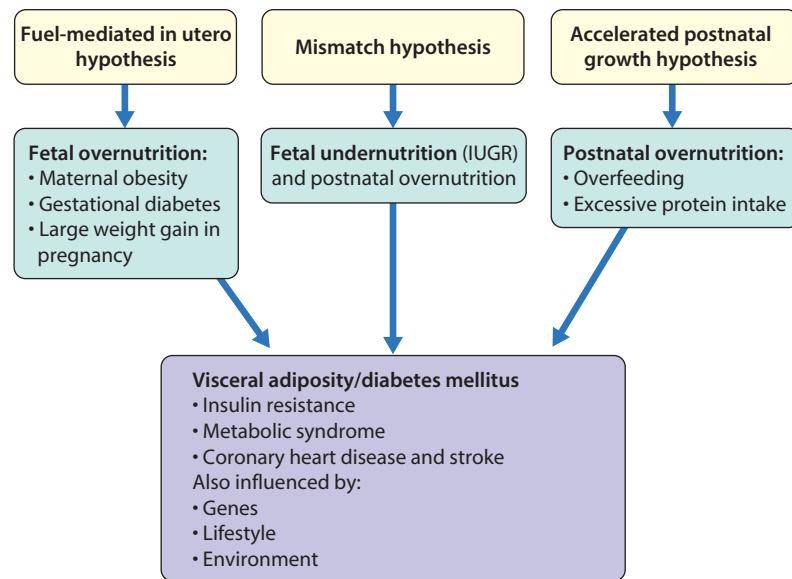


Figure 13.3 Current hypotheses on early metabolic programming of adiposity and related disease. (Adapted from: Koletzko B, Symonds M, Olsen SF. Early Nutrition Programming Project; Early Nutrition Academy: Programming research – where are we and where do we go from here? Am J Clin Nutr 94:2036S–2043S, 2011, with permission.)

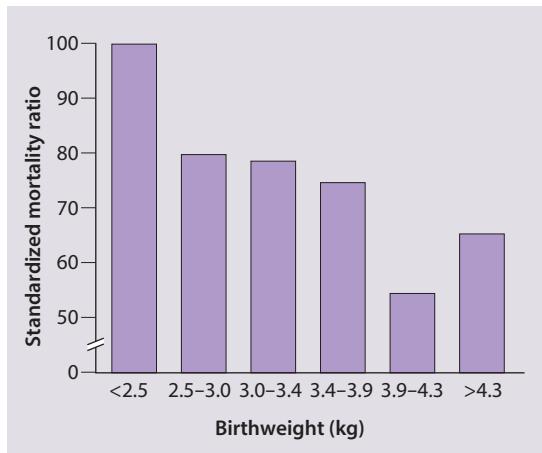


Figure 13.4 Death rates from coronary heart disease according to birthweight showing increased rate in low birthweight babies. (Data from: Barker DJ: Fetal origins of adult disease. In Growing up in Britain: ensuring the healthy future for our children. A study of 4–5 year olds. London, 1999, BMJ Books.)

coronary heart disease, non-insulin-dependent diabetes and hypertension. The 'developmental origins of health and disease' (DOHaD) hypothesis by Barker has generated the concept of developmental programming.

Currently, three hypotheses are proposed: the 'fuel-mediated' *in utero* hypothesis, the accelerated postnatal weight gain hypothesis, and the mismatch hypothesis (Fig. 13.3). These are not mutually exclusive and could have a greater or lesser impact in different circumstances. The association between increased risk of death from coronary heart disease in adults with intrauterine growth restriction (IUGR) is demonstrated in Fig. 13.4. Epigenetic alterations (changes in phenotype or gene expression not due to changes in the DNA sequence, which may be transmissible across generations) are thought to be key mediators of developmental programming.

Summary

Nutritional vulnerability

Infants are particularly vulnerable to inadequate nutrition because of:

- extra nutritional demands for growth (the weight of a term infant doubles by 5 months and trebles by 1 year of age)
- low levels of fat and protein stores
- reduced food intake and increased nutritional demands with illness or following surgery.

Infant feeding

Breastfeeding

Breast milk is the natural food for all infants, and mothers should be encouraged and supported to breastfeed their infant. The development of infant formula feeds resulted in a marked decline in the popularity of breast feeding, but this is gradually being reversed. Exclusive breastfeeding for the first 6 months is the current World Health Organization (WHO) recommendation, which has been endorsed by the UK government.

Shorter periods of breastfeeding can also be advantageous. In 2010, in the UK, 81% of babies were breastfed at birth. Drop-off rates are very high, with only 46% of UK infants still being exclusively breastfed at 1 week of age (Fig. 13.5). A higher proportion of mothers from a managerial and professional background start breastfeeding, compared with mothers from routine and manual occupations, although this gap is closing.

Breastfeeding rates in the UK are lower than many other comparable high-income countries. An international study found that just 34% of babies in the UK received any breast milk at 6 months, compared to 71%

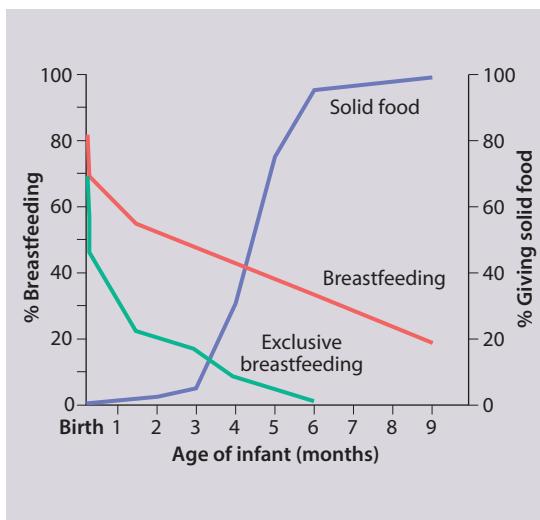


Figure 13.5 Prevalence of breastfeeding, exclusive breastfeeding (no formula milk), and proportion of infants given solid feeds during the first 9 months of life in the UK. This shows the low percentage exclusively breastfed over the first few months of life of infants. (Data from: Infant Feeding Survey, 2010, the latest survey.)

in Norway. Breastfeeding rates in the UK are increasing, but only gradually, despite the widespread promotion of breastfeeding during pregnancy.

Advantages

Breastfeeding should start soon after birth. This is facilitated by placing the baby onto the mother's chest soon after delivery to provide skin-to-skin contact; babies are often alert in the first hour after birth and will suck at the breast. Initial milk in the form of colostrum is small in volume but high in protein and immunoglobulin and other anti-infective agents. It primes the gut microbiome with gut flora which differs markedly from babies fed with formula. The medical advantages of breastfeeding for the infant include:

- reduced risk of developing gastroenteritis and otitis media, and lower respiratory tract infections
- protective effect against necrotizing enterocolitis in extremely preterm infants
- overall increase in IQ (intelligence quotient) score by approximately 3 points
- reduction in risk of SIDS (sudden infant death syndrome)
- lower incidence of obesity, diabetes mellitus and hypertension in later life.

Advantages for the mother are that it:

- promotes close attachment between mother and baby
- delays return of menstruation, allowing iron stores to replenish following pregnancy and childbirth; this also helps with birth spacing
- burns energy stores, helping a return to pre-pregnancy weight
- lowers the risk of developing postnatal depression

- stimulates the release of oxytocin, which causes the muscles in the uterus to contract, helping to reduce postpartum blood loss
- reduces risk of breast and probably ovarian cancer
- is economical, as it does not require the purchase of feeding and sterilizing equipment and infant formula.

In low-income countries, breastfeeding dramatically improves survival during infancy, mainly by reducing gastrointestinal and other infections. The increase in spacing between pregnancies reduces mortality. It has been estimated that 1.3 million to 1.45 million deaths could be prevented in 42 low-income countries alone by increased levels of breastfeeding, making this one of WHO's four main strategies to reduce child mortality.

 **Exclusive breastfeeding in early infancy is life-saving in low- and middle-income countries.**

Physiology

After birth, progesterone levels drop and prolactin levels rise, which stimulates milk secretion by the cuboidal cells of the alveoli in the breast (Fig. 13.6). Secretory activation is achieved by starting to breastfeed shortly after birth followed by frequent suckling. Oxytocin secretion makes the myoepithelial cells around the alveoli contract, which results in the 'let-down' or 'milk ejection reflex'. Mothers may feel their milk 'coming in' with breast fullness about 2–3 days after birth. Milk production is also controlled by feedback inhibitor of lactation (FIL), a polypeptide present in breastmilk, which is responsible for regulating local control of milk production within the breast tissue itself. Build-up of this polypeptide within the milk in the breast results in inhibition of the secretion of milk from the cuboidal cells, which stops the breast becoming too full. Regular feeding or expressing of milk to empty the breast is necessary to remove this polypeptide and promote milk production.

Breastmilk is uniquely designed to match the infant's requirements; for example, the fat concentration increases during feeds, and the content of the milk changes as the infant gets older.

The important infection protection it confers is due to factors such as:

- secretory immunoglobulin A (SigA), the primary protective agent, which coats the intestinal mucosa and prevents bacteria from entering the cells
- human milk oligosaccharides, which function as prebiotics, preventing pathogenic bacteria from attaching to mucosal surfaces
- white blood cells, which can kill micro-organisms
- whey proteins (lysozyme and lactoferrin), which can kill bacteria, viruses and fungi.

In the first few days of life, the volume of milk is low, but water or formula supplements are not required while the supply of breast milk is becoming established. An effective latch, i.e. attachment of the baby to the mother's breast, is essential to ensure good milk transfer and prevent nipple trauma. Healthy, term babies often lose 7%–10% of their birthweight, but should regain their birthweight by 14 days. A baby who loses more than 10%, or fails to regain birthweight by 14 days, should be assessed to rule out an underlying medical problem. Some mothers (and health

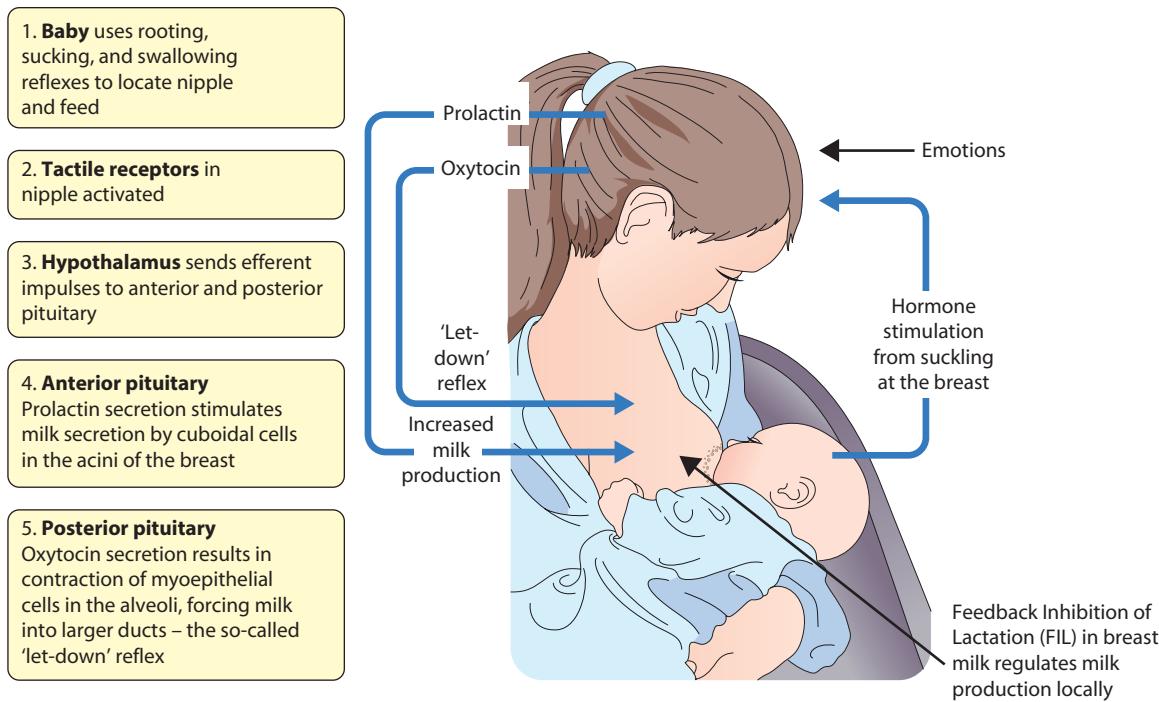


Figure 13.6 Physiology of breastfeeding.

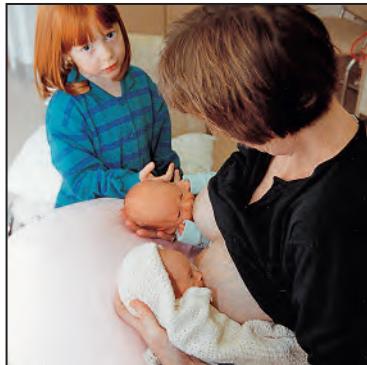


Figure 13.7 Breastfeeding of preterm twins.

professionals) struggle with the fact that the volume of breast milk taken by the infant is unknown. Parents also often worry that when their baby cries or is irritable it is because of insufficient milk. They can be reassured that an adequate volume is being produced if there is audible and visible swallowing, if the infant shows signs of a sustained rhythmic suck, has a moist mouth and is producing regular wet nappies. Weight gain after 2 weeks of age will confirm sufficient intake. Advice from a trained breastfeeding specialist and peer support from mother's groups or the internet can assist. A wide range of advice and videos on breastfeeding is available.

Successful breastfeeding of twins can be achieved (Fig. 13.7) but it is rarely possible to exclusively breastfeed triplets and higher-order births. Preterm infants can be breastfed, but the mother will need to learn how to express milk from the breast until the infant can coordinate sucking and swallowing. Obtaining sufficient milk can be a problem for mothers of extremely premature infants; many neonatal units have donor milk banks to temporarily overcome this problem.

Vitamin K supplementation at birth is recommended as there is insufficient vitamin K in breast milk to reliably prevent bleeding from vitamin K deficiency (haemorrhagic disease of the newborn). It is recommended that all infants (and children up to 5 years) in the UK should be given vitamin D supplements.

Perceived barriers and potential complications of breastfeeding

There are a number of reasons a mother may decide not to breastfeed. These include:

- Dislike of idea of breastfeeding or embarrassment. In the UK it is illegal to ask a breastfeeding mother to stop feeding or leave any public place. Despite this, many mothers report feeling self-conscious breastfeeding in public.
- Other family members cannot help or take part with feeding, unless the mother expresses and the baby accepts milk from a beaker or bottle.
- If the mother returns to work, it may make continuing breastfeeding for the recommended length of time more difficult. Maternity leave allowance and colleagues' attitude to time off work may influence duration of breastfeeding. Partial breastfeeding (in the morning and evening), with expressing during the day at work may be possible.
- Physical breast problems – sore, cracked nipples, thrush, mastitis, inverted nipples, inadequate milk supply.
- Breast milk jaundice – mild, self-limiting, unconjugated hyperbilirubinaemia; advise to continue breastfeeding; assess infant if prolonged (>2 weeks).
- Transmission of drugs – most are transmitted in very low concentration. A few maternal drugs, particularly

Table 13.2 A comparison of human milk, cow's milk and recommended content of infant formula (per 100 ml)

	Mature breast milk	Cow's milk	Infant formula (modified cow's milk)
Energy (kcal)	66	65	60–70/100 ml
Protein (g)	1.0	3.4	1.8–3.0
Carbohydrate (g)	7.0	4.6	9.0–14.0
Casein:whey	40:60	80:20	40:60 to 80:20
Fat (g)	3.8	3.7	4.4–6.0
Sodium (mmol)	0.65	1.9	0.87–2.6
Calcium (mmol)	0.85	3.0	1.25–3.5
Phosphorus (mmol)	0.48	3.0	0.8–2.9
Iron (μ mol)	1.2	0.36	5.4–23

Data from: Koletzko B, editor: *Pediatric Nutrition in Practice*, ed 2, Basel, 2015, Karger.
Formula content is recommended composition by expert group coordinated by ESPGHAN.

- antimetabolites, lithium, radioactive therapy, mean that breastfeeding is contraindicated. Check formulary.
- Risk of transmission of maternal infection – maternal CMV, hepatitis B (if infant not protected) and HIV (breastfeeding not recommended in high-income countries; in low- and middle-income countries breastfeeding with fully suppressive maternal antiretroviral therapy is recommended).
 - In certain rare metabolic disorders (such as galactosaemia, glucose galactose malabsorption, certain long chain fatty acid oxidation disorders), breastfeeding is contraindicated.
 - Tongue-tie, when the frenulum between the dorsum of the tongue and the base of the mouth is short and restricts movement of the tongue, has recently gained attention as a reason for difficulty to latch and feed effectively, to prolong feeding times and growth faltering. Treatment is division of the frenulum. There is considerable debate about indications and efficacy.
- Breastfeeding beyond 6 months without timely introduction of appropriate solids may lead to poor weight gain, iron deficiency and rickets.

Promotion of breastfeeding

Breastfeeding should have as high a public profile as possible. Women who have never seen an infant being breastfed are less likely to want to breastfeed themselves. Education in schools and during pregnancy about the advantages of breastfeeding may be beneficial. Support from peers and health professionals with specialist training may increase duration of breastfeeding, as well as help solve common issues. The WHO recommends continuing breastfeeding until 2 years of age.



Newborn infants of mothers planning to breastfeed should not be given any formula feeds unless unavoidable.

Formula feeding

Infants who are not breastfed require a formula, designed to meet the nutritional needs of infants. Most are based on cow's milk, and their composition continues to be modified to better match the profile of human breast milk. Even after considerable modification, differences remain between formula feeds and breast milk (Table 13.2). Many formula feeds now include prebiotics and probiotics, as well as polyunsaturated fatty acids and nucleotides. Whether or not these provide additional clinical benefit is often uncertain. Given that breastmilk is a biological fluid, whose composition changes during feeds and as the infant matures, it is unlikely that an artificial feed will ever mimic the complexity of breast milk.

There is no evidence that any one of the many brands of formula milk is superior to any other. Feeding equipment should be sterilized, and instructions to prepare the milk followed accurately to avoid infection and ensure the milk is properly constituted.

The WHO has introduced a code of marketing breast milk substitutes which prohibits any advertising of infant formula, bottles and teats and gifts to mothers or inducements to health workers in order to avoid undermining breastfeeding.

Introduction of whole, pasteurized cow's milk as main drink

Breastfeeding or formula feeding is recommended until at least 12 months of age. Pasteurized cow's milk is not recommended as a main drink in place of either breastmilk or infant formula before 12 months of age, as it is associated with increased risk of iron deficiency, due to the low levels of iron present. It can, however, be incorporated into the diet once weaning has commenced (unless there is an allergy to cow's milk), for example, added to mashed potato.

Over the age of 1 year, whole cow's milk can be used in place of infant formula, as solid food should provide adequate iron intake. From 2 years of age, semi-skimmed

cow's milk can be introduced, if there are no concerns with growth and energy intake, and skimmed milk may be used in children over 5 years of age.

Specialized infant formula

In a standard infant formula, the protein is derived from cow's milk protein, the carbohydrate is lactose, and the fat is mainly long-chain triglycerides. There are numerous specialized formula feeds designed for specific medical conditions which modify or replace these constituents. They include:

- preterm formula – increased energy, sodium, calcium, phosphate to match requirements of preterm infants
- extensively hydrolysed and amino acid formula – for treatment of cow's milk protein allergy
- medium-chain triglycerides formula for disorders of fat malabsorption – do not need pancreatic enzymes nor bile salts as directly absorbed into the small intestine
- soya based formula – originally developed for infants with cow's milk protein allergy, but a hydrolysed and amino acid formula is now used as a proportion of these infants are also allergic to soy protein. They are not advised under 6 months and usually avoided in the first year, after which normal soya milk can be

used. This is because of concern that they contain phytoestrogens (plant substances that mimic the effects of endogenous oestrogens), though there is no conclusive evidence of adverse clinical effects

- anti-gastro-oesophageal reflux pre-thickened formulas – contain rice starch or carob bean gum and become more viscous in the stomach with fall in pH. These, as well as thickeners designed to be added to standard formula or given as a paste before a breastfeed, can be used for the treatment of uncomplicated gastro-oesophageal reflux.

Details of all standard and specialist formula feeds can be found in the *British National Formulary for Children*, or *First Steps Nutrition*.

Weaning

The WHO recommend exclusive breastfeeding for 6 months, to prevent gastroenteritis and other infections. After 6 months of age, breast milk becomes increasingly nutritionally inadequate as a sole feed, as it does not provide sufficient energy, vitamins or iron. In many high-income countries, including the UK, complementary feeds are usually introduced at 4–6 months.

Weaning onto solid food is done gradually, often initially with small quantities of pureed fruit, root vegetables



Case history 13.1

Multidisciplinary assessment and gastrostomy insertion

Maya, a 4-year-old girl with spastic cerebral palsy, developed a chest infection. She had been feeding orally on pureed foods and fluids, but meals were taking over an hour to finish. A speech and language therapist assessed the safety of her swallow and a videofluoroscopy undertaken showed she was aspirating fluids but not thickened feeds. Despite manipulation of her diet, sufficient food and fluid intake could not be achieved. She was admitted to her local hospital for a nasogastric tube placement to start supplemental feeds and fluids and referred to the multidisciplinary

feeding clinic. A percutaneous endoscopic gastrostomy (PEG) (Fig. 13.8) was inserted, to allow her oral feeds to be supplemented. Maya was discharged home after her parents completed a competency training package with support in place by community nurses. The PEG was subsequently replaced with a gastrostomy button (Fig. 13.9), to further simplify access.

Maya continues to be reviewed regularly in the feeding clinic to assess her growth and alter her feeding regime as required.



Figure 13.8 Percutaneous endoscopic gastrostomy (PEG) for enteral feeding. Unlike a nasogastric tube, a gastrostomy tube is not usually visible to others and is less likely to be accidentally displaced. (Courtesy of Joanne Hadfield.)



Figure 13.9 Widely used gastrostomy buttons. (Courtesy of Joanne Hadfield.)

or rice. Foods high in salt and sugar should be avoided and honey must not be given until 1 year of age because of risk of infantile botulism. Early introduction of common allergens such as egg and peanut at, or around 4 months of age in infants at high risk of developing IgE-mediated allergy may reduce the risk of developing allergy to these foods.

Additional nutritional support

Children with long-term illnesses may benefit from supplemental nutritional support, which may be provided by the enteral or parenteral route ([Case history 13.1](#)).

Enteral nutrition

Enteral nutrition is used when the digestive tract is functioning, as it maintains gut function and is safe. Feeds are given nasogastrically, by gastrostomy or occasionally via a feeding tube in the jejunum (e.g. if there are problems with vomiting or gastric emptying). In some children who require supplementary feeds due to high energy requirements such as in cystic fibrosis, they can be given continuously overnight, with the child feeding orally during the day. Gastrostomies can either be created endoscopically or surgically. If long-term supplemental enteral nutrition is required (>6 weeks), a gastrostomy is preferred as it avoids repeated replacement of nasogastric tubes which is distressing for the child.

Parenteral nutrition (PN)

'Parenteral' means 'bypassing the gut', and can be used exclusively ('total parenteral nutrition' or 'TPN'), or as an adjunct to enteral feeds to maintain and/or enhance nutrition. The aim is to provide a nutritionally complete feed in an appropriate volume of intravenous fluid. Energy is given as glucose together with a fat emulsion (usually derived from soya bean oil, sometimes combined with fish oil, medium chain triglycerides and olive oil), nitrogen is supplied as synthetic amino acids, resembling the amino acid profile of either egg protein, breast milk or cord blood (depending on the product used). Electrolytes and a full range of vitamins, micronutrients, and trace elements are also given. Clinical deficiencies (such as zinc deficiency) may occur, and monitoring is required.

Many patients, such as extremely preterm infants with an immature gastrointestinal tract, require PN for only a few weeks until they are able to tolerate full enteral feeds. Some children depend on long-term PN, and if their condition is stable can be managed at home, with PN being given overnight so that they are not tied to an infusion pump during the day ([Fig. 13.10](#)). Conditions necessitating long-term PN are short bowel syndrome (e.g. following complicated gastroschisis, or a volvulus), enteropathies (often causing severe diarrhoea in very early life), or a motility disorder such as long-segment Hirschsprung disease. PN is complex and expensive, requires a multidisciplinary team incorporating not only medical and nursing staff but also pharmacists, dietitians, surgeons and interventional radiologists. Short term, it is possible to deliver it via a long line in a peripheral vein (PICC line); long term it is delivered via a central venous catheter (CVC) as this allows infusion of hyperosmolar solutions and reliable venous access. Complications include CVC sepsis or blockage, venous thrombosis and intestinal failure-associated liver disease.



Figure 13.10 Home parenteral nutrition for patients with intestinal failure is associated with good quality of life. This boy has remained well on parenteral nutrition (now 5 nights a week) since he was a newborn infant. His parenteral nutrition is being set up whilst on a camping holiday.

Summary

Additional nutritional support

- Enteral tube feeding can help maintain nutritional status during acute illness, when oral intake is compromised.
- Feeds (bolus or continuous by a pump) can be delivered into the stomach by nasogastric or gastrostomy tubes (preferred when long-term feeding required).
- Parenteral (intravenous) nutrition is used when the gut is incapable of absorbing adequate nutrition to meet requirements.

Faltering growth

Faltering growth is a descriptive term to describe suboptimal weight or rate of weight gain in infants or young children, adjusted for age and sex. If prolonged and severe, it will result in reduction in height or length (stunting) and reduction in head growth and may be associated with delayed development. Terminology around the subject is confusing. It was previously called 'failure to thrive', but the term has fallen out of favour in the UK as it is regarded as somewhat pejorative, but is still used in other countries. Short length or height or suboptimal gain in height is considered under short stature in [Chapter 12](#) (Growth and puberty).

Identifying weight faltering

In clinical practice, faltering weight is often defined as a fall in weight of two or more major centile lines, or weight centile two or more centiles below length/height, or head circumference centile or a weight centile below the 2nd centile for age. Its identification relies on plotting serial measurements of weight, length or height and/or head circumference on a WHO growth chart for boys or girls (see Appendix [Fig. A.1](#) for the charts). Without serial measurements, the trends of growth cannot be seen. One-off

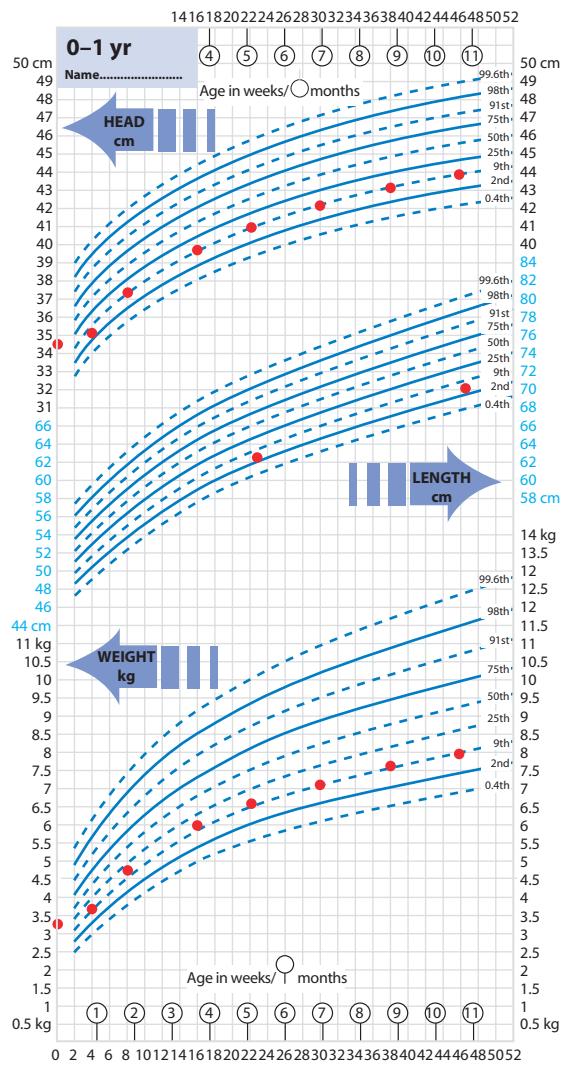


Figure 13.11 Growth chart showing normal weight gain and growth in a constitutionally small infant. The further below the 2nd, and especially the 0.4th, centile, the more likely it is that there will be an organic cause. (Chart © RCPCH, WHO, Department of Health.)

measurements are difficult to interpret, and potential problems can be missed.

Although healthy children's weight will fluctuate, it will usually progress within one centile space (the distance between two major centile lines on the growth chart). However, size at birth is not indicative of the subsequent centile for individuals, as it is determined not only by genes but also by the intrauterine environment. Over the first few months after birth, infants who are large at birth will often cross down centiles (catch-down growth), whereas small babies will move up centiles (catch-up growth) to find their genetic centile growth lines. In addition, babies often lose up to 10% of birthweight in the first few days of life from fluid shifts, but should have regained birthweight by 2 weeks. This is why the UK-WHO growth charts centile lines start at 2 weeks of age, rather than birth. Infants who become acutely ill will often lose weight, but will regain their weight centile within 2 weeks to 3 weeks.

The infant with growth faltering needs to be differentiated from a normal but small or thin baby ([Fig. 13.11](#)). If the child was born preterm, this should be allowed for when plotting growth during the first 2 years of age. Some infants with severe intrauterine growth restriction remain small, though most exhibit catch-up growth.

Clinical features and investigation

If weight/growth faltering is identified, a dietary history should be taken to include:

- history of milk feeding
- age at weaning
- range and type of foods now taken
- mealtime routine and eating and feeding behaviours
- a 3-day food diary – will provide a more detailed and accurate picture of intake
- if possible, observe a meal being taken.

Consider also:

- Was the child born preterm or did the child have intrauterine growth restriction?
- Is the child well with lots of energy or does the child have other symptoms such as diarrhoea, vomiting, cough, or lethargy?
- What is the growth of other family members and are there any illnesses in the family?
- Is the child's development normal?
- Are there psychosocial problems at home?

On examination, look for signs of organic pathology, such as:

- dysmorphic features in genetic conditions
- evidence of nutritional deficiencies such as koilonychia, angular stomatitis
- signs suggestive of chronic respiratory disease
- heart murmur or signs of heart failure from congenital heart disease
- distended abdomen, thin buttocks, misery in malabsorption.

The differential diagnosis is shown in [Fig. 13.12](#). In most, no underlying pathology is identified, the problem being inadequate food intake. When there is an organic cause, which occurs in only about 5%, there are usually symptoms and signs suggestive of the underlying disease. Investigations to be considered are listed in [Box 13.2](#), depending on clinical findings. A full blood count and serum ferritin may be helpful to identify iron-deficiency anaemia, which is usually secondary to inadequate iron intake and correcting it may improve appetite. Coeliac disease and urinary tract infection in particular need to be considered. Although faltering growth is often considered to be a manifestation of poverty (and is certainly the case in poorer societies), studies in the UK have not found an association with low socio-economic status or poor maternal educational attainment. While neglect and safeguarding must always be considered, it is an unusual cause. Evidence for the role of maternal depression is conflicting, with some studies suggesting an association and others being unable to demonstrate a link.

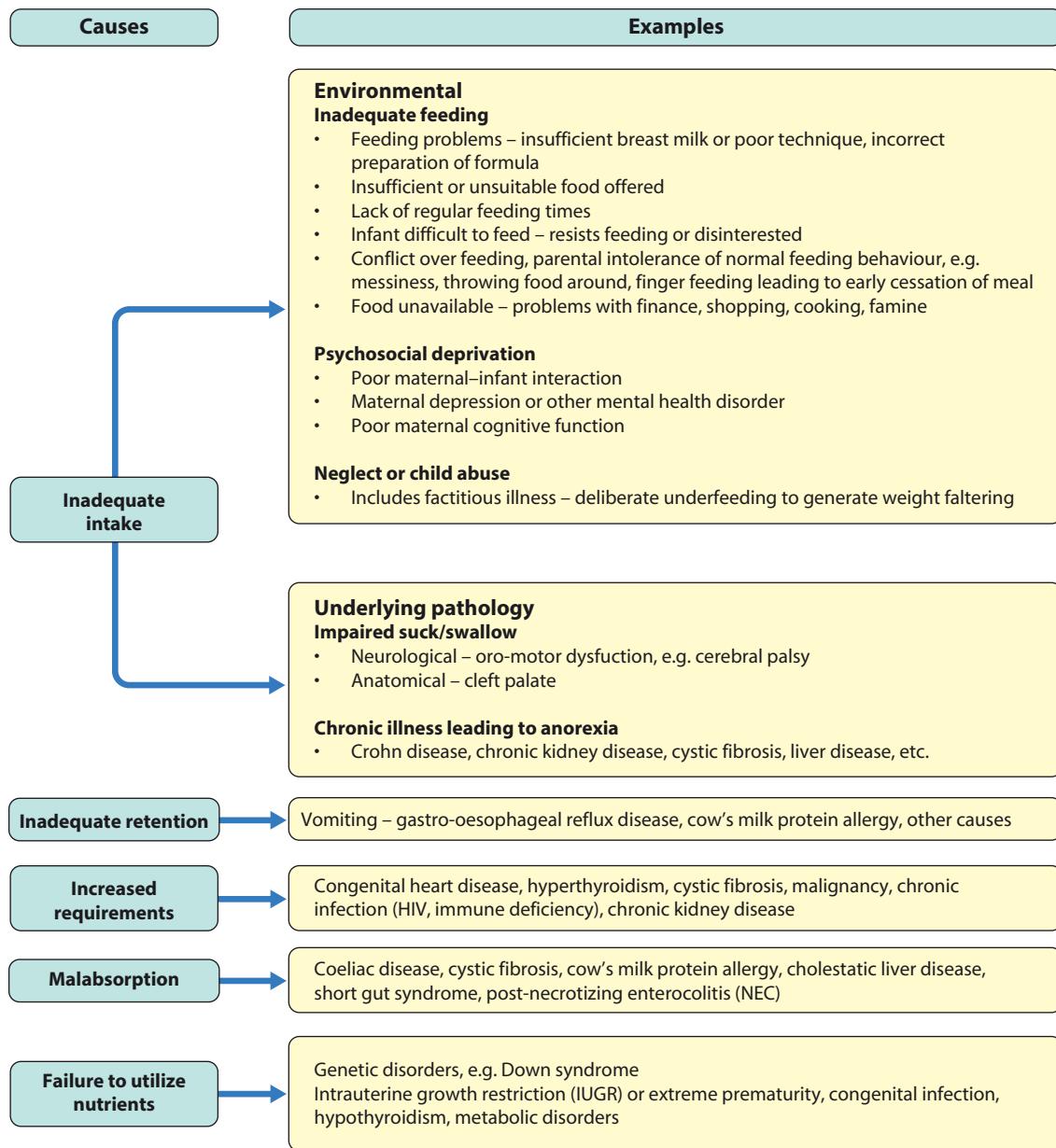


Figure 13.12 Causes of growth faltering.

Management

The management of most faltering growth is carried out in primary care ([Case history 13.2](#)). Using mealtime observations and food diaries, health visitors can assess and support families to improve feeding and increase calorie intake. If indicated, a paediatric dietitian is helpful in assessing the quantity and composition of food intake, recommending strategies for increasing energy intake, and a speech and language therapist has specialist skills with feeding disorders. Input from a clinical psychologist and from social services may also be beneficial. Nursery placement can be helpful in alleviating stress at home and assisting with feeding, as can mothers' or parents' groups with meetings held in person or via the internet. The key outcome measure is to demonstrate weight gain, with a rise up the weight centiles; this usually begins 4 weeks to 8 weeks after intervention.

In children with severe weight faltering, hospital admission may be necessary for active refeeding and multidisciplinary team involvement.

Summary

Faltering growth

- Faltering growth is a description, not a diagnosis.
- Weight, length/height and head circumference measured accurately and plotted on a growth chart is required for its recognition.
- Is present if an infant's weight falls across two centile spaces.
- Also needs to be considered if weight is below the second centile for age or more than two centiles below length/height or head circumference centile.
- Although complex in origin and multifactorial, the final common pathway is usually inadequate food intake.
- If there is underlying pathology, it is usually accompanied by abnormal symptoms or signs.
- Most affected infants and toddlers are managed in primary care by dietary and behavioural modification to improve food intake and by monitoring growth.



Case history 13.2

Weight faltering

Jamie, aged 11 months, was causing concern to his health visitor as he was not putting on weight (Fig. 13.13). She arranged for him to be assessed by his general practitioner, who found that he was otherwise well. His mother was a

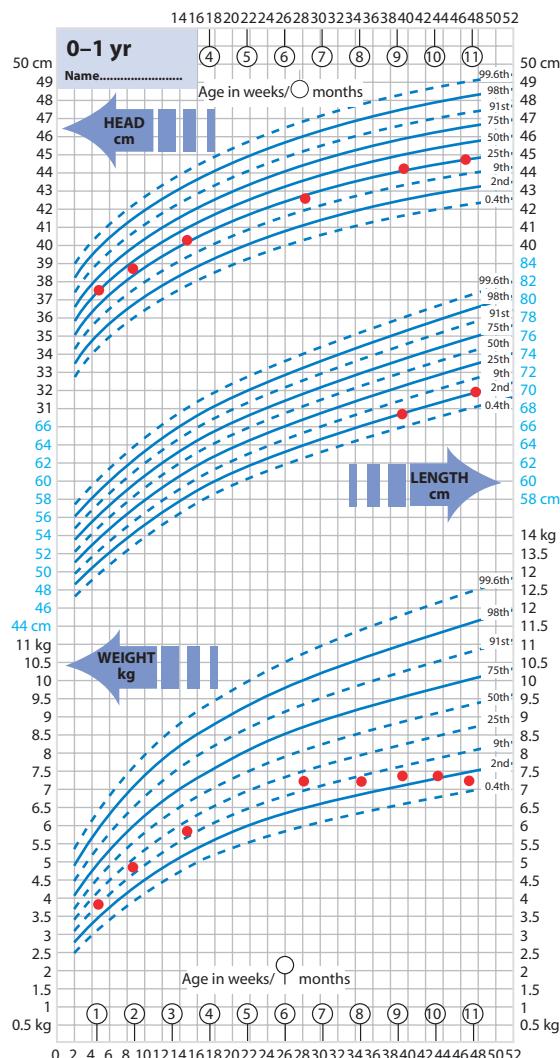


Figure 13.13 Jamie's growth chart. (Chart © RCPCH, WHO, Department of Health.)

Vitamin D deficiency

Vitamin D is derived from two main sources: synthesis in the skin (vitamin D₃) following exposure to ultraviolet B light (UVB) or from the diet (vitamin D₂ or D₃) (Fig. 13.14). The main functions of vitamin D are the regulation of calcium and phosphate metabolism, making it essential for bone health, but it also has functions in regulation of the immune system. The most common cause

of rickets, nutritional vitamin D deficiency, generally results from inadequate sunlight (UVB) exposure and, to a lesser extent, inadequate dietary intake of vitamin D and/or calcium. The pathophysiology of rickets is the same in vitamin D deficiency and inadequate dietary calcium intake (calcipenic rickets), in that inadequate absorption of calcium triggers the secretion of parathyroid hormone which acts in various ways to maintain serum calcium including demineralization of bone. Parathyroid hormone causes renal losses of phosphate,

On visiting the home, the health visitor found Jamie's mother to be tense and anxious about his weight loss. She fed Jamie the same food as she ate herself, together with cow's milk as his main drink, which she had started at 6 months of age. Mealtime was problematic as, after a few mouthfuls, Jamie stopped eating and his mother became frustrated and angry and tried to force him to eat his meal.

Jamie's health visitor suggested strategies for increasing Jamie's food intake (Box 13.1). She continued to provide support and encouragement to his mother and arranged a nursery placement for Jamie. He was weighed regularly, and by 18 months of age he had crossed one centile space upwards, but still ate erratically.

Box 13.1 Strategies for increasing energy intake

Dietary

- Three meals and two snacks each day
- Increase number and variety of foods offered and allow to self-feed, even if messy
- Increase energy density of foods (e.g. add cheese, butter, cream to fortify foods)
- Limit milk intake, use infant formula until 12 months of age
- Avoid excessive intake of fruit juice and diluted cordial drinks

Behavioural

- Offer meals at regular times
- Praise when food is eaten, ignore when not
- Limit mealtime to 30 minutes
- Eat at same time as child
- Avoid mealtime conflict
- Never force feed

Adapted from: Shields B, Wacogne I, Wright CM: Weight faltering and failure to thrive in infancy and early childhood. *BMJ* 245:e5931, 2012.

Box 13.2 Initial investigations to be considered in growth faltering when a pathological cause is suspected

Investigation	Interpreting result
Full blood count and differential white cell count	Anaemia, neutropenia, lymphopenia (immune deficiency)
Serum creatinine, urea, electrolytes, acid-base status, calcium, phosphate	Renal failure, renal tubular acidosis, metabolic disorders
Liver function tests	Liver disease, malabsorption, metabolic disorders
Thyroid function tests	Hypothyroidism or hyperthyroidism
Acute phase reactant, e.g. CRP (C-reactive protein)	Inflammation
Ferritin	Iron-deficiency anaemia
Immunoglobulins	Immune deficiency
IgA tTG (IgA tissue transglutaminase antibodies)	Celiac disease
Urine microscopy, culture, and dipsticks	Urinary tract infection, renal disease
Stool microscopy, culture, and elastase	Intestinal infection, parasites, elastase decreased in pancreatic insufficiency
Karyotype in girls	Turner syndrome
Sweat test, chest X-ray	Cystic fibrosis, other respiratory disorders

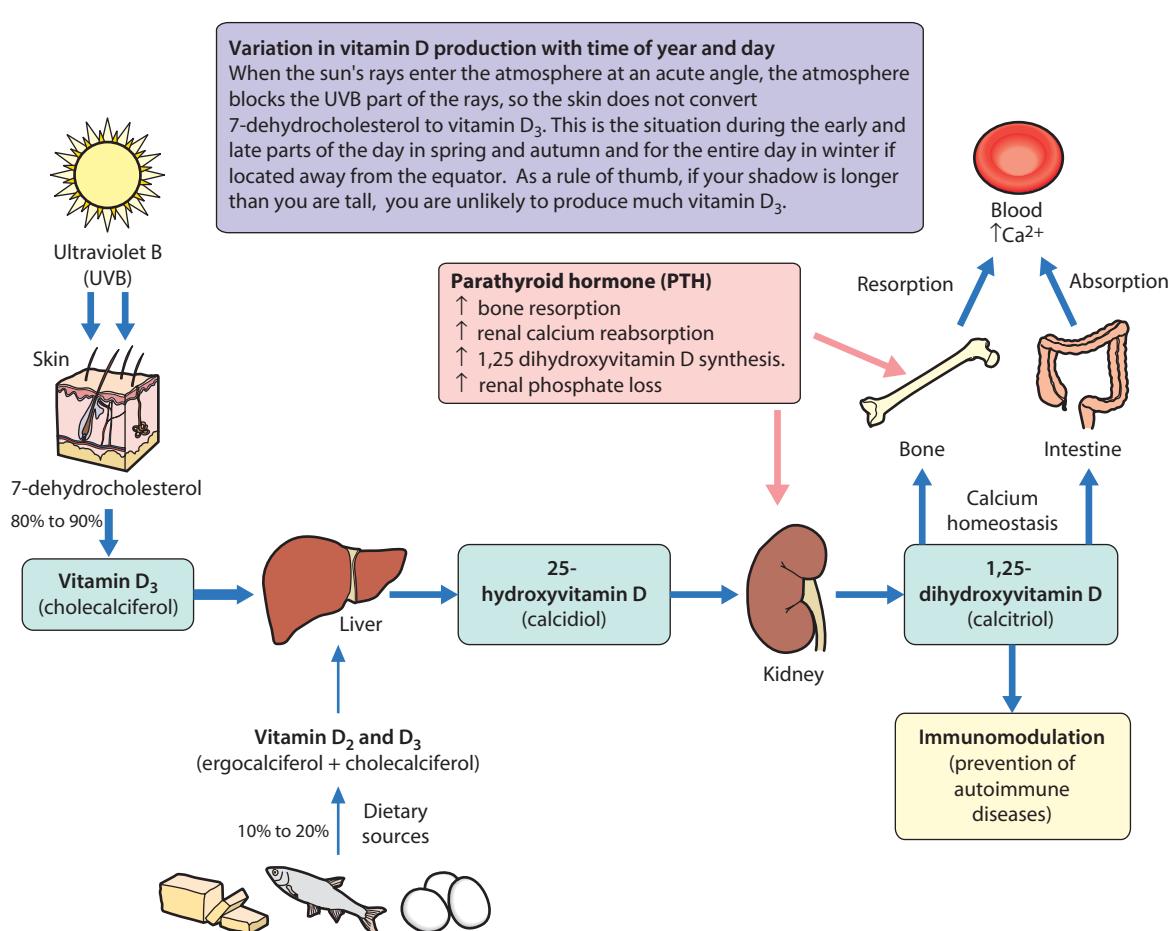


Figure 13.14 Vitamin D metabolism. In most countries, sunlight is the most important source of vitamin D. Vitamin D is not abundant naturally in food, except in fish liver oil, fatty fish, and egg yolk. Vitamin D₂ (ergocalciferol) is the form used to fortify food such as margarine. Vitamin D is hydroxylated in the liver and again in the kidney to produce 1,25-dihydroxyvitamin D, the most active form of the vitamin. Parathyroid hormone (PTH) is secreted in response to low levels of serum calcium. It acts on receptors in bone and kidney to increase calcium resorption (pink arrows).

and the resulting low serum phosphate levels cause the changes in the growth plate which characterize rickets.

Vitamin D deficiency usually presents with tiredness and pain in the leg bones which is worse on exertion. Bony deformity may follow resulting in the classical features of rickets. It can also present with symptoms of hypocalcaemia, e.g. seizures, neuromuscular irritability causing muscle spasm of the hands and feet (tetany), apnoea, stridor, and cardiomyopathy. This presentation is more common before 2 years of age and in adolescence, when a high demand for calcium in rapidly growing bone may result in hypocalcaemia before rickets develops.

Rickets

Rickets signifies a failure in mineralization of bone tissue and characteristic changes in the growth plates within growing bones. Failure of mature bone to mineralize is osteomalacia.

Aetiology

The causes of rickets are listed in [Box 13.3](#). The predominant cause of rickets during the early twentieth century was nutritional vitamin D deficiency due to inadequate intake or insufficient exposure to direct sunlight. Nutritional rickets remains the major cause in low- and middle-income countries. In high-income countries, nutritional rickets has become rare, as formula milk and many foods such as breakfast cereals are supplemented with vitamin D. However, nutritional rickets has re-emerged in high-income countries in black or Asian infants totally breastfed in late infancy. It is also seen in extremely preterm infants due to the difficulty of

providing sufficient nutritional calcium and phosphorus to ensure adequate mineral accretion within the rapidly growing skeleton.

Clinical manifestations

Children with vitamin D deficiency and/or calciopenic rickets are often miserable. The costochondral junctions may be palpable (rachitic rosary), wrists (especially in crawling infants) and ankles (especially in walking infants) may be widened, and there may be a horizontal depression on the lower chest corresponding to attachment of the softened ribs with the diaphragm (Harrison sulcus; [Fig. 13.15](#)). Once the child has started weight-bearing, the legs may become bowed ([Fig. 13.16](#)). One of the earliest clinical signs of rickets is softening of the skull vault (craniotabes), elicited by careful application of pressure over the occipital or posterior parietal bones producing a sensation similar to pressing a ping-pong ball. A comprehensive list of clinical features are listed in [Box 13.4](#) (see also [Case history 13.3](#)).

Diagnosis

This is made from:

- dietary history (prolonged breastfeeding)
- blood tests – biochemical findings depend on the stage of vitamin D deficiency, i.e. degree of decompensation of serum mineral homeostasis. In most cases of established vitamin D deficiency / calciopenic rickets, blood tests reveal a low or normal calcium, low phosphate, high alkaline phosphatase activity, low 25-hydroxyvitamin D, and high parathyroid hormone
- X-ray of the wrist or knee – shows cupping and fraying of the metaphyses and a widened growth plate.

Box 13.3 Causes of rickets

Nutritional (primary) rickets – risk factors

- Living in northern latitudes
- Dark skin
- Decreased exposure to sunlight
- Diets low in calcium, and vitamin D, e.g. exclusive breastfeeding into late infancy or, rarely, toddlers on unsupervised 'dairy-free' diets
- Extreme prematurity – inadequate phosphate intake in breast milk and parenteral nutrition
- Macrobiotic, strict vegan diets
- Prolonged parenteral nutrition in infancy

Intestinal malabsorption

- Small bowel enteropathy (e.g. coeliac disease)
- Pancreatic insufficiency (e.g. cystic fibrosis)
- Cholestatic liver disease
- High phytic acids in diet (e.g. chapattis)

Defective production of 25-hydroxyvitamin D

- Chronic liver disease

Increased breakdown of 25-hydroxyvitamin D

- Enzyme induction by anticonvulsants (e.g. phenobarbital)

Defective production of 1,25-dihydroxyvitamin D

- Chronic kidney disease
- Fanconi syndrome (renal loss of phosphate)
- Inherited disorders (rare) e.g. vitamin D-dependent rickets type 1

Resistance to effect of 1,25-dihydroxyvitamin D

- Vitamin D-dependent rickets type 2

Hypophosphataemic rickets

- X-linked hypophosphataemic rickets
- Other inherited types of hypophosphataemic rickets
- Hypophosphataemia due to primary or secondary tubulopathy
- Lack of bioavailable dietary phosphate (rare)

Rickets

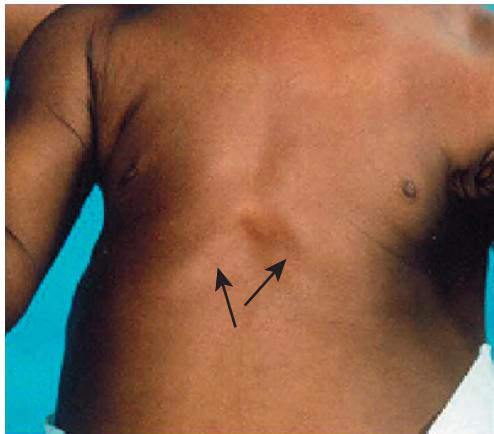


Figure 13.15 Harrison sulcus, indentation of the softened lower ribcage at the site of attachment of the diaphragm. (Courtesy of Nick Shaw.)



Figure 13.16 Severe rickets in a 3-year-old boy secondary to coeliac disease. He has frontal bossing, a Harrison sulcus and bowing of the legs. (Courtesy of Ian Booth.)

Box 13.4 Clinical features of hypocalcaemia and rickets

- Misery
- Poor growth/short stature
- Frontal bossing of skull
- Craniotabes
- Delayed closure of anterior fontanelle
- Delayed dentition
- Enamel hypoplasia
- Ricketty rosary
- Harrison sulcus
- Expansion of metaphyses (especially wrist)
- Bowing of weight-bearing bones
- Pathological fractures
- Hypotonia
- Delayed motor milestones
- Seizures
- Cardiomyopathy/heart failure

Management

Nutritional rickets is managed with vitamin D and ensuring adequate dietary calcium. If compliance is an issue, a single high dose (oral or intramuscular) of vitamin D₃ can be given, followed by the daily maintenance dose. Bone healing starts within 2–4 weeks but may take several years for all bony deformities to resolve. In order to prevent recurrence and maintain optimal bone health, advice on safe sunlight exposure, balanced diet, and correction of predisposing risk factors should be given.

Other vitamin deficiencies

These are shown in [Table 13.3](#).

Summary

Rickets

- Nutritional rickets is an important cause of rickets in the UK. Darker skin colour and prolonged breastfeeding in late infancy without complementary feeding are risk factors.
- Diagnosis – serum calcium is low or normal, phosphorus low, plasma alkaline phosphatase markedly raised, 25-hydroxyvitamin D low and parathyroid hormone raised.
- X-ray features – cupping and fraying of the metaphyses and widened growth plate.



Case history 13.3

Seizures and rickets

Mohammed, a 13-month-old boy, was admitted to the emergency department with a generalized afebrile seizure. This was initially controlled with per rectum diazepam. Some 20 minutes later he had another generalized seizure and needed an intravenous anticonvulsant to control his seizure.

His mother said that he was a healthy child. He was born at term, birthweight 3.1 kg, and was still breastfed. Some weaning foods were started at 7–8 months of age, but he preferred feeding at the breast. He had only recently begun to sit without support.

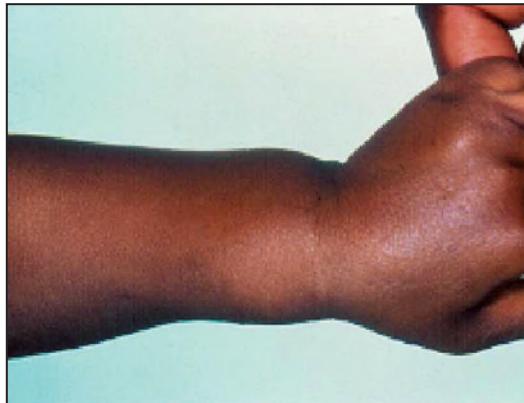


Figure 13.17 Wrist expansion from rickets. (Courtesy of Nick Shaw.)

His weight and head circumference were on the second to ninth centile. He had marked frontal bossing, widened wrist (Fig. 13.17) and other epiphyses, Harrison sulci, wide anterior fontanelle, craniotabes and a rachitic rosary. He would not take his weight on standing.

Investigations showed low plasma calcium and phosphate concentrations, a high alkaline phosphatase and parathyroid hormone, and a very low vitamin D, consistent with vitamin D deficiency/calcioopenic rickets. Liver and renal function tests were normal, and coeliac serology was negative. His wrist X-ray showed characteristic features (Fig. 13.18).

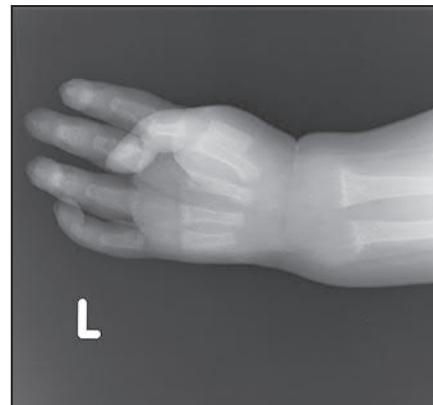


Figure 13.18 X-ray of the child's wrist showing rickets. The ends of the radius and ulna are expanded, rarefied, and cup-shaped, and the bones are poorly mineralized. (Courtesy of Paul Arundel.)

Malnutrition

Worldwide, malnutrition is responsible directly or indirectly for over one-third of all deaths of children under 5 years of age (see Ch. 31, Global child health). Malnutrition from inadequate food intake also continues to occur in high-income countries as a result of poverty, parental neglect or poor education. Mild or moderate malnutrition also occurs in 20%–40% of children in specialist children's hospitals in high-income countries, particularly those with long-term illness. Malnutrition results from anorexia, malabsorption and increased energy requirements because of infection or inflammation. Malnutrition may also result from restrictive diets, which may be iatrogenic or from parental choice, or in older children and adolescents, from dieting to lose weight or eating disorders. Specific nutritional deficiencies, particularly of iron and vitamin D, remain common in high-income countries.

There is increasing concern about the 'double burden of malnutrition' in many low- and middle-income countries as food availability is changing rapidly. Exposure to undernutrition early in life is now increasingly followed by becoming overweight from childhood onwards, with its increased risk of a range of non-communicable

diseases – making it a key factor driving the emerging global epidemic of type 2 diabetes, high blood pressure, stroke, and cardiovascular disease. This combination of negative effects can also pass between generations – for example, maternal obesity increases the likelihood of the child being obese.

Assessment of nutritional status

Assessment is usually with anthropometry.

Anthropometry

Weight and height and mid-upper-arm circumference (MUAC) are key measurements. The WHO recommends that nutritional status is expressed as:

- weight for height – a measure of wasting and an index of acute malnutrition. The weight is plotted against height on a WHO standard growth chart. Severe malnutrition is more than 3 standard deviations (SDs) from the median ('z-score -3'), moderate is 2 to 3 SDs below the median.

Table 13.3 Vitamin deficiencies affecting children

Vitamin	Dietary/environmental sources	When deficiency is encountered	Clinical consequences
Fat-soluble vitamins			
A	Retinol: Liver, fish liver oils, dairy products Carotenoids: in spinach, carrots, mango, papaya	Fat malabsorption conditions e.g. cystic fibrosis Children in low-income countries who do not receive supplements	Increased susceptibility to infection, especially measles Xerophthalmia (dryness of the conjunctiva and cornea) Night blindness
D	90% from ultraviolet B exposure Eggs Fortified foods including margarine, certain yoghurts and breakfast cereals	Children who live further from the Equator, as ultraviolet B levels are low outside summer months Children with darker skin or when exposure to sunlight is limited	Rickets
E	Vegetable oils	Fat malabsorption conditions Preterm infants	Haemolytic anaemia, retinopathy, progressive neuropathy
K	Green leafy vegetables – the richest sources Other vegetables, fruits, dairy produce, vegetable oils, meats and cereals Synthesized by intestinal bacteria Given intramuscularly (occasionally orally) at birth (see Ch. 10, Perinatal medicine)	Newborn infants are vitamin K deficient Seen in children with fat malabsorption	Coagulation abnormalities - lead to bruising/bleeding from vitamin K deficient bleeding (haemorrhagic disease of the newborn)
Water-soluble vitamins			
Thiamine (B₁)	Yeast, brown rice, wheatgerm, nuts, pork, pulses	Deficiency is beri-beri Children from South East Asia with a 'polished rice diet' or those with malnutrition	Cardiomyopathy in infants, also hoarseness, aphonia, encephalopathy, apathy, drowsiness, seizures
Riboflavin (B₂)	Yeast, organ meats (such as liver and kidney), lean meat, milk and milk products, eggs, vegetables, fortified breakfast cereals	Malnutrition	Angular stomatitis, fissuring of lips
Niacin (B₃)	Liver, meat, oily fish, soya, nuts, seeds, pulses, eggs, dairy products, grains	Deficiency is pellagra Malnutrition Regions where maize a major part of the diet	Thick, scaly skin, swollen mouth, fatigue, vomiting and diarrhoea
Pantothenic acid (B₅)	Found in animal and plant products	Very rare as found in almost all foods Can occur in starvation	Fatigue, apathy, paraesthesia, muscle cramps, hypoglycaemia
Pyridoxine (B₆)	Found in a wide variety of foods Also synthesized by intestinal bacteria	Isolated deficiency is rare. Can be found together with B ₁₂ and folic acid deficiency	Microcytic anaemia, glossitis, cheilosis, confusion, increased susceptibility to infection
B₁₂	All animal products, yeast extract	Children on a vegan diet, not receiving supplementation Resection of small intestine where B ₁₂ is absorbed Pernicious anaemia	Megaloblastic anaemia, weakness and fatigue, paraesthesia
Vitamin C	Fresh fruit and vegetables	Deficiency is scurvy Rare but can occur in children with very restrictive diets or neurodisability	Petechiae and bruising, gingivitis, coiled hair, poor growth, irritability; painful joints, impaired wound healing
Folic acid	Green leafy vegetables, yeast extracts, liver, fortified breakfast cereals	Children taking antifolate medications or those with haemolytic conditions Malnutrition	Macrocytic anaemia, neutropenia, thrombocytopenia



Figure 13.19 Mid-upper-arm circumference (MUAC) measurement to identify malnutrition. It is colour-coded; amber is moderate malnutrition, red is severe (<115 mm).

- mid-upper-arm circumference (MUAC) – is related to skeletal muscle mass and is independent of age from 6 months to 5 years. It can be measured easily and repeatedly with a colour-coded tape measure (Fig. 13.19). This is widely used in low- and middle-income countries to screen for malnutrition in the community. Severe malnutrition is MUAC <115 mm in children 6 months to 5 years old.
- height for age – a measure of stunting and an index of chronic malnutrition. Stunting is more than 2 SD (more than 2 z-scores) below median.

Skinfold thickness of the triceps reflects subcutaneous fat stores and can be measured with calipers, but is difficult to measure accurately in young children.

Other methods to assess nutritional status

If indicated, this includes undertaking a detailed dietary assessment, laboratory investigations, such as basic haematological and biochemical indices, micronutrient levels, and body composition measurements.

Consequences of malnutrition

Malnutrition is a multisystem disorder. When severe, immunity is impaired, wound healing is delayed and operative morbidity and mortality increased. There is an increased risk of developing diarrhoea, pneumonia and sepsis. Malnutrition worsens the outcome of illness, e.g. respiratory muscle weakness may delay a child being weaned from mechanical ventilation. Malnourished children are less active and more apathetic. These behavioural abnormalities are rapidly reversed with proper feeding, but prolonged and profound malnutrition can cause permanent impairment in cognitive development.

Severe malnutrition

Severe malnutrition causes protein-calorie malnutrition, which is classified, depending on the presence or absence of oedema, as:

- marasmus
- kwashiorkor
- a combination ('marasmic kwashiorkor').

In marasmus, the child has a wasted, wizened appearance (Fig. 13.20). Oedema is not present. Affected children are often withdrawn and apathetic.



Figure 13.20 Marasmus in a 3-month-old baby who was unable to establish breastfeeding because of a cleft palate.

In kwashiorkor, intravascular protein depletion causes generalized oedema on top of the severe wasting (Fig. 13.21). The child's weight may not be as severely reduced as in marasmus, but this is falsely reassuring, as it is due to the weight of retained fluid. In addition, there may be:

- a 'flaky-paint' skin rash with hyperkeratosis (thickened skin) and desquamation
- a distended abdomen and enlarged liver (usually due to fatty infiltration)
- angular stomatitis
- hair that is sparse and depigmented
- diarrhoea, hypothermia, bradycardia and hypotension
- low plasma albumin, potassium, glucose and magnesium levels.

It is unclear why some children with protein-energy malnutrition develop kwashiorkor and others develop marasmus. There is some evidence that kwashiorkor is a manifestation of primary protein deficiency with energy intake relatively well maintained. It often occurs in communities where infants are not weaned from the breast until about 12 months of age and the subsequent diet is relatively high in starch. Kwashiorkor often develops after an acute intercurrent infection, such as measles or gastroenteritis. In practice, it is sometimes difficult to clearly separate the two, when the term 'marasmic kwashiorkor' is used.

Management

Severe acute malnutrition usually results from limited access to food, poor diets, lack of education, and poor hygiene from poverty. It also occurs as a consequence of war and social disruption, as well as famine and natural disasters.

Most children with severe acute malnutrition have an appetite, are alert and can be managed within the community with ready-to-use therapeutic food (RUTF), which has revolutionized its treatment. It is based on peanut butter mixed with dried skimmed milk, vitamins and minerals, and is consumed directly by the child.

Children with no appetite, severe oedema, a medical complication or are less than 6 months old have complicated severe acute malnutrition and require hospital inpatient care; it has a high mortality, up to 30%. In addition to protein and energy deficiency, there is electrolyte and mineral deficiency (potassium, zinc and magnesium) as well as micronutrient and vitamin deficiency (vitamin A).

Acute management comprises the WHO's 10 essential steps. Stabilization is to:



(a)



(b)

Figure 13.21 Kwashiorkor, a particular manifestation of severe protein–energy malnutrition in some low-income countries, where infants are weaned late from the breast and the young child’s diet is high in starch. A key feature is oedema around the eyes, legs and feet (a). This is demonstrated in (b). There is also redness of the hair (see Figure 31.12 in Ch. 31), hyperkeratosis and depigmentation of the skin.

- treat or prevent hypoglycaemia urgently
- treat or prevent hypothermia
- treat or prevent dehydration – but avoid fluid overload. The standard WHO oral rehydration solution contains too much sodium (Na^+ 75 mmol/l) and too little potassium for severe acute malnutrition; they should be given a special rehydration solution – ReSoMal (rehydration solution for severely malnourished children). Rehydration should be provided orally, by nasogastric tube if necessary. Intravenous fluids are given only for shock
- correct electrolyte imbalance – especially potassium and magnesium. Although plasma sodium may be low, they have excess body sodium
- treat infection – give broad-spectrum antibiotics; fever and other signs may be absent. Treat oral *Candida* if present
- correct micronutrient deficiency – vitamin A and other vitamins; contained in specialized feeds. Introduction of iron is delayed to second week
- initiate feeding – small volumes, frequently, including through the night. Too rapid feeding may result in diarrhoea. Specialized feeds are widely available: initially Formula 75 (75 kcal/100 ml) which is low in protein and sodium and high in carbohydrate is used, subsequently Formula 100 (100 kcal/100 ml) or ready-to-use therapeutic food.

The remaining three steps are provided during rehabilitation:

- achieve catch-up growth
- provide sensory stimulation and emotional support
- provide for follow-up after recovery.

Catch-up growth is a key focus in the rehabilitation phase and the recommended energy and protein requirements are much higher.

Stunting

Approximately 22% of all children under 5 years worldwide were stunted in 2018. This makes them more susceptible to illness and more likely to fall behind at school. As adults, they have an increased risk of becoming obese and developing non-communicable diseases. A 40% reduction in the number of children who are stunted is a global target for 2025, and many multifaceted initiatives are underway.

Summary

Malnutrition

- Worldwide – contributes to about one-third of all childhood deaths.
- Can be identified by measuring weight for height, mid-upper-arm circumference (MUAC), and height for age.
- Marasmus – wasted, wizened appearance, apathetic.
- Kwashiorkor – generalized oedema, sparse and depigmented hair, skin rash, angular stomatitis, distended abdomen, enlarged liver, and diarrhoea.

Obesity

Obesity is the most common nutritional disorder affecting children and adolescents in high-income countries and is rapidly becoming a major problem in low- and middle-income countries in children of more affluent families. Its importance is in its short-term and long-term complications (Box 13.5) and that obese children are likely to become obese adults.

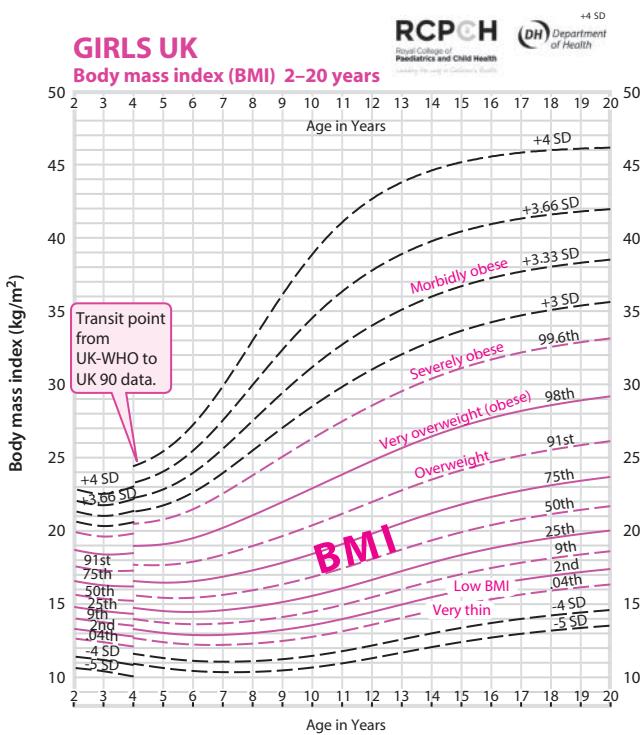


Figure 13.22 Body mass index centile chart for girls aged 2–20 years. (Source: © 2012/13 Royal College of Paediatrics and Child Health, reproduced with permission.)

Box 13.5 Complications of obesity

- Orthopaedic – slipped upper femoral epiphysis, tibia vara (bow legs), abnormal foot structure and function
- Idiopathic intracranial hypertension (headaches, blurred optic disc margins)
- Hypoventilation syndrome (daytime somnolence, sleep apnoea, snoring, hypercapnia, heart failure)
- Non-alcoholic fatty liver disease
- Gall bladder disease/gallstones
- Polycystic ovarian syndrome
- Type 2 diabetes mellitus
- Hypertension
- Abnormal blood lipids
- Other medical sequelae, e.g. asthma, changes in left ventricular mass, increased risk of certain malignancies (endometrial, breast, and colon cancer)
- Psychological sequelae – low self-esteem, teasing, depression

Definitions

In children, the Body Mass Index (BMI) is (weight in kg / (height in m)²) and is expressed as a BMI centile in relation to age-matched and sex-matched population. By convention in the UK, data from 1990 are used (Fig. 13.22). For clinical use, overweight is a BMI over the 91st centile, and obese is a BMI over the 98th centile.

In the UK, the National Child Measurement Programme measures height and weight of children in reception class at school (aged 4–5 years) and in year 6 (aged 10–11 years) to assess overweight and obesity at primary school. The prevalence of overweight (including

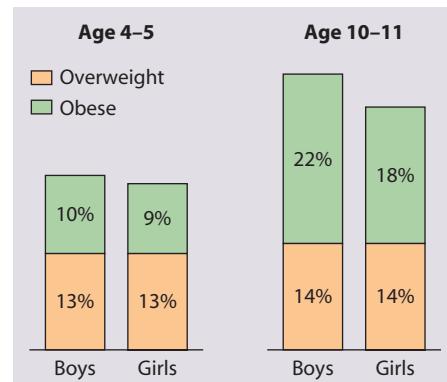


Figure 13.23 Marked increase in obesity and overweight in primary school children between school entry at 4–5 years and at final year at 10–11 years in England, 2018. One in ten children is obese by age 5, rising to one in five by age 11. (Source: National Childhood Measurement Programme 2018/19. Public Health England.)

obesity) between 2006/2007 and 2017/2018 in England is shown in Fig. 13.23. Whereas 22% are overweight or obese at 4 years and 5 years, this increases to 34% of 10- and 11-year-olds.



BMI in children is expressed as a centile, with overweight >91st centile, and obese >98th centile.

Aetiology

The reasons for this marked increase in prevalence are unclear but are due to changes in the nutrition and behaviour relating to diet and activity. Energy-dense foods are

now widely consumed, including sugar-sweetened drinks, high-fat fast foods and processed foods. However, there is no conclusive evidence that obese children eat more than children of normal weight. The National Food Survey showed that UK household energy intake has fallen since the 1970s, the amount of fruit purchased has increased by 75% and the intake of full fat milk has decreased by 80%. However, children's energy expenditure has undoubtedly decreased. Fewer children walk to school; transport in cars has increased; less time at school is spent doing physical activities; and children spend more time in front of small screens (video games, mobile phones, computers, and television), rather than playing outside. Children from low socio-economic homes are more likely to be obese; females from the lowest socio-economic quintile are 2.5 times more likely to be overweight when compared with the highest quintile.

Prevention

There are few randomized controlled trials and most involve complex packages of interventions including decreased fat intake, increased fruit and vegetables, reduction in time spent in front of small screens, increased physical activity, and education. Of these, a reduction in time spent on small screens appears to be the most effective single factor.

Endogenous causes

Oversupply accelerates linear growth and puberty. Obese children are therefore usually relatively tall and will usually be above the 50th centile for height. Therefore, if a child is obese and short with fall-off from height centiles, an endogenous cause, e.g. hypothyroidism and Cushing syndrome, should be considered. In children who are obese with learning disabilities or who are dysmorphic, an underlying syndrome may be present. The most common of these is Prader-Willi (obesity, hyperphagia, poor linear growth, dysmorphic facial features, hypotonia, and undescended testes in males; see Ch. 9, Genetics, and Fig. 9.13). In severely obese children under the age of 3 years, gene defects, e.g. leptin deficiency, are possible causes.

Management

Most obese children are managed in primary care. Specialist paediatric assessment is indicated in any child with complications (see Box 13.5) or if an endogenous cause is suspected.

In the absence of evidence from randomized controlled trials, a pragmatic approach in any individual child, based on consensus criteria, has to be adopted. Tailored clinical intervention should be considered when the child has a BMI at or above 91st centile taking into account the needs of the individual child and family. Consider assessing for comorbidities when the child has a BMI at or above the 98th centile.

Weight maintenance is a more realistic goal than weight reduction and will result in a demonstrable fall in BMI on their centile chart as height increases. It can only be achieved by sustained changes in lifestyle:

- healthier eating – regular meals; eating together as a family; choosing nutrient-rich foods that are lower

in energy and glycaemic index (the glycaemic index is a ranking of carbohydrate-containing foods based on the overall effect on blood glucose level; slowly absorbed foods have a low glycaemic index rating and those more rapidly absorbed a higher rating); increased vegetable and fruit intake; healthier snack food options; decreased portion sizes; drinking water as the main beverage; reduction in sugary drink intake; involvement of the entire family in making sustainable dietary changes

- physical activity can be increased by walking or cycling for transport, undertaking household chores, and playing. Organized exercise programmes have a role, with children and adolescents being encouraged to choose activities that they enjoy and are sustainable (e.g. football, dancing, swimming). At least 60 minutes of moderate or greater intensity physical activity is recommended each day
- limiting television and other small screen recreational activity to less than 2 hours per day.

Drug treatment and surgery

Drug treatment has a part to play in children and young people over the age of 12 years who have physical comorbidities (e.g. orthopaedic problems, sleep apnoea) or severe psychological problems. Orlistat is a lipase inhibitor which reduces the absorption of dietary fat and thus produces steatorrhoea. It may be indicated in exceptional circumstances, if there are severe comorbidities.

Bariatric surgery is generally not considered appropriate in children or young people unless they have achieved or nearly achieved maturity, have a BMI $>40\text{ kg/m}^2$ or more, or

Summary

Obesity

- An increasing major health issue for children, predisposing them to a wide range of medical and psychological problems in childhood and adult life, especially type 2 diabetes mellitus and cardiovascular disease.
- Defined as a BMI $>98\text{th}$ centile of the UK 1990 reference chart for age and sex; overweight is BMI $>91\text{st}$ centile.
- Endogenous causes (hypothyroidism and Cushing syndrome) of obesity are rare, and more likely in a child who is also short with fall-off from height centiles; there are also some rare genetic syndromes.
- Successful management requires sustained changes in lifestyle, with healthier eating, increased physical activity, and reduction in physical inactivity.
- Drug treatment and surgical intervention are only appropriate in a small number of children and young people.
- Lifestyle changes are difficult to achieve and even harder to maintain.
- A cultural change from an obesogenic environment is needed to reduce obesity in children and young people.

BMI between 35 kg/m² and 40 kg/m² with complications, e.g. type 2 diabetes or hypertension, and all other interventions have failed to achieve or maintain weight loss, are fit for anaesthetic and surgery, and commit to long-term follow-up.

Drug and surgical interventions should only be used in conjunction with a dietary, exercise and behavioural weight management programme and be restricted to specialist centres with multidisciplinary expertise in managing severe obesity.

Reducing the prevalence of obesity is a major public health issue and requires multi-component interventions. Programmes such as those providing family support for a healthy lifestyle for infants and young children (HENRY), and MEND (Mind, Exercise, Nutrition, Do it!) Foundation short-term programmes for overweight 7- to 13-year-old children in healthy eating, physical activity and behaviour change have been developed. However, they do not address the availability of unhealthy food or the increasingly obesogenic environment in many countries including the UK. There is recognition in the UK that there needs to be a more 'joined-up' approach to obesity, with integration between health services, local government and other key partners based on the needs of the local population.

Early childhood caries

Early childhood caries (ECC) or caries of primary dentition is a major public health problem worldwide. It is the most common cause for hospitalization in 5- to 9-year-olds; with over 28,000 hospital admissions in this age group in England in 2018, three times as many as for asthma. In England, it accounts for at least 60,000 days missed from school per year, and a national survey showed 12% of 3-year-olds have experience of dental caries; rising to 46% of 8-year-olds in their primary teeth and a similar proportion of 15-year-olds in their permanent teeth. Dental caries can lead to pain, difficulty eating and sleeping, and missing school, and it can adversely affect learning and growth. Children from the most deprived areas have more than twice the level of dental decay than in the least deprived areas.

Aetiology of dental caries

Dental caries (Fig. 13.24) is a dieto-bacterial disease resulting from an interaction between cariogenic diets and bacteria. Dental plaque is a polymicrobial biofilm which forms

on the surface of teeth. The caries process is a result of fermentation of dietary carbohydrates by enzymatic breakdown of sucrose by bacteria (predominantly *Streptococcus mutans* and *Streptococcus sobrinus*, which infants acquire from their mothers) in plaque. This produces acid as a by-product which can demineralize the tooth. When carbohydrates are no longer present, the acid is neutralized by the saliva, and remineralization occurs. If outweighed by demineralization, caries develops. This can progress through the dentine to the pulp which may become inflamed and infected. The frequency of food or beverage intake, regardless of cariogenic potential of specific foods, are independently associated with ECC, as frequent snacking provides the fuel for a sustained acidic environment which promotes demineralization. Other risk factors are sugar-containing foods. Children who drink juice between meals have been shown to have a higher incidence of ECC compared to those who drink water. For babies, milk and water are the safest daytime drinks. Feeding flavoured milk or adding sugar to drinks in a baby bottle before bed and through the night can cause nursing bottle caries due to demineralization, as the sugar is available for a prolonged period and the salivary protection is reduced at night.

Prevention of childhood caries

The cornerstone is diet assessment and counselling. In practice, a 3-day diet diary is provided to the parents and child, in which all meals and snacks consumed are listed. This is followed by an advisory session aimed at helping the family identify hidden sugars. Families can be advised to minimize consumption of cariogenic liquids (e.g. fruit juice, juice drinks, fizzy drinks, etc.), cariogenic solids (e.g. jam/jelly, sweetened cereal, cookies, etc.) and foods with hidden sugars (e.g. tomato ketchup, ready sauces and meals, cereal bars, canned soups, etc.), and to confine higher sugar products to mealtimes.

The top 3 interventions for preventing dental decay are:

- reducing the frequency of consumption of foods and drinks with added sugars, and keeping these products to mealtimes
- use of fluoridated toothpaste twice a day – last thing at night plus at least on one other occasion
- first visit to the dentist when the first baby (deciduous) tooth erupts, which is at about 6 months, and then on a regular basis.

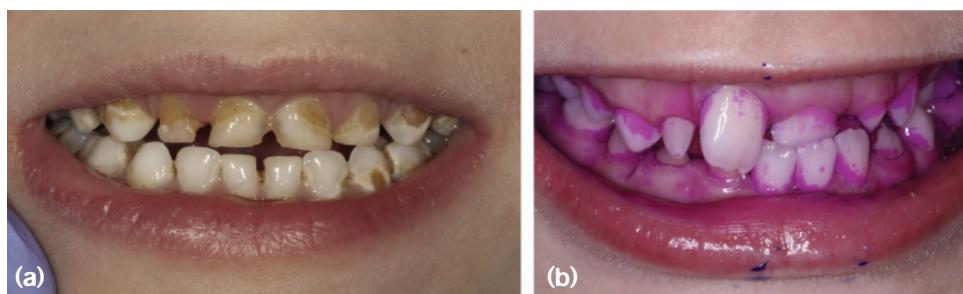


Figure 13.24 (a) Severe early childhood caries affecting the primary teeth of a 4 year old child. (b) Plaque identified by staining following use of a disclosing agent. (From: Clarke L, Stevens C: Preventing dental caries in children: Why improving children's oral health is everybody's business. Paediatrics and Child Health 29:12, 2019, Elsevier.)

Box 13.6 Summary of main points of national guidelines for prevention of caries in children aged 0–6 years

- Advice about prevention of caries in young children:
- Breastfeeding provides the best nutrition for babies
 - From 6 months of age infants should be introduced to drinking from a free-flow cup
 - From age 1 year feeding from a bottle should be discouraged
 - Sugar should not be added to weaning foods or drinks
 - Ask for sugar-free medication where possible
 - Parents or carers should brush or supervise toothbrushing until the age of 7 years
 - As soon as teeth erupt in the mouth, brush them twice daily with fluoridated toothpaste – a flat smear of toothpaste up to 3 years of age, a pea-sized amount of toothpaste thereafter
 - From 3 years onwards – to maintain fluoride concentration levels, spit out after brushing, do not rinse mouth

To facilitate effective tooth brushing, plaque can be visualized using disclosing agents (chewable tablets or solutions). Fluoride in toothpaste has been the single most effective oral health intervention. Water fluoridation is the only way to provide fluoride on a community basis without requiring behaviour change. Currently only 10% of the UK population benefit from a water supply naturally at the optimum level for dental health.

Dental Check By One is a nationwide campaign in the UK, launched in 2018, which aims to spread the message that ‘baby teeth matter’ and to encourage parents and carers to take children to the dentist when teeth first appear, or at the latest by their first birthday. National guidelines for prevention of caries in children aged 0–6 years have been published ([Box 13.6](#)).

Acknowledgements

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Gastroenterology

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Features of gastrointestinal disorders in children:

- Acute abdominal pain requires detailed evaluation to identify surgical, gastrointestinal and extra-gastrointestinal causes.
- Vomiting and diarrhoea are common and usually transient; serious causes are uncommon but important to identify.
- Worldwide, gastroenteritis is one of the most common causes of death in children under 5 years of age.
- The number of children and adolescents developing inflammatory bowel disease is increasing, but in contrast to adults, bowel cancer is extremely rare.

- Constipation is common and often requires long-term treatment.

Acute abdominal pain

Assessment of the child with acute abdominal pain requires considerable skill. The differential diagnosis of acute abdominal pain in children is extremely wide, including both surgical causes and medical conditions, not only of the gastrointestinal tract but also external to it (Fig. 14.1). Of the surgical causes, appendicitis is by far the most common. In children it is essential not to delay

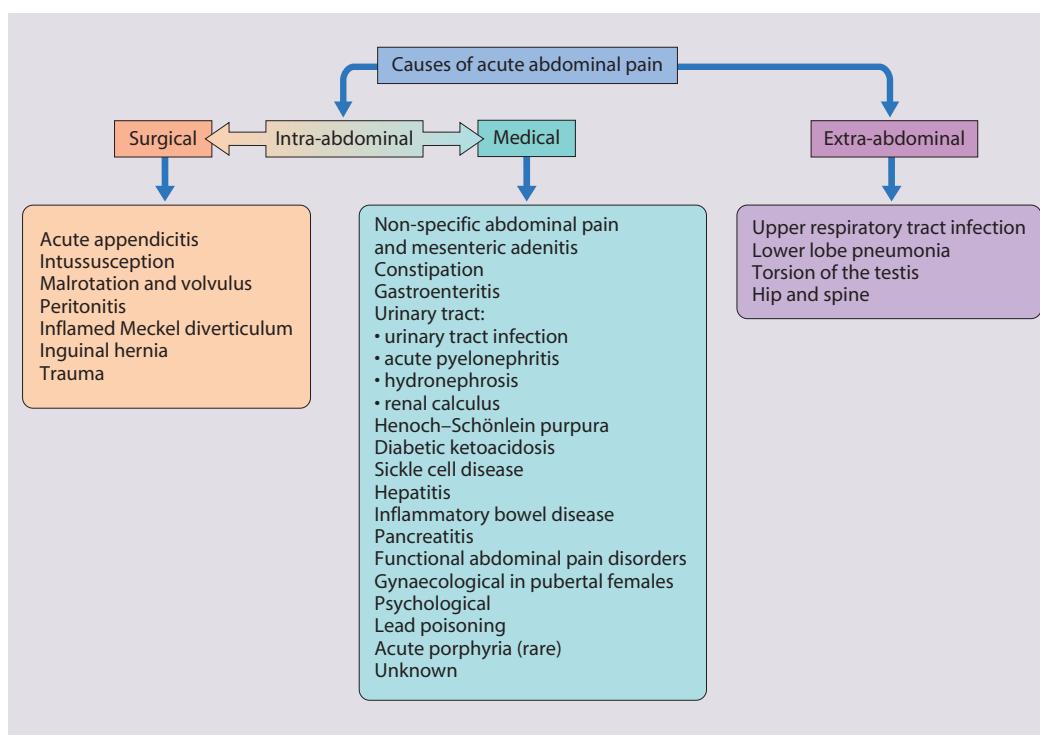


Figure 14.1 Causes of acute abdominal pain.

the diagnosis and treatment of acute appendicitis, as progression to perforation can be rapid. It is easy to belittle the clinical signs of abdominal tenderness in young children. However, in nearly half of the children admitted to hospital with acute abdominal pain, the pain resolves undiagnosed. It is noteworthy that:

- Lower lobe pneumonia may cause pain referred to the abdomen.
- Primary peritonitis is seen in patients with ascites from nephrotic syndrome or liver disease.
- Diabetic ketoacidosis may cause severe abdominal pain.
- Urinary tract infection, including acute pyelonephritis, is a relatively uncommon cause of acute abdominal pain, but must not be missed. A urine sample should be tested, in order to identify not only diabetes mellitus but also conditions affecting the urinary tract.
- Pancreatitis may present with acute abdominal pain and serum amylase should be checked.
- The testes in boys, hernial orifices and hip joints must always be checked.
- Consider gynaecological problems in older females, and if testing for pregnancy is required.



A urine sample should be tested to identify not only diabetes mellitus but also conditions affecting the urinary tract.

Acute appendicitis

Acute appendicitis is the most common cause of abdominal pain in childhood requiring surgical intervention (Fig. 14.2). Although it may occur at any age, it is very uncommon in children under 3 years of age. The clinical features of acute uncomplicated appendicitis are:

- symptoms:
 - anorexia
 - vomiting
 - abdominal pain, initially central and colicky (appendicular midgut colic), but then localizing to the right iliac fossa (from localized peritoneal inflammation)



Figure 14.2 Appendicitis at operation showing a perforated acutely inflamed appendix covered in fibrin. (Courtesy of Anthony Lander.)

- signs:
 - fever
 - abdominal pain aggravated by movement, e.g. on walking, coughing, jumping, bumps on the road during a car journey
 - persistent tenderness with guarding in the right iliac fossa (McBurney's point); however, with a retrocaecal appendix, localized guarding may be absent, and in a pelvic appendix there may be few abdominal signs.

In preschool children:

- It is uncommon but potentially serious.
- The diagnosis is more difficult, particularly early in the disease.
- Perforation may be rapid, as the omentum is less well developed and fails to surround the appendix, and the signs are easy to underestimate at this age.

Appendicitis is a progressive condition and so repeated observation and clinical review every few hours are key to making the correct diagnosis, avoiding delay on the one hand and unnecessary laparotomy on the other.

No laboratory investigation or imaging is consistently helpful in making the diagnosis. A raised neutrophil count is not always present on a full blood count. White blood cells or organisms in the urine are not uncommon in appendicitis as the inflamed appendix may be adjacent to the ureter or bladder. Although ultrasound is no substitute for regular clinical review, it may support the clinical diagnosis (thickened, non-compressible appendix with increased blood flow), and demonstrate associated complications such as an abscess, perforation or an appendix mass, and may exclude other pathology causing the symptoms. In some centres, laparoscopy is available to see whether or not the appendix is inflamed.

Appendectomy is straightforward in uncomplicated appendicitis. Complicated appendicitis includes the presence of an appendix mass, an abscess, or perforation. If there is generalized guarding consistent with perforation, fluid resuscitation and intravenous antibiotics are given prior to laparotomy. If there is a palpable mass in the right iliac fossa and there are no signs of generalized peritonitis, it may be reasonable to elect for conservative management with intravenous antibiotics, with appendicectomy being performed after several weeks. If symptoms progress, laparotomy is indicated. Management should be guided by the surgical team.

Non-specific acute abdominal pain and mesenteric adenitis

Non-specific acute abdominal pain is abdominal pain which resolves in 24–48 hours. The pain is less severe than in appendicitis, and tenderness in the right iliac fossa is variable. It often accompanies an upper respiratory tract infection with cervical lymphadenopathy. In some of these children, the abdominal signs do not resolve and laparoscopy and an appendicectomy is performed. Mesenteric adenitis is often diagnosed in those children in whom large mesenteric nodes are observed and whose appendix is normal, but there are doubts whether this condition truly exists as a diagnostic entity.

Constipation is a common cause of non-specific abdominal pain, which may have an acute onset and be severe and accompanied by vomiting in extreme cases.

Summary

Acute abdominal pain in older children and adolescents

- Exclude medical causes, in particular lower lobe pneumonia, diabetic ketoacidosis, hepatitis, and pyelonephritis.
- Check for strangulated inguinal hernia or torsion of the testis in boys.
- On palpating the abdomen in children with acute appendicitis, guarding and rebound tenderness may be absent or unimpressive, but pain from peritoneal inflammation may be demonstrated on coughing, walking or jumping.
- To distinguish between acute appendicitis and non-specific acute abdominal pain may require close monitoring, joint management between paediatricians and paediatric surgeons, and repeated evaluation in hospital.

Intussusception

Intussusception describes the invagination of proximal bowel into a distal segment. It most commonly involves ileum passing into the caecum through the ileocaecal valve (Fig. 14.3a). Intussusception is the most common cause of intestinal obstruction in infants after the neonatal period. Although it may occur at any age, the peak age of presentation is 3 months to 2 years of age.

The most serious complication is stretching and constriction of the mesentery resulting in venous obstruction, causing engorgement and bleeding from the bowel mucosa, fluid loss, and subsequently bowel perforation, peritonitis and gut necrosis. Prompt diagnosis, immediate fluid resuscitation and urgent reduction of the intussusception are essential to avoid complications.

Presentation is typically with:

- Paroxysmal, severe colicky pain with pallor – during episodes of pain, the child becomes pale, especially around the mouth, and draws up the legs. There is recovery between the painful episodes but subsequently the child may become increasingly lethargic.
- May refuse feeds, may vomit, which may become bile-stained depending on the site of the intussusception.
- A sausage-shaped mass – is often palpable in the abdomen (Fig. 14.3b).
- Passage of a characteristic redcurrant jelly stool comprising blood-stained mucus – this is a characteristic sign but tends to occur later in the illness and may be first seen after a rectal examination.
- Abdominal distension and shock.

Usually, no underlying intestinal cause for the intussusception is found, although there is some evidence that viral infection leading to enlargement of Peyer's patches may form the lead point of the intussusception. An identifiable lead point such as a Meckel diverticulum or polyp is more likely to be present in children over 2 years of age. Intravenous fluid resuscitation is likely to be required

immediately, as there is often pooling of fluid in the gut, which may lead to hypovolaemic shock.

An X-ray of the abdomen may show distended small bowel and absence of gas in the distal colon or rectum. Sometimes the outline of the intussusception itself can be visualized. Abdominal ultrasound is helpful both to confirm the diagnosis (the so-called target/doughnut sign, Fig. 14.3c) and to check response to treatment. Unless there are signs of peritonitis, reduction of the intussusception by rectal air insufflation is usually attempted by a radiologist. This procedure should only be carried out once the child has been resuscitated and is under the supervision of a paediatric surgeon in case the procedure is unsuccessful or bowel perforation occurs. The success rate of this procedure is about 75%. The remaining 25% require operative reduction (Fig. 14.3d). Recurrence of the intussusception occurs in less than 5% but is more frequent after hydrostatic reduction.

Summary

Intussusception

- Usually occurs between 3 months and 2 years of age.
- Clinical features are paroxysmal, colicky pain with pallor, abdominal mass and redcurrant jelly stool.
- Shock is an important complication and requires urgent treatment.
- Reduction is attempted by rectal air insufflation unless peritonitis is present.
- Surgery is required if reduction with air insufflation is unsuccessful or for peritonitis.

Meckel diverticulum

Around 2% of individuals have an ileal remnant of the vitello-intestinal duct, a Meckel diverticulum, which contains ectopic gastric mucosa or pancreatic tissue. Most are asymptomatic but they may present with severe rectal bleeding, which is classically neither bright red nor true melaena. There is usually an acute reduction in haemoglobin. Other forms of presentation include intussusception, volvulus (twisting of the bowel), or diverticulitis, when inflammation of the diverticulum mimics appendicitis. A technetium scan will demonstrate increased uptake by ectopic gastric mucosa in 70% of cases (Fig. 14.4). A negative technetium scan does not exclude the possibility and a laparoscopic examination can be used to make the diagnosis. Treatment is by surgical resection.

Malrotation and volvulus

Malrotation is a congenital abnormality of the midgut, in which the small intestine most commonly lies predominantly on the right-hand side of the abdomen, with the caecum in the right upper quadrant. This results from a failure of the intestine to 'rotate' into the correct position during fetal life and secure or 'fix' the mesentery in the correct position. The reason for this developmental failure is unknown.

Intussusception

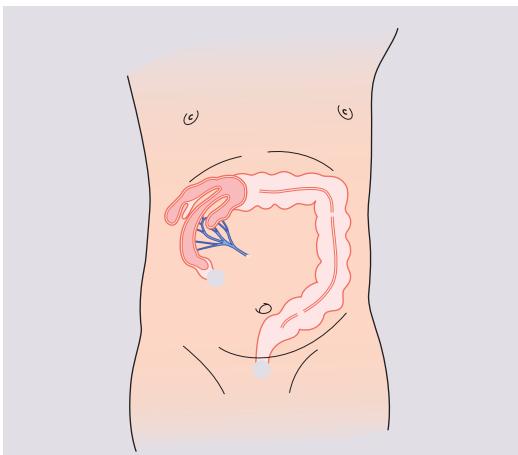


Figure 14.3a Intussusception, showing why the blood supply to the gut rapidly becomes compromised, making relief of this form of obstruction urgent.



Figure 14.3c An abdominal X-ray demonstrating an intussusception (see arrowhead), at reduction using contrast. Reduction is usually with air as it is safer.



Figure 14.3b A child with an intussusception. The mass can be seen in the upper abdomen. The child has become shocked.



Figure 14.3d Intussusception at operation showing the ileum entering the caecum. The surgeon is squeezing the colon to reduce the intussusception. (Courtesy of Anthony Lander.)

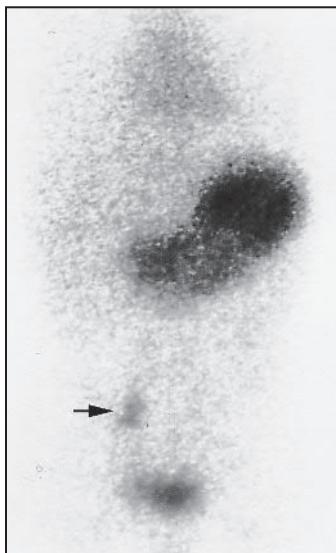


Figure 14.4 Technetium scan showing uptake by ectopic gastric mucosa in a Meckel diverticulum in the right iliac fossa (arrow). The scan has also outlined gastric mucosa in the stomach and excretion into the bladder.

Summary

Meckel diverticulum

- Occurs in 2% of individuals.
- Generally asymptomatic, but may present with bleeding (which may be life-threatening) or intussusception or volvulus.
- Treatment is by surgical resection.

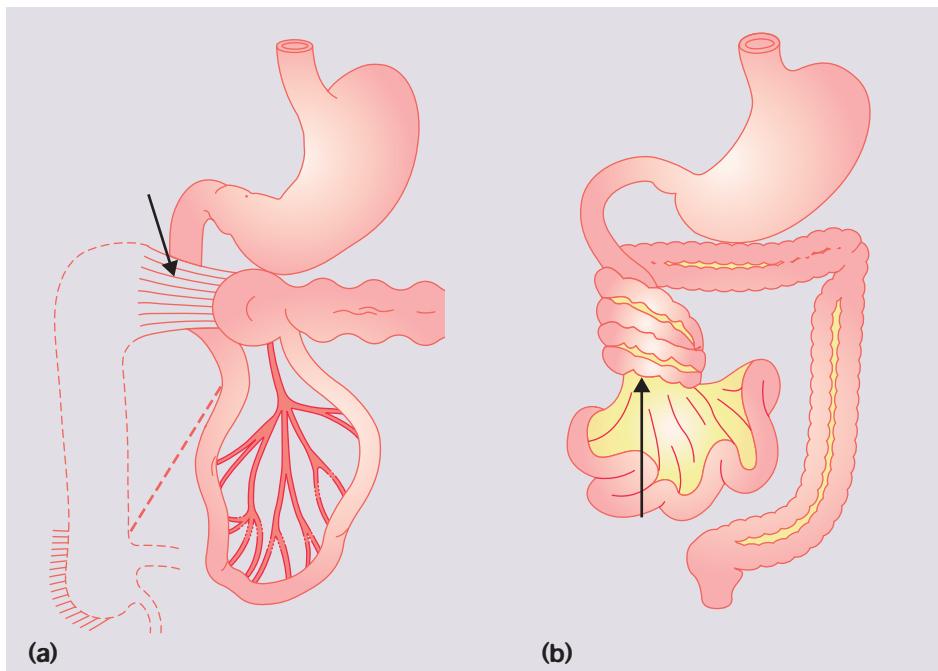


Figure 14.5 (a) The most common form of malrotation, with the caecum remaining high and fixed to the posterior abdominal wall. There are Ladd bands (arrow) obstructing the duodenum. Dotted lines show normal anatomy. (b) Volvulus from rotation of the bowel (arrow). This will result in ischaemia of the small and proximal large intestine.

Summary

Malrotation

- Uncommon but important to diagnose.
- Usually presents in the first 1–3 days of life with intestinal obstruction from Ladd bands obstructing the duodenum or volvulus.
- May present at any age with volvulus causing obstruction and ischaemic bowel.
- Clinical features are bilious vomiting, abdominal pain and tenderness from peritonitis or ischaemic bowel.
- An urgent upper gastrointestinal contrast study is indicated if there is bilious vomiting.
- Treatment is urgent surgical correction.

Fibrous bands called ‘Ladd bands’ tether the caecum to the right upper quadrant and these cause intestinal obstruction by compressing the duodenum (Fig. 14.5a,b). The poorly-tethered gut is able to swing and twist more readily, resulting in volvulus.

There are two presentations:

- obstruction
- obstruction with a compromised blood supply.

Obstruction with bilious vomiting is the usual presentation in the first few days of life but can be seen at a later age. Any child with dark green vomiting needs an urgent upper gastrointestinal contrast study to assess intestinal rotation, unless signs of vascular compromise are present, when an urgent laparotomy is needed. This is a surgical emergency as, when a volvulus occurs, the superior

mesenteric arterial blood supply to the small intestine and proximal large intestine is compromised, and unless it is corrected it will lead to infarction of these areas.

At operation, the volvulus is untwisted, the duodenum mobilized, and the bowel placed in the non-rotated position with the duodenojejunal flexure on the right and the caecum and appendix on the left. The malrotation is not ‘corrected’, but the mesentery broadened. The appendix is generally removed to avoid diagnostic confusion should the child subsequently have symptoms suggestive of appendicitis.

Recurrent abdominal pain

Recurrent abdominal pain is a common childhood problem. It is often defined as episodes of abdominal pain at least 4 times per month sufficient to interrupt normal activities and lasts for at least 2 months. It occurs in about 10% of school-age children. The pain is characteristically perumbilical and the children are otherwise entirely well.

An organic cause needs to be identified but is present in less than 10% of cases (Fig. 14.6). This requires a full history and thorough examination. Particular attention needs to be paid to identify functional constipation, which is common and may cause abdominal pain, and coeliac disease, and inflammatory bowel disease. The perineum should be inspected for anal fissures and other perianal disease and child maltreatment needs to be considered. The child's growth should be checked. The aim is to avoid subjecting the child to unnecessary investigations. ‘Red flag’ features to help identify organic causes are listed in Box 14.1. Investigations are guided by clinical features but baseline screening tests to be considered are listed in Box 14.2.

Causes and assessment of the child with recurrent abdominal pain

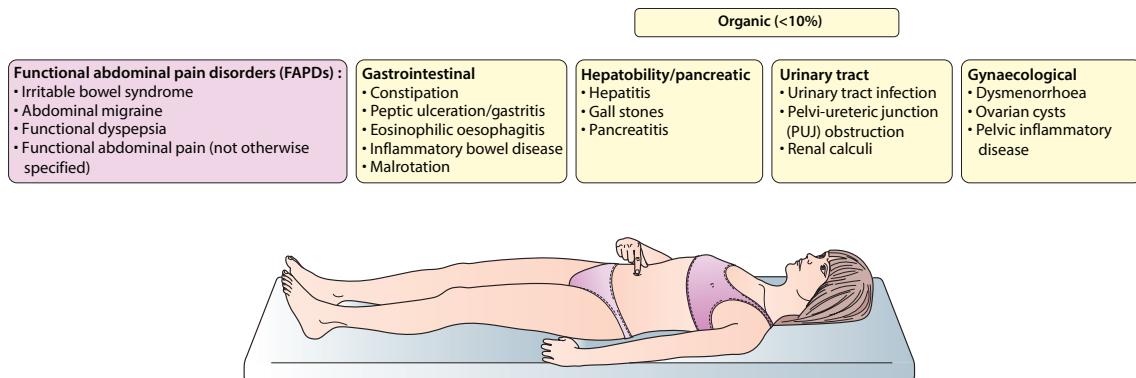


Figure 14.6 Causes and assessment of the child with recurrent abdominal pain.

Box 14.1 Red flags suggesting organic disease

- Persistent pain away from the umbilicus – such as right upper or lower quadrant pain
- Persistent vomiting
- Family history of inflammatory bowel disease, coeliac disease, or peptic ulcer disease
- Epigastric pain at night
- Haematemesis – duodenal ulcer
- Diarrhoea, weight loss, growth faltering, blood in stool – inflammatory bowel disease
- Dysphagia – eosinophilic oesophagitis
- Dysuria, secondary enuresis – urinary tract infection
- Night time waking
- Gastrointestinal blood loss
- Peri-anal disease
- Delayed puberty

Box 14.2 Screening tests to consider to identify organic disorders

- Full blood count with differential
- Erythrocyte sedimentation rate, C-reactive protein for inflammation
- Coeliac serology (including immunoglobulin levels) – as coeliac disease may present with diarrhoea or constipation or as irritable bowel syndrome
- Amylase – for pancreatitis
- Urea and electrolytes
- Liver function tests
- Ultrasound of abdomen
- Thyroid function tests
- Urinalysis / urine culture – to identify urinary tract infection or haematuria from renal calculi
- Faecal calprotectin – as a non-invasive screen for inflammatory bowel disease

A number of symptom complexes are recognized as causing 'functional abdominal pain disorders (FAPDs)'. They are sub-classified (Fig. 14.7) as:

- irritable bowel syndrome (most common)
- abdominal migraine
- functional dyspepsia
- functional abdominal pain (not otherwise specified, i.e. do not meet above classification).

Although described separately, there is considerable overlap between them. Diagnostic criteria have been agreed internationally.

Irritable bowel syndrome (IBS)

A family history is often present. There is a characteristic set of symptoms, with non-specific abdominal pain, often peri-umbilical, related to one or more of:

- defecation
- alteration in stool frequency
- change in appearance of stool (diarrhoea or constipation).

Children with functional constipation also often report pain and distinguishing it from IBS can be problematic. If the abdominal pain resolves with constipation treatment, the child has functional constipation. If pain does not resolve after treatment, the child is likely to have IBS with constipation.

Pathogenesis

IBS is now considered a disorder of visceral hypersensitivity and neurological hypervigilance in combination with psychosocial stressors (see Fig. 14.7). Patients are particularly sensitive to low or high pressure stimuli in the bowel, as shown by children with IBS reporting discomfort at lower rectal distension pressure than controls. These

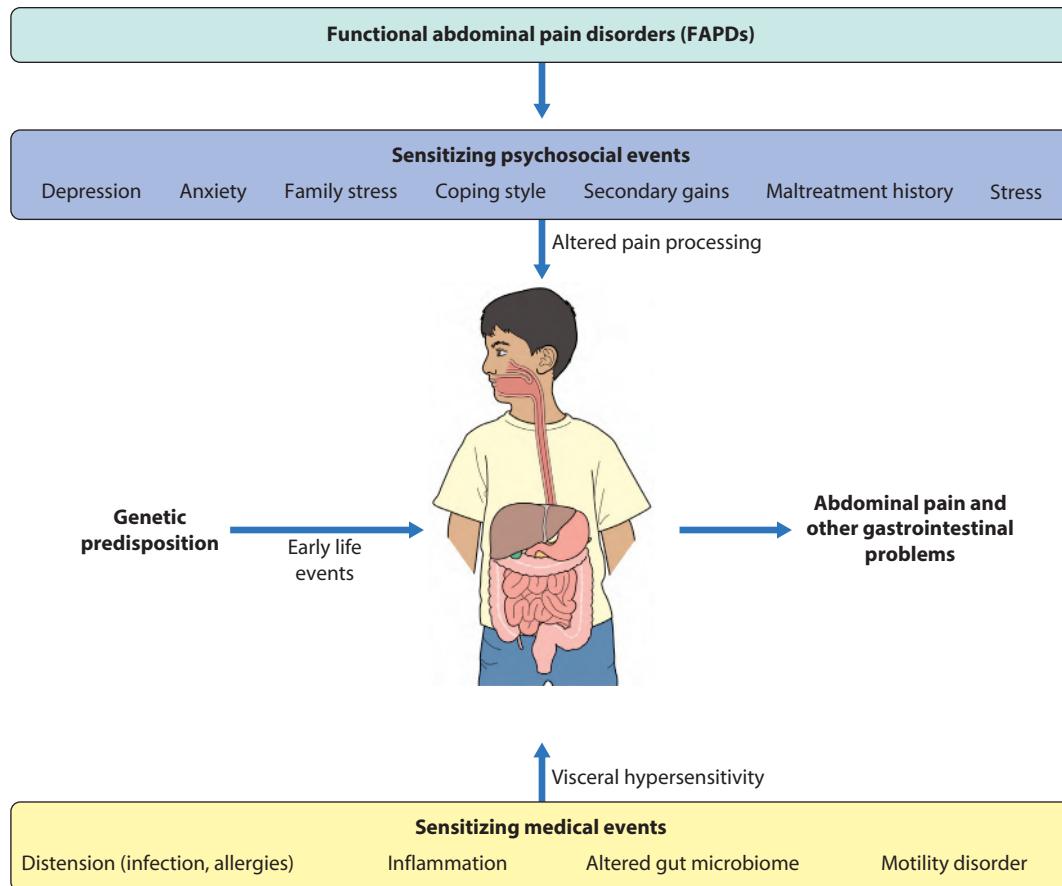


Figure 14.7 Manifestation and pathophysiology of functional abdominal pain disorders (FAPDs) in children.
(Adapted from: Hyams JS, Lorenzo CD, Saps M et al: Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2016;150:1456–1468.)

changes appear to be secondary to insults of the gut-brain-microbiota axis and neuro-immune interactions in the gut, which alter the perception of pain. These insults may vary widely – genetic (e.g. family history of irritable bowel syndrome), early life events (e.g. bowel surgery), environmental (e.g. cow's milk protein allergy, post enteritis), gastrointestinal (e.g. infections, antibiotics) as well as psychosocial triggers (e.g. stress, anxiety, maltreatment). In some children, a vicious cycle of anxiety with escalating pain leading to family distress may develop, accompanied by demands for increasingly invasive investigations.

Abdominal migraine

In abdominal migraine there are paroxysms of intense, acute perumbilical, midline or diffuse abdominal pain, lasting at least an hour, interfering with normal activities. Additional symptoms may be vomiting, nausea, anorexia, headaches, photophobia and pallor. In between episodes, there are long periods (often weeks) of no symptoms interspersed with episodes following a characteristic pattern for the child, with abdominal pain the main symptom. There is often a personal or family history of migraine, and similar triggers to classic migraine (stress, fatigue, travel),

similar associated symptoms (e.g. anorexia, nausea and vomiting), similar relieving factors (e.g. rest and sleep), and can evolve into migraine headaches in adult life.

Functional dyspepsia

This may present with postprandial fullness or early satiety, with or without upper abdominal bloating, nausea or excessive belching, or severe pain or burning in the epigastric area. The pain is not relieved by defecation but may be induced or relieved by eating. There is some evidence for delayed gastric emptying as a result of gastric dysmotility. There is no evidence in children that *Helicobacter pylori* gastritis causes dyspeptic symptoms in the absence of duodenal ulcer.

Management

This is based on a bio-psychosocial model of care. The family need to be confident that their concerns have been fully noted and addressed during the thorough history-taking and examination, and that the child's pain is real and not imaginary. It can be helpful to explain to both the child

and parents that 'sometimes the insides of the intestine become so sensitive that some children can feel the food going round the bends'. It is also necessary to make a distinction between 'serious' and 'dangerous'. These disorders can be serious, if, for example, they lead to substantial loss of schooling, but they are not dangerous. Avoiding triggers and psychosocial factors that exacerbate painful episodes need to be addressed.

Medications may sometimes be indicated. For irritable bowel syndrome, reassurance, dietary manipulations (such as low FODMAP –Fermentable Oligo-saccharides, Di-saccharides, Mono-saccharides And Polyols – diets), anti-spasmodics and alternative therapies may be helpful. For abdominal migraine, treatment with anti-migraine medication may be of benefit if the problem causes school absence. For functional dyspepsia, acid blockade with histamine receptor antagonists and proton pump inhibitors can be offered.

Behaviour modification has been shown to improve coping mechanisms and avoid reinforcement of pain. These include relaxation, distraction and hypnotherapy. Of these techniques, hypnotherapy, with imagined pictures, sound or sensations to distract attention from pain, has been demonstrated to be most effective.

The long-term prognosis is that:

- about half of affected children rapidly become free of symptoms
- in one-quarter, the symptoms take some months to resolve
- in one-quarter, symptoms continue or return in adulthood as irritable bowel syndrome, migraine, or functional dyspepsia.

Peptic ulcer disease

Duodenal ulcers are uncommon in children but should be considered in those with epigastric pain, particularly if it wakes them at night, if the pain radiates through to the back, or when there is a history of peptic ulceration in a first-degree relative. These can be caused by *H. pylori* infection. Initial diagnosis of *H. pylori* infection is generally made with gastric biopsy on endoscopy. Non-invasive tests such as ^{13}C breath test, which detects urease produced by the organism following the administration of ^{13}C -labelled urea by mouth, or stool antigen tests for *H. pylori* are used to confirm successful eradication of *H. pylori* infection. In children, non-invasive tests are not recommended for initial diagnosis and treatment.

Children in whom peptic ulceration is suspected or diagnosed on endoscopy should be treated with proton-pump inhibitors, e.g. omeprazole, and if *H. pylori* is identified, eradication therapy with antibiotics should be given.

Vomiting

Posseting and *regurgitation* are terms used to describe the non-forceful return of milk, but differ in degree. Posseting describes the small amounts of milk that often accompany the return of swallowed air (wind), whereas regurgitation describes larger, more frequent losses. Posseting occurs in nearly all babies from time to time.

Vomiting is the forceful ejection of gastric contents. It is a common problem in infancy and childhood (Fig. 14.8).

It is usually benign and is often caused by feeding disorders or mild gastro-oesophageal reflux or gastroenteritis. Potentially serious disorders need to be excluded, as listed as 'red flag' clinical features in Box 14.3. When assessing the clinical features of vomiting:

- Figures of speech such as 'bringing everything up' need to be picked apart: mild viral vomiting may result in a temporary inability to tolerate solids, but sips of liquids are 'kept down'.
- The word 'bile' may be used by parents or older children to mean 'clear acidic stomach contents'. The presence of green bile in vomit is an emergency, as it suggests that the bowel is obstructed and the flow of bile is reversed.
- In intestinal obstruction, the more proximal the obstruction, the more prominent the vomiting and the sooner it becomes bile-stained, unless the obstruction is proximal to the ampulla of Vater.
- Small quantity of blood in vomit may be swallowed blood, from a cracked nipple in a breastfed baby or nose bleeds in older children. True haematemesis is a 'red flag' clinical feature.
- Abdominal distension in intestinal obstruction becomes increasingly pronounced the more distal the obstruction.
- When accompanying bouts of coughing it needs to be distinguished from spontaneous, unprovoked, vomiting.
- The child who is systemically unwell needs to be identified, as it may be a feature of systemic infection, which may be outside the gastrointestinal tract, especially urinary tract and central nervous system, and other serious illness.

Summary

Vomiting in infants

- Common cause is gastro-oesophageal reflux.
- Feed volumes should be calculated since overfeeding is common in bottle-fed infants.
- If transient, with other symptoms, e.g. fever, diarrhoea or runny nose and cough, most likely to be gastroenteritis or respiratory tract infection, but consider urine infection, sepsis or meningitis.
- If projectile at 2–8 weeks of age, exclude pyloric stenosis.
- If bile-stained, potential emergency – intestinal obstruction, especially intussusception, malrotation or strangulated inguinal hernia? Assess for dehydration and shock. Keep nil by mouth and give intravenous fluids until a diagnosis is reached.

Gastro-oesophageal reflux

Gastro-oesophageal reflux is the involuntary passage of gastric contents into the oesophagus. It is extremely common in infancy. It is caused by functional immaturity of the lower oesophageal sphincter which is inappropriately relaxed. The predominantly fluid diet, a mainly horizontal posture and the short intra-abdominal length of oesophagus in infants all contribute. Most infants with gastro-oesophageal reflux have recurrent regurgitation or vomiting but are putting on weight normally and are

Vomiting

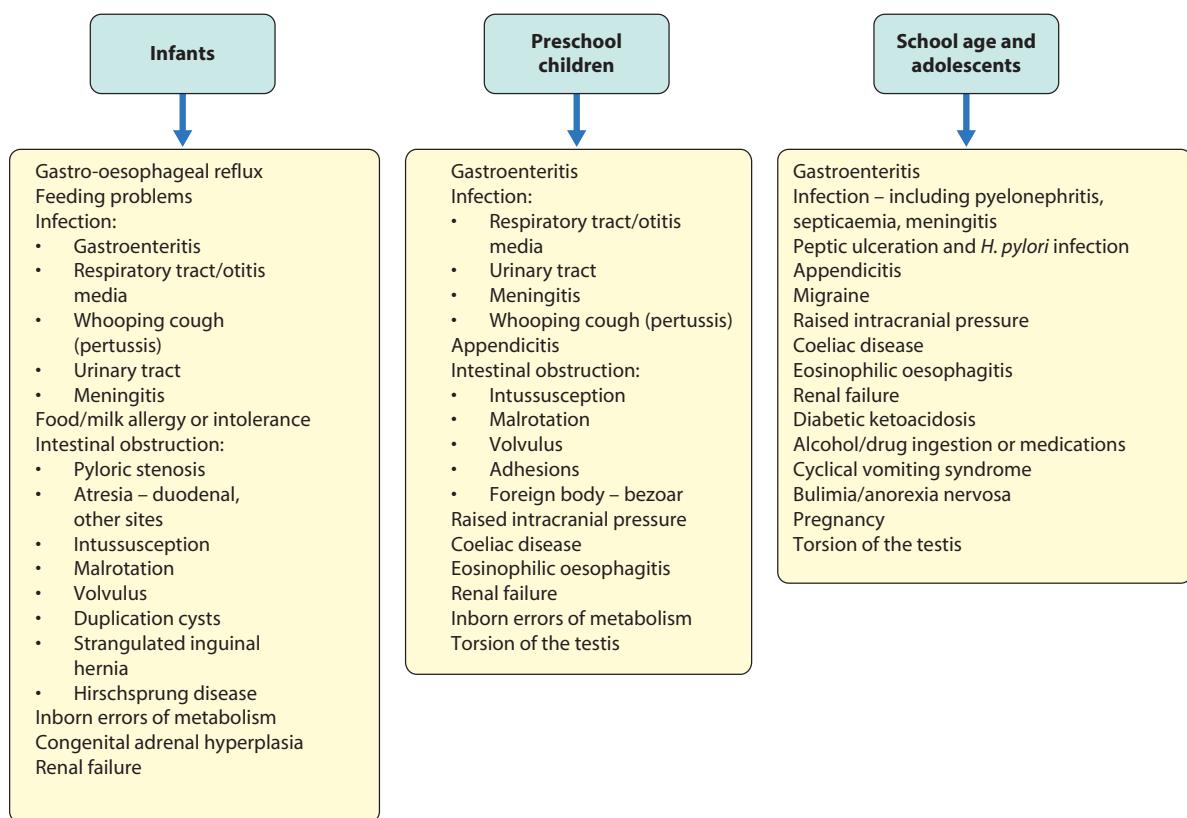


Figure 14.8 Causes of vomiting.

Box 14.3 'Red flag' clinical features in the vomiting child

Bile-stained vomit	Intestinal obstruction (see Ch. 11, Neonatal medicine)
Haematemesis	Oesophagitis, peptic ulceration, oral/nasal bleeding, and oesophageal variceal bleeding
Projectile vomiting, in first few weeks of life	Pyloric stenosis
Vomiting at the end of paroxysmal coughing	Whooping cough (pertussis)
Abdominal tenderness/abdominal pain on movement	Surgical abdomen
Abdominal distension	Intestinal obstruction, including strangulated inguinal hernia, ascites
Hepatosplenomegaly	Chronic liver disease, inborn error of metabolism
Blood in the stool	Intussusception, bacterial gastroenteritis, inflammatory bowel disease
Severe dehydration, shock	Severe gastroenteritis, systemic infection (urinary tract infection, meningitis), diabetic ketoacidosis
Bulging fontanelle or seizures	Raised intracranial pressure, meningitis
Faltering growth	Gastro-oesophageal reflux disease, coeliac disease and other chronic gastrointestinal conditions

otherwise well, although the mess, smell, and frequent changes of clothes (5% of those affected have 6 or more episodes each day) is frustrating for parents and carers.

Whilst common in the first year of life, nearly all symptomatic reflux resolves spontaneously by 12 months of age. This is probably due to a combination of maturation of

the lower oesophageal sphincter, an upright posture and more solids in the diet.

Whilst gastro-oesophageal reflux is usually a benign, self-limited condition, if complications are present (Box 14.4), it is called gastro-oesophageal reflux disease. This is more common in:

- children with cerebral palsy or other neurodevelopmental disorders
- preterm infants
- following surgery for oesophageal atresia or diaphragmatic hernia
- obesity
- hiatus hernia.

Investigation

Gastro-oesophageal reflux is usually diagnosed clinically and no investigations are required. However, they may be indicated if the history is atypical, complications are present, or there is failure to respond to treatment (see [Case history 14.1](#)). Investigations should be overseen by a paediatrician or paediatric gastroenterologist and could include:

- 24-hour oesophageal pH monitoring to quantify the degree of acid reflux, with a pH probe passed through the nose into the lower oesophagus
- wireless pH monitoring, when the probe is placed in the distal oesophagus endoscopically and pH is monitored remotely, which is particularly helpful in children with neurodevelopmental or behavioural problems
- 24-hour impedance monitoring, with a probe in the lower oesophagus, is available in some centres. Weakly acidic or non-acid reflux, which may cause disease, is also measured
- endoscopy including oesophageal biopsies to identify oesophagitis and exclude other causes of vomiting.

A contrast study of the upper gastrointestinal tract is not recommended to diagnose or assess the severity of gastro-oesophageal reflux disease in infants, children and young people.

Management

Uncomplicated gastro-oesophageal reflux has an excellent prognosis and can be managed by parental reassurance, feeding assessment, smaller, more frequent feeds or adding inert thickening agents to feeds (e.g. Carobel). A 1–2-week trial of alginate therapy, which forms a protective gel above stomach contents, may be considered, if these other methods are ineffective.

Gastro-oesophageal reflux disease is managed with stomach acid suppression with either hydrogen receptor antagonists or proton-pump inhibitors (e.g. omeprazole). These drugs reduce the volume of gastric contents and treat acid-related oesophagitis. The evidence for the use of drugs that enhance gastric emptying (e.g. domperidone) is poor, and as they are associated with significant side-effects their use should be discouraged. If the child fails to respond to these measures, other diagnoses such

Box 14.4 Gastro-oesophageal reflux disease

- Faltering growth from severe vomiting
- Oesophagitis – haematemesis, discomfort on feeding or heartburn, iron-deficiency anaemia
- Recurrent pulmonary aspiration – recurrent pneumonia, cough or wheeze, apnoea in preterm infants
- Dystonic neck posturing (Sandifer syndrome)
- Brief resolved unexplained events (apparent life-threatening events)

as cow's milk protein allergy should be considered and further investigations performed.

Surgical management is reserved for children with complications unresponsive to intensive medical treatment or oesophageal stricture. A Nissen fundoplication, in which the fundus of the stomach is wrapped around the intra-abdominal oesophagus, is performed either as an abdominal or as a laparoscopic procedure.

Summary

Gastro-oesophageal reflux

- This is common, but risk is increased if the infant has neuromuscular problems, had surgery to the oesophagus or diaphragm or was premature.
- Investigations are performed if diagnosis is uncertain or gastro-oesophageal reflux disease unresponsive to treatment.
- Gastro-oesophageal reflux disease is treated with feed thickening, stomach acid suppression, or, rarely, fundoplication.

Pyloric stenosis

In pyloric stenosis, there is hypertrophy of the pyloric muscle causing gastric outlet obstruction. It presents at 2–8 weeks of age, irrespective of gestational age. It is more common in boys (4:1), particularly first-born, and there may be a family history, especially on the maternal side.

Clinical features are:

- non-bilious vomiting, which increases in frequency and forcefulness over time, ultimately becoming projectile
- feeds normally after vomiting until dehydration leads to loss of interest in feeding
- weight loss if presentation is delayed.

A hypochloraemic hypokalaemic metabolic alkalaosis develops as a result of vomiting stomach contents. Hyponatraemia may also be present.

Diagnosis

Gastric peristalsis may be seen as a wave moving from left to right across the abdomen ([Fig. 14.10a](#)). Classically, pyloric stenosis has been confirmed by performing a test feed, where the baby is given a milk feed which initially calms the hungry infant, and allows for examination. The diagnosis is made if the pyloric mass, which feels like an olive, is palpable in the right upper quadrant ([Fig. 14.10b](#)). As the stomach is usually overdistended with air, it often needs to be emptied by a nasogastric tube to allow palpation. This has been replaced by ultrasound, which has become the standard diagnostic procedure by visualizing the hypertrophied pylorus ([Fig. 14.10c](#)).

Management

Although the definitive treatment is surgical (pyloromyotomy), this can only be performed safely after acid-base electrolyte imbalances have been corrected, which may take more than 24 hours of intravenous fluid rehydration. Pyloromyotomy involves division of the hypertrophied muscle down to, but not including, the mucosa ([Fig. 14.10d](#)).



Case history 14.1

Gastro-oesophageal reflux disease

Katie, aged 11 months, presented with a history of frequent regurgitation of feeds from a few weeks of life. She had two chest infections which required short hospital admissions. Her parents reported that recent vomit contained small amounts of altered blood. A short trial of feed thickeners, alginate and omeprazole had not improved her

symptoms. A 24-hour oesophageal pH study (off treatment) showed severe ongoing gastro-oesophageal reflux disease (Fig. 14.9a,b). An upper gastro-intestinal endoscopy showed oesophagitis on histology. Symptoms resolved with a higher dose of omeprazole. Her parents also commented on how much better she slept at night.

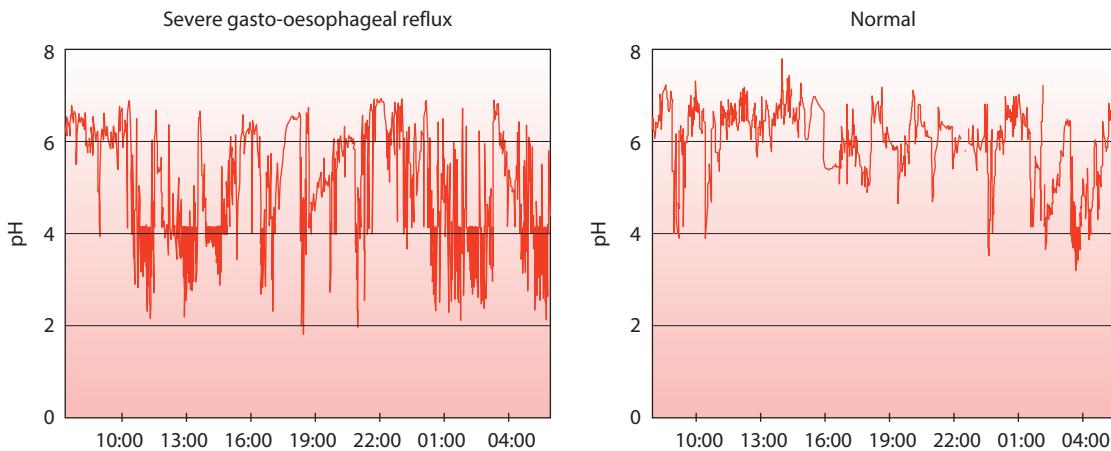


Figure 14.9 (a) Section of an oesophageal pH study showing severe gastro-oesophageal reflux, with frequent drops in pH below 4. (b) Normal pH study for comparison, with pH above 4 for most of the time.

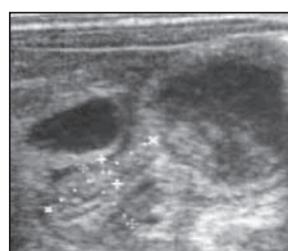
Pyloric stenosis



(a)



(b)



(c)



(d)

Figure 14.10 (a) Visible gastric peristalsis in an infant with pyloric stenosis. (b) Diagram showing a test feed being performed to diagnose pyloric stenosis. The pyloric mass feels like an 'olive' on gentle, deep palpation halfway between the midpoint of the anterior margin of the right ribcage and the umbilicus. (c) Ultrasound examination showing elongated (between crosses) and hypertrophied (between targets) pylorus. (Courtesy of David Hughes.) (d) Pyloric stenosis at operation showing pale, thick pyloric muscle, and pyloromyotomy incision. (Courtesy of Anthony Lander.)



Case history 14.2

Eosinophilic oesophagitis

Arthur, a 14-year-old boy, presents with an intermittent history of a sensation of 'food getting stuck' after eating. His parents report that he takes a long time chewing his food at mealtimes and tends to drink plenty of water whilst eating. He has no other gastrointestinal symptoms and continues to gain weight along his growth centile. His past medical history includes significant eczema and hay fever. Endoscopic and histological assessment revealed features consistent with eosinophilic oesophagitis (Fig. 14.11). He was successfully treated with swallowed corticosteroids and dietary changes.

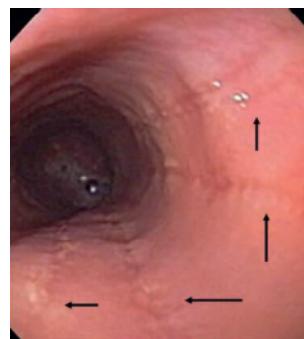


Figure 14.11 A spectrum of endoscopic appearances are associated with eosinophilic oesophagitis ranging from oedema to longitudinal furrowing (arrows) to oesophageal rings described as trachealization. White exudates are commonly seen.

Summary

Pyloric stenosis

- More common in boys and in those with a family history.
- Signs are visible gastric peristalsis, palpable abdominal mass if a test feed is performed, and possible dehydration.
- Associated with hyponatraemia, hypokalaemia, and hypochloraemic alkalosis.
- Diagnosis is confirmed by ultrasound.
- Treated by surgery after rehydration and correction of electrolyte imbalance.

The operation can be performed either as an open procedure via a periumbilical incision or laparoscopically. Postoperatively, the child can usually be fed within a few hours and discharged within a couple of days of surgery.

Eosinophilic oesophagitis

Eosinophilic oesophagitis is an inflammatory condition affecting the oesophagus caused by activation of eosinophils within the mucosa and submucosa. It can present with vomiting, discomfort on swallowing or bolus dysphagia, when food 'sticks in the upper chest'. It is probably an allergic phenomenon, although the precise pathophysiology is unclear. It is more common in children with other features of atopy (asthma, eczema, and hay fever). Diagnosis is by endoscopy (see Case history 14.2) where macroscopically, linear furrows and trachealization of the oesophagus may be seen and, microscopically, eosinophilic infiltration is identified. Treatment is with swallowed corticosteroids in the form of fluticasone or viscous budesonide. Exclusion diets may be of benefit in young children.

Gastroenteritis

In low- and middle-income countries, gastroenteritis remains a major cause of child mortality. In high-income

countries, it is a cause of significant morbidity, particularly in infants and young children. In Europe, children under 3 years old experience 0.5–2 episodes per year, and it remains a common reason for hospital admission in young children. Its incidence has fallen markedly with increased prevention – raised awareness and practice of hand hygiene, improved hygienic preparation and storage of food, safe drinking water, improved sanitation as well as immunization.

The most frequent cause of gastroenteritis in children in high-income countries are viruses. Rotavirus was by far the commonest pathogen causing severe gastroenteritis, but following inclusion of the rotavirus vaccine into the standard immunization schedule, its incidence has fallen markedly and is now very low. Norovirus is now the commonest cause, but results in less severe disease. Other viruses include sapovirus and enteric adenovirus, and astrovirus.

Bacterial causes are less common in high-income countries but may be suggested by the presence of blood in the stools. Clinical features are a poor guide to the pathogen, but *Campylobacter jejuni* infection, *Shigella* and some salmonellae species produce a dysenteric type of infection, with blood and pus in the stool, abdominal pain and tenesmus. *Shigella* infection may also be accompanied by high fever. *Clostridium difficile* causes diarrhoea in children with chronic diseases. Cholera and enterotoxigenic *Escherichia coli* infection are associated with profuse, rapidly dehydrating diarrhoea.

The third cause of gastroenteritis is protozoan parasite infection such as *Giardia* and *Cryptosporidium*, but these rarely cause acute gastroenteritis.

In gastroenteritis there is a sudden change to loose or watery stools of increased frequency and is often accompanied by vomiting. There may be contact with a person with diarrhoea and/or vomiting or recent travel abroad. Dehydration leading to shock is the most serious complication and its prevention or correction is the main aim of treatment.

The following children are at increased risk of dehydration:

- infants, particularly those under 6 months of age or those born with low birthweight
- if they have passed five or more diarrhoeal stools in the previous 24 hours
- if they have vomited more than twice in the previous 24 hours

- if unable to tolerate supplementary fluids
- if they have malnutrition or immune deficiency.

Infants are at particular risk of dehydration compared to older children or adults as they have a high turnover of fluids (100–120 ml/kg per day, i.e. 10% to 12% of bodyweight) as they have:

- a high body water content
- high metabolic rate
- a greater surface area-to-weight ratio, leading to greater insensible water losses (15–17 ml/kg per day)
- immature renal tubular reabsorption
- cannot communicate their need for extra fluids.

Assessment

Clinical assessment of dehydration is difficult. The most accurate measure of dehydration is the degree of weight loss during the period of illness. A recent weight measurement is useful but is often not available and may be misleading if measured on different scales and if clothed differently. The history and examination are used to classify the degree of dehydration as described in Table 6.3 and Fig. 6.7 in Chapter 6. Paediatric Emergencies, as:

- no clinically detectable dehydration (usually <5% loss of body weight)
- clinical dehydration (usually 5%–10% loss of body weight)
- shock (usually >10% loss of body weight). Shock must be identified without delay.

The clinical features also vary according to the serum sodium, i.e. if the dehydration is isonatraemic, hyponatraemic or hypernatraemic.

Isonatraemic and hyponatraemic dehydration

In dehydration, there is a total body deficit of sodium and water. In most instances, the losses of sodium and water are proportional and plasma sodium remains within the normal range (isonatraemic dehydration). When children with diarrhoea drink large quantities of water or other hypotonic solutions, there is a greater net loss of sodium than water, leading to a fall in plasma sodium (hyponatraemic dehydration). This leads to a shift of water from extracellular to intracellular compartments to equilibrate their osmolality. The increase in intracellular volume leads to an increase in brain volume, which may result in seizures, whereas the marked extracellular depletion leads to early and exaggerated peripheral signs of dehydration and increased susceptibility of shock.

Hypernatraemic dehydration

Infrequently, water loss exceeds the relative sodium loss and plasma sodium concentration increases (hypernatraemic dehydration). This usually results from high insensible water losses (high fever or hot, dry environment) or from profuse, low-sodium diarrhoea. The extracellular fluid becomes hypertonic with respect to the intracellular fluid, which leads to a shift of water into the extracellular space from the intracellular compartment. Signs of extracellular fluid depletion are therefore less per unit of fluid loss, and depression

of the fontanelle, reduced tissue elasticity, and sunken eyes and other peripheral signs of dehydration are reduced. This makes this form of dehydration more difficult to recognize clinically, particularly in an obese infant. It is a dangerous form of dehydration as water is drawn out of the brain and cerebral shrinkage within a rigid skull may lead to irritability and abnormal neurological signs. It has become uncommon since adjustment of the sodium content in formula feeds.

Investigation

Usually, no investigations are indicated. Stool culture is required if the child appears septic, if there is blood or mucus in the stools, or if the child is immunocompromised. It may be indicated following recent foreign travel, if the diarrhoea has not improved by day 7, or if the diagnosis is uncertain. Plasma electrolytes, urea, creatinine, and glucose should be checked if intravenous fluids are required or there are features suggestive of hypernatraemia. If antibiotics are started, a blood culture should be taken.

Management

This is shown in Fig. 14.12. Where clinical dehydration is not present on clinical assessment, the aim is to avoid its development. Breastfeeding or other milks should be continued, fluid intake encouraged, and oral rehydration solution offered. If there is clinical dehydration, oral rehydration solution is the mainstay of therapy. Intravenous fluids are only indicated for shock or deterioration or persistent vomiting.

Oral rehydration therapy

This is a key component of the management of gastroenteritis. It contains both sodium and glucose, which increases active sodium and passive water absorption. This works effectively even in the presence of inflammation of the gut, and is therefore effective in diarrhoeal illness. The oral rehydration solution does not 'stop' the diarrhoea, which often continues, but the absorption of water and solutes exceeds secretion and keeps the child hydrated until the infective organism is eradicated. It should be offered in small amounts given frequently, by nasogastric tube if necessary. Coca-Cola and apple juice have a much lower sodium content and higher osmolarity than oral rehydration solution and are unsuitable as oral rehydration solutions.

Hypernatraemic dehydration

If intravenous fluids are required, a rapid reduction in plasma sodium concentration and osmolality will lead to a shift of water into cerebral cells and may result in seizures and cerebral oedema. The reduction in plasma sodium should therefore be slow, over at least 48 hours (with 0.9% saline or 0.9% saline with 5% glucose, tailored to response) and the plasma sodium measured regularly, aiming to reduce it at less than 0.5 mmol/l per hour.

Antidiarrhoeal drugs (e.g. loperamide, Lomotil) and antiemetics

Medications are not indicated for the vomiting or diarrhoea of gastroenteritis in children as it usually resolves in a few days without treatment.

Antibiotics

Antibiotics are not routinely required to treat gastroenteritis, even if there is a bacterial cause. They are only indicated for suspected or confirmed sepsis, extra-intestinal spread of bacterial infection, for salmonella gastroenteritis if aged under 6 months, in malnourished or immunocompromised children, or for specific bacterial infections (e.g. *Clostridium difficile* associated with pseudomembranous colitis, cholera, shigellosis).

Outcome

After diarrhoea has improved, if breastfeeding, continue if possible. Reintroduce solid food and milk. Avoid fruit juices and carbonated drinks. Advise parents about hand washing, that towels used by infected child should not be shared, and that the child should not return to their childcare facility or school until 48 hours after last episode.

In low- and middle-income countries, multiple episodes of diarrhoea are a major contributing factor to the development of malnutrition. Following diarrhoea, nutritional intake should be increased. Zinc supplementation is recommended by WHO in low- and middle-income countries.

Postgastroenteritis syndrome

Infrequently, following an episode of gastroenteritis, the introduction of a normal diet results in a return of watery diarrhoea. In such cases, oral rehydration therapy should be restarted. Inflammation can damage the gut's microvilli, reducing the expression of lactase enzymes. Post-infective lactose intolerance is another cause of foul-smelling loose stool on resuming a normal diet.

Summary

Gastroenteritis

- Results in death of hundreds of thousands of children worldwide every year.
- Is mostly viral, but it can be caused by *Campylobacter*, *Shigella*, and *Salmonella* and other organisms.
- Infants are particularly susceptible to dehydration.
- Oral rehydration solution is the mainstay of treatment and usually effective; intravenous fluid is only required for shock or ongoing vomiting or clinical deterioration.

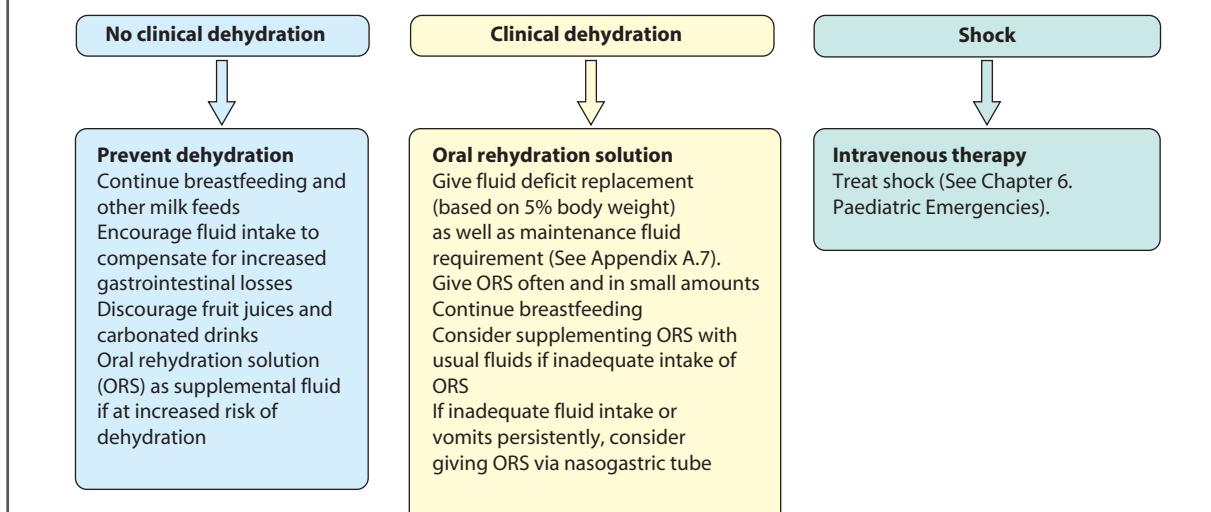
Malabsorption

Disorders affecting the digestion or absorption of nutrients manifest as:

- abnormal stools
- poor weight gain or faltering growth in most but not all cases
- specific nutrient deficiencies, either singly or in combination.

In general, parents know when their children's stools have become abnormal. The true malabsorption stool is difficult to flush down the toilet and has an odour that pervades the whole house. Colour is a poor guide to abnormality. Some disorders affecting the small intestinal mucosa or pancreas (e.g. chronic pancreatic insufficiency in cystic fibrosis) may lead to the malabsorption of many nutrients

Management of gastoenteritis



Oral rehydration solution has saved and continues to save millions of lives worldwide.



In gastroenteritis, death is from shock from dehydration; its prevention or correction is the mainstay of management.

Figure 14.12 Initial management of dehydration due to gastroenteritis. (Adapted from: National Institute for Health and Clinical Excellence (NICE): *Guideline. Diarrhoea and Vomiting in Children under 5*, London, 2009, NICE.)

(pan-malabsorption), whereas others are highly specific, e.g. zinc malabsorption in *acrodermatitis enteropathica*.

Coeliac disease

Coeliac disease is an immune-mediated systemic disorder elicited by gluten and related prolamines (found in wheat, barley and rye) in genetically susceptible individuals. It is characterized by a variable combination of gluten-dependent clinical manifestations, coeliac disease specific antibodies, HLA DQ2 and DQ8 haplotypes and enteropathy. Villi become progressively shorter and then absent, leaving a flat mucosa.

Coeliac disease has a prevalence of about 1 in 100 of the population. However, the so-called 'classical' presentation only has an incidence of around 1 in 3000. The *classical* presentation is of a profound malabsorptive syndrome at 8–24 months of age after the introduction of wheat-containing weaning foods. Associated signs are faltering growth, abdominal distension and buttock wasting, abnormal stools, recurrent abdominal pain and general irritability (see [Case history 14.3](#)).

However, this 'classical' form is no longer the most common presentation and children are now more likely to present less acutely in later childhood. The clinical features of coeliac disease can be highly variable and include mild, non-specific gastrointestinal symptoms, anaemia and growth faltering or with non-gastrointestinal tract signs and symptoms as listed in [Box 14.5](#). Sometimes, it is identified on screening of children at increased risk (type 1 diabetes mellitus, autoimmune thyroid disease, Down syndrome) and first-degree relatives of individuals with known coeliac disease.

The introduction of highly sensitive and specific serological screening tests, IgA anti-tTG (immunoglobulin A tissue transglutaminase antibodies) and IgA EMA (endomysial antibodies), has provided evidence that coeliac disease is much more common than previously thought.

Diagnosis

Although the diagnosis is strongly suggested by positive serology, it is essential to confirm the diagnosis. This can be done by endoscopic biopsy. However, in symptomatic

Box 14.5 Symptoms and signs of coeliac disease

- Diarrhoea – intermittent or chronic
- Nausea / vomiting / abdominal pain / abdominal distension / constipation
- Faltering growth or weight loss
- Delayed puberty
- Short stature
- Unexplained iron-deficiency anaemia resistant to treatment
- Unexplained liver disease
- Lethargy / weakness
- Arthritis / arthralgia
- Neuropathy
- Dermatitis herpetiformis
- Osteoporosis / pathological fractures
- Recurrent aphthous stomatitis
- Dental enamel defects

children with markedly raised IgA tissue transglutaminase titres, if IgA endomysial antibody is also positive, a diagnosis can be made purely on blood tests. In those with a confirmed diagnosis, gluten withdrawal should be followed by resolution of symptoms and catch-up growth.

Management

All products containing wheat, rye, and barley are removed from the diet and this results in resolution of symptoms. Supervision by a dietician is essential. The gluten-free diet should be adhered to for life. Non-adherence to the diet risks the development of micronutrient deficiency, especially osteopenia, and there is a small but definite increased risk in bowel malignancy, especially small bowel lymphoma.

 Children with coeliac disease can present with a wide range of symptoms.

Summary

Coeliac disease

- This is an immune-mediated systemic disorder to gluten and related prolamines (found in wheat, barley and rye) in genetically susceptible individuals.
- Classical presentation is at 8–24 months of age with abnormal stools, faltering growth, abdominal distension, muscle wasting, and irritability.
- Presentation is more often with more subtle symptoms and signs, e.g. anaemia, abdominal pain, short stature, or they are identified on screening.
- Causes a flat mucosa on duodenal biopsy, but this investigation may not be required if non-endoscopy diagnostic criteria are met.
- Treatment is a gluten-free diet for life.

Food allergy

This is described in [Chapter 16 \(Allergy\)](#).

Lactose intolerance

Lactose intolerance is a form of malabsorption, where lactase enzyme is not expressed on the microvilli of the intestine. Lactose is not broken down into glucose and galactose, and this results in recurrent bloating, abdominal pain and foul-smelling 'yeasty' stool whenever dairy products are consumed. Some experience nausea and vomiting. Lactose intolerance is often secondary to viral gastroenteritis and resolves after several months of dairy-free exclusion diet, during which lactase starts to be expressed again. From early adulthood onwards, the rate of lactose intolerance in the population varies widely, from less than 10% in Northern Europe to 95% in parts of Asia and Africa. In rare cases, lactose intolerance can be congenital, in which case it is caused by a genetic inability to produce lactase. Lactase supplements are available, but they are easily denatured by stomach acid, so are not always effective.



Case history 14.3

'Classical' coeliac disease

A 2-year-old boy had a history of poor growth from 12 months of age. His parents had noticed that he tended to be irritable and grumpy and had three or four foul-smelling stools a day. On examination he had wasting of the buttocks, a distended abdomen (Fig. 14.13a) and faltering growth (Fig. 14.13b). He had a moderately elevated IgA anti-tTG with normal IgA immunoglobulin levels. As

his blood tests were not diagnostic of coeliac disease, a duodenal biopsy was performed. This showed subtotal villous atrophy (Fig. 14.13c,d). He was started on a gluten-free diet and, within a few days, his parents commented that his mood had improved and, within a month, he was a 'different child'. He subsequently exhibited good catch-up growth.



Figure 14.13a Coeliac disease causing wasting of the buttocks and distended abdomen.

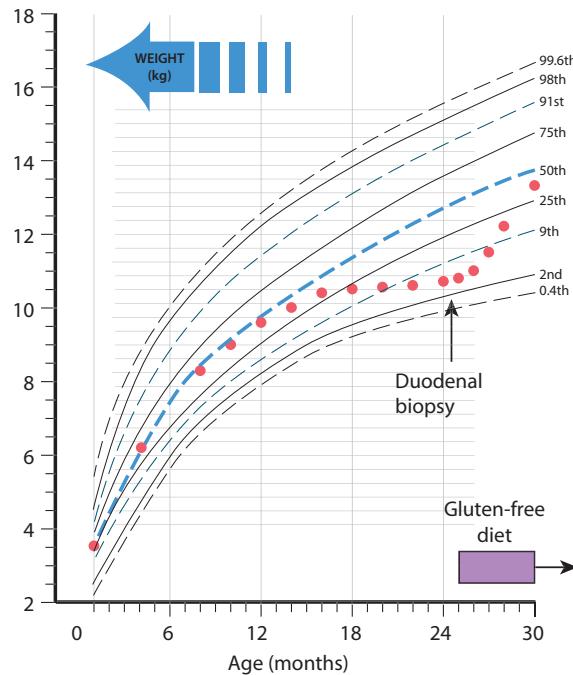


Figure 14.13b Growth chart showing faltering growth and response to a gluten-free diet. (Adapted from: Growth Chart © Royal College of Paediatrics and Child Health.)

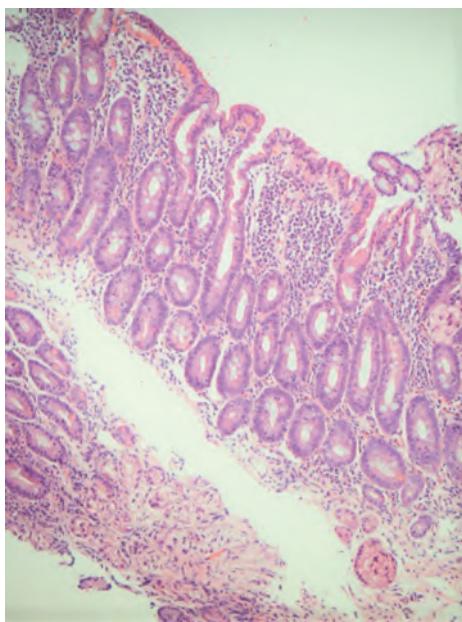


Figure 14.13c Histology of duodenal biopsy showing villous blunting, crypt hyperplasia and intra-epithelial lymphocytosis confirming a diagnosis of coeliac disease. (Courtesy of Professor Marta Cohen.)

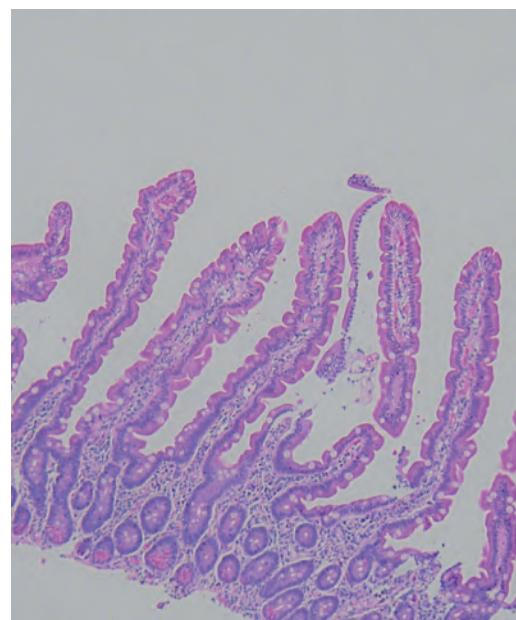


Figure 14.13d Normal duodenal histology shown for comparison. (Courtesy of Professor Marta Cohen.)

Other causes of nutrient malabsorption

These are summarized in Fig. 14.14.

Short bowel syndrome usually occurs when an infant or child has had a large surgical resection. This may be due to congenital atresia, necrotizing enterocolitis, malrotation with volvulus, or a traumatic event such as a road traffic accident. The incidence of patients with short bowel syndrome continues to rise. Depending on the length and type of residual bowel (ileum or jejunum) and if the ileocaecal valve is present, these children may develop malabsorption diarrhoea and malnutrition. If severe, they may require supplemental parenteral nutrition for their intestinal failure. They are at risk from nutritional deficiencies, intestinal failure-associated liver disease, and central line-associated bloodstream infections, and need to be managed by specialist multidisciplinary teams.

Chronic non-specific diarrhoea

This condition, previously known as toddler diarrhoea, is the most common cause of persistent loose stools in preschool children. Characteristically, the stools are of varying consistency, sometimes well formed, sometimes explosive and loose. The presence of undigested vegetables in the stools is common. Affected children are well and thriving. In a proportion of children the diarrhoea may result from undiagnosed coeliac disease or excessive ingestion of fruit juice, especially apple juice. Occasionally the cause is temporary cow's milk allergy following gastroenteritis, when a trial of a cow's milk

protein free diet may be helpful. Once possible underlying causes have been excluded, in the majority of cases the loose stools probably result from dysmotility of the gut (a form of irritable bowel syndrome) and fast-transit diarrhoea; it almost always improves with age.

Summary

Chronic diarrhoea

- In an infant with faltering growth, consider coeliac disease and cow's milk protein allergy.
- Following bowel resection, cholestatic liver disease or exocrine pancreatic dysfunction, consider malabsorption.
- In an otherwise well toddler with undigested vegetables in the stool, consider chronic non-specific diarrhoea.

Inflammatory bowel disease

The incidence of inflammatory bowel disease in children has increased markedly in the last two decades. The reason for this is unclear, but recent evidence suggests a complex interplay between genetics, gut microbiome and mucosal immunity is responsible. A number of genes have been identified that give an increased risk, but this is often in association with increased risks of other autoimmune diseases that do not always coexist with inflammatory bowel disease. Approximately a quarter

Causes of nutrient malabsorption

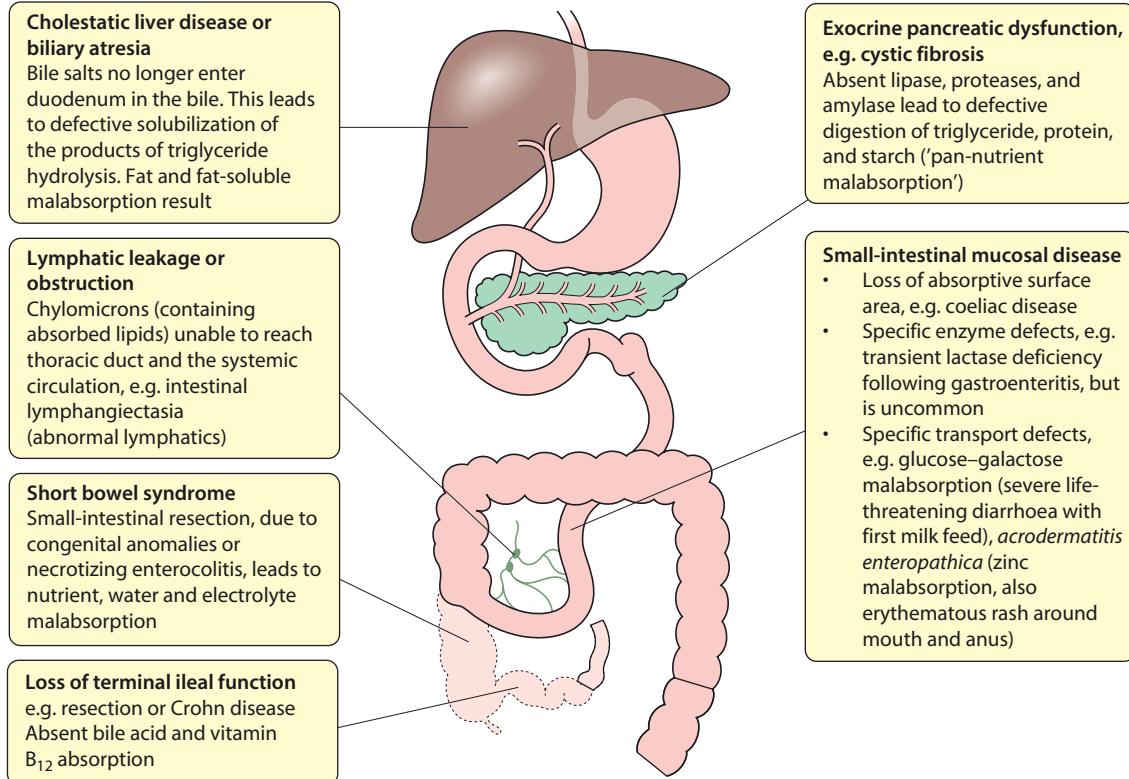


Figure 14.14 Causes of nutrient malabsorption. They are uncommon.

Presentation of Crohn disease in children and young people

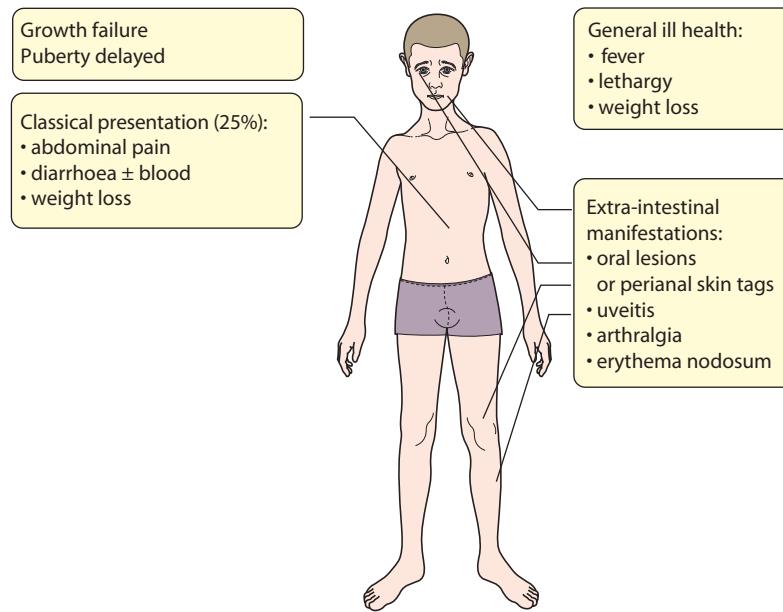


Figure 14.15 Presentation of Crohn disease in children and young people.

of patients present in childhood or adolescence and, in contrast with the adult population, Crohn disease is more common than ulcerative colitis. Crohn disease can affect any part of the gastrointestinal tract from mouth to anus, whereas in ulcerative colitis the inflammation is confined to the colon. Inflammatory bowel disease may cause poor general health, restrict growth, and have an adverse effect on psychological wellbeing. Management requires a specialist multidisciplinary team.

Investigations include:

- Faecal calprotectin – a stool test which is a sensitive marker of gastrointestinal inflammation in children.
- Endoscopy – allows direct visualization of the mucosa, biopsies and therapeutic interventions if required. In paediatric patients it is usually performed under general anaesthetic.
- Wireless capsule endoscopy – a small wireless capsule is either swallowed or delivered into the duodenum endoscopically. It transmits photographs every second, allowing detailed mucosal assessment of the small bowel.

Crohn disease

The clinical features of Crohn disease are summarized in Fig. 14.15. Lethargy and general ill health without gastrointestinal symptoms can be the presenting features, particularly in older children. There may be considerable delay in diagnosis as it may be mistaken for psychological problems. It may also mimic anorexia nervosa. The presence of raised inflammatory markers (platelet count, erythrocyte sedimentation rate, C-reactive protein and faecal calprotectin), iron-deficiency anaemia, and low serum albumin are helpful pointers to a diagnosis or confirming a relapse.

Crohn disease is a transmural, focal, subacute, or chronic inflammatory disease, most commonly affecting the distal ileum and proximal colon. Initially, there are

areas of acutely inflamed, thickened bowel. Subsequently, strictures of the bowel and fistulae may develop between adjacent loops of bowel, between bowel and skin or to other organs (e.g. vagina, bladder).

Diagnosis is based on endoscopic and histological findings on biopsy. Upper gastrointestinal endoscopy, ileocolonoscopy and small bowel assessment by imaging with MRI or wireless capsule endoscopy are required. The histological hallmark is the presence of non-caseating epithelioid cell granulomata, although this is not identified in up to 30% at presentation. Small bowel imaging may reveal narrowing, fissuring, mucosal irregularities and bowel wall thickening.

Remission is induced with nutritional therapy, when the normal diet is replaced by whole protein modular feeds (polymeric diet) for 6–8 weeks. This is effective in 75%. Systemic steroids are required if ineffective.

Relapse is common and immunosuppressant medication (azathioprine, mercaptopurine or methotrexate) is almost always required to maintain remission. Anti-tumour necrosis factor agents (infliximab or adalimumab) may be needed when conventional treatments have failed or at diagnosis of severe disease. Long-term supplemental enteral nutrition may be helpful in correcting growth failure. Surgery may be necessary for complications of Crohn disease – obstruction, fistulae, abscess formation or severe localized disease unresponsive to medical treatment, often manifesting as growth failure. In general, the long-term prognosis for Crohn disease beginning in childhood is good and most patients lead normal lives, despite occasional relapsing disease.



Growth failure and delayed puberty are features of Crohn disease in children and young people.

Ulcerative colitis

Ulcerative colitis is a recurrent, inflammatory and ulcerating disease involving the mucosa of the colon. Characteristically,

the disease presents with rectal bleeding, diarrhoea and colicky pain. Weight loss and growth failure may occur, although this is less frequent than in Crohn disease. Extraintestinal complications include erythema nodosum and arthritis.

The diagnosis is made on endoscopy (upper and ileocolonoscopy) and on the histological features, after exclusion of infective causes of colitis. There is a confluent colitis extending from the rectum proximally for a variable length. In contrast to adults, in whom the colitis is usually confined to the distal colon, 90% of children have pancolitis. Histology reveals mucosal inflammation, crypt damage (cryptitis, architectural distortion, abscesses and crypt loss), and ulceration. If atypical features are noted on endoscopy and histology, small bowel assessment is required to check that extracolonic inflammation suggestive of Crohn disease is not present.

The Paediatric Ulcerative Colitis Activity Index (PUCAI) score is a validated tool used to assess the severity of symptoms and can help categorize severity of disease and assess response to treatment (see [Case history 14.4](#)). In mild disease, aminosalicylates (e.g. mesalazine) are used for induction and maintenance therapy. Disease confined to the rectum and sigmoid colon (less common in children) may be managed with topical steroids. More aggressive or extensive disease requires systemic steroids for acute exacerbations and immunomodulatory therapy, e.g. azathioprine to maintain remission. There is a role for biological therapies in patients with resistant disease but, if ineffective, surgery should not be delayed.

Severe fulminating disease is a medical emergency and requires treatment with intravenous fluids and steroids. If this fails to induce remission, infliximab or ciclosporin may be used.

Colectomy with an ileostomy or ileorectal pouch is undertaken for severe fulminating disease, which may be complicated by a toxic megacolon, or for chronic poorly controlled disease. There is an increased incidence of adenocarcinoma of the colon in adults (1 in 200 risk for each year of disease between 10 and 20 years from diagnosis). Regular colonoscopic screening is performed after 8–10 years from diagnosis dictated by risk factors.

Constipation

Constipation is an extremely common reason for consultation in children, most often between 2 and 4 years of age ([Fig. 14.18](#)). Parents may use the term to describe decreased frequency of defecation, the degree of hardness of the stool or painful defecation. The ‘normal’ frequency of defecation is highly variable and varies with age. Breastfed infants usually have a stool frequency of 4 or more times a day, but may not pass stools for several days and be entirely healthy. It is usually twice a day by 1 year of age. Thereafter, most children have a daily bowel action. Constipation is defined as the presence of two or more of the clinical features:

- the infrequent passage (fewer than three complete stools per week)
- hard, large stool
- ‘rabbit dropping’ stool ([Fig. 14.19](#))
- overflow soiling.

There may be straining or pain and bleeding associated with hard stools or abdominal pain and reduced appetite, which waxes and wanes with passage of stool. Faecal impaction is when there are severe symptoms, overflow soiling and a faecal mass on abdominal examination. The constipation may have been precipitated by dehydration or reduced fluid intake or change in diet or an anal fissure causing pain. It may relate to the child withholding stool (may be accompanied by ‘retentive posturing’ with straight legs, tip-toes with arched back) to avoid distraction from play, or problems with toilet training. In older children there may be anxieties about opening bowels at school or in unpleasant or unfamiliar toilets. It may also be a side effect of medications.

Examination usually reveals a well child whose growth is normal, the abdomen is soft and any abdominal distension is normal for age. The back and perianal area are normal in appearance and position and lower limb neurological examination is normal. A soft faecal mass may sometimes be palpable in the lower abdomen, but is not necessary for the diagnosis. Digital rectal examination should not be performed, though it may sometimes be considered by a paediatric specialist to help identify anatomical abnormalities or Hirschsprung disease.

A primary underlying cause for constipation is rare, but a number of underlying conditions should be considered: ‘red and amber flag’ symptoms and signs indicative of more significant pathology are detailed in [Box 14.6](#). Investigations are not required to diagnose idiopathic constipation, but are carried out as indicated by history or clinical findings. If there is growth faltering or intractable constipation, investigations for hypothyroidism, coeliac disease and hypercalcaemia may be indicated.

Management

This is summarized in [Fig. 14.20](#). Reassurance can be offered that underlying causes have been excluded. Constipation arising acutely in young children, e.g. after an acute febrile illness, usually resolves spontaneously or with the use of maintenance laxative therapy.

In more long-standing constipation, the rectum becomes overdistended, with a subsequent loss of feeling the need to defecate. Involuntary soiling may occur as contractions of the full rectum inhibit the internal sphincter, leading to overflow.

Initial management is to evacuate the overloaded rectum; recovery of normal rectal size and sensation can be achieved but may take a long time. Faecal impaction requires a regimen of stool softeners, initially with a macrogol laxative, e.g. polyethylene glycol (Movicol Paediatric Plain). An escalating dose regimen is administered over 1–2 weeks or until impaction resolves. If this proves unsuccessful, a stimulant laxative, e.g. senna, or sodium picosulphate, may also be required. If the polyethylene glycol is not tolerated, an osmotic laxative (e.g. lactulose) can be substituted.

Maintenance treatment is given following disimpaction or if impaction is not present to ensure ongoing regular, pain-free defecation. Polyethylene glycol (with or without a stimulant laxative) is generally the treatment of choice. The dose should be gradually reduced over a period of months in response to improvement in stool consistency and frequency.

Dietary interventions alone have not been shown to be of benefit in managing constipation in this situation, although



Case history 14.4

Ulcerative colitis

Samuel, a 14-year-old boy, presented with a 3-week history of central abdominal pain and frequent episodes of diarrhoea. This had progressively worsened and the stools had become bloody. He was waking 3–4 times throughout the night to pass stool and was unable to leave the house due to his toileting. On admission to hospital his inflammatory markers (CRP and ESR) were elevated and his faecal calprotectin was extremely high. His score on the Paediatric Ulcerative Colitis

Assessment Index (PUCAI) was severe (Fig. 14.16). An abdominal radiograph was not suggestive of toxic megacolon. He was commenced on intravenous antibiotics and intravenous steroids to treat suspected inflammatory bowel disease. Ileocolonoscopy revealed ulceration throughout the rectum and colon consistent with ulcerative colitis (Fig. 14.17), and histology confirmed the presence of acute severe inflammation with cryptitis and crypt abscess formation.

Circle as shown

Item	Category/Points
Abdominal pain	No pain = 0 Pain can be ignored = 5 Pain cannot be ignored = 10
Rectal bleeding	None = 0 Small amounts = 10 Small amounts with most stools = 20 Large amount (>50% of stool content) = 30
Stool consistency of most stools	Formed = 0 Partially formed = 5 Completely unformed = 10
Number of stools per 24 hours	0–2 = 0 3–5 = 5 6–8 = 10 points >8 = 15
Nocturnal stools (any episode causing wakening)	No = 0 Yes = 10 points
Activity level	No limitation = 0 Occasional limitation = 5 Severely restricted = 10
	Sum of PUCAI = 75

Figure 14.16 The Paediatric Ulcerative Colitis Assessment Index (PUCAI). It is based on history in previous 48 hours; Total score: Remission <10; Mild 10–34; Moderate 35–64; Severe 65–85. This shows Samuel's score of 75 = Severe. (Source: Turner D, Otley AR, Mack D, et al: Development and evaluation of a Pediatric Ulcerative Colitis Activity Index (PUCAI): a prospective multicenter study. *Gastroenterology*. 2007; 133:423. Copyright to The Hospital for Sick Children, Toronto, Canada, 2006.)

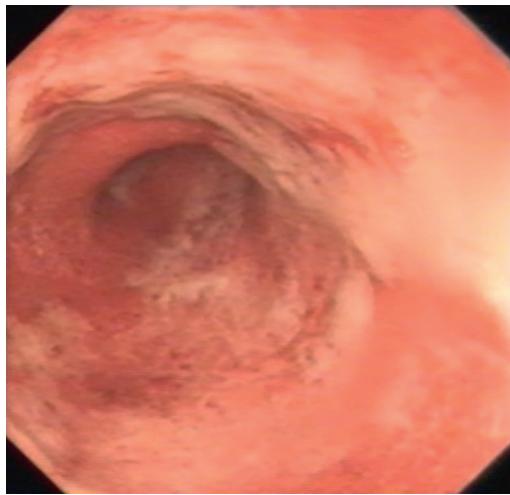


Figure 14.17 Endoscopic appearance showing significant inflammation consistent with the diagnosis of ulcerative colitis.

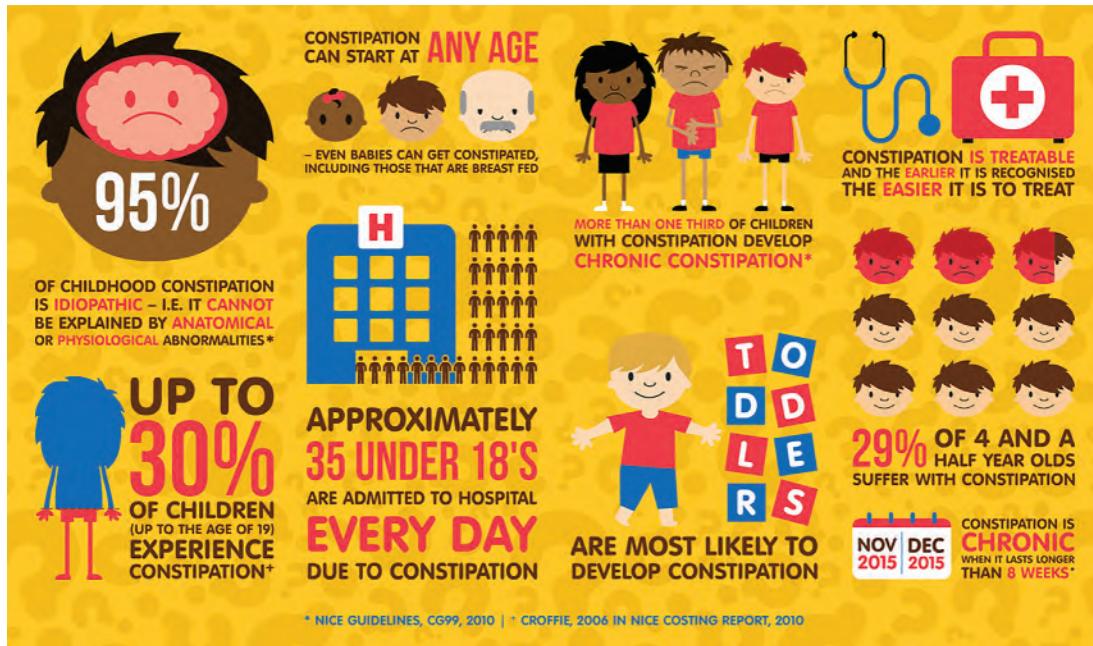


Figure 14.18 Constipation in children. (From: The Children's Bowel and Bladder Charity. www.eric.org.uk, with permission.)

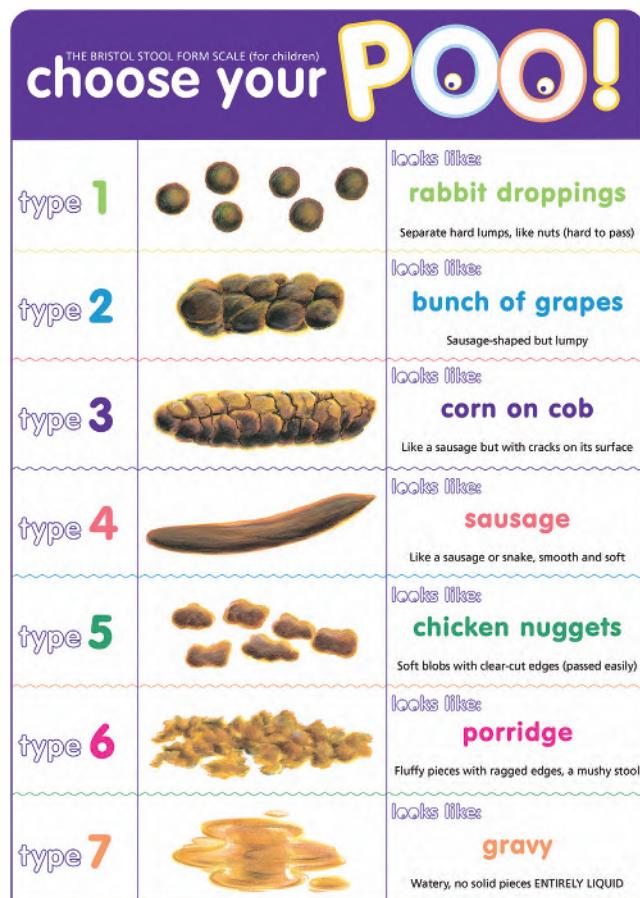
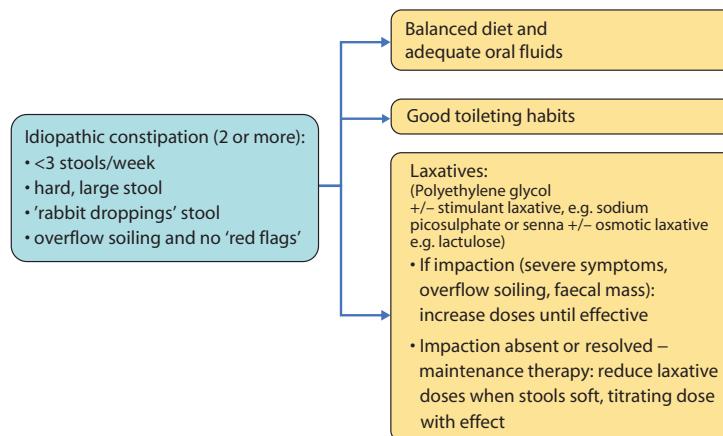


Figure 14.19 Bristol stool chart. This shows description of stools. (From: The Children's Bowel and Bladder Charity. www.eric.org.uk, with permission.)

Box 14.6 ‘Red and amber flag’ symptoms or signs in the child with constipation

‘Red flag’ symptom/signs – urgent referral	Diagnostic concern
Failure to pass meconium within 24 hours of life, constipation from or soon after birth; family history of Hirschsprung disease	Hirschsprung disease
Abdominal distension with vomiting	Hirschsprung disease or intestinal obstruction
Ribbon stool pattern	Anal stenosis
Abnormal lower limb neurology or deformity	Neurological or spinal cord abnormality
Abnormality of lumbosacral or gluteal regions, e.g. sacral dimple above natal cleft, or naevus, hairy patch, central pit, or discoloured skin over the spine	Spina bifida occulta
Abnormal appearance / position / patency of anus	Abnormal anorectal anatomy
Perianal bruising or multiple fissures	Sexual abuse
Perianal fistulae, abscesses, or fissures	Perianal Crohn disease
Amber signs – specialist referral; start treating constipation	Diagnostic concern
Faltering growth / growth failure	Hypothyroidism, coeliac disease, other causes
Constipation triggered by introduction of cow’s milk	Cow’s milk protein allergy

(Based on: National Institute for Health and Clinical Excellence (NICE) guideline: Constipation in children, 2019.)

**Figure 14.20** Summary of the management of constipation. (Based on: National Institute for Health and Clinical Excellence (NICE) guideline: Constipation in children, 2019.)

the child should receive sufficient fluid and a balanced diet. The addition of extra fibre to the diet is not helpful, and may make stools larger and more difficult to pass. Scheduled toileting, e.g. to sit on the toilet after mealtimes to utilize the physiological gastrocolic reflex may be helpful.

The outcome is more likely to be successful if the child is engaged in the treatment process. This requires exploring the child’s concerns and motivation to change. Encouragement by family and health professionals is essential, as relapse is common. The mainstay of treatment is the early, aggressive and prolonged use of laxative medication in a dose that allows the passage of a large, soft stool at least once a day. One needs to emphasize that the use of laxatives is safe, even long-term, as underuse is the commonest reason for treatment failure.

Sometimes the use of behavioural interventions, e.g. a star chart, is helpful to record and reward progress, as well as to motivate the child. Psychological support is sometimes required. National family support organizations have useful materials and resources, e.g. ERIC – The Children’s

Bowel and Bladder Charity. Children of school age are frequently teased as a result stool overflow and this may result in secondary behavioural problems. Management of these children is likely to be more difficult and protracted (see Ch. 24, Child and adolescent mental health).

Occasionally, the faecal retention is so severe that the above regimen is unsuccessful. If oral disimpaction medications are not tolerated or not successful, nasogastric administration of large volume macrogol (Klean Prep) can be administered. Sometimes, evacuation is only possible using enemas or by manual evacuation under an anaesthetic. They should only be performed under specialist supervision, paying particular attention to avoiding distress and embarrassment for the child.

Hirschsprung disease

The absence of ganglion cells from the myenteric and submucosal plexuses of part of the large bowel results in a



Figure 14.21 Abdominal distension from Hirschsprung disease.

narrow, contracted segment. The abnormal bowel extends from the rectum for a variable distance proximally, ending in a normally innervated, dilated colon. In 75% of cases, the lesion is confined to the rectosigmoid, but in 10% the entire colon is involved. Presentation is usually in the neonatal period with intestinal obstruction heralded by failure to pass meconium within the first 24 hours of life. Abdominal distension and later bile-stained vomiting develop (Fig. 14.21). Rectal examination may reveal a narrowed segment and withdrawal of the examining finger often releases a gush of liquid stool and flatus. Temporary improvement in the obstruction following the dilatation caused by the rectal examination can lead to a delay in diagnosis.

Occasionally, infants present with severe, life-threatening Hirschsprung enterocolitis during the first few weeks of life. In later childhood, presentation is with chronic constipation, usually profound, and associated with abdominal distension but usually without soiling. Growth faltering may also be present.

Summary

Hirschsprung disease

- Absence of myenteric plexuses of rectum and variable distance of colon.
- Presentation – usually intestinal obstruction in the newborn period following delay in passing meconium; in later childhood – profound chronic constipation, abdominal distension, and growth faltering.
- Diagnosis – suction rectal biopsy.

Diagnosis is made by demonstrating the absence of ganglion cells, together with the presence of large, acetylcholinesterase-positive nerve trunks on a suction rectal biopsy. Anorectal manometry or barium studies may be useful in giving the surgeon an idea of the length of the aganglionic segment but are unreliable for diagnostic purposes. Management is surgical and usually involves an initial colostomy followed by anastomosis of normally innervated bowel to the anus.

Acknowledgements

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Further reading

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National Institute for Health and Care Excellence (NICE): Diarrhoea and vomiting caused by gastroenteritis in under 5s: Diagnosis and management. Clinical guideline [CG84], London, 2009, NICE.

National Institute for Health and Care Excellence (NICE): Clinical guideline [CG99], Constipation in children and young people: Diagnosis and management, London, 2010, NICE.

National Institute for Health and Care Excellence (NICE): NICE guideline gastro-oesophageal reflux disease in children and young people: Diagnosis and management, London, 2015, NICE.

Websites

Coeliac UK: www.coeliac.co.uk.

ERIC – The Children's Bowel and Bladder Charity: www.eric.org.uk.

Up-to-date reviews on a selection of paediatric gastroenterology topics available at: www.espghan.org.



Infection and immunity

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Features of infection and immunity in children:

- Worldwide, infection, often accompanied by undernutrition, is responsible for the deaths of more than 2.3 million children under 5 years of age annually ([Fig. 15.1](#)).
- In high-income countries, deaths caused by infections are now uncommon. However, infections are the most common cause of acute illness in children, and serious infections still occur, e.g. pneumonia, sepsis, and meningitis, and require early recognition and treatment.
- There has been a rise of multidrug-resistant pathogens over the last two decades, including methicillin-resistant *Staphylococcus aureus* and extended-spectrum beta-lactamase-producing Gram-negative bacteria.
- With air travel, imported ‘tropical diseases’ are now encountered in all countries. Air travel has also contributed to epidemics spreading more rapidly and more widely, e.g. severe acute respiratory syndrome (SARS, caused by SARS coronavirus), and the pandemics caused by COVID-19 (caused by SARS-CoV-2) and H1N1 influenza virus.
- Immunization has played a major role in reducing morbidity and mortality of infections throughout the world.

The febrile child

Most febrile children have a brief, self-limiting viral infection. Mild localized infections, e.g. otitis media or tonsillitis, may be diagnosed clinically. The clinical problem lies in identifying the relatively small proportion of children with a serious infection that needs prompt treatment.

Clinical features

When assessing a febrile child, consider the following:

(i) How is fever identified in children?

Parents usually know if their child has been febrile and this should be considered a valid assessment.

In hospital, it is measured:

- if less than 4 weeks of age, by an electronic thermometer in the axilla
- if aged 4 weeks to 5 years, by an electronic or chemical dot thermometer in the axilla or infrared tympanic thermometer. There are also infrared forehead thermometers.

A fever in children is a temperature over 38.0°C. In general, axillary temperatures underestimate body temperature by 0.5°C.

Children may develop very high temperatures. In general, it is the presence of a fever rather than its height that is important.

(ii) How old is the child?

Febrile infants less than 3 months of age can present with non-specific clinical features (see [Box 11.3](#)) and have a bacterial infection, which cannot be identified reliably on clinical examination alone. During the first few months of life infants are relatively protected against common viral infections because of passive immunity acquired by transplacental transfer of antibodies from their mothers ([Fig. 15.2](#)). Unless a clear cause for the fever is identified in infants less than 3 months, they require urgent investigation with a septic screen ([Box 15.1](#)) and broad-spectrum intravenous antibiotic therapy given immediately to avoid the illness becoming more severe and to prevent spreading of the

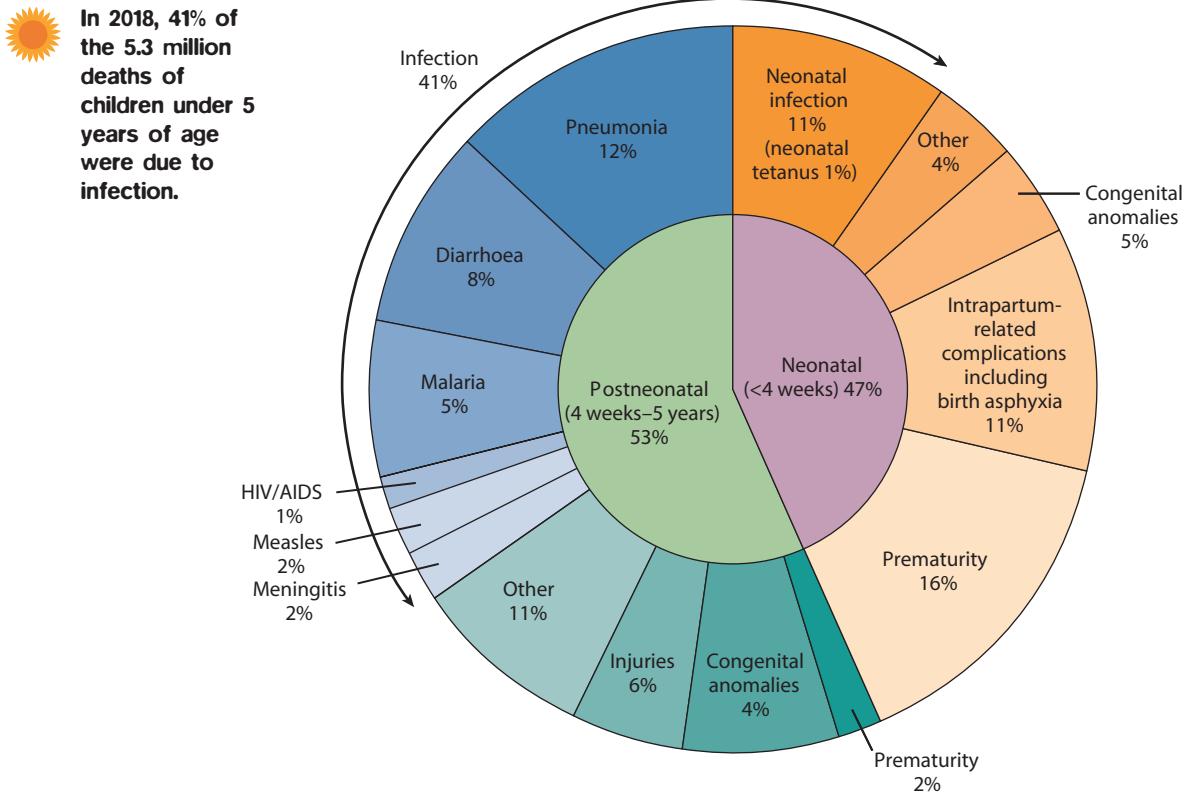


Figure 15.1 Worldwide causes of death in children <5 years. Globally, infection is responsible for 41% of the 5.3 million deaths in children under 5 years of age, 2015. (Data from: WHO and Maternal and Child Epidemiology Estimation Group (MCEE) interim estimates produced in September 2019. www.unicef.org/media/60561/file/UN-IGME-child-mortality-report-2019.pdf.)

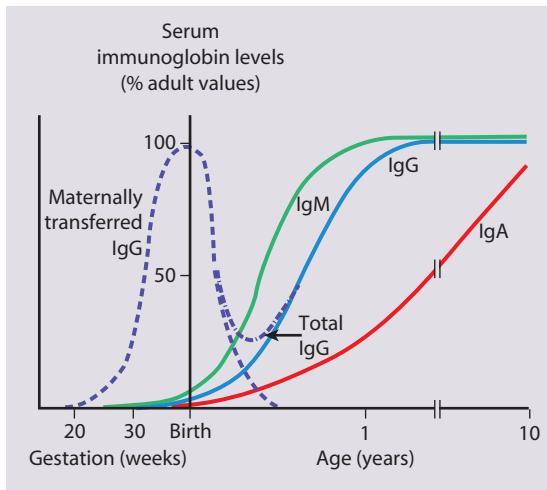


Figure 15.2 Serum immunoglobulin (antibody) levels in the fetus and infant. When maternal immunoglobulin levels decline, infants become susceptible to viral infections.

infection to other sites of the body. This is considered in more detail in the section on late-onset infection in the neonatal infection (Ch. 11, Neonatal medicine).

(iii) Are there risk factors for infection?

These include:

- illness of other family members
- specific illness prevalent in the community

Box 15.1 Septic screen

- Blood culture
- Full blood count including differential white cell count
- Acute phase reactant, e.g. C-reactive protein
- Urine sample

Consider if indicated:

- Chest X-ray
- Lumbar puncture (unless contraindicated)
- Meningococcal and pneumococcal polymerase chain reaction (PCR) on bloodsamples / cerebrospinal fluid (CSF) samples
- PCR for viruses in CSF (especially herpes simplex virus and enteroviruses)
- Serum electrolytes and blood gas including glucose and lactate.

- lack of immunizations
- recent travel abroad (consider malaria, typhoid, and viral hepatitis)
- contact with animals (consider brucellosis, Q fever, and haemolytic uraemic syndrome caused by *Escherichia coli* O157)
- increased susceptibility from immunodeficiency. This is usually secondary such as:
 - Breach of anatomical and physical barriers e.g. burns, central line *in situ*

- Splenectomy for underlying condition, e.g. spherocytosis or auto-splenectomy in sickle cell disease increasing susceptibility to encapsulated organisms (*Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Salmonella* species)
- Immunosuppressive or immune-mediating drugs
- Antibody defects such as in prematurity or loss in nephrotic syndrome
- HIV – in countries with high prevalence of HIV infection, undiagnosed HIV infection in the child must be considered.

Rarely children have a primary immune deficiency including SCID (severe combined immune deficiency) which increases susceptibility to a broad range of pathogens including viruses, bacteria and fungi.

(iv) How ill is the child?

Red flag features suggesting serious illness and the need for urgent investigation and treatment are:

- fever over 38°C if aged less than 3 months
- colour – pale, mottled, or cyanosed

- level of consciousness is reduced, neck stiffness, bulging fontanelle, status epilepticus, focal neurological signs, or seizures
- significant respiratory distress
- shock.

(v) Is there a rash?

Rashes often accompany febrile illnesses. In some, the characteristics of the rash and other clinical features lead to a diagnosis, e.g. a purpuric rash in meningococcal septicaemia; in many, a specific diagnosis cannot be made clinically.

(vi) Is there a focus for infection?

Examination may identify a focus of infection (Fig. 15.3). If identified, investigations and management will be directed towards its treatment. However, if no focus is identified, this is often because it is the prodromal phase of a viral illness, but may indicate a potentially serious bacterial infection, especially urinary tract infection or septicaemia.

The febrile child

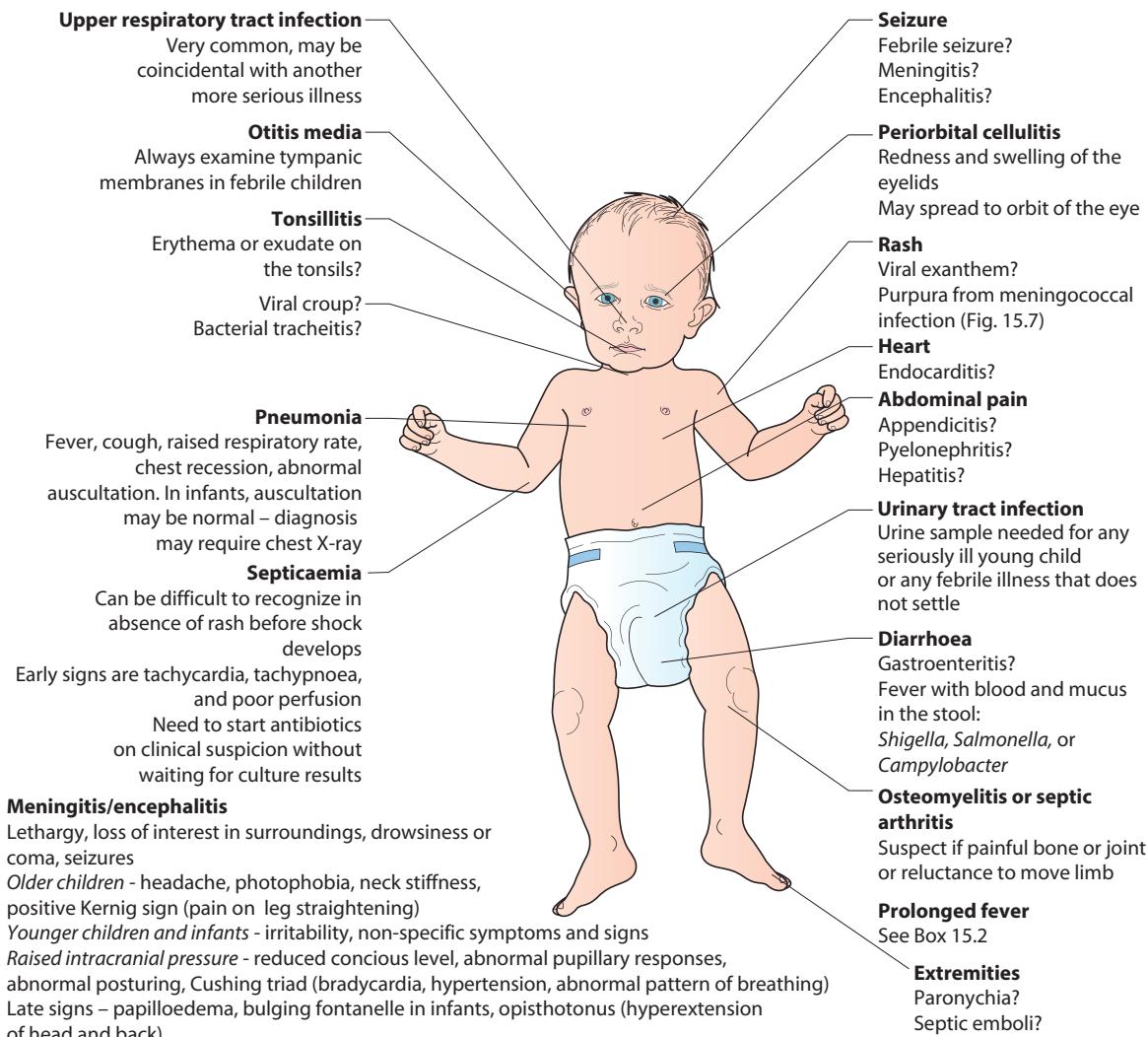


Figure 15.3 Diagnostic clues to evaluating the febrile child.

Management

Children who are not seriously ill can be managed at home with regular review by the parents, as long as they are given clear instructions (e.g. what clinical features should prompt reassessment by a doctor). Children who are significantly unwell, particularly if there is no focus of infection, will require investigations and observation or treatment in a paediatric assessment unit, emergency department, or children's ward. A septic screen will be required (see [Box 15.1](#)).

Parenteral antibiotics should be given immediately to seriously unwell children, e.g. a third-generation cephalosporin such as cefotaxime (<1 month old who have been discharged from hospital) or high-dose ceftriaxone (>1 month old). In infants under 1 month of age, high dose amoxicillin is added to cover for *Listeria* infection. Aciclovir is given if herpes simplex virus (HSV) encephalitis is suspected. Supportive care is given as indicated.

The use of antipyretic agents should be considered in children with fever who appear distressed or unwell. Either paracetamol or ibuprofen can be used. Changing from one to the other should be considered if the child's distress is not alleviated. Alternating them should only be considered if the distress persists or recurs before the next dose is due. Evidence that antipyretics prevent febrile seizures is lacking. There are detailed National Institute for Health and Care Excellence guidelines for the management of the child under 5 years of age with fever.

Summary

The febrile child

- Upper respiratory tract infection is a very common cause.
- Check for otitis media.
- Serious bacterial infection must be considered if there is no focus of infection, especially urinary tract infection or septicaemia, or there are red flag features of potentially life-threatening illness.
- The younger the child, the lower the threshold for performing a septic screen and starting antibiotics.

Serious life-threatening infections

Sepsis

This is considered in [Chapter 6](#) (Paediatric emergencies).

Meningitis

Meningitis occurs when there is inflammation of the meninges covering the brain. This can be confirmed by finding white blood cells in the cerebrospinal fluid (CSF). Viral

infections are the most common cause of meningitis, and although infants may be very unwell at presentation, most are self-resolving. Bacterial meningitis may have severe consequences. Tuberculous meningitis is rare in countries with low tuberculosis (TB) prevalence. It mainly affects children under 5 years of age. Fungal and parasitic meningitis are rare in children and predominantly affect immunocompromised individuals. Causes of non-infectious meningitis include malignancy and autoimmune diseases.

Bacterial meningitis

Bacterial meningitis remains a serious infection in children, although the number of cases in the UK has declined markedly. It has an overall 5% to 10% mortality, with over 10% of survivors left with long-term neurological impairment.

Pathophysiology

Bacterial infection of the meninges usually follows bacteraemia. Much of the damage caused by meningeal infection results from the host response to infection and not from the organism itself. The release of inflammatory mediators and activated leucocytes, together with endothelial damage, leads to cerebral oedema, raised intracranial pressure, and decreased cerebral blood flow. The inflammatory response below the meninges causes a vasculopathy resulting in cerebral cortical infarction, and fibrin deposits may block the resorption of CSF by the arachnoid villi, resulting in hydrocephalus.

Organisms

The organisms that commonly cause bacterial meningitis vary according to the child's age ([Table 15.1](#)). These have changed over time with the introduction of conjugate vaccines (against *H. influenzae* type b [Hib], meningococcal groups B and C, meningococcal groups A, C, Y, and W, and multiple pneumococcal serotypes).

Presentation

The clinical features are listed in [Fig. 15.4](#). The early signs and symptoms of meningitis are non-specific, especially in infants and young children. Only children old enough to talk are likely to describe the classical meningitis symptoms of headache, neck stiffness, and photophobia. However, neck stiffness may also be seen in some children with tonsillitis and cervical lymphadenopathy. As children with meningitis may also have sepsis, signs of shock, such as tachycardia, tachypnoea, prolonged capillary refill time and hypotension, should be sought. Purpura in a febrile child of any age should be assumed to be due to meningococcal sepsis, even if the child does not appear unduly

Table 15.1 Organisms causing bacterial meningitis according to age

<3 months old	Group B streptococcus <i>Escherichia coli</i> and other coliforms <i>Listeria monocytogenes</i>
>3 months	<i>Neisseria meningitidis</i> <i>Streptococcus pneumoniae</i>

Assessment and investigation of meningitis / encephalitis

History	Examination	Investigations to consider
Fever	Fever	Full blood count and differential count
Headache	Purpuric rash (meningococcal disease)	Blood glucose and blood gas (for acidosis)
Photophobia	Neck stiffness (not always present in infants)	Coagulation screen, C-reactive protein
Lethargy	Bulging fontanelle in infants	Urea and electrolytes, liver function tests
Poor feeding/vomiting	Opisthotonus (arching of back)	Culture of blood, throat swab, urine, stool for bacteria
Irritability	Positive Brudzinski/Kernig signs	Samples for viral polymerase chain reaction (PCRs) (e.g. throat swab, nasopharyngeal aspirate, conjunctival swab, stool sample)
Hypotonia	Signs of shock	Lumbar puncture for cerebrospinal fluid (CSF) unless contraindicated (see below for tests on CSF)
Drowsiness	Focal neurological signs	Serum for comparison of convalescent titres
Loss of consciousness	Altered conscious level	PCR of blood and CSF for possible organisms
Seizures	Papilloedema (rare)	If TB suspected: chest X-ray, Mantoux test and/or interferon-gamma release assay, gastric aspirates or sputum for microscopy and culture (and PCR if available)
		Consider CT/MRI brain scan and EEG

Signs associated with neck stiffness

Brudzinski sign – flexion of the neck with the child supine causes flexion of the knees and hips

Kernig sign – with the child lying supine and with the hips and knees flexed, there is back pain on extension of the knee

Contraindications to lumbar puncture (LP):

- Cardiorespiratory instability
- Focal neurological signs
- Signs of raised intracranial pressure, e.g. coma, high BP, low heart rate or papilloedema
- Coagulopathy
- Thrombocytopenia
- Local infection at the site of LP
- If it causes undue delay in starting antibiotics



Best time for LP?
Do as early as possible, but consider contraindications

Typical changes in the CSF in meningitis or encephalitis, beyond the neonatal period

	Aetiology	Appearance	White blood cells	Protein	Glucose
Normal	—	Clear	0–5/mm ³	0.15–0.4 g/L	≥50% of blood
<i>Meningitis</i>	Bacterial	Turbid	Polymorphs:↑↑	↑↑	↓↓
	Viral	Clear	Lymphocytes:↑ (initially may be polymorphs)	Normal/↑	Normal/↓
	Tuberculosis	Turbid/clear/viscous	Lymphocytes:↑	↑↑↑	↓↓↓
<i>Encephalitis</i>	Viral/unknown	Clear	Normal/↑ lymphocytes	Normal/↑	Normal/↓

Figure 15.4 Assessment and investigation of meningitis and encephalitis.

ill at the time; meningitis may or may not be present in this situation.

Investigations

The essential investigations are listed in Fig. 15.4. A lumbar puncture is performed to obtain CSF to confirm the diagnosis, and to identify the organism responsible and its antibiotic sensitivities. Characteristic findings are shown

in Fig. 15.4. However, exceptions can occur; for example, lymphocytes can predominate in bacterial meningitis, e.g. in Lyme disease, and glucose levels can be low in viral meningitis, e.g. enterovirus meningitis. A lumbar puncture should be performed at presentation, as significant delay can prolong the antimicrobial course and length of stay in hospital. Lumbar puncture is usually safe, except if any of the contraindications are present, as listed in Fig. 15.4, as

under these circumstances the procedure carries a risk of coning of the cerebellum through the foramen magnum. In these circumstances, lumbar puncture can be postponed until the child's condition has stabilized. A lumbar puncture done after antibiotics are given can still be helpful, as although cultures may be negative, polymerase chain reaction (PCR) on CSF can still be positive. Even without a lumbar puncture, bacteriological diagnosis can be achieved in about half of the cases from the blood by culture or PCR. Throat swabs should also be obtained for bacterial culture and viral PCRs. A serological diagnosis can be made on convalescent serum 4 weeks to 6 weeks after the presenting illness if necessary.

Management

It is imperative that there is no delay in the administration of antibiotics and supportive therapy in a child with meningitis. The choice of antibiotics will depend on the likely pathogen. A third-generation cephalosporin, e.g. ceftriaxone, is the preferred choice to cover the most common bacterial causes, with the addition of amoxicillin in infants <3 months old to cover *Listeria*. Although still relatively rare in the UK, pneumococcal resistance to penicillin and cephalosporins is increasing rapidly in certain parts of the world. The length of the course of antibiotics given depends on the causative organism and clinical response. Beyond the neonatal period, dexamethasone should be administered when antibiotics are started as it reduces the risk of long-term complications such as deafness.

Cerebral complications

These include:

- *hearing impairment* – inflammatory damage to the cochlear hair cells may lead to deafness. All children who have had meningitis should have an audiological assessment done promptly, as children with hearing impairment may benefit from hearing amplification or a cochlear implant
- *local vasculitis* – this may lead to cranial nerve palsies or other focal neurological lesions
- *local cerebral infarction* – this may result in focal or multifocal seizures, which may subsequently result in epilepsy
- *subdural effusion* – particularly associated with pneumococcal meningitis. This is confirmed by cranial CT or MRI scan. Most resolve spontaneously, but some require neurosurgical intervention
- *hydrocephalus* – may result from impaired resorption of CSF (communicating hydrocephalus) or blockage of the cerebral aqueduct or ventricular outlets by fibrin (non-communicating hydrocephalus). A ventricular shunt may be required
- *cerebral abscess* – the child's clinical condition deteriorates with or without the emergence of signs of a space-occupying lesion. The temperature will continue to fluctuate. It is confirmed on cranial CT or MRI scan. Drainage of the abscess is required together with a long course of antibiotics.

Prophylaxis

Prophylactic treatment with ciprofloxacin to eradicate nasopharyngeal carriage is given to all household contacts for meningococcal meningitis. It is not required for the patient if given a third-generation cephalosporin, as this will eradicate nasopharyngeal carriage. Close contacts of patients with A, C, W or Y infections should be

offered vaccination with the conjugate MenACWY (unless had within the last 12 months). It is not recommended to vaccinate close contacts of patients with meningococcal serogroup B infection.

Partially treated bacterial meningitis

Children are frequently given oral antibiotics for a non-specific febrile illness. If they have early meningitis, this partial treatment with antibiotics may cause diagnostic problems. CSF examination shows a markedly raised number of white cells, but cultures are usually negative. PCR can be helpful in these circumstances. Where the diagnosis is suspected clinically, a full course of antibiotics should be given.

Viral meningitis

More than two-thirds of central nervous system (CNS) infections are viral. Causes include enteroviruses, parechovirus, Epstein–Barr virus (EBV), adenoviruses, and mumps. Mumps meningitis is now rare in the UK due to the measles, mumps, and rubella (MMR) vaccine. Viral meningitis is usually much less severe than bacterial meningitis, and most cases make a full recovery. Infants with viral meningitis caused by parechovirus may present with a 'sepsis'-like syndrome. Diagnosis of viral meningitis can be confirmed by PCR of CSF. Further support for the diagnosis can be made by PCR of stool, urine, nasopharyngeal aspirate, or throat swabs.

Uncommon pathogens and other causes

Where the clinical course is atypical or there is failure to respond to antibiotic and supportive therapy, unusual organisms, e.g. *Mycoplasma* species or *Borrelia burgdorferi* (Lyme disease), TB, or fungal infections need to be considered. Uncommon pathogens are particularly likely in children who are immunocompromised. Recurrent bacterial meningitis may occur in immunodeficient children or in those with structural abnormalities of the skull or meninges that facilitate bacterial access. Aseptic meningitis may be seen in malignancy or autoimmune disorders.

Neonatal meningitis

See Chapter 11.

Summary

Meningitis

- Predominantly a disease of infants and young children.
- Incidence has been reduced markedly by immunization.
- Clinical features:
 - non-specific in infants and young children – fever, poor feeding, vomiting, irritability, lethargy, drowsiness, seizures, or reduced consciousness
 - late signs – bulging fontanelle, neck stiffness, and arched back (opisthotonus).
- Any febrile child with a purpuric rash should be given intramuscular benzylpenicillin immediately and transferred urgently to hospital.

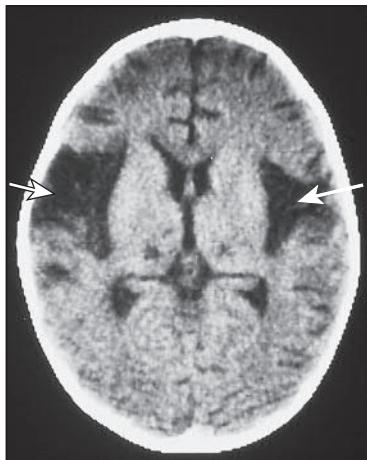


Figure 15.5 Herpes simplex encephalitis. The computed tomography scan shows gross atrophy from loss of neural tissue in the temporoparietal regions (arrows).

Encephalitis/encephalopathy

In meningitis there is inflammation of the meninges, whereas in encephalitis there is inflammation of the brain parenchyma, although the meninges are often also affected. Encephalitis may be caused by:

- direct invasion of the brain by a neurotoxic virus (such as HSV)
- delayed brain swelling following a dysregulated neuroimmunological response to an antigen, usually a virus (postinfectious encephalopathy), e.g. following chickenpox
- a slow virus infection, such as HIV infection or subacute sclerosing panencephalitis (SSPE) following measles.

In encephalopathy from a non-infectious cause, such as a metabolic abnormality, the clinical features may be similar to infectious encephalitis.

The clinical features and investigation of encephalitis are described in Fig. 15.4. Most children present with fever, altered consciousness, and often seizures. Initially, it may not be possible to clinically differentiate encephalitis from meningitis, and treatment for both should be started. The underlying causative organism is only detected in fewer than half of the cases. In the UK, the most common causes of encephalitis are enteroviruses, respiratory viruses (influenza viruses), and herpesviruses (e.g. HSV, varicella zoster virus [VZV], and human herpesvirus 6 [HHV-6]). Worldwide, microorganisms causing encephalitis include *Mycoplasma*, *B. burgdorferi* (Lyme disease), *Bartonella henselae* (cat scratch disease), rickettsial infections (e.g. Rocky Mountain spotted fever), and arboviruses.

HSV is a rare cause of childhood encephalitis but it can have devastating long-term consequences. All children with encephalitis should therefore be treated initially with high-dose intravenous aciclovir (acyclovir) until this diagnosis has been ruled out, because this is a very safe treatment. Most affected children do not have outward signs of herpes infection, such as cold sores, gingivostomatitis, or skin lesions. PCR is used to detect HSV in CSF. As HSV encephalitis is a destructive infection, the electroencephalogram and CT/MRI scan may show focal changes, particularly within the temporal lobes either unilaterally or bilaterally (Fig. 15.5). These tests may be normal initially and need to be repeated

after a few days if the child is not improving. Later confirmation of the diagnosis may be made from HSV antibody production in the CSF. Proven cases of HSV encephalitis or cases where there is a high index of suspicion should be treated with intravenous aciclovir for 3 weeks, as relapses may occur after shorter courses. Untreated, the mortality rate from HSV encephalitis is over 70%, and survivors usually have severe neurological sequelae.

Summary

Encephalitis

- Onset can be insidious and includes behavioural change.
- Consider if HSV could be the cause.
- Treat potential HSV with parenteral high-dose aciclovir until this diagnosis is excluded.

Toxic shock syndrome

Toxin-producing *S. aureus* and group A streptococci can cause this rare syndrome, which is characterized by:

- fever over 39°C
- hypotension
- diffuse erythematous, macular rash.

The toxin can be released from infection at any site, including small abrasions or burns, which may look minor. The toxin acts as a superantigen and, in addition to the aforementioned features, causes organ dysfunction, including:

- mucositis (Fig. 15.6): conjunctivae, oral mucosa, genital mucosa
- gastrointestinal dysfunction: vomiting/diarrhoea
- renal impairment
- liver impairment
- clotting abnormalities and thrombocytopenia
- CNS: altered consciousness.

Intensive care support is required to manage the shock. Areas of infection should be surgically debrided. Antibiotics often include a third-generation cephalosporin (such as ceftriaxone) together with clindamycin,



Figure 15.6 A child with toxic shock syndrome receiving intensive care, including mechanical ventilation via a nasotracheal tube. The lips are red and the eyelids are oedematous from capillary leak. (Courtesy of Professor Mike Levin.)

which acts on the bacterial ribosome to switch off toxin production. Intravenous immunoglobulin may be given to neutralize the circulating toxin. About 1 week to 2 weeks after the onset of the illness, there is desquamation of the palms, soles, fingers, and toes.

A strain of *S. aureus* has emerged in the UK and other countries that produces a toxin called Panton–Valentine leukocidin (PVL). PVL is produced by fewer than 2% of *S. aureus* strains (both methicillin-sensitive *S. aureus* and methicillin-resistant *S. aureus*). PVL-producing *S. aureus* causes recurrent skin and soft-tissue infections, but can also cause necrotizing fasciitis and a necrotizing haemorrhagic pneumonia following an influenza-like illness, both of which carry a high mortality rate. In children, the pro-coagulant state induced by the toxin frequently results in venous thrombosis.

Necrotizing fasciitis/cellulitis

This is a rare, severe subcutaneous infection. It is an uncommon but serious complication of chickenpox in young children. Necrotizing fasciitis often involves tissue planes from the skin down to fascia and muscle. The area involved may enlarge rapidly, leaving poorly perfused necrotic areas of tissue, usually at the centre. There is severe pain and systemic illness, which usually requires intensive care. The invading organism may be *S. aureus* or a group A streptococcus, with or without another synergistic anaerobic organism. Intravenous antibiotic therapy alone is not sufficient to treat this condition. Without surgical intervention and debridement of necrotic tissue, the infection will continue to spread. Clinical suspicion of necrotizing fasciitis warrants urgent surgical consultation and intervention. Intravenous immunoglobulin (IVIG) may also be given.

Specific bacterial infections

Meningococcal infection

Meningococcal infection is a disease that strikes fear into both parents and doctors, as it can kill previously healthy children within hours. Fortunately, it has become uncommon (see immunization section). The septicaemia is usually accompanied by a purpuric rash, which may start anywhere on the body and then spreads. The rash may or may not be present in cases with meningococcal meningitis. Characteristic lesions are non-blanching on palpation (although they may start as maculo-papular lesions), are irregular in size and outline, and may have a necrotic centre (Fig. 15.7). They are



typically larger than 5 mm, although may start as petechiae and increase in size. The septicaemia may progress within hours and the child may require intensive care (Fig. 15.8). Of the main causes of bacterial meningitis, meningococcal infection has the lowest risk of long-term neurological sequelae, with most survivors recovering fully, though limb loss sometimes occurs.



Any febrile child with a purpuric rash or who is very unwell should be given intramuscular benzylpenicillin or intravenous third-generation cephalosporin before urgent transfer to hospital.



Figure 15.8 Meningococcal septicaemia may progress very rapidly and the child may require intensive care. There are widespread purpuric lesions, irregular and varied size with a necrotic centre. (Copyright Keir Shiels.)

Figure 15.7 The glass test for meningococcal purpura. Parents are advised to suspect meningococcal disease if their child is febrile and has a rash that does not blanch when pressed under a glass. (Courtesy of Parviz Habibi.)



Meningococcal septicaemia can kill children in hours. Optimal outcome requires immediate recognition, prompt resuscitation and antibiotics.

Pneumococcal infections

S. pneumoniae is often carried in the nasopharynx of healthy children. Asymptomatic carriage is particularly prevalent among young children and may be responsible for the transmission of pneumococcal disease to other individuals by respiratory droplets. The organism may cause pharyngitis, otitis media, conjunctivitis, sinusitis, as well as 'invasive' disease (pneumonia, bacterial sepsis, and meningitis). Invasive disease, which carries a high burden of morbidity and mortality, mainly occurs in young infants as their immune system responds poorly to encapsulated pathogens such as pneumococci. With the inclusion of the 13-valent pneumococcal vaccine (covering 13 different serotypes) into the routine immunization schedule in the UK, the incidence of invasive disease has declined. Children at increased risk, e.g. due to hyposplenism or asplenia, should also be given daily prophylactic penicillin to prevent infection by strains not covered by the vaccine.

Summary

Pneumococcal infection

- Causes not only minor infections such as otitis media but also severe invasive disease.
- Susceptibility is increased in hyposplenism (e.g. sickle cell disease) and nephrotic syndrome.
- A 13-valent pneumococcal vaccine is included in the UK standard immunization schedule.

H. influenzae infection

Haemophilus influenzae type b (Hib) was an important cause of systemic illness in children, including otitis media, pneumonia, epiglottitis, cellulitis, osteomyelitis, and septic arthritis. It was the second most common cause of meningitis in the UK. Immunization has been highly effective and Hib now rarely causes systemic disease.

Summary

H. influenzae infection

- Can cause severe invasive infections, including sepsis and meningitis.
- Systemic Hib disease is now rare following the introduction of the Hib vaccine.

Staphylococcal and group A streptococcal infections

Staphylococcal and streptococcal infections are usually caused by direct invasion of the organisms. They may also cause disease by releasing toxins, which act as superantigens. Whereas conventional antigens stimulate only a small subset of T cells, which have a specific antigen receptor, superantigens bind to a part of the T-cell receptor which is shared by many T cells and therefore stimulates massive T-cell proliferation and cytokine release. Other diseases following streptococcal infections, such as post-streptococcal glomerulonephritis and rheumatic fever, are immune-mediated.

Scarlet fever

This occurs in association with an exotoxin from group A streptococcal pharyngitis. It is a diffuse, erythematous macular-papular rash with a sandpaper texture, which appears shortly after the pharyngitis (Fig. 15.9a). It usually spreads rapidly to the face, trunk and extremities with increased density around the neck, axillae or groin. There is circumoral pallor with the rash sparing the skin around the mouth. The tongue is initially white but desquamates to leave a red strawberry tongue with prominent papillae (Fig. 15.9b). There may be desquamation around the fingertips and toes. A throat swab may confirm group A streptococcus. Antibiotics such as penicillin V or erythromycin may hasten recovery from streptococcal tonsillitis by, on average, only 16 hours. In order to eradicate group A beta-haemolytic streptococci and prevent rheumatic fever, glomerulonephritis and other complications, 10 days of antibiotic treatment is required. This is indicated in countries where the risk of rheumatic fever is significant, if the child or young person is returning to a closed institution, e.g. boarding school, or is at increased risk of infection.

Impetigo

This is a localized, highly contagious, staphylococcal or streptococcal skin infection, most commonly occurring in infants and young children. It is more common in children with pre-existing skin disease, e.g. atopic eczema. Lesions are usually on the face, neck, and hands and begin as erythematous macules that may become vesicular/pustular or even bullous (Fig. 15.10). Rupture of the vesicles with exudation of fluid leads to the characteristic confluent honey-coloured crusted lesions. Infection is readily spread to adjacent areas and other parts of the body by autoinoculation of the infected exudate. Topical antibiotics (e.g. mupirocin) are sometimes effective for mild cases. Narrow-spectrum systemic antibiotics (e.g. flucloxacillin) are generally needed for more severe infections, although more broad-spectrum antibiotics such as co-amoxiclav or cephalexin have simpler oral administration regimens, taste better, and therefore have better adherence. Affected children should not go to nursery or school until the lesions are dry.



Figure 15.9 Scarlet fever. (a) The diffuse, erythematous macular-papular rash with a sandpaper texture, which appears shortly after the pharyngitis. (b) Red strawberry tongue. The tongue initially has a white coating, but desquamates to result in a red tongue with prominent papillae. (Courtesy of: Don't Forget the Bubbles.)



Figure 15.10 Impetigo showing characteristic confluent honey-coloured crusted lesions. (Courtesy of Dr Paul Hutchins.)



Figure 15.11 Periorbital cellulitis. It should be treated promptly with intravenous antibiotics to prevent spread into the orbit.

Boils

These are infections of hair follicles or sweat glands, usually caused by *S. aureus*. The lesion should be swabbed and then treatment is with systemic antibiotics and occasionally surgical incision. Recurrent boils are usually from persistent nasal carriage in the child or family acting as a reservoir for reinfection. Skin decontamination of the whole family with bodywash, e.g. chlorhexidine, and nasal treatments, e.g. mupirocin, are usually effective at reducing reinfection. Only rarely are they a manifestation of an underlying immunodeficiency.

Periorbital cellulitis

In periorbital (or preseptal) cellulitis there is fever with erythema, tenderness, and oedema of the eyelid or other skin adjacent to the eye (Fig. 15.11) and anterior to the orbital septum. It is almost always unilateral. It may follow local trauma to the skin. In older children, it may spread from a paranasal sinus infection or dental abscess. Periorbital cellulitis should be treated promptly with intravenous antibiotics such as high-dose ceftriaxone to prevent posterior spread of the infection to the orbital tissues causing orbital cellulitis. In orbital cellulitis,

there is proptosis, painful or limited ocular movement with or without reduced visual acuity. It may be complicated by abscess formation, meningitis, or cavernous sinus thrombosis. Where orbital cellulitis is suspected, a CT or MRI scan should be performed to assess the posterior spread of infection and managed in conjunction with an ophthalmologist.

Staphylococcal scalded skin syndrome

This is caused by an exfoliative staphylococcal toxin, which causes separation of the epidermal skin through the granular cell layers. It mainly affects infants and young children, who develop fever and malaise and may have a purulent, crusting, and localized infection around the eyes, nose, and mouth with subsequent widespread erythema and tenderness of the skin. Areas of epidermis separate on gentle pressure (Nikolsky sign), leaving denuded areas of skin (Fig. 15.12), which subsequently dry and heal, generally without scarring. Management is with an intravenous antistaphylococcal antibiotic (e.g. flucloxacillin), analgesia, and monitoring of hydration and fluid balance.



Figure 15.12 Staphylococcal scalded skin syndrome. Its appearance must not be mistaken for a scald from non-accidental injury.

Summary

Staphylococcal and streptococcal infections

- Symptoms are caused by direct invasion of bacteria or by release of toxins.
- Can cause a broad range of diseases, including toxic shock syndrome.
- Immune-mediated diseases following streptococcal infections include glomerulonephritis and rheumatic fever.
- Impetigo is highly contagious.
- Periorbital cellulitis should be treated aggressively with intravenous antibiotics to prevent spread to the orbit or brain.
- Scalded skin syndrome is a rare but serious disease.

Antimicrobial resistance

This has become a major concern in paediatrics, and is fuelled by inappropriate and overuse of antibiotics. Antibiotic stewardship is the umbrella term for interventions to prescribe appropriately, using pathogen-specific, narrow-spectrum antibiotics, in the correct dosage, for the appropriate duration, and performing continual monitoring.

It is a particular problem in neonatal practice as many infants are started on antibiotics empirically because of risk factors for infection or for non-specific clinical signs where infection is considered a possible cause. Antibiotic resistance is an increasing problem in neonatal units globally, particularly for Gram-negative pathogens such as *Escherichia coli* and *Klebsiella* species. Extended spectrum beta-lactamase (ESBL) producing bacteria threaten the use of penicillins and cephalosporins. Carbapenem-resistant Enterobacteriales not only destroy carbapenem (meropenem) antibiotics but other antibiotics such as gentamicin. It highlights the need to follow standardized, restrictive policies for antibiotic use and for narrow-spectrum rather than broad-spectrum antibiotics whenever possible. Antibiotics which drive resistance, e.g. third-generation cephalosporins, in the neonatal period should be avoided unless specifically indicated. If blood cultures are negative, antibiotics should be stopped if there are no signs of infection. Infection prevention should be followed by everyone. Regular infection surveillance should be performed by a multidisciplinary team.

Common viral infections

Many of the common childhood infections present with a fever and rash (Table 15.2). Incubation periods vary from 24

hours to 48 hours for viral gastroenteritis to about 2 weeks for chickenpox, but for some diseases, such as HIV, the length of time between exposure and the development of symptomatic illness may extend to many years.

The infectious period characteristically begins a day or two before the rash appears and, for purposes of nursery/school exclusion, is generally considered to last until the rash has resolved or the lesions have dried up, although this varies depending on the infectious agent. For details about incubation and exclusion periods, see the Public Health England website.

The human herpesviruses

There are currently eight known HHVs that cause infections in humans: HSV-1 and HSV-2, VZV, cytomegalovirus (CMV), EBV, HHV-6, HHV-7, and HHV-8. HHV-8 is associated with Kaposi sarcoma in HIV-infected individuals. The other herpesviruses will be discussed in this section, in order of their prevalence.

The hallmark of most herpesviruses is that, after primary infection, latency is established and there is long-term persistence of the virus within the host, usually in a dormant state. After certain stimuli, reactivation of infection may occur.

Herpes simplex virus infections

HSV usually enters the body through the mucous membranes or skin, and the site of the primary infection may be associated with intense local mucosal damage. HSV-1 is usually associated with lip and skin lesions, and HSV-2 more commonly with genital lesions, but both viruses can cause both types of disease. The wide variety of clinical manifestations are described in the following sections. Treatment is with aciclovir, a viral DNA polymerase inhibitor, which may be used to treat severe symptomatic skin, ophthalmic, cerebral, and systemic infections.

Asymptomatic

Herpes simplex infections are very common and are mostly asymptomatic.

Gingivostomatitis

This is the most common form of primary HSV illness in children. It usually occurs from 10 months to 3 years of age. There are vesicular lesions on the lips, gums, and anterior surfaces of the tongue and hard palate, which often progress to extensive, painful ulceration with bleeding (Fig. 15.13). There is a high fever and the child is very miserable. The illness may persist for up to 2 weeks. Eating and drinking are painful, which may lead to dehydration. Management is symptomatic, but severe disease may necessitate intravenous fluids and aciclovir.

Skin manifestations

Mucocutaneous junctions and damaged skin are particularly prone to infection. 'Cold sores' are recurrent HSV lesions on the gingival/lip margin.

- *Eczema herpeticum* – In this serious condition, widespread vesicular lesions develop on eczematous skin (Fig. 15.14). This may be complicated by secondary bacterial infection, which may result in septicaemia. Treatment is with intravenous aciclovir.

Table 15.2 Causes of fever and a rash

Maculopapular rash		Vesicular, bullous, pustular		
Viral	Human herpes virus-6 (HHV-6) or HHV-7 (roseola infantum) – <2 years old	Viral	Varicella zoster virus – chickenpox, shingles	
	Enterovirus rash		Herpes simplex virus	
	Parvovirus (slapped cheek) – usually school age		Coxsackie virus – hand, foot and mouth	
Bacterial	Measles – uncommon if immunized	Bacterial	Impetigo – characteristic crusting	
	Rubella – uncommon if immunized		Boils	
	Scarlet fever (group A streptococcus)		Staphylococcal bullous impetigo	
Other	Toxic shock syndrome	Other	Staphylococcal scalded skin	
	Rheumatic fever – erythema marginatum		Erythema multiforme; Stevens–Johnson syndrome; toxic epidermal necrolysis	
	<i>Salmonella typhi</i> (typhoid fever) – classically rose spots			
	Lyme disease – erythema migrans	Viral		
	Kawasaki disease		Meningococcal, other bacterial sepsis	
	Systemic onset juvenile idiopathic arthritis		Infective endocarditis	
Petechial, purpuric		Other	Enteroviruses, adenoviruses, and other viral infections	
			Henoch–Schönlein purpura	
			Thrombocytopenia	
			Vasculitis	
			Malaria	

**Figure 15.13** Vesicles with ulceration in gingivostomatitis.**Figure 15.14** Eczema herpeticum.

- *Herpetic whitlows* – These are painful, erythematous, oedematous white pustules on the site of broken skin, typically on fingers. Spread is by autoinoculation from gingivostomatitis and infected adults kissing their children's fingers. A less common cause is contact with genital herpes lesions.

Eye disease

HSV may cause blepharitis or conjunctivitis. It may extend to involve the cornea, producing dendritic ulceration. This can lead to corneal scarring and ultimately loss of vision. Any child with herpetic lesions near or involving the eye requires urgent ophthalmic

assessment involving examination of the cornea by slit-lamp examination.

Disseminated infection

- *Neonatal HSV infection* (see Ch. 11) – The infection may be focal, affecting the skin or eyes, or encephalitis, or may be disseminated. Its morbidity and mortality are high.
- *Infection in the immunocompromised host* – Infection may be severe. Cutaneous lesions may spread to involve adjacent sites, e.g. oesophagitis and proctitis. Pneumonia and disseminated infections involving multiple organs are serious complications.

Summary

Herpes simplex virus infections

- Most are asymptomatic.
- Gingivostomatitis – may necessitate intravenous fluids and aciclovir.
- Skin manifestations – mucocutaneous junctions, e.g. lips and damaged skin.
- Eczema herpeticum – may result in secondary bacterial infection and septicaemia.
- Herpetic whitlows – painful pustules on the fingers.
- Eye disease – blepharitis, conjunctivitis, and corneal ulceration.
- CNS – aseptic meningitis, encephalitis.
- Pneumonia and disseminated infection in the immunocompromised.

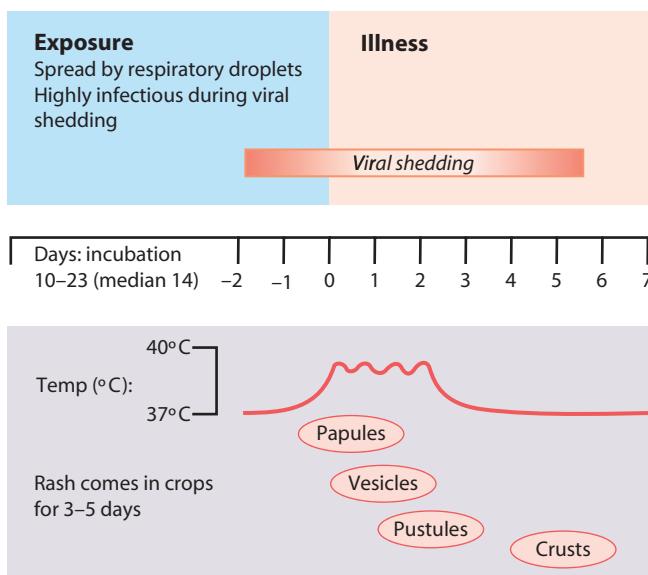
Chickenpox (primary varicella zoster infection)

Clinical features

These are shown in Fig. 15.15. There are a number of rare but serious complications that can occur in previously healthy children:

- Secondary bacterial infection* with staphylococci, group A streptococci, or other organisms. May lead to further complications such as toxic shock syndrome or necrotizing fasciitis. Secondary bacterial infection should be considered where there is onset of a new fever or persistent high fever after the first few days.
- Encephalitis* – this may be generalized, usually occurring early during the illness. In contrast to the encephalitis caused by HSV, the prognosis is good. Most characteristic

Clinical features and complications of chickenpox



Complications

Bacterial superinfection

Staphylococcal
Streptococcal
May lead to toxic shock syndrome or necrotizing fasciitis

Central nervous system

Cerebellitis
Generalized encephalitis
Aseptic meningitis

Immunocompromised

Haemorrhagic lesions
Pneumonitis
Progressive and disseminated infection
Disseminated intravascular coagulation

Typical vesicular rash

- 50–500 lesions start on head and trunk, progress to peripheries. (But may be just a few lesions.)
- Appear as crops of papules, vesicles with surrounding erythema (**Fig. 15.15a**) and pustules at different times for up to one week.
- Lesions may occur on the palate.
- Itchy and scratching; may result in permanent, depigmented scar formation or secondary infection.
- New lesions appearing beyond 10 days suggest defective cellular immunity.



(a)

Figure 15.15 Clinical features and complications of chickenpox. (a) Vesicles with surrounding erythema appearing in crops are characteristic of chickenpox.



Watch for the child with chickenpox whose fever initially settles, but then recurs a few days later – this is likely to be due to secondary bacterial infection.



Beware of admitting a chickenpox contact to a clinical area with immunocompromised children, in whom it can disseminate and cause potentially fatal disease.



Figure 15.16 Herpes zoster (shingles) in a child. Distribution is along the S1 dermatome. (Courtesy of Dr Sam Walters.)

is a VZV-associated cerebellitis. This usually occurs about a week after the onset of rash. The child is ataxic with cerebellar signs. It usually resolves within a month.

- *Purpura fulminans* – this is the consequence of vasculitis in the skin and subcutaneous tissues. It is best known in relation to meningococcal disease and can lead to loss of large areas of skin by necrosis. It may rarely occur after VZV infection due to production of antiviral antibodies, which cross-react and inactivate the inhibitory coagulation factors protein C or protein S. This results in an increased risk of clotting, which most often manifests as purpuric skin rash.

In the immunocompromised host, primary varicella infection may result in severe progressive disseminated disease, which has a mortality of up to 20%. The vesicular eruptions persist and may become haemorrhagic. The disease in the neonatal period is described in [Chapter 10](#).

Treatment and prevention

Oral aciclovir has highly variable absorption and therefore limited benefit, and is not recommended in the UK. Immunocompromised children should be treated with intravenous aciclovir initially. Oral valaciclovir can be substituted at a later point if organ dissemination has not occurred. Human varicella zoster immunoglobulin is recommended as prevention for high-risk immunocompromised individuals with deficient T-cell function following contact with chickenpox. Protection from infection with human varicella zoster immunoglobulin is not absolute, and depends on how soon after contact with chickenpox it is given.

Shingles (herpes zoster)

Shingles is uncommon in children. It is caused by reactivation of latent VZV, causing a vesicular eruption in the dermatomal distribution of sensory nerves. It occurs most commonly in the thoracic region, although any dermatome can be affected ([Fig. 15.16](#)). Children, unlike adults,

rarely suffer neuralgic pain. Shingles in childhood is more common in those who had primary varicella zoster infection in the first year of life. Recurrent or multidermatomal shingles is strongly associated with underlying immunocompromise, e.g. HIV infection. In immunocompromised individuals, reactivated infection can also disseminate to cause severe disease.



Recurrent or multidermatomal shingles suggests a primary or secondary T-cell immune defect.

Summary

Chickenpox

- Clinical features – fever and itchy, vesicular rash, which crops for up to 7 days.
- Complications – secondary bacterial infection, encephalitis; disseminated disease in the immunocompromised.
- Human varicella zoster immunoglobulin – if immunocompromised and in contact with chickenpox or if there is maternal chickenpox shortly before or after delivery.
- Treatment is mainly supportive; intravenous aciclovir for severe chickenpox and for immunocompromised children.

Epstein–Barr virus: infectious mononucleosis (glandular fever)

EBV is the causative agent of infectious mononucleosis, but it is also involved in the pathogenesis of Burkitt lymphoma, lymphoproliferative disease in immunocompromised hosts, and nasopharyngeal carcinoma. The virus has a particular tropism for B lymphocytes and epithelial cells of the oropharynx. Transmission usually occurs by oral contact and the majority of infections are subclinical. Older children, and occasionally young children, may develop a syndrome with:

- fever
- malaise
- tonsillitis/pharyngitis – often severe, limiting fluid and food intake; rarely, breathing may be compromised
- lymphadenopathy – prominent cervical lymph nodes, often with diffuse lymphadenopathy elsewhere.

Other possible features include:

- petechiae on the soft palate
- splenomegaly (50%), hepatomegaly (10%)
- a maculopapular rash (5%)
- jaundice.

Diagnosis is supported by:

- atypical lymphocytes (numerous large T cells seen on blood film)

- a positive monospot test. Detects the presence of heterophile antibodies (i.e. antibodies that react to antigens from phylogenetically unrelated species such as horse red blood cells). Reactive heterophile antibodies in a patient with compatible clinical features are diagnostic for EBV. The test may be negative in young children or in early infection.
- seroconversion with the production of antibodies against viral capsid (VCA IgM and IgG) and nuclear antigen (EBNA). Unnecessary if monospot is positive.

Symptoms may persist for 1 month to 3 months but ultimately resolve. Fatigue is often a prominent feature in adolescents and adults.

Treatment is symptomatic. When the airway is severely compromised, corticosteroids may be considered. In 5% of infected individuals, group A streptococcus is grown from the tonsils. This may be treated with penicillin. Ampicillin or amoxicillin can cause a florid maculopapular rash in children infected with EBV and should therefore be avoided.

Cytomegalovirus

CMV is usually transmitted via saliva, genital secretions, or breastmilk, and rarely via blood products and organ transplants as well as transplacentally. The virus causes mild or subclinical infection in normal paediatric and adult hosts. In high-income countries, about half of the adult population show serological evidence of past infection. In low-income countries, most children have been infected by 2 years of age, often via breastmilk. In the immunocompromised host and the developing fetus, CMV is an important pathogen that can cause considerable morbidity.

CMV may cause a mononucleosis-like syndrome. Pharyngitis and lymphadenopathy are not usually as prominent as in EBV infections. Patients may have atypical lymphocytes on the blood film but are heterophile antibody negative. Maternal CMV infection may result in congenital CMV infection (see Ch. 10), which may be present at birth or manifest at an older age. In the immunocompromised host, CMV can cause retinitis, pneumonitis, bone marrow failure, encephalitis, hepatitis, oesophagitis, and enterocolitis. It is a very important pathogen following bone marrow and organ transplantation. Transplant recipients are closely monitored for evidence of CMV reactivation by sensitive tests such as blood PCR. Interventions used to reduce the risk of transmission of CMV include the use of CMV-negative blood for transfusions and antiviral prophylaxis (ganciclovir); also, if possible, transplant of CMV-positive organs into CMV-negative recipients is avoided.

CMV disease may be treated with intravenous ganciclovir, oral valganciclovir, foscarnet or cidofovir, but each of these drugs can cause serious side-effects.

Human herpesvirus 6 and human herpesvirus 7

HHV-6 and HHV-7 are closely related and have similar presentations, although HHV-6 is more prevalent. Most children are infected with HHV-6 or HHV-7 by the age



Figure 15.17 Macular rash associated with roseola, caused by human herpesvirus (HHV) 6 or 7. It usually appears as the fever wanes, initially on the trunk, and then spreads to the face and extremities. (From: Caserta MT, Human Herpesviruses 6 and 7 (Roseola, Exanthem Subitum): *Principles and Practice of Pediatric Infectious Diseases*, 2018, pp. 1081–1088.e4.)

of 2 years, usually from the oral secretions of a family member. They classically cause roseola infantum (also known as exanthema subitum), characterized by a high fever with malaise lasting a few days, followed by a generalized macular rash, which appears as the fever wanes (see Fig. 15.17). Many children have a febrile illness without rash, and many have a subclinical infection. Exanthema subitum is frequently clinically misdiagnosed as measles or rubella, which are rare in the UK and if suspected should be confirmed by PCR or serology. Another frequent occurrence in primary HHV-6 infection is that infants seen by a doctor during the febrile stage are prescribed antibiotics, and when the rash appears, it is erroneously attributed to an 'allergic' reaction to the drug. Rarely, they may cause aseptic meningitis, encephalitis, hepatitis, or a mononucleosis-like syndrome.

Human parvovirus B19

Human parvovirus B19 (HPV-B19) causes erythema infectiosum or fifth disease (so-named because it was the fifth disease to be described of a group of illnesses with similar rashes), also referred to as 'slapped-cheek syndrome'. Infections can occur at any time of the year, although outbreaks are most common during the spring. Transmission is via respiratory secretions from affected patients, by vertical transmission from mother to fetus and by transfusion of infected blood products. HPV-B19 infects the erythroblastoid red cell precursors in the bone marrow.

HPV-B19 causes a range of clinical syndromes:

- *asymptomatic infection* – common; about 5% to 10% of preschool children and 65% of adults have antibodies
- *erythema infectiosum* – the most common illness, with a viraemic phase of fever, malaise, headache, and myalgia followed by a characteristic rash on the face (slapped cheek) a week later, progressing to a maculopapular, 'lace'-like rash on the trunk and limbs;

Enteroviruses

Human enteroviruses, of which there are many (including the coxsackie viruses, echoviruses, and polioviruses), are a common cause of childhood infection. Transmission is primarily by the faecal–oral and respiratory droplet routes. Following replication in the pharynx and gut, the virus spreads to infect other organs. Infections occur most commonly in the summer and autumn. Over 90% of infections are asymptomatic or cause a non-specific febrile illness, sometimes with a rash usually over the trunk that is blanching or consists of fine petechiae. Some children have a history of loose stools or vomiting, or a contact history. The child is not usually systemically unwell, but if the rash is non-blanching, admission for observation and parenteral antibiotics (such as ceftriaxone) until negative blood cultures have ruled out sepsis is indicated.

Other characteristic clinical syndromes exist and are listed in the following sections. (For poliovirus, see the ‘Immunization’ section below.)

Hand, foot, and mouth disease

Painful vesicular lesions on the hands, feet, mouth, and tongue, and often also on the buttocks. Systemic features are generally mild. The disease subsides within a few days.

Herpangina

Vesicular and ulcerated lesions on the soft palate and uvula causing anorexia, pain on swallowing, and fever. Severe cases may require intravenous fluids and appropriate analgesia.

Summary

Parvovirus

- Usually asymptomatic or erythema infectiosum.
- Can cause aplastic crisis in patients with haemolytic anaemia (e.g. sickle cell disease and thalassaemia) or the fetus (fetal hydrops).

Enteroviruses

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Meningitis/encephalitis

In high-income countries, enteroviruses are the most common cause of viral meningitis. Long-term neurological sequelae are rare; the majority make a full recovery.

Pleurodynia (Bornholm disease)

An acute illness with fever, pleuritic chest pain, and muscle tenderness. There may be a pleural rub, but examination is otherwise normal. Recovery occurs within a few days.

Myocarditis and pericarditis

Both manifestations are rare. Affected children may present with chest pain and/or heart failure associated with a febrile illness and evidence of myocarditis on ECG.

Eczema coxsackium

This is an enterovirus infection affecting young children with eczema, characterized by vesicles, bullae and erosions. It is easily confused with eczema herpeticum. It resolves spontaneously. There is no treatment.

Enteroviral neonatal sepsis syndrome

This rare syndrome occurs in the first few weeks of life, and predominately results from transplacental or intrapartum infection of the infant. It is thought that transplacental infection results in very high viral loads, and the symptoms are consequently often very severe, mimicking bacterial sepsis. Affected infants may present with hypotension and multiorgan failure, requiring intensive care support. Currently, there are no antiviral drugs that are effective against enteroviruses; the use of intravenous immunoglobulin remains controversial.

Enterovirus D68

Infection with enterovirus strain D68 can cause mild to severe symptoms. Most are mild infections including fever, runny nose and cough. Rarely it causes severe respiratory illness or acute flaccid myelitis in children.

Summary

Enterovirus infection

- Mostly asymptomatic or self-limiting illness with rash, which may be petechial.
- Can cause hand, foot, and mouth disease; herpangina; meningitis/encephalitis; myocarditis/pericarditis; and neonatal sepsis syndrome.

Seasonal viral infections

Paediatric wards during the winter are full of infants and children with seasonal viral infections and associated complications. Common infections include respiratory syncytial virus (RSV) (see Ch. 17, Respiratory disorders), coronavirus, human metapneumovirus, rhinovirus and influenza A and B.

Influenza

Influenza is an acute respiratory illness caused predominantly by influenza A or B viruses. It occurs in annual winter outbreaks. Although in many children influenza is an acute, self-limited, uncomplicated disease, in some it is associated with adverse outcomes. Infants and those with underlying immune deficiency, asthma and neurodevelopmental or metabolic disorders are at higher risk, although most deaths from influenza in children occur in previously healthy individuals. Spread is via droplets and children are important vectors for disease within the community. It is highly contagious. The incubation period is 1–4 days. Children can have severe complications of the virus (myocarditis, pericarditis, encephalopathy) or associated bacterial or fungal super-infection. Pneumonia is a major complication.

Treatment for hospitalized children is with neuraminidase inhibitors (oseltamivir or zanamivir), which inhibit viral entry and are most effective given early in the illness. Severely ill children may need intensive care with aggressive management of associated complications. Immunization is the most effective way of preventing infection. Primary school-age children should receive an annual influenza vaccine (see 'Immunization' section below) early in the season.

Summary

Influenza

- Seasonal viral infections are a widespread cause of illness and need for hospitalization in children.
- Influenza can have serious complications in healthy children as well as those with underlying susceptibility.
- Vaccination is the most effective strategy to prevent influenza infection.

COVID-19

COVID-19 disease is caused by a novel coronavirus SARS-CoV-2. Infection rates are much lower in children than adults, and death in childhood rare. Presentation in children is with cough and fever, runny nose and sore throat. Some present with vomiting or diarrhoea. Many are asymptomatic. Rarely, children develop a multi-system inflammatory response (see below).

Uncommon viral infections

Measles

Doctors need to be able to recognize measles. Despite effective vaccines, outbreaks continue to occur due to insufficient immunization coverage to provide herd immunity. Worldwide, measles continues to be a major cause of morbidity and death where immunization is not provided. As with chickenpox and HPV-B19, older children and adults tend to have more severe disease than the very young. For epidemiological tracking of infection, PCR-based or serological confirmation of clinical cases of measles should be undertaken by testing saliva.

Clinical features

These are shown in Fig. 15.18. There are a number of serious complications that can occur in previously healthy children:

- *Encephalitis* occurs in about 1 in 5000 cases, a few days after the onset of the illness. Initial symptoms are headache, lethargy, and irritability, proceeding to seizures and ultimately coma. Mortality is 15%. Serious long-term sequelae include seizures, deafness, hemiplegia, and severe learning difficulties, affecting up to 40% of survivors.
- *Subacute sclerosing panencephalitis (SSPE)* is a rare but devastating illness manifesting, on average, 7 years after measles infection in about 1 in 100,000 cases. Most children who develop SSPE had primary measles infection before 2 years of age. SSPE is caused by a variant of the measles virus, which persists in the CNS. The disorder presents with loss of neurological function, which progresses over several years to dementia and death. The diagnosis is essentially clinical, supported by finding high levels of measles antibody in both blood and CSF, and by characteristic electroencephalogram abnormalities. Since the introduction of immunization against measles, it has become extremely rare.

In low-income countries, where malnutrition and vitamin A deficiency lead to impaired cell-mediated immunity, measles often follows a protracted course with severe complications. Impaired cellular immune responses, such as in HIV infection, may result in a modified or absence of rash, with an increased risk of dissemination, including giant-cell pneumonia or encephalitis.

Treatment

Treatment for measles is supportive. Children who are admitted to hospital should be isolated. In immunocompromised patients, the antiviral drug ribavirin may be used. Vitamin A, which may modulate the immune response, should be given in low-income countries.

Clinical features and complications of measles

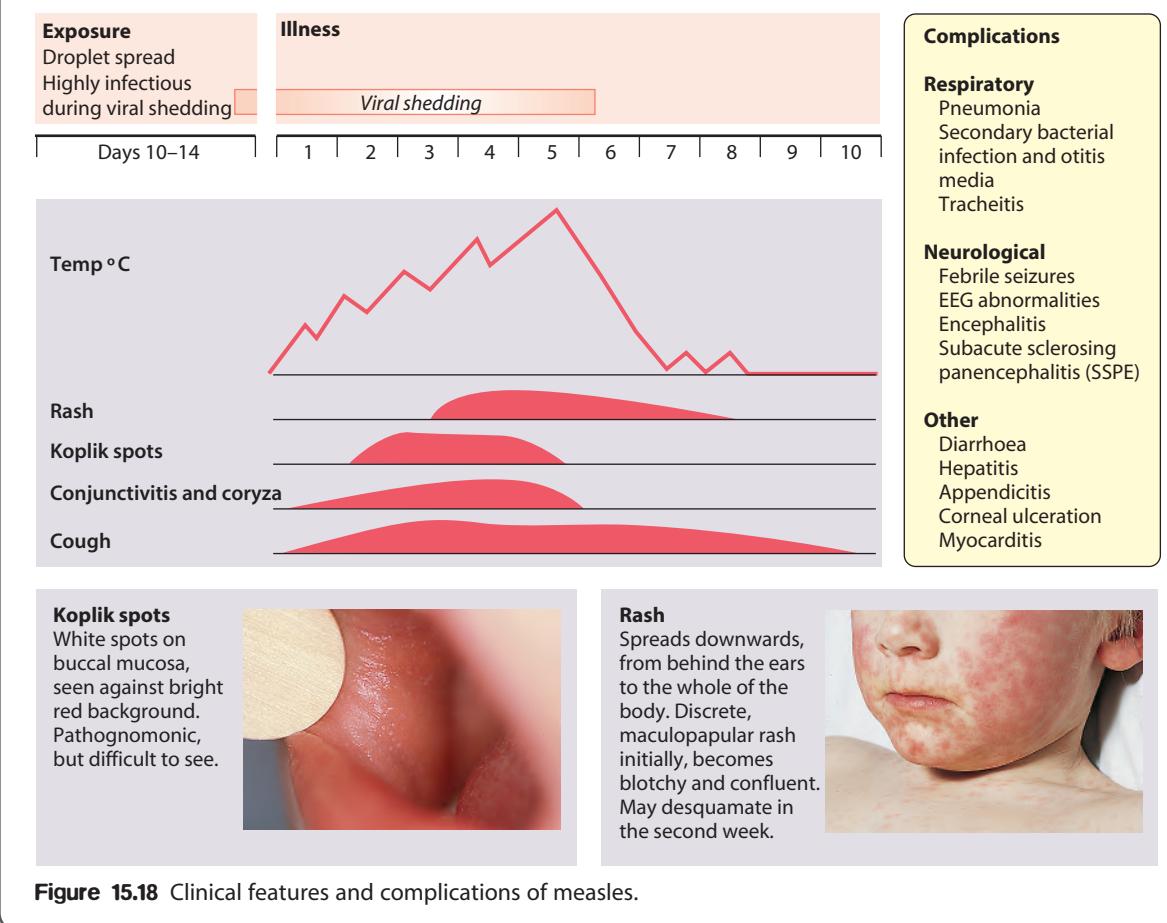


Figure 15.18 Clinical features and complications of measles.

Prevention

Prevention by immunization is the most successful strategy for reducing the morbidity and mortality of measles.



Measles remains a major cause of death in childhood in some low-income countries.

Summary

Measles

- Incidence has declined dramatically since immunization was introduced; but outbreaks still occur when immunization uptake is insufficient for herd immunity.
- Clinical features – fever, cough, runny nose, conjunctivitis, marked malaise, Koplik spots, and maculopapular rash.
- Complications – common if malnourished or immunocompromised; is a major cause of death in some low-income countries.

Mumps

Mumps occurs worldwide, but its incidence has declined dramatically because of the mumps component of the MMR vaccine. Following the decrease in the uptake of the MMR immunization in the late 1990s, there has been a rise in mumps affecting unimmunized children and young people. Mumps usually occurs in the winter and spring months. It is spread by droplet infection to the respiratory tract where the virus replicates within epithelial cells. The virus gains access to the parotid glands before further dissemination to other tissues.

Clinical features

The incubation period is 15 days to 24 days. Onset of the illness is with fever, malaise, and parotitis, but in up to 30% of cases, the infection is subclinical. Only one side of the face may be swollen initially, but bilateral parotid involvement may occur over the next few days. The parotitis is uncomfortable and children may complain of earache or pain on eating or drinking. Examination of the parotid duct may show redness and swelling. Occasionally, parotid swelling may be absent. The fever usually disappears within 3 days to 4 days. Plasma amylase levels are often elevated due to parotid inflammation, and, when associated with abdominal pain, there may be evidence of pancreatic involvement. Infectivity is for up to 7 days after the onset of parotid swelling. The illness is generally mild and self-limiting. Although hearing loss can rarely follow mumps, it is usually unilateral and transient.

Viral meningitis and encephalitis

Lymphocytes are seen in the CSF in about 50%, meningeal signs are only seen in 10%, and encephalitis in about 1 in 5000 cases. The common clinical features are headache, photophobia, vomiting, and neck stiffness.

Orchitis

This is the most feared complication, although it is uncommon in prepubertal males. When it does occur, it is usually unilateral. Although there is some evidence of a reduction in sperm count, infertility is actually very unusual. Rarely, oophoritis, mastitis, and arthritis may occur.

Rubella (German measles)

Rubella is generally a mild disease in childhood. It typically occurs in the winter and spring. It is an important infection, as it can cause severe damage to the fetus (see Ch. 10), though this is now rare. The incubation period is 15–20 days. It is spread by the respiratory route, frequently from a known contact. The prodrome is usually mild with a low-grade fever or none at all. The maculopapular rash is often the first sign of infection, appearing initially on the face and then spreading centrifugally to cover the whole body. It fades in 3–5 days. Lymphadenopathy, particularly the suboccipital and postauricular nodes, is prominent. Complications are rare in childhood but include arthritis, encephalitis, thrombocytopenia, and myocarditis. Clinical differentiation from other viral infections (including enteroviruses) is unreliable. The diagnosis should be confirmed serologically if there is any risk of exposure of a non-immune pregnant woman. There is no effective anti-viral treatment. Prevention therefore lies in immunization.

Summary

Rubella

Generally, a mild illness, but can cause severe abnormalities in congenital infection.

Prolonged fever

Most childhood infections are acute and resolve in a few days. If not, the child needs to be reassessed for complications of the original illness, e.g. a secondary bacterial infection, or the source of infection may not have been identified, e.g. urinary tract infection. Often, the child has developed another unrelated febrile illness. Assessment of prolonged fever is also required for prompt recognition of Kawasaki disease to avoid complications. Causes of prolonged fever are listed in Box 15.2.

Kawasaki disease

Kawasaki disease is a systemic vasculitis. Although uncommon, it is important to establish the diagnosis early, because artery damage may cause morbidity and occasional mortality. Prompt treatment reduces their incidence.

Kawasaki disease mainly affects children of 6 months to 4 years of age, with a peak at the end of the first year of

Box 15.2 Causes of prolonged fever

Infective

- Localized infection: e.g. osteomyelitis
- Bacterial infections: e.g. typhoid, *Bartonella henselae* (cat scratch disease), *Brucella* species
- Deep abscesses: e.g. intra-abdominal, retroperitoneal, pelvic
- Infective endocarditis
- Tuberculosis
- Non-tuberculous mycobacterial infections: e.g. *Mycobacterium avium* complex
- Viral infections: e.g. Epstein–Barr virus, cytomegalovirus, HIV (human immunodeficiency virus)
- Parasitic infections: e.g. malaria, toxocariasis, *Entamoeba histolytica*.

Non-infective

- Systemic onset juvenile idiopathic arthritis
- Systemic lupus erythematosus
- Vasculitis (including Kawasaki disease)
- Inflammatory bowel disease (Crohn disease and ulcerative colitis)
- Sarcoidosis
- Malignancy: e.g. leukaemia, lymphoma, neuroblastoma, Ewing sarcoma
- Macrophage activation syndromes: e.g. haemophagocytic lymphohistiocytosis
- Auto-inflammatory disorders: e.g. familial Mediterranean fever (FMF)
- Drug fever
- Fabricated or induced illness (including Munchausen syndrome by proxy).

life. The disease is more common in children of Japanese and, to a lesser extent, Black-Caribbean ethnicity, than in Caucasians. Its incidence is increasing; there are now about 300 children affected annually in the UK. The aetiology of Kawasaki disease remains unknown.

There is no diagnostic test; instead, the diagnosis is made based on clinical findings alone (Box 15.3). In addition to the classic features, affected children are strikingly irritable and miserable and have a high fever that is difficult to control. Young infants may have ‘incomplete’ symptoms, in which not all the cardinal features are present. The evolution of clinical features is shown in Fig. 15.19. Affected children have high inflammatory markers (C-reactive protein, erythrocyte sedimentation rate, white cell count), with a platelet count that rises typically in the second week of the illness. Children may not have all the clinical features at the same time so it is important to ask about relevant features in the history. Similarly children may have Kawasaki disease and not meet the full diagnostic criteria (incomplete disease). There should remain a high clinical suspicion, particularly for children less than 6 months of age with prolonged fever, even if they do not meet the classic criteria. These children are more likely to have delayed diagnosis and the development of coronary artery aneurysms. The coronary arteries are affected in about one-third of affected children within the first 6 weeks of the illness. This can lead to aneurysms, which can be detected on echocardiography (see Case history 15.1). Subsequent narrowing of the vessels from scar formation

Box 15.3 Clinical criteria to diagnose Kawasaki disease

Presence of fever for at least 5* days with at least four of the five following clinical features:

1. Bilateral bulbar conjunctival injection without exudate.
2. Erythema and cracking of lips, strawberry tongue and/or erythema of oral and pharyngeal mucosa
3. Cervical lymphadenopathy (≥ 1.5 cm diameter), usually unilateral.
4. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like.
5. Erythema and oedema of the hands and feet in acute phase and/or desquamation around the nails in subacute phase.

*The diagnosis can be made with 4 days of fever when at least four clinical features (particularly redness and swelling of the hands and feet) are present. (Reprinted from: *Circulation* 2001;103:335-335. © 2001 American Heart Association, Inc., with permission.)

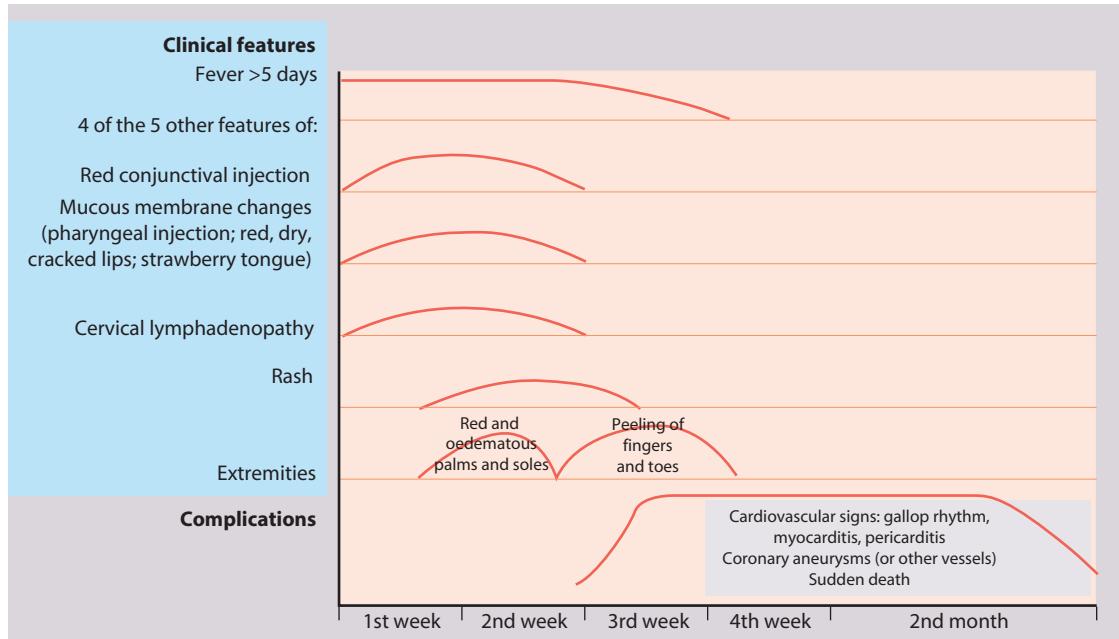


Figure 15.19 Kawasaki disease. Evolution of clinical features in Kawasaki disease.



Case history 15.1

Kawasaki disease

This 2-year-old boy developed a high fever of 2 days' duration. Examination showed a miserable child with mild conjunctivitis, a rash, and cervical lymphadenopathy. A viral infection was diagnosed and his mother was reassured. When he presented to hospital 3 days later, he was noted to have cracked red lips (Fig. 15.20a). He was admitted and a full septic screen, including a lumbar puncture, was performed and antibiotics started. The following day, he was still febrile and irritable; his C-reactive protein

and erythrocyte sedimentation rate were extremely high. Kawasaki disease was suspected and he was treated with intravenous immunoglobulin and oral aspirin. His clinical condition improved and he became afebrile the following morning. An echocardiogram at this stage showed no aneurysms of the coronary arteries, which are the most serious complication associated with delayed diagnosis and treatment. On the 15th day of the illness there was peeling of the fingers and toes (Fig. 15.20b).



Figure 15.20 (a) Red, cracked lips and conjunctival inflammation; and (b) peeling of the fingers, which developed on the 15th day of the illness. (Courtesy of Professor Mike Levin.)

can result in myocardial ischaemia and sudden death. Mortality is 0.5%.

Prompt treatment with intravenous immunoglobulin, ideally given within the first 10 days, has been shown to lower the risk of coronary artery aneurysms. Aspirin is also given; as there is no evidence anti-inflammatory doses reduce the risk of coronary artery aneurysms, many specialists use aspirin in low-dose for its antiplatelet effects to reduce the risk of thrombosis. Children suspected of having the disease but who do not have all the clinical features should still be considered for treatment. Echocardiography should be performed when the diagnosis is first suspected, and at 4–6 weeks to identify coronary artery aneurysms. Sometimes, fever persists or recurs despite initial treatment (resistant Kawasaki disease) and these children may be given a second dose of intravenous immunoglobulin or corticosteroids or infliximab (a monoclonal antibody against tumour necrosis factor- α). Children with coronary artery aneurysms require long-term low-dose aspirin and lifelong follow-up.



Prolonged fever – consider – is it Kawasaki disease?

Summary

Kawasaki disease

- Mainly affects infants and young children.
- The diagnosis is made on clinical features – fever over 5 days and four other features of non-purulent conjunctivitis, red mucous membranes, cervical lymphadenopathy, rash, red and oedematous palms and soles, or peeling of fingers and toes. Children with Kawasaki disease are often strikingly miserable, which is not improved by oral antipyretic agents.
- ‘Incomplete’ cases can occur, especially in infants, so a high index of suspicion should be maintained in a persistently febrile child.
- Complications – coronary artery aneurysms and sudden death.
- Initial treatment – intravenous immunoglobulin and aspirin.

Paediatric multisystem inflammatory syndrome

A small number of children appear to develop a severe, systemic inflammatory response to SARS-CoV-2 infection. Although the pathophysiology is not well understood it is thought to result from an abnormal immune response to the virus. Affected children develop persistent fever, evidence of inflammation (neutrophilia, lymphopenia, high CRP) and single or multi-organ failure. Gastrointestinal symptoms, rash and conjunctivitis are common. Many of these children have features consistent with Kawasaki disease but are generally older children or adolescents. Some develop severe inflammatory shock and require intensive care support. Cardiac involvement includes myocarditis, coronary artery abnormalities, valve involvement and pericardial effusion. Features may overlap with Kawasaki disease, bacterial sepsis or toxic shock. Antibiotics are often started until infection is

ruled out. Treatment currently includes immunomodulation with intravenous immunoglobulin (IVIG), low-dose aspirin and corticosteroids. Children are often SARS-CoV-2 PCR negative but serology positive. The full spectrum of disease and optimal treatment is incompletely understood.

Tuberculosis

The decline in the incidence and mortality from TB in high-income countries was hailed as an example of how public health measures and antimicrobial therapy can dramatically modify a disease. However, TB is again becoming a public health problem, partly through its increased incidence in patients with HIV infection, and with the emergence of multidrug-resistant *Mycobacterium tuberculosis* strains (MDR-TB). Spread of TB is almost invariably by the respiratory route. Close proximity, a large infectious load in the index case (related to pulmonary cavitation and sputum smear positivity), and underlying immunodeficiency enhance the risk of transmission. There is an important distinction between latent TB (an asymptomatic infection state) and TB disease (active TB). Latent TB is more likely to progress to active TB in infants and young children compared with adults. In contrast to adults, children are generally not infectious, because their disease is typically paucibacillary. Children usually acquire TB from an infected adult in the same household.

Clinical features

These are outlined in Fig. 15.21.

Diagnosis

Diagnosis of TB in children is even more difficult than in adults. The clinical features of active TB are often non-specific, such as prolonged fever, malaise, anorexia, weight loss, or focal signs of infection (e.g. lymph node swelling in TB lymphadenitis). The majority (about three-quarters) of cases with active TB have pulmonary TB; extrapulmonary disease is less common, and includes TB lymphadenitis, osteoarticular TB, genitourinary TB, and TB meningitis.

Spontaneous sputum samples are generally unobtainable from children under about 8 years of age, but induced sputum samples can be obtained at any age. Children usually swallow sputum, so gastric washings on three consecutive mornings can be used to identify *M. tuberculosis* originating from the lung, using special staining techniques for acid-fast bacilli (Ziehl–Neelsen stains or auramine stains) and mycobacterial cultures. To obtain these washings, a nasogastric tube is passed and secretions are washed out of the stomach with saline (before food intake). Urine, lymph node tissue, CSF, and radiological examinations should also be performed as appropriate. Although it is difficult to culture TB from children, the rise of MDR-TB makes it important to try to grow the organism so that antibiotic sensitivity can be assessed. PCR-based methods for the detection of *M. tuberculosis* are used in parallel with mycobacterial cultures, but provide limited information regarding drug resistance and do not replace cultures. Whole genome sequencing of samples has been introduced in England since 2017 and provides genotypic data on mutations associated with resistance. However, phenotypic resistance from cultures is still vital to ensure the most appropriate drug regimen is prescribed.

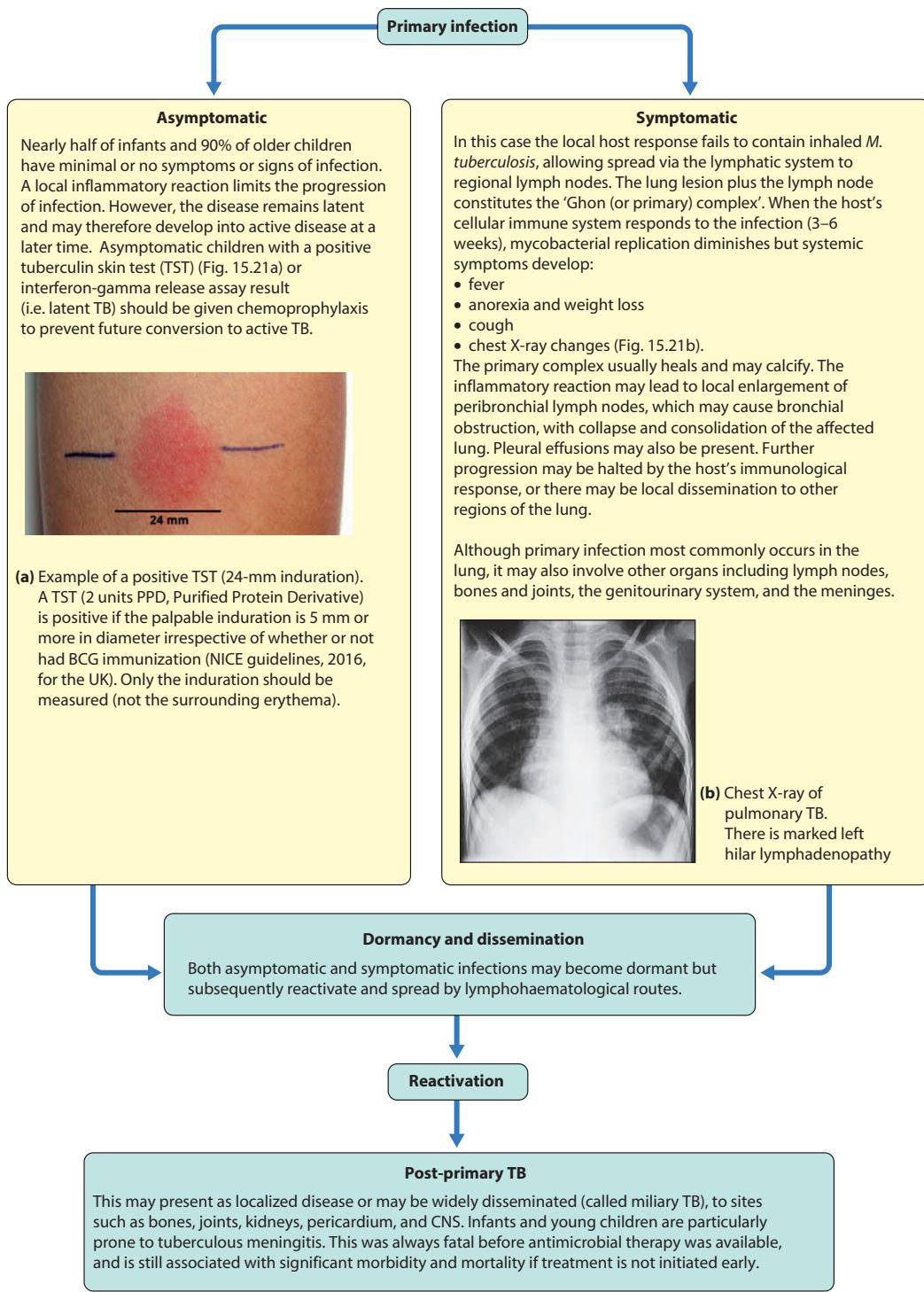


Figure 15.21 Clinical features of tuberculosis.

If TB is suspected, a tuberculin skin test (TST; also called Mantoux test) is performed by injecting purified protein derivative of tuberculin into the forearm (2 units intradermal injection, read after 48 hours to 72 hours as induration measured in millimetres). Because purified protein derivative is a mixture of proteins, some of which are expressed by both *M. tuberculosis* and BCG (*Bacillus Calmette-Guérin*), the TST may be positive because of past BCG vaccination rather than TB infection. Most international guidelines therefore suggest that a history of BCG immunization should be taken into account when interpreting the test result. The UK recommendations deviate

from this; NICE (National Institute for Health and Care Excellence) guidance suggests an induration of 5 mm or more should be considered to be positive, regardless of prior BCG vaccination. Other countries use different cut-offs (typically 10 mm).

Interferon-gamma release assays (IGRAs) are newer, blood-based tests for TB. They assess the response of T cells to *in vitro* stimulation, with a small number of antigens expressed by *M. tuberculosis* but not by BCG. Positive results therefore indicate TB infection rather than BCG vaccination. However, a negative IGRA result does not reliably rule out TB infection. Also, there is increasing

evidence that IGRAAs perform worse in children compared with adults. Neither IGRA nor the TST can distinguish between latent TB and active TB, so correlation with clinical signs and symptoms is required. As 20% of children with TB disease have a negative TST and/or IGRA, decision to treat is made on clinical and microbiological assessment, and TB should not be excluded in a child with a negative immune assay.

Coinfection with HIV makes the diagnosis even more difficult. With advanced immunocompromise and malnutrition, both TST and IGRA can be false negative. Contact history, radiology, and possibly tissue diagnosis become even more important. One must avoid making an incorrect diagnosis of TB on chest X-ray appearances alone, as lymphoid interstitial pneumonitis can have a similar appearance and occurs in 20% of HIV-infected children. In view of the overlapping epidemiology, all individuals with TB should be tested for HIV, and vice versa.

Treatment

Quadruple therapy (rifampicin, isoniazid, pyrazinamide, ethambutol) is the recommended initial combination, unless MDR-TB is strongly suspected (e.g. when a household member has been recently diagnosed with MDR-TB). This is decreased to rifampicin and isoniazid alone after 2 months, by which time antibiotic sensitivities are often known. Fixed dose combination drugs are available, particularly for older children and adolescents. These can reduce overall pill burden and improve compliance but there is an urgent need for more child friendly drug preparations to improve adherence in young children. Treatment for uncomplicated pulmonary TB or TB lymphadenitis is usually for 6 months; longer treatment courses are required for osteoarticular TB, TB meningitis, or disseminated disease. Compliance is crucial; families and young people can be supported in a number of ways in the community including directly observed therapy (DOTS) and video observed therapy (VOTS). In adolescents, pyridoxine is given weekly to prevent peripheral neuropathy associated with isoniazid therapy, a complication that does not occur in young children. In tuberculous meningitis, dexamethasone is given initially, to decrease the risk of long-term sequelae.

Asymptomatic children who are Mantoux or IGRA positive and therefore latently infected should also be treated (e.g. with rifampicin and isoniazid for 3 months or isoniazid alone for 6 months) as this will decrease the risk of reactivation (i.e. conversion to active TB) later in life.

Prevention and contact tracing

BCG immunization has been shown to reduce the incidence of TB, but its protective effect is incomplete (i.e. BCG-vaccinated children can still acquire TB infection). In the UK, BCG is recommended at birth for high-risk groups only and is not given routinely to any age group. BCG, which is a live vaccine, should not be given to HIV-positive or other immunocompromised children due to the risk of severe local reactions and dissemination. BCG can cause a local reaction, often forming a blister with surrounding erythema 2–6 weeks after the infection. This can ooze and scab. This is normal and will resolve. BCG can also cause non-suppurative and suppurative lymphadenitis. Non-suppurative lymphadenitis will resolve without additional treatment. The optimal management of suppurative lymphadenitis is unclear

and may involve aspiration, surgical excision, medical management or watch and wait.

As most children are infected by a household contact, it is essential to screen other family members for TB infection. Children who are exposed to individuals with pulmonary TB should be assessed for evidence of latent TB (by TST and IGRA). Children under 2 years of age who had close contact with a sputum smear-positive pulmonary TB person should be started on prophylactic anti-tuberculosis antibiotics because of the risk of infection and progression to disease is high at this age, and the immune assays are least reliable in this age group.

Non-tuberculous mycobacterial infections

There are numerous non-tuberculous mycobacteria found in the environment. Immunocompetent individuals rarely suffer from diseases caused by these organisms. They occasionally cause persistent lymphadenitis in young children, who are otherwise well, primarily affecting the cervicofacial region. The skin overlying the node often becomes violaceous and thin. Where technically possible without risk of damage to the facial nerve, the most commonly used treatment approach is complete lymph node excision, as biopsy or partial excision can result in formation of a chronic fistula and poor healing. Alternative treatment approaches are 'watchful waiting' (no intervention, as in the majority of cases spontaneous resolution occurs over several months), or treatment with antimycobacterial antibiotics. Unlike TB, these organisms are transmitted via soil and water, and therefore contact tracing is not required.

Non-tuberculous mycobacteria may cause disseminated infection in immunocompromised individuals. *Mycobacterium avium-intracellulare* infections are particularly common in patients with advanced HIV disease. These infections do not respond to conventional TB treatment, and require a combination regimen of different antimycobacterial drugs. Recently, chronic pulmonary non-tuberculous mycobacterial infections have become an increasing problem in adolescents and adults with cystic fibrosis. Treatment of these infections is often difficult, and only successful in some instances.

Summary

Tuberculosis

- TB affects millions of children worldwide; low but increasing incidence in many high-income countries.
- Clinical features follow a sequence – primary infection, then latency, which may be followed by conversion to active TB months to years later.
- Diagnosis is often difficult, so the decision to treat is then based on contact history, tuberculin skin test and interferon-gamma release assay results, X-ray findings, and clinical features.
- Adherence to drug therapy can be problematic but is essential for successful treatment.
- Contact tracing and identification of children with latent TB are important.
- TB is more difficult to diagnose and more likely to disseminate in immunocompromised individuals.

Tropical infections

Although tropical infections must be considered, most febrile children who have a recent travel history to a tropical region have a non-tropical infection (e.g. a common

viral infection). The most common or most serious imported infections are outlined in Fig. 15.22.



A febrile child returning from the tropics
– most common causes are non-tropical infections, but consider malaria and typhoid fever as well as other tropical infections.

An approach to the febrile child returning from the tropics

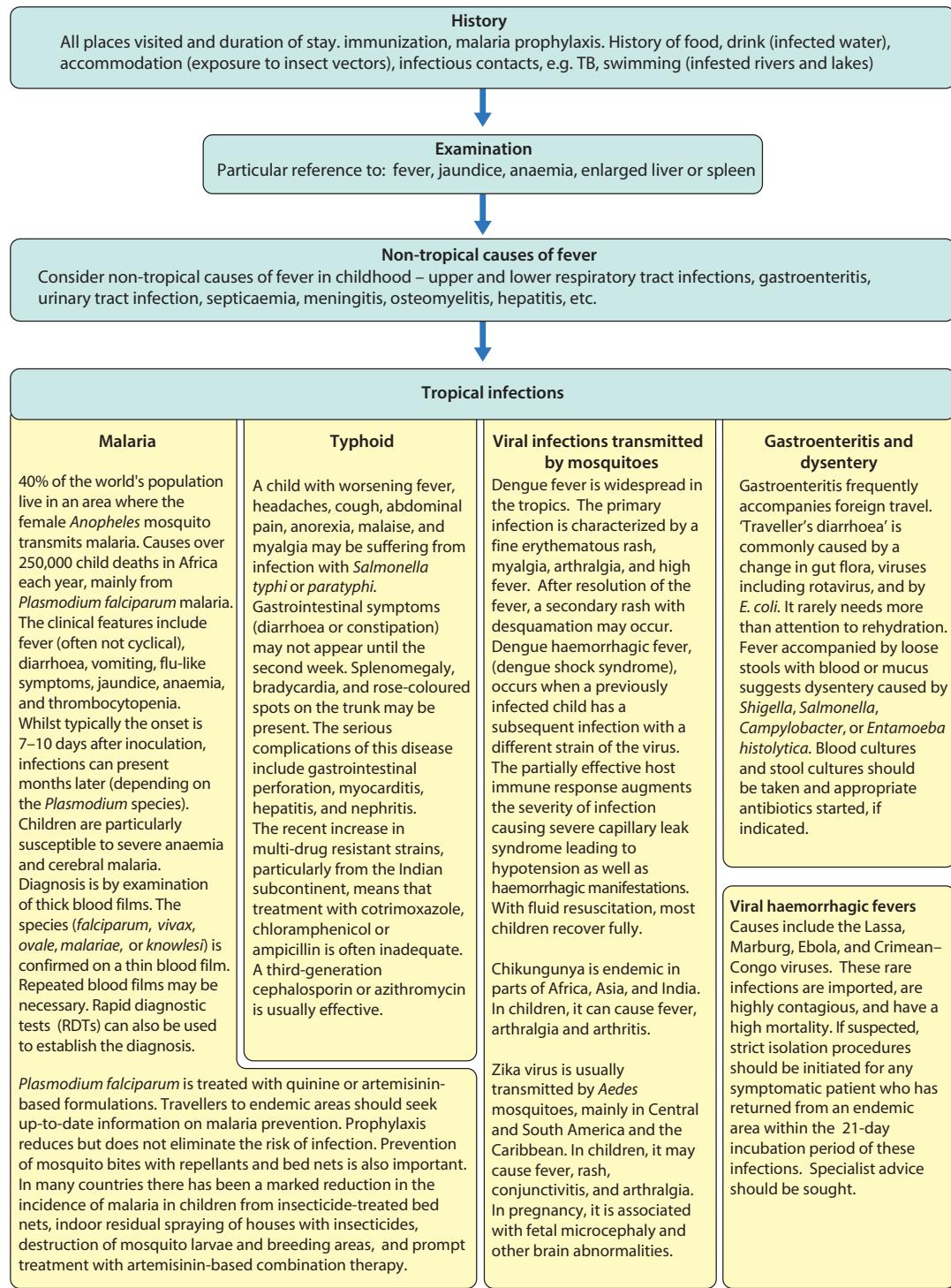


Figure 15.22 An approach to the febrile child returning from the tropics.

HIV infection

Globally there are over 2.8 million children and adolescents living with HIV infection, mostly in sub-Saharan Africa. Though there has been a decline in the number of children becoming infected each year, there were still an estimated 160,000 new infections in children under 14 years in 2018. There are around 15 million children who have lost a parent to HIV-related causes. The major route of HIV infection in children is mother-to-child transmission, which occurs during pregnancy (intrauterine), at delivery (intrapartum), or through breastfeeding (postpartum). The virus may also be transmitted to children iatrogenically as a result of lapses in infection prevention and control (IPC) measures such as by infected blood products or contaminated needles, or through sexual abuse.

Diagnosis

In children over 18 months of age, HIV infection is diagnosed by detecting antibodies against the virus. Children less than 18 months of age who are born to infected mothers will have transplacental maternal IgG HIV antibodies; therefore, at this age a positive antibody test confirms HIV exposure but not HIV infection. The most sensitive test for HIV diagnosis before 18 months of age is HIV DNA PCR, but internationally the most commonly used test is the viral load assay, which measures RNA copies/ml. All infants born to HIV-infected mothers should be tested for HIV infection, whether or not they are symptomatic. A first test for evidence of any in-utero infection is undertaken at birth. Establishing that the infant is uninfected then relies on at least two further negative tests for the viral genome (HIV DNA or RNA PCR) after cessation of post-exposure prophylaxis (antiretroviral, ART). This is confirmed by the loss of maternal HIV antibodies from the infant's circulation after 18 months of age.

Clinical features

Without treatment, about 20% of HIV-infected infants progress rapidly to symptomatic disease and onset of acquired immune deficiency syndrome (AIDS) in the first year of life; however, other infected children remain asymptomatic for months or even years before progressing to clinical disease. Some asymptomatic children are only identified in adolescence at routine screening following diagnosis in another family member. Clinical presentation varies with the degree of immunocompromise. Children with mild immunocompromise may only have lymphadenopathy or parotid enlargement; if moderate, they may have recurrent bacterial infections, candidiasis, chronic diarrhoea, and lymphocytic interstitial pneumonitis (Fig. 15.23). This lymphocytic infiltration of the lungs may be caused by a response to the HIV infection itself, or it may be related to EBV infection. Severe AIDS diagnoses include opportunistic infections, e.g. *Pneumocystis jirovecii (carinii)* pneumonia (PCP), severe growth faltering, encephalopathy (Fig. 15.24), and malignancy, although the latter was rare in untreated children who tended to die of other causes before developing malignancy. More than one clinical feature is often present. An unusual constellation of symptoms, especially if infectious, should alert one to the possibility of HIV infection.

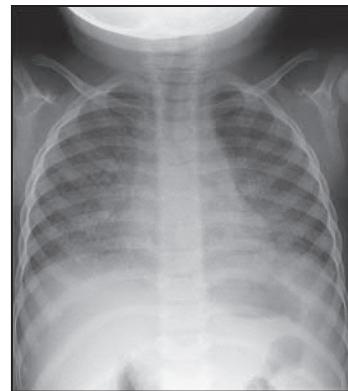


Figure 15.23 Lymphocytic interstitial pneumonitis in a child with human immunodeficiency virus infection. There is diffuse reticulonodular shadowing with hilar lymphadenopathy.



Figure 15.24 A CT scan in a child with HIV encephalopathy showing diffuse increase in cerebrospinal fluid spaces from cerebral atrophy and volume loss.



Children with persistent lymphadenopathy, hepatosplenomegaly, recurrent fever, parotid swelling, thrombocytopenia, or any suggestion of serious, persistent, unusual, recurrent infections should be tested for HIV.

Treatment

Combination antiretroviral therapy should be started in all children regardless of CD4 counts once the diagnosis of HIV infection has been confirmed. As in adults, combinations of three (or four) drugs are used. Prophylaxis against PCP with cotrimoxazole is prescribed for infants who are HIV-infected, and for older children with low CD4 counts.

Other aspects of management include:

- Immunization, which is important because of the higher risk of infections, and should follow the routine vaccination schedule, with the exception that BCG should not be given as it is a live vaccine that can cause disseminated disease. Vaccination against influenza, hepatitis A and B, and VZV should be considered.

- Multidisciplinary management of children, if possible in a family clinic, where they can be seen together with other members of their family who may be HIV infected and where the team includes an adult specialist. The team will need to address issues such as adherence to medication, disclosure of HIV diagnosis, and planning for the future.
- Regular follow-up, with particular attention paid to weight, developmental progress, and clinical signs and symptoms of disease. Effective ART has transformed HIV infection into a chronic disease with the vast majority of perinatally infected children surviving into adulthood. Family HIV clinics in the UK increasingly manage adolescents and young adults, providing services to address issues such as difficulties with adherence, stigma, safe sex practices, fertility, and pregnancy.

Reduction of vertical transmission

Mothers who are most likely to transmit HIV to their infants are those with a high HIV viral load and more advanced disease. Where mothers are not taking ART and breastfeed, 25% to 40% of infants become infected with HIV. Avoidance of breastfeeding reduces the rate of transmission by about 4% for every 6 months that the child is breastfed. In high-income countries, perinatal transmission of HIV has been reduced to less than 1% by using a combination of interventions:

- use of effective ART during pregnancy and intrapartum to achieve an undetectable maternal viral load at the time of delivery
- postexposure prophylaxis with ART given to the infant for 2–4 weeks after birth
- avoidance of breastfeeding
- active management of labour and delivery, to avoid prolonged rupture of the membranes and unnecessary instrumentation (e.g. forceps delivery)
- prelabour caesarean section if the mother's viral load is detectable close to the expected date of delivery.

In low- and middle-income countries, WHO recommends lifelong ART for all pregnant mothers with HIV infection, whatever their CD4 count, and to exclusively breastfeed their babies for the first 6 months before weaning, and continue to breastfeed as long as they wish until 24 months. ART, as postexposure prophylaxis, should be given to the newborn (whether breast or formula fed) for the first 4 weeks of life.



Antenatal antiretroviral treatment, active management of labour and delivery, and avoidance of breastfeeding can reduce the vertical transmission rate of HIV to less than 1%.

Summary

HIV

- There are 2.8 million children (<15 years) worldwide infected with HIV.
- Treatment includes combination ART and prophylaxis against *Pneumocystis jirovecii* pneumonia.
- The majority of perinatally infected children are surviving into adulthood if ART is available and adhered to.
- Raises complex psychosocial issues for the family and healthcare providers, including when and what to tell the HIV-infected child (and the siblings), confidentiality, and adherence support.

Lyme disease

This disease, caused by the bacterium *Borrelia burgdorferi*, was first recognized in a cluster of children with arthritis in Lyme, Connecticut. It also occurs in the UK, and other European countries and parts of Asia and North America. *Borrelia burgdorferi* is transmitted by hard ticks, which have a range of hosts including sheep, foxes and many small mammals including hedgehogs. However, in only half of the cases is there a history of a preceding tick bite. In adults, most ticks attach to the legs but in children (because questing ticks tend to be at the top of long grasses) they may attach anywhere including in the hairline.

Infections occur most commonly from June to September, but can occur throughout the year. Tick populations are expanding their habitats, possibly due to climate change and altered land management. They are found on the edge of woods and any grassy areas including in urban parks. Travel history particularly to Central and Eastern Europe and North-Eastern states of the USA should be elicited.

Clinical features

Following an incubation period of 4 days to 30 days, an erythematous macule at the site of the tick bite enlarges to cause the classical skin lesion known as erythema migrans (Fig. 15.25), a painless red expanding lesion with a bright red outer spreading edge. It is not usually itchy. During early disease, the skin lesion may be accompanied by fever, headache, malaise, myalgia, arthralgia, and lymphadenopathy. Usually, these features fluctuate over several weeks and then resolve. Influenza-like symptoms outside the flu season should prompt suspicion. Dissemination of infection in the early stages is rare, but may lead to cranial nerve palsies (particularly of the facial nerve), meningitis, arthritis, or carditis.



Figure 15.25 Lyme disease. Site of tick bite and red, expanding rash, erythema migrans. Further examples of the rash in Lyme disease can be seen in support of NICE Guideline on Lyme disease at <https://www.nice.org.uk/guidance/ng95/resources/lyme-disease-rash-images-pdf-4792273597>.

The late stage of Lyme disease occurs after weeks to months with neurological, cardiac, and joint manifestations. Neurological disease includes fluctuating fatigue, meningoencephalitis and/or peripheral, central or autonomic neuropathies. Cardiac disease includes myocarditis and heart block. Joint disease is more commonly reported in the USA and varies from brief migratory arthralgia to acute asymmetric monoarthritis and oligoarthritis of the large joints. Recurrent attacks of arthritis are common. In 10% of cases, chronic erosive joint disease occurs months to years after the initial attack.

Diagnosis

This is based on clinical and epidemiological features and serology. Serology will be negative in early disease, and will therefore not be helpful at presentation with erythema migrans. Seroconversion occurs 4–6 weeks following tick attachment. Isolation of the organism is difficult and is not routinely undertaken.

Treatment

The drug of choice for early uncomplicated Lyme disease in children aged 8 years or over is doxycycline, and for younger children, amoxicillin. Intravenous treatment with ceftriaxone is required for carditis or neurological disease. NICE has guidelines for clinicians on investigation and treatment of Lyme disease in children.

Immunization

Immunization saves millions of lives every year, as well as preventing morbidity and disability and parents from taking time off work to look after their sick children. The most notable success of immunization has been the global eradication of smallpox in 1980. Polio has been eliminated globally other than in Afghanistan and Pakistan, and neonatal and maternal tetanus remains in only 13 countries. Also, through herd immunity, the whole population

benefits by reduced pathogen exposure of unvaccinated individuals. Vaccine coverage rates to achieve this varies according to how contagious an infection is (the reproductive ratio of an infection [R_0], the number of individuals infected by one individual). A highly infectious disease such as measles (12–18 individuals infected by one individual) requires 95% vaccine coverage; for rubella it is only 80%.

Differences exist in the composition and scheduling of immunization programmes in different countries, and schedules change as new vaccines become available. Developing new vaccines and incorporating them into national programmes is a long and very expensive process, involving not only development of the new vaccine, but large efficacy trials, licensing, organization of their implementation, consistent supply and safety monitoring. Finance is often another major issue. The process usually takes 3–10 years, though was greatly curtailed for the development and introduction of COVID-19 vaccines.

The majority of vaccines are:

- Live attenuated vaccines, e.g. MMR, rotavirus, BCG – modified organisms
- Inactivated vaccines, e.g. inactivated polio (IPV), influenza – whole organisms obtained by chemical or heat treatment
- Subunit vaccines, e.g. diphtheria, pneumococcal, human papillomavirus (HPV), hepatitis B (HBV) – contain antigens of the organism, and usually require adjuvants.

The UK routine immunization schedule for 2020 is shown in Fig. 15.26; the latest version is available on the Department of Health website.

Rationale behind the current immunization programme

- *Diphtheria* – infection causes local disease with membrane formation affecting the nose, pharynx, or larynx, or systemic disease with myocarditis and neurological manifestations. There were about 60,000 annual notifications and 3000 deaths in the 1920s and 1930s, but immunization has practically eradicated the disease in the UK (Fig. 15.27a).
- *Pertussis* – clinical features are described in Chapter 17. Epidemics were associated with 60,000 to 160,000 cases each year. In 1974, after claims of an association between neurological conditions and pertussis vaccination, vaccination rates fell and was followed by a large pertussis outbreak, showing how epidemics can recur when immunization rates fall (Fig. 15.27b). The safety concerns were not substantiated in subsequent studies, but a less reactogenic acellular (aP) vaccine replaced the whole-cell vaccine and immunization age was changed to an earlier age when fewer neurological conditions present. However, it took several years to restore confidence in the vaccine. In 2012, after a number of infants less than 3 months old died from pertussis in the UK, pertussis immunization for pregnant women was introduced to provide infants with passive immunity prior to routine pertussis immunization.
- *Haemophilus influenzae type B* – causes invasive disease primarily in young children. The number of

	2 months	3 months	4 months	1 year	2–7 years	3 years 4 months	12–13 years	14 years
Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae</i> type b and hepatitis B (DTaP/IPV/Hib/HepB)	6 in 1	6 in 1	6 in 1					
Pneumococcal conjugate vaccine (PCV)		PCV		PCV				
Rotavirus (oral)	Rotavirus	Rotavirus						
Meningococcal B vaccine (MenB)	MenB		MenB	MenB				
Meningococcal group C (MenC/MenACWY)								MenACWY
Hib/MenC				Hib/Men C				
Measles, mumps, and rubella (MMR)				MMR		MMR		
Intranasal influenza vaccine (annual from 2–6 years)					Flu vaccine			
Diphtheria, tetanus, pertussis, polio, (DTaP/IPV)						4 in 1		
Human papillomavirus (HPV) Boys and girls, 2 doses 6 months apart							HPV	
Diphtheria, tetanus, polio (Td/IPV)								3 in 1

Figure 15.26 Routine immunization schedule in the UK (2020). There is also a selective immunization programme for infants born to hepatitis B infected mothers and for BCG at birth in areas of the country with a high TB incidence or parents or grandparents born in a high incidence country. (Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/849165/PHE_childhood_immunisation_schedule_Jan2020.pdf.)

reports of infection dropped dramatically after the introduction of the Hib vaccine (Fig. 15.27c), but a gradual rise from 1988 occurred because protection was not maintained throughout childhood. This was addressed with a Hib catch-up programme, and to prevent a further resurgence, a Hib booster dose has been introduced at 12 months of age.

- *Poliovirus infection* – epidemics occurred in the 1940s and 1950s and caused paralytic poliomyelitis in many children. Oral polio vaccine (OPV) carried a small risk of vaccine associated paralytic polio (about one case in 1.5 million doses). Inactivated polio vaccine (IPV) is now used as it does not carry this risk. There were only 33 cases globally in 2018 (Fig. 15.27d).
- *Meningococcal immunization* – meningococcal C disease was a major cause of meningitis in the late 1990s; the marked fall in the number of reports of group C disease in all age groups following the introduction of the vaccine is shown in Fig. 15.27e. Invasive disease is now well controlled and has fallen to only 43 cases in 2018/2019. The number of cases of meningococcal B has reduced since introduction of the vaccine. Due to a rise in meningococcal W disease across all age groups, ACWY conjugate vaccine was introduced for adolescents as they have a high rate of carriage. Reduction in carriage has resulted in a gradual reduction of cases for all ages.
- *Measles* – there were on average 400,000 notifications and 86 deaths annually in the 1950s and 1960s (Fig. 15.27f), both of which declined markedly following introduction of the measles vaccine. However, public confidence in the vaccine was severely damaged by huge media coverage of an assertion of a possible

association between it and autism in a paper in the Lancet (see Fig. 15.27f). Although this has been discredited, vaccine uptake rates fell and took some time to recover. Although only 90% of children are protected from primary vaccination with MMR at 12 months of age, the introduction of a preschool booster of MMR has reduced the proportion of susceptible school-age children and measles in the community. Although MMR coverage in England in 2019 was 95% for the 1st dose and 87% for the 2nd dose, the number of measles notifications in England and Wales increased to 991, mostly from Europe, and has resulted in the UK losing its WHO measles elimination status. The MMR vaccine includes immunization against mumps; reduced vaccine coverage in the past has resulted in its re-emergence in young adults; congenital rubella is now very rare.

- *Pneumococcal vaccination* – introduced into the UK immunization programme in 2006. Prior to this, more than 500 children under 2 years of age developed invasive pneumococcal disease in England and Wales each year. In 2010, a 13-valent conjugate vaccine (PCV, effective against 13 serotypes) was introduced, which protects against about 90% of the disease-causing pneumococcal serotypes.
- *Rotavirus vaccine* – has resulted in a marked reduction in the number of acute gastroenteritis-associated hospital admissions in young children.
- *Human papillomavirus vaccine* – provides protection against the two strains (human papillomavirus 16 and human papillomavirus 18) that cause 70% of cervical cancer. Initially given only to girls, but now also to boys as it can cause penile cancer in males

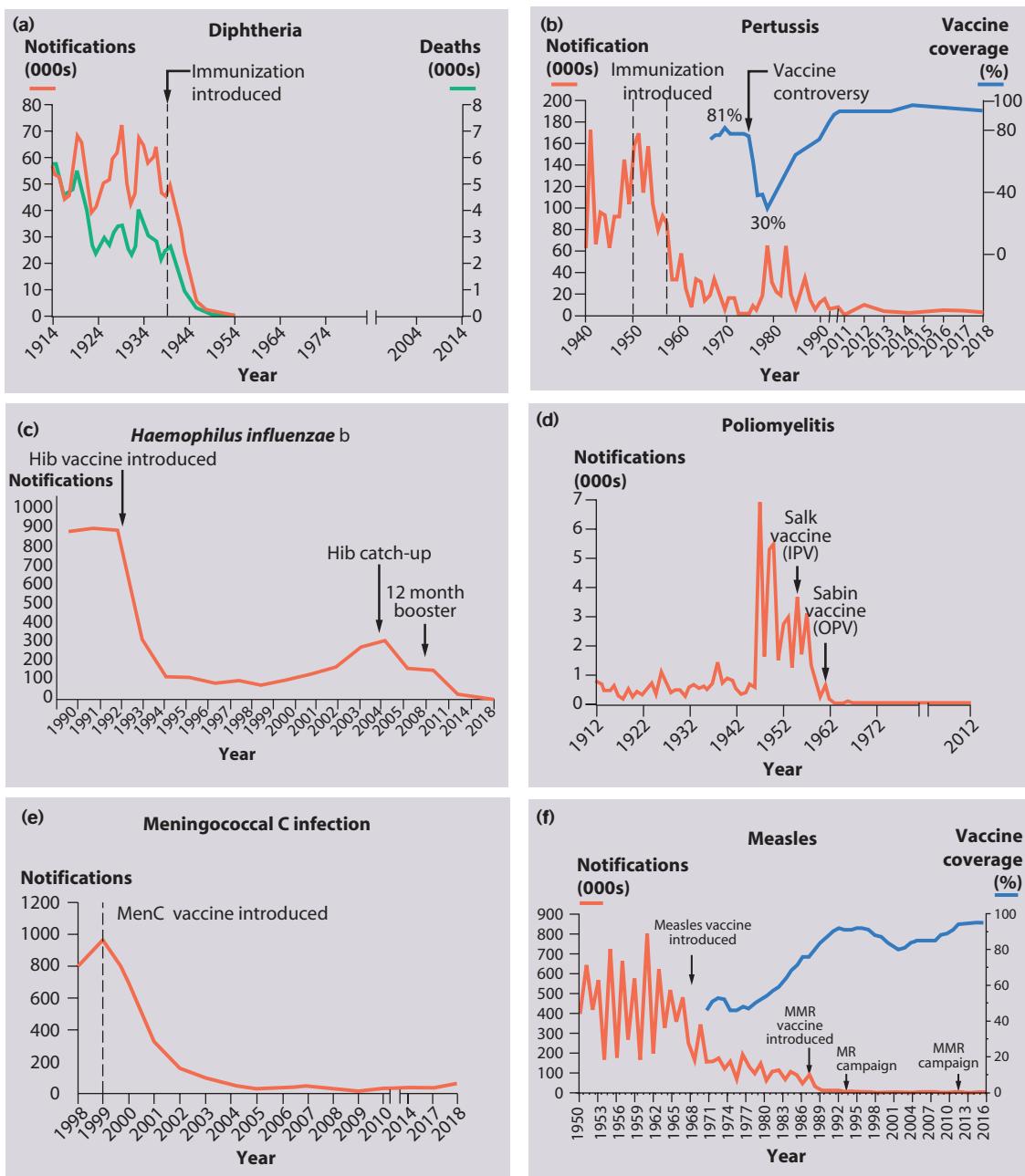


Figure 15.27 Effect of immunization on the number of notifications in England and Wales. (a) Diphtheria; (b) pertussis; (c) *Haemophilus influenzae* type b in children under 5 years of age; (d) poliomyelitis; (e) meningococcal disease; and (f) measles. (Data from Public Health England.)

- as well as anal cancer and head and neck cancer in both sexes.
- Influenza vaccine* – offered to young children as they are at higher risk of hospital admission than older children and are an important source of infection, as ‘super-spreaders’. Limited effectiveness during some seasons and suboptimal uptake.
- Hepatitis B vaccine* – now given as part of the routine immunization schedule. If mothers are hepatitis B surface antigen (HBsAg)-positive, it is also given at birth, 1 month, 2 months, and 12 months of age. Babies born to highly infectious e-antigen (HBeAg)-positive mothers should additionally receive hepatitis B immunoglobulin at birth.

- BCG (Bacillus Calmette–Guérin) immunization* – in the UK is given in the neonatal period and targeted to those at increased risk (live in high risk area, parent or grandparent born in a high-incidence country). The main value of BCG is in the prevention of disseminated disease (including meningitis) in younger children, hence the rationale for changing the timing of vaccination from early adolescence to the neonatal period.
- Varicella vaccination* – a live, attenuated varicella-zoster virus vaccine is available and given routinely in some countries, but not in the UK. It may be given to the siblings of ‘at-risk’ children (e.g. those undergoing chemotherapy).

Global immunization programme

Routine childhood immunization was provided for more than 116 million infants in 2018; the challenge is to provide it for the remaining 20 million undervaccinated or unvaccinated children. There is also considerable concern about the disruption caused by the COVID-19 pandemic, and that many children will not receive their scheduled vaccines.

Contraindications

Vaccination should be postponed if the child has an acute illness; however, a minor infection without fever or systemic features is not a contraindication. Following vaccination, there may be swelling and discomfort at the injection site and a mild fever and malaise. Some vaccines, such as MMR vaccine, may be followed by fever or malaise 7 days to 10 days later. Live vaccines should not be given to children who are immunocompromised, on or in contact with a child on immunosuppressive therapy (except in children with HIV infection on ART in whom MMR vaccine can be given), and advice should be obtained if the mother was on immunosuppressive therapy during pregnancy. A child who has had an anaphylactic reaction to a vaccine should not be given a repeat dose. Rare adverse reactions, which may not be identified during clinical trials, need to be reported. For example, an association between a rotavirus vaccine and an increased risk of intussusception, which had not been identified on clinical trials, led to its replacement with safer vaccines. Local guidelines about vaccination and its contraindications should be followed.

Vaccine confidence

The increasing number of people who refuse to vaccinate their children, often referred to as vaccine hesitancy, has become a major problem globally. Reasons for this are complex. Some of the issues are:

- Many parents have never encountered any of the diseases in immunization schedules, reducing their concern about the severity of the diseases.
- Vaccine safety – concern about side-effects or that they cause other diseases. The claim that MMR may be associated with autism generated huge adverse publicity and a decline in vaccine uptake in many countries.
- Societies have become less tolerant of risk.
- Belief that body is overwhelmed by vaccines.
- Distrust of health services.
- Formation of groups who are against specific vaccines or vaccines in general through personal conviction, religion, culture or socio-economic issues, and may use social media to generate fear.

These highlight the need to improve engagement with the public to better understand and respond to their concerns.

Immunodeficiency

Immunodeficiency may be:

- Primary (uncommon) – a genetically determined defect in the immune system
- Secondary (more common) – caused by breach of anatomical and physical barriers, e.g. burns, functional hypoplasia or splenectomy, immune-suppressive or immune-mediating drugs, antibody loss, e.g. nephrotic syndrome, malnutrition, or HIV.

Primary immunodeficiencies

Although primary immune deficiencies are rare, there are more than 250 genetically recognized disorders, with new disorders continually being identified. Most result from inherited defects in immune system development or function, and many are inherited as X-linked or autosomal recessive disorders. There may be a family history of parental consanguinity and unexplained death, particularly in boys. The clinical presentation is highly variable, however they should be considered in children with SPUR infections: Severe (e.g. meningitis or peritonitis), Persistent (e.g. does not improve with usual antibiotics), Unusual (e.g. *Pneumocystis jirovecii* or *Burkholderia cepacia*), or Recurrent (appear to have resolved but reappear). A family history of immune-deficiency and faltering growth, chronic diarrhoea and severe eczema from early infancy are additional presentations. The clinical presentation of the different primary immune deficiencies is shown in Fig. 15.28.

Investigation

This is directed towards the most likely cause (Table 15.3) and should not all be done on initial testing. A full blood count (and differential), immunoglobulin levels (IgM, IgG, IgA, IgE) and lymphocyte subsets will give a general indication of white cell numbers and types and antibody levels. An HIV test should be done if there is faltering growth, complement levels if there is a history of opportunistic infection and phagocytic function if invasive pyogenic infections. Further investigations should be directed by an immunologist and can quantify the essential components of the immune system and also provide a functional assessment of immunocompetence. Genetic testing can reveal known single-gene defects or novel diagnoses based on rapidly evolving exome and whole genome sequencing.

Management

Management options depend on underlying immune defect and can include:

Antimicrobial prophylaxis:

- For T-cell and neutrophil defects – cotrimoxazole to prevent PCP and itraconazole or fluconazole to prevent other fungal infections

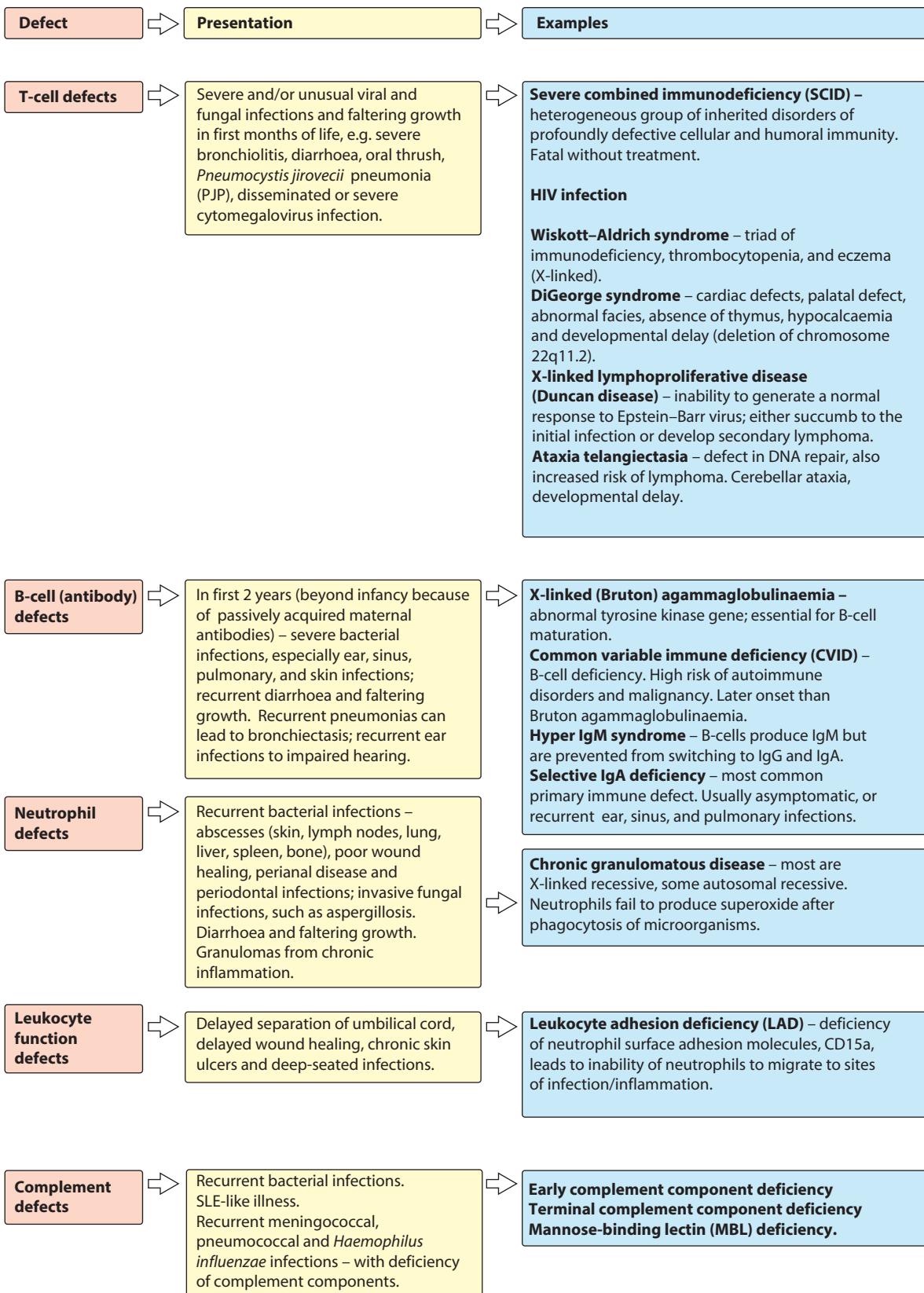


Figure 15.28 Clinical presentation of primary immunodeficiency.

Table 15.3 Investigation to identify primary immunodeficiency – *first line investigations in italics*.

Immune defect	Investigations
Cellular (T cells)	<i>Full blood count (including lymphocyte count)</i> <i>Lymphocyte subsets (to assess CD3⁺ [total T cell], CD4⁺ [helper T cell], and CD8⁺ [cytotoxic T cell] numbers)</i> Ability of T cells to proliferate in response to mitogen
Antibody (humoral; B cells)	<i>Immunoglobulin levels (IgG, IgM, IgA, and IgE)</i> IgG subclasses (in children >2 years) Specific antibody responses (e.g. vaccine-induced antibodies to tetanus and pneumococci) <i>Lymphocyte subsets (to assess B-cell numbers)</i>
Combined (B and T cells)	Investigations as above
Neutrophils	Specific genetic/molecular tests for severe combined immunodeficiency <i>Full blood count (to assess neutrophil numbers/neutropenia)</i> <i>Nitroblue tetrazolium test (NBT test) – abnormal in chronic granulomatous disease (most laboratories now use newer assays to determine superoxide production)</i> Tests for leucocyte adhesion deficiency – CD11b/CD18 expression Tests of chemotaxis (neutrophil mobility)
Complement/mannose-binding lectin	<i>Tests of classical and alternative complement pathways (CH50, AP50)</i> Assays for individual complement proteins Mannose-binding lectin levels
Additional tests	<i>HIV test</i>

- For B-cell defects – antibiotic prophylaxis (e.g. azithromycin) to prevent recurrent bacterial (e.g. chest, ear, sinus) infections

Antibiotic treatment:

- Prompt treatment of infections
- Appropriate choice of antibiotics to cover likely organisms
- Generally longer courses, with low threshold for intravenous therapy

Screening for end-organ disease:

- E.g. CT chest scan in children with antibody deficiency to detect bronchiectasis

Immunoglobulin replacement therapy:

- For children with antibody deficiency
- Can be given intravenously, which may require central venous (Portacath or Hickman) line insertion, or subcutaneously

Bone marrow transplantation:

- E.g. for severe combined immunodeficiency, chronic granulomatous disease
- Can be matched sibling donor, matched unrelated donor, or haploidentical (parental) transplant

Gene therapy:

- Currently an evolving area and not widely available.

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Centers for Disease Control and Prevention, Atlanta, GA, USA: www.cdc.gov.

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Meningitis Research Foundation: www.meningitis.org.
Useful teaching material on meningitis.

Public Health England:

For incubation and exclusion periods, see www.gov.uk/health-protection/infectious-diseases.

UK Department of Health Green Book: www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book. *Up-to-date information on vaccines and the immunization programme in the UK.*

UK Department of Health Immunisation Schedule: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/849165/PHE_childhood_immunisation_schedule_Jan2020.pdf. *Up-to-date information on the immunization programme in the UK.*

UNAIDS: www.unaids.org. *Worldwide information on HIV.*

World Health Organization: www.who.int.



Allergy

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Features of allergic disorders in children:

- Up to 40% of children in the UK have one or more allergic disorders (eczema, allergic rhinitis, or asthma) and 3%-6% have food allergy.
- They have increased in prevalence in the UK and in many other countries, both high- and low-income.
- They cause significant morbidity and can be fatal – about 20 children or young people die from asthma and 2 from food anaphylaxis in the UK each year.

An abnormal immune system may result in:

- allergic diseases
- immune deficiencies
- autoimmune disorders – either organ-specific (e.g. type I diabetes mellitus) or systemic (e.g. systemic lupus erythematosus).

Explanations of some of the terms used in 'allergy' are listed in **Box 16.1**.

Mechanisms of allergic disease

Many genes have been linked to the development of allergic disease. Polymorphisms or mutations in these genes lead to a susceptibility to allergy. Intact barrier function of the skin appears to be important. Alterations in the filaggrin gene are associated with increased risk of eczema and food allergy.

Allergic diseases occur when individuals make an abnormal immune response to harmless environmental

stimuli, usually proteins. Allergy is an 'epigenetic condition' where the environment interacts with these genes. The developing immune system must be 'sensitized' to

Box 16.1 Allergy definitions

- *Hypersensitivity* – objectively reproducible symptoms or signs following exposure to a defined stimulus (e.g. food, drug, pollen) at a dose that is usually tolerated by most people
- *Allergy* – a hypersensitivity reaction initiated by specific immunological mechanisms. This can be IgE-mediated (e.g. peanut allergy) or non-IgE-mediated (e.g. coeliac disease)
- *Atopy* – a personal and/or familial tendency to produce IgE antibodies in response to ordinary exposures to potential allergens, usually proteins. Strongly associated with asthma, allergic rhinitis and conjunctivitis, eczema and food allergy
- *Anaphylaxis* – a serious allergic reaction with bronchial, laryngeal, or cardiovascular involvement that is rapid in onset and may cause death
- *Immune tolerance* – the absence of an active immune response against a particular antigen, e.g. the absence of an allergic immune response to peanut or house dust mite
- *Sensitization* – a positive test to an allergen, either by skin prick test, or specific IgE. Does not equate to allergy unless a clinical reaction is initiated on exposure. However, the higher the number of positive tests, the more likely the person is going to be "allergic"

an allergen before an allergic immune response develops. Only a few stimuli account for most allergic disease:

- inhalant allergens, e.g. house-dust mite, plant pollens, pet dander and moulds
- ingestant allergens, e.g. egg, cow's milk, nuts, wheat, seeds, legumes, seafood and fruits
- insect stings/bites, drugs, and natural rubber latex.

Allergic immune responses are classified as IgE mediated or non-IgE mediated. IgE-mediated allergic reactions have a characteristic clinical course:

- an early phase, occurring within minutes of exposure to the allergen, caused by release of histamine and other mediators from mast cells. Causes urticaria, angioedema, sneezing, vomiting, bronchospasm and/or cardiovascular shock
- a late phase response may also occur after 4–6 hours, especially in reactions to inhalant allergens. This causes nasal congestion in the upper airway, and cough and bronchospasm in the lower airway.
A potential late phase response in food allergy is why children need to be observed in hospital for several hours after a moderate or severe food allergy reaction.

The majority of severe life-threatening allergic reactions are IgE mediated.

Non-IgE-mediated allergic immune responses usually have a delayed onset of symptoms and more varied clinical course.

The hygiene hypothesis

It is not clear why the prevalence of allergic diseases has increased in many countries and the speed of this change suggests an environmental cause. A consistent observation is that the risk is lower in younger children of large families and in children raised on farms. These findings have led to the hygiene hypothesis, which proposes that the increased prevalence is due to altered microbial exposure associated with modern living conditions (Fig. 16.1). Although the hypothesis remains the leading explanation for the increase in allergic disease, it is mainly supported by indirect evidence.

Clinical evaluation

History and examination

An allergy-focused history is the cornerstone to a correct diagnosis. The child and family may not volunteer a history of allergic disease as they have come to consider the symptoms as normal, e.g. the child who coughs most nights or has a blocked nose most of the time may not perceive this as abnormal. As allergic diseases are multi-system, in addition to the signs of individual allergic diseases, examination may reveal:

- mouth breathing (Fig. 16.2a). Children who habitually breathe with their mouth open may have an obstructed nasal airway from rhinitis, and there may also be a history of snoring or obstructive sleep apnoea
- an allergic salute (Fig. 16.2b), from rubbing an itchy nose

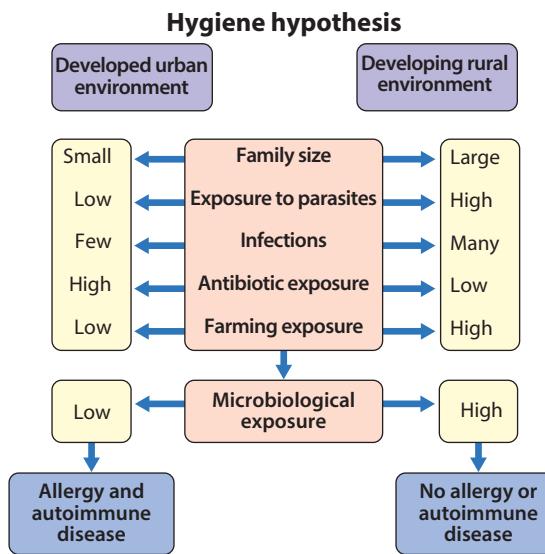


Figure 16.1 Hygiene hypothesis.

- pale and swollen inferior nasal turbinates from rhinitis
- hyperinflated chest or Harrison sulci from chronic undertreated asthma
- atopic eczema affecting the limb flexures
- allergic conjunctivitis; may be accompanied by prominent creases (Dennie–Morgan folds) and blue-grey discolouration below the lower eyelids.

Growth needs to be checked, especially in those with food allergy, where dietary restrictions or malabsorption can lead to nutritional deficiencies or compromise, and in those treated with high-dose inhaled/nasal/topical corticosteroids.

Investigations

Skin prick tests

Skin prick testing is performed for food and inhaled allergens, and sometimes for investigating drug or insect sting allergies. A drop of allergen (either an extract or the fresh food) is placed on the skin, the site is marked and the skin is pricked with a lancet (Fig. 16.3). After 15 minutes any wheals are measured to determine if positive. Providing antihistamines have been stopped 48–72 hours before testing, negative tests suggest that allergy is unlikely. Test results can only be interpreted in the context of a detailed history.

IgE blood tests

Raised total IgE is an indication of atopy in a child. For investigating food or inhaled allergy, such as to milk, grass pollen, etc, specific IgE tests are required. Food that the child is already eating without symptoms should not be tested as it may yield a false positive result. The greater the response, the more likely the child is to be allergic. Negative results make IgE-mediated allergy unlikely.

More recently developed 'component' blood tests to specific components of the allergen can provide more specific information.

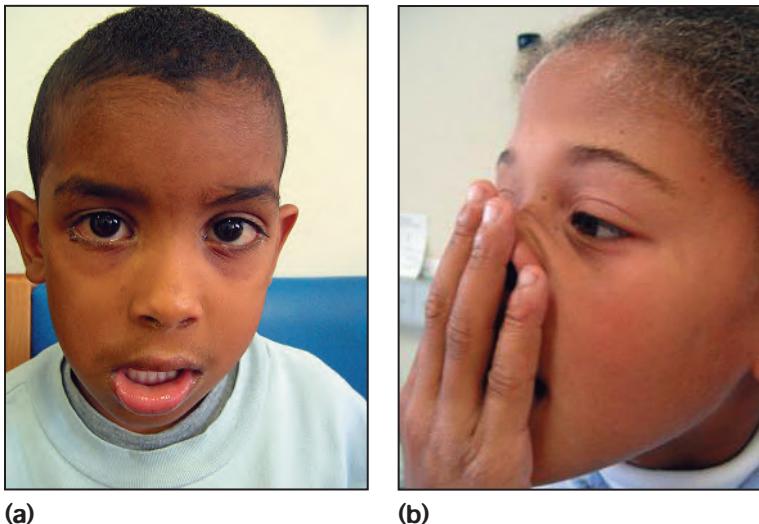


Figure 16.3 Skin-prick testing for IgE-mediated allergy. A drop of the allergen is placed on the skin, the site is marked, and pricked with a needle, and any weals measured. Weals of 4 mm or greater are considered positive. Multiple positive results are present. (Courtesy of Dr Pete Smith.)

Spirometry and other lung function tests

May be performed to provide information about lung function to diagnose or monitor asthma or lung inflammation.

Allergen challenge

If results from the history and investigations are not clear, or if the child is thought to have grown out of an allergy, an allergen challenge may be performed. This is usually a food challenge for food allergy. The child is given increasing quantities of the food, starting with a tiny amount, until a full portion is reached. Sometimes these are 'placebo controlled', where the child and parents do not know which of the challenges involves the food or a placebo. The test should be performed in a hospital with full resuscitation facilities available, with close monitoring for signs of anaphylaxis. Similarly, drug challenges are also sometimes performed.

Organization of care

The individual diseases are managed by general practitioners, general paediatricians or organ-specific specialists, e.g. eczema by dermatologists, asthma by respiratory paediatricians. However, allergic diseases coexist and it is

Figure 16.2 Allergic facies. (a) There is a habitually open mouth due to mouth breathing. (b) An allergic salute, from rubbing an itchy nose. (Courtesy of Professor George Du Toit.)

therefore helpful to consider allergy as a systemic disease. The role of paediatric allergists is to identify triggers to avoid and to manage children with multisystem or severe disease. The management of specific allergic diseases and conditions is described in the following section.

Age of onset of allergic conditions

Allergic children develop individual allergic disorders at different ages:

- Eczema and food allergy usually develop in infancy.
- Allergic rhinitis, conjunctivitis and asthma begin most often in preschool and primary school years.
- Allergic disorders often coexist; for example, most children with food allergy have a history of early-onset eczema and most children with asthma have some degree of allergic rhinitis.

Prevention of allergic diseases

Many interventions have been tested for preventing allergic disease but only one has shown definite reduced risk of allergy to date. This is the induction of 'immune tolerance' by feeding common food allergens such as egg and peanut to young infants to reduce their risk of developing egg or peanut allergy. This is now often suggested in infant feeding guidelines for countries where food allergy is common, such as the UK, US and Australia. However, when multiple food allergens have been introduced together, the effect is limited due to difficulty feeding infants sufficient food allergens for long enough to prevent all food allergy. Thus, the impact of using immune tolerance to prevent food allergy is limited. Other approaches tried without success include probiotics (live bacteria such as *Lactobacillus*), prebiotics (non-digestible oligosaccharides), nutritional supplements (e.g. omega-3 fatty acids, vitamin D, antioxidants, trace elements), medications (e.g. antihistamines, immunotherapy), and skin moisturizers. There is some evidence house dust avoidance by covering mattresses may benefit some dust-sensitized children with asthma.

Summary

Paediatric allergy

- Includes food allergy, eczema, allergic rhinitis and conjunctivitis, asthma, urticaria, insect sting hypersensitivity, drug allergy and anaphylaxis.
- Occurs when a genetically susceptible person reacts abnormally to an environmental antigen.
- Different allergic diseases often coexist – if a child has one, look for others.

Food allergy and food intolerance

Presentation varies between countries, cultures, with the agent and the child's age:

- in infants – the most common causes are egg, cow's milk and nuts
- in older children – peanut, tree nut, fish, shellfish and sesame.

As food allergy is an allergy to the food protein, many other foods can be implicated, particularly in cultures and settings with diverse food intakes. Fruits, legumes and seeds are also common causes of IgE mediated food allergies.

Food allergy is most commonly primary, where children usually react on first exposure. It can also be secondary to cross-reactivity between proteins present in fresh fruits/ vegetables/nuts and those present in pollens, e.g. a child who can eat apples may develop allergy to apples when older if they become allergic to birch tree pollen, because the apple and birch pollen share a very similar protein. This common condition is termed the 'pollen food allergy syndrome' and generally leads to mild allergic reactions, often causing an itchy mouth but rarely systemic symptoms.

Non-IgE mediated food allergy typically occurs hours after ingestion and usually involves the gastrointestinal tract. Food allergy and intolerance are different from food aversion, where the person refuses the food for psychological or behavioural reasons.

Clinical features

Food allergy occurs when a pathological immune response is mounted against a specific food protein. It is usually *IgE-mediated*, with a history of allergic symptoms varying from urticaria to facial swelling to anaphylaxis, usually 10–15 minutes (up to 2 hours) after ingestion of a food.

Over 80% of children with food allergy present in the first year of life; many have atopic eczema. *Non-IgE-mediated food allergy* typically occurs hours after ingestion and usually involves the gastrointestinal tract, with diarrhoea, vomiting, abdominal pain and sometimes faltering growth. It sometimes presents in an infant with blood in the stools in the first few weeks of life from proctitis, or rarely with severe repetitive vomiting in an infant following milk or rice which can result in shock (food protein-induced enterocolitis syndrome). Eosinophilic esophagitis presents with persistent vomiting and difficulty swallowing in young children; and in older children with difficulty

swallowing, and impaction of food in the oesophagus. A *non-immunological hypersensitivity reaction to a specific food* is called food intolerance. An example of each in relation to cow's milk is shown in Fig. 16.4.

Diagnosis

The clinical history is key in food allergy diagnosis. Food allergy should be suspected if typical symptoms occur following exposure to a particular food. For IgE-mediated food allergy, the most helpful confirmatory tests are skin-prick tests and measurement of specific IgE antibodies in blood as described above.

Management

The management of a food-allergic child involves avoidance of the relevant food(s). This can be very difficult as the most common food allergens are common ingredients in the diet, and may be present in small quantities in many foods. Food labelling legislation requires all common food allergens to be clearly disclosed. The advice of a paediatric dietitian can help patients avoid foods to which they are allergic, find appropriate alternatives, and avoid nutritional deficiencies. If a child is diagnosed with one allergy, related allergies need to be considered; 20% of children with egg allergy have peanut sensitization and may be peanut allergic and children with peanut allergy will often have a tree nut allergy.

Proteins with an unstable tertiary structure may be rendered non-allergenic by heat degradation or other forms of processing. For example, in milk and egg allergy, many children will be able to tolerate egg or milk in a baked form, where the change in the protein epitope brought about by cooking at high temperatures makes the food less allergenic. So, some children are allergic to runny egg, but can tolerate eating cooked egg or egg in baked foods.

In addition to dietary management, the child and family must be able to manage an allergic reaction. Written self-management plans and adequate training should be provided. Mild reactions (rash, swelling of lips/face/eyes) are treated with non-sedating antihistamines. Severe reactions (i.e. with cardiovascular, laryngeal or bronchial involvement) are treated with adrenaline given intramuscularly by autoinjector (e.g. EpiPen), which the child or parent should carry with them at all times.

Immunotherapy for food allergy involves giving the child minute amounts of the food they are allergic to, and building up that amount over time. There is a substantial risk of significant allergic reaction during this treatment and it is highly resource intensive. The Food and Drug Administration in the USA have approved a product for peanut immunotherapy, but this is not recommended in the UK; although it increases threshold of reactivity it also increases risk of allergic reactions and anaphylaxis. It is unclear whether food allergen immunotherapy has a positive effect on quality of life.

Food allergy to cow's milk and egg often resolves in early childhood, and gradual reintroduction under supervision of a paediatric dietitian may be possible for these foods. Food allergy to nuts and seafood usually persists through to adulthood.



The diagnosis of food allergy should not be made lightly – dietary restrictions and fear of accidental reactions make a major impact on family life.

Examples of food allergy and hypersensitivity to milk

Condition	Clinical manifestation
IgE-mediated food allergy • Immediate cow's milk allergy	The clinical features of an acute allergic reaction are listed in (a). A 6-month-old breastfed infant developed widespread urticaria immediately after the first formula feed. Skin-prick test was strongly positive (8 mm weal) to cow's milk, confirming the diagnosis of IgE-mediated cow's milk allergy. Widespread urticaria and lip swelling after milk ingestion are shown in (b) and (c).
	(a) Clinical features of an acute allergic reaction: Mild reaction <ul style="list-style-type: none">Urticaria and itchy skinFacial swelling Severe reaction <ul style="list-style-type: none">WheezeStridorAbdominal pain, vomiting, diarrhoeaShock, collapse
	
	
Non-IgE-mediated cow's milk allergy	A 4-month-old infant, formula fed since birth, has loose stools and faltering growth. Skin-prick test to cow's milk is negative (0 mm weal). Elimination of cow's milk results in resolution of symptoms, which return on trial re-introduction.
Non-allergic food hypersensitivity • Temporary lactose intolerance	Previously well 12-month-old infant develops diarrhoea and vomiting. The vomiting settles but watery stools continue for several weeks. <ul style="list-style-type: none">Stool sample – no pathogens but positive for reducing substances.Diagnosis – temporary lactose intolerance following viral gastroenteritis.

Figure 16.4 Examples of food allergy and hypersensitivity to milk. (a) Clinical features of an acute allergic reaction. (b, c) Widespread urticaria and lip swelling after milk ingestion. (Courtesy of Dr Pete Smith.)

Summary

Food allergy

- Affects up to 6% of children.
- The most common causes are egg, milk, nuts, seafood, wheat, legumes, seeds and fruits.
- Diagnosis of IgE-mediated food allergy is based on a suggestive history supported by skin-prick tests or specific IgE antibodies in blood.
- Supervised food challenge is sometimes necessary to clarify the diagnosis.
- Those at risk of a severe reaction, e.g. with previous anaphylaxis or coexistent asthma, should carry an adrenaline autoinjector.

Eczema

Eczema can be either atopic (where there is evidence of IgE antibodies to common allergens) or non-atopic. Atopic eczema is classified as an allergic disease as many

affected children have a family history of allergy, at least 50% develop other allergic diseases and IgE antibodies to common allergens are usually present. Filaggrin gene mutations have been identified as the key genetic risk factor for eczema development due to impairment of skin barrier function, which then leads to cutaneous sensitization to inhalant and food allergens. This means that filaggrin gene mutations predispose to food allergy, asthma and hay fever as well as eczema. Up to 40% of young infants with severe eczema have an IgE-mediated food allergy. Eczema is considered further in Chapter 25 (Dermatological disorders).

Allergic rhinitis and conjunctivitis (rhinoconjunctivitis)

This can also be atopic (associated with IgE antibodies to common inhalant allergens) or non-atopic. Rhinoconjunctivitis is classified according to the pattern and severity of symptoms experienced. Therefore it may be intermittent or persistent and mild, moderate or severe. In temperate climates it is often classified as seasonal (related to seasonal grass, weed or tree

Box 16.2 Range of treatment for allergic rhinoconjunctivitis

- Allergen avoidance
- Nasal saline irrigation if tolerated
- Second-generation non-sedating antihistamines
- Nasal inhaled corticosteroid (ensure adequate technique)
- Eye drops: cromoglycate or else steroids under ophthalmology supervision
- Leukotriene receptor antagonists, e.g. montelukast
- Allergen immunotherapy

pollens) and perennial (related to perennial allergens such as house-dust mite or pets). It affects up to 20% of children and can severely disrupt their lives. In addition to its classic presentation of coryza and conjunctivitis, it can also present as 'cough-variant rhinitis' due to a post-nasal drip or as a chronically blocked nose causing sleep disturbance with impaired daytime behaviour and concentration. Allergic rhinitis is associated with eczema, sinusitis and adenoidal hypertrophy and is closely associated with asthma.

Initial treatment is shown in [Box 16.2](#). Children who remain symptomatic may be given specific allergen immunotherapy which can be highly effective. Solutions of the allergen are injected subcutaneously or administered sublingually regularly over several years, to develop immune tolerance. Subcutaneous immunotherapy must be carried out under specialist supervision due to the risk of anaphylaxis. Sublingual immunotherapy is usually the initial choice as it is safer.

Asthma

Allergy is an important component of asthma. Affected children often have IgE antibodies to Aeroallergens (house-dust mite; tree, grass and weed pollens; moulds; animal danders). Aeroallergen avoidance is difficult to achieve but measures to reduce exposure to house dust mite in the home may be helpful. For those who also have food allergy, uncontrolled asthma is a risk factor for severe and even fatal food allergic reactions. Management of asthma is described in [Chapter 17](#) (Respiratory disorders).

Urticaria and angioedema

Urticaria presents as hives or redness and results from local vasodilation and increased permeability of capillaries and venules. These changes are dependent on activation of skin mast cells, which release a range of mediators including histamine. It is itchy. Urticaria may involve deeper tissues to produce swelling (angioedema), especially of the lips and soft tissues around the eyes. While hives and angioedema can be a symptom of an IgE-mediated allergic reaction, not all hives are due to allergy.

Hives and angioedema due to IgE-mediated allergy will occur very shortly after exposure to the potential allergen (<1 hour), are reproducible, i.e. they happen whenever the child is exposed to the allergen, and resolve within 2–4 hours of allergen removal. Acute urticaria can also

occur after a viral infection; the rash usually lasts for days rather than hours.

Chronic urticaria (persisting >6 weeks) is usually non-allergic. Treatment is with second-generation non-sedating antihistamines, which may need to be increased up to four times the standard dose. In refractory cases anti-IgE antibody (omalizumab) may be used.

Angioedema without urticaria is a feature of C1 esterase inhibitor deficiency, which results in hereditary angioedema. This very rare condition is due to an inability to control the complement cascade. This needs specialist review.

Drug allergy

Drug allergies occur in children but are not common. Only a minority who are labelled 'drug allergic' are truly allergic; usually the label of drug allergy arises because a viral illness, for which the child has been prescribed antibiotics, causes a skin rash. A detailed history is required of the nature and timing of the rash in relation to taking the antibiotics. Any mucous membrane, widespread skin or systemic involvement may suggest a more severe drug allergy such as Stevens–Johnson syndrome (see [Ch. 25](#)) or DRESS (drug rash with eosinophilia and systemic symptoms).

Allergy skin and blood tests may be used to support a diagnosis of drug allergy. A drug challenge may be the only way to conclusively confirm or refute the diagnosis. Drug challenge is not safe after a severe drug reaction – an alternative drug should be sought instead of re-exposing the patient to the same drug(s).

Vaccines

True vaccine allergy in infants and children is rare. When present, it may be caused by gelatin, latex or antibiotics in the vaccine. There is often concern about giving vaccines to children with food allergy. However, multiple studies have shown that egg-allergic children can safely have MMR and nasal flu vaccine due to negligible egg protein content. Yellow fever vaccine does have a quantifiable level of egg protein; if required in egg-allergic children it should be given in hospital. Vaccines do not cause allergies.

Insect sting hypersensitivity

In the UK this arises mainly from bee and wasp stings. Allergic reactions may be:

- local, cutaneous – most reactions
- systemic – severe systemic reactions are rare in childhood.

Children with a local reaction, even if large, or a mild systemic skin reaction are unlikely to develop a severe reaction in the future and the family can be reassured. Those who had a severe systemic reaction, or have significant anxiety about a further reaction, should be offered an adrenaline autoinjector. They may wish to consider allergen immunotherapy especially if the risk of re-sting is high, or if the fear of re-sting has a big impact on the child's quality of life.



Figure 16.5 Example of a MedicAlert bracelet providing warning about severe allergy, in this instance to nuts.

Anaphylaxis

The immediate management of serious and potentially life-threatening allergic reaction is described in [Chapter 6](#) (Paediatric emergencies).

In children, the most common cause of anaphylaxis is food allergy, but can also be caused by insect stings, drugs and may even be idiopathic. Those at risk of anaphylaxis should carry an adrenaline autoinjector device on their person at all times and consider a MedicAlert bracelet ([Fig. 16.5](#)) or necklace. Some organizations recommend carrying two adrenaline autoinjectors, in case one misfires or a further dose is needed.

Acknowledgements

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Respiratory disorders

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Features of respiratory disorders in children:

- Respiratory disorders are common: In the UK, they account for half of acute consultations with general practitioners in young children.
- Respiratory disorders are the commonest reason for acute paediatric hospital admissions.
- Asthma is the commonest chronic childhood illness in the UK.
- Modern management of cystic fibrosis has markedly extended life expectancy.

Predisposition to individual respiratory disorders varies with age; for example, the type of acute respiratory infections children experience at different ages is shown in **Figure 17.1**. Infants and young children are particularly susceptible to viral infections following loss of protective maternal antibodies. Age also affects severity of illness; in general, neonates and infants are the most severely affected. The growing lungs of children are also particularly vulnerable to the long-term effects of environmental pollution and toxins, including cigarette smoke, which increases the lifetime risk of several diseases including asthma and chronic obstructive pulmonary disease in adult life.

Risk factors for respiratory disease in children or young people include:

- parental – genetic predisposition, maternal smoking during pregnancy
- in the child or young person – prematurity or low birthweight, especially with bronchopulmonary dysplasia, congenital heart disease, disorders causing muscle weakness, reduced immune function, lack or incomplete immunization or cigarette use or vaping
- environmental – household or air pollution, number of siblings, allergens, low socio-economic status, cigarette smoke and vaping.

Presentation of respiratory disorders in children can be with either the clinical features of:

- *Upper respiratory tract* – coryza, sore throat, earache, sinusitis, cough or stridor.
- *Lower respiratory tract*:
 - *Cough* – The character and nature of the cough may suggest a particular diagnosis. In general, wet or moist cough suggests that there are extra secretions.
 - *Increased rate of breathing* – Whilst the normal ranges for respiratory rate are wide, particularly for younger children, tachypnoea is one of the most sensitive signs of illness. However, this is not specific for respiratory problems and also occurs in heart failure, metabolic disorders and sepsis.

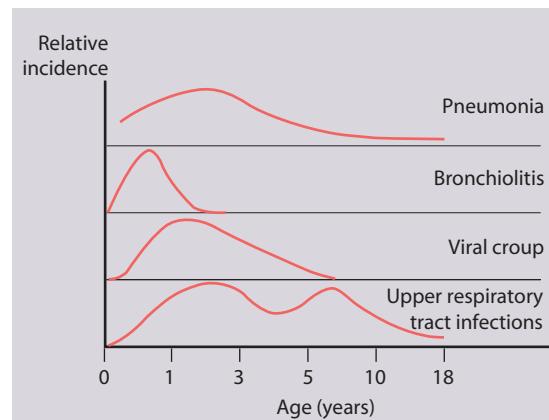


Figure 17.1 Age distribution of acute respiratory infections in children.



Figure 17.2 Marked sternal recession in an infant, indicating increased work of breathing.

- **Increased work (effort) of breathing** – An increase in resistance in the airways or lungs will result in an increase in the effort required to achieve adequate gas exchange. A conscious child will try to keep blood carbon dioxide and oxygen levels normal. If the resistance is increased in the upper airway, then effort is increased in inspiration. If the resistance is increased in the lower airway, then effort is increased in expiration. This is a specific indicator of respiratory illness.
- **Chest recession** – In infants and young children, chest recession is an important indicator of increased work of breathing, as they have compliant chest walls (Fig. 17.2). It is dynamic, occurring with each breath due to an acute change in the effort required to overcome airway resistance. The recession can be above the ribs (suprasternal), involve the chest wall (sternal) or below the ribs (subcostal). As chest wall muscles are relatively weak, and the diaphragm is relatively strong, when the work of breathing increases the breathing pattern becomes abdominal. This leads to 'see-sawing' of the chest and abdomen, with the chest moving in whilst the abdomen moves out during inspiration. This contrasts with later childhood or adult life, when even if there is increased work of breathing, the stiffer chest wall and diaphragm move together, with both moving outwards during inspiration. Whilst recession can still be seen, it tends to be between the ribs (intercostal).
- **Extra respiratory noises** – Flow of air against a resistance will lead to the generation of sounds. A stethoscope makes lower airway sounds easier to hear. Musical noises, e.g. wheeze, suggest partial obstruction. Coarser sounds, e.g. crackles, suggest increased secretions.
- **Reduced oxygen saturation** – In air, this is a sensitive marker of respiratory illness. Oxygen saturation can also be low in children with cardiac conditions, but is less likely to increase to the normal range with supplemental oxygen. Specially designed probes are required according to the child's size.

Impending respiratory failure is suggested by:

- cyanosis persistent grunting
- reduced oxygen saturation despite oxygen therapy
- rising pCO₂ on blood gas
- exhaustion, confusion, reduced conscious level.

Additional respiratory support will be required (see Ch. 6, Paediatric emergencies).

Summary

The clinical features of respiratory tract disorders in infants and young children are:

- Cough.
- Respiratory noises – wheeze, stridor, crackles.
- Increased rate of breathing.
- Increased work of breathing – dynamic chest recession.
- Reduced oxygen saturation which improves with supplemental oxygen and respiratory support if necessary.

Upper respiratory tract infections

Children have an average of five upper respiratory tract infections (URTIs) per year in the first few years of life, but some infants and primary school-age children have as many as 10–12 per year. Approximately 80% of all respiratory infections are URTIs; the term embraces a number of different conditions:

- common cold (coryza)
- sore throat (pharyngitis, including tonsillitis)
- acute otitis media
- sinusitis (relatively uncommon).

The child may have a combination of these conditions. Cough may be troublesome and may be secondary to attempts to clear upper airway secretions or a postnasal drip. URTIs may cause:

- difficulty in feeding in infants as their noses are blocked and this obstructs breathing
- febrile seizures.

Hospital admission may be required if feeding and fluid intake is inadequate.

The common cold (coryza)

This is the most common infection of childhood. Classical features include a clear or mucopurulent nasal discharge and nasal blockage. The most common pathogens are viruses – rhinoviruses (of which there are >100 different serotypes), coronaviruses, and respiratory syncytial virus (RSV).

Advice for parents that colds are self-limiting and there is no specific curative treatment may reduce anxiety and save unnecessary visits to doctors. Pain is best treated with paracetamol or ibuprofen. Antibiotics are of no benefit as the common cold is viral in origin and secondary bacterial infection is very uncommon. Cough may persist for up to 4 weeks after a common cold.

Sore throat (pharyngitis and tonsillitis)

Pharyngitis is usually caused by a viral infection (adenovirus, enterovirus or rhinovirus) and results in inflammation of the pharynx and soft palate with variably enlarged and tender local lymph nodes. Tonsillitis is a form of pharyngitis causing intense inflammation of the tonsils, often with a purulent exudate and may be caused by group A beta-haemolytic streptococci and Epstein-Barr



(a)

(b)

(c)

(d)

Figure 17.3 Appearance of the eardrum. (a) Normal; (b) acute otitis media; (c) otitis media with effusion; and (d) grommet. (Courtesy of Mr N Shah, Mr N Tolley, Mr Williamson, and Mr R Thevasagayam.)

virus (infectious mononucleosis or glandular fever). The tonsillitis of group A beta-haemolytic streptococci may produce a toxin responsible for the rash of scarlet fever (see Fig. 15.9a, Ch. 15, Infection and immunity). Marked constitutional disturbance, such as headache, apathy and abdominal pain is more common with bacterial infection, but it is not possible to distinguish clinically between viral and bacterial causes, and less than a third of cases of tonsillitis are caused by bacteria.

Antibiotics such as penicillin V or erythromycin hasten recovery from streptococcal tonsillitis on average by only 16 hours. However, antibiotics may be indicated to eradicate beta haemolytic streptococci to prevent rheumatic fever in high incidence countries or in children at increased risk of severe infection. This requires 10 days of oral antibiotics. Rarely, children may require hospital admission for intravenous fluid administration and analgesia if they are unable to swallow solids or liquids. Amoxicillin is best avoided as it may cause a widespread maculopapular rash if the tonsillitis is due to infectious mononucleosis.

Children with recurrent tonsillitis or its complications (e.g. peritonsillar abscess – quinsy) and those with sleep disordered breathing (e.g. obstructive sleep apnoea) may benefit from tonsillectomy and/or adenoidectomy. However, as acute sore throat is very common in children, in order to prevent unnecessary surgery strict indications for the operation have been adopted in some countries. In the UK, surgery is usually deferred until a child has had either seven or more episodes of significant sore throat in the preceding 12 months, or five or more episodes in each of the two previous years, or three or more episodes in each of the previous three years.

Tonsils and adenoids increase in size until about 8 years of age and then gradually regress. In young children, the adenoids grow proportionately faster than their airway. Narrowing the airway is therefore greatest between 2 and 8 years. For children where sleep disordered breathing is suspected, parents should be encouraged to obtain video recordings of the child during sleep, as these can help make decisions about the need for sleep recordings or surgery.

Acute otitis media

Infants and young children are prone to acute otitis media because their Eustachian tubes are short, horizontal, and function poorly. Most children will have at least one episode of acute otitis media and up to 20% will have three or more episodes. It is most common at 6–12 months of age. It causes earache and fever.

Summary

Acute otitis media

- This is diagnosed by examining the tympanic membrane, which should be visualized in all febrile children.
- Antibiotics marginally shorten the duration of pain but do not reduce hearing loss.
- If recurrent, may result in otitis media with effusion, which may cause speech and learning impairment from hearing loss.

Every child with a fever should have their tympanic membranes examined (Fig. 17.3a–d). In acute otitis media, the tympanic membrane is bright red and bulging with loss of the normal light reflection (Fig. 17.3b). Occasionally, there is acute perforation of the eardrum with pus visible in the external canal. Pathogens include RSV, rhinovirus, pneumococcus, *Haemophilus influenzae* and *Moraxella catarrhalis*. Complications include mastoiditis (see Fig. 2.14a) and meningitis, but these are rare. Pain should be treated with regular analgesia and may be required for up to a week. Otitis media usually resolves spontaneously. Antibiotics marginally shorten the duration of pain but have not been shown to reduce the risk of hearing loss. Neither decongestants nor antihistamines are beneficial.

Recurrent ear infections can lead to otitis media with effusion (also called glue ear; Fig. 17.3c). Children are usually asymptomatic apart from possible decreased hearing. The eardrum is dull and retracted, often with a visible fluid level. Otitis media with effusion is very common between the ages of 2 and 7 years. It usually resolves spontaneously, but may cause conductive hearing loss and interfere with normal speech development. There is no evidence of long-term benefit from the use of antibiotics, steroids, or decongestants. Nasal inflation, where the child breaths out through a nostril to inflate a small balloon, may help by opening the eustachian tube, but the child usually needs to be school-aged to perform it. If hearing does not improve, surgery may be considered, with insertion of tympanostomy tubes (grommets; Fig. 17.3d) with or without the removal of adenoids, but benefits often do not last more than 12 months.

Sinusitis

Infection of the paranasal sinuses may occur with viral URTIs. Occasionally, there is secondary bacterial infection,

with pain, swelling and tenderness over the cheek from infection of the maxillary sinus. As the frontal sinuses do not develop until late childhood, frontal sinusitis is uncommon in the first decade of life. Antibiotics and analgesia are used for acute sinusitis.

Upper airways obstruction

Severe upper airways obstruction results in choking, to clear the airway (see Ch. 6). Complete obstruction of the upper airway rapidly leads to respiratory failure and death. It may occur acutely as a result of an inhaled foreign body, or inhalation burns.

Partial obstruction of the upper airway leads to increased work of breathing accompanied by additional noises on breathing. Variable upper airway obstruction leads to stertor (snoring when asleep), and fixed partial airway obstruction leads to stridor, a high-pitched, musical, whistling sound. A brief explanation of why upper airway obstruction leads to stridor rather than wheeze is given in Figure 17.4. The causes of stridor are listed in Box 17.1. By far the most common cause is viral laryngotracheobronchitis ('croup').

The severity of upper airways obstruction is best assessed clinically by the characteristics of the stridor (none, only on crying, at rest, or biphasic) and the degree of accompanying chest retraction (none, only on crying, at rest). Severe obstruction also leads to increasing respiratory rate, heart rate, and agitation. Central cyanosis, drooling of saliva from inability to swallow it or reduced level of consciousness suggest impending complete airway obstruction and the need for intubation. Pulse oximetry can reliably detect hypoxaemia but, in contrast to parenchymal lung disease, it is a late feature in upper airways obstruction.

Total obstruction of the upper airway may be precipitated by examination of the throat using a spatula. Avoid looking at the throat of a child with upper airways obstruction unless full resuscitation equipment and personnel are at hand.

Croup

Viral croup accounts for over 95% of laryngotracheal infections in children. Parainfluenza viruses are the most common cause, but it may be triggered by rhinovirus, RSV and influenza. It typically occurs from 6 months to 6 years of age but the peak incidence is in the second year of life. It is most common in the autumn. The typical features are coryza and fever followed by:

- hoarseness due to inflammation of the vocal cords
- a barking cough, like a sea lion, due to tracheal oedema and collapse
- harsh stridor
- variable degree of difficulty breathing with chest recession
- the symptoms often starting, and being worse, at night.

When the upper airway obstruction is mild, the stridor and chest recession disappear when the child is at rest and the

Box 17.1 Causes of acute stridor (upper airway obstruction)

Common causes

Viral laryngotracheobronchitis ('croup')

Foreign body

Rare causes

Laryngeal oedema (anaphylaxis and recurrent croup)

Inhalation of smoke and hot fumes in fires

Trauma to the throat

Retropharyngeal abscess

Bacterial tracheitis or epiglottitis

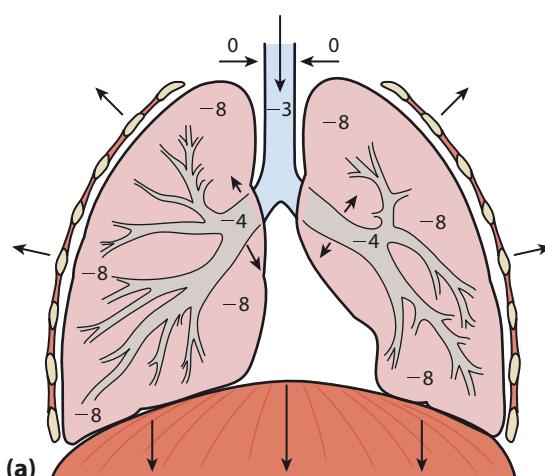
Severe lymph node swelling (malignancy, tuberculosis, infectious mononucleosis, measles)

Hypocalcaemia

Vocal cord dysfunction

Diphtheria (exceedingly rare)

Inhalation



Exhalation

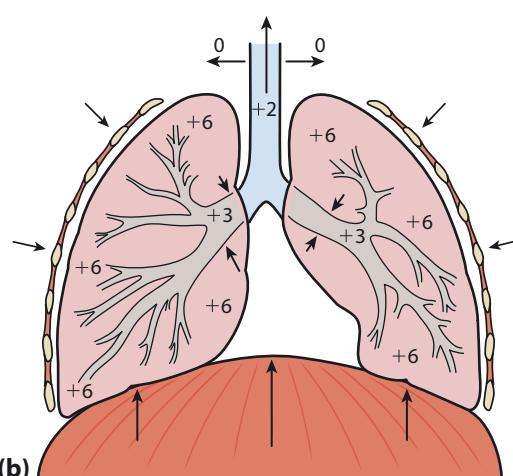


Figure 17.4 In normal breathing, during inspiration the negative intrapleural pressure dilates the intrathoracic airways but collapses the extrathoracic airway (a); and on exhalation positive intrapleural pressure does the opposite (b). This explains why extrathoracic obstruction causes difficulty in inspiration, whereas intrathoracic obstruction causes problems on exhalation. Numbers represent pressures at different points.

child can usually be managed at home. Parents should be advised to observe the child closely for signs of increasing severity. The decision to manage the child at home or in hospital is influenced not only by the severity of the illness but also by the time of day, ease of access to hospital, the child's age (with a lower threshold for admission for those <12 months old due to their narrow airway calibre), and parental understanding and confidence about the disorder.

Inhalation of warm moist air is a traditional and widely used therapy but it has not been proven to be beneficial. Oral dexamethasone, oral prednisolone, or nebulized steroids (budesonide) reduce the severity and duration of croup, and either one is first-line therapy for croup causing chest recession at rest. They have been shown to reduce the need for hospitalization.

If the upper airways obstruction is severe, nebulized epinephrine (adrenaline) with oxygen by face mask provides rapid but transient improvement. The child must continue to be observed closely for 2–3 hours after administration as its benefit is temporary, but the therapy is useful whilst waiting for the corticosteroids to take effect. Intubation for viral croup has become extremely unusual since the introduction of steroid therapy. Some children have a pattern of recurrent croup, which may be related to atopy.

Bacterial tracheitis and acute epiglottitis

Bacterial tracheitis and acute epiglottitis have similar clinical features. The latter is now very rare since children in most countries are immunized against *H. influenzae* type b (Hib). Presentation is with a very ill-looking child with a high fever, and drooling saliva as they are unable to swallow it. In contrast to croup, their stridor is soft (see [Case history 17.1](#)). Children with bacterial tracheitis also have copious, thick airway secretions. They have rapidly progressive airways obstruction. Bacterial tracheitis is typically caused by infection with *Staphylococcus aureus*.

If the diagnosis of either bacterial tracheitis or epiglottitis is suspected, urgent hospital admission and treatment are required. Calm administration of oxygen with nebulized adrenaline will usually offer some temporary benefit. Treatment must be initiated without delay. A senior anaesthetist, paediatrician, and ear, nose, and throat (ENT) surgeon should supervise maintenance of the airway, and the child should be intubated under controlled conditions with a general anaesthetic. Rarely, this is impossible and urgent tracheostomy is required. Only after the airway is secured should blood be taken for culture and intravenous antibiotics started.



Case history 17.1

Acute stridor

Amyra, a 14-month-old girl, woke up at 2 a.m. with marked noisy breathing on inspiration and a loud cough. She had been well until that evening when she developed a runny nose and fever of 38.1°C. Her mother gave her a dose of paracetamol suspension. Her noisy breathing scared her mother, who called an ambulance. In the emergency department she was noted to have a temperature of 37.9°C, was alert but had marked inspiratory stridor and moderate chest recession, particularly on inspiration.

What diagnosis would you make and how would you manage it?

A diagnosis of viral croup was made. The history is characteristic, including the stridor being worse at night. She does not have the clinical features of bacterial tracheitis or epiglottitis, which are important to exclude ([Table 17.1](#)). Management, in accordance with her disease severity, is to give a single dose of steroids, either orally or nebulized. She was given oral dexamethasone followed by observation and, after 2 hours, was discharged home as her stridor and work of breathing had improved.

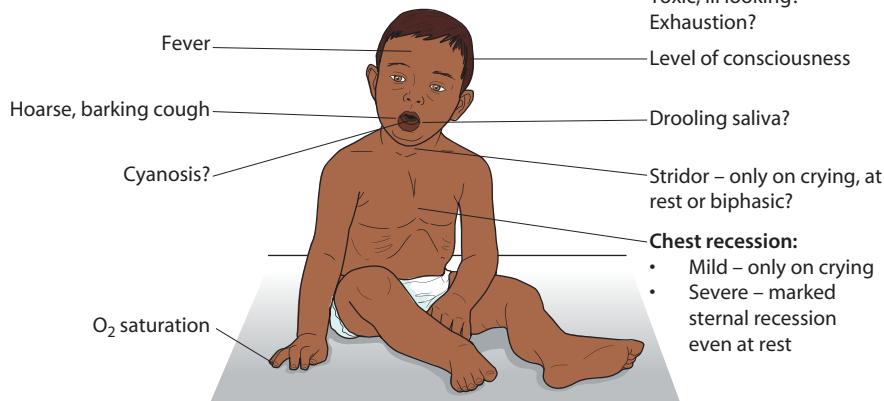
Table 17.1 Clinical features of croup (viral laryngotracheitis) and bacterial tracheitis/epiglottitis

	Croup	Bacterial tracheitis and epiglottitis
Onset	Over days	Over hours
Preceding coryza	Yes	No
Cough	Severe, barking	Absent or slight
Able to drink	Yes	No
Drooling saliva	No	Yes
Appearance	Unwell	Toxic, very ill
Fever	<38.5°C	>38.5°C
Stridor	Harsh, rasping	Soft, whispering
Voice, cry	Hoarse	Muffled, reluctant to speak

Summary

The child with acute stridor

Clinical features to assess



Other causes of stridor

When a child with acute stridor presents with atypical features or a poor response to treatment, other causes need to be considered (see Box 17.1). If a child has an abrupt onset of stridor without infection, consider anaphylaxis or inhaled foreign body.

Chronic stridor is usually due to a structural problem, either from intrinsic narrowing or collapse of the laryngotracheal airway, e.g. laryngomalacia (floppy larynx), subglottic stenosis, or external compression (e.g. vascular ring, where the trachea and oesophagus are compressed by blood vessels, most often a double aortic arch, lymph nodes or tumours). Investigations are sometimes required to determine the cause.

Laryngomalacia is common and is due to the soft, immature cartilage of the upper larynx collapsing on inspiration causing airway obstruction. Although it is a congenital anomaly, it usually presents at about 4 weeks of age when inspiratory flow rates are sufficient to generate the stridor, which is worse when the infant is agitated, feeding or lying on his/her back. If the child is thriving, no treatment or further investigation is required. It resolves by 2 years.

Lower respiratory tract infections

Lower respiratory tract infections (LRTI) are common in children. They include bronchiolitis, bronchitis and pneumonia. About half of all cases are viral in origin. Around 1 in 3 children in the UK develop bronchiolitis during their first year of life. After 12 months of age approximately 3 in 100 children per year will have a LRTI.

Bronchiolitis

Bronchiolitis is the most common serious respiratory infection of infancy, resulting in admission to hospital

of 2%–3% of all infants during annual winter epidemics; 90% are aged 1–9 months. RSV is the pathogen in 80%, and the remainder are accounted for by parainfluenza virus, rhinovirus, adenovirus, influenza virus, and human metapneumovirus. There is evidence that co-infection with more than one virus, particularly RSV and human metapneumovirus, may lead to a more severe illness.

Coryzal symptoms precede a cough and breathlessness. The characteristic findings are shown in Figure 17.5. Feeding difficulty due to dyspnoea is often the reason for admission to hospital. Recurrent apnoea is a serious complication, especially in young infants. Infants born prematurely who develop bronchopulmonary dysplasia, those with other underlying lung disease, such as cystic fibrosis, or those who have congenital heart disease are most at risk from severe bronchiolitis.

Investigations and decision to admit

Pulse oximetry should be performed on all children with suspected bronchiolitis. No other investigations are routinely recommended. In particular, chest X-ray or capillary blood gases are only indicated if respiratory failure is suspected.

Hospital admission is indicated if any of the following are present:

- apnoea (observed or reported)
- persistent oxygen saturation of <92% when breathing air
- inadequate oral fluid intake (<70% of usual volume)
- severe respiratory distress – grunting, marked chest recession, or a respiratory rate over 70 breaths/minute.

Management

This is supportive. Humidified oxygen is delivered via nasal cannulae or head box at a concentration adjusted according to pulse oximetry. The infant is monitored for apnoea.

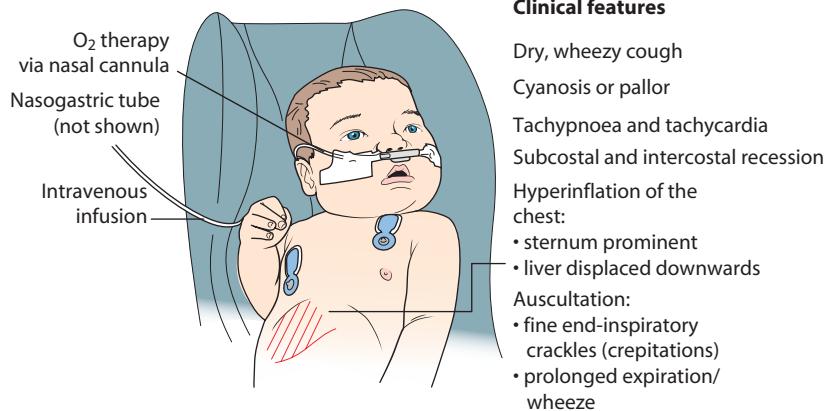


Figure 17.5 Clinical features of bronchiolitis in an infant requiring hospital care.

There is no evidence of benefit from the use of mist, nebulized hypertonic saline, antibiotics, corticosteroids or bronchodilators such as salbutamol or ipratropium. Fluids may need to be given by nasogastric tube or intravenously. If the infant remains hypoxic despite standard nasal cannula oxygen, heated, humidified high flow nasal cannula oxygen (HHFNCO) may be beneficial by allowing higher flows of oxygen to be delivered comfortably, although its role in bronchiolitis has not been determined. In some infants, non-invasive respiratory support with continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or mechanical ventilation is required.

RSV is highly infectious, and infection control measures, particularly good hand hygiene, cohort nursing, and gowns and gloves, have been shown to prevent cross-infection to other infants in hospital.

Most infants recover from the acute infection within 2 weeks. However, as many as half will have recurrent episodes of cough and wheeze (see the following section). Rarely, following adenovirus infection, the illness may result in permanent damage to the airways (bronchiolitis obliterans).

Prevention of bronchiolitis

A monoclonal antibody to RSV (palivizumab) given monthly by intramuscular injection reduces the number of hospital admissions in high-risk preterm infants. Its use is limited by cost and the need for multiple injections.

Pneumonia

The incidence of pneumonia peaks in infancy and old age, but is relatively high in childhood. It is a major cause of childhood mortality in low- and middle-income countries and more than 600,000 children die each year from pneumonia worldwide. Viruses are the most common cause in young children beyond the neonatal period, whereas bacteria are more common in neonates and older children. In clinical practice, it is difficult to distinguish between viral and bacterial pneumonia and in more than half of cases no causative pathogen is identified.

The likely pathogen varies according to age:

- Newborn – organisms from the mother's genital tract, particularly group B streptococcus, but also Gram-negative enterococci and bacilli.

Clinical features

- Dry, wheezy cough
- Cyanosis or pallor
- Tachypnoea and tachycardia
- Subcostal and intercostal recession
- Hyperinflation of the chest:
 - sternum prominent
 - liver displaced downwards
- Auscultation:
 - fine end-inspiratory crackles (crepitations)
 - prolonged expiration/wheeze



Causes of acute respiratory distress in an infant:

- Bronchiolitis
- Viral episodic wheeze
- Pneumonia
- Heart failure
- Foreign body
- Anaphylaxis
- Pneumothorax or pleural effusion
- Metabolic acidosis
- Severe anaemia.

- Infants and young children – respiratory viruses such as RSV are commonest. Bacterial infections include *Streptococcus pneumoniae*, *H. influenzae* and *Staphylococcus aureus*. *Bordetella pertussis* and *Chlamydia trachomatis* can also cause pneumonia at this age.
- Children over 5 years – *Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, and *Chlamydia pneumoniae* are the main causes.
- At all ages *Mycobacterium tuberculosis* should be considered.

Immunization with Hib and pneumococcal vaccines has markedly reduced the incidence of pneumonia from *Haemophilus influenzae* and invasive *Streptococcus pneumoniae*.

Clinical features and investigations

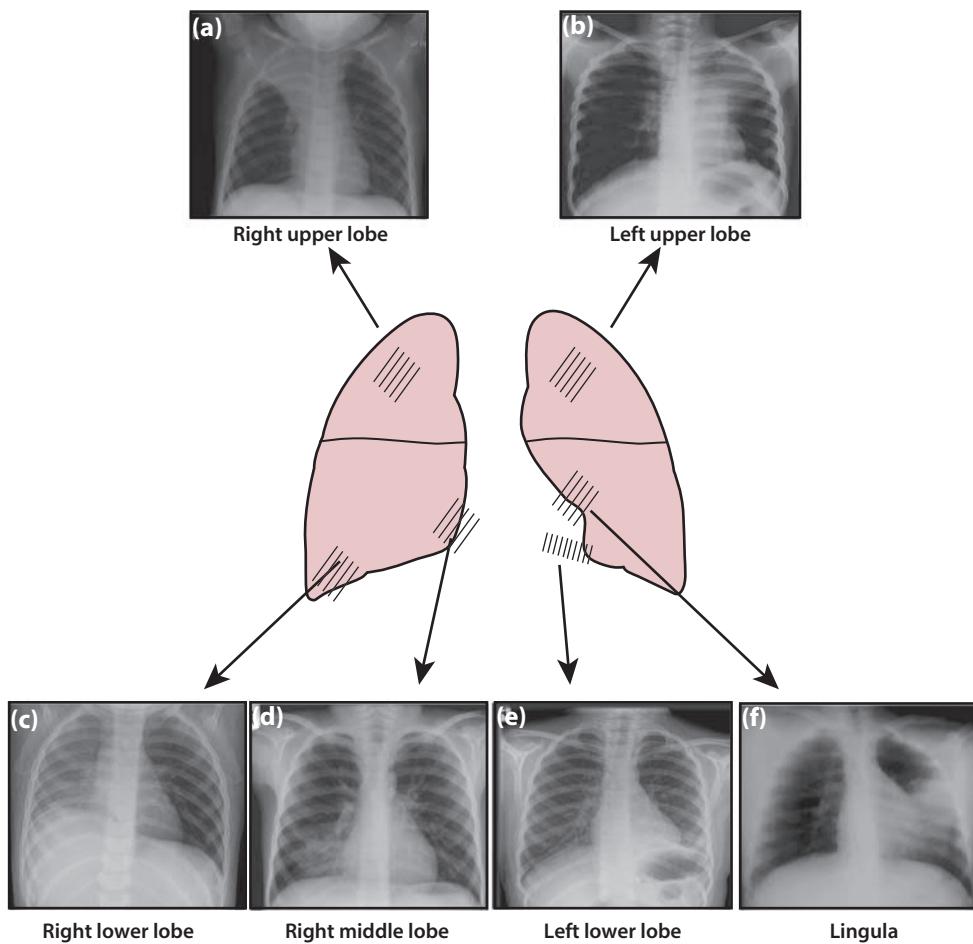
Fever, cough and shortness of breath are the most common presenting symptoms. These are usually preceded by a URTI. Other symptoms include lethargy, poor feeding, and appearing 'unwell'. Some children do not have a cough at presentation. Localized chest, abdominal, or neck pain is a feature of pleural irritation.

Examination reveals tachypnoea and increased work of breathing. The most sensitive clinical sign of pneumonia is raised respiratory rate so this must always be measured in a febrile child. The classic signs of consolidation are localized dullness on percussion, decreased breath sounds, bronchial breathing and end-inspiratory coarse crackles, although these signs are often absent in young children. The percussion note will be 'stony dull' if there is an accompanying effusion or empyema. Oxygen saturation may be decreased.

A chest X-ray is only necessary if there is doubt about the diagnosis (Fig. 17.6). Neither a chest X-ray nor blood tests, including full blood count and acute-phase reactants, are able to reliably differentiate between a viral and bacterial cause. When the pneumonia is associated with a pleural effusion, this is initially sterile (para-pneumonic effusion) but can become infected (empyema) (Fig. 17.7). When this happens, the fluid becomes increasingly viscous, and fibrin strands form, leading to septations.

Management

Evidence-based guidelines for the management of pneumonia in childhood have been published (British



- Consolidation of the right upper lobe with loss of volume of this lobe. The horizontal fissure has been shifted upwards.
- Left upper lobe consolidation.
- Right lower lobe consolidation with volume loss on the right. The heart silhouette is clearly seen but the right hemidiaphragm is raised and partially obscured.
- A normal right hemidiaphragm but partial loss of the right heart border typical of right middle lobe consolidation.
- Left lower lobe consolidation. The diaphragm is not clearly seen behind the cardiac silhouette.
- Lingular consolidation with obvious loss of the left heart border.

Figure 17.6 Chest X-ray interpretation in pneumonia. A guide to the radiological appearances of pneumonia in different lobes of the lung. The diagram shows the horizontal fissures, and shading illustrates the key finding in each lobar consolidation.

Thoracic Society). Most affected children can be managed at home but indications for admission include oxygen saturation <92%, recurrent apnoea, grunting and/or an inability to maintain adequate fluid/feed intake. General supportive care for children requiring admission should include oxygen for hypoxia and analgesia for pain. Intravenous fluids should be given if necessary to correct dehydration and maintain adequate hydration and sodium balance. Physiotherapy has no proven role.

The choice of antibiotic is determined by the child's age and the severity of illness. Newborns require broad-spectrum intravenous antibiotics. Most older infants can be managed with oral amoxicillin, with broader-spectrum antibiotics such as co-amoxiclav reserved for complicated or unresponsive pneumonia. For children over 5 years of age, either amoxicillin or an oral macrolide such

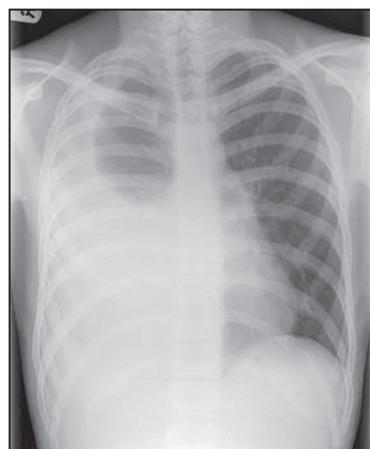


Figure 17.7 Right-sided empyema.

as clarithromycin is the treatment of choice. There is no advantage in giving intravenous rather than oral treatment in mild/moderate pneumonia unless the child is vomiting.

Small sterile parapneumonic effusions occur in up to one-third of children with pneumonia and usually resolve once the pneumonia is treated. Persistent fever despite 48 hours of antibiotics in a child with an effusion suggests it has become infected. This is a pleural empyema; the fluid becomes increasingly viscous, and fibrin strands form, leading to septations, and drainage may be required. The percutaneous placement of a small-bore chest drain under ultrasound guidance with regular instillation of a fibrinolytic agent to break down the fibrin strands is usually effective. Video-assisted thoracoscopic surgery or even thoracotomy and decortication is sometimes necessary in refractory cases.

Prognosis and follow-up

Follow-up is not required for a child with a simple pneumonia who makes a full clinical recovery. Those with a lobar collapse or persistent symptoms should have a repeat chest X-ray after 4–6 weeks to confirm resolution. Virtually all children with pneumonia, even those with empyema, make a full recovery in high-income countries.

Summary

Pneumonia

- Community acquired pneumonia can be diagnosed clinically and treated with oral antibiotics.
- Fever, cough and tachypnoea are sensitive but non-specific features.
- Grunting, crackles and/or a dull percussion note on auscultation in a child with fever and cough are more specific indicators.
- Hypoxia, recurrent apnoea, grunting and/or inability to maintain adequate fluids or feeds should prompt referral to hospital.

Whooping cough (pertussis)

This highly contagious respiratory infection is caused by *Bordetella pertussis*, which produces pertussis toxin. A related organism, *Bordetella parapertussis*, causes a similar illness but it does not produce pertussis toxin and the illness is usually milder and shorter. Pertussis is endemic, with epidemics every few years. After a week of coryza (catarrhal phase), the child develops a characteristic paroxysmal or spasmodic cough followed by a characteristic inspiratory whoop (paroxysmal phase). The spasms of cough are often worse at night and may culminate in vomiting (tussive vomiting). During a paroxysm, the child goes red or blue in the face, and mucus flows from the nose and mouth. The whoop may be absent in infants, but apnoea is common at this age. Epistaxis and subconjunctival haemorrhage can occur due to vigorous coughing. The paroxysmal phase lasts up to 3 months. The symptoms gradually decrease (convalescent phase), but may persist for many months. Complications such as pneumonia, seizures and bronchiectasis are uncommon

but there is still a significant mortality, particularly in infants who have not yet completed their primary vaccinations at 4 months. Infants and young children suffering severe spasms of cough or cyanotic attacks should be admitted to hospital and isolated from other children.

The organism can be identified early in the disease from culture of a pernasal swab, although PCR (polymerase chain reaction) is more sensitive. It can also be diagnosed serologically. Characteristically, there is a marked lymphocytosis ($>15 \times 10^9/L$) on a blood count. Although macrolide antibiotics eradicate the organism, they decrease symptoms only if started during the catarrhal phase. Siblings, parents and school contacts are at risk and close contacts should receive macrolide prophylaxis. Unimmunized infant contacts should be vaccinated. Immunization reduces the risk of developing pertussis and the severity of disease if affected but does not guarantee protection. The level of protection declines steadily during childhood and most cases are now in young people over 15 years old. Reimmunization of mothers during pregnancy is recommended in the UK and a number of other countries as it reduces the risk of pertussis in the first few months of the infant's life, when it is most dangerous.

Summary

Pertussis

- Caused by *Bordetella pertussis*.
- Paroxysmal cough followed by inspiratory whoop and vomiting; in infants, apnoea rather than whoop, which is potentially dangerous.
- Diagnosis is usually clinical. It is suggested by marked lymphocytosis on a blood film and confirmed by culture / PCR from a pernasal swab.

Asthma

Asthma is the most common chronic respiratory disorder in childhood. About 14% of children are diagnosed as having asthma in the UK. Worldwide, there has been an increase in the incidence of asthma over the last 40 years, but this has now plateaued in most high-income countries. Although the symptoms of asthma can be readily controlled in most children, it is an important cause of school absence, restricted activity, and anxiety for the child and family. There are still about 20 deaths from asthma in children and young people each year in the UK.

Pathophysiology of asthma

An outline of the pathophysiology of asthma is shown in Figure 17.8.

Clinical features

Asthma should be suspected in any child with wheezing on more than one occasion, particularly if this persists between viral illnesses (interval symptoms). What is meant by 'wheeze' should be clarified, as parents and children often mean something different from doctors. Demonstrating or describing the sound (e.g. 'a whistling in the chest when your child breathes out') can be helpful.

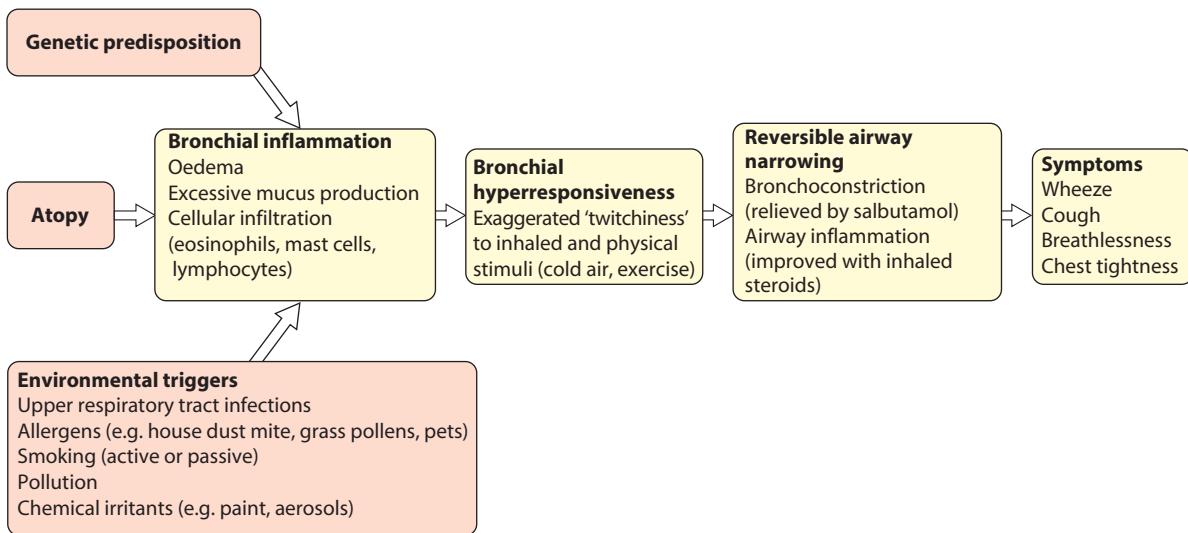


Figure 17.8 Pathophysiology of asthma.

Ideally, the presence of wheeze is confirmed on auscultation during an acute episode to distinguish it from transmitted upper respiratory noises, which are often loud and easy to hear in children. Asthmatic wheeze is a polyphonic (multiple pitch) noise as multiple airways of different sizes are affected. A chronic dry cough is common in children with asthma but is rarely the only symptom.

Key features associated with asthma in the history include:

- wheeze, cough and breathlessness worse at night and in the early morning
- wheeze and breathlessness with non-viral triggers
- interval symptoms, i.e. symptoms between acute exacerbations
- personal or family history of an atopic disease
- positive response to asthma therapy.

Once suspected, the pattern or phenotype should be further explored by asking:

- How frequent are the symptoms?
- What triggers the symptoms? Specifically, are sport and general activities affected by the asthma?
- How often is sleep disturbed by asthma?
- How severe are the interval symptoms between exacerbations?
- How much school has been missed due to asthma?

Examination of the chest is usually normal between attacks. In long-standing asthma there may be hyperinflation of the chest, and on auscultation a prolonged expiratory phase and generalized polyphonic (musical) expiratory wheeze. Onset of the disease in early childhood may result in Harrison sulci (Fig. 17.9). Evidence of atopy should be sought, by examination of the nasal mucosa for allergic rhinitis and the skin for eczema. Growth should be plotted, but is usually normal. The presence of a wet cough productive of sputum, finger clubbing or growth faltering suggests a condition characterized by chronic infection such as cystic fibrosis rather than asthma.

The preschool child

Diagnosing asthma in preschool children is often difficult. Approximately half of all children wheeze at some time

during the first 3 years of life. There are two main patterns of wheezing (Fig. 17.10):

- viral episodic wheezing
- multiple trigger wheeze.

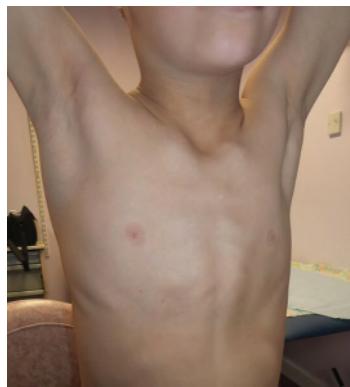


Figure 17.9 The depressions at the base of the thorax associated with the muscular insertion of the diaphragm are called Harrison sulci, and are associated with chronic obstructive airways disease such as asthma during childhood from chronic increased work of breathing.

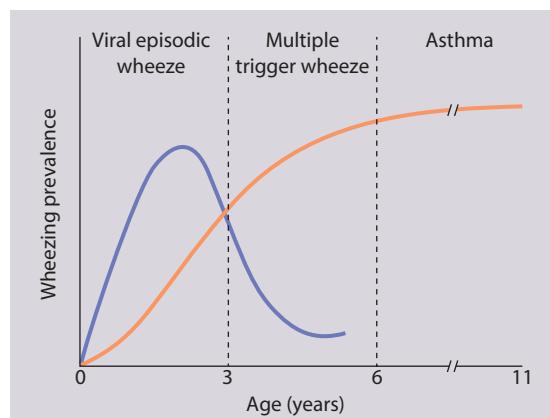


Figure 17.10 Prevalence of wheeze in children caused by the major phenotypes by age.

Viral episodic wheeze

Most wheezy preschool children have *viral episodic wheeze*, triggered by viral upper respiratory tract infections, with no interval symptoms between episodes. It is thought to result from an abnormal immune response to viral infection causing inflammation and obstruction of the small airways. Risk factors include maternal smoking during and/or after pregnancy, prematurity and male sex. A family history of asthma or allergy is not a risk factor, but a family history of early viral wheezing is common. It usually resolves by 5 years of age, presumably from increased airway size.

Multiple trigger wheeze and asthma

Multiple-trigger wheeze is used to describe wheezy episodes triggered by many stimuli which can include viral infections, cold air, dust, animal dander and exercise. A significant proportion have asthma. The presence of asthma risk factors increases the likelihood the child has asthma and will benefit from asthma treatment, e.g. salbutamol during acute events and inhaled steroids over longer periods. Risk factors are more than 3 episodes a year of cough and wheeze for more than 10 days with viral infections, cough and wheeze between episodes, laughing or excitement causing wheeze, allergic sensitization, eczema, food allergy or family history of asthma.

Investigations

In children less than 5 years old, the diagnosis of asthma is based on history, examination and response to treatment. Specific investigations such as skin prick testing to identify sensitization to inhaled allergens may help determine the precise phenotype and determine whether changes to the child's environment might improve symptoms. A chest X-ray is not necessary unless other conditions need to be excluded.

In children >5 years old, if diagnosis is uncertain, investigations may include:

- peak expiratory flow rate (PEFR) – measured with peak flow meters, which are simple to use, portable and useful for serial measurements (see Fig. 2.16 and Appendix Fig. A.5). The child should fully inhale before placing the mouthpiece between their teeth and sealing tightly with their lips. A sharp, fast exhalation will provide an estimate of the maximum rate of exhalation and this is achieved very early in exhalation (usually the first 0.2 seconds). Poorly controlled asthma leads to increased variability in peak flow rate, with both diurnal variability (morning usually lower than evening) and day-to-day variability.
- spirometry – a non-invasive measure of flow through the airways larger than the bronchioles (Fig. 17.11). It involves blowing out as hard and fast as possible for as long as possible. To generate reliable results children must be able to fully expire whilst completing each test. This provides a measurement of the volume expired in the first second (forced expiratory volume in 1 second – FEV₁) and the total volume of expired air (forced vital capacity – FVC). Asthma classically produces obstructive spirometry in which FEV₁ is reduced but FVC remains normal (resulting in a FEV₁:FVC ratio <80%). Children with mild to moderate asthma may have normal spirometry when well.

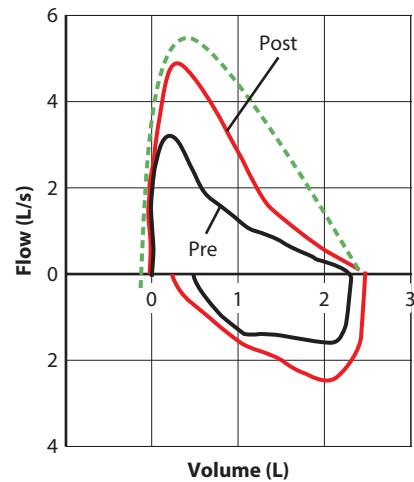


Figure 17.11 Typical spirometry results for a child with poorly controlled asthma before and after salbutamol. The pre-bronchodilator flow-volume loop (black) shows severe airway obstruction, with normal expiration shown in green. Following administration of salbutamol, there is an increase in flow, and a significant increase in the forced expiratory volume in 1 second (FEV₁) (red).

- bronchodilator reversibility – identified by showing an improvement before and after a dose of inhaled bronchodilator (by ≥20% in PEFR or ≥12% in FEV₁).
- exhaled nitric oxide concentration (FeNO, fractional exhaled nitric oxide) – if available, is a marker of airway inflammation, and is elevated in untreated asthma and allergic rhinitis. It is recommended by NICE as a helpful test in diagnosis of asthma in children if there is diagnostic uncertainty.

Differential diagnosis

A small number of children with persistent or recurrent wheeze will have other causes (Box 17.2).

Management of asthma

Medications used to treat children with asthma are shown in Table 17.2. A wider range of biological treatments are becoming available, but these are only required for a small proportion of asthmatic children.

Box 17.2 Causes of recurrent or persistent childhood wheeze

- Viral episodic wheeze
- Multiple trigger wheeze
- Asthma
- Recurrent anaphylaxis (e.g. in food allergy)
- Chronic aspiration
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Bronchiolitis obliterans
- Tracheo-bronchomalacia

Table 17.2 Drugs in asthma

Type of drug	Drug
Bronchodilators	
Short-acting β_2 -agonists (rescue inhalers)	Salbutamol Terbutaline
Long-acting β_2 -agonists (LABA)	Salmeterol Formoterol
Anticholinergic bronchodilator	Ipratropium bromide
Preventer therapy	
Inhaled steroids	Budesonide Beclometasone Fluticasone Mometasone
Methylxanthines	Theophylline
Leukotriene receptor antagonists (LTRA)	Montelukast
Oral steroids	Prednisolone
Anti-IgE monoclonal antibody	Omalizumab
Anti-IL5 monoclonal antibody	Mepolizumab

Bronchodilator therapy

Inhaled β_2 -agonists are the most commonly used and most effective bronchodilators. *Short-acting β_2 -agonists* (SABAs – often called *rescue inhalers*) such as salbutamol or terbutaline have a rapid onset of action (maximum effects after 10–15 min), are effective for 2–4 hours and have few side-effects.

They are used ‘as required’ for increased symptoms and in high doses for acute asthma attacks. Use of a SABA more than 2 times per week should prompt the need to start preventer therapy. Some international guidelines now recommend that these should not be used alone to treat asthma.

By contrast, *long-acting β_2 -agonists* (LABAs) such as salmeterol or formoterol are effective for 12 hours. They are not used in acute asthma and should not be used without an inhaled corticosteroid (use as a single treatment is associated with increased mortality). LABAs are useful in exercise-induced asthma.

Ipratropium bromide, an anticholinergic bronchodilator, is sometimes given to young infants when other broncho-dilators are found to be ineffective or in the treatment of severe acute asthma.

Preventer therapy

Inhaled corticosteroids (ICS)

Prophylactic drugs are effective only if taken regularly. *Inhaled corticosteroids* (often called *preventers*) are the most effective inhaled prophylactic therapy. They decrease airway inflammation, resulting in decreased symptoms, asthma exacerbations and bronchial hyperactivity. They have no clinically significant side-effects when given in low dose, although they can cause mild reduction in height velocity, but this is usually followed by catch-up growth in late childhood. Systemic side-effects, including impaired growth, adrenal suppression and altered bone metabolism may occur when high doses are used.

To reduce the risk of side-effects, treatment with inhaled corticosteroids should always be at the lowest dose possible. Treatment for many children is effective at very low doses.



Always monitor the growth of children with asthma, especially if taking regular inhaled or oral corticosteroids.

Add-on therapy

The first choice of add-on therapy in a child over 5 years is a LABA, whereas in children under 5 years, an oral *leukotriene receptor antagonist* such as montelukast is recommended. The latter can also be used in older children when symptoms are not controlled by the addition of a LABA. *Slow-release oral theophylline* is an alternative; however, its use is limited in children by the high incidence of side-effects (vomiting, insomnia, headaches, poor concentration). Antibiotics are of no value in the absence of a bacterial infection and neither cough medicines nor decongestants are beneficial. Antihistamines, e.g. loratadine and nasal steroids are useful in the treatment of allergic rhinitis.

MART therapy

There has been a recent move towards the use of combined ICS and LABA inhalers as maintenance and reliever therapy (MART). Most regimens require a small regular dose of ICS/LABA to be given with scope for increasing the daily dose up to four-fold if required. There is little evidence that this approach is effective in children and young people, and the potential benefits are extrapolated from adult studies and observational data.

Additional therapies for children and young people with severe asthma

Oral *prednisolone*, usually given on alternate days to minimize the adverse effect on growth, is required only in severe persistent asthma where other treatments have failed. Injectable monoclonal antibodies that act against IgE (omalizumab) and interleukin 5 (IL-5) (mepolizumab) are also available for selected children with severe asthma. IgE is the natural antibody that mediates allergy and IL-5 is a cytokine that mediates eosinophil activation. Children requiring these treatments should be managed by a specialist paediatric asthma service.

Escalating and de-escalating treatment

The British Guideline on Asthma Management uses a stepwise approach, starting treatment with the step most appropriate to the severity of the asthma and aiming for optimal control of symptoms. Complete control is defined as the absence of daytime or night-time symptoms, no limit on activities (including exercise), no need for reliever use, normal lung function, and no exacerbations (need for hospitalization or oral steroids) in the previous 6 months. Once a diagnosis has been established all children should be on a regular preventer. Treatment is stepped up when asthma control is poor and stepped down when control is good. For children 12 years and younger the current guideline is summarized in **Figure 17.12**. Older children should follow adult protocols and guidance which typically use higher doses of ICS and a greater range of biologics.

Treatment of asthma in children

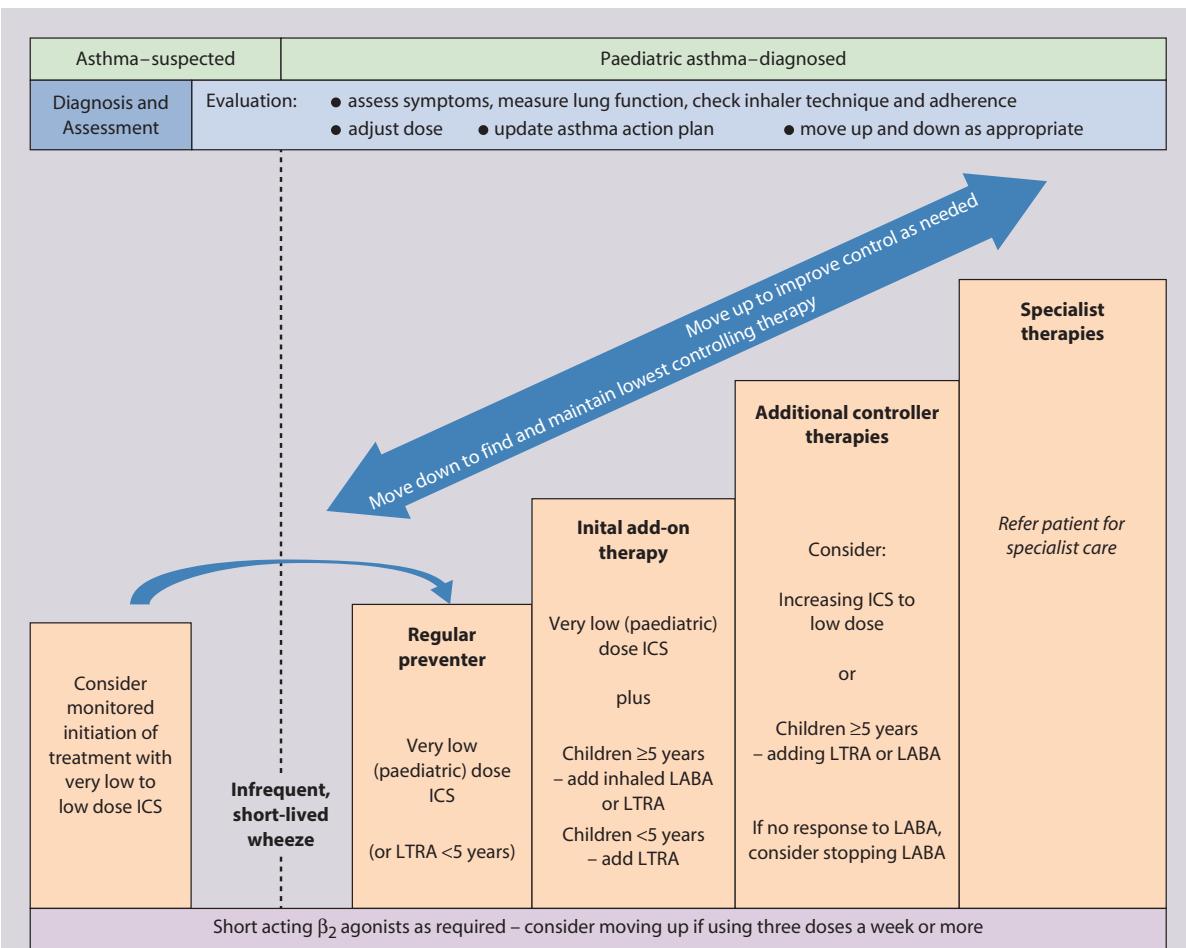


Figure 17.12 A stepwise approach to the treatment of asthma in children 0–12 years. Very low dose ICS include doses up to 200 mcg and low doses are up to 400 mcg of beclomethasone dipropionate (CFC-MDI) equivalent per day. ICS, inhaled corticosteroid; LTRA, leukotriene receptor antagonist; LABA, long-acting β_2 -agonist. (From: Scottish Intercollegiate Guideline Network (SIGN), British guideline on the management of asthma, Edinburgh, 2019, SIGN publication 158. Available at: <http://www.sign.ac.uk>. By kind permission of the Scottish Intercollegiate Guidelines Network.)

Allergen avoidance and other nonpharmacological measures

In children who have allergy to house dust mite, the use of dust-mite-impermeable bedding may reduce exacerbations of asthma requiring hospitalization. Allergen immunotherapy is effective for treating atopic asthma due to a single allergen, but its use is limited by the risk of systemic allergic reactions associated with the treatment (see Ch. 16, Allergy). Parents should be advised about the harmful effects of inhaling second-hand cigarette smoke and e-cigarette vapour.

Acute asthma

Assessment

With each acute attack, duration of symptoms, treatment already given, and the course of previous attacks should be noted. The severity of an attack needs to be classified as:

- mild
- moderate

- severe
- life-threatening.

The clinical features which determine this are shown in Figure 17.13.

Criteria for admission to hospital

Children require hospital admission if, after high-dose inhaled bronchodilator therapy, they:

- have not responded adequately clinically, i.e. there is persisting breathlessness or tachypnoea
- are becoming exhausted
- still have a marked reduction in their predicted (or usual best) peak flow rate or FEV₁ (<50%)
- have a reduced oxygen saturation (<92% in air).

A chest X-ray is indicated only if there are unusual features (e.g. asymmetry of chest signs suggesting pneumothorax, lobar collapse) or signs of severe infection. In children, blood gases are only indicated in life-threatening or refractory cases and are often normal until the child is *in extremis*.

Determining severity of acute asthma

Determine the severity of the attack (see Fig. 17.14):

- Mild
- Moderate
- Severe
- Life-threatening

This is determined by clinical features shown.

Too breathless to talk – severe

Increased work of breathing
Check respiratory rate:

- Tachypnoea – varies with age; poor guide to severity

Chest recession:

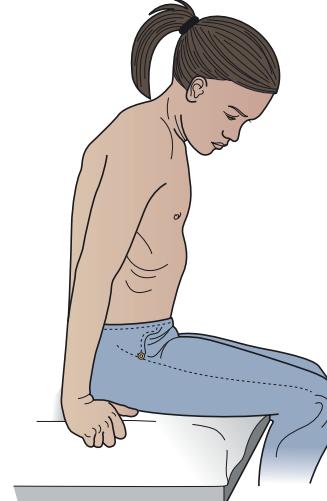
- Moderate – some intercostal recession
- Severe – use of accessory neck muscles
- Life-threatening – poor respiratory effort

Auscultation:

- Wheeze
- Silent chest – poor air entry from poor expiratory effort or exhaustion in life-threatening

Cardiovascular:

- Tachycardia – varies with age; better guide to severity than respiratory rate but affected by β_2 -agonists
- Arrhythmia, hypotension – life-threatening



**Altered consciousness, agitation or confusion – in life-threatening
Exhaustion – life-threatening**

Tongue:

- Cyanosis in life-threatening

Peak flow (% predicted or best or usual measurement):

- Moderate >50%
- Severe 33–50%
- Life-threatening <33%

O₂ saturation:

- Moderate $\geq 92\%$
- Severe or life-threatening <92%

Is there a trigger for the attack?:

- URTI or other viral illness
- Allergen, e.g. animal dander
- Exercise
- Cold air

Causes of acute breathlessness in the older child:

- Asthma
- Pneumonia or lower respiratory tract infection
- Foreign body
- Anaphylaxis
- Pneumothorax or pleural effusion
- Metabolic acidosis – diabetic ketoacidosis, inborn error of metabolism, lactic acidosis
- Severe anaemia
- Heart failure
- Panic attacks (hyperventilation).

Figure 17.13 Assessment of the child or young person with acute asthma to determine severity of the attack.

Management

Acute breathlessness is frightening for both the child and the parents. Calm and skillful management is the key to their reassurance. Oxygen, inhaled bronchodilators and steroids form the foundation of acute asthma treatment.

Management is summarized in Figure 17.14. As soon as the diagnosis has been made, if the oxygen saturation is $<92\%$, oxygen therapy should be given. All children should be given a β_2 -bronchodilator; the dose and frequency is varied according to severity of the attack, the child's age and response to therapy. It should be given with a meter dosed inhaler and spacer unless the attack is severe to life-threatening, when a nebulizer driven by high-flow oxygen may be indicated. The addition of nebulized ipratropium and/or nebulized magnesium to the initial therapy in severe asthma is probably beneficial. A short course (3–5 days) of oral prednisolone expedites recovery in moderate or severe acute asthma.

Inhaled therapies may not be delivered in therapeutic concentrations to severely affected areas of the lung that are under-ventilated, so intravenous therapy has a role in the few children who fail to respond adequately to inhaled bronchodilator therapy. Magnesium sulphate, salbutamol and aminophylline are all potentially

beneficial. Magnesium sulphate is usually the first-line intravenous agent, but can cause profound hypotension. For both intravenous salbutamol and aminophylline, a loading dose is given over 20 minutes, followed by continuous infusion during which ECG and blood electrolytes should be monitored. If the child is already on oral theophylline, the loading dose of aminophylline should be omitted. Nausea and vomiting are common with aminophylline. Intravenous salbutamol can cause tachycardia and lactic acidosis. Antibiotics are only given if there are clinical features of bacterial infection. Occasionally, these measures are insufficient and mechanical ventilation is required.

Patient education

Prior to discharge from hospital after an acute admission, the following should be reviewed with the child and family:

- When drugs should be used (regularly or 'as required').
- How to use the drug (inhaler technique) (see Figs. 17.15–17.17).
- What each drug does (relief vs prevention).

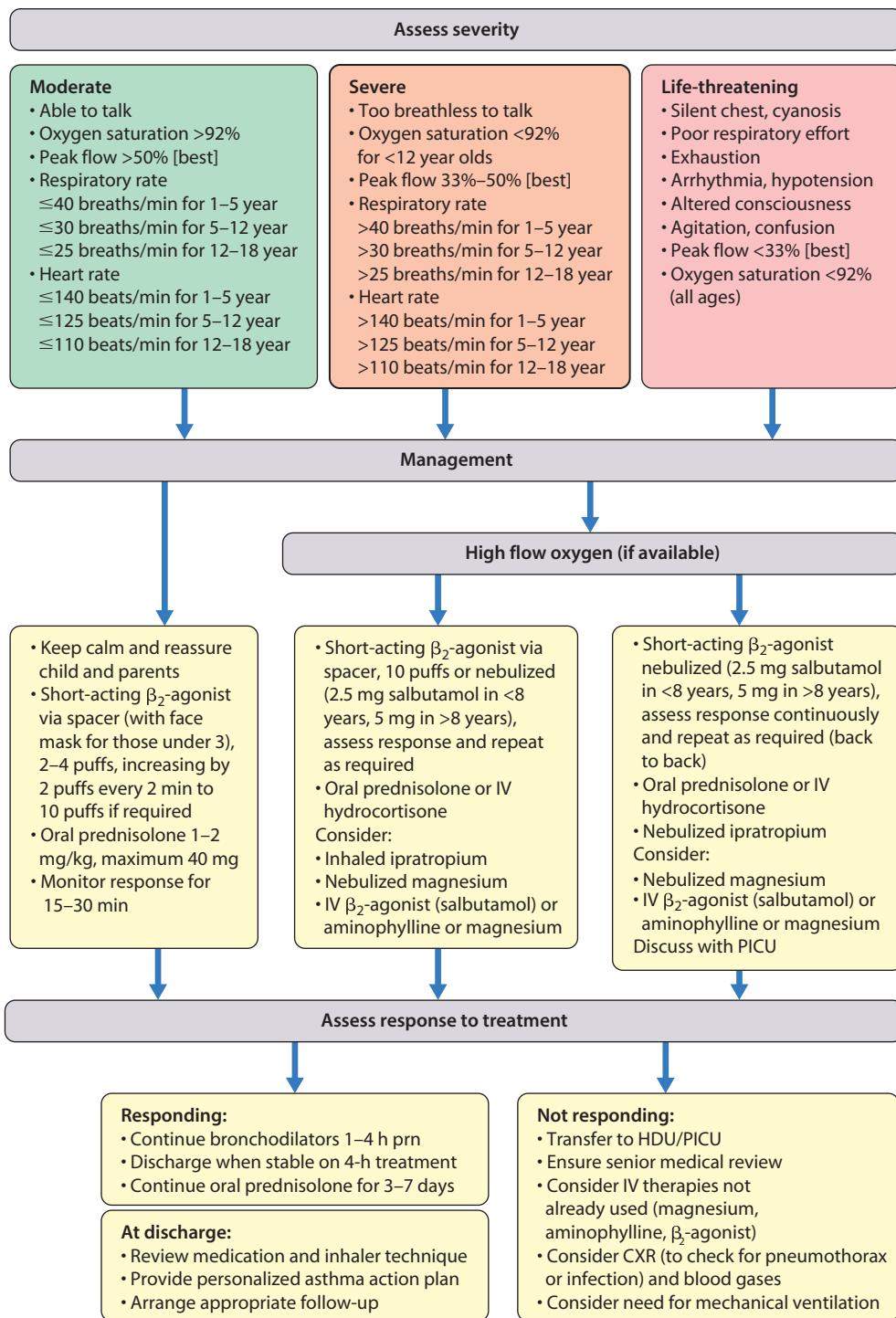


Figure 17.14 Management of acute asthma. (Adapted and modified from: The Scottish Intercollegiate Guideline Network/British Thoracic Society, July 2019.)

- How often and how much can be used (frequency and dosage).
- What to do if asthma worsens (a written personalized asthma action plan should be completed: see Appendix Fig. A.4 for an example).

The child and parents need to be aware that increasing symptoms (cough, wheeze and breathlessness), reduced ability to participate in activities and increased use of bronchodilators all indicate poorly controlled asthma. Some asthmatics find it difficult to identify gradual

deterioration – measurement of peak flow rate at home helps with this. Children and young people with difficult asthma may be given an emergency supply of oral steroids to keep at home and use for acute exacerbations as detailed in their asthma action plan.

Outcomes are better for children with asthma who have a package of educational measures, but no single component has been shown to be beneficial in isolation. Periodic assessment and review by a healthcare professional is required and is outlined in Figure 17.18. For children who are old enough to perform lung function testing this should include spirometry.

Choosing the correct inhaler

Inhaled drugs may be administered via a variety of devices, chosen according to the child's age and preference.

- *Pressurized metered dose inhaler and spacer* (Fig. 17.15).
 - Appropriate for all age groups – 0–2 years, spacer with face mask; ≥3 years, spacer with mouthpiece.
 - A spacer is recommended for all children as it increases drug deposition to the lungs and reduces oropharyngeal deposition and therefore systemic side-effects.
 - Useful for acute asthma attacks when poor inspiratory effort may impair the use of inhalers direct to the mouth.
- *Breath-actuated metered dose inhalers* (e.g. *Autohaler, Easi-Breathe*) – from 6 years. Less coordination needed than a pressurized metered dose inhaler without spacer. Useful for delivering β_2 -agonists when 'out and about' in older children.
- *Dry powder inhaler* – from 4 years (Fig. 17.16). Needs a good inspiratory flow, therefore less good in severe asthma and during an asthma attack. Also easy to use when 'out and about' in older children.
- *Nebulizer* – any age (Fig. 17.17). A far less efficient method of drug delivery than metered-dose inhalers (MDI) plus spacer due to variation in droplet size. Should always be administered using high-flow oxygen not air. Only used in acute asthma where oxygen is needed.



Figure 17.15 Pressurized metered dose inhaler and spacer. Suitable for all ages, with face mask if under 2 years of age.

Many children fail to respond to treatment because their inhaler is not appropriate for their age or they have poor inhaler technique. Inhaler technique should be taught and then assessed at every review.



Figure 17.16 Dry powder inhaler, 4 years and older.



Figure 17.17 Nebulizer: all ages. Only used in acute asthma where oxygen is needed in addition to inhaled drugs.

Cough

The cough reflex functions to expel unwanted material, including mucus, from the airway below the glottis. In most children, episodes of cough are due to tracheobronchial spread of URTIs caused by viruses and do not indicate the presence of long-term or serious underlying respiratory disease. In about half of children with acute cough, the symptoms will settle by 10 days, but in up to

10% it will persist for up to 4 weeks. Coughing following any respiratory tract illness tends to persist for longer if there is ongoing exposure to environmental cigarette smoke as this impairs ciliary function. The significance of parental smoking on children is often underestimated. If both parents smoke, young children are twice as likely to have recurrent cough and wheeze than in non-smoking households. In the older child, active smoking is an important factor. A cough lasting more than 8 weeks is considered chronic.

Periodic assessment of the child or young person with asthma

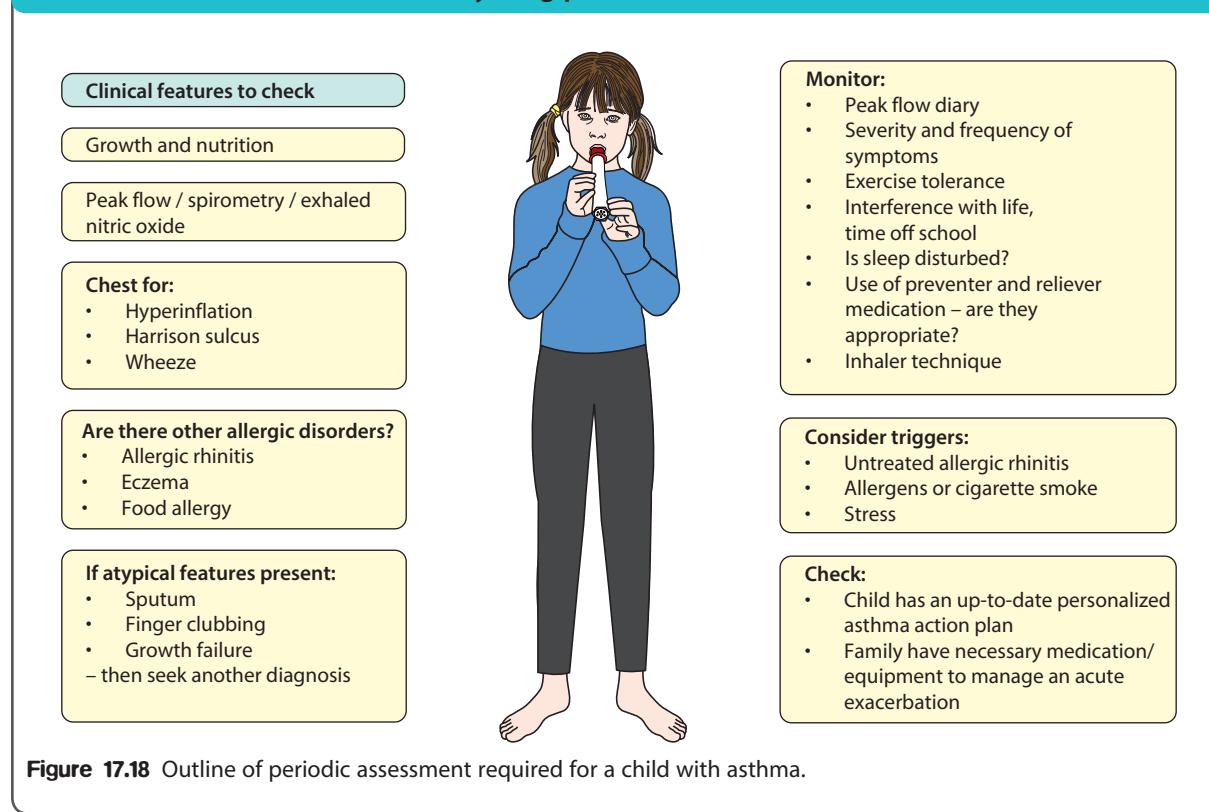


Figure 17.18 Outline of periodic assessment required for a child with asthma.

Chronic cough

The causes are listed in **Box 17.3**. By far the commonest reason for this is that the child has had a series of respiratory tract infections in rapid succession. This often happens when a child enters school or nursery for the first time and is much more common if there are older siblings. However, some infections, such as pertussis and RSV and *Mycoplasma*, can cause a cough that persists for weeks or months but eventually remits spontaneously. These coughs are typically *dry*. Chronic wet cough (i.e. sounding like there is excess sputum in the airways) or a productive cough after an acute infection may indicate unresolved lobar changes following pneumonia, persistent bacterial bronchitis (see the following section), or suppurative lung disease.



If the cough is ‘wet’ (i.e. sounding like there is excess sputum in the airways) or if the cough is productive, further investigation is required. Children rarely expectorate and therefore sputum is not commonly seen.

Protracted bacterial bronchitis (PBB)

PBB is the leading cause of chronic wet cough in young children (<8 years) in high-income countries. It is caused by bacterial infection of the conducting airways (the trachea, bronchi and bronchioles), in contrast to pneumonia which is caused by infection in the airspaces. Affected children are otherwise well, but often miss school and have disturbed sleep. Causative organisms

Box 17.3 Causes of chronic or recurrent cough

- Recurrent respiratory infections
- Persistent bacterial bronchitis (will be persistently wet)
- Following specific respiratory infections (e.g. pertussis, respiratory syncytial virus, *Mycoplasma*)
- Asthma (only if accompanied by wheezing)
- Persistent lobar collapse following pneumonia
- Suppurative lung diseases (e.g. cystic fibrosis, ciliary dyskinesia or immune deficiency)
- Recurrent aspiration (\pm gastro-oesophageal reflux)
- Inhaled foreign body
- Cigarette smoking (active or passive)
- Tuberculosis
- Habit cough
- Airway anomalies (e.g. tracheo-bronchomalacia, tracheo-oesophageal fistula)

include *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Staphylococcus aureus*. PBB is a clinical diagnosis based on chronic wet cough, the absence of symptoms or signs suggesting another cause such as bronchiectasis and resolution of cough following antibiotic treatment. Although improvement with treatment is part of the diagnostic criteria, relapse of cough is common. Frequent relapse (recurrent PBB) is associated with a subsequent diagnosis of bronchiectasis.

Less common causes of chronic cough

Aspiration of feeds can cause cough, wheeze and recurrent lower respiratory tract infections. It can occur during or after feeding due to gastro-oesophageal reflux disease or swallowing disorders. Aspiration is more common in children with cerebral palsy. Rarely it is due to an anatomical anomaly, e.g. H-type tracheo-oesophageal fistula.

Inhaled foreign body needs to be considered in any cough with acute onset respiratory symptoms, unilateral respiratory signs or a chronic cough with a persistent radiological abnormality. It occurs most commonly in children aged 6 months to 3 years. The aspirated material is most often food, but can be bits off toys, or coins. A history of choking is present in >80%, but only when specifically asked about. Radio-opaque foreign bodies can be readily identified on plain chest X-ray (Fig. 17.19). A radiolucent foreign body such as a peanut is more difficult to diagnose (see Case history 17.2). Removal is using a rigid-bronchoscope.

In any child with a severe, persistent cough, tuberculosis should be considered (see Ch. 15).

Bronchiectasis

Bronchiectasis is irreversible dilatation of the bronchial tree, which can be confirmed on a CT scan. In practice, it is diagnosed by the presence of clinical features of chronic suppurative lung disease, namely recurrent episodes of chronic wet cough, coarse crackles on auscultation and

finger clubbing. It is confirmed by radiological demonstration of bronchial dilatation (Fig. 17.21a,b). The early stages of bronchiectasis may be indistinguishable from PBB. There is evidence that mild bronchiectasis can be reversible if appropriately treated, with suitable antibiotics or the causative factor, e.g. foreign body is removed.

Generalized bronchiectasis may be due to cystic fibrosis, primary ciliary dyskinesia, immunodeficiency, or

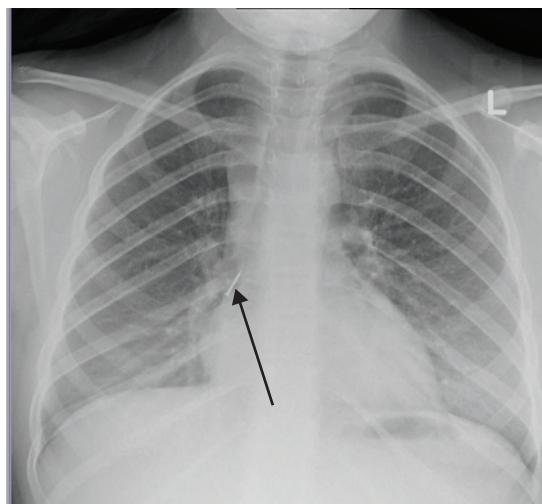


Figure 17.19 Chest X-ray showing a pin (arrow) in the right main bronchus.

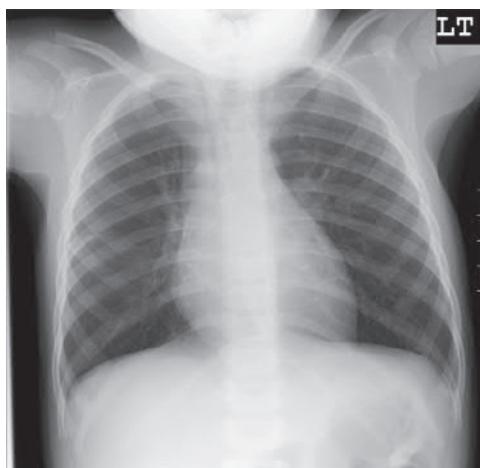


Case history 17.2

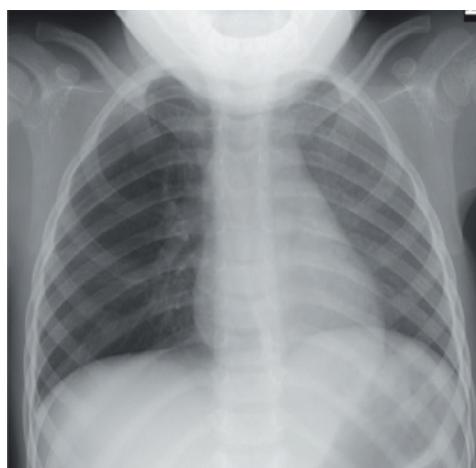
Foreign body inhalation

A previously well 3-year-old boy choked on some peanuts. His mother took him to the emergency department where a chest X-ray was done, which was normal. She returned as he developed a severe cough and wheeze over the next 5 days. As peanuts are radiolucent, an inspiratory (normal view) and expiratory film need to be requested as a foreign

body typically acts as a 'ball-valve' and there is under-expansion during inspiration but over-expansion during expiration. An expiratory chest X-ray revealed a hyperlucent right lung and mediastinal shift (Fig. 17.20a,b). Bronchoscopy was performed and revealed a peanut wedged in the right main bronchus.



(a)



(b)

Figure 17.20 Peanut inhalation, with peanut in right main bronchus acting as a ball valve, so inspiratory film (a) is normal whereas expiratory film (b) shows hyperlucency of right lung and mediastinal shift.

chronic aspiration. Focal bronchiectasis is due to previous severe pneumonia, congenital lung abnormality, or obstruction by a foreign body. Treatment is based on optimizing airway clearance as well as the prevention and treatment of lower airways infections.



(a)



(b)

Figure 17.21 Bronchiectasis on CT scan of the chest. (a) Generalized, with enlargement of the bronchi throughout the left and right lung fields and (b) focal, with changes in the right upper lobe.

Cystic fibrosis (CF)

CF is the commonest life-limiting inherited condition in Caucasians. It has an incidence of 1 in 2500 live births and carrier rate of 1 in 25. It is less common in other ethnic groups. Average life expectancy has increased from a few years to the late thirties, with a projected life expectancy for current newborns into the fifties.

The fundamental problem in CF is a defective protein called the CF transmembrane conductance regulator (CFTR). This is a cyclic AMP-dependent chloride channel found in the membrane of cells. The gene for CFTR is located on chromosome 7. Nearly 2000 different gene mutations have been discovered causing a number of distinct defects in CFTR, but by far the most frequent mutation (about 78%) in the UK is Phe508Del. Some genotypes are known to be associated with milder disease and pancreatic sufficiency. CFTR mutations can be grouped into six classes based on the way the CFTR protein is affected (Fig. 17.22).

Pathophysiology

CF is a multisystem disorder, which results from abnormal ion transport across epithelial cells. In the airways this leads to a reduction in the airway surface liquid layer causing impaired ciliary function and retention of thick, mucopurulent secretions which are prone to infection. Defective CFTR also causes dysregulation of inflammation and defence against infection. In the intestine, thick viscid meconium leads to meconium ileus in 10%–20% of infants. The pancreatic ducts also become blocked with thick secretions, causing pancreatic enzyme deficiency and malabsorption. Abnormal function of the sweat glands results in excessive concentrations of sodium and chloride in the sweat.

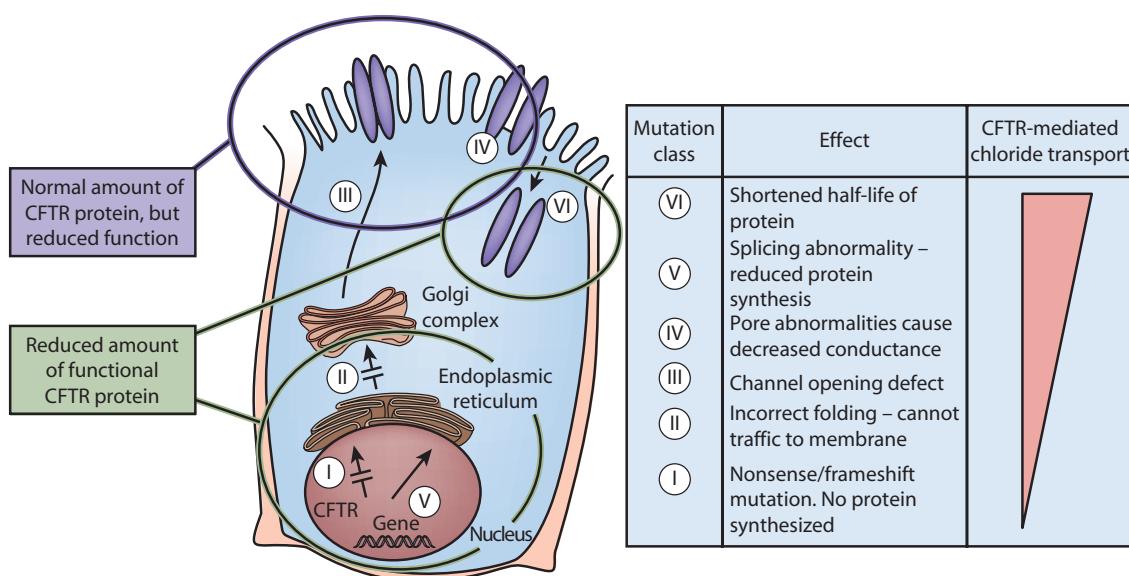


Figure 17.22 Effect of different classes of mutations on the function of the CFTR protein. Phe508del is a class II mutation. G551D is a class III mutation. Newer therapies are targeting specific classes of mutation and are potentially a major advance in treatment.

Newborn screening

All UK infants are screened for CF as part of the newborn screening programme. If the blood spot sample has elevated immunoreactive trypsinogen (IRT), it is tested for the common CFTR mutations. A second blood spot is obtained if IRT is elevated but only one or no mutations are detected. Infants considered to be at significant risk of the disease are referred to a specialist centre for a sweat test. Screening reduces diagnostic delay and lowers the risk of developing established lung disease or faltering growth.

Diagnosis

The gold standard diagnostic procedure is a sweat test. Sweating is stimulated by applying a low-voltage current to pilocarpine applied to the skin. The sweat is collected into a special capillary tube or absorbed onto a weighed piece of filter paper. A raised sweat chloride concentration ($>60\text{ mmol/L}$) confirms the diagnosis. Diagnostic errors are common if there is an inadequate volume of sweat collected. Confirmation of diagnosis can be made by testing for CFTR mutations.

Clinical features

Respiratory

In the UK, nearly all children with CF are now identified by newborn blood spot screening. In a handful of cases it is with recurrent chest infections, faltering growth, or malabsorption (Box 17.4). CF lung disease is characterized by a vicious circle of infection, inflammation and lung damage. Early bacterial pathogens include *Staphylococcus aureus* and *Haemophilus influenzae*. Subsequent pathogens include *Pseudomonas aeruginosa* and *Burkholderia cepacia* complex. These infections can be eradicated if treated early; if not the infection can become chronic, which is associated with lung damage and bronchiectasis (Fig. 17.23). Severe CF lung disease causes a persistent, 'wet' cough, productive of purulent sputum. It can also cause haemoptysis and pneumothorax. On examination there is chest hyperinflation due to air trapping, coarse inspiratory crepitations, and/or expiratory wheeze and finger clubbing. Historically, 95% of individuals with CF died from respiratory failure. However, new treatments (CFTR modulators) appear to markedly improve outcomes for some patients.

About 15% of older children and adolescents with CF develop asthma-type symptoms and obstructive patterns on spirometry due to allergic sensitization and exposure to *Aspergillus fumigatus*, a ubiquitous environmental fungus. This can result in patchy chest X-ray changes, acute respiratory symptoms, e.g. chest tightness, breathlessness and a reduction in lung function. A diagnosis of allergic broncho-pulmonary aspergillosis (ABPA) is confirmed if there are elevated and rising specific IgE antibodies to *Aspergillus* in the presence of clinical features. Treatment is with oral steroids and antifungal agents, e.g. itraconazole.

Gastrointestinal

Over 90% of children with CF have pancreatic exocrine insufficiency (lipase, amylase, and proteases), resulting in maldigestion and malabsorption. Untreated, this

Box 17.4 Clinical features of cystic fibrosis

Newborn

- Diagnosed through newborn screening
- Meconium ileus

Infancy

- Prolonged neonatal jaundice
- Growth faltering
- Recurrent chest infections
- Malabsorption, steatorrhoea

Young child

- Bronchiectasis
- Rectal prolapse
- Nasal polyp
- Sinusitis

Older child and adolescent

- Allergic bronchopulmonary aspergillosis
- Diabetes mellitus
- Cirrhosis and portal hypertension
- Distal intestinal obstruction (meconium ileus equivalent)
- Pneumothorax or recurrent haemoptysis
- Infertility in males

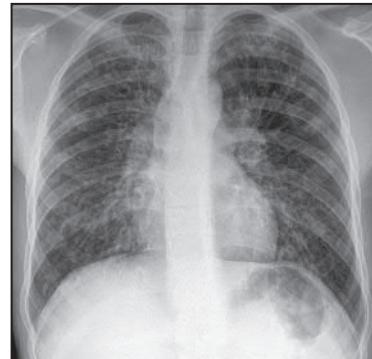


Figure 17.23 A chest X-ray in cystic fibrosis showing hyperinflation, marked peribronchial shadowing, bronchial wall thickening and ring shadows.

leads to faltering growth with frequent large, pale, and greasy stools (steatorrhoea). Pancreatic insufficiency can be diagnosed by demonstrating low faecal elastase. Thick inspissated bowel contents can cause bowel obstruction with vomiting, abdominal distension, and failure to open bowels. In neonates this is called meconium ileus and frequently requires surgery. In older children it is called distal intestinal obstruction syndrome and can usually be managed medically with laxatives such as oral Gastrograffin.

Other complications

The incidence of CF-related diabetes (CFRD) increases with age due to decreasing pancreatic endocrine function. All children are screened annually from the age of 10 years with a glucose tolerance test or a continuous glucose monitoring system (CGMS). CFRD is different from

type 1 and type 2 diabetes but has features of both. It does not present with diabetic ketoacidosis (DKA); instead it causes a gradual reduction in lung function or failure to gain weight which can be difficult to identify. It is treated with insulin.

Up to one-third of adolescent patients have evidence of liver disease, with hepatomegaly on liver palpation, abnormal liver function on blood tests, or an abnormal ultrasound. Only 5%–10% require treatment. Regular ursodeoxycholic acid improves bile flow. Rarely, the liver disease progresses to cirrhosis, portal hypertension, and ultimately liver failure. Liver transplantation is generally successful in CF-related liver failure.

Males are virtually always infertile due to absence of the vas deferens, although they can father children through intracytoplasmic sperm injection. Some females with CF have reduced fertility due to increased viscosity of cervical mucus and poor nutritional status. Pregnancy can also cause significant deterioration in lung function. Many, however, tolerate pregnancy well.

Management

Effective CF management requires a multidisciplinary team (MDT) approach. Patients should be reviewed every 2–3 months and be seen by the MDT from a specialist CF centre at least annually (Fig. 17.24). The aim of management is to prevent progression of the lung disease (monitored using spirometry) and to maintain adequate nutrition and growth. Psychologists play a particularly important role in the overall delivery of care. The psychological repercussions of CF and the associated treatment burden on affected children and their families is considerable.

Respiratory management

The key aspects of CF respiratory management are airway clearance and the aggressive treatment of lower respiratory infection. From diagnosis, children should have twice daily chest physiotherapy to clear airways

Periodic review of the child or young person with cystic fibrosis

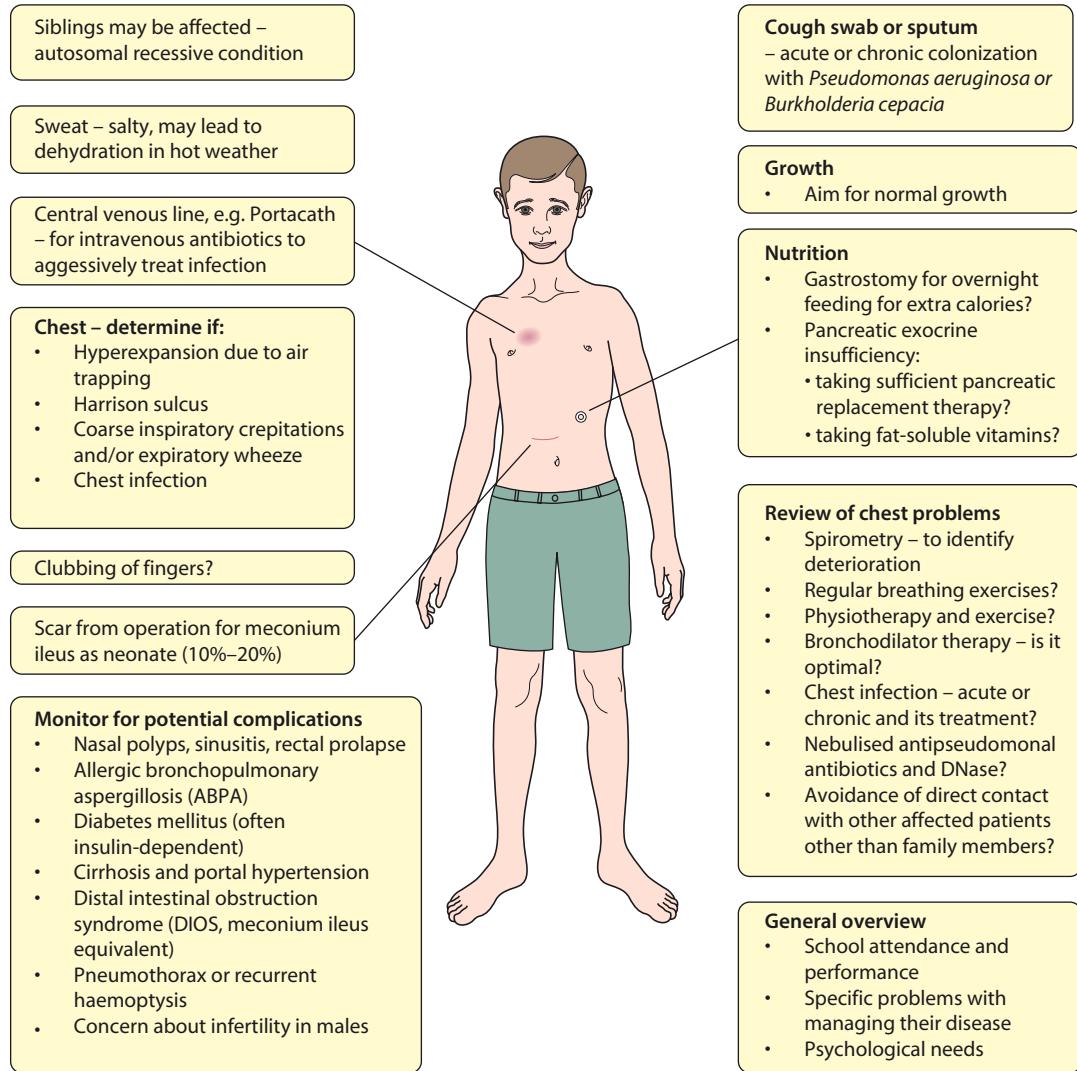


Figure 17.24 Periodic review of the child or adolescent with cystic fibrosis.

secretions. In younger children, parents are taught to perform percussion and postural drainage. Older patients perform controlled deep breathing exercises and use a variety of physiotherapy devices. Physical exercise is beneficial and should be encouraged. Nebulized mucolytics such as DNase and hypertonic saline decrease the viscosity of secretions and the number of infective exacerbations. Infective exacerbations are treated with oral or intravenous antibiotics depending on how unwell the child is. Intravenous antibiotics are usually given for 10–14 days via a peripheral long line and courses may be completed at home. Children requiring frequent courses of IV antibiotics may benefit from insertion of an implantable venous access device (Portacath). Respiratory microbiology samples (sputum or cough swabs) are obtained at every clinic to monitor for infection. In the UK, young children receive prophylactic oral flucloxacillin to prevent *Staphylococcus aureus* infection. New isolates of *Pseudomonas aeruginosa* should be eradicated using antibiotics (nebulized and/or oral and/or IV), which are successful in 80% of cases. If the infection becomes chronic, daily nebulized anti-pseudomonal antibiotics reduce symptoms and lung function decline. Due to the risk of cross-infection, outpatient clinics must be segregated according to cultured organisms and contact between CF patients is avoided.

Bilateral lung transplantation is the only therapeutic option for end-stage CF lung disease, but this is infrequently needed in children. Survival at 5 years is <50%. Meticulous assessment and expert post-transplant care are essential.

Nutritional management

Dietary status should be assessed regularly. Pancreatic insufficiency is treated with oral enteric-coated pancreatic replacement therapy taken with all meals and snacks containing fat. Dosage is adjusted according to fat content and clinical response. In most children with CF, a normal healthy diet is encouraged. In some with more advanced disease, additional calories are required. This can often be achieved with nutritional supplements, but in some, overnight feeding via a gastrostomy is used. Children who are pancreatic insufficient also require fat-soluble vitamin (A, D, E and K) supplements.

CFTR modulators

There are three broad classes of drugs that can alter the functional expression of CFTR: potentiators, correctors and amplifiers.

CFTR potentiators (such as ivacaftor) enable CFTR protein at the cell surface to function more effectively as a chloride channel. In patients with a class III mutation (such as G551D), they reduce sweat chloride to near normal levels and increase lung function and weight.

CFTR correctors (such as lumacaftor, tezacaftor and elexacaftor) help the CFTR protein to fold correctly and get to the cell surface. When used in combination with the potentiator ivacaftor they show promising results in individuals with the common Phe508del genetic mutation, although they are not as beneficial as ivacaftor in patients with class III mutations.

Recent studies using a combination of two correctors, and a potentiator (triple therapy) have shown exciting results in older children and young people homozygous

and heterozygous for Phe508del. Many find that they feel better, with increased appetite, weight gain and in some cases improved lung function. The availability of these treatments varies by country, and not all combinations of genetic mutations are suitable for treatment. Despite early hopes, gene therapy has not yet proven to be a useful treatment in CF.

Summary

Cystic fibrosis

- Is the commonest inherited life-limiting condition affecting Caucasians.
- Is a multi-system disorder affecting the lungs, pancreas, liver and gastrointestinal tract.
- Treatment aims to prevent progressive respiratory failure due to repeated cycles of infection and maintain adequate growth and nutrition.
- New treatments with CFTR modulators appear to improve the outlook for some individuals.

 Cystic fibrosis should be considered in any child with recurrent infections, loose stools or faltering growth.

Primary ciliary dyskinesia (PCD)

This is usually an autosomal recessive condition. It results in abnormal structure or function of cilia lining the respiratory tract. This leads to impaired mucociliary clearance. Affected children have recurrent infection of the upper and lower respiratory tracts, which, if untreated, may lead to bronchiectasis. They characteristically have a recurrent productive cough, purulent nasal discharge, and chronic ear infections.

During embryonic development, the action of the cilia allows lateralization to occur. This is crucial to determine which side organs develop, e.g. the heart on the left, the liver on the right. Thus ciliary action is responsible for normal organ situs, and almost 50% of individuals with PCD have Kartagener syndrome with dextrocardia and situs inversus (major organs are in the mirror position of normal).

The diagnosis of PCD is made by examination of the structure and function of the cilia of nasal epithelial cells brushed from the nose in combination with genetic testing. Nasal nitric oxide is almost always low and can be used as a screening test prior to cilia studies. Treatment is as for other causes of bronchiectasis.

Immunodeficiency

Children with immunodeficiency may develop severe, unusual, or recurrent chest infections. The immune deficiency may be secondary to an illness, e.g. malignant disease or treatment such as corticosteroids or chemotherapy. Less commonly, it is due to HIV infection or a primary immune deficiency. Different types of immune deficiency predispose to different lung infections: IgG deficiency predisposes to infections with polysaccharide-capsulated bacteria such as

S. pneumoniae; cell-mediated immunodeficiencies make one susceptible to opportunistic infections such as *Pneumocystis jirovecii* and fungi, and neutrophil-killing defects predispose to staphylococcal infection (see Ch. 15).

Sleep-disordered breathing

During REM (rapid eye movement) sleep, the control of breathing becomes unstable and there is relaxation of voluntary muscles in the upper airway and chest. This makes upper airway collapse more likely.

Sleep-disordered breathing occurs either due to airway obstruction, central hypoventilation, or a combination of both. Key aspects include loud snoring, witnessed pauses in breathing (apnoeas), restlessness, and disturbed sleep. However, symptoms alone are neither a sensitive nor specific marker of actual difficulties. Up to 12% of pre-pubescent school children snore, but true estimates of the prevalence of obstructive sleep apnoea resulting in gas-exchange abnormalities range from 0.7%–3%.

Obstructive sleep apnoea leads to excessive daytime sleepiness or hyperactivity, learning and behaviour problems, faltering growth and, in severe cases, pulmonary hypertension. In childhood, it is usually due to upper airway obstruction secondary to adenotonsillar hypertrophy. Predisposing causes of sleep-disordered breathing are neuromuscular disease (e.g. Duchenne muscular dystrophy), craniofacial abnormalities (e.g. Pierre Robin sequence), dystonia of upper airway muscles (e.g. cerebral palsy), and severe obesity. Children with Down syndrome have anatomical upper airway restriction as well as hypotonia and are particularly at risk. These high-risk groups should be screened for sleep-disordered breathing.

The most basic assessment is overnight pulse oximetry, which can be performed in the child's home. The frequency and severity of periods of desaturation can be quantified. Normal oximetry does not exclude the condition, but means that severe physical consequences are unlikely. Polysomnography is required in more complex cases. This includes monitoring of heart rate, respiratory effort, airflow, CO₂ and video recording. It provides more information about gas exchange and can distinguish between central and obstructive events. Sometimes more detailed electrophysiological assessment is needed to assess neurological arousals and sleep staging.

If adenotonsillar hypertrophy is present, adenotonsillectomy usually dramatically improves their condition (Fig. 17.25). Medical treatments such as topical steroid nasal sprays and antihistamines may improve symptoms in milder cases. If severe hypoxaemia is seen on the sleep study, there is increased risk of perioperative complications. For children with other sleep-related breathing disorders or persistent obstruction following medical and surgical intervention, nasal or face mask continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) may be required at night.

Congenital central hypoventilation syndrome is a rare congenital condition resulting in disordered central control of breathing as well as other autonomic dysfunction. In severe cases, life-threatening hypoventilation occurs during sleep, which may result in death in infancy. Long-term ventilation, during sleep, is the mainstay of treatment.

Summary

Sleep disordered breathing

- Obstructive sleep apnoea is usually due to adenotonsillar hypertrophy, and surgical removal of tonsils and adenoids may improve symptoms markedly.

Respiratory care in children with complex needs

Tracheostomy

The number of children of all ages with a tracheostomy is increasing. Indications are listed in Table 17.3. If a child with a tracheostomy develops sudden and severe breathing difficulties, it may be that the tracheostomy tube is blocked with secretions and needs urgent suction or changing. If this does not relieve the difficulty in breathing, respiratory support is given via the tracheostomy tube. All children with a tracheostomy should have a spare tracheostomy tube with them at all times, and a carer competent to change it.

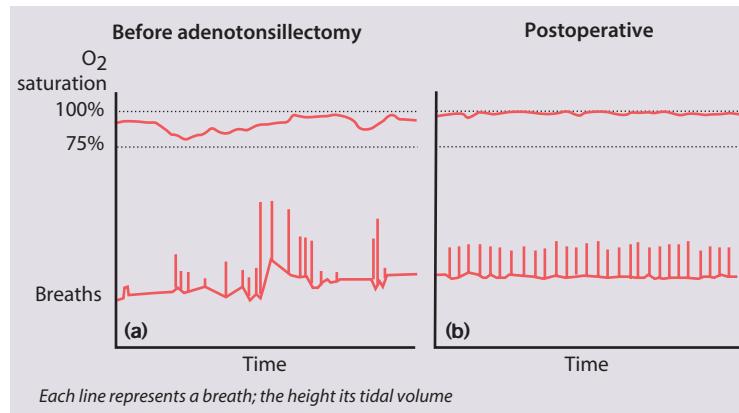


Figure 17.25 Extract from cardiorespiratory monitoring in a child with obstructive sleep apnoea. (a) Irregular breathing with periodic pauses associated with oxygen desaturation; and (b) post-adenotonsillectomy, the breathing is regular and the desaturation has resolved. (Courtesy of Dr Parviz Habibi.)

Table 17.3 Indications for tracheostomy in children

Narrow upper airways	Subglottic stenosis Laryngeal anomalies (e.g. atresia, haemangiomas, webs) Pierre Robin sequence (small jaw and cleft palate) Other craniofacial anomalies (e.g. Crouzon disease)
Lower airway anomalies	Severe tracheo-bronchomalacia
Long-term ventilation	Muscle weakness Head or spinal injury
Wean from artificial ventilation	Any prolonged period of ventilation
Airway protection	To facilitate clearance of secretions

**Figure 17.26** Long-term non-invasive respiratory support given overnight via nasal mask to a child with muscle weakness.

Long-term ventilation

An increasing number of children are receiving long-term respiratory support. Preterm infants with severe bronchopulmonary dysplasia may require additional oxygen for many months. Children with sleep-disordered breathing due to neuromuscular diseases such as Duchenne muscular dystrophy will benefit in both quality and duration of life from nocturnal respiratory support. This requires BiPAP (bilevel positive airway pressure), which can be delivered non-invasively by a nasal mask or full face mask (Fig. 17.26). Children who have more severe respiratory failure may need 24-hour respiratory support via a

**Figure 17.27** Long-term ventilation via a tracheostomy.

tracheostomy (Fig. 17.27). In some severe and progressive conditions difficult ethical decisions need to be made about admission for intensive care and whether to initiate long-term ventilation.

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Cardiac disorders

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Recent developments in paediatric cardiac disease:

- Congenital cardiac lesions are increasingly identified on antenatal ultrasound screening (over 50%, with over 70% of severe lesions).
- Most lesions are diagnosed by echocardiography, the mainstay of diagnostic imaging.
- Magnetic resonance imaging allows three-dimensional reconstruction of complex cardiac disorders, assessment of haemodynamics and flow patterns, and assists interventional cardiology, reducing the need for cardiac catheterization.
- Most defects can be operated by definitive surgery at the initial operation.
- An increasing number of defects (60%) are treated non-invasively, e.g. persistent ductus arteriosus.
- New therapies are available to treat pulmonary hypertension and delay transplantation.
- The overall infant cardiac surgical mortality has been reduced from approximately 20% in 1970 to 1.8% in 2016.

Epidemiology

Heart disease in children is mostly congenital. It is the most common single group of structural malformations in infants:

- 8 per 1000 liveborn infants have significant cardiac malformations, 30% of which require intervention in the first year of life.
- minor abnormalities of the cardiovascular system are present in up to 53.2 per 1000 live births, e.g. a

bicuspid aortic valve can be identified on screening in up to 5% of live births

- about 1 in 10 stillborn infants have a cardiac anomaly.

The nine most common anomalies account for 80% of all lesions (**Box 18.1**), but:

- about 10%–15% have complex lesions with more than one cardiac abnormality and
- about 10%–15% also have a non-cardiac abnormality.

Box 18.1 The most common congenital heart lesions

- Left-to-right shunts (breathless)
 - Ventricular septal defect 30%
 - Persistent arterial duct 12%
 - Atrial septal defect 7%
- Right-to-left shunts (blue)
 - Tetralogy of Fallot 5%
 - Transposition of the great arteries 5%
- Common mixing (breathless and blue)
 - Atrioventricular septal defect (complete) 2%
- Outflow obstruction in a well child (asymptomatic with a murmur)
 - Pulmonary stenosis 7%
 - Aortic stenosis 5%
- Outflow obstruction in a sick neonate (collapsed with shock)
 - Coarctation of the aorta 5%

Aetiology

Genetic causes are increasingly recognized in the aetiology of congenital heart disease, now in more than 10%. These may affect whole chromosomes, point mutations, or microdeletions (Table 18.1). Cardiac screening should be part of the care of children with multi-system genetic disorders. Polygenic abnormalities probably explain why having a child with congenital heart disease doubles the risk for subsequent children, and the risk is higher still if either parent has congenital heart disease. A small number are related to external teratogens.

Circulatory changes at birth

In the fetus, the left atrial pressure is low, as relatively little blood returns from the lungs. The pressure in the right atrium is higher than in the left, as it receives all the systemic venous return including blood from the placenta. The flap valve of the foramen ovale is held open, blood flows across the atrial septum into the left atrium, and then into the left ventricle, which in turn pumps it to the upper body (Fig. 18.1 and see Fig. 10.9).

With the first breaths, resistance to pulmonary blood flow falls and the volume of blood flowing through the lungs increases six-fold. This results in a rise in the left atrial pressure. Meanwhile, the volume of blood returning to the right atrium falls as the placenta is excluded from the circulation. The change in the pressure difference

causes the flap valve of the foramen ovale to close. The arterial duct (ductus arteriosus), which connects the pulmonary artery to the aorta in fetal life, will normally close within the first few hours or days. Some infants with congenital heart lesions rely on blood flow through the duct (duct-dependent circulation). Their clinical condition will deteriorate dramatically when the duct closes, which is usually at 1–2 days of age but occasionally later.

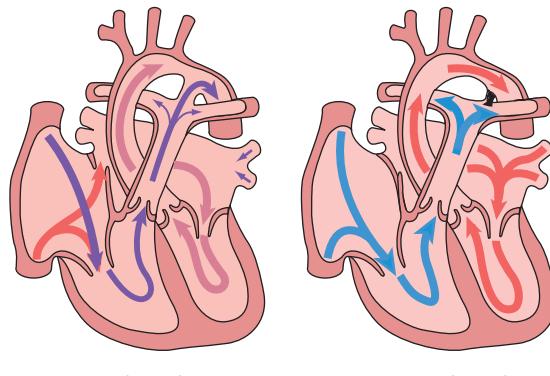


Figure 18.1 Changes in the circulation from the fetus to the newborn. When congenital heart lesions rely on blood flow through the duct (a duct-dependent circulation), there will be a dramatic deterioration in the clinical condition when the duct closes.

Table 18.1 Causes of congenital heart disease

	Cardiac abnormalities	Frequency
Maternal disorders		
Rubella infection	Peripheral pulmonary stenosis, PDA	30%–35%
Systemic lupus erythematosus	Complete heart block (anti-Ro and anti-La antibody)	35%
Diabetes mellitus	Incidence increased overall	2%
Maternal drugs		
Warfarin therapy	Pulmonary valve stenosis, PDA	5%
Fetal alcohol syndrome	ASD, VSD, tetralogy of Fallot	25%
Chromosomal abnormality		
Down syndrome (trisomy 21)	Atrioventricular septal defect, VSD	30%
Edwards syndrome (trisomy 18)	Complex	60%–80%
Patau syndrome (trisomy 13)	Complex	70%
Turner syndrome (45XO)	Aortic valve stenosis, coarctation of the aorta	15%
Chromosome 22q11.2 deletion	Aortic arch anomalies, tetralogy of Fallot, common arterial trunk	80%
Williams syndrome (7q11.23 microdeletion)	Supravalvular aortic stenosis, peripheral pulmonary artery stenosis	85%
Noonan syndrome (PTPN11 mutation and others)	Hypertrophic cardiomyopathy, atrial septal defect, pulmonary valve stenosis	50%
Duchenne muscular dystrophy	Cardiomyopathy	78% by age 20

ASD, atrial septal defect; PDA, persistent ductus arteriosus; VSD, ventricular septal defect.

Presentation

Congenital heart disease presents with:

- antenatal cardiac ultrasound diagnosis
- detection of a heart murmur
- heart failure
- shock
- cyanosis.

It may also be detected on oxygen saturation screening for critical congenital heart disease (see Ch. 10, Perinatal medicine).

Antenatal diagnosis

Checking the anatomy of the fetal heart has become a routine part of the fetal anomaly scan performed in high-income countries between 18 weeks' and 20 weeks' gestation and can lead to 70% of those infants who require surgery in the first 6 months of life being diagnosed antenatally. If an abnormality is detected, detailed fetal echocardiography is performed by a paediatric cardiologist. Any fetus at increased risk, e.g. with suspected Down syndrome, where the parents have had a previous child with heart disease, or where the mother has congenital heart disease is also checked with detailed fetal echocardiography. Early diagnosis allows the parents to be counselled. Depending on the diagnosis, some choose termination of pregnancy; the majority continue with the pregnancy and can have their child's management planned antenatally. Mothers of infants with duct-dependent lesions likely to need treatment within the first 2 days of life may be offered delivery at or close to a cardiac centre.

Heart murmurs

The most common presentation of more minor congenital heart disease is with a heart murmur. Even so, the vast majority of children with murmurs have a normal heart. They have an 'innocent murmur', which can be heard at some time in almost 30% of children. It is obviously important to be able to distinguish an innocent murmur from a pathological one.

Hallmarks of an innocent ejection murmur are (all have an 'S', 'innoSent'):

- aSymptomatic
- Soft blowing murmur
- Systolic murmur only, not diastolic
- left Sternal edge.

Also:

- normal heart sounds with no added sounds
- no parasternal thrill
- no radiation.

During a febrile illness or anaemia, innocent or flow murmurs are often heard because of increased cardiac output. Therefore, it is important to examine the child when such other illnesses have been corrected.

Differentiating between innocent and pathological murmurs can be difficult. If a murmur is thought to be significant, or if there is uncertainty about whether it is

innocent, the child should be seen by an experienced paediatrician to decide about referral to a paediatric cardiologist for echocardiography. Full examination must include palpation of the femoral pulses, measurement of peripheral oxygen saturations and blood pressure. A chest radiograph and electrocardiography (ECG) may help with the diagnosis beyond the neonatal period.

Many newborn infants with potential shunts have neither symptoms nor a murmur at birth, as the pulmonary vascular resistance is still high. Therefore, conditions such as a ventricular septal defect (VSD) or ductus arteriosus may only become apparent at several weeks of age when the pulmonary vascular resistance falls.



**The features of an innocent murmur can be remembered as the five Ss:
'InnoSent' murmur = aSymptomatic, Soft,
Systolic, left Sternal edge**

Heart failure

Symptoms

- Breathlessness (particularly on feeding or exertion)
- Sweating
- Poor feeding
- Recurrent chest infections.

Signs

- Poor weight gain or faltering growth
- Tachypnoea
- Tachycardia
- Heart murmur, gallop rhythm
- Enlarged heart
- Hepatomegaly
- Cool peripheries.

Signs of right heart failure (ankle oedema, sacral oedema, and ascites) are rare in high-income countries, but may be seen with long-standing rheumatic heart disease or pulmonary hypertension, with tricuspid regurgitation and right atrial dilatation.

In the first week of life, heart failure (Box 18.2) usually results from left heart obstruction, e.g. coarctation of the

Box 18.2 Causes of heart failure

- Neonates – obstructed (duct-dependent) systemic circulation
 - Hypoplastic left heart syndrome
 - Critical aortic valve stenosis
 - Severe coarctation of the aorta
 - Interruption of the aortic arch
- Infants (high pulmonary blood flow)
 - Ventricular septal defect
 - Atrioventricular septal defect
 - Large persistent ductus arteriosus
- Older children and adolescents (right or left heart failure)
 - Eisenmenger syndrome (right heart failure only)
 - Rheumatic heart disease
 - Cardiomyopathy

Table 18.2 Types of presentation with congenital heart disease

Type of lesion	Left-to-right shunt	Right-to-left shunt	Common mixing	Well children with obstruction	Sick neonates with obstruction
Symptoms	Breathless or asymptomatic	Blue	Breathless and blue	Asymptomatic	Collapsed with shock
Examples	ASD VSD PDA	Tetralogy of Fallot TGA	AVSD Complex congenital heart disease	AS PS Adult-type CoA	Coarctation HLHS

AS, aortic stenosis; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CoA, coarctation of the aorta; HLHS, hypoplastic left heart syndrome; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TGA, transposition of the great arteries; VSD, ventricular septal defect.

aorta. If the obstructive lesion is very severe, then arterial perfusion may be predominantly by right-to-left flow of blood via the arterial duct, so-called duct-dependent systemic circulation (see Fig. 18.2). Closure of the duct under these circumstances rapidly leads to severe acidosis, collapse and death unless ductal patency is restored ([Case history 18.1](#)).

After the first week of life, progressive heart failure is most likely due to a left-to-right shunt ([Case history 18.2](#)). During the subsequent weeks, as the pulmonary vascular resistance falls, there is a progressive increase in left-to-right shunt and increasing pulmonary blood flow. This causes pulmonary oedema and breathlessness.

Such symptoms of heart failure will increase up to the age of about 3 months but may later subsequently improve as the pulmonary vascular resistance rises in response to the left-to-right shunt. If left untreated, these children will develop Eisenmenger syndrome, which is irreversibly raised pulmonary vascular resistance resulting from chronically raised pulmonary arterial pressure and flow. Blood flow across the shunt will now be from right to left, and the young adult will be blue from cyanosis. If this develops, the only surgical option is a heart-lung transplant, if available, although medication is now available to palliate the symptoms.

Cyanosis

- Peripheral cyanosis (blueness of the hands and feet, or around the mouth) may occur when a child is cold or unwell from any cause or with polycythaemia.
- Central cyanosis, seen on the tongue as a slate blue colour, is associated with a fall in arterial blood oxygen tension. It can only be recognized clinically if the concentration of reduced haemoglobin in the blood exceeds 50 g/L, so it is less pronounced if the child is anaemic.
- Check with a pulse oximeter that an infant's oxygen saturation is normal ($\geq 94\%$). Persistent cyanosis in an otherwise well infant is nearly always a sign of structural heart disease.

Cyanosis in a newborn infant with respiratory distress (respiratory rate >60 breaths/min) may be due to:

- cardiac disorders – cyanotic congenital heart disease
- respiratory disorders, e.g. respiratory distress syndrome (surfactant deficiency), meconium aspiration, pulmonary hypoplasia
- persistent pulmonary hypertension of the newborn – failure of the pulmonary vascular resistance to fall after birth
- infection – septicaemia from group B streptococcus and other organisms
- inborn error of metabolism – metabolic acidosis and shock.

Whether the presentation of congenital heart disease is with a heart murmur, heart failure, cyanosis or shock depends on the underlying anatomic lesion causing:

- left-to-right shunt
- right-to-left shunt
- common mixing
- outflow obstruction in the well or sick child.

This is summarized in [Table 18.2](#).

Diagnosis

If congenital heart disease is suspected, a chest radiograph and ECG ([Box 18.3](#)) should be performed. Although rarely diagnostic, they may be helpful in establishing that there is an abnormality of the cardiovascular system and as a baseline for assessing future changes. Echocardiography, combined with Doppler ultrasound, enables almost all causes of congenital heart disease to be diagnosed. Even when a paediatric cardiologist, or paediatrician with expertise in cardiology (PEC) is not available locally, a specialist echocardiography opinion may be available via telemedicine, or else transfer to the cardiac centre will be necessary. An urgent specialist opinion is required if the child is haemodynamically unstable, if there is severe heart failure, if there is cyanosis, when the oxygen saturations are less than 94% due to heart disease, and when there are reduced volume pulses.



Case history 18.1

Shock

A 2-day-old baby had been discharged home the day after delivery following a normal routine examination. He suddenly collapsed and was rushed to hospital. He was pale, with grey lips. The right brachial pulse could just be felt, the femoral pulses were impalpable, and his liver was markedly enlarged. Blood gases showed a severe metabolic acidosis.

The differential diagnosis was:

- congenital heart disease
- septicaemia
- inborn error of metabolism.

He was ventilated and treated with volume support. Blood cultures were taken and antibiotics started for possible sepsis. Blood and urine samples were taken for an amino acid screen and urine for organic acids. As the femoral pulses remained impalpable, a prostaglandin infusion was started. Within 2 hours, he was pink and well perfused and the acidosis was resolving. Severe coarctation of the aorta (Fig. 18.2) was diagnosed on echocardiography. He had developed shock from a left heart outflow tract obstruction once the arterial duct had closed.



Maintaining ductal patency is the key to early survival in neonates with a duct-dependent circulation.

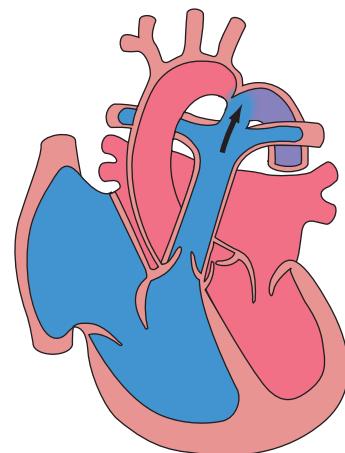


Figure 18.2 Duct-dependent coarctation. The systemic circulation is maintained by blood flowing right to left across the ductus arteriosus – a duct-dependent systemic circulation.



Case history 18.2

Heart failure

A 5-week-old female infant was referred to hospital because of wheezing, poor feeding and poor weight gain during the previous 2 weeks. Before this she had been well. Her routine neonatal examination had been normal. She was tachypnoeic (50–60 breaths/min) and there was some sternal and intercostal recession. The pulses were normal. There was a thrill, a pansystolic murmur at the lower left sternal edge and a slightly accentuated pulmonary component to the second heart sound. There were scattered wheezes. The liver was enlarged, palpable at two finger-breadths

below the costal margin. The ECG was unremarkable. The chest radiograph showed cardiomegaly and increased pulmonary vascular markings. An echocardiogram showed a moderate-sized ventricular septal defect (VSD; Fig. 18.3). Treatment was medical with diuretics and captopril. The VSD closed spontaneously at 18 months.

This infant developed heart failure from a moderate VSD presenting at several weeks of age when the pulmonary resistance fell, causing increased left-to-right shunting of blood. The defect closed spontaneously.

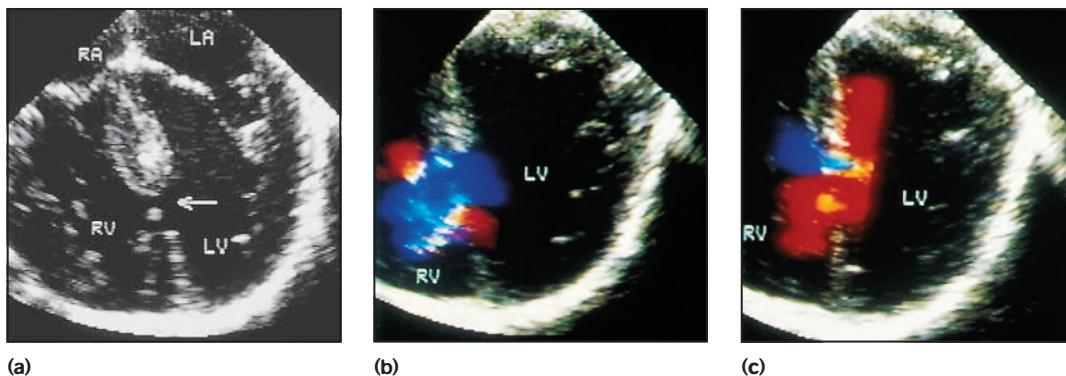


Figure 18.3 (a) Echocardiogram showing a medium-sized muscular ventricular septal defect (arrow); (b) the colour Doppler shows a left-to-right shunt (blue) during systole; and (c) there is also a small right-to-left shunt (red) during diastole. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Box 18.3 ECG in children**Important features**

- Arrhythmias
- Superior QRS axis (negative deflection in AVF; see Fig. 18.4f)
- Right ventricular hypertrophy (upright T wave in V₁ over 1 month of age; see Fig. 18.5d)
- Left ventricular strain (inverted T wave in V₆; see Fig. 18.13d)

Pitfalls

- P-wave morphology is rarely helpful in children
- Partial right bundle branch block – most are normal children, although it is common in ASD (atrial septal defect)
- Sinus arrhythmia is a normal finding

Nomenclature

The European (as opposed to American) system for naming congenital heart disease is referred to as sequential segmental arrangement. The advantage is that it is not necessary to remember the pattern of an eponymous syndrome, e.g. tetralogy of Fallot. The disadvantage is that it is long-winded. The idea is that each component is described in turn, naming the way the atria, then the ventricles, and then the great arteries are connected. Hence, a normal heart will be described as *situs solitus* (i.e. the atria are in the correct orientation), concordant atrioventricular connection and concordant ventriculo-arterial connection. Therefore, a heart of any complexity can be described in a logical step-by-step process. This system is not described here, as it is beyond the scope of this book.

Summary**Presentation of congenital heart disease**

- Antenatal ultrasound screening – increasing proportion detected antenatally.
- Detection of a heart murmur – need to differentiate innocent from pathological murmur.
- Cyanosis – if duct dependent, prostaglandin to maintain ductal patency is vital for initial survival.
- Heart failure – usually from left-to-right shunt when pulmonary vascular resistance falls.
- Shock – when duct closes in severe left heart obstruction.
- Oxygen saturation screening for critical congenital heart disease – if performed.

Left-to-right shunts

These are:

- atrial septal defects (ASDs)
- VSDs
- persistent ductus arteriosus (PDA).

Atrial septal defect

There are two main types of ASD:

- secundum ASD (80% of ASDs; Fig. 18.4a)
- partial atrioventricular septal defect (AVSD or primum ASD, less common; Fig. 18.4b).

Both present with similar symptoms and signs, but their anatomy is quite different. The secundum ASD is a defect in the centre of the atrial septum involving the foramen ovale.

Partial AVSD is a defect of the atrioventricular septum and is characterized by:

- an interatrial communication between the bottom end of the atrial septum and the atrioventricular valves (primum ASD)
- abnormal atrioventricular valves, with a left atrioventricular valve which has three leaflets and tends to leak (regurgitant valve).

Clinical features**Symptoms**

- None (commonly)
- Recurrent chest infections/wheeze
- Arrhythmias (fourth decade onwards).

Physical signs

- An ejection systolic murmur best heard at the upper left sternal edge – due to increased flow across the pulmonary valve because of the left-to-right shunt (Fig. 18.4c).
- A fixed and widely split second heart sound (often difficult to hear) – due to the right ventricular stroke volume being equal in both inspiration and expiration.
- With a partial AVSD, an apical pansystolic murmur will be heard from atrioventricular valve regurgitation.

Investigations**Chest radiograph**

The chest radiograph (Fig. 18.4d) shows cardiomegaly, enlarged pulmonary arteries, and increased pulmonary vascular markings.

ECG

- Secundum ASD – partial right bundle branch block is common (but may occur in normal children), right axis deviation due to right ventricular enlargement (Fig. 18.4e).
- Partial AVSD – a ‘superior’ QRS axis (mainly negative in AVF; Fig. 18.4f). This occurs because there is a defect of the middle part of the heart where the atrioventricular node is. The displaced node then conducts to the ventricles superiorly, giving the abnormal axis.

Echocardiography

This will delineate the anatomy and is the mainstay of diagnostic investigations.

Management

Children with significant ASD (large enough to cause right ventricle dilatation) will require treatment. For secundum

ASDs, this is by cardiac catheterization with insertion of an occlusion device (Fig. 18.4g), but for partial AVSD surgical correction is required. Treatment is usually undertaken at about 3 years to 5 years of age in order to prevent right heart failure and arrhythmias in later life.

Ventricular septal defects

VSDs are common, accounting for 30% of all cases of congenital heart disease. There is a defect anywhere in the ventricular septum, perimembranous (adjacent to the tricuspid valve) or muscular (completely surrounded by muscle). They can most conveniently be considered according to the size of the lesion.

Small VSDs

These are smaller than the aortic valve in diameter, perhaps up to 3 mm.

Clinical features

Symptoms

- Asymptomatic.

Physical signs

- Loud pan-systolic murmur at lower left sternal edge (loud murmur implies smaller defect)
- Quiet pulmonary second sound (P_2).

Atrial septal defect

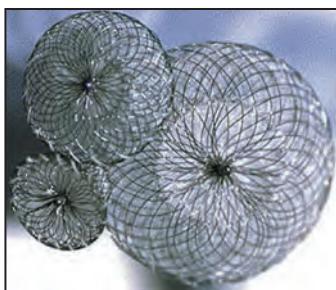
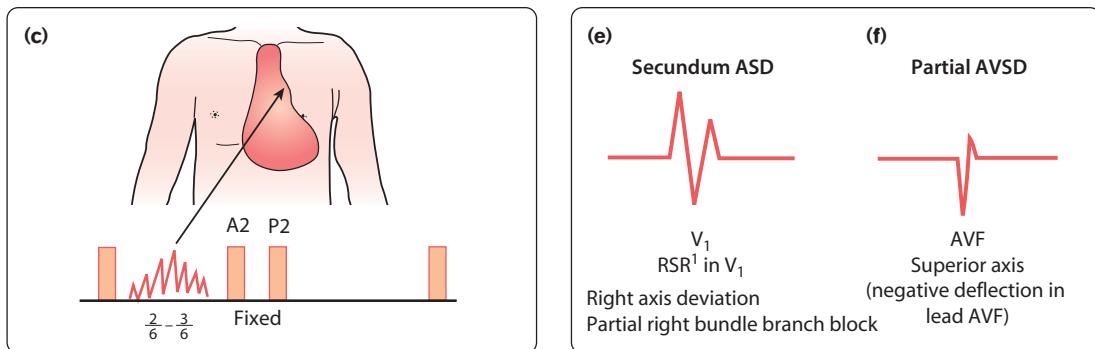
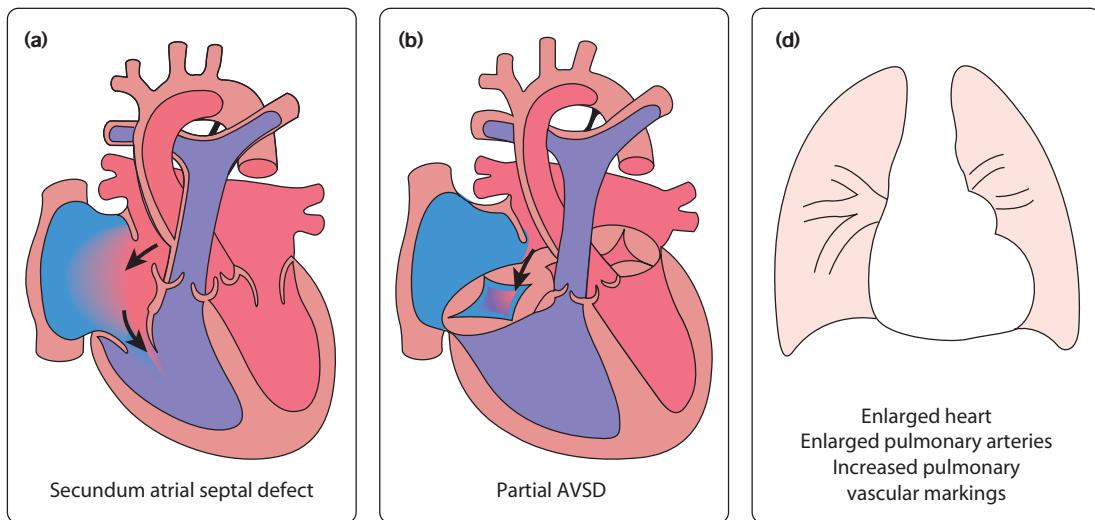


Figure 18.4 Atrial septal defect. (a) The ostium secundum atrial septal defect is a deficiency of the foramen ovale and surrounding atrial septum; (b) partial atrioventricular septal defect (AVSD) is a deficiency of the atrioventricular septum; (c) murmur; (d) chest radiograph; (e and f) ECG; and (g) examples of an occlusion device used to close secundum atrial septal defects.

Investigations

Chest radiograph

- Normal.

ECG

- Normal.

Echocardiography

- Demonstrates the precise anatomy of the defect. It is possible to assess its haemodynamic effects using Doppler echocardiography. There is no pulmonary hypertension.

Management

These lesions will close spontaneously. This is ascertained by the disappearance of the murmur with a normal ECG on follow-up by a paediatrician or paediatric cardiologist and by a normal echocardiogram. While the VSD is present, prevention of bacterial endocarditis is by maintaining good dental hygiene and avoiding body piercings or tattoos.

Large VSDs

These defects tend to be the same size or bigger than the aortic valve (Fig. 18.5a).

Clinical features

Symptoms

- Heart failure with breathlessness and faltering growth after 1 week old
- Recurrent chest infections.

Physical signs (Fig. 18.5b)

- Tachypnoea, tachycardia and enlarged liver from heart failure
- Active precordium
- Soft pan-systolic murmur or no murmur (implying large defect)
- Apical mid-diastolic murmur (from increased flow across the mitral valve after the blood has circulated through the lungs)
- Loud pulmonary second sound (P_2) – from raised pulmonary arterial pressure.

Large ventricular septal defect

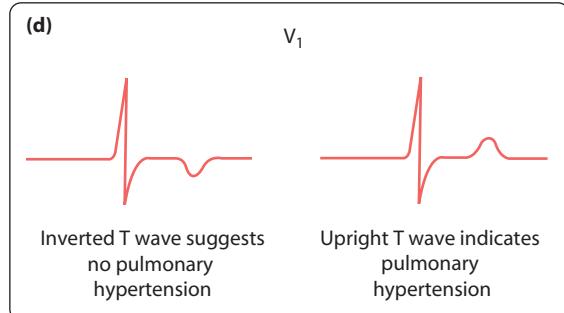
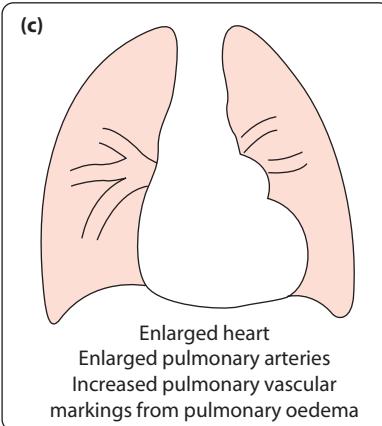
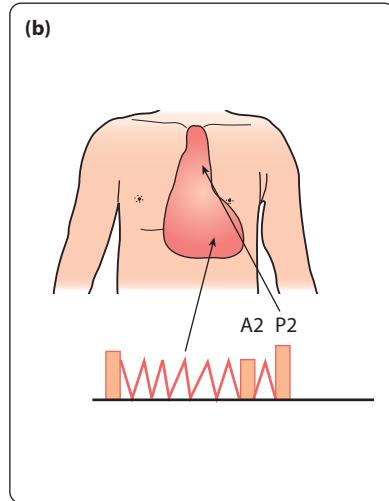
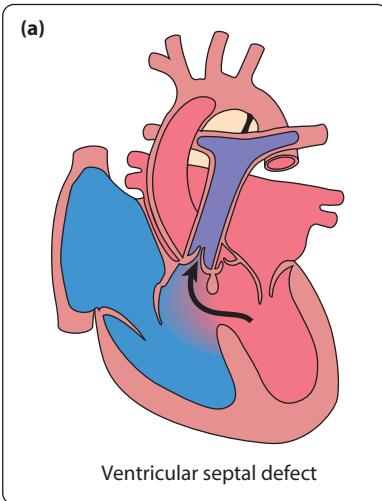


Figure 18.5 Ventricular septal defect. (a) Ventricular septal defect showing a left-to-right shunt; (b) murmur; (c) chest radiograph; and (d) ECG.

Investigations

Chest radiograph (Fig. 18.5c)

- Cardiomegaly
- Enlarged pulmonary arteries
- Increased pulmonary vascular markings
- Pulmonary oedema.

ECG (Fig. 18.5d)

- Biventricular hypertrophy by 2 months of age.

Echocardiography

- Demonstrates the anatomy of the defect, haemodynamic effects and high pulmonary pressure (due to high flow).

Management

Drug therapy for heart failure is with diuretics, often combined with captopril. Additional calorie input is required. There is always high pulmonary pressure (pulmonary hypertension) in children with large VSD and left-to-right shunt, which will ultimately lead to irreversible damage of the pulmonary capillary vascular bed (see the 'Eisenmenger syndrome' section below). To prevent this, surgery is usually performed at 3 months to 6 months of age in order to:

- manage heart failure and faltering growth
- prevent permanent lung damage from pulmonary hypertension and high blood flow.

Persistent ductus arteriosus (persistent arterial duct)

The ductus arteriosus connects the pulmonary artery to the descending aorta. In term infants, it normally closes shortly after birth. In PDA it has failed to close by 1 month after the expected date of delivery due to a defect in the constrictor mechanism of the duct. The flow of blood across a PDA is then from the aorta to the pulmonary artery (i.e. left to right), following the fall in pulmonary vascular resistance after birth. In the preterm infant, the presence of a PDA is not from congenital heart disease but due to prematurity. This is described in [Chapter 11](#) (Neonatal medicine).

Clinical features

Most children present with a continuous murmur beneath the left clavicle (Fig. 18.6a). The murmur continues into diastole because the pressure in the pulmonary artery is lower than that in the aorta throughout the cardiac cycle. The pulse pressure is increased, causing a collapsing or bounding pulse. Symptoms are unusual, but when the duct is large there will be increased pulmonary blood flow with heart failure and pulmonary hypertension. Many of these infants were preterm.

Investigations

The chest radiograph and ECG are usually normal, but if the PDA is large and symptomatic the features on

Persistent ductus arteriosus

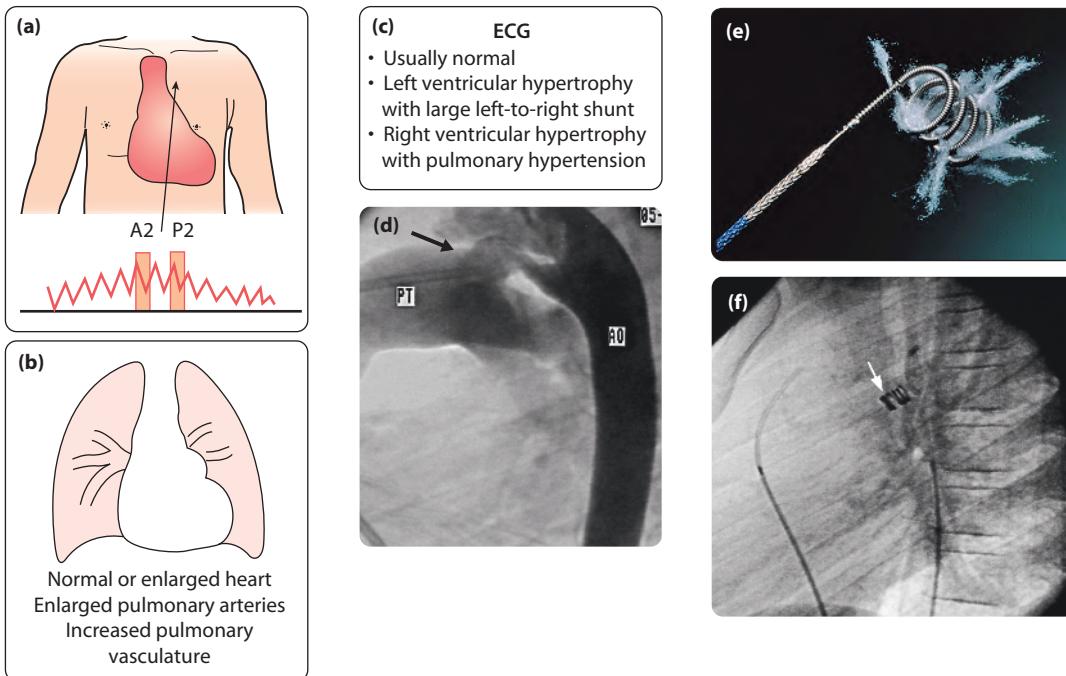


Figure 18.6 Persistent ductus arteriosus. (a) Murmur; (b) chest radiograph; (c) ECG; (d) a persistent ductus arteriosus visualized on angiography (arrow); (e) a coil used to close ducts. It is passed through a catheter via the femoral artery or vein; and (f) angiogram to show coil in the duct (arrow). AO, aorta; PT, pulmonary trunk.

Summary

Left-to-right shunts

Lesion	Symptoms	Signs	Management
ASD			
Secundum	None	ESM at ULSE Fixed split S ₂	Catheter device closure at 3–5 years of age
Partial AVSD	None	ESM at ULSE Fixed split S ₂ Pansystolic murmur at apex	Surgery at 3 years of age
VSD			
Small (80%–90% of cases)	None	Pan-systolic murmur at LLSE	None
Large (10%–20% of cases)	Heart failure	Active precordium, loud P ₂ , soft murmur, tachypnoea, hepatomegaly	Diuretics, captopril, calories Surgery at 3–6 months of age
PDA	None	Continuous murmur at ULSE ± bounding pulses	Coil or device closure at cardiac catheter at 1 year of age, or ligation in preterm

ASD, atrial septal defect; AVSD, atrioventricular septal defect; ESM, ejection systolic murmur; LLSE, lower left sternal edge; PDA, persistent ductus arteriosus; ULSE, upper left sternal edge; VSD, ventricular septal defect.

chest radiograph (Fig. 18.6b) and ECG (Fig. 18.6c) are indistinguishable from those seen in a patient with a large VSD. However, the duct is readily identified on echocardiography.

Management

Closure is recommended to abolish the lifelong risk of bacterial endocarditis and of pulmonary vascular disease. Closure is with a coil or occlusion device introduced via a cardiac catheter ideally at about 1 year of age (Fig. 18.6d–f). Occasionally, surgical ligation is required.

Right-to-left shunts

These are:

- tetralogy of Fallot
- transposition of the great arteries.

Presentation is with cyanosis (blue, oxygen saturations $\leq 94\%$, or collapsed), usually in the first week of life.

Hyperoxia (nitrogen washout) test

The test is sometimes used to help determine the presence of heart disease in a cyanosed neonate. The infant is placed in 100% oxygen (headbox or ventilator) for 10 minutes. If the right radial arterial partial pressure of oxygen (PaO_2) from a blood gas remains low ($< 15 \text{ kPa}$, 113 mmHg) after this time, a diagnosis of 'cyanotic' congenital heart disease can be made if lung disease and persistent pulmonary hypertension of the newborn have

been excluded. If the PaO_2 is over 20 kPa, it is not cyanotic heart disease. Blood gas analysis must be performed as oxygen saturations are not reliable enough in this range.

Management of the cyanosed neonate

- Stabilize the airway, breathing, and circulation (ABC), with mechanical ventilation if necessary.
- Start prostaglandin E infusion (5 ng/kg per min). Most infants with cyanotic heart disease presenting in the first few days of life are duct dependent, i.e. there is reduced mixing between the pink oxygenated blood returning from the lungs and the blue deoxygenated blood from the body. Maintenance of ductal patency is the key to early survival of these infants (Fig. 18.7). Observe for potential side-effects of prostaglandin – apnoea, jitteriness and seizures, flushing, vasodilatation and hypotension.

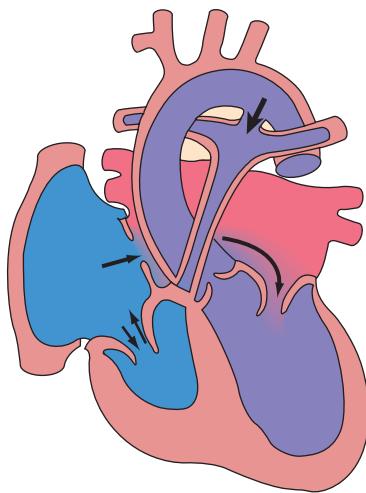
Tetralogy of Fallot

This is the most common cause of cyanotic congenital heart disease (Fig. 18.8a).

Clinical features

In tetralogy of Fallot, as implied by the name, there are four cardinal anatomical features:

- a large VSD
- overriding of the aorta with respect to the ventricular septum
- subpulmonary stenosis causing right ventricular outflow tract obstruction
- right ventricular hypertrophy as a result.



Pulmonary atresia with intact septum

Figure 18.7 An example of cyanotic congenital heart disease from duct-dependent pulmonary circulation – the pulmonary circulation is maintained by blood flowing left to right across the duct. Maintaining ductal patency with prostaglandin is crucial for early survival.

Symptoms

Most are diagnosed:

- antenatally or
- following the identification of a murmur in the first 2 months of life. Cyanosis at this stage may not be obvious, although a few present with severe cyanosis in the first few days of life.

The classical description of severe cyanosis, hypercyanotic spells and squatting on exercise developing in late infancy, is now rare in high-income countries, but still common where access to the necessary paediatric cardiac services is not readily available. It is important to recognize hypercyanotic spells, as they may lead to myocardial infarction, cerebrovascular accidents and even death if left untreated. They are characterized by a rapid increase in cyanosis, usually associated with irritability or inconsolable crying because of severe hypoxia and breathlessness and then pallor because of tissue acidosis. On auscultation, there is a very short murmur or no murmur during a spell.

Signs

- Clubbing of the fingers and toes will develop in older children.
- A loud harsh ejection systolic murmur at the left sternal edge from day 1 of life (Fig. 18.8b). With increasing right ventricular outflow tract obstruction, which is predominantly muscular and below the pulmonary valve the murmur will shorten and cyanosis will increase.

Tetralogy of Fallot

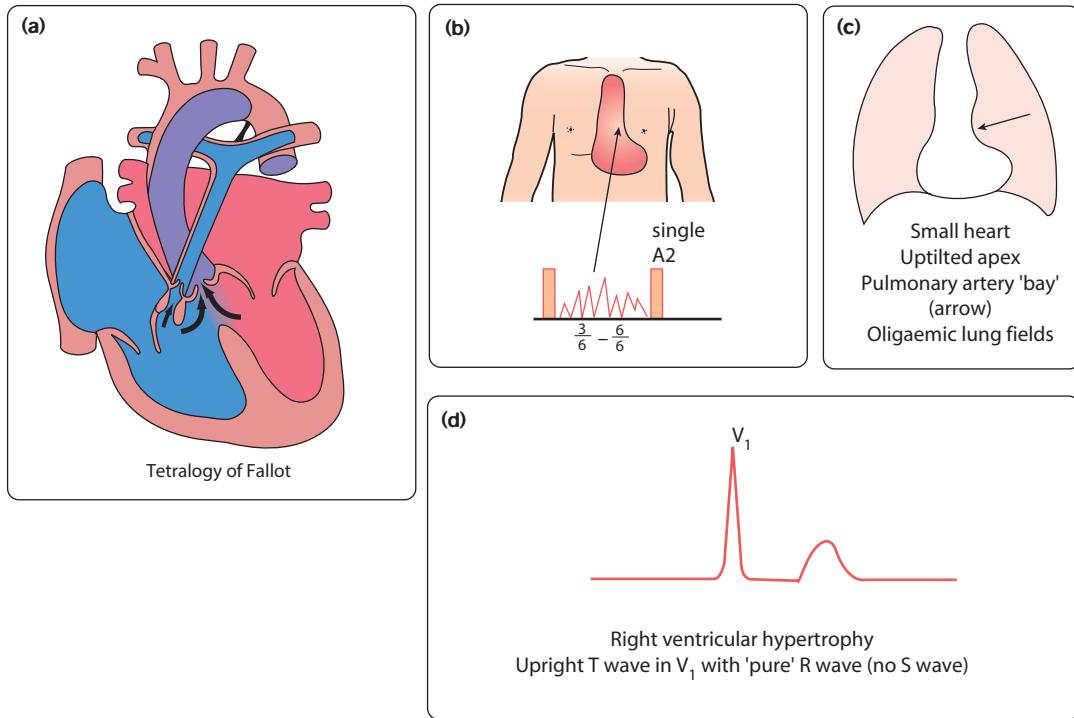


Figure 18.8 Tetralogy of Fallot. (a) The right ventricular outflow tract obstruction results in blood flowing from right to left across the ventricular septal defect; (b) murmur; (c) chest radiograph; and (d) ECG.

Investigations

Chest radiograph (Fig. 18.8c)

A radiograph will show a relatively small heart, possibly with an upturned apex (boot shaped) due to right ventricular hypertrophy, more prominent in the older child. There may be a right-sided aortic arch, but characteristically there is a pulmonary artery 'bay', a concavity on the left heart border where the convex-shaped main pulmonary artery and right ventricular outflow tract would normally be profiled. There may also be decreased pulmonary vascular markings reflecting reduced pulmonary blood flow.

ECG (Fig. 18.8d)

Normal at birth. Right ventricular hypertrophy when older.

Echocardiography

This will demonstrate the cardinal features, but cardiac catheterization (or MRI scan) may be required to show the detailed anatomy of the coronary arteries if not seen on echocardiography.

Management

- Initial management is medical, with definitive surgery at around 6 months of age. It involves closing the VSD and relieving right ventricular outflow tract obstruction, sometimes with an artificial patch which extends across the pulmonary valve.
- Infants who are very cyanosed in the early neonatal period require a shunt to increase pulmonary blood flow. This is usually done by surgical placement of an artificial tube between the subclavian artery and the pulmonary artery (a modified Blalock–Taussig shunt), or by balloon dilatation or stent insertion in the right ventricular outflow tract.
- Hypcyanotic spells are usually self-limiting and followed by a period of sleep. If prolonged (beyond about 15 min), they should be given prompt treatment, according to need, with:
 - sedation and pain relief (morphine is excellent)
 - intravenous propranolol (or an α adrenoceptor agonist), which probably works both as a peripheral vasoconstrictor and by relieving the subpulmonary muscular obstruction that is the cause of reduced pulmonary blood flow
 - intravenous volume administration
 - bicarbonate to correct acidosis
 - muscle paralysis and artificial ventilation in order to reduce metabolic oxygen demand.

Transposition of the great arteries

The aorta is connected to the right ventricle and the pulmonary artery is connected to the left ventricle (discordant ventriculo-arterial connection). The blue blood is therefore returned to the body and the pink blood is returned to the lungs (Fig. 18.9a). There are two parallel circulations – unless there is mixing of blood between them, this condition is incompatible with life. Fortunately, there are a number of naturally occurring associated anomalies, e.g. VSD, ASD and PDA as well as therapeutic interventions which can achieve this mixing in the short term.

Clinical features

Symptoms

Cyanosis is the predominant symptom. It may be profound and life-threatening. If not detected antenatally, presentation is usually on day 2 of life when ductal closure leads to a marked reduction in mixing of the desaturated and saturated blood. Cyanosis will be less severe and presentation delayed if there is more mixing of blood from associated anomalies, e.g. an ASD.

Physical signs (Fig. 18.9b)

- Cyanosis is always present.
- The second heart sound is often loud and single.
- Usually no murmur but may be a systolic murmur from increased flow or stenosis within the left ventricular (pulmonary) outflow tract.

Investigations

Chest radiograph (Fig. 18.9c)

This may reveal the classic findings of a narrow upper mediastinum with an 'egg on side' appearance of the cardiac shadow (due to the anteroposterior relationship of the great vessels, narrow vascular pedicle, and hypertrophied right ventricle, respectively). Increased pulmonary vascular markings are common due to *increased* pulmonary blood flow.

ECG (Fig. 18.9d)

This is usually normal.

Echocardiography

This is essential to demonstrate the abnormal arterial connections and associated abnormalities.

Management

- In the sick cyanosed neonate, the key is to improve mixing.
- Maintaining the patency of the ductus arteriosus with a prostaglandin infusion is mandatory.
- A balloon atrial septostomy may be a life-saving procedure, which needs to be performed in 20% of those with transposition of the great arteries (Fig. 18.9e–g). A catheter with an inflatable balloon at its tip is passed through the umbilical or femoral vein and then on through the right atrium and foramen ovale. The balloon is inflated within the left atrium and then pulled back through the atrial septum. This tears the atrial septum, renders the flap valve of the foramen ovale incompetent and so allows mixing of the systemic and pulmonary venous blood within the atrium.
- All patients with transposition of the great arteries will require an operation, which is usually the arterial switch procedure in the neonatal period. In this operation, performed in the first few days of life, the pulmonary artery and aorta are transected above the arterial valves and switched over. In addition, the coronary arteries have to be transferred across to the new aorta. More complex forms of transposition will need alternative operations.

Transposition of the great arteries

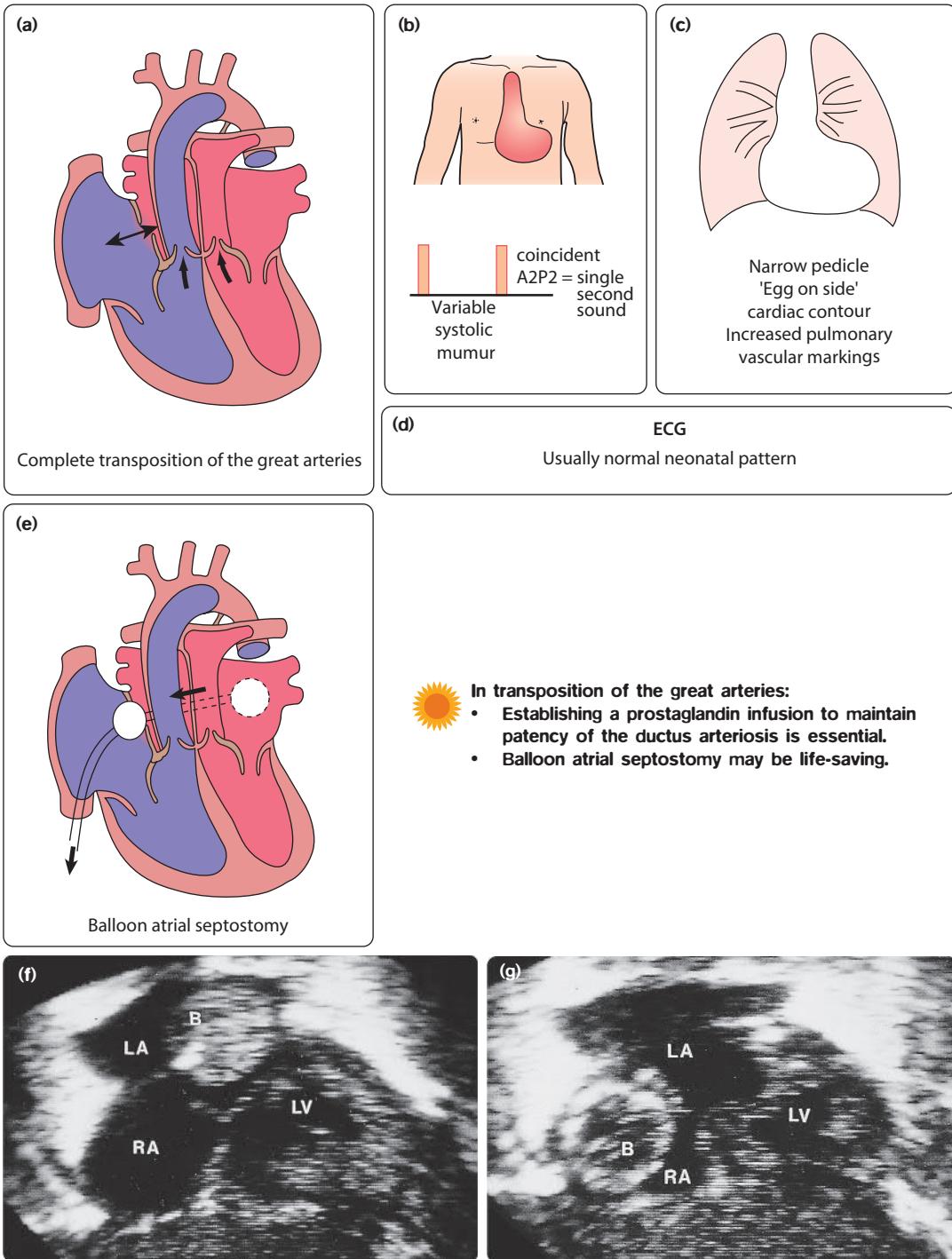


Figure 18.9 Transposition of the great arteries. **(a)** Transposition of the great arteries. There must be mixing of blood between the two circulations for this to be compatible with life; **(b)** heart sounds; **(c)** chest radiograph; **(d)** ECG; **(e)** balloon atrial septostomy. A balloon (about 2 ml) is pulled through the atrial septum from the left atrium to the right atrium in order to increase the size of the atrial defect. This is done with echocardiographic guidance; **(f)** echocardiogram showing balloon in the left atrium; and **(g)** balloon has been pulled through the atrial septum and is now in the right atrium. B, balloon; LA, left atrium; LV, left ventricle; RA, right atrium.

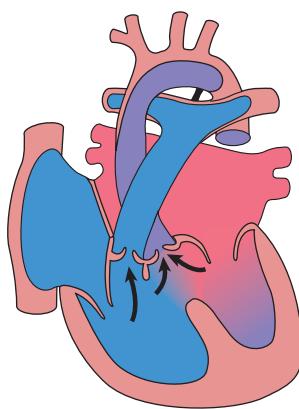
Summary

Cyanotic congenital heart disease

Lesion	Clinical features	Management
Tetralogy of Fallot	Loud murmur at upper left sternal edge Clubbing of fingers and toes (older) Hypercyanotic spells	Surgery at 6–9 months of age
Transposition of the great arteries	Neonatal cyanosis No murmur	Prostaglandin infusion Balloon atrial septostomy Arterial switch operation in neonatal period
Eisenmenger syndrome	No murmur Right heart failure (late)	Medication to delay transplantation

Eisenmenger syndrome

If high pulmonary blood flow due to a large left-to-right shunt or common mixing is not treated at an early stage, the pulmonary arteries become thick walled and the resistance to flow increases (Fig. 18.10). Gradually, those children that survive become less symptomatic as the shunt decreases. Eventually, at about 10–15 years of age, the shunt reverses and the young person becomes blue, which is Eisenmenger syndrome. This situation is progressive and the adult will die in right heart failure at a variable age, usually in the fourth or fifth decade of life. Treatment is aimed at prevention of this condition, with early intervention for high pulmonary blood flow. Transplantation is not readily available although medication to palliate pulmonary vascular disease is now available (see the ‘Pulmonary hypertension’ section below).



Eisenmenger syndrome

Figure 18.10 Eisenmenger syndrome with right-to-left shunting from pulmonary vascular disease following increased pulmonary blood flow and pulmonary hypertension with large ventricular septal defect.

Common mixing (blue and breathless)

These include:

- AVSD (complete)
- complex congenital heart disease, e.g. tricuspid atresia.

Atrioventricular septal defect (complete)

This is most often seen in children with Down syndrome (Fig. 18.11). A complete AVSD is a defect in the middle of the heart with a single five-leaflet (common) valve between the atria and ventricles, which stretches across the entire atrioventricular junction and tends to leak. As there is a large defect there is high pulmonary artery pressure.

Features of a complete AVSD are:

- presentation on antenatal ultrasound screening
- cyanosis at birth or heart failure at 2 weeks to 3 weeks of life
- no murmur heard, but the lesion is detected on routine echocardiography screening in a newborn infant with Down syndrome
- there is always a superior axis on the ECG
- management is to treat heart failure medically (as for large VSD) and surgical repair at 3 months to 6 months of age.

Complex congenital heart disease

It is difficult to generalize about these conditions (tricuspid atresia, mitral atresia, double inlet left ventricle, common arterial trunk – truncus arteriosus) because their main presenting feature depends on whether cyanosis or heart failure is more predominant. Tricuspid atresia is the most common.

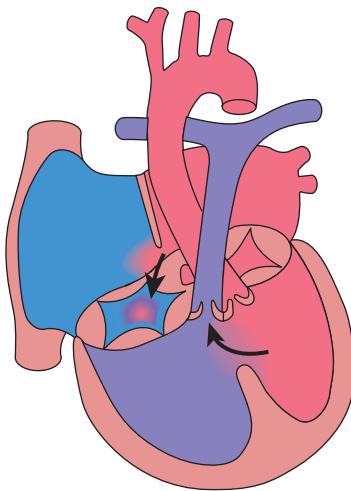


Figure 18.11 Atrioventricular septal defect. Complete atrioventricular septal defect, with a common atrioventricular valve between a large atrial and ventricular component to the atrioventricular septal defect.

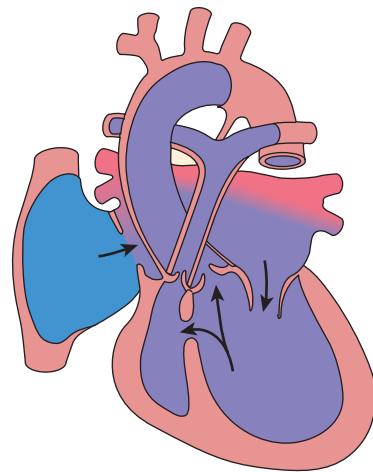


Figure 18.12 Tricuspid atresia. In tricuspid atresia, there is only one effective ventricle because of complete absence of the tricuspid valve.

Tricuspid atresia

In tricuspid atresia (Fig. 18.12) only the left ventricle is effective, the right being small and non-functional.

Clinical features

There is 'common mixing' of systemic and pulmonary venous return in the left atrium. Presentation is with cyanosis in the newborn period if duct dependent, or the child may be well at birth and become cyanosed or breathless.

Management

Early palliation (as with all the common mixing complex diseases) is performed to maintain a secure supply of blood to the lungs at low pressure, by:

- a Blalock-Taussig shunt insertion (between the subclavian and pulmonary arteries) in children who are severely cyanosed

- pulmonary artery banding operation to reduce pulmonary blood flow if breathless.

Completely corrective surgery is not possible with most, as there is often only one effective functioning ventricle. Palliation is performed (Glenn or hemi-Fontan operation connecting the superior vena cava to the pulmonary artery after 6 months of age and a Fontan (total cavo-pulmonary connection) operation to also connect the inferior vena cava to the pulmonary artery at 3–5 years of age).

Thus, the left ventricle drives blood around the body and systemic venous pressure supplies blood to the lungs. The Fontan operation results in a less than ideal functional outcome but has the advantages of relieving cyanosis and removing the long-term volume load on the single functional ventricle.

Summary

Common mixing

Lesion	Clinical features	Management
Atrioventricular septal defect (complete)	Down syndrome (often) Cyanosis at birth Breathless at 2–3 weeks of life	Treat heart failure medically Surgical repair at 3 months
Complex disorders (e.g. tricuspid atresia)	Cyanosis Breathless	Shunt (Blalock-Taussig) or pulmonary artery banding, then surgery (Glenn and later Fontan operation)

Outflow obstruction in the well child

These lesions are:

- aortic stenosis
- pulmonary stenosis
- adult-type coarctation of the aorta.

Aortic stenosis

The aortic valve leaflets are partly fused together, giving a restrictive exit from the left ventricle (Fig. 18.13a). There may be one to three aortic leaflets. Bi-cuspid aortic valve is a common lesion seen in up to 1% of the population and may be inherited. Aortic stenosis may not be an isolated lesion. It is often associated with mitral valve stenosis and coarctation of the aorta, and their presence should always be excluded.

Clinical features

Most present with an asymptomatic murmur. Those with severe stenosis may present with reduced exercise tolerance, chest pain on exertion, or syncope.

In the neonatal period, those with *critical* aortic stenosis and a duct-dependent systemic circulation may present with severe heart failure leading to shock.

Physical signs (Fig. 18.13b)

- Small volume, slow rising pulses
- Carotid thrill (always)

- Ejection systolic murmur maximal at the upper right sternal edge radiating to the neck
- Delayed and soft aortic second sound
- Apical ejection click.

Investigations

Chest radiograph (Fig. 18.13c)

Normal or prominent left ventricle with post-stenotic dilatation of the ascending aorta (aortopathy).

ECG (Fig. 18.13d)

There may be left ventricular hypertrophy.

Management

In children, regular clinical and echocardiographic assessment is required in order to assess when to intervene. Children with symptoms on exercise or who have a high resting pressure gradient (>64 mmHg) across the aortic valve will undergo balloon valvotomy. Balloon dilatation in older children is generally safe and uncomplicated, but in neonates this is much more difficult and dangerous.

Most neonates and children with significant aortic valve stenosis requiring treatment in the first few years of life will eventually require aortic valve replacement. Early treatment is therefore palliative and directed towards delaying this for as long as possible.

Aortic stenosis

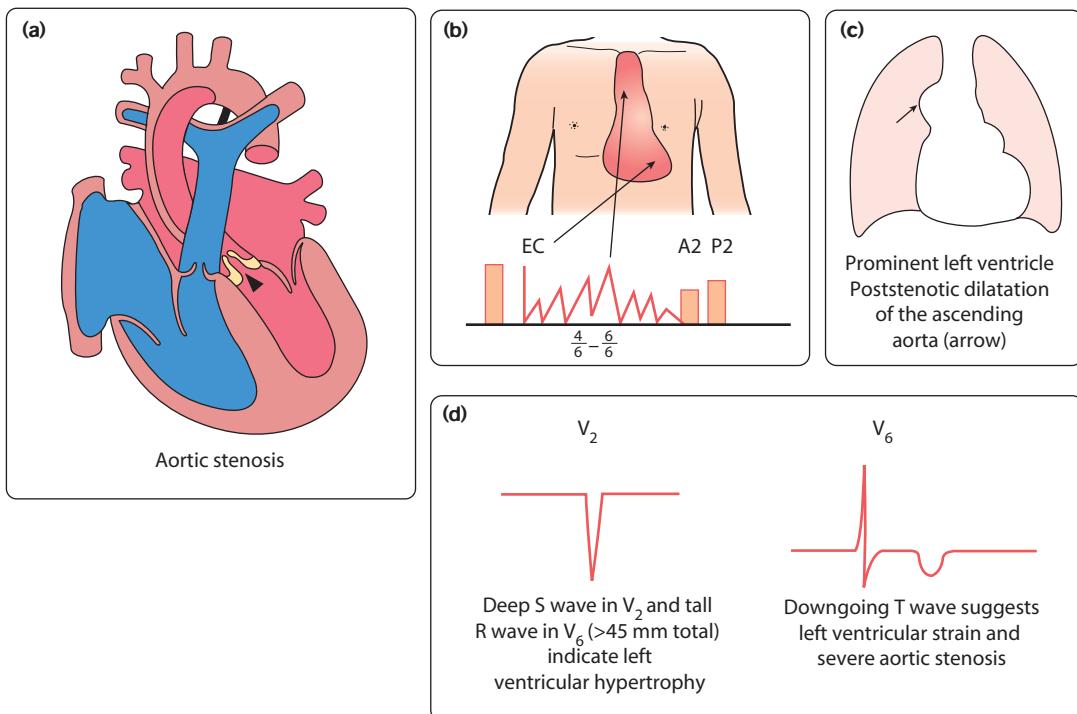


Figure 18.13 Aortic stenosis. (a) Aortic stenosis; (b) murmur; (c) chest radiograph; and (d) ECG.

Pulmonary stenosis

The pulmonary valve leaflets are partly fused together, giving a restrictive exit from the right ventricle.

Clinical features

Most are asymptomatic (Fig. 18.14a). It is diagnosed clinically. A small number of neonates with *critical* pulmonary stenosis have a duct-dependent pulmonary circulation and present in the first few days of life with cyanosis.

Physical signs (Fig. 18.14b)

- An ejection systolic murmur best heard at the upper left sternal edge; thrill may be present.
- An ejection click best heard at the upper left sternal edge.
- When severe, there is a prominent right ventricular impulse (heave).

Investigations

Chest radiograph (Fig. 18.14c)

Normal or post-stenotic dilatation of the pulmonary artery.

ECG (Fig. 18.14d)

Shows evidence of right ventricular hypertrophy (upright T wave in V₁).

Management

Most children are asymptomatic and when the pressure gradient across the pulmonary valve on Doppler echocardiography becomes markedly increased (> about 64 mmHg), intervention will be required. Transcatheter balloon dilatation is the treatment of choice in most children.

Adult-type coarctation of the aorta

This uncommon lesion (Fig. 18.15a) is not duct dependent. It gradually becomes more severe over many years. It is much more common for coarctation to present in the neonatal period (see below).

Clinical features (Fig. 18.15b)

- Asymptomatic.
- Systemic hypertension in the right arm.
- Ejection systolic murmur at upper sternal edge.
- Collaterals heard with continuous murmur at the back.
- Radio-femoral delay. This is due to blood bypassing the obstruction via collateral vessels in the chest wall and hence the pulse in the legs is delayed.

Investigations

Chest radiograph (Fig. 18.15c)

- 'Rib notching' due to the development of large collateral intercostal arteries running

Pulmonary valve stenosis

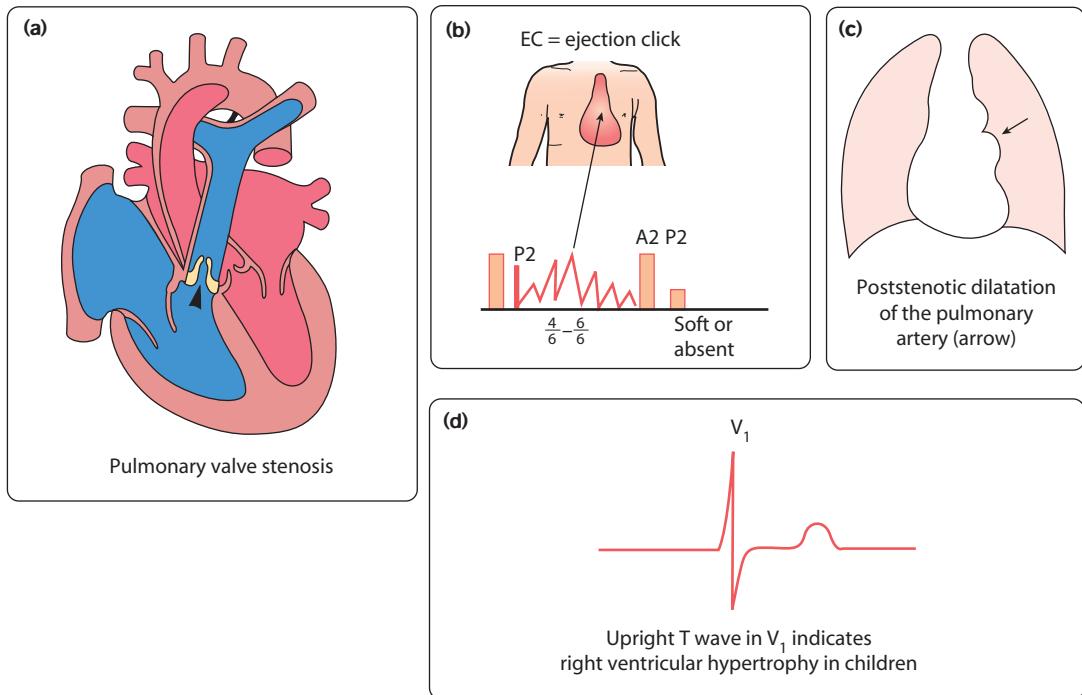


Figure 18.14 Pulmonary valve stenosis. (a) Pulmonary valve stenosis; (b) murmur; (c) chest radiograph; and (d) ECG.

- under the ribs posteriorly to bypass the obstruction
- '3' sign, with visible notch in the descending aorta at site of the coarctation.

ECG

- Left ventricular hypertrophy (Fig. 18.15d).

Management

When the condition becomes severe, as assessed by echocardiography, a stent may be inserted at cardiac catheter. Sometimes surgical repair is required.

Outflow obstruction in the sick infant

These lesions include:

- coarctation of the aorta
- interruption of the aortic arch
- hypoplastic left heart syndrome.

Clinical features are:

- presentation as sick infants with heart failure and shock in the neonatal period, unless diagnosed on antenatal ultrasound or oxygen saturation screening.

Summary

Outflow obstruction in the well child

Lesion	Signs	Management
Aortic stenosis	Murmur, upper right sternal edge; carotid thrill	Balloon dilatation
Pulmonary stenosis	Murmur, upper left sternal edge; no carotid thrill	Balloon dilatation
Coarctation (adult type)	Systemic hypertension Radio-femoral delay	Stent insertion or surgery

Adult-type coarctation of the aorta

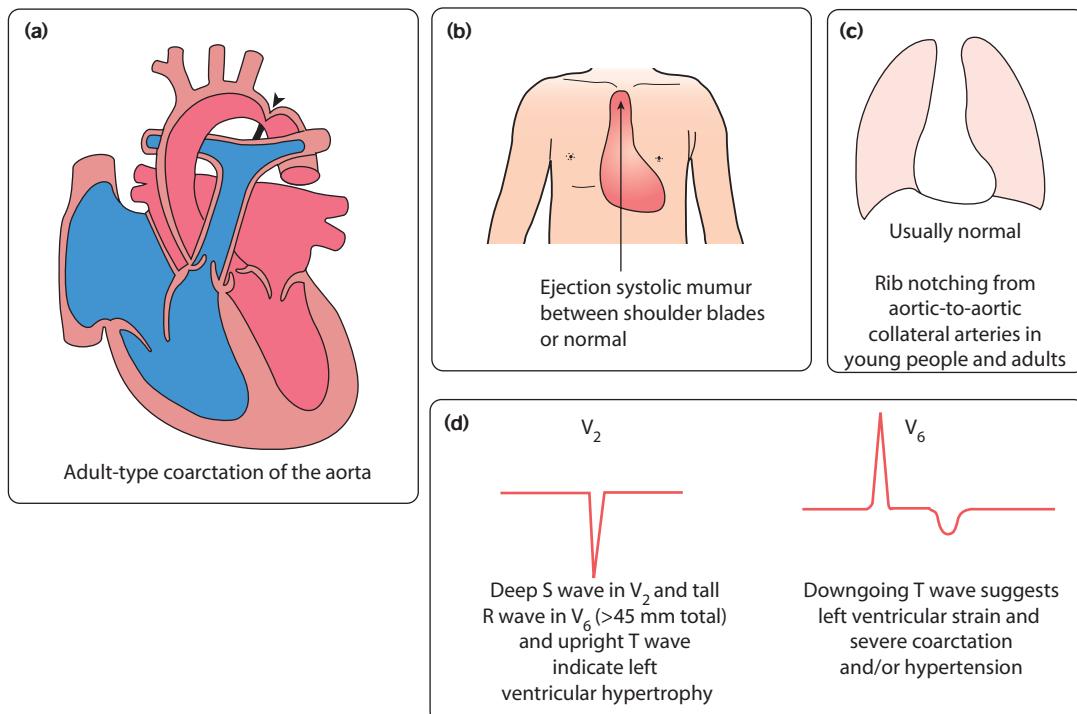


Figure 18.15 Adult-type coarctation of the aorta. (a) Adult-type coarctation of the aorta. There is narrowing of the aorta distal to the left subclavian artery adjacent to the insertion of the arterial duct; (b) murmur; (c) chest radiograph; and (d) ECG.

Management is:

- resuscitate (ABC)
- prostaglandin should be commenced at the earliest opportunity
- referral to a cardiac centre for early surgical intervention.

Coarctation of the aorta

This is due to arterial duct tissue encircling the aorta just at the point of insertion of the duct (see Fig. 18.2). When the duct closes, the aorta also constricts, causing severe obstruction to the left ventricular outflow. This is the most common cause of collapse due to left outflow obstruction.

Clinical features

Examination on the first day of life is usually normal. Neonates usually present with acute circulatory collapse at about 2 days of age when the duct closes.

Physical signs

- A sick baby, with severe heart failure
- Absent femoral pulses
- Severe metabolic acidosis.

Investigations

Chest radiograph

Cardiomegaly from heart failure and shock.

ECG

Normal.

Management

This is the same as for all sick infants with outflow obstruction. Surgical repair is performed soon after diagnosis.

Interruption of the aortic arch

- Uncommon, with no connection between the proximal aorta and distal to the arterial duct, so that the cardiac output is dependent on right-to-left shunt via the duct (Fig. 18.16).
- A VSD is usually present.
- Presentation is with shock in the neonatal period as above.
- Complete correction with closure of the VSD and repair of the aortic arch is usually performed within the first few days of life.
- Association with other conditions (DiGeorge syndrome – absence of thymus, palatal defects, immunodeficiency and hypocalcaemia, and chromosome 22q11.2 microdeletion).

Hypoplastic left heart syndrome

In this condition there is underdevelopment of the entire left side of the heart (Fig. 18.17). The mitral valve is small or

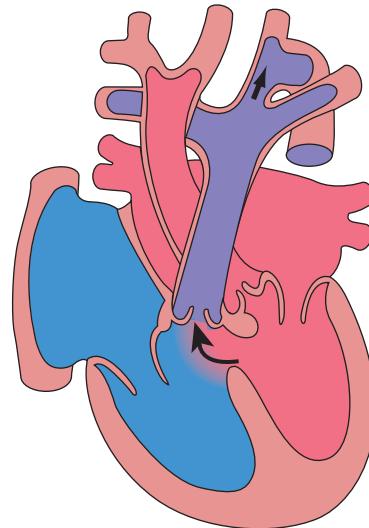


Figure 18.16 Interruption of the aortic arch. The lower body circulation is maintained by right-to-left flow of blood across the duct.

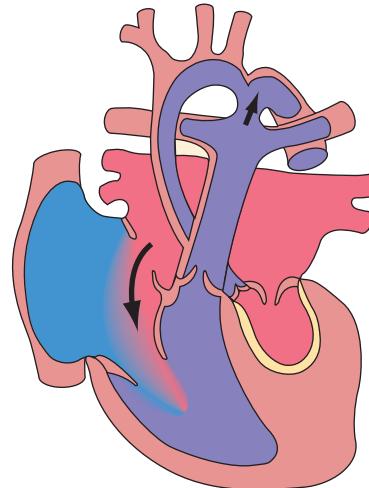


Figure 18.17 Hypoplastic left heart syndrome. The entire left side of the heart is underdeveloped.

atretic, the left ventricle is diminutive, and there is usually aortic valve atresia. The ascending aorta is very small, and there is almost invariably coarctation of the aorta.

Clinical features

These children may be detected antenatally at ultrasound screening. This allows for effective counselling and prevents the child from becoming sick after birth. They may be identified on oxygen saturation screening. If they do present after birth, they are the sickest of all neonates presenting with a duct-dependent systemic circulation. There is no flow through the left side of the heart, so ductal constriction leads to profound acidosis and rapid cardiovascular collapse. There is weakness or absence of all peripheral pulses, in contrast to weak femoral pulses in coarctation of the aorta.

Summary

Left heart outflow obstruction in the sick infant – duct-dependent lesions

Lesion	Clinical features	Management
Coarctation of the aorta	Circulatory collapse Absent femoral pulses	Maintain ABC Prostaglandin infusion
Interruption of the aortic arch	Circulatory collapse Absent femoral pulses and absent left brachial pulse	Maintain ABC Prostaglandin infusion
Hypoplastic left heart syndrome	Circulatory collapse All peripheral pulses absent	Maintain ABC Prostaglandin infusion

Management

The management of this condition consists of a difficult neonatal operation called the Norwood procedure. Children who have complex lesions or are small for gestational age undergo hybrid procedures that are a combination of cardiac catheter and surgical operation. This is followed by a further operation (Glenn or hemi-Fontan) at about 6 months of age and again (Fontan) at about 3 years of age.

Care following cardiac surgery

Most children recover rapidly following cardiac surgery and are back at nursery or school within a month. Exercise tolerance will be variable and most children can be allowed to find their own limits. Restricted exercise is advised only for children with severe residual aortic stenosis and for ventricular dysfunction.

Most of the children are followed up in specialist cardiac clinics. Most lead normal, unrestricted lives, but any change in symptoms, e.g. decreasing exercise tolerance or palpitations, requires further investigation. An increasing number of adolescents and young adults require revision of surgery performed in early life. The most common reason for this is replacement of artificial valves and relief of postsurgical suture line stenosis, e.g. recoarctation or pulmonary artery stenosis.

Cardiac arrhythmias

Sinus arrhythmia is normal in children and is detectable as a cyclical change in heart rate with respiration. There is acceleration during inspiration and slowing on expiration (the heart rate changing by up to 30 beats/min).

Supraventricular tachycardia

This is the most common childhood arrhythmia. The heart rate is rapid, between 250 and 300 beats/min. It can cause poor cardiac output and pulmonary oedema. It typically presents with symptoms of heart failure in the neonate or young infant. It is a cause of *hydrops fetalis* and intrauterine death. The term re-entry tachycardia is used because

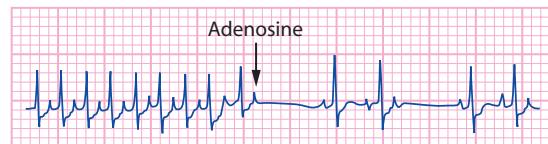


Figure 18.18 Rhythm strip showing supraventricular re-entry tachycardia, in which there is a narrow complex (<120 ms or three small squares) tachycardia of 250–300 beats/min, and response to treatment with adenosine.

a circuit of conduction is set up, with premature activation of the atrium via an accessory pathway. There is rarely a structural heart problem, but an echocardiogram should be performed both to review cardiac anatomy as well as evidence of poor function.

Investigation

The ECG will generally show a narrow complex tachycardia of 250–300 beats/min (Fig. 18.18). It may be possible to discern a P wave after the QRS complex due to retrograde activation of the atrium via the accessory pathway. If heart failure is severe, there may be changes suggestive of myocardial ischaemia, with T-wave inversion in the lateral precordial leads. When in sinus rhythm, a short P–R interval may be discernible. In the Wolff–Parkinson–White syndrome, the early antegrade activation of the ventricle via the pathway results in a short P–R interval and a delta wave and a wide QRS complex.

Management

In the severely ill child, prompt restoration of sinus rhythm is the key to improvement. This is achieved by:

- circulatory and respiratory support – tissue acidosis is corrected, positive pressure ventilation if required
- vagal stimulating manoeuvres, e.g. carotid sinus massage or cold ice pack to face, successful in about 80%
- intravenous adenosine – the treatment of choice. This is safe and effective, inducing atrioventricular block after rapid bolus injection. It terminates the tachycardia by breaking the re-entry circuit that is set up between the atrioventricular node and

- accessory pathway. It is given incrementally in increasing doses
- electrical cardioversion with a synchronized direct current shock (0.5–2 J/kg body weight) if adenosine fails.

Once sinus rhythm is restored, maintenance therapy will be required, e.g. with flecainide or sotalol. Digoxin can be used on its own when there is no overt pre-excitation wave (delta wave) on the resting ECG, but propranolol can be added in the presence of pre-excitation. Even though the resting ECG may remain abnormal, 90% of children will have no further attacks after infancy. Treatment is therefore stopped at 1 year of age if there is no Wolff-Parkinson-White Syndrome. Those who have Wolff-Parkinson-White syndrome need to be assessed to ensure they cannot conduct quickly, and this may be undertaken as young adults, with atrial pacing. This will reduce the small chance of sudden death in such patients. Those who relapse or are at risk are usually treated with percutaneous radiofrequency ablation or cryoablation of the accessory pathway.

Congenital complete heart block

This is a rare condition (Fig. 18.19) that is usually related to the presence of anti-Ro or anti-La antibodies in maternal serum. These mothers will have either manifest or latent connective tissue disorders. Subsequent pregnancies are often affected. This antibody appears to prevent normal development of the electrical conduction system in the developing heart, with atrophy and fibrosis of the atrioventricular node. It may cause fetal hydrops, death *in utero* and heart failure in the neonatal period. However, most remain symptom free for many years, but a few become symptomatic with presyncope or syncope. All children with symptoms require insertion of an endocardial pacemaker. There are other rare causes of complete heart block.

Other arrhythmias

Long QT syndrome may be associated with sudden loss of consciousness during exercise, stress or emotion, usually in late childhood. It may be mistakenly diagnosed as epilepsy. If unrecognized, sudden death from ventricular tachycardia may occur. There are many genetic causes and inheritance is autosomal dominant; there are several phenotypes. It has been associated with erythromycin therapy, electrolyte disorders and head injury.

It is one of the group of channelopathies caused by specific gene mutations. Abnormalities of the sodium, potassium or calcium channels lead to gain or loss of function. Anyone with a family history of sudden unexplained death or a history of syncope on exertion should be assessed.



Figure 18.19 Electrocardiography of congenital complete heart block. The P waves and QRS complexes are dissociated.

Atrial fibrillation, atrial flutter, ectopic atrial tachycardia, ventricular tachycardia and ventricular fibrillation occur in children, but all are rare. They are most often seen in children who have undergone surgery for complex congenital heart disease.

Syncope

Transient loss of consciousness is usually due to syncope, when it is associated with a loss of postural tone with spontaneous recovery. It is caused by a transient impairment of brain oxygen delivery, generally due to impaired cerebral perfusion (see also Ch. 29, Neurological disorders).

This is common in adolescents and is usually benign, but rarely it is due to cardiac disease, which may be life-threatening. The causes are:

- vasovagal syncope – is in response to a range of provocation and stressors. These may be from just standing up too quickly (a symptom of 'orthostatic intolerance'), to the sight of blood or needles or to a sudden unexpected pain. There is usually a prodrome of dizziness and light-headed feeling and abnormal vision often with nausea, sweating, or pallor. When associated with jerking movements, it can easily be misdiagnosed as an epileptic seizure. In most episodes there is a maladaptive drop in blood pressure; in a significant minority there is a marked fall in heart rate and in a few there is asystole
- cardiac syncope – may be arrhythmic, from heart block, supraventricular tachycardia, ventricular tachycardia, e.g. associated with long QT syndrome or structural, associated with aortic stenosis, hypertrophic cardiomyopathy.

Features suggestive of a cardiac cause are:

- symptoms on exercise – potentially dangerous
- family history of sudden unexplained death
- palpitations.

Check blood pressure and for signs of cardiac disease (murmur, femoral pulses, signs of Marfan syndrome). Investigate all presenting with transient loss of consciousness with a standard 12-lead ECG, and check the corrected Q-T interval.

Chest pains

Rarely due to cardiac disease in children. Only those occurring with palpitations or on exertion suggest a possible cardiac origin. Those occurring at rest usually require no further investigation, but if occurring in a child with known heart disease or on exercise, then they should be taken more seriously.

Rheumatic fever

Acute rheumatic fever is a multisystem autoimmune response to a group A streptococcus (GAS) infection. It mainly affects children aged 5–15 years, and may progress

to rheumatic heart disease. Worldwide, it is estimated that there are approximately 470,000 new cases of acute rheumatic fever and 275,000 deaths attributed to rheumatic heart disease each year. Most are in low- and middle-income countries or indigenous populations, where it affects about 19 per 100,000 school-age children, in contrast to <2 per 100,000 school-age children in high-income countries. The higher incidence in low- and middle-income countries mainly relates to environmental factors, especially household overcrowding. Difference in streptococcal virulence may also be a factor. Antibiotic treatment of streptococcal pharyngitis plays only a minor role in reducing incidence; a 10-day course of antibiotics for GAS pharyngitis is required for prevention of acute rheumatic fever.

Clinical features

After a latent interval of 2–6 weeks following GAS pharyngitis, or occasionally streptococcal pyoderma, there is an acute febrile illness with polyarthritis and often carditis. Less common is presentation with Sydenham chorea. The clinical features and diagnostic criteria are shown in Fig. 18.20.

There is usually evidence of prior GAS infection, and acute phase reactants (CRP and ESR) are raised from systemic inflammation. Cardiac evaluation is with ECG and echocardiography, which should be performed serially to identify carditis, if possible.

Rheumatic heart disease

The most common form of long-term damage is to the cardiac valves from scarring and fibrosis of the valve tissue of the heart. If there have been repeated attacks of acute rheumatic fever with carditis, this may occur as early as the second decade of life, but usually symptoms do not develop until early adult life. Although the mitral valve is the most frequently affected valve, aortic, tricuspid and, rarely, pulmonary valve disease may occur.

Management

Immediate management is focused on alleviation of symptoms. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used for arthritis, both for acute inflammation and prevention of new joint involvement. Aspirin has been used

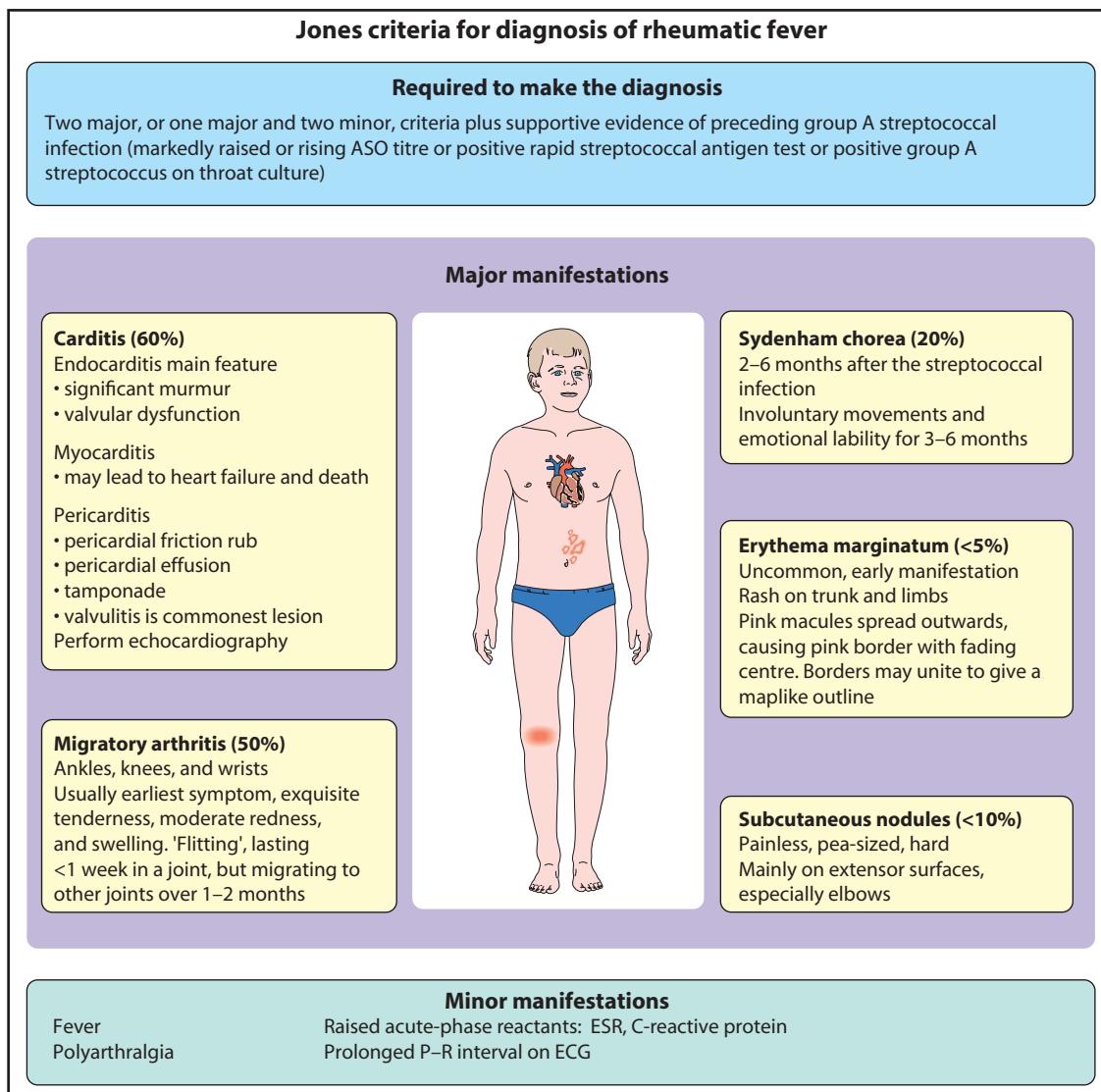


Figure 18.20 Jones criteria for diagnosis of rheumatic fever. If acute rheumatic fever is suspected, carditis should be diagnosed by echocardiography, if possible. In moderate to high-risk populations, monoarthritis or polyarthralgia may be considered a major manifestation of arthritis and monoarthralgia a minor manifestation instead of polyarthralgia.

traditionally to suppress the inflammatory response of the joints and heart, but has largely been superseded by naproxen as it has fewer side-effects. With severe carditis, cardiac failure may need to be treated; occasionally glucocorticoids may be given. Although bed rest has been traditional, its efficacy is uncertain. Sydenham chorea is usually managed with psychological, educational and social support until it resolves. GAS carriage is eradicated with penicillin; household contacts with GAS-positive throat cultures should also be treated. Disease activity can be monitored with serial CRP measurements.

Recurrence of GAS infection should be prevented as severity of eventual rheumatic valvular disease relates to the number of childhood episodes of acute rheumatic fever. Prophylaxis is most effectively achieved with monthly injections of benzathine penicillin. Alternatively, penicillin can be given orally daily, but it is less effective and compliance may be a problem. Changing to oral medication may be appropriate for young adults who have remained free of further attacks of acute rheumatic fever. The length of prophylaxis is controversial. Many recommend prophylaxis for either 10 years after the last episode of acute rheumatic fever or until the age of 21 years, whichever is the longer. Attention to minimizing the pain associated with parenteral antibiotic prophylaxis assists with continuing compliance.

Infective endocarditis

All children of any age with congenital heart disease (except secundum ASD), including neonates, are at risk of infective endocarditis. The risk is highest when there is a turbulent jet of blood, as with a VSD, coarctation of the aorta and PDA or if prosthetic material has been inserted at surgery. It may be difficult to diagnose, but should be suspected in any child or adult with a sustained fever, malaise, raised erythrocyte sedimentation rate, unexplained anaemia or haematuria. The presence of the classical peripheral stigmata of infective endocarditis should not be relied upon.

Clinical signs

- Fever
- Anaemia and pallor
- Splinter haemorrhages in nailbed
- Clubbing (late)
- Necrotic skin lesions ([Fig. 18.21](#))
- Changing cardiac signs
- Splenomegaly
- Neurological signs from cerebral infarction
- Retinal infarcts
- Arthritis/artralgia
- Haematuria (microscopic).

Diagnosis

Multiple blood cultures should be taken before antibiotics are started. Detailed cross-sectional echocardiography may confirm the diagnosis by identification of vegetations but can never exclude it. The vegetations consist of fibrin and platelets and contain infecting organisms. Acute-phase reactants are raised and can be useful to monitor response to treatment.



Figure 18.21 Widespread infected emboli and infarcts in a child with bacterial endocarditis. The tip of the third toe is gangrenous.

The most common causative organism is α -haemolytic streptococcus (*Streptococcus viridans*). Bacterial endocarditis is usually treated with high-dose penicillin in combination with an aminoglycoside, giving 6 weeks of intravenous therapy and checking that the serum level of the antibiotic will kill the organism. If there is infected prosthetic material, e.g. prosthetic valves, VSD patches or shunts, there is less chance of complete eradication and surgical removal may be required.

Prophylaxis

The most important factor in prophylaxis against endocarditis is good dental hygiene that should be strongly encouraged in all children with congenital heart disease along with avoidance of body piercing and tattoos.

Antibiotic prophylaxis is *no longer recommended in the UK for most cardiac conditions*, but may be required in those at high risk, such as those with prosthetic valves or artificial conduits placed at previous heart surgery when undergoing:

- dental treatment, however, trivial
- surgery which is likely to be associated with bacteraemia.

Myocarditis/cardiomyopathy

Dilated cardiomyopathy (a large, poorly contracting heart) may be inherited, secondary to metabolic disease or may result from a direct viral infection of the myocardium. It should be suspected in any child with an enlarged heart and heart failure who has previously been well. The diagnosis is readily made on echocardiography. Treatment is symptomatic with diuretics and angiotensin-converting enzyme inhibitors and carvedilol, a β -adrenoceptor blocking agent. The role of steroids and immunoglobulin infusion is controversial. Myocarditis usually improves spontaneously, but some children ultimately require heart transplantation. Other cardiomyopathies (hypertrophic/restrictive) are rare in childhood and are usually related to a systemic disorder (e.g. Hurler, Pompe or Noonan syndromes).

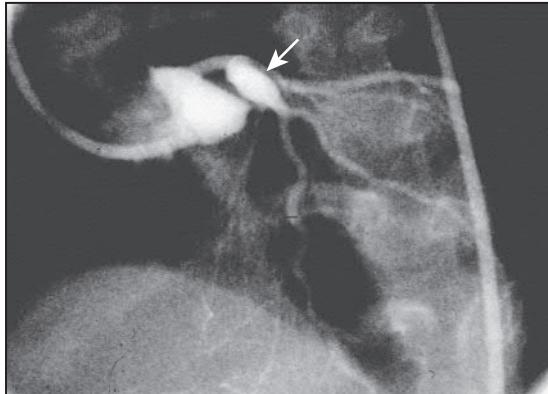


Figure 18.22 Kawasaki disease. Angiogram showing coronary artery aneurysm.

Kawasaki disease

This mainly affects children of 6 months to 5 years of age. Clinical features are described in [Chapter 15](#) (Infection and immunity). It is uncommon (9/100,000 children in the UK, 322/100,000 in Japan) but is doubling in frequency every 10 years and can cause significant cardiac disease. It is the commonest cause of acquired heart disease in children in high-income countries. An echocardiogram is performed at diagnosis and at 4–6 weeks, which may show a pericardial effusion, myocardial disease (poor contractility), endocardial disease (valve regurgitation), or coronary disease with aneurysm formation, which can be giant ($>/= 10$ or >8 mm in diameter). If the coronary arteries are abnormal, angiography ([Fig. 18.22](#)) or magnetic resonance imaging will be required. The risk of coronary artery aneurysm is high and treatment with intravenous immunoglobulin should be given as soon as possible.

Paediatric inflammatory multisystem syndrome temporarily associated with COVID-19 (PIMS-TS)

A small number of children develop a severe systemic inflammatory response associated with COVID-19 infection. It shares a number of features in common with Kawasaki disease, staphylococcal and streptococcal toxic shock syndromes, bacterial sepsis and macrophage activation syndromes. Those who have cardiac disease may present with shock, typically 3–4 weeks after suspected or proven COVID-19 infection. On echocardiography they have may severe cardiac dysfunction or coronary artery aneurysms.

Pulmonary hypertension

This is of increasing importance in paediatric cardiology, as there is now effective medication for most causes. It can be caused by a number of different diseases ([Box 18.4](#)). From the cardiac perspective, most children

Box 18.4 Causes of pulmonary hypertension

- Pulmonary arterial hypertension
 - Idiopathic: sporadic or familial
 - Post-tricuspid shunts (e.g. VSD, AVSD, PDA)
 - HIV infection
 - Persistent pulmonary hypertension of the newborn
- Pulmonary venous hypertension
 - Left-sided heart disease
 - Pulmonary vein stenosis or compression
- Pulmonary hypertension with respiratory disease
 - Chronic obstructive lung disease or bronchopulmonary dysplasia in preterm infants
 - Interstitial lung disease
 - Obstructive sleep apnoea or upper airway obstruction
- Pulmonary thromboembolic disease
- Pulmonary inflammatory or capillary disease.

AVSD, atrioventricular septal defect; HIV, human immunodeficiency virus; PDA, persistent ductus arteriosus; VSD, ventricular septal defect.

with pulmonary hypertension (high pulmonary artery pressure, mean >25 mmHg) have a large post-tricuspid shunt with high pulmonary blood flow and low resistance, e.g. VSD, AVSD or PDA. The pressure falls to normal if the defect is corrected by surgery within 6 months of age. If these children are left untreated, however, the high flow and pressure cause irreversible damage to the pulmonary vascular bed (pulmonary vascular disease), which is not correctable other than by heart/lung transplantation.

Many medical therapies are now available, which may act on the pulmonary vasculature on the cyclic guanosine monophosphate pathway (e.g. inhaled nitric oxide, intravenous magnesium sulphate and oral phosphodiesterase inhibitors including sildenafil) or endothelin receptor antagonists such as oral bosentan or on the cyclic adenosine monophosphate pathway (intravenous prostacyclin or inhaled iloprost). These medications allow transplantation to be delayed for many years.

Acknowledgements

We would like to acknowledge contributors to this chapter in previous editions, whose work we have drawn on: Andrew Redington (1st, 2nd Editions), Robert Tulloh (3rd, 4th, 5th Editions).

Further reading

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Kidney and urinary tract disorders

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Features of kidney and urinary tract disorders in children:

- Many structural abnormalities of the kidneys and urinary tract are identified on antenatal ultrasound screening.
- Urinary tract infection, vesicoureteric reflux, and urinary obstruction have the potential to damage the growing kidney.
- Nephrotic syndrome is usually steroid sensitive and only rarely leads to chronic kidney disease.
- Chronic renal disorders may affect growth and development.

Assessment of renal function

The kidney has multiple functions:

- filtering water-soluble salts and ions from the blood whilst not filtering out large molecules
- the reabsorption of necessary filtered small molecules, such as glucose and amino acids
- the dilution or concentration of urine to optimize fluid balance
- the regulation of blood pressure
- the metabolism of vitamin D
- the regulation of acid-base balance.

The assessment of 'renal function' encapsulates a range of variables including plasma creatinine and urea, serum electrolytes, blood pressure, urinary concentration and electrolytes, and urine output. In children:

- Plasma creatinine (a product of muscle breakdown) – is generally used to assess and monitor renal function.

However, the normal range of serum creatinine increases throughout childhood, accompanying increasing muscle mass and height. Creatinine level does not become abnormally high until renal function is markedly reduced.

- Plasma urea – is raised in acute kidney injury and chronic kidney disease and increases before the rise in creatinine. However, it is not as specific as it also rises in dehydration, catabolic states, high protein diet and gastrointestinal bleeding. High urea levels may cause nausea, vomiting and headaches.
- Estimating glomerular filtration rate – is a more accurate way of monitoring renal function (by using the formula $eGFR = 31 \times \text{height (cm)} / \text{creatinine (micromol/l)}$). The glomerular filtration rate (GFR) is low in the newborn infant and is especially low in premature infants; the GFR at 28 weeks' gestation is only 10% of the term infant. In term infants, the corrected GFR (20–30 ml/min per 1.73 m^2) rapidly rises until 1–2 years of age when the adult rate of 80 ml/min to 120 ml/min per 1.73 m^2 is achieved.
- Formal GFR measurement – is performed measuring clearance of a substance that is freely filtered by the glomerulus and not reabsorbed by the tubules. Inulin is now used in the UK but involves intravenous administration of inulin followed by serial blood tests to measure its clearance. Formal GFRs are not routinely used apart from prior to chemotherapy or research.
- Urinary protein loss – occurs before the fall in GFR in chronic kidney disease.
- Urine osmolality is an indicator of how well the kidneys can concentrate the urine and hence how well they are functioning.

Radiological investigations

Radiological investigations of the kidneys and urinary tract are used to identify anatomical and functional abnormalities (Table 19.1).

Congenital anomalies

Since the introduction of antenatal ultrasound screening, most significant structural congenital anomalies of the kidneys and urinary tract (CAKUT) are identified antenatally and are managed prospectively. Abnormalities are identified in 1 in 1000 births. They are potentially important because they may:

- be associated with abnormal renal development or function (chronic kidney disease)
- predispose to urinary tract infection
- involve urinary obstruction which requires surgical treatment
- be associated with non-renal congenital anomalies.

The antenatal detection and early treatment of urinary tract anomalies provide an opportunity to minimize or prevent progressive renal damage. However, minor

abnormalities are also detected, most commonly mild unilateral pelvic dilatation, which does not require intervention but may lead to over-investigation, unnecessary treatment, and unwarranted parental anxiety.

Anomalies detectable on antenatal ultrasound screening

Absence of both kidneys (renal agenesis) – As amniotic fluid is mainly derived from fetal urine, there is severe oligohydramnios resulting in Potter sequence (Fig. 19.1a,b), which is fatal due to failure of development of fetal lungs.

Multicystic dysplastic kidney (MCDK) – Results from the failure of union of the ureteric bud (which forms the ureter, pelvis, calyces, and collecting ducts) with the nephrogenic mesenchyme. It is a non-functioning structure with large fluid-filled cysts with no renal tissue and no connection with the bladder (Fig. 19.2). Half will have involuted by 2 years of age, and nephrectomy is indicated only if it remains very large or hypertension develops, but this is rare. MCDKs do not produce urine and, if they are bilateral, Potter sequence will result.

Cystic dysplastic kidneys can be caused by *autosomal recessive polycystic kidney disease* (ARPKD; Fig. 19.3) or *autosomal dominant polycystic kidney disease* (ADPKD; Fig. 19.4), and *renal cysts and diabetes*. In contrast to a

Table 19.1 Radiological investigations of the kidneys and urinary tract

Radiology	
Ultrasound	Standard imaging procedure of the kidneys and urinary tract. Provides anatomical assessment but not function. Excellent at visualizing urinary tract dilatation, stones, and nephrocalcinosis (small, multiple calcium deposits within renal parenchyma) Advantages: non-invasive, mobile Disadvantages: operator dependent, may not detect all renal scars
Micturating cystourethrogram (MCUG)	Contrast introduced into the bladder through urethral catheter Can visualize bladder and urethral anatomy. Detects vesicoureteric reflux (VUR) and urethral obstruction Disadvantages: invasive and unpleasant investigation especially beyond infancy, high radiation dose, and can introduce infection
CT scan kidneys and ureters	To accurately identify position of kidney stones. Intravenous uograms are not performed in children
Plain abdominal X-ray	Identifies unsuspected spinal abnormalities May identify renal stones, but poor at showing nephrocalcinosis
Nuclear medicine	
DMSA scan (^{99m}Tc dimercaptosuccinic acid)	<i>Static</i> scan of the renal cortex Detects functional defects, such as scars or areas of non-functioning renal tissue, but very sensitive, so need to wait at least 2 months after a urinary tract infection to avoid diagnosing false 'scars'
MAG3 renogram (mercaptop-acetyl-triglycine, labelled with ^{99m}Tc)	<i>Dynamic</i> scan, isotope-labelled substance MAG3 excreted from the blood into the urine. Measures drainage. Best performed with a high urine flow so furosemide often given. In children old enough to cooperate (usually >4 years of age), scan during micturition can be used to identify VUR (indirect cystogram)
Functional test	
Bladder flow urodynamics	To assess how well bladder is emptying together with flow rates. Bladder abnormalities can contribute to recurrent UTIs

Some congenital anomalies of the kidneys and urinary tract (CAKUT)

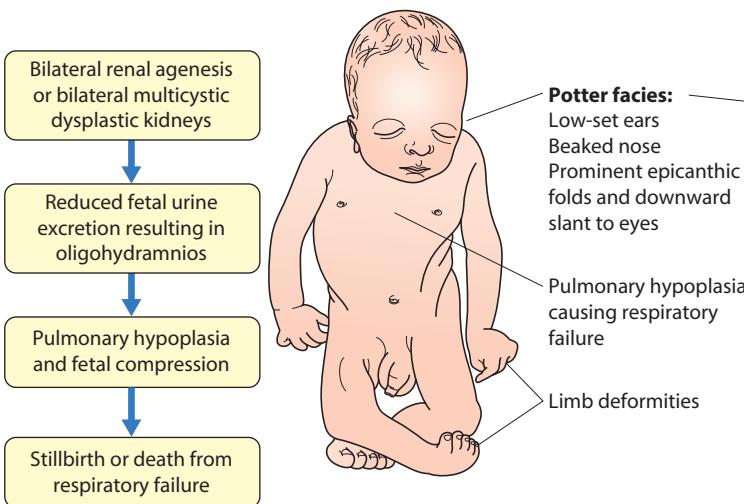


Figure 19.1b Facies in Potter sequence.

Figure 19.1a Features of Potter sequence. Intrauterine compression of the fetus from oligohydramnios caused by lack of fetal urine causes a characteristic facies, lung hypoplasia, and postural deformities including severe talipes. The infant may be stillborn or die soon after birth from respiratory failure.

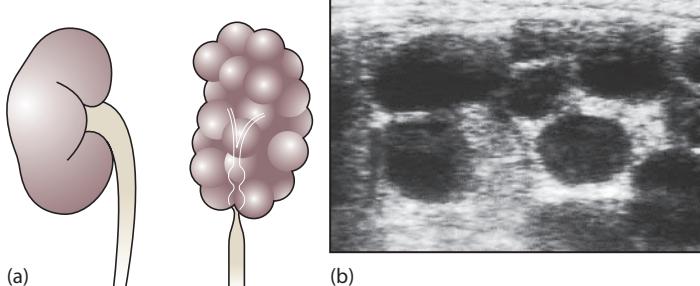


Figure 19.2 (a) Normal left kidney and multicystic dysplastic kidney (MCDK) on right. The kidney is replaced by cysts of variable size, with atresia of the ureter; and (b) renal ultrasound showing multiple discrete cysts of variable size.

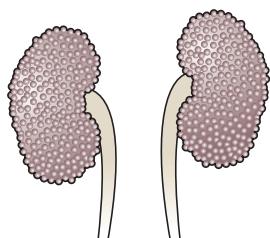


Figure 19.3 Autosomal recessive polycystic kidney disease (ARPKD). There is diffuse bilateral enlargement of both kidneys.

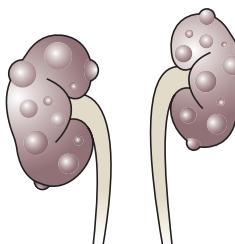


Figure 19.4 Autosomal dominant polycystic kidney disease (ADPKD). There are bilateral separate cysts of varying size between normal renal parenchyma. The kidneys are enlarged.

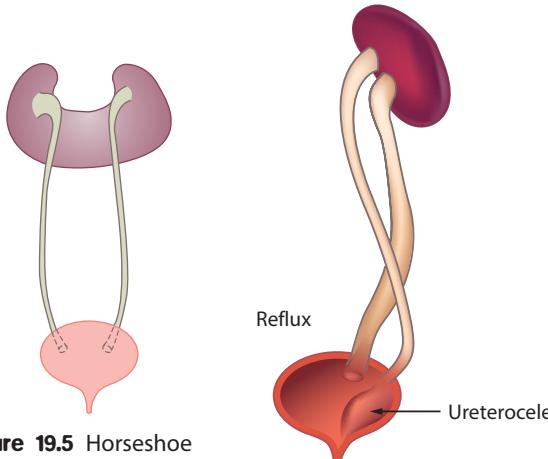


Figure 19.5 Horseshoe kidney.

Figure 19.6 Duplex kidney showing ureterocele of upper moiety and reflux into lower pole moiety.



Figure 19.7 Prune-belly syndrome (absent musculature syndrome). The name arises from the wrinkled appearance of the abdomen. It is associated with a large bladder, dilated ureters, and cryptorchidism. (Courtesy of Jane Deal.)

Urinary tract obstruction

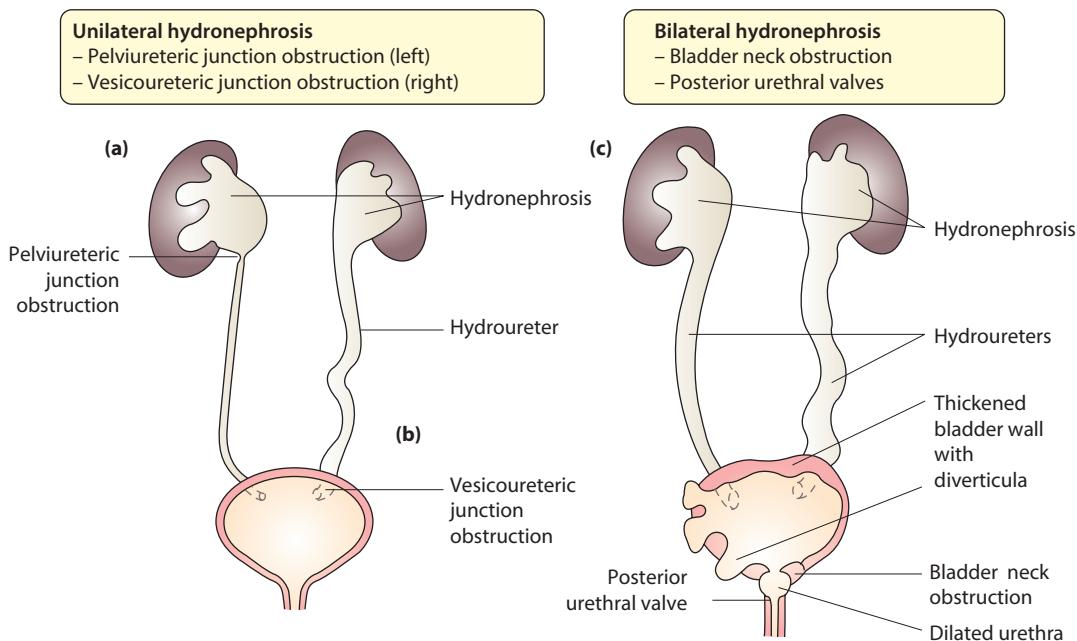


Figure 19.8 Obstruction to urine flow results in dilatation of the urinary tract proximal to the site of obstruction. Obstruction may be at the pelviureteric (labeled **a**) or vesicoureteric junction (labeled **b**) causing unilateral hydronephrosis, or at the bladder neck or urethra (labeled **c**) causing bilateral hydronephrosis.

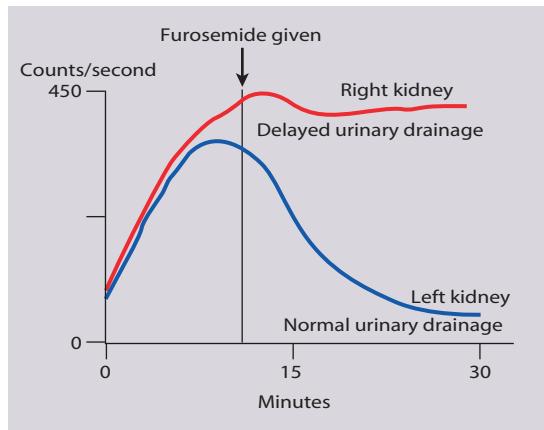


Figure 19.9 Graph from dynamic nuclear medicine scan MAG3 showing delayed excretion from a pelviureteric junction obstruction.

multicystic dysplastic kidney, in these disorders some or normal renal function is maintained but both kidneys are always affected. ADPKD has an incidence of 1 in 1000; the main symptoms in childhood are hypertension, and it causes chronic kidney disease requiring renal replacement in late adulthood. It is associated with several extra-renal features including cysts in the liver and pancreas, cerebral aneurysms, and mitral valve prolapse.

A *pelvic kidney* or a *horseshoe kidney* (Fig. 19.5), when the lower poles are fused in the midline, result from abnormal caudal migration of the kidneys. The abnormal position may predispose to infection or obstruction of urinary drainage.

Duplex kidneys can vary from simply a bifid renal pelvis to complete division with two ureters. These ureters may have an abnormal drainage so that the ureter from the lower pole moiety often refluxes, whereas the upper pole ureter may drain ectopically into the urethra or vagina or may prolapse into the bladder (ureterocele) and urine flow may be obstructed (Fig. 19.6).

Failure of fusion of the infraumbilical midline structures results in exposed bladder mucosa (*bladder extrophy*). Absence or severe deficiency of the anterior abdominal wall muscles is frequently associated with a large bladder and dilated ureters (*megacystis-megaureter*) and cryptorchidism, the *prune-belly syndrome* (Fig. 19.7).

Urinary tract obstruction

Obstruction to urine flow may occur at the pelvi-ureteric or vesicoureteric junction, at the bladder neck (e.g. due to disruption of the nerve supply, neuropathic bladder), or at the posterior urethra in a boy due to mucosal folds or a membrane, known as posterior urethral valves. The consequences of obstruction to urine flow are shown in [Figure 19.8](#) and [Figure 19.9](#). At worst, this results in a dysplastic kidney which is poorly functioning, and may contain cysts. In the most severe and bilateral cases Potter sequence is present. Renal dysplasia can also occur in association with severe intrauterine vesicoureteric reflux (VUR), in isolation, or associated with rare syndromes affecting multiple systems, e.g. VACTERL (vertebral, anorectal, cardiac, tracheoesophageal fistula, oesophageal atresia, renal and limb abnormalities).

Postnatal management

An example of a protocol for infants with antenatally diagnosed anomalies is shown in [Fig. 19.10](#). Prophylactic antibiotics may be started at birth to try to prevent urinary tract infection (UTI), although practice varies between centres. As the newborn kidney has a low GFR, urine flow is low and mild outflow obstruction may not be evident in the first few days of life. The ultrasound scan should therefore be delayed for a few weeks. However, bilateral hydronephrosis in a male infant warrants investigations

including an ultrasound and micturating cystourethrogram (MCUG) shortly after birth to exclude posterior urethral valves, which always requires urological intervention such as cystoscopic ablation ([Case history 19.1](#)).

Vesicoureteric reflux

VUR is a developmental anomaly of the vesicoureteric junctions. The ureters are displaced laterally and enter directly into the bladder rather than at an angle, with a shortened or absent intramural course. Severe cases may be associated with renal dysplasia. It may be familial (30%–50% in first-degree relatives), occur temporarily after a urinary tract infection (UTI) or occur with bladder pathology, e.g. a neuropathic bladder or urethral obstruction. Its severity varies significantly ([Fig. 19.12](#)). Mild reflux often resolves with age, but VUR that is severe enough to cause dilatation of the ureter may have significant long-term impact:

- Urine returning to the bladder from the ureters after voiding results in incomplete bladder emptying, which encourages infection.
- The kidneys may become infected (pyelonephritis) if reflux is severe enough to reach the kidney.
- Bladder voiding pressure is transmitted to the renal papillae which may contribute to renal damage if voiding pressures are high.

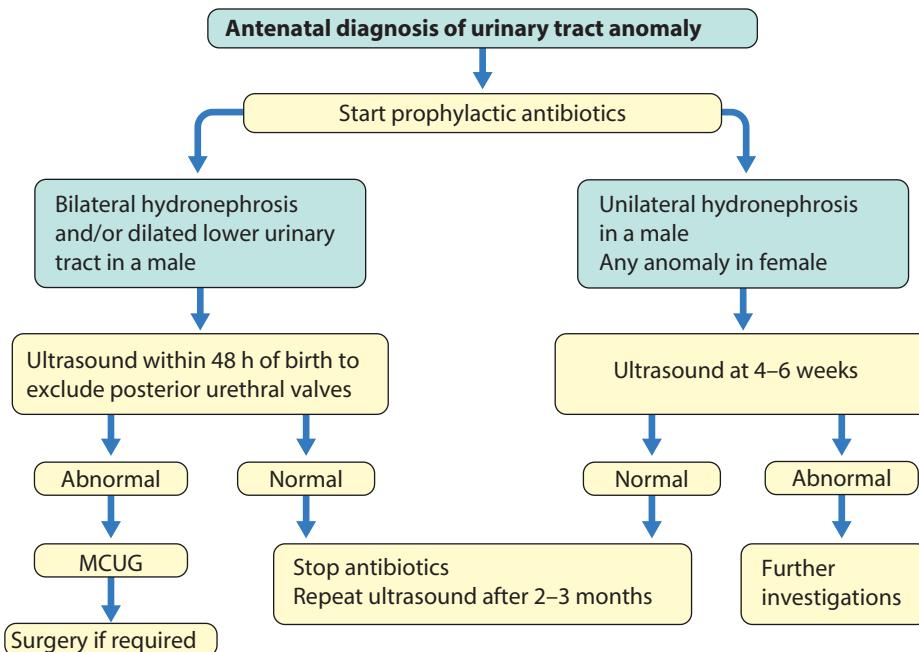


Figure 19.10 An example of a protocol for the management of infants with antenatally diagnosed urinary tract anomalies. MCUG, micturating cystourethrogram.



Case history 19.1

Posterior urethral valves

Bilateral hydronephrosis was noted on antenatal ultrasound at 20 weeks' gestation in a male fetus. There was progressive hydronephrosis, poor renal growth with reduced renal cortex, and decreasing volume of amniotic fluid on repeated scans (Fig. 19.11a). After birth, a urethral catheter was inserted and prophylactic antibiotics were started. An urgent ultrasound showed bilateral hydronephrosis with small dysplastic kidneys and cyst formation. A micturating cystourethrogram showed severe, bilateral vesicoureteric reflux, a small thickened bladder, and a dilated posterior urethra (Fig. 19.11b). Posterior urethral

valves were confirmed on cystoscopy and ablated surgically. Subsequent progress of the patient, called Caden, is described in Case history 19.4.



Bilateral hydronephrosis in a male infant requires urgent investigation to exclude posterior urethral valves.

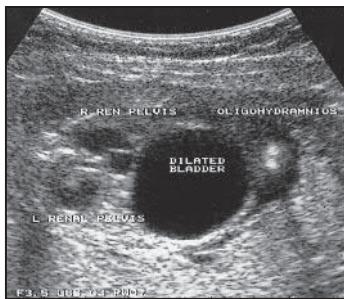


Figure 19.11a Antenatal ultrasound scan in an infant with urinary outflow obstruction from posterior urethral valve. (Courtesy of Karl Murphy.)

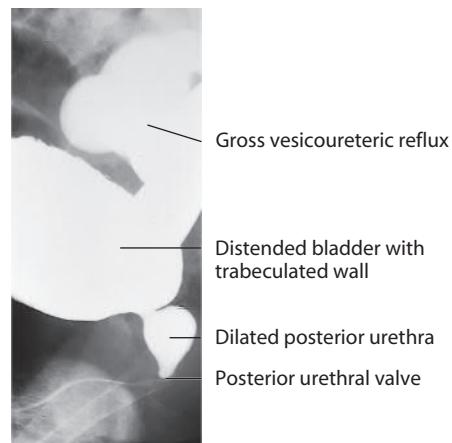


Figure 19.11b Micturating cystourethrogram (MCUG) in the same patient.

Infection may damage renal tissue, leaving a 'scar', resulting in a shrunken, poorly functioning segment of kidney (reflux nephropathy). If scarring is bilateral and severe, progressive chronic kidney disease may develop. Progressive scarring needs an assessment of the bladder and may be an indication for surgical intervention. There is increased risk of hypertension in childhood or early adult life, which is estimated to be up to 10%.

Urinary tract infection (UTI)

About 3%–7% of girls and 1%–2% of boys have at least one symptomatic UTI before the age of 6 years, and 12%–30% of them have a recurrence within a year. UTI may involve the kidneys (pyelonephritis), when it is usually associated with fever and systemic involvement, or may be due to cystitis, when there may be no fever. UTI in childhood is important because:

- up to half of patients have a structural abnormality of their urinary tract
- pyelonephritis may damage the growing kidney by forming a scar, predisposing to hypertension and to progressive chronic kidney disease if the scarring is bilateral.

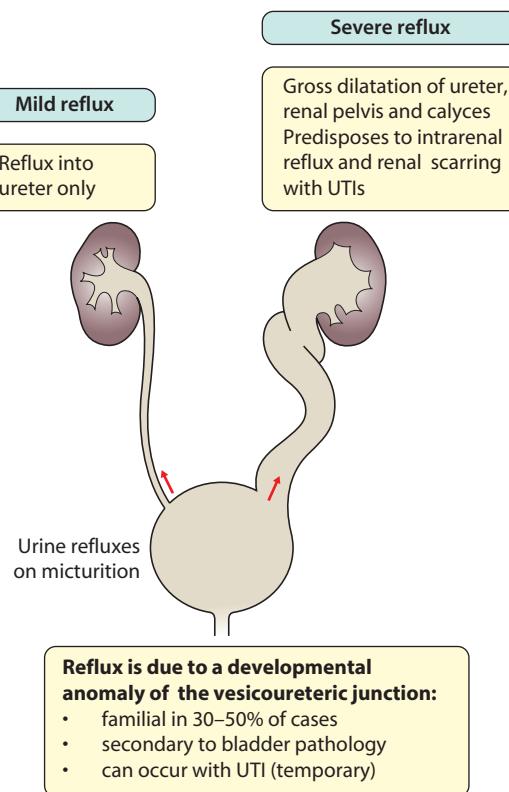


Figure 19.12 Vesicoureteric reflux.

There are NICE (National Institute for Health and Care Excellence) guidelines on UTI in children, updated in 2017.

Clinical features

Presentation of UTI varies with age (Box 19.1). In infants, symptoms are non-specific; fever is usually but not always present, and septicaemia may develop rapidly. As infants and toddlers cannot articulate their symptoms, the classical symptoms of dysuria, frequency, and loin pain only become evident with increasing age. Serious illness from septicaemia is described in Chapter 6 (Paediatric emergencies). Dysuria alone is usually due to cystitis, or vulvitis in girls or balanitis in boys. Dysuria can also be secondary to bladder neck compression from constipation. Symptoms suggestive of a UTI may also occur following sexual abuse.

Collection of samples

The most common error in the management of UTI in children, and especially in infants, is failure to establish

Box 19.1 Presentation of urinary tract infection in infants and children

Infants	Children
• Fever	• Dysuria, frequency and urgency
• Vomiting	• Abdominal pain or loin tenderness
• Lethargy or irritability	• Fever with or without rigors (exaggerated shivering)
• Poor feeding/faltering growth	• Lethargy and anorexia
• Jaundice	• Vomiting, diarrhoea
• Septicaemia	• Haematuria
• Offensive urine	• Offensive/cloudy urine
• Febrile seizure (>6 months)	• Febrile seizure
	• Recurrence of enuresis

the diagnosis properly in the first place. If the diagnosis of a UTI is not made, the opportunity to prevent renal damage may be missed. UTI is also easily overdiagnosed by overzealous interpretation of urine dipstick results and contamination of urine samples on collection; this results in unnecessary treatment and investigation.

For the child in nappies, urine can be collected by:

- a 'clean-catch' sample into a waiting clean pot when the nappy is removed. This is the recommended method. The child can be encouraged to pass urine by gently rubbing their lower abdomen with gauze, soaked in cold water (sometimes called the 'Quick-wee technique') (Fig. 19.13).
- an adhesive plastic bag applied to the perineum after careful washing, although there may be contamination from the skin or faeces
- a urethral catheter if there is urgency in obtaining a sample and no urine has been passed
- suprapubic aspiration, when a fine needle attached to a syringe is inserted directly into the bladder just above the symphysis pubis under ultrasound guidance; it may be used in severely ill infants requiring urgent diagnosis and treatment, but it is an invasive procedure, and rarely used.

In the older child, urine can be obtained by collecting a midstream sample. Careful cleaning and collection are necessary, as contamination with both white cells and bacteria can occur from under the foreskin in boys, and from reflux of urine into the vagina during voiding in girls.

Ideally, the urine sample should be observed under a microscope to identify organisms and cultured straight away. This is indicated in all infants and children under the age of 3 years with a suspected UTI. If this is not possible, the urine sample should be refrigerated to prevent the overgrowth of contaminating bacteria. Urinary white cells are not a reliable feature of a UTI, as they may lyse during storage and may be present in febrile children without a UTI and in children with balanitis or vulvovaginitis. Dipsticks can be used as a screening test. Urine culture should still be performed if a UTI is suspected unless both leukocyte esterase and nitrite are negative, as this makes a UTI unlikely. Urine culture should be performed if the clinical symptoms and dipstick tests do not correlate (Table 19.2).

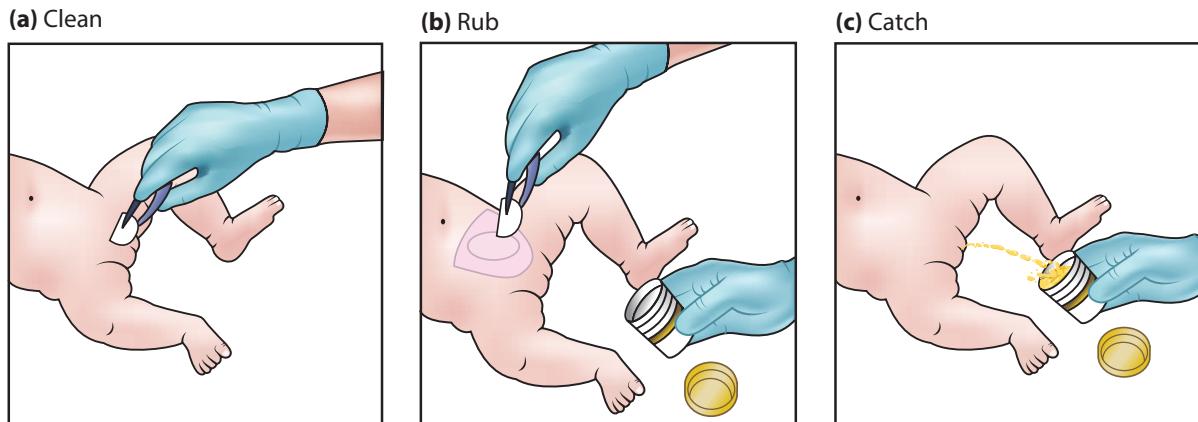


Figure 19.13 A method to obtain a 'clean-catch' sample of urine in infants and toddlers (the Quick-wee technique).

Table 19.2 Interpretation of results of dipstick testing in children 3 years and older

Leukocyte esterase and nitrite positive	Regard as UTI
Leukocyte esterase negative and nitrite positive	Start antibiotic treatment if clinical evidence of UTI
Leukocyte esterase positive and nitrite negative	Diagnosis depends on urine culture
Leukocyte esterase and nitrite negative	Only start antibiotic treatment if clinical evidence of UTI
Blood, protein, and glucose present on stick testing	Diagnosis depends on urine culture
	UTI unlikely. Repeat or send urine for culture if clinical history suggests UTI
	Useful in any unwell child to identify other diseases, e.g. nephritis, diabetes mellitus, but will not discriminate between children with and without UTIs

A bacterial culture of more than 10^5 colony-forming units (CFU) of a single organism per millilitre in a properly collected specimen gives a 90% probability of infection. If the same result is found in a second sample, the probability rises to 95%. A growth of mixed organisms usually represents contamination, but if there is doubt, another sample should be collected. Any bacterial growth of a single organism per millilitre in a catheter sample or suprapubic aspirate is considered diagnostic of infection.



A urine sample should be tested in all infants with an unexplained fever $>38^\circ\text{C}$.

Bacterial and host factors that predispose to infection

Infecting organism

UTI is usually the result of bowel flora entering the urinary tract via the urethra, although it can be haemogenous, e.g. in the newborn. The most common organism is *Escherichia coli*, followed by *Klebsiella*, *Proteus*, *Pseudomonas*, and *Enterococcus faecalis*. *Proteus* infection is more commonly diagnosed in boys than in girls, possibly because of its presence under the prepuce. *Proteus* infection predisposes to the formation of phosphate stones by splitting urea to ammonia, and thus alkalinizing the urine. *Pseudomonas* infection may indicate the presence of some structural abnormality in the urinary tract affecting drainage, and it is also more common in children with plastic catheters and ureteric stents.

Host factors

The risk of infection is increased by:

- antenatally diagnosed renal or urinary tract abnormality including VUR. If urinary tract abnormality was not identified on antenatal screening or was not followed-up, it will be identified when investigations are performed.
- incomplete bladder emptying – may be because of constipation, infrequent voiding, resulting in bladder enlargement, neuropathic bladder or vesicoureteric reflux.

Investigation

Infants presenting with a first UTI should have an ultrasound to identify:

- serious structural abnormalities and urinary obstruction
- renal defects (although it is not the gold standard for detecting renal scars).

The extent to which a child with a UTI should have further investigations is controversial. This is not only because of the invasive nature and radiation burden of the tests but also because of the lack of an evidence base to show that investigation improves outcome (unless urinary obstruction is demonstrated). Mild VUR usually resolves spontaneously and operative intervention to stop mild VUR has not been shown to decrease renal damage. There has, therefore, been a move away from extensive investigation of all children with UTIs, focusing on children who have recurrent UTIs or those associated with atypical features which include:

- seriously ill or septicaemia
- poor urine flow
- abdominal or bladder mass
- raised creatinine
- failure to respond to suitable antibiotics within 48 hours
- infection with atypical (non-*E. coli*) organisms.

If urethral obstruction is suspected on ultrasound (abnormal bladder in a boy), MCUG should be performed promptly. Functional scans (i.e. DMSA or MAG-3) should be deferred for 3 months after a UTI, unless the ultrasound is suggestive of obstruction, to avoid missing a newly developed scar and because of false-positive results from transient inflammation. The need for any investigations in a child with only bladder symptoms (lower UTI/cystitis) is also controversial.

Management

- All infants under 3 months of age with suspicion of a UTI or if seriously ill should be referred immediately to hospital. They require intravenous antibiotic therapy (e.g. co-amoxiclav) for at least

5–7 days followed by oral prophylaxis ([Case history 19.2](#)).

- Infants aged over 3 months and children with acute pyelonephritis/upper UTI (bacteriuria and fever $\geq 38^\circ\text{C}$ or bacteriuria and loin pain/tenderness even if fever is $<38^\circ\text{C}$) are treated with intravenous antibiotics if there is concern about sepsis or with oral antibiotics (e.g. trimethoprim for 7 days). If intravenous antibiotics are used, this is usually for 2–4 days followed by oral antibiotics for a total of 7–10 days. The choice of antibiotic is adjusted according to sensitivity on urine culture, for example *Enterococcus* spp. are often resistant to cephalosporins.
- Children with cystitis/lower UTI (dysuria but no systemic symptoms or signs) can be treated with oral antibiotics such as trimethoprim or nitrofurantoin for a shorter course, e.g. 5 days.

Medical measures for the prevention of UTI

The aim is to ensure washout of organisms that ascend into the bladder from the perineum; and to reduce the

presence of aggressive organisms in the stool, perineum, and under the foreskin:

- high fluid intake to produce a high urine output
- regular voiding
- ensure complete bladder emptying by encouraging the child to try a second time to empty his bladder after a minute or two, commonly known as double voiding, which empties any urine residue or refluxed urine returning to the bladder
- treatment and/or prevention of constipation
- good perineal hygiene
- *Lactobacillus acidophilus*, a probiotic to encourage colonization of the gut by this organism and reduce the number of pathogenic organisms that might potentially cause invasive disease
- antibiotic prophylaxis. This is controversial as evidence that giving antibiotic prophylactically to prevent infection is better than prompt treatment is lacking. They are often given in children under 2 years to 3 years of age with a congenital abnormality of the kidneys or urinary tract, following an upper UTI or those with severe reflux until out of nappies. Low-dose trimethoprim is used most often, but nitrofurantoin or cephalexin may be given. Broad-spectrum, poorly absorbed antibiotics such as amoxicillin should be avoided.



Case history 19.2

Urinary tract infection

Jack, a 2-month-old infant, stopped feeding and had a high, intermittent fever. He was referred to hospital, where he had an infection screen. Urine microscopy showed more than 100 white blood cells and cultured more than 10^5 *E. coli* CFU/ml. He was treated with intravenous antibiotics. An ultrasound showed that the left kidney was smaller than the right kidney with dilated ureters. He was started on prophylactic antibiotics. A DMSA (dimercaptosuccinic acid) scan ([Fig. 19.14](#)) performed 3 months later confirmed bilateral renal scarring, with the left kidney

contributing 33% of renal function. The MCUG ([Fig. 19.15](#)) showed bilateral vesicoureteric reflux. At 4 years of age, the reflux had resolved and antibiotic prophylaxis was stopped. His blood pressure, urine protein-to-creatinine ratio, and renal growth and function continue to be monitored in clinic.

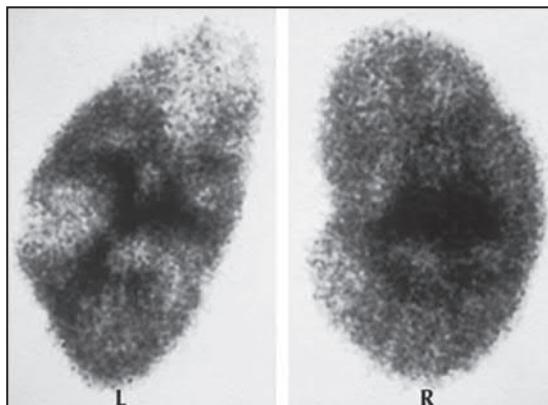


Figure 19.14 DMSA (dimercaptosuccinic acid) scan showing bilateral renal scarring, more severe on left upper pole.



Figure 19.15 Micturating cystourethrogram (MCUG) showing bilateral vesicoureteric reflux with ureteric dilatation and dilated clubbed calyces on the right.

Follow-up of children with recurrent UTIs, renal scarring, or reflux

In these children:

- Urine should be dipsticked with any non-specific illness in case it is caused by a UTI and urine sent for microscopy and culture if suggestive of UTI.
- Consider prophylactic oral antibiotics to reduce infections although breakthrough infection can still occur.
- Circumcision in boys may sometimes be considered as there is evidence that it reduces the incidence of UTI.
- Bladder urodynamics assessment can detect incomplete bladder emptying or neuropathic bladder which may require intermittent clean catheterization to reduce risk of infections.
- Anti-VUR surgery may be indicated if there is progression of scarring with ongoing higher grade VUR.
- Blood pressure should be checked annually if renal dysplasia and scars are present.
- Urinalysis is performed to check for proteinuria which is indicative of progressive chronic kidney disease.
- Regular assessment of renal growth and function is necessary if there are bilateral defects because of the risk of progressive chronic kidney disease.

Enuresis

Primary nocturnal enuresis

This is considered in [Chapter 24](#) (Child and adolescent mental health).

Daytime enuresis

This is a lack of bladder control during the day in a child old enough to be continent (over the age of 3–5 years). Nocturnal enuresis is also usually present. It may be caused by:

- lack of attention to bladder sensation: a manifestation of a developmental or behavioural problem, although it may occur in otherwise normal children who are too preoccupied with what they are doing to respond to the sensation of a full bladder
- detrusor instability (sudden, urgent urge to void induced by sudden bladder contractions)
- bladder neck weakness
- a neuropathic bladder (bladder is enlarged and fails to empty properly, irregular thick wall, and is associated with spina bifida and other neurological conditions)
- a UTI (rarely in the absence of other symptoms)

Summary

A 2-year-old child with a urinary tract infection

Why important?

Up to half have a structural abnormality of their urinary tract
Pyelonephritis may damage the growing kidney by forming a renal scar, which may result in hypertension and chronic kidney disease

Diagnosis secure?

- Suggestive clinical features?
- Upper or lower urinary tract infection?
- Urine sample properly collected and processed?
- Culture of single organism $>10^5/\text{ml}$ if clean catch or mid-stream urine or else any organisms on suprapubic aspirate or catheter sample?

Predisposing factors?

Incomplete bladder emptying
Constipation
Vesicoureteric reflux

Why investigate?

To identify serious structural abnormalities, urinary obstruction, renal scars, vesicoureteric reflux

What investigation?

- Ultrasound of kidneys and urinary tract
- Further investigations if atypical features or urethral obstruction in boy on ultrasound

Management

Treat infection with antibiotics:

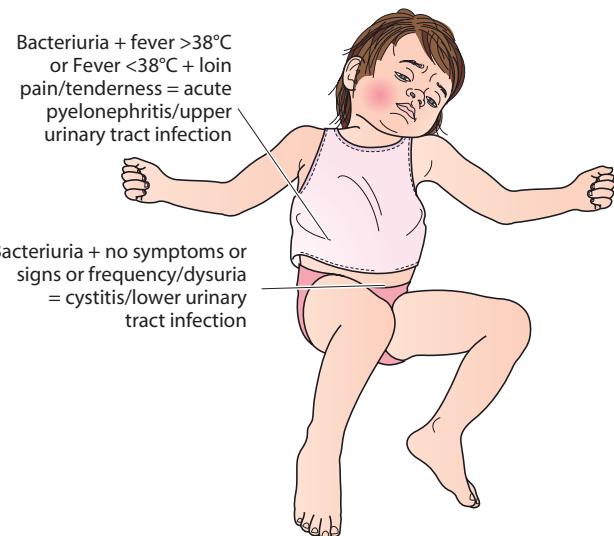
- Upper UTI and sepsis – IV then oral
- No sepsis or lower UTI – oral

Advice about medical preventative measures to consider:

- High fluid intake
 - Regular voiding, double micturition
 - Prevent or treat constipation
 - Good perineal hygiene
 - *Lactobacillus acidophilus*
- Advise to check urine culture if develops clinical features suggestive of non-specific illness

If renal scarring or reflux on investigation, or develops recurrent UTIs:

- Consider low-dose antibiotic prophylaxis
- Monitor blood pressure, renal growth



- constipation
- an ectopic ureter causes constant dribbling and child is always damp.

Examination may reveal evidence of a neuropathic bladder, i.e. the bladder may be distended, there may be abnormal perineal sensation and anal tone, or abnormal leg reflexes and gait. Sensory loss in the distribution of the S2, S3, and S4 dermatomes should be sought. A spinal lesion may be present. Girls who are dry at night but wet on getting up are likely to have pooling of urine from an ectopic ureter opening into the vagina.

A urine sample should be dipsticked and, if abnormal, sent for microscopy, culture, and sensitivity. Other investigations are performed if indicated. An ultrasound may show bladder pathology, with incomplete bladder emptying or thickening of the bladder wall. Urodynamic studies may be required. An X-ray of the spine may reveal a vertebral anomaly. An MRI scan may be required to confirm or exclude a spinal defect such as tethering of the cord.

Affected children in whom a neurological cause has been excluded may benefit from star charts, bladder training, and pelvic floor exercises. Constipation should be treated. A small portable alarm with a pad in the pants, which is activated by urine, can be used when there is lack of attention to bladder sensation. Anticholinergic drugs, such as oxybutynin, to dampen down bladder contractions, may be helpful if other measures fail.

Secondary (onset) nocturnal enuresis

The loss of previously achieved urinary continence may be due to:

- emotional upset, which is the most common cause
- UTI
- polyuria from an osmotic diuresis in diabetes mellitus or a renal concentrating disorder, e.g. sickle cell disease or chronic kidney disease or very rarely diabetes insipidus, which can be central or nephrogenic.

Investigation should include:

- testing a urine sample for infection, glycosuria, and proteinuria using a dipstick
- assessment of urinary concentrating ability by measuring the osmolality of an early morning urine sample. Rarely, a formal water deprivation test may be needed to exclude a urinary concentrating defect
- ultrasound of the renal tract.

Summary

Enuresis

Daytime enuresis

- Consider possible causes: developmental or behavioural, bladder instability or neuropathy, UTI, constipation, ectopic ureter.

Secondary (onset) enuresis

- Consider – emotional upset, UTI, polyuria from an osmotic diuresis in diabetes mellitus or a renal concentrating disorder.

Proteinuria

Transient proteinuria may occur during febrile illnesses or after exercise and does not require investigation. Persistent proteinuria is significant and should be quantified by measuring the urine protein-to-creatinine ratio in an early morning sample (normal protein-to-creatinine ratio <20 mg/mmol).

A common cause is orthostatic (postural) proteinuria when proteinuria is only found when the child is upright during the day. It can be diagnosed by measuring the urine protein-to-creatinine ratio in a series of early morning urine specimens. The prognosis is excellent and further investigations are not necessary. Other causes of proteinuria, which need further evaluation, are listed in [Box 19.2](#).

Nephrotic syndrome

In nephrotic syndrome, heavy proteinuria results in a low plasma albumin and oedema. The cause of most cases of primary childhood nephrotic syndrome is unknown, but a few cases are secondary to systemic diseases such as Henoch-Schönlein purpura and other vasculitides, e.g. SLE (systemic lupus erythematosus), infections (e.g. malaria) or allergens (e.g. bee sting). Clinical signs of the nephrotic syndrome are:

- periorbital oedema (particularly on waking), often the earliest sign
- scrotal or vulval, leg, and ankle oedema ([Fig. 19.16](#))
- ascites
- breathlessness due to pleural effusions and abdominal distension
- infection such as peritonitis, septic arthritis, or sepsis due to loss of protective immunoglobulins in the urine.

[Case history 19.3](#) shows typical presentation, and initial investigations are listed in [Box 19.3](#).

Box 19.2 Causes of proteinuria

- Orthostatic proteinuria
- Glomerular abnormalities
 - Nephrotic syndrome
 - Glomerulonephritis
 - Abnormal glomerular basement membrane
- Increased glomerular filtration pressure
- Reduced renal mass in chronic kidney disease
- Hypertension
- Tubular proteinuria



Figure 19.16 Gross oedema of the scrotum and legs as well as abdominal distension from ascites.



Case history 19.3

Nephrotic syndrome

Zakariya developed periorbital oedema (Fig. 19.17) which improved during the day. He was seen by several doctors who diagnosed allergy, conjunctivitis, and hay fever. When he developed ascites and bilateral leg oedema his urine was dipsticked and showed 4+ protein and nephrotic syndrome was diagnosed. Periorbital oedema is often the initial sign of nephrotic syndrome but diagnosis is often delayed until other complications develop. Investigations performed are

Box 19.3 Investigations performed at presentation of nephrotic syndrome

- Urine protein – on test strips (dipstick) to confirm heavy proteinuria ($\geq 3+$ protein)
- Full blood count to assess whether there is an infection. Also a high haemoglobin suggests intravascular fluid depletion
- Urea, electrolytes, creatinine, albumin
Hyponatraemia is common in presentation of nephrotic syndrome. Intravascular fluid depletion is indicated by high urea and/or creatinine
- Complement levels – C3, C4 to differentiate from other causes of proteinuria such as postinfectious glomerulonephritis, when C3 will be low, or SLE, when both C3 and C4 are low
- Antistreptolysin O or anti-DNAse B titres and throat swab to differentiate from poststreptococcal glomerulonephritis
- Urinary sodium concentration which can be helpful to indicate intravascular fluid depletion if low ($<10 \text{ mmol/L}$) in a child who is oedematous
- Hepatitis B and hepatitis C screen to detect secondary causes of nephrotic syndrome caused by hepatitis B and C viruses. This will also alter the treatment
- Malaria screen if recent travel abroad as may cause nephrotic syndrome

listed in Box 19.3. He is most likely to have steroid-responsive nephrotic syndrome, and the clinical course is outlined in Fig. 19.18.



Figure 19.17 Facial oedema in nephrotic syndrome which improves during the day and is often misdiagnosed as an allergy.

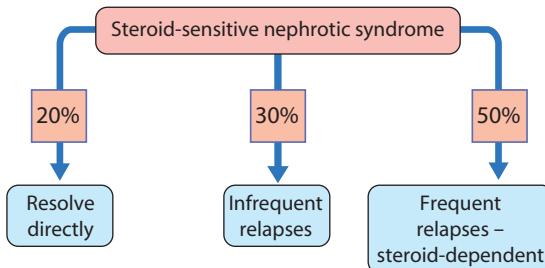


Figure 19.18 Clinical course in steroid-responsive nephrotic syndrome.



Periorbital oedema – is it nephrotic syndrome?

Steroid-sensitive nephrotic syndrome

In 85%–90% of children with nephrotic syndrome, the proteinuria resolves with corticosteroid therapy (steroid-sensitive nephrotic syndrome; see Fig. 19.18). These children do not progress to chronic kidney disease. It is more common in boys than in girls, in Asian children than in Caucasians, and there is an association with atopy. It is often precipitated by respiratory infections. Features suggesting steroid-sensitive nephrotic syndrome are:

- age between 1–10 years
- no macroscopic haematuria
- normal blood pressure
- normal complement levels
- normal renal function.

Management

The most widely used protocol is to initially give oral corticosteroids (60 mg/m^2 per day of prednisolone), unless there are atypical features. After 4 weeks, the dose is reduced to 40 mg/m^2 on alternate days for 4 weeks and then weaned or stopped. The median time for the urine to become free of protein is 11 days. Extending the duration of corticosteroid therapy does not reduce the relapse rate. Children who do not respond to 4–6 weeks of corticosteroid therapy or have atypical features may have a more complex diagnosis and require a renal biopsy. Renal histology in steroid-sensitive nephrotic syndrome is usually normal on light microscopy but fusion of the specialized epithelial cells that invest the glomerular capillaries (podocytes) is seen on electron microscopy. For this reason, it is called minimal change disease.

The child with nephrotic syndrome is susceptible to several serious complications at presentation or relapse:

- Hypovolaemia – during the initial phase of oedema formation, the intravascular compartment may

- become volume depleted. The child who becomes hypovolaemic characteristically complains of abdominal pain and may feel faint. There is peripheral vasoconstriction and urinary sodium retention. A low urinary sodium (<10 mmol/L) and a high haemoglobin concentration or packed cell volume of red blood cells are indications of hypovolaemia, which requires urgent treatment with intravenous fluid (0.9% saline or 4.5% albumin solution) as the child is at risk of vascular thrombosis and shock. Increasing peripheral oedema, assessed clinically and by daily weight, may cause discomfort and respiratory compromise. If severe, this may need treatment with intravenous 20% albumin infusion with furosemide. Care must be taken with the use of 20% albumin as it may precipitate pulmonary oedema and hypertension from fluid overload, and also with diuretics, which may cause or worsen hypovolaemia.
- *Thrombosis* – a hypercoagulable state, due to urinary losses of antithrombin III, thrombocytosis which may be exacerbated by steroid therapy, increased synthesis of clotting factors, and increased blood viscosity from the raised haematocrit, all predispose to thrombosis. This may affect the lungs, brain, limbs, and splanchnic circulation with potentially catastrophic results.
 - *Infection* – children in relapse are at risk of infection with encapsulated bacteria, especially *Pneumococcus*. Spontaneous peritonitis may occur. Pneumococcal and seasonal influenza vaccination is recommended. Penicillin prophylaxis is used whilst the child is in relapse (i.e. heavily proteinuric due to immunoglobulin urinary losses along with albumin). Chickenpox and shingles should be treated with aciclovir.
 - *Hypercholesterolaemia* – this correlates inversely with the serum albumin, but the cause of the hyperlipidaemia is not fully understood.

Prognosis

This is summarized in Fig. 19.18. Relapses are identified by parents on urine testing. The side-effects of corticosteroid therapy may be reduced by an alternate-day

regimen. If relapses are frequent, or if a high maintenance dose is required, involvement of a paediatric nephrologist is advisable as steroid-sparing agents may be considered to enable reduction in steroid use. Possible steroid-sparing agents include the immunomodulator levamisole, the immunosuppressant mycophenolate mofetil, calcineurin inhibitors such as tacrolimus and for difficult cases the anti-CD20 B-cell monoclonal antibody rituximab.

Steroid-resistant nephrotic syndrome

These children should be referred to a paediatric nephrologist (Table 19.3) as a renal biopsy is indicated. Management of the oedema is by diuretic therapy, salt restriction, angiotensin-converting enzyme inhibitors, and sometimes nonsteroidal anti-inflammatory drugs, which may reduce proteinuria. Up to 30% have mutations in genes involved in podocyte function in the glomerular basement membrane. Genetic testing is recommended as it assists in management decisions.

Congenital nephrotic syndrome

Congenital nephrotic syndrome presents in the first 3 months of life. It is rare. The most common kind is recessively inherited and the gene frequency is particularly high in Finland. In the UK, it is more common in consanguineous families. Genetic testing is recommended as over 70% have an underlying genetic defect. Traditionally, this condition has been associated with high mortality, usually due to complications of hypoalbuminaemia, but with intensive nutritional management, complications are now related to progressive chronic kidney disease. The albuminuria is so severe that unilateral nephrectomy may be necessary for its control, followed by dialysis for severe chronic kidney disease, which is continued until the child is no longer nephrotic and is old enough for renal transplantation. However, some children have milder disease and may not need renal replacement in childhood.



An oedematous child – test for proteinuria to check for nephrotic syndrome.

Table 19.3 Steroid-resistant nephrotic syndrome

Cause	Specific features	Prognosis
Focal segmental glomerulosclerosis	Most common Familial or idiopathic	30% progress to stage 5 chronic kidney disease; 20% respond to tacrolimus, or rituximab Recurrence post-transplant is common
Mesangiocapillary glomerulonephritis (membranoproliferative glomerulonephritis)	More common in older children Haematuria and low complement level present	Decline in renal function over many years Treated with ACE inhibitors and/or immunosuppression with mycophenolate mofetil
Membranous nephropathy	Associated with hepatitis B May precede SLE (systemic lupus erythematosus)	Most remit spontaneously within 5 years

Summary

Nephrotic syndrome

- Clinical signs: oedema – periorbital, scrotal or vulval, leg, and ankle; ascites; pleural effusions.
- Diagnosis: heavy proteinuria and low plasma albumin.

Steroid-sensitive nephrotic syndrome

- Characteristic features: 1–10 years old; no macroscopic haematuria; and normal blood pressure, complement levels, and renal function.
- Management: oral corticosteroids.

Steroid-resistant nephrotic syndrome

- Renal biopsy and genetic testing if unresponsive or atypical features.
- Complications: hypovolaemia, thrombosis, infection (pneumococcal), hypercholesterolaemia.
- Prognosis: may resolve or else there may be infrequent or frequent relapses.

Haematuria

Urine that is red in colour or tests positive for haemoglobin on urine sticks should be examined under the microscope to confirm haematuria (>10 red blood cells per high-power field). Glomerular haematuria is suggested by brown urine, the presence of abnormally shaped red cells (because they deform as they pass through the basement membrane), and casts, and is often accompanied by proteinuria. Lower urinary tract haematuria

is usually red, occurs at the beginning or end of the urinary stream, is not accompanied by proteinuria, and is unusual in children.

UTI is the most common cause of haematuria (Box 19.4), although this is seldom the only symptom. The history and examination may suggest the diagnosis, e.g. a family history of stone formation or nephritis or a history of trauma. A plan of investigation is outlined in Box 19.5.

A renal biopsy may be indicated if:

- there is significant persistent proteinuria
- there is recurrent macroscopic haematuria
- renal function is abnormal
- the complement levels are persistently abnormal.

Acute glomerulonephritis

The causes of acute glomerulonephritis in childhood are listed in Box 19.6. Increased glomerular cellularity restricts glomerular blood flow, and therefore glomerular filtration is decreased. This leads to:

- decreased urine output and volume overload
- hypertension, which may cause seizures
- oedema, characteristically initially periorbital
- haematuria and proteinuria.

Management is by attention to both water and electrolyte balance and the use of diuretics when necessary. Rarely, there may be a rapid deterioration in renal function (rapidly progressive glomerulonephritis). This may occur with any cause of acute glomerulonephritis, but is uncommon when the cause is poststreptococcal. If left untreated, irreversible chronic kidney disease may occur over weeks or months, so renal biopsy and subsequent treatment with immunosuppression and plasma exchange may be necessary.

Haematuria

Box 19.4 Causes of haematuria

Non-glomerular

- Infection (bacterial, viral, tuberculosis, schistosomiasis)
- Trauma to genitalia, urinary tract, or kidneys
- Stones
- Tumours
- Sickle cell disease
- Bleeding disorders
- Renal vein thrombosis
- Hypercalciuria

Glomerular

- Postinfectious glomerulonephritis
- Henoch–Schönlein purpura and all other vasculitides (see Box 19.6)
- IgA nephropathy
- Genetic disorders of collagen in basement membrane, e.g. Alport syndrome, thin basement membrane disease

Box 19.5 Investigation of haematuria

All patients

- Urine microscopy (with phase contrast) and culture
- Urinary protein:creatinine and calcium:creatinine ratios
- Kidney and urinary tract ultrasound
- Plasma urea, electrolytes, creatinine, calcium, phosphate, albumin
- Full blood count, coagulation screen, sickle cell screen

If suggestive of glomerular haematuria

- ESR, complement levels, and anti-double stranded DNA antibodies
- Throat swab and antistreptolysin O/anti-DNAse B titres
- Hepatitis B and C screen
- Renal biopsy if indicated (see text)
- Test family for blood in urine
- Hearing test (if Alport syndrome suspected)

Box 19.6 Causes of acute glomerulonephritis

- Postinfectious (including streptococcus)
- Vasculitis (Henoch–Schönlein purpura or, rarely, SLE [systemic lupus erythematosus], microscopic polyarteritis, polyarteritis nodosa)
- IgA nephropathy and mesangiocapillary glomerulonephritis
- Antiglomerular basement membrane disease (Goodpasture syndrome) – very rare

Poststreptococcal and postinfectious glomerulonephritis

Usually follows a streptococcal sore throat or skin infection and is diagnosed by evidence of a recent streptococcal infection (culture of the organism, raised ASO/anti-DNAse B titres), and low complement C3 levels that return to normal after 3–4 weeks. Long-term prognosis is good.

Henoch–Schönlein purpura

Henoch–Schönlein purpura is the combination of some of the following features:

- characteristic skin rash on extensor surfaces
- arthralgia
- periarticular oedema
- abdominal pain
- glomerulonephritis.

It usually occurs between the ages of 3 and 10 years, is twice as common in boys, peaks during the winter months, and is often preceded by an upper respiratory infection. It is postulated that genetic predisposition and antigen exposure increase circulating IgA levels and disrupt IgG synthesis. The IgA and IgG interact to produce complexes that activate complement and are deposited in affected organs, precipitating an inflammatory response with vasculitis.

Clinical findings

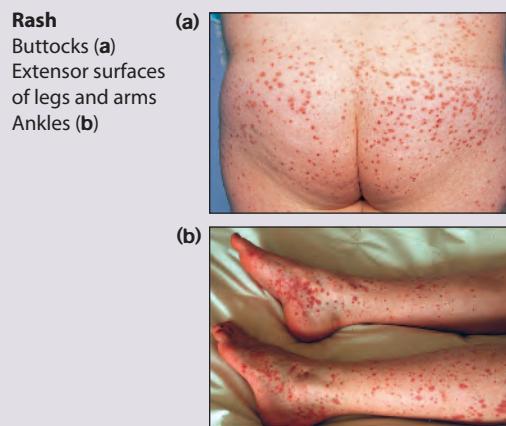
At presentation, affected children often have a fever. The *rash* is the most obvious feature (Fig. 19.19). It is symmetrically distributed over the buttocks, the extensor surfaces of the arms and legs, and the ankles. The trunk is usually spared. The rash may initially be urticarial, rapidly becoming maculopapular and purpuric, is characteristically palpable, and may recur over several weeks. The rash is the first clinical feature in about 50% and is the cornerstone of the diagnosis, which is clinical.

Joint pain occurs in two-thirds of patients, particularly of the knees and ankles. There is *periarticular oedema*. Long-term damage to the joints does not occur, and symptoms usually resolve before the rash goes.

Colicky abdominal pain occurs in many children and, if severe, can be treated with corticosteroids. Gastrointestinal involvement can cause haematemesis and melaena. Intussusception can occur and can be particularly difficult to diagnose under these circumstances. Ileus, protein-losing enteropathy, orchitis, and occasionally central nervous system involvement are other rare complications.

Renal involvement is common, but is rarely the first symptom. Over 80% have microscopic or macroscopic haematuria or mild proteinuria. These children usually

Henoch–Schönlein purpura



Joint pain and swelling

Knees and ankles (b)

Abdominal pain

Haematemesis and melaena
Intussusception

Renal

Microscopic/macrosopic haematuria (80%)
Nephrotic syndrome (rare)

Figure 19.19 Main clinical manifestations of Henoch–Schönlein purpura. (a) Rash on buttocks; and (b) rash around the extensor surfaces of the legs and slight joint swelling. (a, Courtesy of Michael Markiewicz. b, Courtesy of Tauny Southwood.)

make a complete recovery. If proteinuria is more severe, nephrotic syndrome may result. Risk factors for progressive chronic kidney disease are heavy proteinuria, oedema, hypertension, and deteriorating renal function, when a renal biopsy will determine if treatment is necessary. All children with Henoch–Schönlein purpura should be followed for a year to detect those with persisting haematuria or proteinuria (5%–10%). Children who have persistent renal involvement or required treatment for Henoch–Schönlein purpura nephritis require long-term follow-up. This is necessary as hypertension and progressive chronic kidney disease may develop after an interval of several years.

IgA nephropathy

This may present with episodes of macroscopic haematuria, commonly in association with upper respiratory tract infections. Histological findings and management are as for Henoch–Schönlein purpura, which may be a variant of the same pathological process but not restricted to the kidney. The prognosis in children is better than that in adults.

Genetic abnormalities of glomerular basement membrane

Abnormalities of the collagen in the basement membrane of the glomerulus can lead to Alport syndrome or thin basement membrane disease. This should be suspected if there is a family history of haematuria and/or chronic kidney disease due to Alport syndrome or of unknown

cause. The most common form of Alport syndrome is an X-linked recessive disorder that progresses to severe chronic kidney disease by early adult life in males and is associated with nerve deafness and ocular defects. There are also forms of Alport syndrome which are autosomal dominant or recessive. Other collagen abnormalities cause a milder phenotype and lead to thin basement membrane disease. This also requires long-term follow-up to detect proteinuria and chronic kidney disease, which can develop in later life, but is delayed if proteinuria is treated early with ACE inhibitors.

Vasculitis

The most common vasculitis to involve the kidney is Henoch–Schönlein purpura. However, renal involvement may occur in rarer vasculitides such as polyarteritis nodosa, microscopic polyarteritis, and granulomatosis with polyangiitis (formerly known as Wegener granulomatosis). Characteristic symptoms are fever, malaise, weight loss, skin rash, and arthropathy with prominent involvement of the respiratory tract in granulomatosis with polyangiitis. ANCA (antineutrophil cytoplasm antibodies) are present and diagnostic in these diseases. Renal angiogram may demonstrate the presence of aneurysms in polyarteritis nodosa. Renal involvement may be severe and rapidly progressive. Treatment is with corticosteroids, plasma exchange, and intravenous cyclophosphamide, and increasingly biological monoclonal antibody therapy.

Systemic lupus erythematosus (SLE)

SLE predominantly affects female teenagers and young adults although it can occur at any age and also in males. It is much more common in certain ethnic groups (Asian and Afro-Caribbean). It is characterized by the presence of multiple autoantibodies, including antibodies to double-stranded DNA. The C3 and C4 components of complement may be low, particularly during active phases of the disease. Haematuria and proteinuria are indications for renal biopsy, as immunosuppression is always necessary and its intensity will depend on the severity of renal involvement.

Summary

Acute glomerulonephritis

- Cause: usually postinfectious or follows a streptococcal infection, but also vasculitis (including Henoch–Schönlein purpura), IgA nephropathy, and genetic abnormalities of the glomerular basement membrane.
- Clinical features: oedema (especially around the eyes), hypertension, decreased urine output, haematuria and proteinuria.
- Management: fluid and electrolyte balance, diuretics, monitor for rapid deterioration in renal function.

Hypertension

Identification of hypertension relies on correct measurement of blood pressure (see Fig. 2.15). Blood pressure increases with age and height and readings should be plotted on a centile chart. Hypertension is blood pressure

Box 19.7 Causes of hypertension

- Renal**
 - Renal parenchymal disease
 - Renovascular, e.g. renal artery stenosis
 - Polycystic kidney disease (autosomal recessive polycystic kidney disease and autosomal dominant polycystic kidney disease)
 - Renal tumours
- Coarctation of the aorta**
- Catecholamine excess**
 - Pheochromocytoma
 - Neuroblastoma
- Endocrine**
 - Congenital adrenal hyperplasia
 - Cushing syndrome or corticosteroid therapy
 - Hyperthyroidism
- Essential hypertension**
 - A diagnosis of exclusion in children, although increasingly common especially in children who are obese and with obstructive sleep apnoea

above 95th percentile for age, height and gender (see Appendix Table A.1 or the electronic calculator <https://www.mdcalc.com/aap-pediatric-hypertension-guidelines>). Children who are overweight or obese are at increased risk. Symptomatic hypertension in children is usually secondary to renal, cardiac, or endocrine causes (Box 19.7).

Presentation includes vomiting, headaches, facial palsy, hypertensive retinopathy, seizures, or proteinuria. Faltering growth and cardiac failure are the most common features in infants. Pheochromocytoma may also cause paroxysmal palpitations and sweating.

Some causes are correctable, e.g. nephrectomy for unilateral scarring, angioplasty for renal artery stenosis, surgical repair of coarctation of the aorta, resection of a pheochromocytoma, but in most cases medical treatment is necessary with antihypertensive medications such as calcium channel blockers, ACE inhibitors and angiotensin 2 receptor blockers (ARBs).

Early detection of hypertension is important. All children with a renal tract abnormality should have their blood pressure checked annually throughout life. Children with a family history of essential hypertension should be encouraged to restrict their salt intake, avoid obesity, and have their blood pressure checked regularly.

Renal masses

An abdominal mass identified on palpating the abdomen should be investigated promptly by ultrasound scan. The causes of palpable kidneys are shown in Box 19.8. Bilaterally enlarged kidneys in early life are most frequently due to autosomal recessive polycystic kidney disease (ARPKD), which is associated with hypertension, hepatic fibrosis, and progression to chronic kidney disease. This form of polycystic kidney disease must be distinguished from ADPKD (autosomal dominant polycystic kidney disease), which has a more benign prognosis in childhood with onset of progressive chronic kidney disease in adulthood, although hypertension is found in at least 30% of affected children.

Box 19.8 Causes of palpable kidneys**Unilateral**

- Multicystic dysplastic kidney
- Compensatory hypertrophy of normal kidney
- Obstructed hydronephrosis
- Renal tumour (Wilms tumour)
- Renal vein thrombosis

Bilateral

- Autosomal recessive polycystic kidneys
- Autosomal dominant polycystic kidneys
- Tuberous sclerosis
- Renal vein thrombosis

Renal calculi

Renal stones are uncommon in childhood ([Fig. 19.20](#)). When they occur, predisposing causes must be sought:

- UTI
- structural anomalies of the urinary tract
- metabolic abnormalities.

The most common are phosphate stones associated with infection, especially with *Proteus*. Calcium-containing stones occur in idiopathic hypercalciuria, the most common metabolic abnormality, and with increased urinary urate and oxalate excretion. Deposition of calcium in the parenchyma (nephrocalcinosis) may occur with hypercalciuria, hyperoxaluria, and distal renal tubular acidosis. Nephrocalcinosis may be a complication of furosemide therapy in the neonate. Cystine and xanthine stones are rare.

Presentation may be with haematuria, loin or abdominal pain, UTI, or passage of a stone. Stones that are not passed spontaneously should be removed, by either lithotripsy or surgery, and any predisposing structural anomaly repaired if possible. A high fluid intake is recommended in all affected children. If the cause is a metabolic abnormality, specific therapy may be possible.

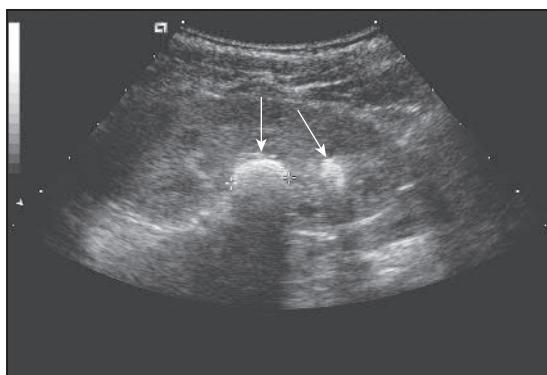


Figure 19.20 Renal ultrasound showing a staghorn calculus (arrows).

Box 19.9 Causes of Fanconi syndrome**Idiopathic****Secondary to inborn errors of metabolism**

- Cystinosis (an autosomal recessive disorder causing intracellular accumulation of cystine)
- Glycogen storage disorders
- Lowe syndrome (oculocerebrorenal dystrophy)
- Galactosaemia
- Fructose intolerance
- Tyrosinaemia
- Wilson disease (hepatolenticular degeneration)

Acquired

- Drugs and toxins, e.g. gentamicin, amphotericin
- Heavy metals

Renal tubular disorders

Abnormalities of renal tubular function may occur at any point along the length of the nephron and affect any of the substances handled by it (see [Fig. 19.22](#)).

Fanconi syndrome (generalized proximal tubular dysfunction)

Proximal tubule cells reabsorb essential salts, ions and small molecules which have been filtered out by the glomerulus. They are among the most metabolically active in the body, so are especially vulnerable to cellular damage. The cardinal features are excessive urinary loss of amino acids, glucose, phosphate, bicarbonate, sodium, calcium, potassium, and magnesium. The causes are listed in [Box 19.9](#). Fanconi syndrome should be considered in a child presenting with:

- polydipsia and polyuria
- salt depletion and dehydration
- hyperchloraemic metabolic acidosis
- rickets
- faltering or poor growth.

Specific transport defects

See [Fig. 19.21](#).

Acute kidney injury

Acute kidney injury (AKI) is a sudden, potentially reversible, reduction in renal function. Oliguria (<0.5 ml/kg per hour) is usually present. It is stratified into levels of severity by the pRIFLE ([Table 19.4](#)) and KDIGO ([Table 19.5](#)) criteria, two of the most widely used diagnostic criteria for AKI. pRIFLE uses changes in estimated creatinine clearance (eGFR), KDIGO uses serum creatinine (SCr) and changes in urine output.

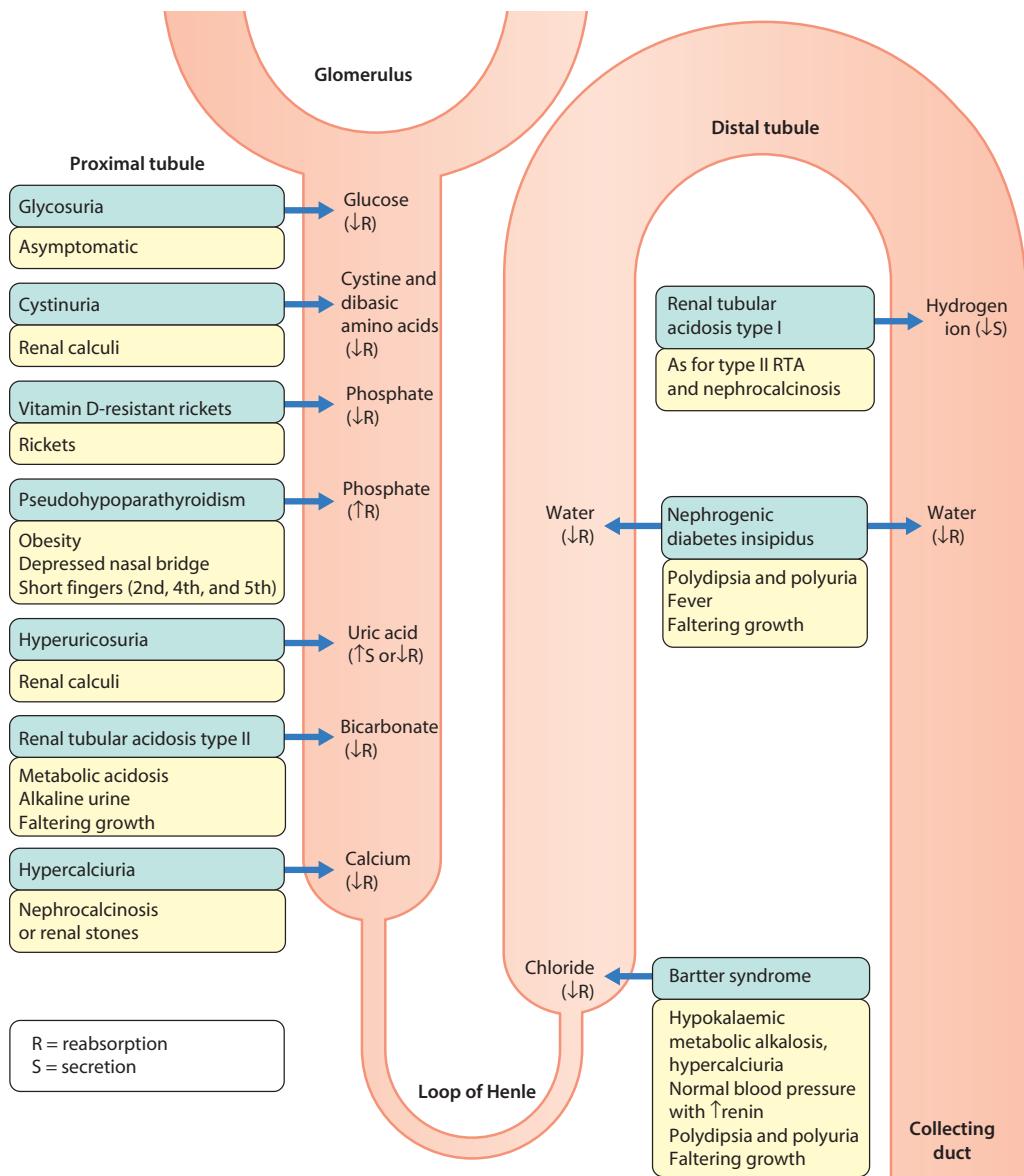


Figure 19.21 Schematic diagram of specific transport defects in some renal tubular disorders.

The cause(s) of acute kidney injury may be (see Box 19.10):

- prerenal: the most common cause in children
- renal: there is salt and water retention; blood, protein, and casts are often present in the urine; and there may be symptoms specific to an accompanying disease (e.g. haemolytic uraemic syndrome [HUS])
- postrenal: from urinary obstruction.

Acute-on-chronic renal failure is suggested by the child having faltering growth, anaemia, and disordered bone mineralization (renal osteodystrophy).

Management

Children with acute kidney injury should have their circulation and fluid balance meticulously monitored. Medication that may adversely affect renal function should be reviewed

and minimized. Investigation by ultrasound scan will identify obstruction of the urinary tract, the small kidneys of chronic kidney disease, or large, bright kidneys with loss of cortical medullary differentiation typical of an acute process.

Prerenal failure

This is suggested by hypovolaemia. The fractional excretion of sodium is very low as the body tries to retain volume. The hypovolaemia needs to be urgently corrected with fluid replacement and circulatory support if acute tubular injury and necrosis are to be avoided.

Renal failure

If there is circulatory overload, restriction of fluid intake and challenge with a diuretic may increase urine output sufficiently to allow gradual correction of sodium and water balance. A high-calorie, normal protein diet will decrease

catabolism, uraemia, and hyperkalaemia. Emergency management of metabolic acidosis, hyperkalaemia, and hyperphosphataemia is shown in **Table 19.6**. If the cause of renal failure is not obvious, a renal biopsy should be performed to identify rapidly progressive glomerulonephritis, as this may need immediate treatment with immunosuppression. The two most common renal causes of acute renal failure in children in the UK are haemolytic uraemic syndrome and acute tubular necrosis, the latter usually in the setting of multisystem failure in the intensive care unit or following cardiac surgery.

Table 19.4 pRIFLE (paediatric Risk, Injury, Failure, Loss, End stage renal disease) classification system

	Estimated creatinine clearance (eCCI)	Urine output
Risk	Decrease by 25%	<0.5 ml/kg/hr for 8 hours
Injury to the kidney	Decrease by 50%	<0.5 ml/kg/hr for 16 hours
Failure of kidney function	Decrease by 75% or <35 mL/min/1.73 m ²	<0.3 ml/kg/hr for 24 hours or anuric for 12 hours
Loss of kidney function	Persistent renal failure >4 weeks	Not applicable
End stage renal disease	Persistent renal failure >3 months	Not applicable

(Source: McCaffrey J, Kumar Dhakal A, Milford DV, Webb NJA, Lennon R: Recent developments in the detection and management of acute kidney injury. Arch Dis Child 102:91–96, 2017.) RRT, renal replacement therapy; eGFR, estimated glomerular filtration rate.

Box 19.10 Causes of acute kidney injury

Prerenal	Renal	Postrenal
<ul style="list-style-type: none"> Hypovolaemia: <ul style="list-style-type: none"> gastroenteritis burns sepsis haemorrhage nephrotic syndrome Circulatory failure Heart failure 	<ul style="list-style-type: none"> Vascular: <ul style="list-style-type: none"> haemolytic uraemic syndrome vasculitis embolus renal vein thrombosis Tubular: <ul style="list-style-type: none"> acute tubular necrosis ischaemic toxic obstructive Glomerular: <ul style="list-style-type: none"> glomerulonephritis Interstitial: <ul style="list-style-type: none"> interstitial nephritis pyelonephritis 	<ul style="list-style-type: none"> Obstruction: <ul style="list-style-type: none"> congenital, e.g. posterior urethral valves acquired, e.g. blocked urinary catheter, renal and ureteric stones

Table 19.5 KDIGO (Kidney Disease: Improving Global Outcomes) classification system

SCr (Serum creatinine)	Urine output
Stage 1 Increase 1.5–1.9 × baseline or increase >/= 27 micromol/L	<0.5 ml/kg/hr for 6–12 hours
Stage 2 Increase 2–2.9 × baseline	<0.5 ml/kg/hr for >/= 12 hours
Stage 3 Increase >3 × baseline or SCr >/= 354 micromol/L or initiation of RRT or eGFR <35 mL/min/1.73 m ²	<0.5 ml/kg/hr for >/= 24 hours or Anuric for >/= 12 hours

(Source: McCaffrey J, Kumar Dhakal A, Milford DV, Webb NJA, Lennon R: Recent developments in the detection and management of acute kidney injury. Arch Dis Child 102:91–96, 2017.) RRT, renal replacement therapy; eGFR, estimated glomerular filtration rate.

Table 19.6 Some metabolic abnormalities in acute renal failure and their therapy

Metabolic abnormality	Treatment
Metabolic acidosis	Sodium bicarbonate
Hyperphosphataemia	Calcium carbonate Dietary restriction
Hyperkalaemia	Calcium gluconate if ECG changes Salbutamol (nebulized or intravenous) Dietary restriction
	Calcium exchange resin Glucose and insulin Renal replacement therapy

Postrenal failure

This requires assessment of the site of obstruction and relief by nephrostomy or bladder catheterization. Surgery can be performed once fluid volume and electrolyte abnormalities have been corrected.

Renal replacement therapy

Renal replacement therapy in acute kidney injury is indicated when there is:

- failure of conservative management
- hyperkalaemia
- severe hyponatraemia or hypernatraemia
- pulmonary oedema or severe hypertension due to volume overload
- severe metabolic acidosis
- multisystem failure.

Peritoneal dialysis or haemodialysis can be undertaken for acute kidney injury. However, if the child requires inotropes – e.g. in sepsis or heart failure – continuous venovenous haemofiltration provides gentle, continuous dialysis and fluid removal. Acute kidney injury in childhood generally carries a good prognosis for renal recovery unless complicating a life-threatening condition, e.g. severe sepsis, following cardiac surgery or multisystem failure.

Summary

Acute kidney injury

- Prerenal: most common cause in children, from hypovolaemia and circulatory failure.
- Renal: most often haemolytic uraemic syndrome or multisystem failure.
- Postrenal: from urinary obstruction.
- Management: treat underlying cause, metabolic abnormalities, renal replacement if necessary.

Haemolytic uraemic syndrome

HUS is a triad of acute renal failure, microangiopathic haemolytic anaemia, and thrombocytopenia. Typical HUS is secondary to gastrointestinal infection with verocytotoxin-producing *E. coli* O157:H7, acquired through contact with farm animals or eating uncooked beef, or, less often, *Shigella*. It follows a prodrome of bloody diarrhoea. The toxin from these organisms enters the gastrointestinal mucosa and preferentially localizes to the endothelial cells of the kidney where it causes intravascular thrombogenesis. The coagulation cascade is activated and clotting is normal (unlike in disseminated intravascular coagulation). Platelets are consumed in this process and microangiopathic haemolytic anaemia (low serum haemoglobin, high serum lactate dehydrogenase) results from damage to red blood cells as they circulate through the microcirculation, which is occluded. Other organs such as the brain, pancreas, and heart may also be involved.

With early supportive therapy, including dialysis, the typical diarrhoea-associated HUS usually has a good prognosis, although long-term follow-up is necessary as there may be persistent proteinuria and the development of hypertension and progressive chronic kidney disease. By contrast, atypical HUS has no diarrhoeal prodrome, may be genetic, and may relapse frequently. A monoclonal anti-terminal complement complex antibody, eculizumab, has greatly improved the prognosis of this condition, which previously had a high risk of hypertension, progressive chronic kidney disease and mortality. However, it is very expensive and the duration of treatment is unknown.



Haemolytic uraemic syndrome – the triad of:

- acute kidney injury
- haemolytic anaemia
- thrombocytopenia.

Chronic kidney disease

Chronic kidney disease is progressive loss of renal function due to numerous conditions and has five stages as shown in Table 19.7. Stage 5 chronic kidney disease, with GFR less than 15 ml/min per 1.73 m^2 , is much less common in children than in adults, with an incidence of only 10 per million of the child population each year. Congenital and familial causes are more common in childhood than are acquired diseases (Table 19.8).

Table 19.7 Grading of severity of chronic kidney disease

Stage	Estimated glomerular filtration rate	Description
1	>90 ml/min per 1.73 m^2	Normal renal function but structural abnormality or persistent haematuria or proteinuria
2	60–89 ml/min per 1.73 m^2	Mildly reduced function, asymptomatic
3	30–59 ml/min per 1.73 m^2	Moderately reduced renal function, renal osteodystrophy
4	15–29 ml/min per 1.73 m^2	Severely reduced renal function with metabolic derangements and anaemia. Need to make plans for renal replacement therapy
5	<15 ml/min per 1.73 m^2	End stage renal failure, renal replacement therapy required

Table 19.8 Causes of chronic kidney disease

Cause	%
Congenital anomalies of kidney and urinary tract	53
Glomerular disease	19
Familial/hereditary	13
Systemic diseases affecting kidneys	4
Tubulointerstitial diseases	5
Miscellaneous renal diseases (PKD, metabolic, etc)	6

(Data from: UK Renal Registry, 22nd Report, 2020.)

Clinical features

Severe chronic kidney disease presents with:

- anorexia and lethargy
- polydipsia and polyuria
- faltering growth/growth failure
- bony deformities from renal osteodystrophy (renal rickets)
- hypertension
- acute-on-chronic renal failure (precipitated by infection or dehydration)
- incidental finding of proteinuria
- unexplained normochromic, normocytic anaemia.

Many children with chronic kidney disease have had their renal disease detected before birth by antenatal ultrasound or have previously identified renal disease. Symptoms rarely develop before renal function falls to less than one-third of normal or chronic kidney disease stage 4.

Management

The aims of management are to prevent the symptoms and metabolic abnormalities of chronic kidney disease, to allow normal growth and development, and to preserve residual renal function. The management of these children should be conducted in a specialist paediatric nephrology centre.

Nutrition

Poor appetite, nausea and vomiting are common. Improving nutrition using calorie supplements and nasogastric or gastrostomy feeding may be necessary to optimize growth. Protein intake should not be restricted and instead needs to be sufficient to maintain growth and a normal albumin. Food containing potassium and phosphate need restriction under the guidance of a paediatric renal dietitian.

Prevention of renal osteodystrophy

Phosphate retention and hypocalcaemia due to decreased activation of vitamin D lead to secondary hyperparathyroidism, which results in osteitis fibrosa and osteomalacia of the bones. Phosphate restriction by decreasing the dietary intake of milk products, calcium carbonate as a

phosphate binder, and activated vitamin D supplements help to prevent renal osteodystrophy.

Control of salt and water balance and acidosis

Many children with chronic kidney disease caused by congenital structural malformations and renal dysplasia have an obligatory loss of salt and water. They need salt supplements and free access to water. In other causes of chronic kidney disease, such as steroid resistant nephrotic syndrome or if the patient is anephric, fluid and salt restriction are very important to prevent fluid overload, hypertension and pulmonary oedema. Treatment with bicarbonate supplements is necessary to prevent acidosis.

Anaemia

Reduced production of erythropoietin and circulation of metabolites that are toxic to the bone marrow result in anaemia. This responds well to the administration of recombinant human erythropoietin, which is administered subcutaneously.

Hormonal abnormalities

Many hormonal abnormalities occur in progressive chronic kidney disease. Most importantly, there is growth hormone resistance with high growth hormone levels but poor growth. Recombinant human growth hormone has been shown to be effective in improving growth for up to 5 years of treatment, but whether it improves final height remains unknown. Many children with stage 4 and stage 5 chronic kidney disease have delayed puberty and a subnormal pubertal growth spurt.

Dialysis and transplantation

It is now possible for all children to enter renal replacement therapy programmes when stage 5 chronic kidney disease is reached. The optimum management is by renal transplantation ([Case history 19.4](#)). Technically, this is difficult in very small children and a minimum weight, e.g. 10kg, needs to be reached before transplantation to avoid renal vein thrombosis. Kidneys obtained from living related donors have a higher success rate than deceased donor kidneys, which are matched as far as possible to the recipient's HLA (human leukocyte antigen) type. Patient survival is high and first-year graft survival is around 97% for living related and 96% for deceased kidneys in the UK. Graft losses from both acute and chronic rejection or recurrent disease mean that the 5-year graft survival is reduced to 89% for living related kidneys and 86% for deceased donor kidney transplants, and some children need retransplantation. Current immunosuppression is mainly with combinations of tacrolimus and mycophenolate mofetil and prednisolone, and there is increasing use of minimal steroid regimens which improve growth.

Ideally, a child should receive a transplant before dialysis is required, but if this is not possible, a period of dialysis may be necessary. Peritoneal dialysis, either by cycling overnight using a machine (continuous cycling peritoneal dialysis) or by manual exchanges over 24 hours (continuous ambulatory peritoneal dialysis), can be done by the parents at home and is therefore less disruptive to family



Case history 19.4

Renal transplantation

Caden was born with a severe form of posterior urethral valves and had chronic kidney disease from birth (see Fig. 19.11a,b). He was managed for the first 3 years with intensive nutritional input. He underwent treatment for UTIs and received medications including salt supplements and erythropoietin. He needed to have his bladder augmented and went on to dialysis briefly (Fig. 19.22) before he had a live related transplant from his father at the age of 4 years. He is now growing and developing well although he continues to need immunosuppressants and occasionally suffers from UTIs.



Figure 19.22 Caden enjoying treats whilst on dialysis. Children with chronic kidney disease have a diet restricted in potassium and phosphate, which means no chocolate, crisps, or pizza – unless on the dialysis machine!

life and the child's schooling. Haemodialysis is an alternative and has been usually done in hospital three to four times a week although paediatric home haemodialysis is increasingly adopted and improves quality of life and outcomes.

Summary

Chronic kidney disease

- Causes: congenital (structural malformations and hereditary nephropathies) most common.
- Presentation: abnormal antenatal ultrasound, anorexia and lethargy, polydipsia and polyuria, faltering growth/growth failure, renal rickets (osteodystrophy), hypertension, proteinuria, anaemia.
- Management: nutrition and nasogastric or gastrostomy feeding, phosphate restriction and activated vitamin D to prevent renal osteodystrophy, salt supplements and free access to water to control salt and water balance, bicarbonate supplements to prevent acidosis, erythropoietin to prevent anaemia, growth hormone, and dialysis and transplantation.

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Further reading

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British Association of Paediatric Nephrology: renal.org/bapn/homepage.

Emedicine: emedicine.medscape.com/pediatrics_general.
Details about a range of paediatric nephrology conditions.

International Pediatric Nephrology Association (IPNA):
ipna-online.org/patient-education. *Links to paediatric renal patient support organizations throughout the world.*

Royal College of Paediatrics and Child Health/British Kidney Patient Association and British Association for Paediatric Nephrology – InfoKid: www.infokid.org.uk. *Information for parents and carers about children's kidney conditions.*

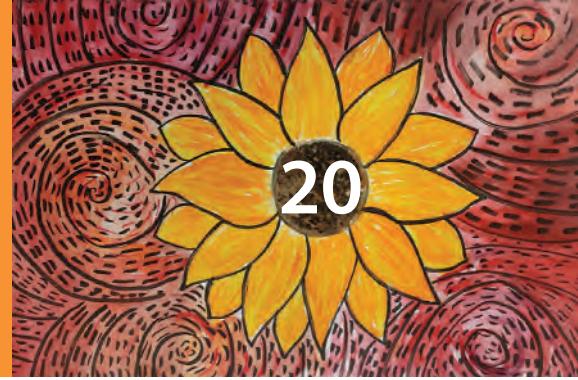
The Renal Association – Rare Renal: rarerenal.org. *Provides up-to-date information for clinicians and patients on rare*

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Genital disorders

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Features of genital disorders in children:

- Hydroceles, and inguinal hernias result from failure of closure of the processus vaginalis
- Undescended testes are frequently identified on neonatal and infant physical examination (NIPE)
- The acute scrotum is a surgical emergency.
- Vulvovaginitis is common in girls.

Inguinoscrotal conditions

Embryology

In the fetus, the testis descends from its origin on the posterior abdominal wall, down the inguinal canal into the scrotum, guided by a ligament, the gubernaculum ([Fig. 20.1a](#)). The structures that are found in the scrotum in a male (testis, vas and blood vessels) or labium in a female (attachment of the round ligament of the uterus) pass through the abdominal wall and pick up layers corresponding to those of the abdominal wall. In a male these make up the coverings of the spermatic cord. In both males and females there is a remnant of peritoneal invagination, the processus vaginalis ([Fig. 20.1b](#)), which, if it remains patent and in continuity with the abdomen, explains why abdominal contents or fluid can become a hydrocele or hernia, respectively ([Fig. 20.1c-d](#)).

Inguinal hernia

Inguinal hernias are common, occurring in up to 5% of boys, and are even more common in premature babies. A hernia is usually caused by a persistently patent processus vaginalis and emerges from the deep inguinal ring through the inguinal canal. This is an indirect hernia; direct hernias are uncommon in children.

A hernia presents as a lump in the groin which may extend into the scrotum ([Fig. 20.2](#)) or labium. They are usually asymptomatic but may be intermittent, becoming visible during straining or coughing. On examination, sometimes a lump can be palpated in the groin.

The contents of the hernia may become irreducible (incarcerated), causing pain and sometimes intestinal obstruction or damage to the testis (strangulation) from progressive oedema from venous and lymphatic obstruction. In these circumstances the lump is tender and the child may be irritable and may vomit. The risk of incarceration is much higher in infants than in older children.

Most hernias can be successfully reduced by 'taxis' (gentle compression in the line of the inguinal canal) with good analgesia. Surgery can then be performed when any oedema has settled and the child is well. If reduction is impossible, emergency surgery is required because of the risk of compromise of the bowel or testis. In girls, the ovary may descend into the hernia. If the ovary becomes incarcerated, it cannot be reduced in the same way as bowel and requires formal surgical reduction.

Treatment of inguinal herniae (see [Fig. 20.1c](#)) is by open or laparoscopic surgery.

In laparoscopic hernia repair, the internal ring is closed from inside the peritoneal cavity, which has the advantage over the open repair of not risking damage to the vas and vessels (which are handled in open herniotomy).



Prompt surgical repair is indicated for inguinal hernias in infants to lower the risk of incarceration.

Hydrocele

A hydrocele has the same underlying anatomy as a hernia, but the patent processus vaginalis is not wide enough for bowel to pass through, but can fill with fluid. Hydroceles are usually asymptomatic and sometimes appear blue. They are usually identified during the routine newborn and infant physical examination (NIPE). They may present during a viral illness in infants, when fluid in the

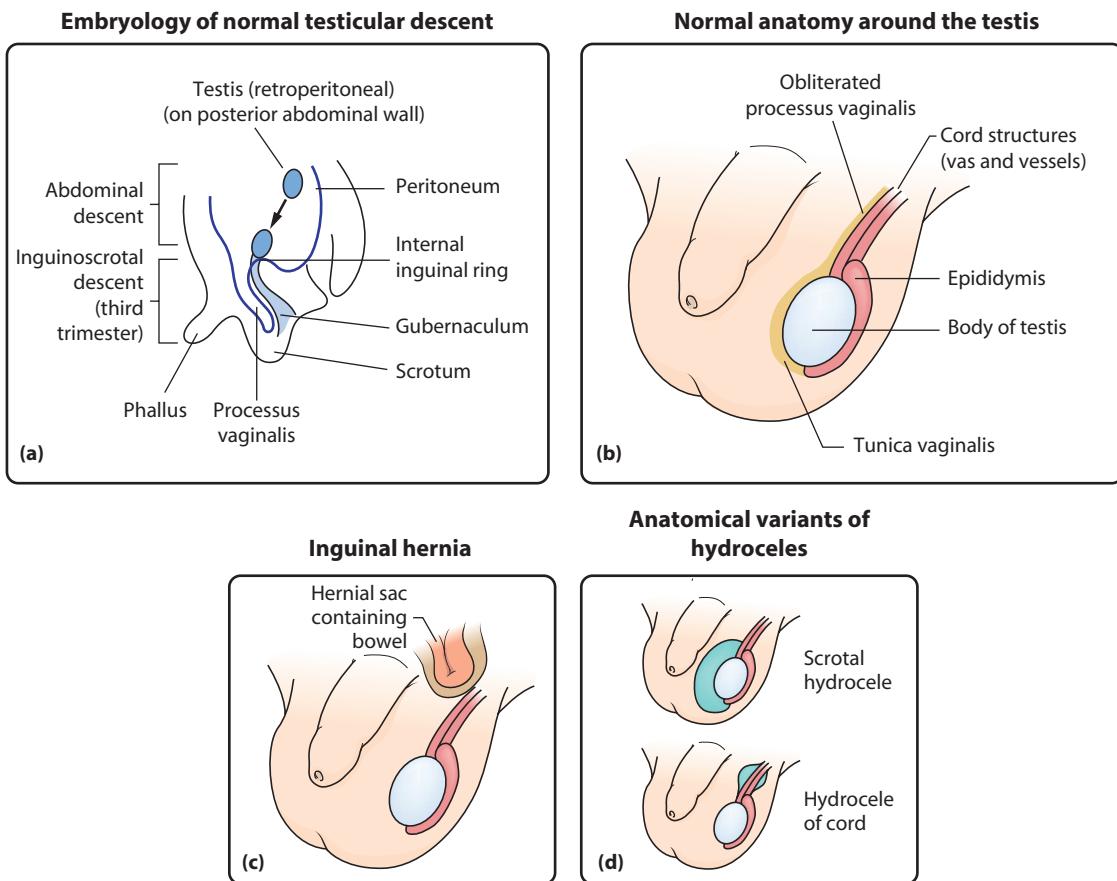


Figure 20.1 (a) Normal embryology of testicular descent; (b) normal groin structures showing remnant of processus vaginalis above and medial to cord structures; (c) relationship of inguinal hernia sac to cord; and (d) variants of hydrocele from patent processus vaginalis.

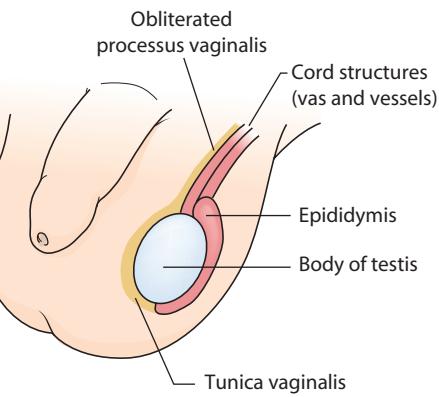


Figure 20.2 Bilateral inguinal hernias in 2-month-old boy. (Courtesy of Mike Coren.)

intra-abdominal cavity increases and passes down the patent processus vaginalis.

It is usually possible to feel the testis, however tense the hydrocele. Sometimes the hydrocele is separate from

Normal anatomy around the testis



Anatomical variants of hydroceles

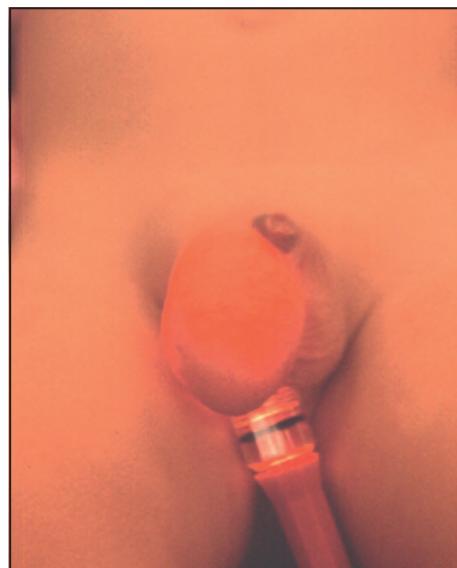
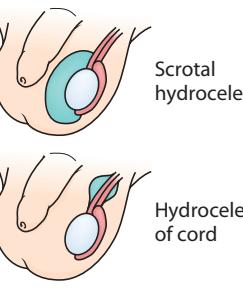


Figure 20.3 Transilluminated right hydrocele. (Courtesy of Anette Jacobsen.)

the testis (see Fig. 20.1d) as it is in the cord. The key to differentiating a hernia from a hydrocele is the ability to 'palpate above' a hydrocele. Hydroceles usually transilluminate (Fig. 20.3).

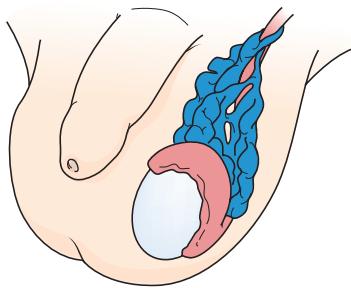


Figure 20.4 Varicocele showing convoluted vessels occupying much of the left hemiscrotum.

Although the processus vaginalis is often patent at birth it usually closes within months. Congenital hydroceles therefore usually resolve spontaneously, and can be managed expectantly. Surgery may be considered if it persists beyond the first two years of life, but resolution may take longer than this. In a girl, a hydrocele is much less common than in boys.

Varicocele

This is a scrotal swelling comprising dilated (varicose) testicular veins and occurs in up to 15% of boys, usually at puberty (*Fig. 20.4*). It is usually asymptomatic, but may cause a dull ache. On examination it may have a bluish colour and feel like a 'bag of worms'. Sometimes the testis is smaller or softer than normal. Management is conservative if asymptomatic. Occlusion of the gonadal veins can be achieved by surgical ligation – through the groin laparoscopically or by radiological embolization.

Undescended testis

Most undescended testes originate from arrest of the testis along its normal pathway of descent (see *Fig. 20.1a*). An undescended testis is present in up to 5% of newborn term infants but is more common in premature infants. By three months of age, only 1% are still undescended. The diagnosis should ideally be made at the routine newborn and infant physical examination (NIPE) of the newborn (*Chapter 10*, Perinatal medicine).

The testes may be felt in the scrotum or may need to be coaxed by gentle pressure along the line of the inguinal canal into the scrotum.

An undescended testis may be palpable or impalpable. A palpable undescended testis is usually felt in the groin, but cannot be manipulated into the scrotum. Occasionally it can be palpated below the external inguinal ring but outside the scrotum – the so-called 'ectopic' testis.

If the testis is impalpable, it may be in the inguinal canal, but cannot be identified or it may be intra-abdominal or absent. If there are bilateral impalpable testes, consider if the karyotype must be established to exclude a disorder of sex development.

A testis may also be retractile, when the testis is present in the inguinal canal but can be manipulated into the scrotum with ease and without tension. Action of the cremaster muscle (as seen in eliciting the cremasteric reflex by light touch on the inner thigh) pulls up the testis. Parents of boys with a retractile testis often report that the testis is sometimes obvious, particularly when the boy is warm and relaxed, and sometimes not. Testes should be therefore always be examined in a warm, relaxed environment.

Investigations and management

Imaging is not helpful in the assessment of an undescended testis.

If an undescended testis is identified on the routine newborn and infant physical examination (NIPE) the decision to operate should be delayed for several months as some will subsequently descend spontaneously.

Orchidopexy is the surgical placement of the testis in the scrotum, and is performed within the first year of life:

- to allow self-examination as adults – an undescended testis is dysplastic, and has a 10-fold increased risk of malignancy later in life. Bringing the testis down does not change this risk, but being able to perform self-examination as an adult means that any lumps developing are readily palpable and treatable.
- for cosmetic reasons – to achieve the same, symmetrical appearance as other boys. This may be of psychological benefit. If the testis is absent, a prosthesis can be inserted when older.
- to reduced risk of torsion and trauma compared to groin location.
- to improve fertility – the testis needs to be in the scrotum, below body temperature, in order to allow spermatogenesis. The effect is probably marginal in unilateral undescended testis but is more important if bilateral. There is some evidence that delaying orchidopexy beyond the first two years of life adversely affects testicular development.

When a testis is *impalpable*, about 10% have regressed in development and are, in fact, absent. Abdominal laparoscopy allows both diagnosis and treatment.

When a testis is *retractile*, follow-up is recommended because some high testes require surgery to place them in the scrotum. Whether or not this is true ascent of the testis is controversial.



Undescended testes should be referred to a paediatric surgeon when detected. If surgery is required, the optimum time is within the first year of life.

Testicular pain ('the acute scrotum')

Torsion of the testis

This is commonest in post-pubertal boys (*Fig. 20.5a*), but may occur at any age, including the newborn. It is usually very painful, with redness and oedema of the scrotal skin. However, the pain may be localized to the groin or lower abdomen, highlighting the need to always examine the testes in a boy presenting with sudden-onset pain in the groin, abdomen or scrotum. It must be distinguished from an incarcerated hernia. An undescended testis is at increased risk of torsion, as is a testis lying transversely on its attachment to the spermatic cord (the so-called 'clapper bell' testis).

Torsion of the testis must be treated within hours of the onset of symptoms to lower the risk of testicular loss. In fact, surgical exploration in any acute scrotal presentation is mandatory unless torsion can be excluded with certainty (see below). Fixation of the contralateral testis is also performed because of the increased risk of a contralateral torsion. Outcome is variable, depending on time to correction. If delayed, testicular loss is likely.

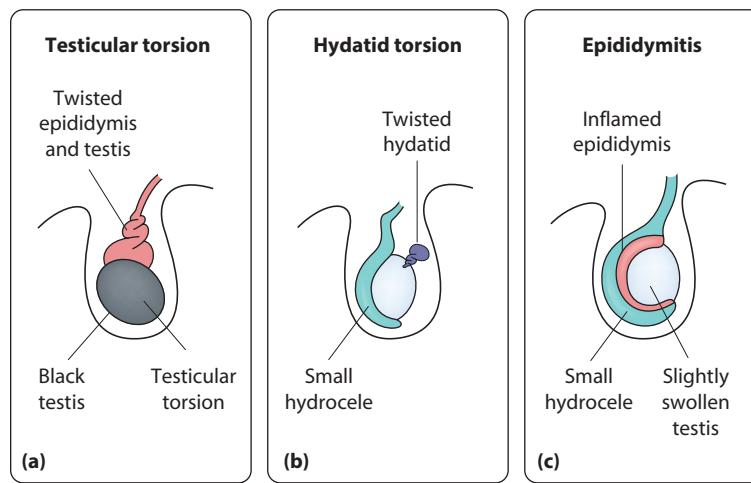


Figure 20.5 (a) Testicular torsion; (b) hydatid torsion; and (c) epididymitis.

In perinatal testicular torsion, testicular loss is almost inevitable, and as a result some surgeons will not perform surgical exploration urgently but rather let the dead testis atrophy. The unilateral remaining testis can be fixed electively when the infant is older.

Torsion of appendix testis

A testicular appendage (hydatid of Morgagni) is a Mullerian remnant usually located on the upper pole of the testis. Torsion of the appendix testis (Fig. 20.5b) tends to affect prepubertal boys and is more common than torsion of the testis. Pain evolves over days, but is not as dramatic as in testicular torsion. Scrotal exploration and excision of the appendage is often necessary because it cannot be differentiated reliably from torsion of the testis. If a 'blue dot' can be seen through the scrotal skin and pain is controlled with analgesia, surgery may not be necessary.

Other acute inguinoscrotal conditions

Infection may cause an acute scrotum. *Epididymo-orchitis* (Fig. 20.5c) is commoner in infants and small children, and more likely with a pre-existing urological or anorectal malformation. As it may be indistinguishable from torsion, scrotal exploration may be necessary. Doppler ultrasound of flow pattern in the testicular blood vessels may allow differentiation of epididymitis from torsion of the testis, but must not replace clinical evaluation. A urine sample should be obtained to identify an associated urinary tract infection. Pus should be sent at operation for microbiology to characterize the nature of the infection, but infection may be bacterial or viral. Antibiotics are started empirically.

In *idiopathic scrotal oedema* there is redness and swelling extending beyond the scrotum into the thigh, perineum and suprapubic area, but the testis is normal and non-tender. It requires analgesia and review. It may recur. An *incarcerated hernia* may also cause an acute scrotum, although symptoms usually affect the groin.

Trauma to the scrotum is an uncommon cause of testicular damage, but may need surgical exploration, debridement and repair. Sexual abuse needs to be considered in all genital injuries.

Recurrent scrotal pain in boys can be difficult to manage. Any associated symptoms or signs such as swelling or redness should be regarded as intermittent testicular torsion and the testes fixed. Sometimes prophylactic fixation is required to exclude intermittent torsion as a cause for recurrent pain.



Torsion of the testis must be excluded (by emergency exploration if necessary) in boys with an 'acute scrotum'. Delay leads to testicular loss.

Abnormalities of the penis

The foreskin

A normal foreskin does not retract in infancy, and retraction should not be attempted. At 1 year of age, about half of uncircumcised boys have a non-retractile (normal) foreskin. Only 1% of boys over 16 years old have a non-retractile foreskin. The prepuce develops adherent to the underlying glans, and acts as protection to the non-keratinized glanular and meatal squamous epithelium in an environment where urine can cause inflammation or even ulceration. This can manifest as ammoniacal dermatitis (napkin rash) in infants and young children, where the preputial opening can be reddened and sore. It usually only needs reassurance and attention to routine hygiene.

This needs to be differentiated from infection, or balanoposthitis, where the redness is more extensive, and, crucially, there is a purulent discharge. The infection is usually bacterial and needs antibiotic treatment, either topical or systemic.

Ballooning of the foreskin on urination is a common cause of parental concern. It can look dramatic but seldom causes any trouble. It has no functional consequence, does not represent obstruction, and does not need intervention.

Another cause of parental concern is sub-preputial smegma. It appears as a lump which grows briefly, seemingly under the non-retractile or partially retractile foreskin. It is yellowish and malleable, and simply comprises desquamated skin and secretions. There is no need to intervene – it will discharge in due course (with typical appearance of smegma – 'cottage cheese'; Fig. 20.6) when the preputial adhesions break down.

Non-retractile foreskin and phimosis

When traction is applied (gently) to a normal foreskin, the skin at the preputial opening is seen to evert, even if it does not necessarily open up (Fig. 20.7). A foreskin that is pathologically non-retractile will not do this, and will truly render the glans 'muzzled' (Greek word 'phimos'). This differentiates a foreskin that is simply non-retractile (i.e. normal, physiological) from one which is problematic (phimosis).



Figure 20.6 Smegma. (Courtesy of Anette Jacobsen, Singapore.)



Figure 20.7 Normal foreskin in an infant. (Courtesy of Anette Jacobsen, Singapore.)

The commonest condition that gives rise to a true phimosis is balanitis xerotica obliterans (BXO), which gives rise to progressive scarring which can extend onto the glans, and ultimately into the urethra. **Fig. 20.8** shows its typical appearance. Circumcision is indicated.

Paraphimosis

Paraphimosis is an irreducible retracted foreskin, most common in post-pubertal boys. The glans swells, and if the prepuce is not reduced it may result in compromise of the blood supply to the glans. Treatment (by reduction) is an emergency, which may require general anaesthesia. Paraphimosis is no longer considered to require circumcision unless the foreskin is abnormal (as with BXO).

Circumcision

Circumcision remains a tradition in Jewish and Muslim religions and is a non-religious cultural preference in North America.

Medical reasons for circumcision include:

- BXO causing a true phimosis
- recurrent balanoposthitis causing refractory symptoms
- prophylaxis of recurrent urinary infection, especially in the presence of a congenital uropathy (such as posterior urethral valves or vesicoureteric reflux) or if renal reserve is limited
- if access to the urethra is required reliably for intermittent catheterization, e.g. spina bifida

There is some evidence that circumcision affords protection against transmission of HIV and HPV (human papillomavirus), and there are programmes promoting circumcision in newborn infants and young adult males in some countries with high prevalence of HIV infection.



Figure 20.8 Balanitis xerotica obliterans (BXO) causing a true phimosis. (Courtesy of Alun Williams).

Complications following circumcision are uncommon, but include bleeding, ulceration of exposed granular skin and subsequent meatal stenosis.

 **A non-retractile foreskin is normal in preschool children.**

Hypospadias

This has an incidence of up to 1 in 200 boys. It is thought to arise from failure of development of ventral closure of tissues of the penis.

Typically there are three features, although their occurrence is variable:

- abnormal site of ventral urethral meatus – the urethral meatus is variable in position (**Fig. 20.9**), but in most (80%) is on the distal shaft or glans penis (**Fig. 20.10a**)
- ventral curvature of the shaft of the penis (formerly called 'chordée') (**Fig. 20.10b**), more apparent on erection
- hooded appearance of the foreskin – characteristic in appearance because of ventral foreskin deficiency but of no functional significance.

There is rarely an associated or underlying disorder of sex development, and only rarely another congenital urinary tract abnormality.

Management

Surgery may be performed for functional or cosmetic reasons. The ultimate aim of hypospadias surgery is to allow a boy to pass urine in a straight line whilst standing, and to have a straight erection. Surgery, if needed, is usually performed in the first two to three years of life. The commonest surgical complications are breakdown of the repair or meatal narrowing. It is important that a boy with hypospadias is not circumcised before the repair, as the tissue of the prepuce may be used in the repair itself.

 **Infants with hypospadias must not be circumcised, to preserve tissue for reconstruction.**

'Buried' penis

Parents are sometimes concerned that a boy's penis looks small. This is usually from variations in penoscrotal skin attachment or a fat pad in overweight children making the penis look buried. It improves with growth of the penis after puberty.

Hypospadias

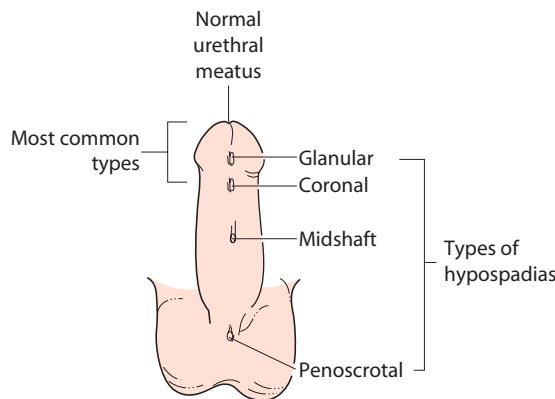


Figure 20.9 Varieties of hypospadias.

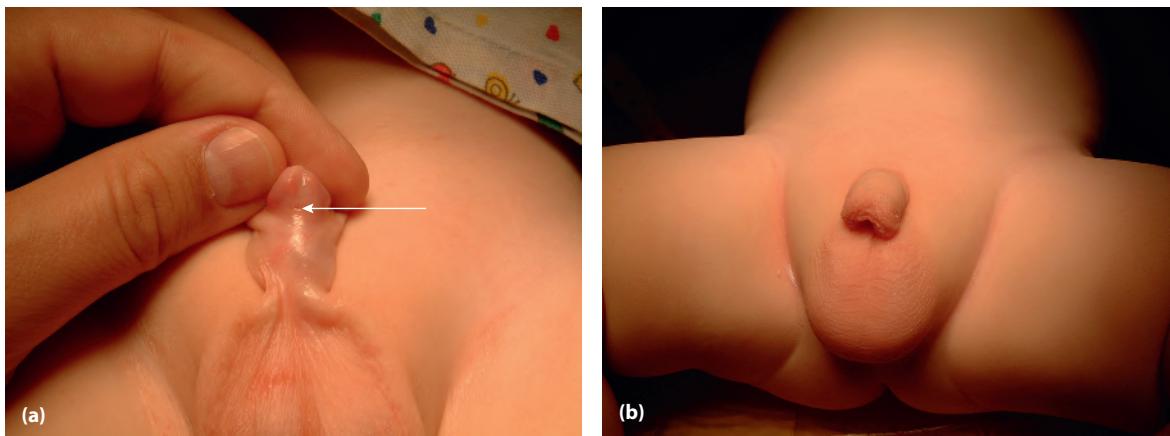


Figure 20.10 (a) Penile shaft in coronal hypospadias showing the urethral meatus (arrow). (b) Dorsal hooded prepuce and ventral curvature of the penis (chordee) in hypospadias. (Courtesy of Nic Alexander.)

Summary

Genital conditions in male infants

Inguinal hernia/hydrocele

- Surgical repair of inguinal hernias in infants should be performed promptly to prevent bowel incarceration and strangulation.
- Hydroceles identified on routine newborn and infant physical examination (NIPE) usually resolve spontaneously.

Undescended testis

- Common – up to 5% of term boys at birth, 1% at 3 months of age.
- If testis undescended but palpable – requires orchidopexy.
- If undescended and impalpable – may require laparoscopy to identify if a testis is present.
- If bilateral impalpable testes – urgent karyotype is essential.
- Retractile testes – usually do not require surgery.

Acute scrotal conditions

- May occur at any age but torsion of testis must be considered not only for acute pain of the scrotum but also for acute abdominal and groin pain.
- Scrotal surgical exploration is required unless torsion of the testis can be reliably excluded.

Non-retractile foreskin

- Is normal in preschool children.
- Circumcision is not recommended routinely but is still traditional in some communities worldwide.

Hypospadias

- 1 in 200 boys.
- Ventral urethral meatus at abnormal site, penile curvature and hooded foreskin.
- Surgery may be required in first 2–3 years of life.
- Infants with hypospadias must not be circumcised.

Genital disorders in girls

Normal anatomy

Recognition of the normal female anatomy and its variations is crucial in order to avoid incorrectly diagnosing them as pathological conditions and to recognize disorders of sex differentiation in the newborn, female genital mutilation and sexual abuse.

Vulvovaginitis / vaginal discharge

The commonest problem is redness of the vulva. In infants, this is often due to a nappy rash due to ammoniacal dermatitis. Less often, the vulvovaginitis is infective, occasionally with *Candida* infection. Vaginal discharge is common, and is usually innocuous unless it is green or offensive, when it may indicate infection. Foreign bodies are more often suspected than found; they are actually rare. The 'red flag' symptom is a bloody vaginal discharge, which needs referral to a specialist as vaginal rhabdomyosarcoma is a rare but important cause in preschool girls.

Labial adhesions

Fusion of the labia minora can be a cause of local irritation in the prepubertal girl. There is usually an adequate orifice for the passage of urine. The characteristic appearance is of superficial fusion of the labia minora with a translucent (or even slightly bluish) area of flimsy tissue between the labia. The appearance sometimes raises parental concern about abnormal vaginal development, although these conditions are rare. Unless the labial adhesion causes significant symptoms, no specific treatment is required. Topical corticosteroids or oestrogens can be helpful to lyse the adhesions, especially if it allows the underlying introital anatomy to be seen, but re-adhesion is common. Examination under anaesthesia, or formal 'division of adhesions' should be undertaken only exceptionally because of the high rate of recurrence.



Blood-stained vaginal discharge must be investigated.

Summary

Genital conditions in female infants

- Vulvovaginitis in infants is usually due to nappy rash.
- Labial adhesions tend to recur; no treatment is indicated unless symptomatic.

Acknowledgements

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Further reading

Wilcox, DT & Thomas DFM (2021). *Essentials of paediatric urology*, ed 3, CRC Press.



Liver disorders

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Features of liver disorders in children:

- Prolonged neonatal jaundice (>14 days of age if term, >3 weeks if preterm) requires investigation to identify liver disease (elevated conjugated jaundice).
- The earlier in life biliary atresia is diagnosed and treated surgically, the better the prognosis.
- Chronic hepatitis B virus (HBV) infection in children can be prevented.
- Hepatitis C is curable with oral antiviral drugs, so children and mothers at risk need to be screened.
- Liver transplantation is an effective therapy for acute or chronic liver failure, with a greater than 80% 20-year survival rate.

Many of the clinical features and complications of liver disease are shown in [Figure 21.1](#).



Liver disease in children is uncommon and should be managed by national centres.

Neonatal cholestasis

Physiological jaundice in newborns is common but 90% will have resolved by 2 weeks (3 weeks if preterm). Prolonged (or persistent) neonatal jaundice requires prompt investigation to distinguish unconjugated (resolves spontaneously) from conjugated which indicates liver disease. Early diagnosis and management of neonatal liver disease improves prognosis.

The differential diagnosis of prolonged jaundice in infancy is shown in [Box 21.1](#).



In prolonged (persistent) jaundice, always look to see if the stools are pale, which suggests bile duct obstruction or severe liver disease.

Biliary atresia

This occurs in 1 in 15,000 live births. There is progressive fibrosis and obliteration of the extrahepatic and intrahepatic biliary tree. Without intervention, chronic liver failure develops and death occurs within 2 years. The exact aetiology is unknown. Clinical presentation is with mild jaundice and pale stools (the colour may fluctuate but becomes increasingly pale as the disease progresses) (see [Case history 21.1](#)). They have normal birthweight followed by faltering growth. Hepatomegaly is often present initially. Splenomegaly develops later due to portal hypertension.

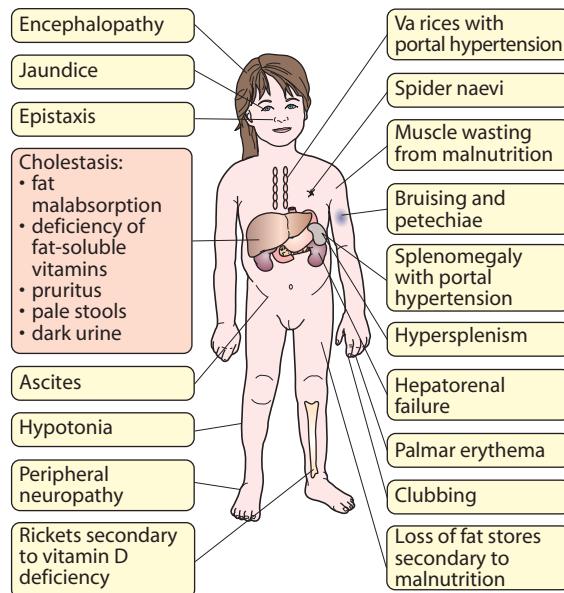


Figure 21.1 Symptoms and signs of hepatic dysfunction. Most common presentation is with jaundice, bleeding disorders and growth faltering.

Box 21.1 Causes of prolonged (persistent) neonatal jaundice**Unconjugated**

- Breastmilk jaundice
- Infection (particularly urinary tract)
- Haemolytic anaemia, e.g. G6PD deficiency
- Hypothyroidism
- High gastrointestinal obstruction
- Crigler–Najjar syndrome

Conjugated ($>25 \mu\text{mol/L}$)**Bile duct obstruction**

- Biliary atresia
- Choledochal cyst

Neonatal hepatitis syndrome

- Congenital infection
- Inborn errors of metabolism
- α_1 -Antitrypsin deficiency
- Galactosaemia
- Tyrosinaemia (type 1)
- Errors of bile acid synthesis
- Progressive familial intrahepatic cholestasis
- Cystic fibrosis
- Intestinal failure-associated liver disease – associated with long-term parenteral nutrition

Intrahepatic biliary hypoplasia

- Alagille syndrome

Investigations

There is a raised conjugated bilirubin with a raised gamma glutamyl transferase (GGT) and abnormal liver function tests. A fasting abdominal ultrasound may demonstrate a contracted or absent gallbladder, though it may be normal. The diagnosis is confirmed by a cholangiogram (ERCP [endoscopic retrograde cholangiopancreatography] or operative), which fails to outline a normal biliary tree. Liver biopsy initially demonstrates neonatal hepatitis with features of extrahepatic biliary obstruction developing with time.

Treatment

Palliative surgery with a Kasai hepatoportoenterostomy (a loop of jejunum is anastomosed to the cut surface of the porta hepatis) bypasses the fibrotic ducts and facilitates drainage of bile from any remaining patent ductules. Early surgery increases the success rate, with 60% clearing the jaundice if performed before 60 days. Even with successful clearance of jaundice, the disease progresses in most children who may develop cholangitis and cirrhosis with portal hypertension. Nutrition and fat-soluble vitamin supplementation is essential. If the Kasai is unsuccessful, liver transplantation is essential. Biliary atresia is the single most common indication for liver transplantation in the paediatric age group.

Choledochal cysts

These are cystic dilatations of the extrahepatic biliary system. They may be detected on antenatal ultrasound scan, present with neonatal jaundice or, in older children with abdominal pain, a palpable mass, jaundice, or cholangitis. The diagnosis is established by ultrasound or magnetic resonance cholangiopancreatography. Treatment is by surgical excision of the cyst with the formation of a Roux-en-Y anastomosis to the biliary duct. Future complications include cholangitis and a 2% risk of malignancy, which may develop in any part of the biliary tree.

Neonatal hepatitis syndrome

In neonatal hepatitis syndrome, there is prolonged neonatal jaundice and hepatic inflammation. There are many causes (Box 21.1). Babies may have a low birthweight and faltering growth. Other clinical features depend on the diagnosis. Jaundice may be severe and differentiation from biliary atresia is essential. Liver biopsy is often non-specific but shows giant cell hepatitis and extramedullary haemopoiesis.

Alagille syndrome

This is a rare autosomal dominant condition with widely varying penetrance even within families. Clinical presentation is with a characteristic triangular facies (Fig. 21.4), skeletal abnormalities (including butterfly vertebrae), congenital heart disease (classically peripheral pulmonary stenosis), renal tubular disorders, and defects in the eye. Infants may be profoundly cholestatic with severe pruritus and faltering growth. Identifying the gene mutations confirms the diagnosis. Treatment is to provide nutrition and fat-soluble vitamins. Pruritus is profound and difficult to manage. A small number will require liver transplant, but most survive into adult life. Mortality is most likely secondary to the cardiac disease.

Progressive familial intrahepatic cholestasis

These autosomal recessive disorders all affect bile salt transport. Clinical presentation is with jaundice, intense pruritus, faltering growth, rickets, and in some cases diarrhoea and hearing loss. Older children may present with gallstones.

The diagnosis is confirmed by identifying mutations in bile salt transport genes. Treatment is with nutritional support and fat-soluble vitamins. Newer drugs include ileal bile acid transporter inhibitors (IBAT) which prevent bile salt reabsorption and improve pruritus. Progression of fibrosis is usual with most requiring liver transplantation.



Case history 21.1

Biliary atresia

A term infant, birthweight 3.4 kg, was initially breastfed and developed mild jaundice on the 3rd day of life. At 5 weeks she was still jaundiced. She was constantly hungry on an infant formula. On questioning, her stools were pale (Fig. 21.2) but there were no other features of liver disease.

Investigations revealed:

- Serum bilirubin 160 micromol/L, with 140 micromol/L conjugated.

She was referred to a national paediatric liver centre, where further investigations revealed:

- Alanine transferase elevated – 120 IU/L,
- Gamma glutamyl transferase elevated – 430 IU/L.
- Ultrasound – absent gallbladder despite 4 hours of fasting.

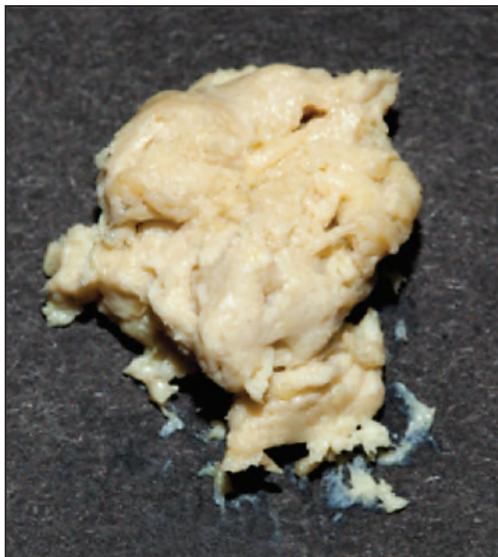


Figure 21.2 Pale stool secondary to biliary atresia.

Treatment with fat-soluble vitamins and ursodeoxycholic acid were commenced. Feeds were changed to a high MCT (medium chain triglyceride) feed and she settled on to a 3-hour feeding pattern. No other causes of conjugated jaundice were identified.

An operative cholangiogram confirmed biliary atresia and she underwent a Kasai portoenterostomy at 6 weeks of age. Figure 21.3 shows her a few months after her operation.

At 4 years of age she had developed increasing splenomegaly. Endoscopy identified oesophageal varices. She remains stable at the age of 6 years.



In prolonged (persistent) neonatal jaundice, early diagnosis of biliary atresia improves the prognosis. All term infants who are jaundiced at 2 weeks should be investigated for liver disease.



Figure 21.3 Several months after successful bile drainage by hepatoperoenterostomy (Kasai procedure) for biliary atresia. The scar is from her surgery.



(a)



(b)

Figure 21.4 The typical facial features of a child with Alagille syndrome with (a) pointed chin and (b) wide spaced eyes and prominent forehead.

Neonatal metabolic liver disease

α_1 -Antitrypsin deficiency

It is inherited as an autosomal recessive disorder with an incidence of 1 in 2000 to 1 in 4000 in the UK. There are many phenotypes of the protease inhibitor (Pi) which are coded on chromosome 14, with liver disease primarily associated with the protein phenotype PiZZ. Abnormal folding of the protease α_1 -antitrypsin is associated with accumulation of the protein within the hepatocytes and hence liver disease in infancy and childhood. The lack of circulating α_1 -antitrypsin results in emphysema in adults, especially if there is exposure to cigarette smoke.

The majority of children who present with α_1 -antitrypsin deficiency will either have prolonged neonatal jaundice or, less commonly, bleeding due to vitamin K deficiency (haemorrhagic disease of the newborn). Hepatomegaly is present. The diagnosis is confirmed by estimating the level of α_1 -antitrypsin in the plasma and identifying the protein phenotype. Approximately 50% of children have a good prognosis, but the remainder will develop liver disease (cirrhosis, splenomegaly and portal hypertension) and may require transplantation. Pulmonary disease is not significant in childhood, but may develop in adult life. Advice to avoid smoking (both active and passive) should be given. The disorder can be diagnosed antenatally.

Galactosaemia

This very rare disorder has an incidence of 1 in 23,000 to 1 in 44,000. The infants develop poor feeding, vomiting, jaundice, and hepatomegaly when fed milk. Liver failure, cataracts, and developmental delay are inevitable if it is untreated. A rapidly fatal course with shock, haemorrhage, and disseminated intravascular coagulation, often due to Gram-negative sepsis, may occur.

On investigating prolonged (persistent) jaundice, it can be identified by detecting galactose, a reducing substance, in the urine. The diagnosis is made by measuring the enzyme galactose-1-phosphate-uridyl transferase in red cells. A recent blood transfusion may mask the diagnosis. A galactose-free diet prevents progression of liver disease, but ovarian failure and learning difficulties may occur later.

Other causes

Neonatal hepatitis may occur following prolonged parenteral nutrition. Rare causes include tyrosinaemia type 1, cystic fibrosis, lipid and glycogen storage disorders, peroxisomal disorders, and inborn errors of bile acid synthesis.

Viral hepatitis

The clinical features of acute viral hepatitis include nausea, vomiting, abdominal pain, lethargy, and jaundice; however, 30% to 50% of children do not develop jaundice. A large tender liver is common and 30% will have splenomegaly. The liver transaminases are usually markedly elevated. Coagulation is usually normal.

Hepatitis A

Hepatitis A virus is an RNA virus which is spread by faecal–oral transmission. The incidence of hepatitis A in childhood has fallen as socio-economic conditions have improved. Many adults are now not immune. Vaccination is required for travellers to endemic areas.

The disease may be asymptomatic, but the majority of children have a mild illness and recover both clinically and biochemically within 2 weeks to 4 weeks. Some may develop prolonged cholestatic hepatitis (which is self-limiting), or fulminant hepatitis. Chronic liver disease does not occur.

Diagnosis can be confirmed by detecting IgM antibody to the virus. There is no treatment and no evidence that bed rest or change of diet is effective. Close contacts should be vaccinated within 2 weeks of the onset of the illness. In those at increased risk, e.g. chronic liver disease, HNIG (human normal immunoglobulin) should be considered.

Hepatitis B

Hepatitis B virus (HBV) is a DNA virus that is an important cause of acute and chronic liver disease worldwide, with high prevalence and carrier rates in sub-Saharan Africa and the Far East (Fig. 21.5). HBV is transmitted by:

- perinatal transmission from carrier mothers or horizontal spread within families
- inoculation with infected blood via blood transfusion, needlestick injuries, or renal dialysis
- among adults it can also be transmitted sexually.

Infants who contract HBV perinatally are asymptomatic, but at least 90% become chronic carriers. Older children who contract HBV may be asymptomatic or have classical features of acute hepatitis. The majority will resolve spontaneously, but 1% to 2% develop fulminant hepatic failure, while 5% to 10% become chronic carriers.

The diagnosis is made by detecting HBV antigens and antibodies. IgM antibodies to the core antigen (anti-HBc) are positive in acute infection. Hepatitis B surface antigen (HBsAg) denotes ongoing infectivity. There is no treatment for acute HBV infection.

Chronic hepatitis B

Approximately 30% to 50% of asymptomatic carrier children will develop chronic HBV liver disease, which may progress to cirrhosis in 10%. There is a long-term risk of hepatocellular carcinoma. Current treatment regimens for chronic HBV have poor efficacy. Interferon or pegylated interferon (a long-acting formulation) treatment for chronic hepatitis B is successful in 50% of children infected horizontally and 30% of children infected perinatally. Oral antiviral therapy such as entecavir and tenofovir are licensed for treatment in children >2 years and clears the virus in 25%. Long-term treatment may be required.

Prevention

Prevention of HBV infection is important. Immunization with HBV vaccine is now part of the routine immunization schedule in the UK and many other countries. In addition, all pregnant women are screened antenatally for HBsAg, and if identified as HBsAg-positive are offered additional doses of the vaccine for their infants starting at birth. If

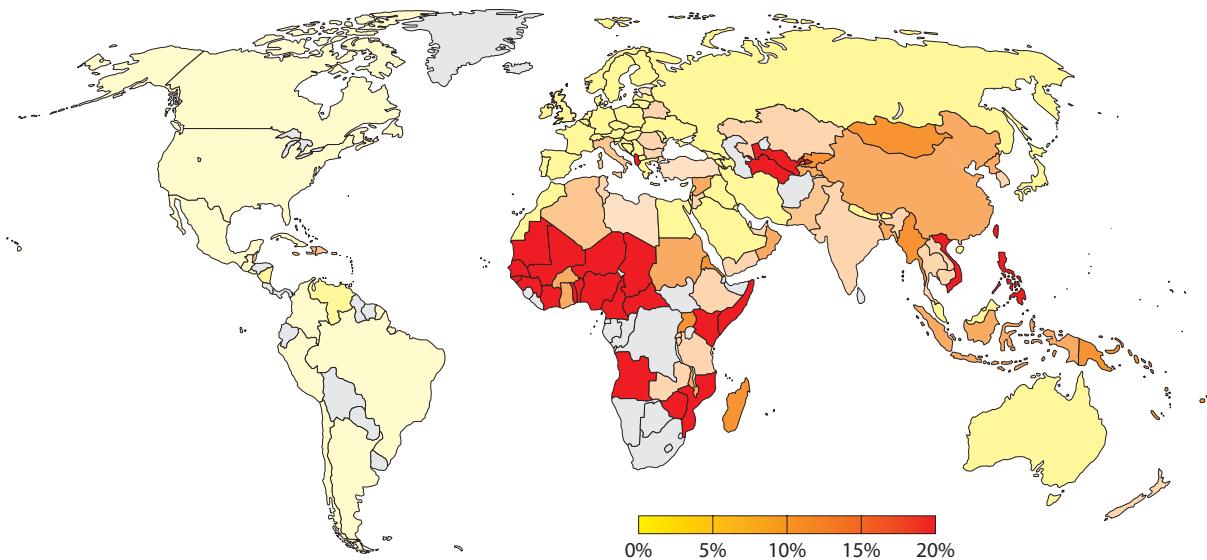


Figure 21.5 Global HBsAg prevalence. (From: Razavi-Shearer D, Gamkrelidze I, Nguyen MH et al. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. Lancet Gastroenterol Hepatol 2018; 3(6):383–403.)

the mother is also hepatitis B e antigen (HBeAg)-positive, giving the infant hepatitis B immunoglobulin shortly after birth may also be advised.. Antibody response to the vaccination course should be checked at 12 months in infants of HBsAg-positive mothers, as 5% require further vaccination. Other members of the family should also be vaccinated. Neonatal vaccination has reduced the incidence of HBV-related cancer in endemic countries.

Summary

Hepatitis B virus (HBV)

- Perinatal transmission from carrier mothers should be prevented by maternal screening and giving the infant a course of hepatitis B vaccine with hepatitis B immunoglobulin if indicated.
- Hepatitis B immunization is part of the routine immunization schedule in many countries including the UK.
- Infection may result in chronic HBV liver disease, which may progress to cirrhosis and hepatocellular carcinoma.

Hepatitis C

Hepatitis C virus (HCV) is an RNA virus that was responsible for 90% of post-transfusion hepatitis until the screening of donor blood was introduced in 1991. In the UK, about 1 in 2000 donors have HCV antibodies. The prevalence is high among intravenous drug users. Vertical transmission is now the most common cause of HCV transmission in children. Six percent of transmission occurs from infected mothers, but is twice as common if there is co-infection with HIV. It seldom causes an acute

infection, but the majority become chronic carriers, with a 20% to 25% lifetime risk of progression to cirrhosis or hepatocellular carcinoma. Oral direct acting antiviral drugs such as sofosbuvir and ledipasvir, the combination of sofosbuvir plus ribavirin, and glecaprevir and pibrentasvir are 98%–100% curative and licensed in children >3 years in the US and >12 years in Europe. Effective therapy for HCV prevents significant liver disease and liver cancer, highlighting the need to screen high-risk mothers and children. Treatment is not indicated before 3 years of age, as HCV may resolve spontaneously following vertically acquired infections.

Hepatitis D virus

Hepatitis D virus (HDV) is a defective RNA virus that depends on hepatitis B virus for replication. It occurs as a co-infection with hepatitis B virus or as a superinfection causing an acute exacerbation of chronic hepatitis B virus infection. Cirrhosis develops in 50% to 70% of those who develop chronic HDV infection.

Hepatitis E virus

This is an RNA virus that is enterally transmitted, usually by contaminated water. It is found worldwide but is more prevalent in low-income countries. Hepatitis E virus causes a mild self-limiting illness in most people and is known to be transmitted by blood transfusion or eating infected pork. In pregnant women it causes fulminant hepatic failure with a high mortality rate.

Seronegative (non-A to G) hepatitis

Clinical presentation is similar to hepatitis A. When a viral aetiology of hepatitis is suspected but not identified, it is known as seronegative hepatitis.

Epstein–Barr virus

Children with Epstein–Barr virus infection are usually asymptomatic. Some 40% have hepatitis with marked hepatosplenomegaly, which may become fulminant. Less than 5% are jaundiced.

Acute liver failure (fulminant hepatitis)

Acute liver failure in children is the development of massive hepatic necrosis with subsequent loss of liver function, with or without hepatic encephalopathy. The disease is uncommon, but has a high mortality. Most are caused by infection and metabolic conditions (Table 21.1). The child may present within hours or weeks with jaundice, encephalopathy, coagulopathy, hypoglycaemia, and electrolyte disturbance. Early signs of encephalopathy include alternate periods of irritability and confusion with drowsiness. Older children may be aggressive and unusually difficult. Complications include cerebral oedema, haemorrhage from gastritis or coagulopathy, sepsis and pancreatitis.

Diagnosis

Bilirubin may be normal in the early stages, particularly with metabolic disease. Transaminases are greatly elevated (10–100 times normal), alkaline phosphatase is increased, coagulation is very abnormal, and plasma ammonia is elevated. It is essential to monitor the acid–base balance, blood glucose and coagulation times. An EEG will show acute hepatic encephalopathy and a CT scan may demonstrate cerebral oedema.

Management

Early referral to a national paediatric liver centre is essential.

Steps to stabilize the child prior to transfer include:

- maintaining the blood glucose (>4 mmol/L) with intravenous dextrose
- preventing sepsis with broad-spectrum antibiotics and antifungal agents
- preventing haemorrhage, particularly from the gastrointestinal tract, with intravenous vitamin K and H₂-blocking drugs or proton pump inhibitors
- prevent cerebral oedema by fluid restriction and mannitol diuresis if oedema develops.

Table 21.1 Causes of acute liver failure

Children <2 years old	Children >2 years
Infection (most common is herpes simplex)	Seronegative hepatitis
Metabolic disease	Paracetamol overdose
Seronegative hepatitis	Mitochondrial disease
Drug induced	Wilson disease
Gestational alloimmune liver disease	Autoimmune hepatitis

Features suggestive of a poor prognosis are a shrinking liver, rising bilirubin with falling transaminases, a worsening coagulopathy, or progression to coma. Without liver transplantation, 70% of children who progress to coma will die.

Liver disease in older children

The causes of chronic liver disease are listed in Box 21.2. The clinical presentation varies from an apparent acute hepatitis to the insidious development of hepatosplenomegaly, cirrhosis, and portal hypertension with lethargy and malnutrition. The most common causes are hepatitis viruses (B or C), autoimmune hepatitis and non-alcoholic fatty liver disease, but Wilson disease should always be excluded.

Autoimmune hepatitis and sclerosing cholangitis

The mean age of presentation is 7 years to 10 years. It is more common in girls. It may present as an acute hepatitis, as fulminant hepatic failure or chronic liver disease with autoimmune features such as skin rash, arthritis, haemolytic anaemia, or nephritis. Diagnosis is based on elevated total protein, hypergammaglobulinaemia (IgG >20 g/L); positive autoantibodies, a low serum complement (C4); and typical histology. Autoimmune hepatitis may occur in isolation or in association with inflammatory bowel disease, coeliac disease, or other autoimmune diseases. Ninety percent of children with autoimmune hepatitis will respond to prednisolone and azathioprine. Sclerosing cholangitis is treated with ursodeoxycholic acid.

Cystic fibrosis

Cystic fibrosis is a multi-organ genetic disease due to abnormalities in the cystic fibrosis transmembrane regulator (CFTR), described in detail in Chapter 17 (Respiratory disorders). Liver disease is the second most common cause of death after respiratory disease. The most common liver abnormality is hepatic steatosis (fatty liver). It may be associated with protein energy malnutrition or micronutrient deficiencies. Steatosis does not generally progress, and treatment involves ensuring optimal nutritional support. More significant liver disease arises from thick tenacious bile with abnormal bile acid concentration leading to progressive biliary fibrosis. Cirrhosis and portal hypertension develop in 20% of children by

Box 21.2 Causes of chronic liver disease in older children

- Postviral hepatitis B, C
- Autoimmune hepatitis and sclerosing cholangitis
- Drug-induced liver disease (NSAIDs)
- Cystic fibrosis
- Wilson disease
- Fibropolycystic liver disease
- Non-alcoholic fatty liver disease
- α_1 -Antitrypsin deficiency

mid-adolescence. Early liver disease is difficult to detect by biochemistry, ultrasound or radioisotope scanning. Liver histology includes fatty liver, focal biliary fibrosis, or focal nodular cirrhosis. Supportive therapy includes endoscopic treatment of varices and nutritional therapy and treatment with ursodeoxycholic acid. Experience with the new CFTR modulators in cystic fibrosis-related liver disease (CFLD) is limited, but some may cause increased transaminases. Liver transplantation may be considered for those with end-stage liver disease, either alone or in combination with a heart-lung transplant.

Wilson disease

Wilson disease is an autosomal recessive disorder with an incidence of 1 in 200,000. Many mutations have now been identified. The basic genetic defect is a combination of reduced synthesis of caeruloplasmin (the copper-binding protein) and defective excretion of copper in the bile, which leads to an accumulation of copper in the liver, brain, kidney, and cornea. Wilson disease rarely presents in children under the age of 3 years. In those presenting in childhood, a hepatic presentation is more obvious, but subtle neurological damage is likely to be present. They may present with almost any form of liver disease, including acute hepatitis, fulminant hepatitis, cirrhosis, and portal hypertension. Neuropsychiatric features are more common in those presenting from the second decade onwards and include deterioration in school performance, mood and behaviour change, and extrapyramidal signs such as incoordination, tremor, and dysarthria. Renal tubular dysfunction, with vitamin D-resistant rickets, and haemolytic anaemia also occur. Copper accumulation in the cornea (Kayser–Fleischer rings) (Fig. 21.6) is not seen before 7 years of age.

A low serum caeruloplasmin and copper is characteristic, but not universal. Urinary copper excretion is increased and this further increases after administering the chelating agent penicillamine. However, the diagnosis is confirmed by the finding of elevated hepatic copper on liver biopsy or identification of the gene mutation (ATP7B).

Treatment is with penicillamine or trientine. Both promote urinary copper excretion, reducing hepatic and central nervous system copper. Zinc is given to reduce copper absorption. Pyridoxine is given to prevent peripheral neuropathy. Zinc is used in asymptomatic children

identified by screening families with an index case. Neurological improvement may take up to 12 months of therapy. About 30% of children with Wilson disease will die from hepatic complications if untreated. Liver transplantation is considered for children with acute liver failure or severe end-stage liver disease.

Fibropolycystic liver disease (ciliopathies)

This is a range of inherited conditions affecting the development of the intrahepatic biliary tree. Presentation is with liver cystic disease or fibrosis and renal disease.

Congenital hepatic fibrosis presents in children over 2 years old with hepatosplenomegaly, abdominal distension, and portal hypertension. It differs from cirrhosis in that liver function tests are normal in the early stage. Liver histology shows large bands of hepatic fibrosis containing abnormal bile ductules. Complications include portal hypertension with varices and recurrent cholangitis. Cystic renal disease may coexist and may cause hypertension or renal dysfunction. Indications for liver transplant include severe recurrent cholangitis or deterioration of renal function requiring renal transplant, in which case a combined transplant would be offered.

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease is the single most common cause of chronic liver disease in the high-income world. It is a spectrum of disease, ranging from simple fatty deposition (steatosis) through to inflammation (steatohepatitis), fibrosis, cirrhosis, hepatocellular carcinoma and end-stage liver failure. In childhood, it may be associated with a metabolic syndrome or with obesity. The prognosis in childhood is uncertain; few develop cirrhosis in childhood in contrast to 8% to 17% of adults. They are usually asymptomatic, although some complain of vague right upper quadrant abdominal pain or lethargy. The diagnosis is often suspected following the incidental finding of an echogenic liver on ultrasound or mildly elevated transaminases carried out for some other reason. Liver biopsy demonstrates marked steatosis with or without inflammation or fibrosis. The pathogenesis is not fully understood but may be linked to insulin resistance. Treatment targets weight loss through diet and exercise, which may lead to liver function tests returning to normal.

Complications of chronic liver disease

Nutrition

Effective nutrition is essential. It may improve and stabilize patients with liver disease. Barriers to effective nutrition include:

- *fat malabsorption* – long chain fat is not effectively absorbed without bile. Therefore, medium chain triglyceride containing milk (specialist formula) is required if children are persistently cholestatic, as it does not require bile micelles for absorption. Up to 40% of fat needs to be long chain fat to prevent



Figure 21.6 Kayser–Fleischer rings from copper in the cornea in a child with Wilson disease.

Table 21.2 The effects of fat-soluble vitamin deficiency

Fat-soluble vitamin	Effect of deficiency
Vitamin K	Bleeding diathesis including intracranial bleeding
Vitamin A	Retinal changes in infants and night blindness in older children
Vitamin E	Peripheral neuropathy, haemolysis, and ataxia
Vitamin D	Rickets and fractures

- essential fatty acid deficiency. Fat-soluble vitamins are carried on the long chain fats and hence deficiency is common unless these vitamins are supplemented
- *protein malnutrition* – poor intake combined with high catabolic rate of the diseased liver makes protein malnutrition common at presentation of liver disease. Protein intake should not be restricted unless the child is acutely encephalopathic
 - *anorexia* – when unwell children cannot take the required amount of nutrition and many will require nasogastric tube feeding or occasionally parenteral nutrition.

Fat-soluble vitamins

All fat-soluble vitamins (Table 21.2) can be given orally. Monitoring of the levels and adjustment of dose is required to prevent deficiency. In severe deficiency, intramuscular administration may be required.

Pruritus

Severe pruritus is associated with cholestasis, although the aetiology is not clear. Pruritis is difficult to manage and may lead to excoriation of the skin. Treatment includes:

- loose cotton clothing, avoiding overheating, keep nails short
- moisturizing the skin with emollients
- medication – phenobarbital to stimulate bile flow; cholestyramine, a bile salt resin to absorb bile salts; ursodeoxycholic acid, an oral bile acid to solubilize the bile; rifampicin, an enzyme inducer; and the new ileal bile acid transporter inhibitors (IBATs).

Encephalopathy

This occurs in end-stage liver disease and may be precipitated by gastrointestinal haemorrhage, sepsis, sedatives, renal failure, or electrolyte imbalance. It is difficult to diagnose in children as the level of consciousness may vary throughout the day. Infants present with irritability and sleepiness, while older children present with abnormalities in mood, sleep rhythm, intellectual performance and behavior disturbance. Plasma ammonia may be elevated and an EEG is always abnormal. Oral lactulose and a non-absorbable oral antibiotic (e.g. rifaximin) will help reduce the ammonia by lowering the colonic pH and increasing gut transit time.



Figure 21.7 This is a liver that has been removed at the time of transplant in a child with severe cholestasis. The liver is green due to intrahepatic and parenchymal cholestasis. The nodular surface is indicative of cirrhosis and regenerative nodules.



Figure 21.8 Cirrhosis and portal hypertension. Malnutrition with loss of fat and muscle bulk; distended abdomen from hepatosplenomegaly and ascites; scrotal swelling from ascites; and no jaundice, despite advanced liver disease.

Cirrhosis and portal hypertension

Cirrhosis is the end result of many forms of liver disease. It is defined pathologically as extensive fibrosis with regenerative nodules. It may be secondary to hepatocellular disease or to chronic bile duct obstruction (biliary cirrhosis) (Fig. 21.7). The main pathophysiological effects of cirrhosis are diminished hepatic function and portal hypertension with splenomegaly, varices, and ascites (Fig. 21.8). Hepatocellular carcinoma may develop.

Children with compensated cirrhosis may be asymptomatic if liver function is adequate. They will not be jaundiced and may have normal liver function tests. As the cirrhosis increases, however, the results of deteriorating liver function and portal hypertension become obvious. Physical signs include jaundice, palmar (Fig. 21.9) and



Figure 21.9 Palmar erythema in a child with biliary atresia.



Figure 21.10 Facial telangiectasia, spider naevi, and mild jaundice in a child with progressive familial intrahepatic cholestasis type 2.

plantar erythema, telangiectasia and spider naevi (Fig. 21.10), malnutrition, and hypotonia. Dilated abdominal veins and splenomegaly suggest portal hypertension, although the liver may be shrunken and impalpable.

Investigations include:

- screening for the known causes of chronic liver disease
- upper gastrointestinal endoscopy to detect the presence of oesophageal varices and/or erosive gastritis
- abdominal ultrasound – may show a shrunken liver and splenomegaly with gastric and oesophageal varices
- liver biopsy – may be difficult because of increased fibrosis but may indicate the aetiology (e.g. typical changes in congenital hepatic fibrosis, copper storage).

As cirrhosis decompensates, biochemical tests may demonstrate an elevation of aminotransferases and alkaline phosphatase. The plasma albumin falls and the prothrombin time becomes increasingly prolonged.

Oesophageal varices

These are an inevitable consequence of portal hypertension and may develop rapidly in children. They are best diagnosed by upper gastrointestinal endoscopy. Acute bleeding is treated with blood transfusions and H₂-blockers (e.g. ranitidine) or omeprazole. Octreotide infusion, vasopressin analogues, endoscopic band ligation, or sclerotherapy may be effective. Portacaval shunts may preclude liver transplantation, but radiological placement of a stent between the hepatic and portal veins (transjugular intrahepatic portosystemic shunt, TIPS) can be used as a temporary measure if transplantation is being considered.

Ascites

Ascites is a major problem (Fig. 21.11). The pathophysiology of ascites is uncertain, but contributory factors include hypoalbuminaemia, sodium retention, renal impairment and fluid redistribution. It is treated by sodium and fluid restriction and diuretics. Additional therapy for refractory ascites includes albumin infusions or paracentesis.



Figure 21.11 Tense ascites in a baby with end-stage liver disease.

Spontaneous bacterial peritonitis

This should always be considered if there is undiagnosed fever, abdominal pain, tenderness, or an unexplained deterioration in hepatic or renal function. A diagnostic paracentesis should be performed and the fluid sent for white cell count and differential and culture. Treatment is with broad-spectrum antibiotics.

Renal failure

This may be secondary to renal tubular acidosis, acute tubular necrosis, or functional renal failure (hepatorenal syndrome).

Liver transplantation

Liver transplantation is an accepted therapy for acute or chronic end-stage liver failure and has revolutionized the prognosis for these children. Transplantation is also considered for some hepatic malignancy (hepatoblastoma or hepatocellular carcinoma).

The indications for transplantation in chronic liver failure are:

- severe malnutrition unresponsive to intensive nutritional therapy
- complications refractory to medical management (bleeding varices, resistant ascites)
- failure of growth and development
- poor quality of life.

Liver transplant evaluation includes assessment of the vascular anatomy of the liver and exclusion of irreversible disease in other systems. Absolute contraindications include sepsis, untreatable cardiopulmonary disease or cerebrovascular disease.

There is considerable difficulty in obtaining small organs for children. Most children receive part of an adult's liver, either a cadaveric graft or more recently from a living related donor. A cadaveric organ may either be reduced to fit the child's abdomen (reduction hepatectomy) or split (shared between an adult and child).

Complications post-transplantation include:

- primary non-function of the liver (5%)
- hepatic artery thrombosis (10%–20%)
- biliary leaks and strictures (20%)
- rejection (30%–60%)
- sepsis, the main cause of death.

In large national centres, the overall 1-year survival is approximately 90%, and the overall 20-year survival is greater than 80%. Most deaths occur in the first 3 months. Children who survive the initial postoperative period usually do well. Long-term studies indicate normal psychosocial development and quality of life in survivors.

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Further reading

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Websites

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Malignant disease

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Features of malignant disease in children:

- The pattern of malignant disease varies with age and between continents.
- Awareness of clinical presentation is important as early diagnosis may improve outcome.
- Prognosis for many types of malignant disease has improved markedly, but often involves intensive therapy, multiple clinical assessments, investigations and hospital admissions over many years.
- Management is conducted by specialist centres, but in the UK shared care networks allow supportive care to be provided by hospitals and community nearer home.

Cancer in children is not common:

- Around 1 child in 500 develops cancer by 15 years of age.
- Each year, in Western countries, there are 120 to 140 new cases per million children aged under 15 years (1500 new cases each year in the UK).

The types of disease (Fig. 22.1) are very different from adults, where carcinomas of the lung, breast, bowel, and prostate predominate. The age at presentation varies with the different types of disease:

- Leukaemia affects children at all ages (although there is an early childhood peak).
- Neuroblastoma and Wilms tumour (known as embryonal tumours) are almost always seen in the first 6 years of life.
- Hodgkin lymphoma and bone tumours have their peak incidence in adolescence and early adult life.

Despite significant improvements in survival over the last four decades (Fig. 22.2), cancer is the most common disease causing death in childhood (beyond the neonatal period). Overall, 5-year survival of children with all forms of cancer is about 75%, most of whom can be considered cured, although cure rates vary considerably between diagnoses. This improved life expectancy can be attributed to the introduction of multi-agent chemotherapy, improved supportive care, and specialist multidisciplinary management. However, for some children, the price of survival is long-term medical or psychosocial difficulties with over 60% childhood cancer survivors living with at least one chronic condition related to their cancer or its treatment.

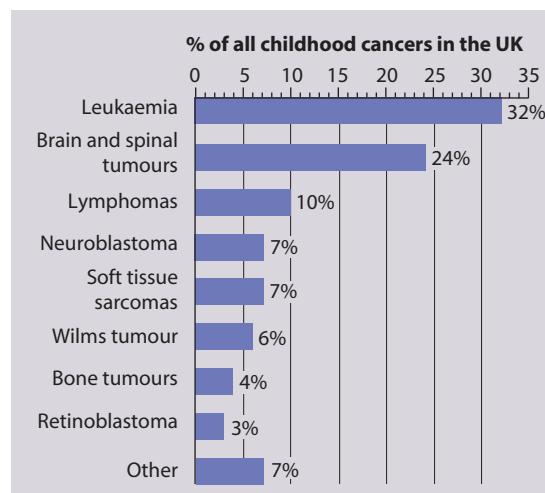


Figure 22.1 Relative frequency of different types of cancer in children in the UK.

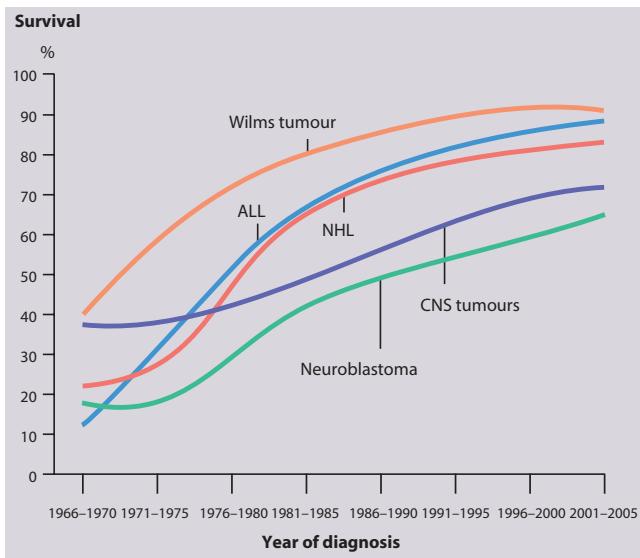


Figure 22.2 Five-year survival rates showing the considerable improvement over the 50 years from 1966 to 2005. ALL, acute lymphoblastic leukaemia; CNS, central nervous system; NHL, non-Hodgkin lymphoma. (From: National Registry of Childhood Tumours, Childhood Cancer Research Group, with permission.)

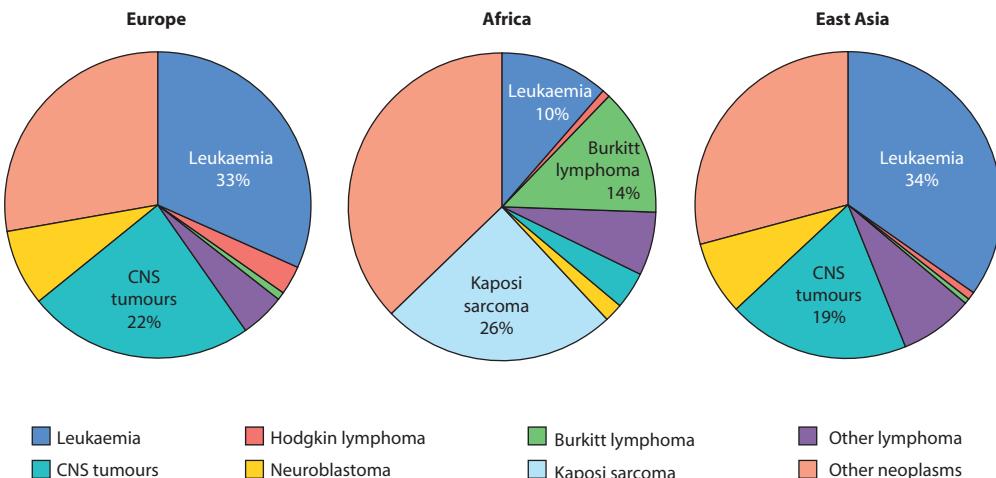


Figure 22.3 International distributions of cancer in children highlighting much higher frequency of Burkitt lymphoma and Kaposi sarcoma in Africa than in Europe or East Asia populations. (Data from: *Global Cancer Facts and Figures*, ed 2, 2011, American Cancer Society.)



For children in the Western world, leukaemia is the most common malignancy followed by brain tumours.

Aetiology

In most cases, the aetiology of childhood cancer is unclear, but it is likely to involve interaction between environmental factors (e.g. viral infection) and host genetic susceptibility. In fact, there are very few established environmental risk factors. Cancer is usually sporadic but may be inherited, although in most cases a specific gene mutation is unknown. Research initiatives, such as the 100,000 genome project in the UK, may better elucidate the genetic causes of childhood cancer.

One well-established example of an inherited cancer is bilateral retinoblastoma (associated with a mutation within the RB gene, on chromosome 13). There are also syndromes associated with an increased risk of cancer in childhood, e.g. Down syndrome and leukaemia, and neurofibromatosis and glioma. Identification of biological characteristics of specific tumour cells may help elucidate the basic pathogenetic mechanisms behind their origin.

Examples of infection-related childhood cancers include Burkitt lymphoma, Hodgkin lymphoma and nasopharyngeal carcinoma (Epstein–Barr virus), liver carcinoma (hepatitis B), and Kaposi sarcoma (HIV and human herpes virus 8). Viral-mediated Burkitt lymphoma and Kaposi sarcoma are the most common childhood cancers in Africa, but account for a very small proportion of childhood cancer in Western countries (Fig. 22.3).

Clinical presentation

Cancer in children can present with wide-ranging symptoms and signs but typical presentations are:

- a localized mass
- the consequences of disseminated disease, e.g. bone marrow infiltration, causing systemic ill-health
- the consequences of pressure from a mass on local structures or tissue, e.g. airway obstruction secondary to enlarged lymph nodes in the mediastinum.

Presentation can also be as an acute emergency (Table 22.1).

Investigations

Initial symptoms can be very non-specific, and this can lead to a delay in diagnosis. Once a diagnosis of malignancy is suspected, the child should be referred immediately to a specialist centre for further investigation.

Radiology

The location of solid tumours and evidence of any metastases are identified, using a combination of ultrasound, plain X-rays, CT and MRI scans. Nuclear medicine imaging (e.g. radiolabelled technetium bone scan) may be useful to identify bone or bone marrow disease or, using special markers, MIBG scans localize tumours of neural crest origin, e.g. neuroblastoma. Positron emission tomography (PET) enables identification of metabolically active cells and is increasingly used in staging and assessment of response to treatment of certain diseases, including Hodgkin lymphoma and sarcoma.

Table 22.1 Oncological emergencies

Haematological	Bone marrow failure – anaemia, thrombocytopenia, neutropenia Hyperleukocytosis (white cell count $>100 \times 10^9/L$) Coagulopathy – bleeding, DIC
Infection	Bacterial, viral, fungal Sepsis
Neurological	Raised intracranial pressure (obstructive hydrocephalus) Spinal cord compression
Metabolic/ Endocrine	Tumour lysis syndrome (on initiating chemotherapy; risk of acute renal failure) Hypercalcaemia SIADH (syndrome of inappropriate anti-diuretic hormone) Diabetes insipidus
Other	Superior vena cava obstruction (SVCO) Airway obstruction Cardiac tamponade

Tumour marker studies

Increased urinary catecholamine excretion (e.g. VMA, vanillylmandelic acid, and HVA, homovanillic acid) is useful in confirming the diagnosis of neuroblastoma. High α -fetoprotein (α FP) production is often observed in germ cell and liver tumours and can be used to monitor treatment response.

Pathology

Typically, diagnoses are confirmed histologically, either by bone marrow aspiration (leukaemia) or by biopsy for most solid tumours, although this may not always be possible for brain tumours. Histological techniques such as immunohistochemistry are routinely used to differentiate tumour types. Molecular and genetic techniques are also used to confirm diagnosis (e.g. translocation of chromosomes 11 and 22 in Ewing sarcoma) and to predict prognosis (e.g. amplification of the myc oncogene associated with a poor prognosis in neuroblastoma).

Management

Once malignancy is suspected, the parents and child need to be seen and the diagnostic pathway explained to them. Detailed investigation to define the extent of the disease (staging) is paramount to planning treatment. Children are usually treated as part of national and international collaborative studies that offer consistency in care and have contributed to improvements in outcome.

In the UK, children with cancer are initially investigated and treated in specialist centres where experienced multidisciplinary teams can provide the intensive medical and psychosocial support required. Treatment plans are agreed by the multidisciplinary team. Subsequent management is often shared between the specialist centre, referral hospital, and local services within the community, to provide the optimum care with the least disruption to the family. This requires all team members to have the required expertise and work to shared protocols.

Teenagers and young adults

Survival statistics suggest that older teenagers and young adults have poorer outcomes than children and constitute a distinct population. This relates both to the specific types of cancer, biological behaviour of their tumours and to their particular social/psychological needs. This has prompted the development of age-appropriate treatment protocols, facilities, and support networks.

Treatment

Treatment may involve chemotherapy, surgery, or radiotherapy, alone or for most children in combination.

Chemotherapy

Cytotoxic chemotherapy agents target cells that are rapidly proliferating and typically cause cell death by interfering with DNA replication/repair mechanisms, cell division, or metabolic pathways.

Chemotherapy is used:

- as primary curative treatment, e.g. in acute lymphoblastic leukaemia
- to control primary or metastatic disease before definitive local treatment with surgery and/or radiotherapy (neoadjuvant treatment), e.g. in sarcoma or neuroblastoma
- as adjuvant treatment to deal with residual disease and to eliminate presumed micrometastases, e.g. after initial local treatment with surgery in Wilms tumour.

High-dose therapy with stem cell rescue

The limitation of chemotherapy (and radiotherapy) is the risk of irreversible damage to normal tissues, particularly bone marrow. Transplantation of bone marrow stem cells can be used as a strategy to intensify the treatment of patients with the administration of potentially lethal doses of chemotherapy and/or radiation. The source of stem cells may be allogeneic (from a compatible donor) or autologous (from the patient him/herself, harvested beforehand, while the marrow is uninvolved or in remission). Allogeneic transplantation is principally used in the management of high-risk or relapsed leukaemia and autologous stem cell support is used most commonly in the treatment of children with solid tumours whose prognosis is poor using conventional chemotherapy, e.g. high-risk neuroblastoma.

Targeted therapies and immunotherapy

A growing understanding of the molecular biology of cancer has led to the increasing development and use of targeted therapies. Examples include:

- cancer growth inhibitors including tyrosine kinase inhibitors, e.g. imatinib that targets the fusion gene (BCR-ABL) that causes Philadelphia chromosome positive (Ph+) acute lymphatic leukaemia and chronic myeloid leukaemia
- monoclonal antibodies, such as rituximab (anti-CD20) for lymphoma and anti-GD2 for treatment of high-risk neuroblastoma
- CAR (chimeric antigen receptor) T-cell therapy, a type of immunotherapy which involves the genetic engineering of T cells to kill leukaemia cells.

Radiotherapy

Radiotherapy uses high-energy radiation to kill cancer cells. It has most commonly been administered as 'external beam' photon radiotherapy. Proton beam radiotherapy is a different way of delivering radiotherapy and can be more precisely targeted at a tumour, reducing the dose (and potential damage) to normal adjacent structures, while maintaining cure rate in certain types of cancer. Proton beam therapy has recently become available for children in the UK. In addition, radiotherapy can be administered as an intravenous medicine (e.g. radioactive iodine for thyroid cancer or MIBG therapy for high-risk neuroblastoma). Occasionally brachytherapy (insertion of radioactive material) may be used in children. Radiotherapy has an important role in the treatment of some tumours, but risk of damage to growth and function of normal tissue is greater in a child than an adult. The need for adequate

protection of normal tissues and for careful positioning and immobilization of the patient during treatment raises practical difficulties, particularly in young children, who may require a daily general anaesthetic for the duration of treatment. Cranial radiotherapy in children under the age of 3 years is particularly problematic because of the significant risk of severe damage to cognitive development.

Surgery

In contrast to adult cancer treatment, most children with solid tumours require adjuvant or neo-adjuvant treatment. Therefore initial surgery is frequently restricted to biopsy to establish diagnosis, and more extensive operations are usually undertaken to remove residual tumour after chemotherapy and/or radiotherapy.

Supportive care and side-effects of disease and treatment

Cancer and its treatment produces frequent, predictable, and often severe multisystem side-effects (Fig. 22.4). Supportive care is an important part of management and improvements in this aspect of cancer care have contributed to the increasing survival rates. Patients must have access to immediate care throughout their treatment as potential complications can present as an emergency, as outlined above.

Infection from immunosuppression

Due to both treatment (chemotherapy or wide-field radiation) and underlying disease, children with cancer are immunocompromised and at risk of serious infection. Children with fever and neutropenia must be admitted promptly to hospital for cultures and treatment with broad-spectrum antibiotics. Some important opportunistic infections associated with therapy for cancer include *Pneumocystis jiroveci* pneumonia (especially in children with leukaemia), disseminated fungal infection (e.g.

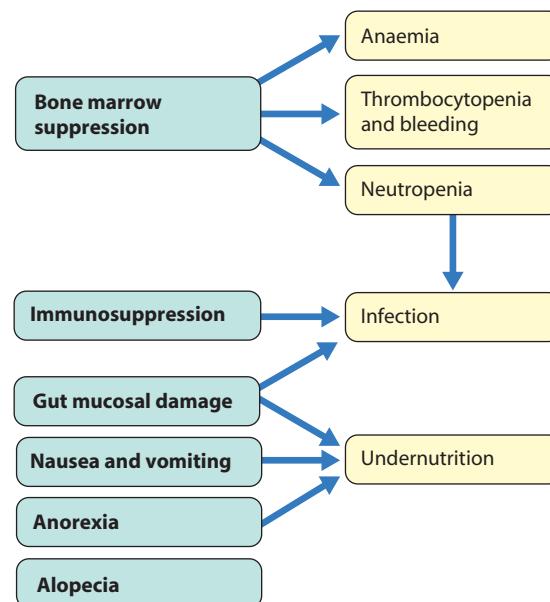


Figure 22.4 Short-term side-effects of chemotherapy.

aspergillosis and candidiasis) and coagulase-negative staphylococcal infections of central venous catheters.

Most common viral infections are no worse in children with cancer than in other children, but measles and varicella zoster (chickenpox) may have atypical presentation and can be life-threatening. If non-immune, immunocompromised children are at risk from contact with measles or varicella, some protection can be afforded by prompt administration of immunoglobulin or zoster immune globulin. Aciclovir is used to treat established varicella infection, but no treatment is available for measles. During chemotherapy and from 6 months to a year subsequently, the use of live vaccines is contraindicated due to depressed immunity. After this period, reimmunization against common childhood infections is recommended. Flu vaccines are recommended for children on treatment. UK data from 2020 suggests that children with cancer are not at increased risk of severe infection with COVID-19. More data is being collected internationally on this.



Fever with neutropenia requires hospital admission, investigation and treatment.

Bone marrow suppression

Anaemia may require blood transfusions. Thrombocytopoenia presents the risk of bleeding, and considerable blood product support may be required, particularly for children with leukaemia, those undergoing intensive therapy requiring bone marrow transplantation, and in the more intensive solid tumour protocols.

Gastrointestinal damage, nausea and vomiting, and nutritional compromise

Mouth ulcers are common, painful and, when severe, can prevent a child eating adequately. Many chemotherapy agents are nauseating and induce vomiting, which may be only partially prevented by the routine use of antiemetic drugs. These two complications can result in significant nutritional compromise and supplementary nasogastric or parenteral feeding regimes may be needed. Chemotherapy-induced gut mucosal damage also causes diarrhoea and may predispose to Gram-negative infection.

Drug-specific side-effects

Many individual drugs have specific side-effects: e.g. cardiotoxicity with doxorubicin; renal failure and deafness with cisplatin; haemorrhagic cystitis with cyclophosphamide; and neuropathy with vincristine. The extent of these side-effects is not always predictable and patients require careful monitoring during and, in some cases, after treatment is complete.

Pain

Pain in children with cancer can be from many causes, including:

- disease infiltration or direct pressure on other organs
- side-effects of cancer treatment, such as mouth or skin sores
- surgical procedures.

Paediatric palliative care specialists are often part of the wider cancer multidisciplinary team and can also provide expertise in pain management.

Other supportive care issues

Fertility preservation

Some patients may be at risk of infertility as a result of their cancer treatment. Appropriate fertility preservation techniques may involve surgically moving a testis or ovary out of the radiotherapy field; sperm banking (which should be offered to boys mature enough to achieve this); and consideration of newer techniques such as cryopreservation of ovarian cortical tissue or testicular tissue should be considered, although the long-term efficacy of this is still uncertain.

Venous access

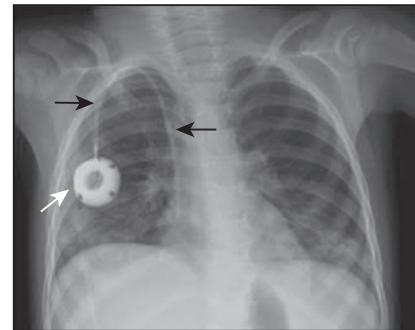
The discomfort of multiple venepunctures for blood sampling and intravenous infusions can be avoided with central venous catheters. Different types of catheter are used including tunneled venous catheters (Hickman lines) and implantable ports. A port is similar to a tunneled catheter but is left entirely under the skin (Fig. 22.5a, b). Central venous catheters can remain *in situ* for many months if not years, but they carry a risk of infection and can become blocked or split.

Psychosocial support

The diagnosis of a potentially fatal illness has an enormous and long-lasting impact on the whole family. They need the opportunity to discuss implications of the diagnosis and its



(a)



(b)

Figure 22.5 (a) A central venous catheter allows pain-free blood tests and injections for this child on chemotherapy, which has caused the alopecia. (b) A port device (white arrow) visualized on a chest X-ray. The black arrows show the central line.

treatment, and their anxiety, fear, guilt and sadness. Most will benefit from the counselling and practical support provided by health professionals. Help with practical issues, including transport, finances, accommodation, and care of siblings, is an early priority. The provision of detailed written material for parents will help them understand their child's disease and treatment. The children themselves, and their siblings, need an age-appropriate explanation of the disease. Once treatment is established and the disease appears to be under control, families should be encouraged to return to as normal a lifestyle as possible. Early return to school is important and children with cancer should not be allowed to under-achieve the expectations previously held for them. It is easy to underestimate the severe stress that persists within families in relation to the uncertainty of the long-term outcome. This often manifests itself as marital problems in parents and behavioural difficulties in both the child and siblings.

Summary

Malignant disease in children

- Uncommon, but affects 1 in 500 by 15 years of age.
- Can present with a localized mass, or its pressure effects, or disseminated disease.
- Treatment may involve chemotherapy, surgery, radiotherapy, or high-dose therapy with stem cell rescue.
- Fever with neutropenia must be investigated and treated urgently.
- Measles and varicella zoster infection are potentially life-threatening.
- A multidisciplinary team is required to provide supportive care and psychosocial support.
- Supportive care includes not only management of side-effects but also of pain and fertility preservation.
- Psychosocial support – includes not only the patient and parents but also siblings and other family and community members.

Leukaemia

Acute lymphoblastic leukaemia (ALL) accounts for 80% of leukaemia in children. Most of the remainder is acute myeloid leukaemia/acute non-lymphocytic leukaemia (AML/ANLL). Chronic myeloid leukaemia and other myeloproliferative disorders are rare.

Clinical presentation

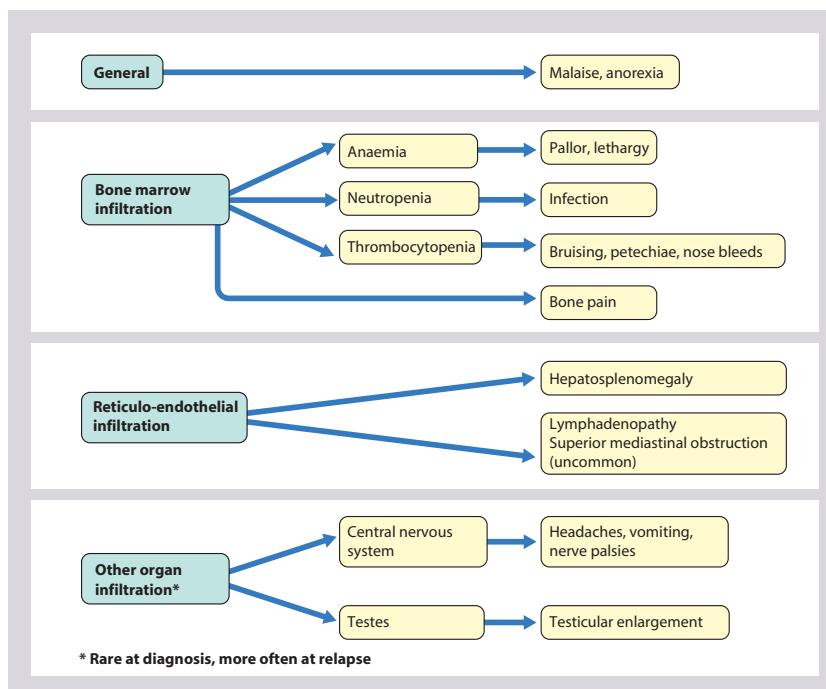
Presentation of ALL peaks at 2–5 years of age. Clinical symptoms and signs result from disseminated disease and systemic ill-health from infiltration of the bone marrow or other organs with leukemic blast cells (Fig. 22.6). In most children, leukaemia presents insidiously over several weeks (see *Case history 22.1*) but in some children the illness presents and progresses very rapidly.

Investigations

In most but not all children, the full blood count is abnormal, with low haemoglobin, thrombocytopenia, and evidence of circulating leukemic blast cells. Bone marrow examination is essential to confirm the diagnosis and to identify immunological and cytogenetic characteristics which give useful prognostic information. A coagulation screen should be performed as approximately 10% of patients with acute leukaemia have disseminated intravascular coagulation (DIC) at the time of diagnosis. These patients may present with haemorrhagic or thrombotic complications. A lumbar puncture is performed to identify disease in the CSF. Chest X-ray is required to identify a mediastinal mass characteristic of T-cell disease.

Both ALL and AML are classified by morphology. Immunological phenotyping further subclassifies ALL; the common B-cell (75%) and T-cell (15%) subtypes are the most frequent. Prognosis and some aspects of clinical presentation vary according to different subtypes, and treatment intensity is adjusted accordingly.

Figure 22.6 Signs and symptoms of acute leukaemia.





Case history 22.1

Disseminated disease, e.g. bone marrow infiltration, causing systemic ill-health

A 4-year-old girl was generally unwell, lethargic, looking pale, and occasionally febrile over a period of 9 weeks. Two courses of antibiotics for recurrent sore throat failed to result in any benefit. Her parents returned to their general practitioner when she developed a rash. Examination showed pallor, petechiae, modest generalized lymphadenopathy, and mild hepatosplenomegaly. A full blood count showed:

- Haemoglobin 83 g/L
- White blood cells $15.6 \times 10^9/\text{L}$
- Platelets $44 \times 10^9/\text{L}$.

Blast cells were seen on the peripheral blood film. CSF examination was normal. Bone marrow examination confirmed acute lymphoblastic leukaemia (Fig. 22.7).

Diagnosis: Acute lymphoblastic leukaemia.

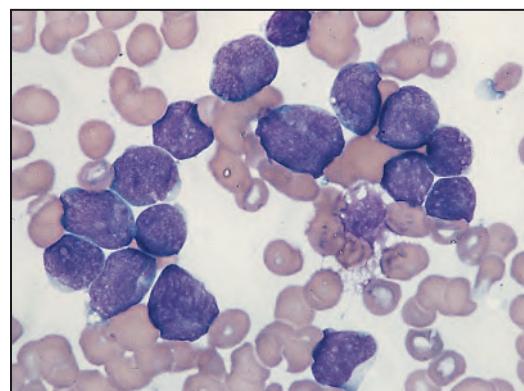


Figure 22.7 Leukemic blast cells on a bone marrow smear.

Management of acute lymphoblastic leukaemia

A number of factors contribute to prognosis in ALL including age, white cell count at presentation, cytogenetics of the leukemic cells, and response to treatment. The intensity of therapy is adapted according to risk (Table 22.2).

Remission induction

Before starting treatment of the disease, anaemia may require correction with blood transfusion, risk of bleeding minimized by transfusion of platelets, and infection must be treated. Additional hydration and allopurinol (or urate oxidase when the white cell count is high and the risk is greater) are given to protect renal function against the effects of rapid cell lysis. Remission implies eradication of the leukemic blasts and restoration of normal marrow function. Combination chemotherapy including steroids is given and current induction treatment schedules achieve remission rates of 95%.

Intensification

A block of intensive chemotherapy is given to consolidate remission. This improves cure rates but at the expense of increased toxicity.

Central nervous system

Cytotoxic drugs penetrate poorly into the central nervous system (CNS). As leukemic cells in this site may survive effective systemic treatment, treatment with intrathecal chemotherapy is used to prevent CNS relapse. Patients with evidence of CNS disease at diagnosis receive additional doses of intrathecal chemotherapy during induction.

Continuing therapy

Chemotherapy of modest intensity is continued over a relatively long period of time, up to 3 years from diagnosis. Cotrimoxazole prophylaxis is given routinely to prevent *Pneumocystis* pneumonia.

Treatment of relapse

High-dose chemotherapy, with or without total body irradiation followed by bone marrow transplantation, is used as an alternative to conventional chemotherapy after a relapse. CAR (chimeric antigen receptor) T-cell therapy (using genetically engineered T-cell receptors) is also being used to treat relapsed B cell ALL in selected patients.

Table 22.2 Prognostic factors in acute lymphoblastic leukaemia

Prognostic factor	High-risk features
Age	<1 year or >10 years
Tumour load (measured by the white cell count)	$>50 \times 10^9/\text{L}$
Cytogenetic/molecular genetic abnormalities in tumour cells	e.g. MLL rearrangement, t(4;11) hypodiploidy (<44 chromosomes)
Speed of response to initial chemotherapy	Persistence of leukemic blasts in the bone marrow
Minimal residual disease (MRD) assessment (submicroscopic levels of leukaemia detected by PCR)	Detectable MRD after induction therapy

Brain tumours

In contrast to adults, brain tumours in children are almost always primary rather than metastatic and 60% are infratentorial (located below the tentorium cerebelli). They are the most common solid tumour in children and are the leading cause of childhood cancer deaths in the UK. Types of brain tumour in children (Fig. 22.8) include:

- Astrocytoma (~40%) – varies from (low grade) to highly malignant (high grade, *glioblastoma multiforme*).
- Medulloblastoma (~20%) – arises in the midline of the posterior fossa. May seed through the CNS via the CSF and up to 20% have spinal metastases at diagnosis.
- Ependymoma (~8%) – most common site is IVth ventricle but may arise anywhere in CSF spaces. 10% are slow growing low grade but the remainder present as aggressive tumours requiring complete resection and radiotherapy for cure.
- Brainstem glioma (6%) – malignant tumours associated with a very poor prognosis.

Brain tumours – sites, presentation and typical case histories

(a)

Supratentorial:
• Cortex – astrocytoma

Midline:
• Craniopharyngioma

Infratentorial:
• Cerebellar – medulloblastoma, astrocytoma, ependymoma
• Brainstem – brainstem glioma

Spinal cord:
• Astrocytoma, ependymoma

Headache and behaviour changes – is there raised intracranial pressure?

Clinical presentation

All ages

- Persistent or recurrent vomiting
- Problems with balance, coordination or walking
- Behavioural change
- Abnormal eye movements
- Seizures (without fever)
- Abnormal head position – wry neck, head tilt or persistent stiff neck

Child/Teenager

- Persistent or recurrent headache
- Blurred or double vision
- Lethargy
- Deteriorating school performance
- Delayed or arrested puberty, slow growth

Infants

- Developmental delay/regression
- Progressive increase in head circumference, separation of sutures, bulging fontanelle
- Lethargy

Site of tumour and clinical features specific to anatomical position

Supratentorial – cortex

- Seizures
- Hemiplegia
- Focal neurological signs

Midline

- Visual field loss – bitemporal hemianopia
- Pituitary failure – growth failure, diabetes insipidus, weight gain

Cerebellar and IVth ventricle

- Truncal ataxia
- Coordination difficulties
- Abnormal eye movements

Brainstem

- Cranial nerve defects
- Pyramidal tract signs
- Cerebellar signs – ataxia
- Often no raised intracranial pressure

MRI Scans

(b)

(c)

(d)

(e)

Typical case history

(b) 14-year-old. Aggressive behaviour at school, headaches, seizure
MRI scan – (Fig. 22.8b)
Diagnosis – **astrocytoma – glioblastoma multiforme**
Management – surgery, radiotherapy +/- chemotherapy, but prognosis poor (<30% survival)
Astrocytomas – commonly found in the cerebral hemispheres, thalamus and hypothalamus. For posterior fossa tumours, see below.

(c) 10-year-old complaining of headaches, vomiting, poor growth, struggling to see the board at school.
MRI scan – (Fig. 22.8c)
Diagnosis – **craniopharyngioma**
Management – surgical excision +/- radiotherapy
Prognosis – good survival but risk of long-term visual impairment and lifelong, complex pituitary insufficiency

(d) 3-year-old vomiting in the mornings, unsteady on his feet, new-onset convergent squint.
MRI scan – (Fig. 22.8d)
Diagnosis – **medulloblastoma**
Management – surgery, chemotherapy, radiotherapy.
Prognosis – survival rates are improving with 5-year survival about 50%
Other posterior fossa tumours:
Astrocytoma – cystic, slow growing. Good prognosis following surgery.
Ependymoma – most are aggressive tumours

(e) 4-year-old. Refuses to walk, unable to climb stairs, squint, facial asymmetry and drooling.
MRI scan – (Fig. 22.8e)
Diagnosis – **brainstem glioma**. But not for biopsy as too hazardous.
Management – palliative radiotherapy
Prognosis – very poor (<10% survival)

Figure 22.8 (a) Location of brain tumours. Clinical features of brain tumours. MRI scans showing (b) fronto-parietal mass; (c) large midline suprasellar mass; (d) cerebellar mass; and (e) brainstem mass.

- Craniopharyngioma (4%) – a developmental tumour arising from the squamous remnant of Rathke pouch. It is not truly malignant but is locally invasive and grows slowly in the suprasellar region.
- Atypical teratoid/rhabdoid tumour – a rare type of aggressive tumour that most commonly occurs in young children.

Clinical features

The developmental age of the child is important as presentation varies according to age and their ability to report symptoms (see Fig. 22.8 – Clinical presentation). Signs and symptoms are often related to evidence of raised intracranial pressure but focal neurological signs may be detected depending on the site of the tumour. Papilloedema may be present, but can be a late sign and difficult to detect.

Spinal tumours, primary or metastatic, can present with back pain, peripheral weakness of arms or legs, or bladder/bowel dysfunction, depending on the level of the lesion.



Persistent back pain in children warrants investigation with MRI scan.

Investigations

Brain tumours are best characterized on MRI scan. Magnetic resonance spectroscopy can be used to examine the biological activity of a tumour and aid radiological diagnosis. Some tumour types can metastasize within the CSF and a lumbar puncture is therefore required for complete staging of the disease. Lumbar puncture must not be performed without neurosurgical advice if there is any suspicion of raised intracranial pressure.

Management

Surgery is usually the first treatment and is aimed at treating hydrocephalus, providing a tissue diagnosis and attempting maximum resection. In some cases the anatomical position of the tumour means biopsy is not safe, e.g. tumours in the brainstem and optic pathway. Even tumours which are histologically ‘benign’ can threaten survival. The use of radiotherapy and/or chemotherapy varies with tumour type and the age of the patient.

Neurorehabilitation and late effects

A brain tumour is an acquired brain injury. The functional implications of the site of the tumour, the potential hazards of surgery and the importance of radiotherapy in treatment all combine to place children with brain tumours at particular risk of sequelae. In the acute phase, neurorehabilitation including physiotherapy, occupational therapy, speech and language therapy may be required to support optimal recovery. Survivors living with disability, growth, endocrine, neuropsychological, and educational problems require complex care management into adulthood.

Lymphomas

Lymphomas are malignancies of the cells of the immune system and can be divided into Hodgkin and non-Hodgkin lymphoma (NHL). NHL is more common in childhood, while Hodgkin lymphoma is seen more frequently in adolescence.



Figure 22.9 PET scan showing active disease in Hodgkin lymphoma in the right cervical and axillary nodes.

Hodgkin lymphoma

Clinical features

Classically presents with painless lymphadenopathy, most frequently in the neck. Lymph nodes are much larger and firmer than the benign lymphadenopathy commonly seen in young children. The lymph nodes may cause airway or SVC (superior vena cava) obstruction (see Case history 22.2). The clinical history is often long (several months), and systemic symptoms (sweating, weight loss, fever and pruritus – the so-called ‘B’ symptoms) are uncommon, even in more advanced disease.

Investigations

Lymph node biopsy, radiological assessment of all nodal sites and bone marrow biopsy are used to stage disease and determine treatment.

Management

Combination chemotherapy with or without radiotherapy. Positron emission tomography (PET) scanning is used in the UK to monitor treatment response and guide further management (Fig. 22.9).

Overall, about 80% of all patients can be cured. Even with disseminated disease, about 60% can be cured.

Non-Hodgkin lymphoma

T-cell non-Hodgkin lymphoma usually presents with a mediastinal mass with varying degrees of marrow infiltration. The mediastinal mass may cause superior vena cava obstruction presenting with dyspnoea, facial swelling and flushing venous distension in the neck and distended veins in the upper chest and arms (Fig. 22.10). These children need rapid assessment in a unit with Paediatric Intensive Care facilities.

B-cell non-Hodgkin lymphoma may present with lymphadenopathy in the head and neck or abdomen with a short history of illness. Abdominal disease presents with pain from intestinal obstruction, a palpable mass or even intussusception in cases with involvement of the ileum.



Figure 22.10 Venous distension over the chest wall secondary to superior vena cava obstruction from T-lymphoblastic lymphoma.



Case history 22.2

Pressure from a mass on local structures or tissue, e.g. airway obstruction secondary to enlarged lymph nodes

A 14-year-old girl complained of a cough for 2 weeks which was non-productive and worse at night. She had seen her general practitioner and her chest was clear. She returned 2 weeks later, as she had noticed a swelling in her neck. On examination, she had a large anterior cervical lymph node which was non-tender. On referral to hospital, she had a chest X-ray, which showed a large mediastinal mass (Fig. 22.11).

Differential diagnosis

- T-cell non-Hodgkin lymphoma/acute leukaemia
- Hodgkin lymphoma

Her full blood count was normal. A biopsy of the mass was consistent with a diagnosis of Hodgkin lymphoma.

Diagnosis: Hodgkin lymphoma.

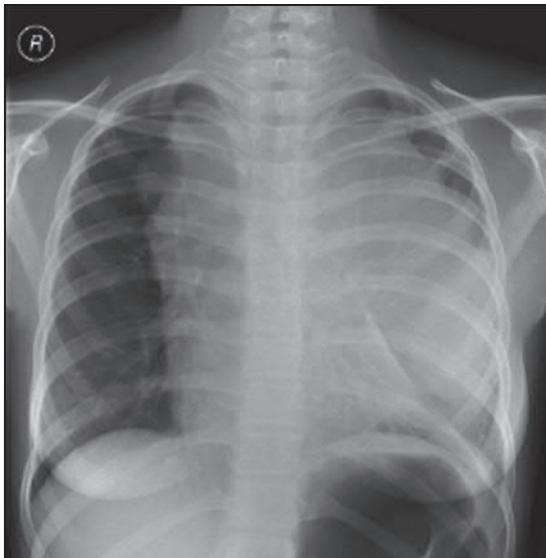


Figure 22.11 Chest X-ray showing a large mediastinal mass.



Figure 22.12 Burkitt lymphoma involving facial bones. (Courtesy of Liz Molyneux.)

Investigations

Biopsy, radiological assessment of all nodal sites (CT or MRI), and examination of the bone marrow and CSF.

Management

Multiagent chemotherapy. The majority of patients now do well and survival rates of over 80% are expected for both T-cell and B-cell disease. Relapse confers a poor prognosis.

Burkitt lymphoma

Burkitt lymphoma is a type of B-cell non-Hodgkin lymphoma and has three variants. The *endemic variant* most commonly occurs in children living in malaria endemic regions of the world and is the most common childhood cancer in Africa. Epstein–Barr virus (EBV) infection is found in nearly all patients as chronic malaria is believed to reduce resistance to EBV. The disease characteristically involves the jaw or other facial bone (Fig. 22.12), and it is not uncommon for patients to present with advanced stage disease. In the Western world cases are *sporadic* and can be associated with EBV infection. *Immunodeficiency-associated* Burkitt lymphoma is usually associated with HIV infection or occurs in patients on immunosuppression post-transplant. Treatment is with multi-agent chemotherapy.

Neuroblastoma

Neuroblastoma and related tumours arise from neural crest tissue in the adrenal medulla and sympathetic nervous system. It is a biologically unusual tumour in that spontaneous regression sometimes occurs in very young infants and there is a spectrum of disease from the benign (ganglioneuroma) to the highly malignant (neuroblastoma). Neuroblastoma is most common before the age of 5 years.

Clinical features

At presentation (Box 22.1), most children have an abdominal mass, but the primary tumour can lie anywhere along the sympathetic chain from neck to the pelvis. Classically, the abdominal primary is of adrenal origin, but at presentation the tumour mass is often large and complex, crossing the midline and enveloping major blood vessels and lymph nodes. Paravertebral tumours may invade through adjacent intervertebral foramen and cause spinal cord compression requiring emergency intervention to prevent devastating long-term neurological damage. Over the age of 2 years, clinical symptoms are mostly from metastatic disease, particularly bone pain, bone marrow suppression causing weight loss, and malaise (see Case history 22.3).

Box 22.1 Presentation of neuroblastoma

Common	Less common
Pallor	Paraplegia
Weight loss	Cervical lymphadenopathy
Abdominal mass	Proptosis
Hepatomegaly	Periorbital bruising
Bone pain	Skin nodules
Limp	Opsoclonus myoclonus (or dancing eye syndrome)

Investigations

Characteristic clinical and radiological features with raised urinary catecholamine metabolite levels (VMA/HVA) suggest neuroblastoma. Confirmatory biopsy is usually obtained and evidence of metastatic disease detected with bone marrow sampling and MIBG scan (as in Fig. 22.14).

Age, stage and biology of disease at diagnosis are the major factors which influence prognosis. Unfortunately, the majority of children over 1 year present with advanced

disease and have a poor prognosis. Increasingly, information about the biological characteristics of neuroblastoma is being used to guide therapy and prognosis. Amplification of the *MYCN* oncogene predicts aggressive behaviour of the tumour and evidence of deletion or gain of genetic material on part of one or more chromosomes (as compared with a change in the number of copies of whole chromosomes) is also associated with a poorer prognosis.

Management

Localized primaries without metastatic disease can often be cured with surgery alone and in some infants (even when metastatic to skin, liver or bone marrow – MS neuroblastoma) may resolve spontaneously.

Metastatic disease in older children is treated with chemotherapy, including high-dose therapy with autologous stem cell rescue, surgery, and radiotherapy. Risk of relapse is high and the prospect of cure for children with metastatic disease is still little better than 40%. Immunotherapy (with anti-GD2) and the use of 'maintenance' treatment with differentiating agents (retinoic acid) are now established in treating those with high-risk disease.


Case history 22.3
Neuroblastoma

Jack, a 3-year-old boy, was taken to his general practitioner by his mother because he was not eating as well as usual and had a distended abdomen. Recently, he appeared reluctant to walk and sometimes cried when he was picked up. His grandmother thought he had lost weight. On examination, the general practitioner confirmed that he seemed generally miserable and pale. He was concerned to note a large abdominal mass. He was referred directly to his local hospital.

Differential diagnosis and specific investigations

An initial ultrasound examination confirmed the abdominal mass and an MRI scan characterized a very large upper

abdominal mass in complex relationship with the left kidney and the major vessels but extending towards the midline, suggestive of neuroblastoma (Fig. 22.13). Subsequent investigations confirmed bone marrow infiltration by tumour cells and a positive MIBG scan showing uptake at the primary and distant sites consistent with metastatic disease (Fig. 22.14).

Diagnosis: Metastatic neuroblastoma.

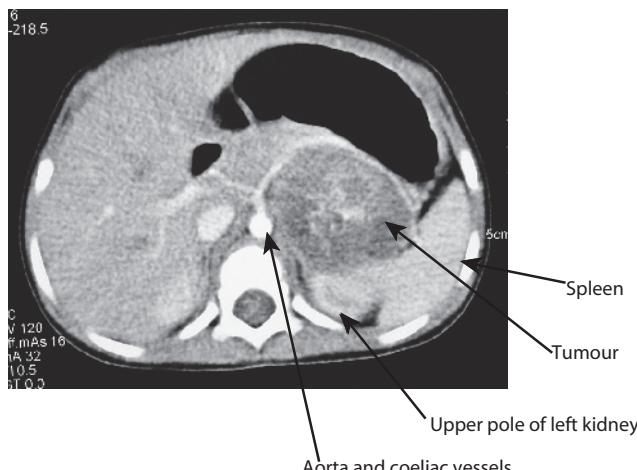


Figure 22.13 Transverse MRI image showing a large left-sided primary neuroblastoma arising from the adrenal region and distorting coeliac and mesenteric blood vessels.



Figure 22.14 The MIBG scan 'maps' metastatic tumour. This image shows the lower half of the abdomen, pelvis, and legs. The dark areas are evidence of high isotope uptake and the pattern is consistent with widespread metastatic disease. (Normal uptake from excretion of isotope into urine in the bladder has been blocked in this exposure.)

Wilms tumour (nephroblastoma)

Wilms tumour originates from embryonal renal tissue and is the most common renal tumour of childhood. Over 80% of patients present before 5 years of age and it is very rarely seen after 10 years of age.

Clinical features

Most children present with a large abdominal mass, often found incidentally in an otherwise well child. Other clinical features are listed in [Box 22.2](#).

Investigations

Ultrasound and/or CT/MRI ([Fig. 22.15](#)) is usually characteristic, showing an intrinsic renal mass distorting the normal structure. Staging is to assess for distant metastases (usually lung), initial tumour resectability and function of the contralateral kidney.

Management

In the UK, children receive initial chemotherapy followed by delayed nephrectomy, after which the tumour is staged histologically and subsequent treatment is planned according to the surgical and pathological findings. Radiotherapy is restricted to those with more advanced disease. Initial nephrectomy followed by chemotherapy is an approach taken in some countries. Around 5% of patients have bilateral disease at diagnosis, and their management is directed to preserve as much renal function as possible.

Box 22.2 Presentation of Wilms tumour

Common	Less common
Abdominal mass	Abdominal pain
Haematuria	Anorexia Anaemia (haemorrhage into mass) Hypertension Screening – infants with Beckwith-Wiedemann syndrome (see Chapter 10, Perinatal medicine)

Prognosis is good, with more than 80% of all patients cured. Cure rate for patients with metastatic disease at presentation (~15%) is over 60%, but relapse carries a poor prognosis.

Soft tissue sarcomas

Sarcomas are cancers of connective tissue such as muscle or bone. Rhabdomyosarcoma is the most common form of soft tissue sarcoma in childhood. The tumour is thought to originate from primitive mesenchymal tissue and there are a wide variety of primary sites, resulting in varying presentations and prognosis.

Clinical features

- *Head and neck* are the most common sites of disease (40%), causing, e.g. proptosis, nasal obstruction, or blood-stained nasal discharge.
- *Genitourinary tumours* may involve the bladder, paratesticular structures, or the female genitourinary tract. Symptoms include dysuria and urinary obstruction, scrotal mass, or blood-stained vaginal discharge.
- *Metastatic disease* (lung, liver, bone, or bone marrow) is present in approximately 15% of patients at diagnosis and is associated with a particularly poor prognosis.

Investigations

Biopsy and full radiological assessment of primary disease and any evidence of metastasis ([Fig. 22.16](#)).

Management

Multimodality treatment (chemotherapy, surgery, and radiotherapy) is used, dependent on the age of the patient and site, size, and extent of disease. The tumour margins are deceptively ill-defined, and attempts at primary surgical excision are often unsuccessful and are not attempted unless this can be achieved without mutilation or irreversible organ damage. Overall cure rates are about 65%.

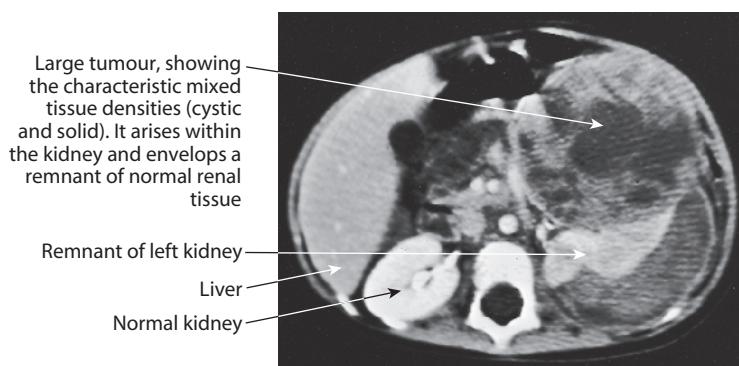
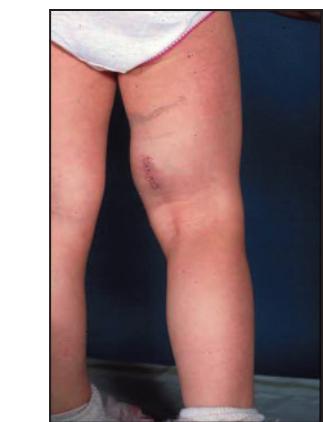


Figure 22.15 Large Wilms tumour arising within the left kidney, showing characteristic cystic and solid tissue densities.



(a)



(b)

Figure 22.16 Rhabdomyosarcoma. (a) Soft tissue mass of lower limb. The scar is from a biopsy. (b) MRI scan of a child presenting with proptosis of the right eye. It shows a right periorbital soft tissue mass displacing the globe and compressing other orbital structures. Histology confirmed the diagnosis of rhabdomyosarcoma.

Bone tumours

Malignant bone tumours are uncommon before puberty. Osteosarcoma is more common than Ewing sarcoma, but Ewing sarcoma is seen more often in younger children. Both have a male predominance.

Clinical features

The limbs are the most common site. Persistent localized bone pain is the characteristic symptom, usually preceding the detection of a mass, and is an indication for early X-ray. At diagnosis, most patients are otherwise well.

Investigations

Plain X-ray is followed by MRI and bone scan (Fig. 22.17a–c). A bone X-ray shows destruction and variable periosteal new bone formation. In Ewing sarcoma, there is often a substantial soft tissue mass. Chest CT is used to assess for lung metastases, bone scan, whole body MRI or PET for bony metastases and bone marrow sampling to exclude marrow involvement.

Management

In both tumours, treatment involves the use of combination chemotherapy given before surgery. Whenever possible, amputation is avoided by using *en bloc* resection of tumours with endoprosthetic resection (Fig. 22.17d). In Ewing sarcoma, radiotherapy is also used in the management of local disease, especially when surgical resection is impossible or incomplete, e.g. in the pelvis or axial skeleton.

Retinoblastoma

Retinoblastoma is a malignant tumour of retinal cells and, although rare, accounts for about 5% of severe visual impairment in children. It may affect one or both eyes. All bilateral tumours are hereditary, as are about 20% of unilateral cases. The retinoblastoma susceptibility gene is on chromosome 13, and the pattern of inheritance is dominant, but with incomplete penetrance. Most children present within the first 3 years of life. Children from families with the hereditary form of the disease should be screened regularly from birth.

Clinical features

The most common presentation of unsuspected disease is when a white pupillary reflex is noted to replace the normal red one (Fig. 22.18) or with a squint.

Investigations

MRI and examination under anaesthetic. Tumours are frequently multifocal.

Treatment

The aim is to cure, yet preserve vision. Biopsy is not undertaken and treatment is based on the ophthalmological findings. Enucleation of the eye may be necessary for more advanced disease. Chemotherapy is used, particularly in bilateral disease, to shrink the tumour(s), followed by local laser treatment to the retina. Radiotherapy may be used in advanced disease, but it is more often reserved for the treatment of recurrence. In the UK, retinoblastoma is managed in a limited number of specialist centres with dedicated ophthalmology, oncology and clinical genetics input. Most patients are cured, although many are visually impaired. There is a significant risk of second malignancy (especially sarcoma) among survivors of hereditary retinoblastoma.

Kaposi sarcoma

Kaposi sarcoma is a low-grade cancer that arises from the cells of the blood or lymph vessels and is triggered by human herpes virus-8. Although very rare in children in the UK, the prevalence of HIV infection in sub-Saharan Africa means that it is one of the most common paediatric malignancies in this region. Whilst adults typically present with a purple/brown skin rash, these appearances are less common in children who may have only generalized lymphadenopathy suggestive of lymphoma. Diagnosis

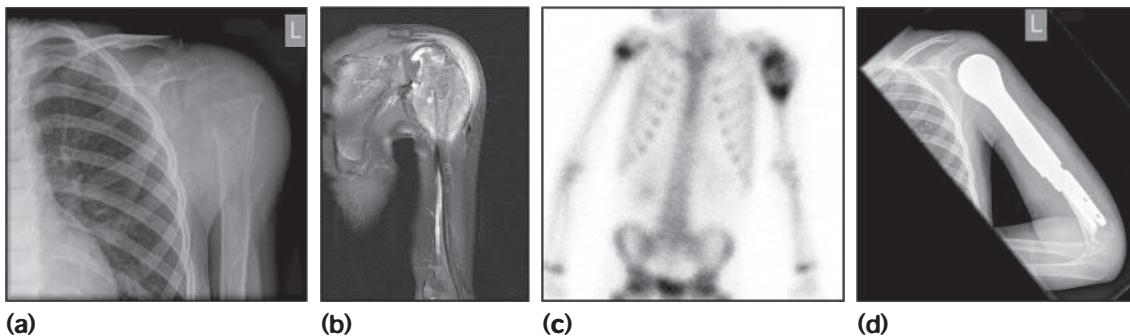


Figure 22.17 Ewing sarcoma of the humerus. (a) Plain X-ray shows a destructive bone lesion within the proximal humeral metaphysis; (b) MRI shows a large destructive soft tissue mass arising from the proximal metadiaphysis of the left humerus; (c) bone scan shows prominent abnormal tracer uptake in the proximal left humerus; and (d) post-surgery, most of the humerus has been resected and replaced by a metallic prosthesis.



Figure 22.18 White pupillary reflex in retinoblastoma.

requires biopsy confirmation. Treatment involves a combination of chemotherapy and antiretroviral therapy.

Rare tumours

Liver tumours

Primary malignant liver tumours are mostly hepatoblastoma (65%) or hepatocellular carcinoma (25%). Presentation is usually with abdominal distension or with a mass. Pain and jaundice are rare. Elevated serum α FP (alpha-fetoprotein) is detected in nearly all cases of hepatoblastoma and in some cases of hepatocellular carcinoma. Management includes chemotherapy, surgery and, in inoperable cases, liver transplantation. The majority of children with hepatoblastoma can now be cured, but the prognosis for children with hepatocellular carcinoma is less satisfactory.

Germ cell tumours

Germ cell tumours (GCTs) may be benign or malignant. They arise from the primitive germ cells which migrate from yolk sac endoderm to form gonads in the embryo. Benign tumours are most common in the sacrococcygeal region, and most malignant germ cell tumours are found in the gonads. Serum markers (α FP and β -HCG) are



Figure 22.19 Lytic bone lesions on a skull X-ray in Langerhans cell histiocytosis.

invaluable in confirming the diagnosis and in monitoring response to treatment. Malignant germ cell tumours are very sensitive to chemotherapy, and a good outcome can be expected for disease at most sites, including the brain.

Langerhans cell histiocytosis

Langerhans cell histiocytosis (LCH) is a rare disorder characterized by an abnormal proliferation of histiocytes (a type of dendritic antigen-presenting cells). Whether it truly represents a malignancy remains uncertain, however its sometimes aggressive behaviour and its response to chemotherapy place it within the practice of oncologists. Clinically, its manifestations include:

- bone lesions – present at any age with pain, swelling, or even fracture. X-ray reveals a characteristic lytic lesion with a well-defined border, often involving the skull (Fig. 22.19)
- diabetes insipidus – may be associated with skull disease with proptosis and hypothalamic infiltration
- systemic LCH – the most aggressive form which tends to present in infancy with a seborrhoeic rash (Fig. 22.20) and soft tissue involvement of the gums, ears, lungs, liver, spleen, lymph nodes, and bone marrow. This form of LCH is usually progressive and requires chemotherapy, although spontaneous regression may occur.

The prognosis is variable, but most patients are cured.



Figure 22.20 Rash in systemic Langerhans cell histiocytosis. It is often mistaken for seborrhoeic dermatitis or eczema.

Long-term survivors

Improved survival rates means an ever-increasing population of adult survivors of childhood cancer. Over half have at least one residual problem as a consequence of either the disease or its treatment (Table 22.3).

All survivors need regular long-term follow-up to provide appropriate treatment or advice. This need for specialist multidisciplinary follow-up continues into adulthood, and its provision presents a challenge within adult healthcare services. Until recently, the majority of survivors have remained under the care of paediatric oncologists, although specialist adult clinics are being established. Some survivors will require specific counselling for problems such as poor or asymmetric growth, infertility and sexual dysfunction, and advances in the use of adult growth hormone. Assisted reproductive technology has enhanced the lives of many patients. The risk of second

cancer is small, but nevertheless survivors are at increased risk and this may rise with increasing survival rates. When new treatment protocols for childhood cancers are developed, there is a need to reduce, whenever possible, the toxicity of treatment to spare adverse short-term and long-term effects.

Palliative and end-of-life care

Palliative care assists with symptom management, psychosocial support for the child and family, attention to practical needs and spiritual care throughout the child's illness. If a child relapses, further treatment may be considered. A reasonable number can still be cured and others may have a further significant remission with good-quality life. However, for some children, a time comes when death is inevitable, and the staff and family must make the decision to concentrate on end-of-life care (see Ch. 5, Care of the sick child and young person).

Most parents prefer to care for their terminally ill child at home, but will need practical help and emotional support. Pain control and symptom relief are a serious source of anxiety for parents, but they can often be achieved successfully at home. Health professionals with experience in palliative and end-of-life care for children work together with the family and local healthcare workers. Some families may choose for the child's care to be provided in conjunction with a children's hospice. After the child's death, families should be offered continuing contact with an appropriate member of the team who looked after their child, and be given support through their bereavement.



With adequate support from health professionals, end-of-life care for children can often be provided at home.

Table 22.3 Some problems that may occur following cure of childhood cancer

Problem	Cause
Specific organ dysfunction	Nephrectomy for Wilms tumour Toxicity from chemotherapy, e.g. renal from cisplatin or ifosfamide, cardiac from doxorubicin or mediastinal radiotherapy
Growth/endocrine problems	Growth and other pituitary hormone deficiencies from irradiation Bone growth retardation and deformity at sites of irradiation
Infertility	Gonadal irradiation Alkylating agent chemotherapy (cyclophosphamide, ifosfamide)
Mental health disorders	Post-traumatic stress disorder, healthcare-related anxiety
Neuropsychological problems	Cranial irradiation (particularly at age <5 years) Brain surgery
Second malignancy	Irradiation Alkylating agent chemotherapy
Social/educational disadvantage	Chronic ill health Absence from school

Summary

Presentation of malignant disease in children

Brain tumours:

All ages

- Persistent or recurrent vomiting
- Problems with balance, coordination or walking
- Behavioural change
- Abnormal eye movements
- Seizures (without fever)
- Abnormal head position – wry neck, head tilt or persistent stiff neck

Child/Teenager

- Persistent or recurrent headache
- Blurred or double vision
- Lethargy
- Deteriorating school performance
- Delayed or arrested puberty, slow growth

Infants

- Developmental delay/regression
- Progressive increase in head circumference, separation of sutures, bulging fontanelle
- Lethargy

Retinoblastoma:

- Screening if positive family history
- White pupillary reflex or squint

Lymphomas:

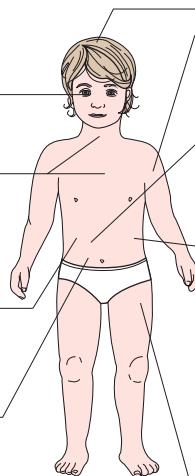
- Enlarged lymph nodes in the neck or abdomen
- Mediastinal mass – may cause superior vena caval obstruction

Wilms tumour:

- Large abdominal mass in a well child
- Occasionally anorexia, abdominal pain, haematuria

Langerhans cell histiocytosis:

- Seborrhoeic rash
- Widespread soft tissue infiltration
- Bone pain, swelling or fracture
- Diabetes insipidus



Soft tissue sarcomas:

- Mass any site

Neuroblastoma:

- Abdominal mass
- Spinal cord compression
- Weight loss and malaise
- Pallor, bruising
- Bone pain

Acute lymphoblastic leukaemia (ALL):

- Malaise, anorexia
- Pallor, lethargy
- Infections
- Bruising, petechiae, nose bleeds
- Lymphadenopathy
- Hepatosplenomegaly
- Bone pain

Malignant bone tumours:

- Localized bone pain

Preschool (<5 years old)	School-age	Adolescence
Acute lymphoblastic leukaemia (ALL) – peak incidence Non-Hodgkin lymphoma	Acute lymphoblastic leukaemia (ALL)	Acute lymphoblastic leukaemia (ALL) Hodgkin lymphoma
Neuroblastoma	Brain tumours	Malignant bone tumours
Wilms tumour		Soft tissue sarcomas
Retinoblastoma		

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Further reading

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Hains R, Goldman A, Rapoport A, Meiring M, editors: Oxford textbook of palliative care in children, ed 3, Oxford, 2021, Oxford University Press.

Pizzo PA, Poplack DG: Principles and practice of pediatric oncology, ed 7, Lippincott, 2015, Williams and Wilkins. Comprehensive textbook.

Websites

CCLG (Children's Cancer and Leukaemia Group): www.cclg.org.uk. Association of healthcare professionals involved in the treatment and care of children and younger teenagers with cancer, underpins all the activity in paediatric oncology in the UK.

Cure4Kids: www.cure4kids.org. Dedicated to improving healthcare for children with cancer and other catastrophic diseases around the globe. Provides continuing medical education and communication tools to healthcare professionals and scientists worldwide.

HeadSmart: <https://www.headsmart.org.uk>. Guide to early diagnosis of brain tumours in infants, children and young people.

TCT (Teenage Cancer Trust): www.teenagecancertrust.org. TCT create world-class cancer services for young people in the UK, providing life-changing care and support.

Haematological disorders

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Features of haematological disorders in children:

- Changes in the blood count during childhood mean that it is important to use age-adjusted normal ranges.
- Iron deficient anaemia is common.
- Causes of haemolytic anaemia include sickle cell (SC) disease, thalassaemia, G6PD deficiency, and hereditary spherocytosis.
- The most common inherited causes of abnormal bleeding are haemophilia A and B and von Willebrand disease (vWD).
- Petechiae or purpura may be non-thrombocytopenic (Henoch–Schönlein purpura, sepsis, trauma) or thrombocytopenic (immune thrombocytopenia, leukaemia, disseminated intravascular coagulation).

Haemopoiesis is the process which maintains lifelong production of haemopoietic (blood) cells. The main site of haemopoiesis throughout postnatal life is the bone marrow. All haemopoietic cells are derived from *haemopoietic stem cells*, which are crucial for normal blood production; deficiency of these stem cells causes bone marrow failure disorders (e.g. aplastic anaemia) because stem cells are required for the ongoing replacement of dying cells. Haemopoietic stem cells can also be used for treatment, e.g. cells from healthy donors can be transplanted into children with bone marrow failure (*stem cell transplantation*).

Haematological values at birth and the first few weeks of life

Features are:

- At birth, the haemoglobin concentration (Hb) in both term and preterm infants is high, 140 g/L to 215 g/L, to compensate for the low oxygen concentration in the fetus. The Hb falls naturally over the first few weeks of life due to reduced red cell production, reaching a nadir of around 100 g/L at 2 months of

age (Fig. 23.1). Normal haematological values at birth and during childhood are shown in the *Appendix* (Table A.4).

- Preterm babies have a steeper fall in Hb to a mean of 65 g/L to 90 g/L at 4 weeks to 8 weeks chronological age; this is mainly due to reduced red blood cell production and lifespan.
- The main haemoglobin at birth (~60%) both in term and preterm babies is HbF (fetal haemoglobin) (Table 23.1). Almost all of the remaining haemoglobin at birth is HbA (adult haemoglobin). In healthy babies, HbF gradually falls to around 1% at the age

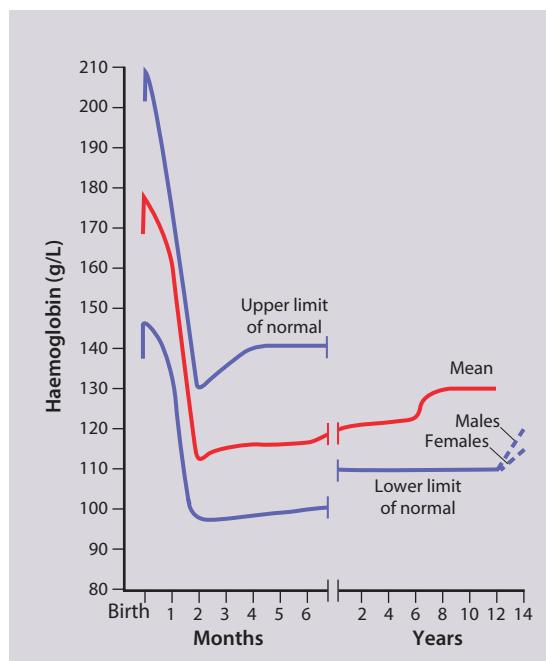
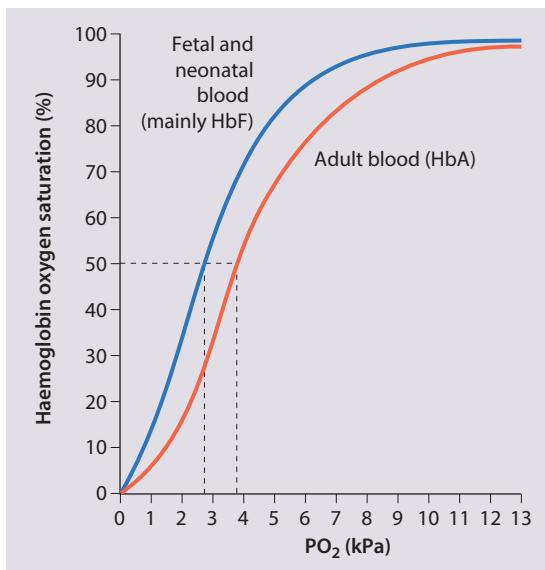


Figure 23.1 Changes in haemoglobin concentration with age, showing that the haemoglobin is high at birth, falling to its lowest concentration at 2 months to 3 months of age.

Table 23.1 Haemoglobins in haemoglobinopathies

	HbA	HbA ₂	HbF	HbS
Newborn	25%	1%	74%	–
Adult	97%	2%	–	–
β-Thalassaemia trait	>90%	↑	↑	–
β-Thalassaemia major	–	↑	↑	–
Sickle cell trait	✓	✓	↑	✓
Sickle cell disease	–	✓	↑	✓

**Figure 23.2** Oxygen dissociation curve showing the left shift of HbF compared with HbA. HbF-containing red cells have a higher affinity for oxygen and hold on to oxygen, delivering less to the tissues.

of 12 months at the same time as HbA gradually rises. HbF has a higher affinity for oxygen than HbA and is therefore better able to hold on to oxygen, an advantage in the relatively hypoxic environment of the fetus (Fig. 23.2).

- Normal blood volume at birth varies with gestational age. It is increased by delayed clamping of the umbilical cord. In healthy term infants the average blood volume is 80 ml/kg; in preterm infants the average blood volume is 100 ml/kg.
- Stores of iron, folic acid, and vitamin B₁₂ in term and preterm babies are adequate at birth. However, in preterm infants, stores of iron and folic acid are lower and are depleted more quickly, leading to deficiency after 2 months to 4 months if the recommended daily intakes are not maintained by supplements.
- White blood cell counts in neonates are higher than in older children ($10\text{--}25 \times 10^9/\text{L}$).
- Platelet counts at birth are within the normal adult range ($150\text{--}400 \times 10^9/\text{L}$).

Summary

Haemoglobin at birth

- The Hb concentration is high at birth (>140 g/L) but falls to its lowest level at 2 months of age.
- HbF is gradually replaced by HbA during infancy.

Anaemia

Anaemia is defined as a Hb below the normal range. The normal range varies with age, so anaemia can be defined as:

- neonate: Hb less than 140 g/L
- 1 month to 12 months of age: Hb less than 100 g/L
- 1 year to 12 years of age: Hb less than 110 g/L.

Anaemia results from one or more of the following mechanisms:

- reduced red cell production – either due to red cell aplasia or qualitatively abnormal erythropoiesis (e.g. iron deficiency, the most common cause of anaemia)
- increased red cell destruction (*haemolysis*)
- blood loss – relatively uncommon cause in children.

There may be a combination of these three mechanisms, e.g. *anaemia of prematurity*.

Using this approach, the principal causes of anaemia are shown in Fig. 23.3 and a diagnostic approach to identifying their causes is shown in Fig. 23.4.

 **The definition of anaemia varies with age:**
Hb <100g/L in infants (post neonatal), Hb <110g/L from 1 year old to 12 years old.

Iron deficiency

The main causes of iron deficiency are:

- inadequate intake
- malabsorption
- blood loss.

Inadequate intake of iron is common in infants because additional iron is required for the increase in blood volume accompanying growth and to build up the child's iron stores (Fig. 23.5). A 1-year-old infant requires an intake of iron which is about the same as an adult male but only half that of an adult female.

Iron may come from:

- breast milk (low iron content but 50% of the iron is absorbed)
- infant formula (supplemented with adequate amounts of iron)
- cow's milk (low iron content and poor bioavailability, so poor source of iron)
- solids introduced at weaning, e.g. cereals (cereals are supplemented with iron but only 1% is absorbed).

Iron stores in infants are increased by delayed cord clamping at birth, from increased transfusion of placental blood.

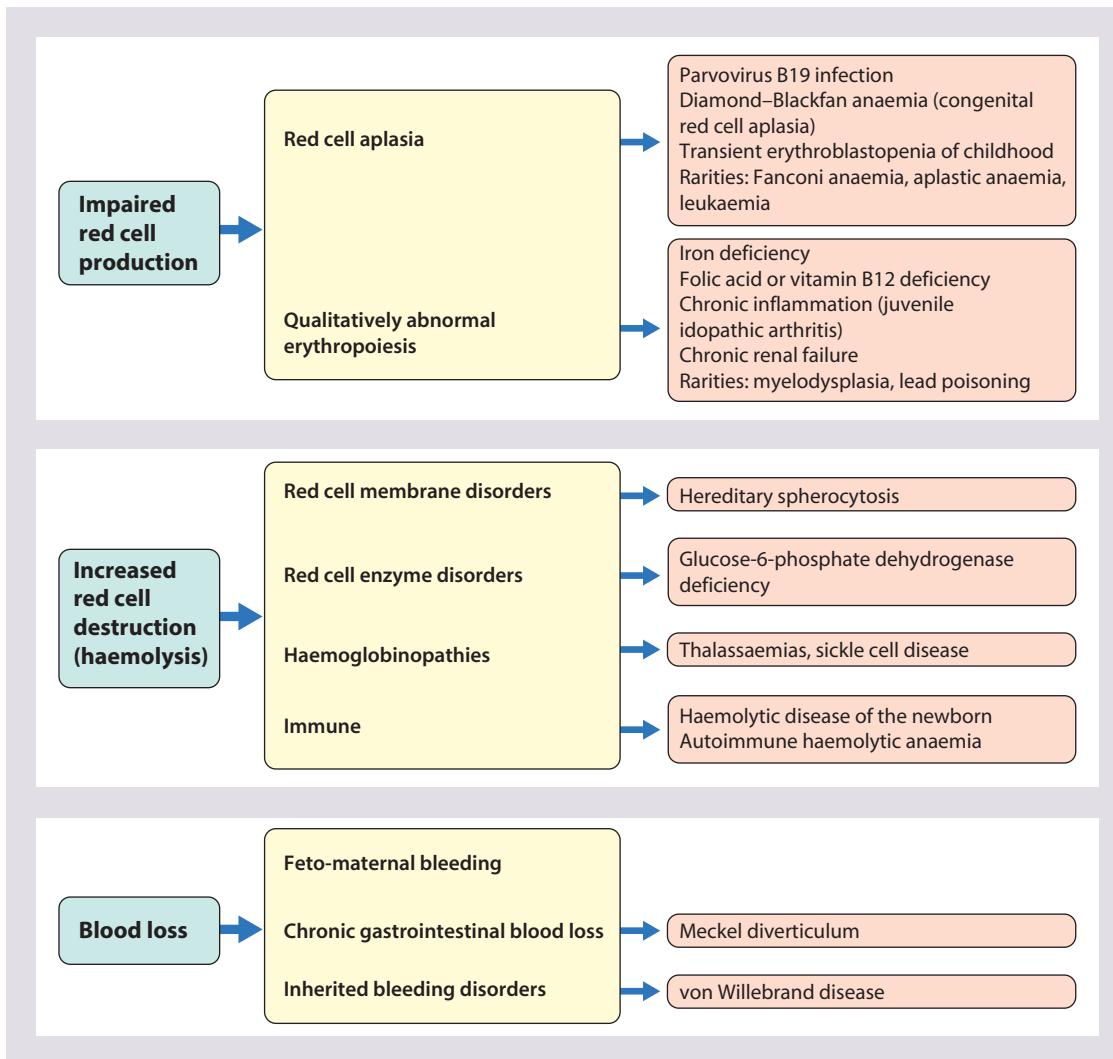


Figure 23.3 Causes of anaemia in infants and children.

Iron deficiency may develop because of a delay in the introduction of mixed feeding beyond 6 months of age in fully breast-fed infants or to a diet with insufficient iron-rich foods, especially if it contains a large amount of cow's milk (Box 23.1). Iron absorption is increased when eaten with food rich in vitamin C (fresh fruit and vegetables) and is inhibited by tannin in tea.



Infants should not be fed unmodified cow's milk as its iron content is low and bioavailability is poor.

Clinical features

Most infants and children are asymptomatic until the Hb drops below 60 g/L to 70 g/L. As the anaemia worsens, children tire easily and young infants feed more slowly than usual. The history should include asking about blood loss and symptoms or signs suggesting malabsorption. They may appear pale but pallor is an unreliable sign unless confirmed by pallor of the conjunctivae, tongue or palmar creases. Some children have 'pica', a term which describes the inappropriate eating of non-food materials

such as soil, chalk, gravel, or foam rubber (see Case history 23.1). There is evidence that iron deficiency anaemia may be detrimental to behaviour and intellectual function.

Diagnosis

The diagnostic clues are:

- microcytic, hypochromic anaemia, with low MCV (Mean Cell Volume), and MCH (Mean Cell Haemoglobin)
- low serum ferritin.

The other main causes of microcytic anaemia are:

- β -thalassaemia trait (usually children of Asian, Arab or Mediterranean origin)
- anaemia of chronic disease (e.g. due to chronic kidney disease).

Children with α -thalassaemia trait (usually children of African or Far Eastern ethnicity) also have a microcytic/hypochromic blood picture but most of these children are not anaemic.

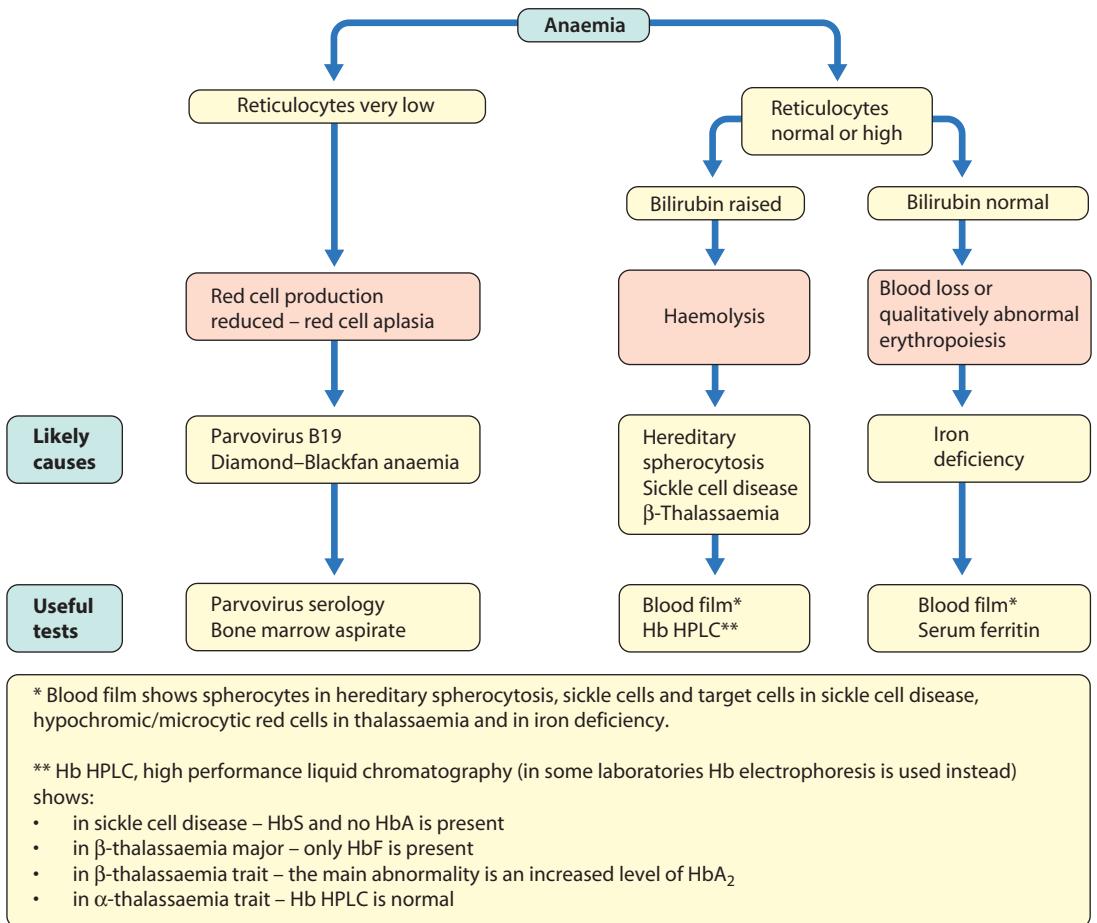


Figure 23.4 Simple diagnostic approach to anaemia in children.

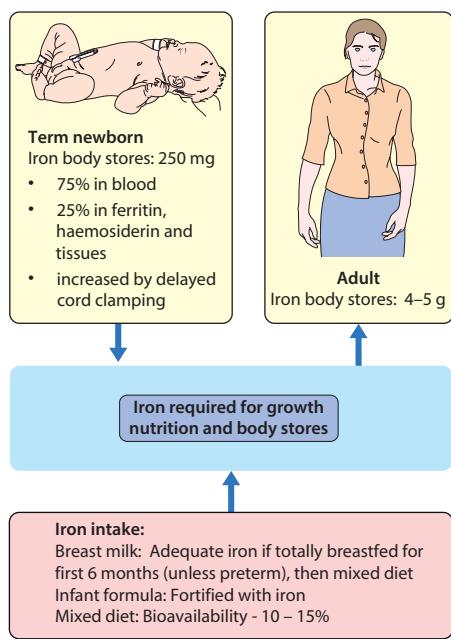


Figure 23.5 Iron requirements during childhood.

Box 23.1 Dietary sources of iron

High in iron

- Red meat – beef, lamb
- Liver, kidney
- Oily fish – pilchards, sardines, etc.

Average iron

- Pulses, beans, and peas
- Fortified breakfast cereals with added vitamin C
- Wholemeal products
- Dark green vegetables – broccoli, spinach, etc.
- Dried fruit – raisins, sultanas
- Nuts and seeds – cashews, peanut butter, etc.

Foods to avoid in excess in toddlers

- Cow's milk
- Tea: tannin inhibits iron uptake
- High-fibre foods: phytates inhibit iron absorption

Management

For most children, management involves *dietary advice* and supplementation with *oral iron*. The best tolerated preparations are Sytron (sodium iron edetate) or Niferex (polysaccharide iron complex) – unlike some other



Case history 23.1

Iron deficiency anaemia

Ayesha, aged 2 years, was noted to look pale when she attended her general practitioner for an upper respiratory tract infection. A blood count showed Hb 50.0 g/L, MCV 54 fL (normal 72–85 fL) and MCH 16 pg (normal 24–39 pg). She was drinking three pints of cow's milk per day and was a very fussy eater, refusing meat. She had started eating soil when playing in the garden.

Because of the inappropriately large volume of milk she was drinking, she was not sufficiently hungry to eat solid food. Replacing some of the milk with iron-rich food and treatment with oral iron produced a rise in the Hb to 75 g/L within 4 weeks. Her pica (eating non-food materials) stopped. Oral iron was continued until her Hb had been normal for 3 months.

preparations these do not stain the teeth. Iron supplementation should be continued until the Hb is normal and then for a minimum of a further 3 months to replenish the iron stores. With good compliance, the Hb will rise by about 10 g/L per week. Failure to respond to oral iron usually means the child is not getting the treatment. However, investigation for other causes, in particular mal-absorption (e.g. due to coeliac disease) or chronic blood loss (e.g. due to Meckel diverticulum), is advisable if the history or examination suggests a non-dietary cause or if there is failure to respond to therapy in compliant families. Blood transfusion should never be necessary for dietary iron deficiency. Even children with a Hb as low as 20 g/L to 30 g/L due to iron deficiency have arrived at this low level over a prolonged period and can tolerate it.

Treatment of iron deficiency with normal Hb

Some children have biochemical evidence of iron deficiency (e.g. low serum ferritin) but have not yet developed anaemia. Whether these children should be treated with oral iron is controversial. In favour of treatment is the knowledge that iron is required for normal brain development and there is evidence that iron deficiency anaemia is associated with behavioural and intellectual impairment, which may be reversible with iron therapy. However, it is not yet clear whether treatment of subclinical iron deficiency confers significant benefit. Treatment also carries a risk of accidental poisoning with oral iron, which is very toxic. A simple strategy is to provide dietary advice to increase oral iron and its absorption in all children with subclinical deficiency and to offer parents the option of additional treatment with oral iron supplements.



Treatment of iron deficiency anaemia is with dietary advice and oral iron therapy for several months.

Red cell aplasia

There are three main causes of red cell aplasia in children:

- congenital red cell aplasia ('Diamond–Blackfan anaemia')

- transient erythroblastopenia of childhood
- parvovirus B19 infection (this infection causes red cell aplasia in children with inherited haemolytic anaemias and not in healthy children).

The diagnostic clues to red cell aplasia are:

- low reticulocyte count despite low Hb
- normal bilirubin
- negative direct antiglobulin test (Coombs test)
- absent red cell precursors on bone marrow examination.

Diamond–Blackfan anaemia (DBA) is a rare (5–7 cases/million live births) cause of severe, lifelong anaemia usually presenting at 2–3 months of age. Most cases are caused by genetic mutations in one of the ribosomal protein (RP) genes. There is a family history of DBA in 20% of cases; the remaining 80% are sporadic. Some children with DBA have other congenital anomalies, such as short stature or abnormal thumbs, which are a clue to the diagnosis. Treatment is by oral steroids, monthly red blood cell transfusions or, in very severe cases, stem cell transplantation.

Unlike DBA, transient erythroblastopenia of childhood (TEC) is triggered by viral infection and always recovers, usually within several weeks. These children have no family history and no congenital anomalies.

Increased red cell destruction (haemolytic anaemia)

Haemolytic anaemia is caused by increased red blood cell destruction either in the circulation (intravascular haemolysis) or in the liver or spleen (extravascular haemolysis). While the lifespan of a normal red cell is 120 days, in haemolysis, red cell survival may be reduced to a few days. In mild haemolysis, the bone marrow compensates by producing more red cells. This means that haemolysis only leads to anaemia when the bone marrow is no longer able to fully compensate.

The main cause of haemolysis in children is *intrinsic* abnormalities of the red blood cells which lead to their premature destruction:

- red cell membrane disorders (e.g. hereditary spherocytosis)
- red cell enzyme disorders (e.g. glucose-6-phosphate dehydrogenase deficiency)
- haemoglobinopathies (abnormal haemoglobins, e.g. β -thalassaemia major, sickle cell disease).

The diagnostic clues to haemolysis are:

- anaemia with a normal white cell count and platelet count
- the spleen and/or liver may be moderately enlarged (due to extramedullary haemopoiesis)
- raised reticulocyte count (on the blood film this is called 'polychromasia' as the reticulocytes have a characteristic lilac colour on a stained blood film)
- unconjugated bilirubinaemia and increased urinary urobilinogen
- abnormal appearance of the red cells on a blood film (e.g. spherocytes, sickle shaped or very hypochromic) (Fig. 23.6)

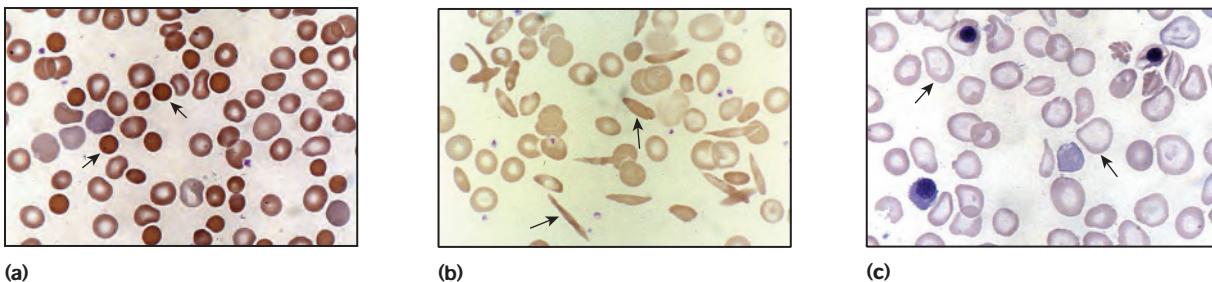


Figure 23.6 Abnormally shaped red blood cells help make the diagnosis in haemolytic anaemias. (a) Spherocytes (arrows) in hereditary spherocytosis; (b) sickle cells (arrows) in sickle cell disease; and (c) hypochromic cells (arrows) in thalassaemia.

- positive direct antiglobulin test (only if an immune cause, as this test identifies antibody-coated red blood cells)
- increased red blood cell precursors in the bone marrow.

Hereditary spherocytosis

Hereditary spherocytosis (HS) occurs in 1 in 5000 births in Caucasians. It usually has an autosomal dominant inheritance, but in 25% there is no family history. The disease is caused by mutations in genes which encode important red cell membrane proteins, such as spectrin or ankyrin. In HS the red blood cells become spherical in shape (spherocytes) because the red cell loses part of its membrane each time it passes through the spleen. Spherocytes are less deformable than normal red blood cells and are therefore destroyed prematurely in the spleen.

Clinical features

The disorder is often suspected because of the family history. The clinical features, which are highly variable, include:

- *jaundice* – usually develops during childhood but may be intermittent; may cause severe haemolytic jaundice in the first few days of life
- *anaemia* – presents in childhood with mild anaemia (Hb 90–110 g/L), but the Hb may transiently fall during infections
- *mild to moderate splenomegaly* – depends on the rate of haemolysis
- *aplastic crisis* – uncommon, transient (2–4 weeks), caused by parvovirus B19 infection
- *gallstones* – due to increased bilirubin excretion
- some children are completely asymptomatic and HS may be identified during a routine blood test.

Diagnosis and management

The blood film is usually diagnostic but more specific tests are available (e.g. dye binding assay or genetic testing). Autoimmune haemolytic anaemia is also associated with spherocytes but this can be excluded by a positive direct antibody test.

Most children have mild chronic haemolytic anaemia and the only treatment they require is oral folic acid as they have a raised folic acid requirement secondary to

their increased red blood cell production. Splenectomy is beneficial but is only indicated for poor growth or troublesome symptoms of anaemia (e.g. severe tiredness, loss of vigour) or needing blood transfusions. It is usually deferred until after 7 years of age because of the risks of post-splenectomy sepsis. Prior to splenectomy all patients should be vaccinated against *Haemophilus influenzae* (Hib), meningitis ACWY, meningitis B and *Streptococcus pneumoniae*, and lifelong daily oral penicillin prophylaxis is advised. Aplastic crisis due to parvovirus B19 infection is treated by red cell transfusions over the 3-week to 4-week period when no red blood cells are produced. If gallstones are symptomatic, cholecystectomy may be necessary.

Glucose-6-phosphate dehydrogenase deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common red cell enzymopathy affecting over 100 million people worldwide. It has a high prevalence (10%–20%) in individuals originating from central Africa, the Mediterranean, the Middle East, and the Far East. Many different mutations of the gene have been described, leading to different clinical features in different populations.

G6PD is the rate-limiting enzyme in the pentose phosphate pathway and is essential for preventing oxidative damage to red cells. Red cells lacking G6PD are susceptible to oxidant-induced haemolysis (usually caused by certain drugs; see Box 23.2). G6PD deficiency is X-linked and therefore mainly causes symptoms in males. Females who are heterozygotes are usually clinically normal as they have about half the normal G6PD activity.

Clinical manifestations

Children usually present clinically with:

- *neonatal jaundice* – onset is typically in the first 3 days of life. Worldwide it is the most common cause of severe neonatal jaundice requiring exchange transfusion
- *acute haemolysis* – precipitated by:
 - infection, the most common precipitating factor
 - certain drugs (see Box 23.2)
 - fava beans (broad beans; other types of beans do not cause haemolysis)
 - naphthalene in mothballs.

Box 23.2 Drugs, chemicals and food which can cause haemolysis in children with G6PD deficiency (British National Formulary for Children 2020).

Definite risk drugs

- Sulphonamides (including co-trimoxazole)
- Fluoroquinolones (ciprofloxacin)
- Nitrofurantoin

Possible risk drugs

- Quinine (acceptable in acute malaria)
- Chloroquine (acceptable in acute malaria and chemoprophylaxis)
- Aspirin (in high doses)
- Sulfonylureas

Chemicals and food

- Naphthalene in mothballs
- Fava beans (broad beans) in some G6PD variants

Haemolysis due to G6PD deficiency is associated with fever, malaise, abdominal pain, and the passage of dark urine, as it contains haemoglobin as well as urobilinogen as the haemolysis is mainly intravascular. The Hb often falls rapidly and may drop below 50 g/L over 24–48 hours.

Diagnosis and management

Between episodes, almost all patients have a completely normal blood picture and no jaundice or anaemia. The diagnosis is made by identifying a low level of G6PD activity in red blood cells. During a haemolytic crisis, G6PD levels may be misleadingly elevated to a normal level due to the higher enzyme concentration in reticulocytes, which are produced in increased numbers during the crisis. A repeat assay is then required once the haemolytic episode is over to confirm the diagnosis. Parents should be given advice about the signs of acute haemolysis to look out for (jaundice, pallor, and dark urine) and provided with a list of drugs, chemicals, and food to avoid (Box 23.2). Transfusions are rarely required, even for acute episodes.

Haemoglobinopathies

These are red blood cell disorders which cause haemolytic anaemia because of reduced or absent production of HbA (α -thalassaemias and β -thalassaemias) or because of the production of an abnormal haemoglobin (e.g. sickle cell disease). α -Thalassaemias are caused by deletions (occasionally mutations) in the α -globin gene. β -Thalassaemia and sickle cell disease are caused by mutations in the β -globin gene. Clinical manifestations of the haemoglobinopathies affecting the β -chain are delayed until after 4–6 months of age when most of the HbF present at birth has been replaced by HbA (Fig. 23.7, Table 23.1).

Sickle cell disease

This is one of the most common inherited disorders in children in many European countries, including the UK (prevalence 1 in 2000 live births). The inheritance is autosomal recessive. Sickle cell (SC) disease is the collective name given to haemoglobinopathies in which HbS is inherited. HbS forms as a result of a point mutation in codon 6 of the

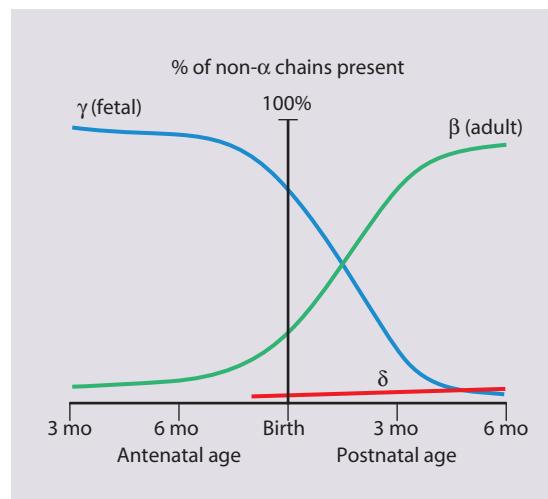


Figure 23.7 Changes in haemoglobin chains in the fetus and infancy.

β -globin gene, which causes a change in the amino acid encoded from glutamic acid to valine. Sickle cell disease is most common in patients whose parents originate from tropical Africa, the Caribbean, Central India, and the Middle East. HbS is rare in families of northern European extraction but changing patterns of migration mean that sickle cell disease is now a clinical problem in most parts of the world.

There are three main forms of sickle cell disease:

- *Sickle cell anaemia (HbSS)* – patients are homozygous for HbS, i.e. virtually all their haemoglobin is HbS; they have small amounts of HbF and no HbA because they have the sickle mutation in both β -globin genes.
- *HbSC disease (HbSC)* – affected children inherit HbS from one parent and HbC from the other parent (HbC is formed as a result of a different point mutation in β -globin), so they also have no HbA because they have no normal β -globin genes.
- *Sickle β -thalassaemia* – affected children inherit HbS from one parent and β -thalassaemia trait from the other. They have no normal β -globin genes and most patients can make no HbA and therefore have similar symptoms to those with sickle cell anaemia.

Individuals who inherit HbS from one parent and a normal β -globin gene from the other parent, are *carriers* (i.e. they have *sickle cell trait*). Although approximately 40% of their haemoglobin is HbS, patients with sickle cell trait are asymptomatic. However, they can transmit HbS to their offspring. Sickle trait can only be identified as a result of blood tests.

Pathogenesis of sickling

In all forms of sickle cell disease, HbS polymerizes within red blood cells forming rigid structures which deform the red cells into a sickle shape. Irreversibly sickled red cells have a reduced lifespan and may be trapped in the microcirculation, resulting in blood vessel occlusion (vaso-occlusion) and therefore ischaemia in an organ or bone. This is exacerbated by low oxygen tension, dehydration, and cold.

The clinical manifestations of sickle cell disease vary widely between different individuals. Disease severity also

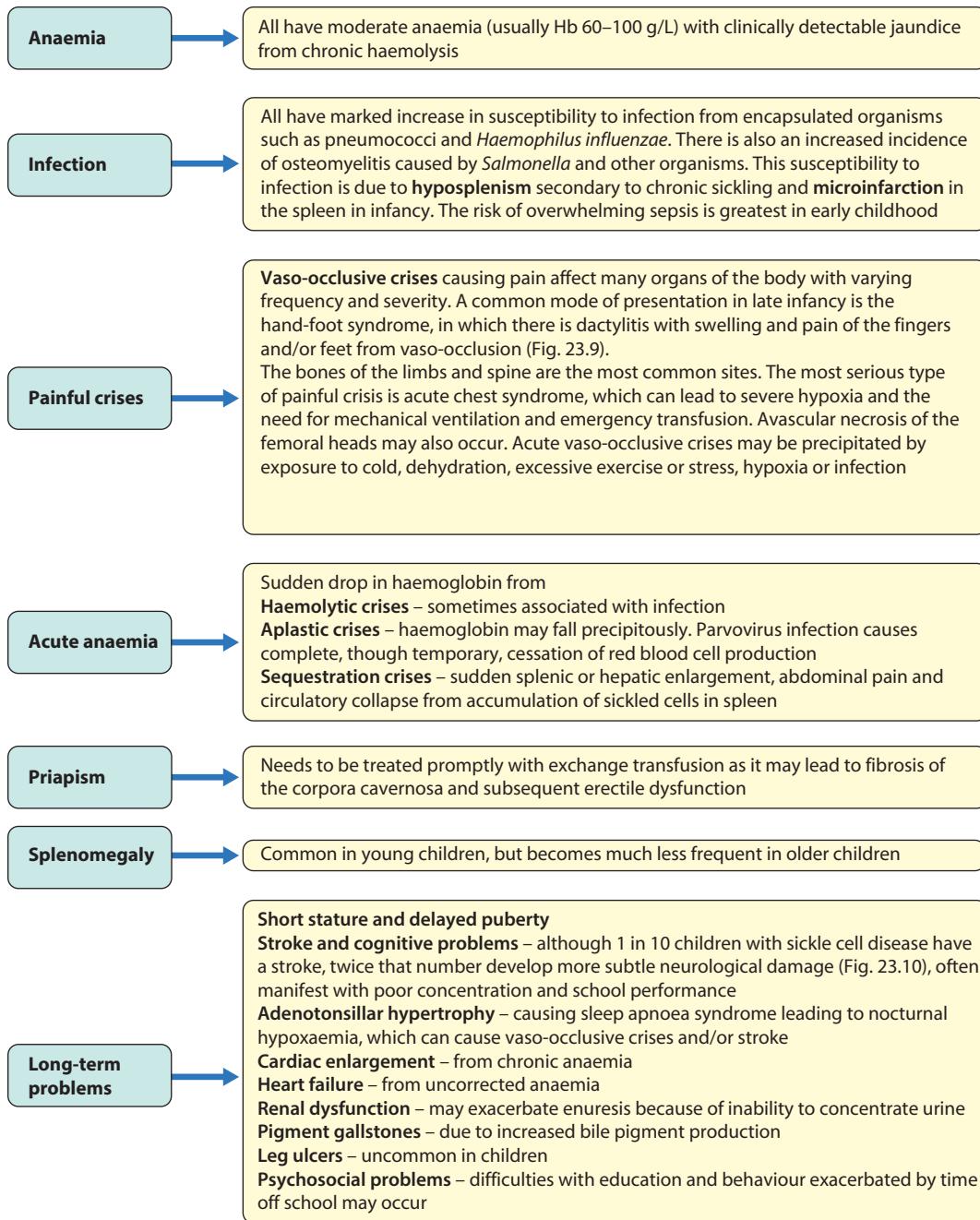


Figure 23.8 Clinical manifestations of sickle cell disease.

varies with different forms of sickle cell disease; in general, HbSS is the most severe form of the disease. One of the most important factors which modifies severity of sickle cell disease is the amount of HbF. While most patients with sickle cell disease have HbF levels of 1%, genetic variation means that some patients naturally produce more HbF (e.g. 10%–15% of their haemoglobin may be HbF), and this often reduces disease severity. As a result, considerable research is being carried out into drugs that increase HbF.



Clinical features

These are listed in Fig. 23.8. (See also Figs. 23.9 and 23.10.)

Figure 23.9 Dactylitis in sickle cell disease.

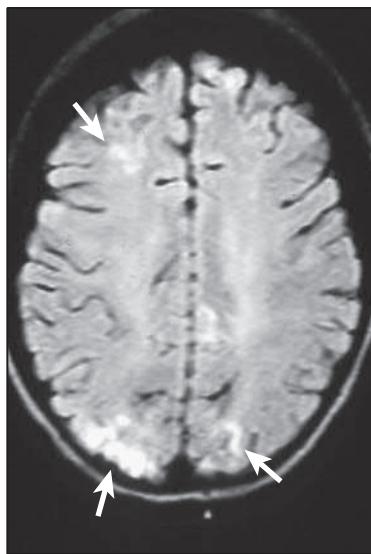


Figure 23.10 Magnetic resonance image of the brain in sickle cell disease showing multiple cerebral infarcts (arrows).

Management

Prophylaxis – Because spleen function is severely impaired in most patients, they are particularly susceptible to infection with encapsulated organisms, e.g. *Streptococcus pneumoniae* and *Haemophilus influenzae* type B, and therefore all affected children should be fully immunized, including against pneumococcal, *Haemophilus influenzae* type B and meningococcus infection. To ensure full coverage of all pneumococcal subgroups, daily oral penicillin throughout childhood should be given. Vaso-occlusive crises should be minimized by avoiding exposure to cold, dehydration, excessive exercise, undue stress, or hypoxia. This requires practical measures such as dressing children warmly, giving drinks especially before exercise, and taking extra care to keep children warm after swimming or when playing outside in the winter.

Treatment of acute painful episodes, also known as painful 'crises' – Painful crises should be treated with oral or intravenous analgesia according to need (may require opiates) and good hydration (oral or intravenous as required); infection should be treated with antibiotics; oxygen should be given if the oxygen saturation is reduced. Exchange transfusion is indicated for severe acute chest syndrome and stroke.

Prevention of chronic problems – Children who have recurrent painful vaso-occlusive crises or acute chest syndrome (see [Case history 23.2](#)) benefit from hydroxycarbamide, a drug which increases HbF production and helps protect against further episodes. Many clinicians now offer hydroxycarbamide to asymptomatic children with HbSS to help improve long-term outcome of sickle cell disease. It requires monitoring for side-effects, especially white blood cell suppression. The most severely affected children (1%–5%) who have had a stroke or who do not respond to hydroxycarbamide may be offered a bone marrow transplant, which is currently the only cure for sickle cell disease.

Prognosis

Sickle cell disease is a cause of premature death due to one or more of the severe complications; around 50% of



Case history 23.2

Acute sickle chest syndrome

Princess, a 9-year-old girl with known sickle cell anaemia (HbSS), presented with increasing chest pain for 6 hours. She had a non-productive cough. On examination, she had a fever of 39.7°C. Her breathing was laboured, respiratory rate increased and there was reduced air entry at both bases. Investigations:

- haemoglobin 60 g/L, white blood cells (WBC) $14 \times 10^9/L$, platelets $350 \times 10^9/L$
- chest X-ray (see [Fig. 23.11](#))
- oxygen saturation – 89% in air
- arterial PO_2 – 9.3 kPa (70 mmHg) breathing face-mask oxygen
- blood cultures were taken and viral titres performed.

A diagnosis of acute sickle chest syndrome was made, a potentially fatal condition. She was given oxygen by continuous positive airways pressure (CPAP). An exchange transfusion was performed. Broad-spectrum antibiotics were commenced. She responded well to treatment.

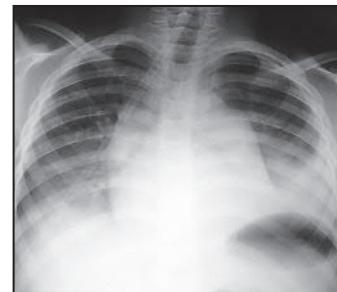


Figure 23.11 Chest X-ray in acute sickle chest syndrome showing bilateral lower zone consolidation. (Courtesy of Parviz Habibi.)

patients with the most severe form of sickle cell disease in high-income countries with established sickle cell disease treatment programmes die before the age of 40 years. However, the mortality rate during childhood in these settings is around 3%, usually from bacterial infection. Childhood mortality in sickle cell disease is significantly higher in sub-Saharan Africa, where the majority will not live to adulthood.

Prenatal diagnosis and screening

Many high-income countries with a relatively high prevalence of haemoglobinopathies, including the UK, perform neonatal screening using the dried blood spots (Guthrie test) collected in the first week of life for neonatal biochemical screening. Early diagnosis of sickle cell disease allows penicillin prophylaxis to be started in early infancy. Prenatal diagnosis is available in many countries and is undertaken by DNA testing following chorionic villus sampling or amniocentesis in the first trimester of pregnancy, allowing couples an option to prevent the birth of an affected child.

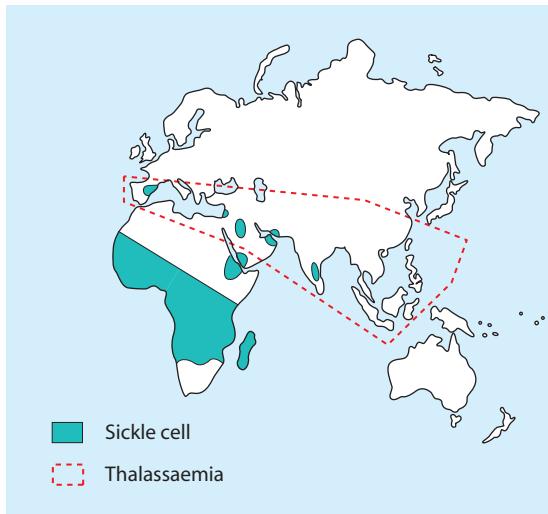


Figure 23.12 Ethnic origin of most families with sickle cell disease and thalassaemia.

Haemoglobin SC disease

Children with SC disease usually have a nearly normal haemoglobin level and fewer painful episodes than those with HbSS, but they may develop proliferative retinopathy in adolescence. Their eyes should be checked periodically. They are also prone to develop osteonecrosis of the hips and shoulders.

Sickle cell trait

This is asymptomatic and is not considered as a disease. Potential carriers should be screened prior to general anaesthesia to make sure that additional effort to prevent hypoxia is made since sickling is theoretically possible if carriers are exposed to low oxygen tension.

β -Thalassaemias

The β -thalassaemias occur most often in people from the Indian subcontinent, Mediterranean, and Middle East (Fig. 23.12). There are two main types of β -thalassaemia:

- β -thalassaemia major, also now called transfusion dependent thalassaemia (TDT) – This is the most severe form of the disease. HbA, which is a tetramer of two alpha and two beta globin chains ($\alpha_2\beta_2$), cannot be produced because these patients inherit two abnormal β -globin genes, one from each parent.
- β -thalassaemia intermedia, also now called non-transfusion dependent thalassaemia, NTDT – This form of the disease is milder and of variable severity. The β -globin mutations allow a small amount of HbA and a large amount of HbF to be produced.

Clinical features (Fig. 23.13)

- severe anaemia, typically presenting at 4–6 months of age, together with mild/moderate jaundice
- faltering growth / growth failure
- extramedullary haemopoiesis manifest as hepatosplenomegaly and/or bone marrow expansion causing the classical facies of maxillary overgrowth and skull bossing.

These clinical signs are very rare in the UK and high-income countries as they are completely prevented by effective blood transfusion (see below).

Management

β -Thalassaemia major is uniformly fatal without regular blood transfusions, so all patients are given lifelong monthly transfusions of red blood cells. The aim is to maintain the Hb above 95–100 g/L in order to reduce growth failure and prevent bone deformation. Repeated blood transfusion causes chronic iron overload, which if untreated causes cardiac failure, liver cirrhosis, diabetes, infertility, and growth failure. For this reason, all patients are treated with iron chelation, usually with an oral iron chelator drug, such as deferasirox, starting from 2 years to 3 years of age. Patients who comply well with transfusion and chelation have a greater than 90% chance of living into their forties and beyond. Those with poor compliance have a high mortality in early adulthood from iron overload. The complications of multiple transfusions are shown in Box 23.3. An alternative treatment for β -thalassaemia major is bone marrow transplantation from a matched sibling donor, which is currently the only cure.

Prenatal diagnosis

For parents who are both heterozygous for β -thalassaemia trait, there is a 1 in 4 risk of having an affected child. Prenatal diagnosis of β -thalassaemia (DNA analysis from chorionic villus sampling or amniocentesis in the first trimester of pregnancy) should be offered together with genetic counselling to help parents to make informed decisions about whether or not to continue the pregnancy.

β -Thalassaemia trait

Individuals with β -thalassaemia trait, who have one mutated and one normal β -globin gene, are usually asymptomatic. Anaemia is mild or absent but the MCV is reduced (60–70 fl) as is the mean cell haemoglobin (MCH; 18–22 fl). The diagnosis is made using high performance liquid chromatography (HPLC) of a peripheral blood sample which shows an increased percentage of HbA₂ (usually to about 5%). β -Thalassaemia trait can cause confusion with mild iron deficiency because of the reduced MCV and MCH, but can be distinguished by measuring serum ferritin, which is low in iron deficiency but not in β -thalassaemia trait. To avoid unnecessary iron therapy, serum ferritin levels should be measured in patients with mild anaemia and microcytosis prior to starting iron supplements.

α -Thalassaemias

Healthy individuals have four α -globin genes. The manifestation of α -thalassaemia syndromes depends on the number of functional α -globin genes.

The most severe α -thalassaemia, α -thalassaemia major (also known as Hb Barts hydrops fetalis) is caused by deletion of all four α -globin genes, so no HbA ($\alpha_2\beta_2$) can be produced. It occurs mainly in families of South-East Asian origin and presents in mid-trimester with fetal hydrops (oedema and ascites), which is always fatal *in utero* or within hours of delivery. The only long-term survivors of α -thalassaemia major are those who have received monthly intrauterine transfusions until delivery followed by lifelong monthly transfusions after birth. The diagnosis is made by Hb HPLC, which shows mainly Hb Barts (a tetramer of four gamma globin chains, γ^4).

When only three of the α -globin genes are deleted (*HbH disease*), affected children typically have

Clinical features and complications of β -thalassaemia major (transfusion dependent thalassaemia)

Pallor

Jaundice

Bossing of the skull
Maxillary overgrowth

Splenomegaly and
hepatomegaly

Need for repeated
blood transfusions
Complications shown in
Box 22.3



Figure 23.13 Facies in β -thalassaemia showing maxillary overgrowth and skull bossing in a child with β -thalassaemia intermedia, (non-transfusion dependent thalassaemia).

Box 23.3 Complications of long-term blood transfusion in children

Iron deposition – the most important (all patients)

- Heart – cardiomyopathy
- Liver – cirrhosis
- Pancreas – diabetes
- Pituitary gland – impaired growth and sexual maturation
- Skin – hyperpigmentation

Antibody formation (10%)

- Allo-antibodies to transfused red cells in the patient make finding compatible blood very difficult
- Infection – now uncommon

Infection – now uncommon

- Hepatitis A, B, C
- HIV
- Malaria
- Prions (e.g. new variant Creutzfeldt-Jakob disease)

Venous access (common problem)

- Often traumatic in young children
- Central venous access device (e.g. Portacath) may be required; these predispose to infection

mild–moderate anaemia but occasional patients are transfusion dependent.

As with sickle cell trait and β -thalassaemia trait, individuals with α -thalassaemia trait are asymptomatic. Alpha thalassaemia trait is caused by deletion of one or two α -globin genes and may cause confusion with iron deficiency as the red blood cells have a reduced MCV and MCH.

Anaemia in the newborn

Reduced red blood cell production – The two main causes in the newborn are congenital infection with parvovirus B19 and congenital red cell aplasia (Diamond–Blackfan anaemia), as outlined above. In both cases, the Hb is low and the red blood cells look normal but the reticulocyte count is low and the bilirubin is normal.

Increased red cell destruction (haemolytic anaemia) – The main causes of haemolytic anaemia in neonates is haemolytic disease of the newborn (HDN). However, as described above, intrinsic genetic disorders of the red blood cell, such as red cell membrane disorders (e.g. HS), red cell enzyme disorders (e.g. G6PD deficiency), and haemoglobinopathies, may also present in the neonatal period.

HDN is due to antibodies against blood group antigens. The most important antibodies are those directed against the Rh antigens (anti-D, anti-c and anti-E antibodies), the

ABO blood group antigens (anti-A or anti-B antibodies) and Kell antigens (anti-Kell antibodies). For HDN to develop, the mother is always negative for the relevant antigen (e.g. rhesus D-negative) and the baby is always positive; the mother then makes antibodies against the baby's blood group antigen and these antibodies cross the placenta into the baby's circulation causing fetal or neonatal haemolytic anaemia. The diagnostic clue to this type of haemolytic anaemia is a positive direct anti-globulin test (Coombs test). This test is only positive in antibody-mediated anaemias and so is negative in all the other types of haemolytic anaemia. (These conditions are considered further in Ch. 11, Neonatal medicine.)

Blood loss

The main causes are:

- Feto-maternal haemorrhage (occult bleeding into the mother).
- Twin-to-twin transfusion (bleeding from one twin into the other one).
- Blood loss around the time of delivery (e.g. placental abruption).

The main diagnostic clue is severe anaemia with a raised reticulocyte count and normal bilirubin.

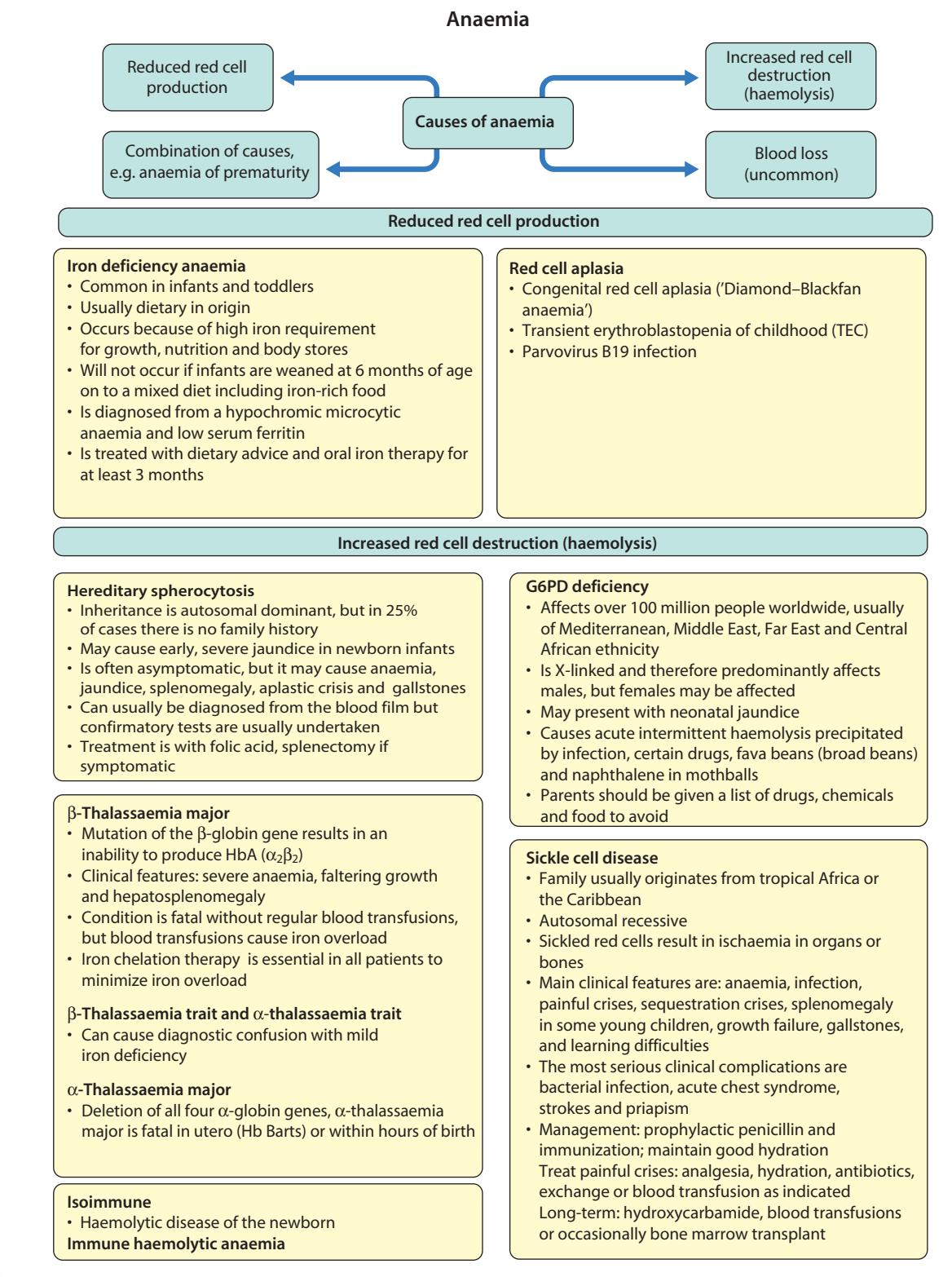
Anaemia of prematurity

The main causes are:

- inadequate erythropoietin production
- reduced red cell lifespan

- frequent blood sampling whilst in hospital if extremely preterm or require intensive care
- iron and folic acid deficiency (after 2–3 months). Delayed cord clamping at birth reduces the risk.

Summary



Bone marrow failure syndromes

Bone marrow failure (also known as aplastic anaemia) is a rare condition characterized by a reduction or absence of all three main blood cell lineages in the bone marrow (red cell lineage, white blood cell lineages, and megakaryocyte/platelet lineage) leading to peripheral blood pancytopenia. It may be inherited or acquired. The acquired cases may be due to viruses (especially hepatitis viruses), drugs (such as sulphonamides, chemotherapy), or toxins (such as benzene, glue); however, many cases are labelled as 'idiopathic' because a specific cause cannot be identified.

Bone marrow failure may be partial or complete. It may start as failure of a single lineage but progress to involve all three cell lines.

The clinical presentation is with:

- anaemia due to reduced red cell numbers
- infection due to reduced white cell numbers (especially neutrophils)
- bruising and bleeding due to thrombocytopenia.

Inherited aplastic anaemia

These disorders are all rare.

Fanconi anaemia

This is the most common of the rare inherited aplastic anaemias. It is an autosomal recessive condition caused by mutations in one of the many *FANCA* genes, most commonly *FANCA*. The majority of children have congenital anomalies, including short stature, abnormal radii and thumbs, renal malformations, microphthalmia, and pigmented skin lesions. Children may present with one or more of these anomalies as the signs of bone marrow failure do not usually become apparent until the age of 5–6 years. The diagnosis is made by demonstrating increased chromosomal breakage of peripheral blood lymphocytes and/or by genetic analysis of the *FANCA* genes to identify the causative mutations. This test can be used to identify affected family members or for prenatal diagnosis. Affected children are at high risk of death from bone marrow failure or transformation to acute leukaemia. The recommended treatment is bone marrow transplantation using normal donor marrow from an unaffected sibling or matched unrelated marrow donor.

Shwachman–Diamond syndrome

This rare autosomal recessive disorder is characterized by bone marrow failure, together with signs of pancreatic exocrine failure and skeletal abnormalities. Most are caused by mutations in the *SBDS* gene, which can be used for identifying unusual cases or prenatal diagnosis. Most affected children have an isolated neutropenia or mild pancytopenia. Like Fanconi anaemia, there is an increased risk of transforming to acute leukaemia.

Bleeding disorders

Normal haemostasis

Haemostasis describes the normal process by which blood coagulation is initiated and terminated in a tightly

regulated manner. This is to ensure that blood vessel wall injuries are rapidly repaired, and the resulting clot is contained within the area of vessel wall injury. It takes place via a series of interactions involving cellular and plasma factors.

There are five main components:

1. *Coagulation factors* – are produced (mainly by the liver) in an inactive form and are activated when coagulation is initiated (usually by tissue factor (TF), which is released by vessel injury).
2. *Coagulation inhibitors* – these either circulate in plasma or are bound to endothelium and inactivate clotting factor complexes. These are necessary to prevent widespread coagulation throughout the body once coagulation has been initiated.
3. *Fibrinolysis* – this process ensures that excess fibrin deposition at the site of injury is either prevented or rapidly removed due to activity of the key enzyme plasmin.
4. *Platelets* – are vital for haemostasis as they aggregate at sites of vessel injury to form the primary haemostatic plug, which is then stabilized by fibrin.
5. *Blood vessels* – both initiate and limit coagulation. Intact vascular endothelium secretes prostaglandin I₂ and nitric oxide (which promote vasodilatation and inhibit platelet aggregation). Damaged endothelium releases TF and procoagulants (e.g. collagen and von Willebrand factor, vWF) and there are inhibitors of coagulation on the endothelial surface (thrombomodulin, antithrombin and protein S).

The endpoint of the coagulation is the generation of thrombin. Thrombin generation occurs as a result of a large number of enzymatic reactions, which is orchestrated by both positive and negative feedback loops. The traditional view of the blood coagulation pathway was a 'cascade' model of reactions in distinct 'intrinsic' and 'extrinsic' pathways. This has now been replaced by a 'cellular model' with three main components – the initiation, amplification and propagation of clot formation. At the same time as the coagulation reaction, there is continuous negative feedback from anti-coagulant factors to limit the extent to which the coagulation factors remain activated. This, and enzymatic degradation of thrombin, ensures that hemostasis is maintained at all times.

Diagnostic approach

Defects in the coagulation factors, in platelet number or function, or in the fibrinolytic pathway are associated with an increased risk of bleeding. In contrast, defects in the naturally occurring inhibitors of coagulation (e.g. antithrombin) or in the vessel wall (e.g. damage from vascular catheters) are associated with thrombosis. In some cases, both procoagulant and anticoagulant abnormalities can occur at the same time, as seen in disseminated intravascular coagulation (DIC).

The diagnostic evaluation of an infant or child for a possible bleeding disorder includes:

- identifying features in the clinical presentation that suggest the underlying diagnosis, as indicated in **Box 23.4**
- initial laboratory screening tests to determine the most likely diagnosis (**Table 23.2**)
- specialist investigation to characterize a deficiency or exclude important conditions that can present with normal initial investigations, e.g. mild vWD, factor XIII deficiency and platelet function disorders.

Box 23.4 Helpful clinical features in evaluating bleeding disorders**Age of onset**

- Neonate – in 20% of haemophiliacs, bleeding occurs in the neonatal period, usually with intracranial haemorrhage or bleeding after circumcision
- Toddler – haemophiliacs may present when starting to walk
- Adolescent – von Willebrand disease may present with menorrhagia

Family history

- Family tree – detailed family tree required
- Gender of affected relatives (if all boys, suggests haemophilia)

Bleeding history

- Previous surgical procedures and dental extractions – if uncomplicated, suggests bleeding tendency is acquired rather than inherited

- Presence of systemic disorders
- Drug history, e.g. anticoagulants
- Unusual pattern or inconsistent history – consider non-accidental injury

Pattern of bleeding

- Mucous membrane bleeding and skin haemorrhage – characteristic of platelet disorders or von Willebrand disease
- Bleeding into muscles or into joints – characteristic of haemophilia
- Scarring and delayed haemorrhage – suggestive of disorders of connective tissue, e.g. Marfan syndrome, osteogenesis imperfecta or factor XIII deficiency

Table 23.2 Investigations in haemophilia A and von Willebrand disease

	Haemophilia A	von Willebrand disease
PT	Normal	Normal
APTT	↑↑	↑ or normal
Factor VIII:C	↓↓	↓ or normal
vWF Antigen	Normal	↓
RiCoF (activity)	Normal	↓
Ristocetin-induced platelet aggregation	Normal	Abnormal
vWF multimers	Normal	Variable

APTT, activated partial thromboplastin time; PT, prothrombin time; RiCoF, ristocetin cofactor, measures von Willebrand disease activity; vWF, von Willebrand factor.

The most useful initial screening tests are:

- full blood count and blood film
- prothrombin time (PT) – tests for deficiencies in the intrinsic pathway in the traditional coagulation model involving factors II, V, VII and X
- activated partial thromboplastin time (APTT) – tests for deficiencies in the extrinsic pathway involving factors II, V, VIII, IX, X, XI and XII
- if PT or APTT is prolonged, a 50:50 mix with normal plasma will distinguish between possible factor deficiency or presence of inhibitor
- thrombin time – tests for deficiency or dysfunction of fibrinogen
- quantitative fibrinogen assay
- D-dimers – to test for fibrin degradation products
- biochemical screen, including renal and liver function tests.

The ‘bleeding time’ is no longer used to investigate platelet disorders, as it is unreliable. It has been replaced by *in vitro* tests of platelet function.

In the neonate, the levels of all clotting factors except factor VIII (FVIII) and fibrinogen are lower; preterm infants have even lower levels. Therefore the results have to be compared with normal values in infants of a similar gestational and postnatal age. In view of this, and because it is often difficult to obtain good-quality neonatal samples, it is often necessary to exclude an inherited coagulation factor deficiency by performing genetic analysis both on the child and their parents.

Haemophilia

The most common severe inherited coagulation disorders are haemophilia A and haemophilia B. Both have X-linked recessive inheritance. In haemophilia A, there is FVIII deficiency ([Fig. 23.14](#)); it has a frequency of 1 in 5000 male births. Haemophilia B (FIX deficiency) has a frequency of 1 in 30,000 male births. Two-thirds of newly diagnosed infants have a family history of haemophilia, whereas one-third are sporadic. Identifying female carriers requires a detailed family history, analysis of coagulation factors and DNA analysis. Prenatal diagnosis is available using DNA analysis.

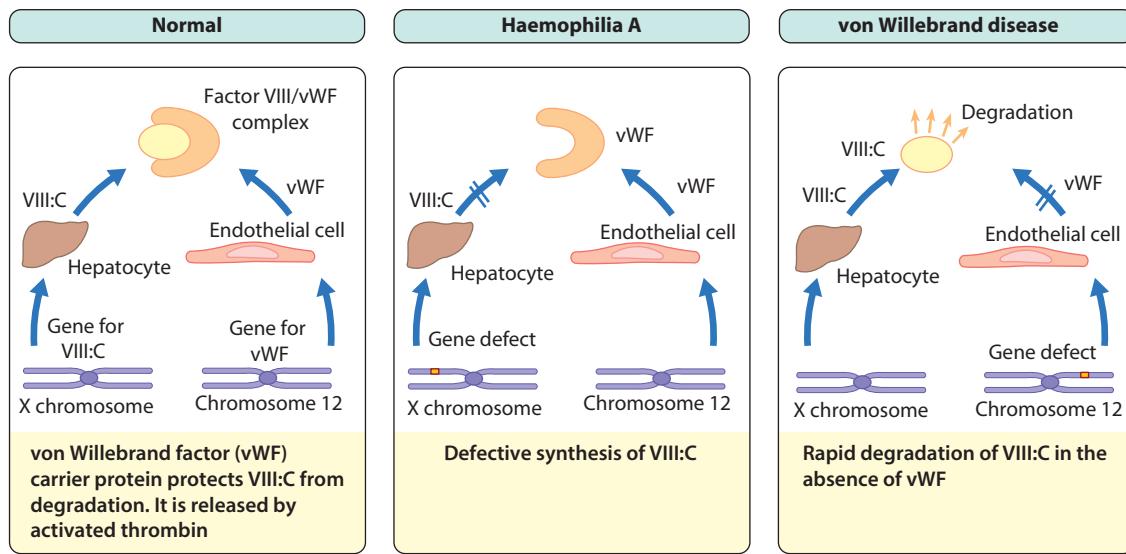


Figure 23.14 Factor VIII synthesis: normal, haemophilia A and von Willebrand disease.

Table 23.3 Severity of haemophilia

Factor VIII	Severity	Bleeding tendency
<1%	Severe	Spontaneous joint/muscle bleeds
1%–5%	Moderate	Bleed after minor trauma
>5%–40%	Mild	Bleed after surgery

Clinical features

The disorder is graded as severe, moderate, or mild, depending on the FVIII (or IX in haemophilia B) level (Table 23.3). The hallmark of severe disease is recurrent spontaneous bleeding into joints and muscles, which can lead to crippling arthritis if not properly treated (Fig. 23.15). Many of these children have large bruises from trivial pressure such as being picked up or knocking a cot rail, and in those with no family history this may lead to the suspicion of non-accidental injury. Towards the end of the first year of life, when they start to crawl or walk (and fall over), children begin to develop muscle and joint bleeds. Almost 40% of cases present in the neonatal period, particularly with large cephalhaematomas, intracranial haemorrhage, bleeding post circumcision or prolonged oozing from heel stick and venepuncture sites. The severity usually remains constant within a family.

Management

Prophylactic FVIII and IX given intravenously is considered to be the standard of care in all children with severe haemophilia A and B, respectively, to reduce the risk of chronic joint damage. The goal is to maintain a trough factor concentration of at least 1% to prevent all bleeds. Primary prophylaxis usually begins around 1 year and is given every 2–3 days. If peripheral venous access is poor, a central venous access device (e.g. Portacath) may be



Figure 23.15 Severe arthropathy from recurrent joint bleeds in haemophilia. The aim of modern management is to prevent this from occurring.

required. Prophylaxis has been shown to result in better joint function in adult life. Parents are usually taught to give replacement therapy at home, and many children are able to administer their own treatment from 7 years to 8 years of age.

During acute bleeding episodes, recombinant factor concentrate is given by prompt intravenous infusion. If recombinant products are unavailable, highly purified, virally inactivated plasma-derived products should be used. The quantity required depends on the site and nature of the bleed. In general, raising the circulating level to 30% of normal is sufficient to treat minor bleeds and simple joint bleeds. Major surgery or life-threatening bleeds require the level to be raised to 100% and then maintained at 30% to 50% for up to 2 weeks to prevent secondary haemorrhage. This can only be achieved by regular infusion of factor concentrate (usually 8–12-hourly for FVIII, 12–24-hourly for FIX, or by continuous infusion) and by closely monitoring plasma levels. *Intramuscular injections, aspirin, and nonsteroidal anti-inflammatory drugs should be avoided in all patients with haemophilia.* Complications are listed in Box 23.5.

Box 23.5 Complications of treatment of haemophilia**Inhibitors, i.e. antibodies to FVIII or FIX**

- Develop in 30% of patients with haemophilia A, but only 3% of patients with haemophilia B
- Reduce or completely inhibit the effect of treatment
- Usually treated with immune tolerance induction which involves regular exposure to large quantities of factor treatment for a long time

Transfusion-transmitted infections

- Hepatitis A, B, and C
- HIV
- Other, e.g. prions, parvovirus B19

Vascular access

- Peripheral veins – may be difficult to cannulate
- Central venous access devices may become infected or thrombosed

Desmopressin (DDAVP), which stimulates release of endogenous FVIII and vWF, may allow mild haemophilia A to be managed without the use of blood products. It is given by infusion. Adequate levels can be achieved to enable minor surgery and dental extraction to be undertaken. DDAVP is ineffective in haemophilia B.

Designated haemophilia centres normally supervise the management of children with bleeding disorders. They provide a multidisciplinary approach with expert medical, nursing, and laboratory input. Specialized physiotherapy is needed to preserve muscle strength and avoid damage from immobilization. Psychosocial support is an integral part of maintaining compliance.

Patient support organizations such as the Haemophilia Society may provide families with helpful information and advocacy.

von Willebrand disease (vWD)

Von Willebrand factor (vWF) is a large glycoprotein produced in the vascular endothelium and has two major roles:

- It facilitates platelet adhesion to damaged endothelium.
- It acts as the carrier protein for FVIII, protecting it from inactivation and clearance.

vWD results from either a quantitative or qualitative deficiency of vWF. This causes defective platelet plug formation and, since vWF is a carrier protein for FVIII, patients with vWD also are effectively deficient in FVIII (see Fig. 23.14).

There are many different mutations in the vWF gene resulting in many different types of vWD. The inheritance is usually autosomal dominant. The most common subtype, type 1 (60%–80%), is usually fairly mild and is often not diagnosed until puberty or adulthood.

Clinical features

These are:

- bruising
- excessive, prolonged bleeding after surgery
- mucosal bleeding such as epistaxis and menorrhagia.

In contrast to haemophilia, spontaneous soft tissue bleeding such as large haematomas and haemarthroses are uncommon.

Management

Treatment depends on the type and severity of the disorder. Type 1 vWD can usually be treated with DDAVP, which causes secretion of both FVIII and vWF into plasma. DDAVP should be used with caution in children less than 1 year of age as it can cause hyponatraemia due to water retention and may cause seizures, particularly after repeated doses, and if fluid intake is not strictly regulated. More severe types of vWD have to be treated with *plasma-derived* FVIII concentrate, as DDAVP is ineffective and recombinant FVIII concentrate contains no vWF. Recombinant vWF has undergone clinical trials and may soon be licensed for use in adult patients. *Intramuscular injections, aspirin, and nonsteroidal anti-inflammatory drugs should be avoided in all patients with vWD.*

Acquired disorders of coagulation

The main acquired disorders of coagulation affecting children are those secondary to:

- vitamin K deficiency, causing vitamin K deficient bleeding (haemorrhagic disease of the newborn), see Chapter 10, Perinatal medicine
- liver disease
- immune thrombocytopenia (ITP)
- disseminated intravascular coagulation (DIC).

Vitamin K is essential for the production of active forms of factors II, VII, IX, X, and for the production of naturally occurring anticoagulants such as protein C and protein S. Vitamin K deficiency therefore causes reduced levels of all of these factors. The main clinical consequence of this is a prolonged prothrombin time and an increased risk of bleeding. Children may become deficient in vitamin K due to:

- inadequate intake (e.g. neonates, long-term chronic illness with poor intake)
- malabsorption (e.g. coeliac disease, cystic fibrosis, obstructive jaundice)
- vitamin K antagonists (e.g. warfarin).

Thrombocytopenia

Thrombocytopenia is a platelet count less than $150 \times 10^9/L$. The risk of bleeding depends on the level of the platelet count:

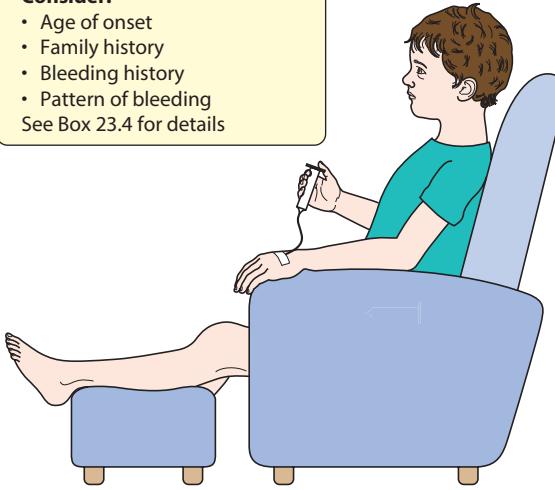
- severe thrombocytopenia (platelets $<20 \times 10^9/L$) – risk of spontaneous bleeding
- moderate thrombocytopenia (platelets $20\text{--}50 \times 10^9/L$) – at risk of excess bleeding during operations or trauma but low risk of spontaneous bleeding
- mild thrombocytopenia (platelets $50\text{--}150 \times 10^9/L$) – low risk of bleeding unless there is a major operation or severe trauma.

Thrombocytopenia may result in bruising, petechiae, purpura and mucosal bleeding (e.g. epistaxis, bleeding from gums when brushing teeth). Major haemorrhage

Summary

The child with abnormal bleeding – into soft tissues, mucocutaneous or following surgery

Acquired disorders	Inherited disorders
<p>Vitamin K deficiency:</p> <ul style="list-style-type: none"> mainly neonates or early infancy <p>Liver disease</p> <p>Thrombocytopenia:</p> <ul style="list-style-type: none"> immune, DIC, etc. <p>Consider:</p> <ul style="list-style-type: none"> Age of onset Family history Bleeding history Pattern of bleeding <p>See Box 23.4 for details</p>	<p>Haemophilia A (factor VIII deficiency) and haemophilia B (factor IX deficiency):</p> <ul style="list-style-type: none"> Are X-linked recessive disorders affecting males Presentation of severe disease – usually with recurrent spontaneous bleeding into joints and muscles at about 1 year of age Treatment – recombinant FVIII concentrate for haemophilia A or recombinant FIX concentrate for haemophilia B. Desmopressin (DDAVP) to treat mild haemophilia A Treatment complications – inhibitors and intravenous access <p>von Willebrand disease (vWD):</p> <ul style="list-style-type: none"> Results from either a quantitative or qualitative deficiency of von Willebrand factor (vWF) Autosomal dominant Presentation – mucosal bleeding, e.g. epistaxis or menorrhagia in adolescence or excessive, prolonged bleeding after surgery Treatment – mild disease with DDAVP, severe disease with plasma-derived FVIII concentrate



in the form of severe gastrointestinal haemorrhage, haematuria, and intracranial bleeding is much less common. The causes of easy bruising and purpura are listed in **Table 23.4**. While purpura may signify thrombocytopenia, it also occurs with a normal platelet count from platelet dysfunction and vascular disorders.

Immune thrombocytopenia (ITP)

ITP is the most common cause of thrombocytopenia in childhood. It has an incidence of around 4 per 100,000 children per year. It is usually caused by destruction of circulating platelets by antiplatelet IgG autoantibodies. The reduced platelet count may be accompanied by a compensatory increase of megakaryocytes in the bone marrow.

Clinical features

Most children present between the ages of 2 years and 10 years, with onset often 1 week to 2 weeks after a viral infection or vaccination. In the majority of children, there is a short history of days or weeks. Affected children develop petechiae, purpura, and/or superficial bruising (see **Case history 23.3**). ITP can also cause epistaxis and other mucosal bleeding but profuse bleeding is uncommon, despite the fact that the platelet count often falls to less than $10 \times 10^9/L$. Intracranial bleeding is a serious but rare complication, occurring in 0.1% to 0.5%, mainly in those with a long period

of severe thrombocytopenia. In about 80% of children, the disease is acute, benign, and self-limiting, usually remitting spontaneously within 6 weeks to 8 weeks. The following definitions are used in ITP based on duration:

- Newly-diagnosed ITP: Duration ≤ 3 months
- Persistent ITP: Duration 3–6 months
- Chronic ITP: Duration ≥ 6 months.

Treatment recommendations vary according to the duration of ITP.

Diagnosis

ITP is a diagnosis of exclusion, so careful attention must be paid to the history, clinical features, and blood film to ensure that more serious disorders, such as inherited thrombocytopenias, aplastic anaemia and leukaemia, are not missed. In the younger child, a congenital cause (such as Wiskott–Aldrich or Bernard–Soulier syndromes) should be considered. Any atypical clinical features, such as the presence of anaemia, neutropenia, hepatosplenomegaly, or marked lymphadenopathy, should prompt a bone marrow examination to exclude acute leukaemia or aplastic anaemia. However, in most children with isolated thrombocytopenia and non-life-threatening mucosal bleeding, treatment can be given without prior bone marrow examination. Systemic lupus erythematosus (SLE) should also be considered in adolescents.

Table 23.4 Causes of purpura or easy bruising

Platelet count reduced, i.e. thrombocytopenia	
<i>Increased platelet destruction or consumption</i>	
Immune	Immune thrombocytopenic purpura (ITP) Systemic lupus erythematosus (SLE) Alloimmune neonatal thrombocytopenia
Non-immune	Haemolytic uraemic syndrome Thrombotic thrombocytopenic purpura Disseminated intravascular coagulation (DIC) Congenital heart disease Giant haemangiomas (Kasabach–Merritt syndrome) Hypersplenism
<i>Impaired platelet production</i>	
Congenital	Fanconi anaemia Wiskott–Aldrich syndrome Bernard–Soulier syndrome
Acquired	Aplastic anaemia Marrow infiltration (e.g. leukaemia) Drug-induced
Platelet count normal	
<i>Platelet dysfunction</i>	
Congenital	Rare disorders, e.g. Glanzmann thrombasthenia, Hermansky Pudlak syndrome type 2
Acquired	Uraemia, cardiopulmonary bypass
<i>Vascular disorders</i>	
Congenital	Rare disorders, e.g. Ehlers–Danlos, Marfan syndrome, hereditary haemorrhagic telangiectasia
Acquired	Meningococcal and other severe infections Vasculitis, e.g. Henoch–Schönlein purpura, SLE Scurvy



Case history 23.3

Immune thrombocytopenic purpura (ITP)

Sian, aged 5 years, developed bruising and a skin rash over 24 hours. She had had an upper respiratory tract infection the previous week. On examination she appeared well but had a purpuric skin rash with some bruises on the trunk and legs (Fig. 23.16). There were three blood blisters on her tongue and buccal mucosa, but no fundal haemorrhages, lymphadenopathy, or hepatosplenomegaly. Urine was

normal on dipstick testing. A full blood count showed Hb 115 g/L with normal indices, WBC and differential normal, platelet count $17 \times 10^9/\text{L}$. The platelets on the blood film were large; the film was otherwise normal. A diagnosis of ITP was made and she was discharged home. Her parents were counselled and given emergency contact names and telephone numbers. They were also given literature on the condition and advised that she should avoid contact sports but should continue to attend school. Over the next 2 weeks she continued to develop bruising and purpura but was asymptomatic. By the third week, she had no new bruises, and her platelet count was $25 \times 10^9/\text{L}$; the blood count and film showed no new abnormalities. The following week, the platelet count was $74 \times 10^9/\text{L}$ and a week later it was $200 \times 10^9/\text{L}$. She was discharged from follow-up.



Figure 23.16 Bruising and purpura from immune thrombocytopenic purpura.



In children with immune thrombocytopenic purpura, in spite of impressive cutaneous manifestations and extremely low platelet count, the outlook is good, and most will remit quickly without any intervention.

Management

Most children can be managed at home and do not require hospital admission. Treatment is controversial. Most children do not need any therapy even if their platelet count is less than $10 \times 10^9/L$ but treatment should be given if there is evidence of major bleeding (e.g. intracranial or gastrointestinal haemorrhage) or persistent minor bleeding that affects daily life such as excessive epistaxis or menstrual bleeding. The treatment options include oral prednisolone or intravenous immunoglobulin, and both have significant side-effects. Platelet transfusions are reserved for life-threatening haemorrhage as they raise the platelet count only for a few hours. The parents need immediate 24-hour access to hospital treatment, and the child should avoid trauma, as far as possible, and contact sports while the platelet count is very low.

Chronic ITP

Chronic ITP occurs in 20% of affected children. In the majority, treatment is mainly supportive; drug treatment is only offered to children with chronic persistent bleeding that affects daily activities or impairs quality of life.

Children with significant bleeding are rare and require specialist care. A variety of treatment modalities are available, including thrombopoietin receptor agonists (TPO-RA) such as eltrombopag (available as an oral daily dose) or romiplostim (given as weekly subcutaneous injections). Rituximab, a humanized monoclonal antibody directed against B cells, can also be given as second-line treatment if TPO-RA is not available. Splenectomy can be effective for this group but is mainly reserved for children who fail drug therapy as it significantly increases the risk of infection and patients require lifelong antibiotic prophylaxis. If ITP in a child becomes chronic, regular screening for SLE should be performed, as the thrombocytopenia may predate the development of autoantibodies.

Disseminated intravascular coagulation

DIC describes a disorder characterized by coagulation pathway activation leading to diffuse fibrin deposition in the microvasculature and consumption of coagulation factors and platelets.

Summary

The child with petechiae or purpura

Non-thrombocytopenic

Henoch–Schönlein purpura

- Lesions confined to buttocks, extensor surfaces of legs and arms
- Swollen painful knees and ankles
- Abdominal pain
- Haematuria

Sepsis

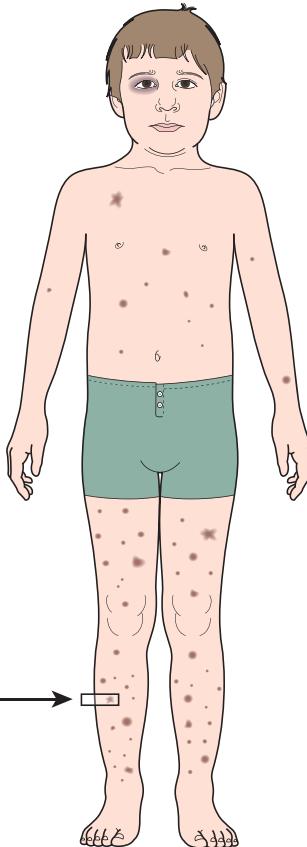
- Meningococcal or viral
- Clinical features – fever, septicaemia, meningitis
- Rash in meningococcal sepsis – positive glass test
- If suspected, give parenteral penicillin immediately

Trauma

- Accidental or non-accidental

Other causes (rare)

Positive glass test – rash does not blanch when pressed



Thrombocytopenia

Immune thrombocytopenia (ITP)

- 2–10 years
- Widespread petechiae and purpura and superficial bruising
- Distinguish from acute leukaemia and aplastic anaemia – clinical features, full blood count and blood film
- Bone marrow examination not required if only the platelet count is low and characteristic clinical features
- Is acute, benign and self-limiting in about 80% of children
- Treatment – controversial, usually not required unless there is major or persistent bleeding

Leukaemia

- Clinical features – malaise, infection, pallor, hepatosplenomegaly, lymphadenopathy
- Blood count – also low Hb, blasts on film, confirmed on bone marrow

Disseminated intravascular coagulation (DIC)

- Critically ill – severe sepsis or shock or extensive tissue damage

Other causes (uncommon)

The most common causes of activation of coagulation are severe sepsis or shock due to circulatory collapse, e.g. in meningococcal septicaemia, or extensive tissue damage from trauma or burns. DIC may be acute or chronic and is likely to be initiated through the tissue factor pathway. The predominant clinical feature is bruising, purpura, and haemorrhage. However, the pathophysiological process is characterized by microvascular thrombosis and purpura fulminans may occur.

No single test reliably diagnoses DIC. However, DIC should be suspected when the following abnormalities coexist – thrombocytopenia, prolonged PT, prolonged APTT, low fibrinogen, raised fibrinogen degradation products (such as D-dimers), and microangiopathic haemolytic anaemia. There is also usually a marked reduction in the naturally occurring anticoagulants, protein C and protein S, and antithrombin.

The most important aspect of management is to treat the underlying cause of the DIC (usually sepsis) while providing intensive care. Supportive care may be provided with fresh frozen plasma (to replace clotting factors), cryoprecipitate and platelets. The use of heparin remains controversial.

Thrombosis in children

Thrombosis is uncommon in children and about 95% of venous thromboembolic events are secondary to underlying disorders associated with hypercoagulable states such as severe sepsis, dehydration and disseminated intravascular coagulation. It is often exacerbated by indwelling central venous catheters. Thrombosis of cerebral vessels usually presents with signs of a stroke. (The condition is considered further in Ch. 11 and Ch. 29.) Rarely, children may inherit abnormalities in the coagulation and fibrinolytic pathway that increase their risk of developing clots even in the absence of underlying predisposing factors. These conditions are termed congenital prothrombotic disorders (thrombophilias). They are:

- protein C deficiency
- protein S deficiency
- antithrombin deficiency
- factor V Leiden
- prothrombin gene G20210A mutation.

Proteins C and S and antithrombin are natural anticoagulants and their deficiencies are inherited in an autosomal dominant manner. Heterozygotes are also predisposed to thrombosis, usually venous, during the second or third decade of life and only rarely in childhood. Homozygous deficiency of protein C and protein S are very uncommon and present with life-threatening thrombosis with widespread haemorrhage and purpura into the skin (known as ‘purpura fulminans’) in the neonatal period. Homozygous antithrombin deficiency is not seen, probably because it is lethal in the fetus.

Factor V Leiden is an inherited abnormality in the structure of the coagulation protein factor V, which makes it resistant to degradation by activated protein C as part of the body's normal anticoagulant mechanism. The prothrombin gene mutation is associated with high levels of plasma prothrombin.

Secondary or acquired causes of thrombosis are:

- catheter-related thrombosis
- DIC
- hypernatraemia
- polycythaemia (e.g. due to congenital heart disease)
- malignancy
- SLE and persistent antiphospholipid syndrome.

Diagnosis

Although inherited thrombophilia is very uncommon, these disorders predispose to life-threatening thrombosis and so it is important not to miss the diagnosis in any child presenting with an unexplained thrombotic event. Therefore, screening tests for the presence of an inherited thrombophilia should be carried out in the following situations:

- any child with unanticipated or extensive venous thrombosis, ischaemic skin lesions, or neonatal purpura fulminans
- any child with a positive family history of neonatal purpura fulminans.

The screening tests are assays for protein C and protein S, antithrombin assay, polymerase chain reaction (PCR) for factor V Leiden, and for the prothrombin gene mutation.

Mutations in factor V (factor V Leiden) and the prothrombin gene, respectively, are present in 5% and 2% of the northern European population. Children with protein C deficiency or factor V Leiden have 4 times to 6 times higher risk of developing recurrent thromboses. The risk increases significantly if these conditions are inherited together. Therefore it is reasonable to screen children who develop thrombosis for all of these factors in order to plan the best management to prevent thrombosis. In the UK, current practice is not to screen asymptomatic children for genetic defects that are not going to affect their medical management, e.g. on the basis of family history alone, until they are old enough to receive appropriate counselling and make decisions for themselves.

Summary

Thrombosis

All children with thrombosis should be screened for inherited or acquired predisposing disorders.

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Haemophilia: World Federation of Haemophilia: www.wfh.org or The Haemophilia Society: www.haemophilia.org.uk.

Sickle Cell Society: www.sicklecellsociety.org.

UK Thalassaemia Society: www.ukts.org.



Child and adolescent mental health

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Features of child mental health:

- Good mental health in childhood and adolescence is a stronger predictor of high satisfaction in adult life than any other factor including wealth, education and physical health.
- Mental health is as integral a component of good medical care as physical assessment or management of maltreatment.
- Mental health is complex. There is seldom a single cause for a mental health problem, and biological, psychological and social factors all contribute to its evolution.

In this chapter we will focus on any emotion or behaviour that is sufficiently impairing that it forms part of a paediatric consultation, and consider what clinicians can do to help. Mental health has many confusing definitions. When we refer to mental health ‘problems’ we mean any

emotional or behavioural difficulty that adversely affects the child or young person’s (CYP’s) life. Mental health ‘disorders’ are diagnosed in a subset of these individuals. They are usually more severe and are defined according to diagnostic criteria used in psychiatry.

Some statistics relating to mental health in CYPs in England are:

- More than 50% of all mental health problems are established by 14 years of age and 75% by age 24.
- There was only a small increase in the overall prevalence of mental health problems in 5- to 16-year-olds between 1999 and 2017, from 9.7% to 11.2% respectively. This increase was mostly driven by an increase in the rate of emotional problems.
- Mental health problems among 5–19 year olds are mainly emotional, behavioural or hyperactivity. Their rates vary markedly with age (Fig. 24.1). Almost a quarter of 17–19-year-old girls have one or more

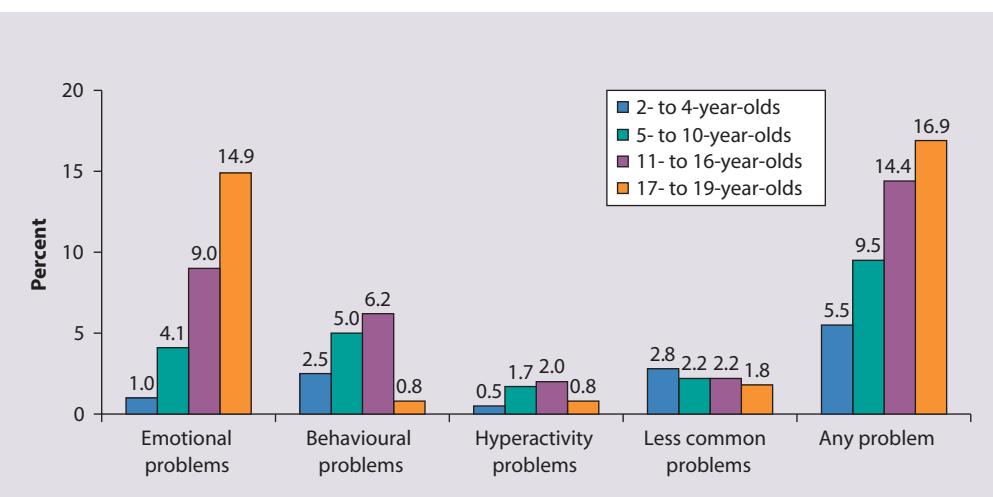


Figure 24.1 Rates of different types of problems in 5- to 19-year-olds by age. Rates of mental health problems vary with age. (From: Mental Health of Children and Young People in England, 2017. NHS Digital, 2018.)

- mental health problem, with emotional problems such as anxiety and depression being the most prevalent.
- There are strong correlations between the presence of developmental and (some) chronic physical conditions and the presence of mental health problems (Fig. 24.2). However, comorbid and secondary mental health problems often go unrecognized and untreated as there is a tendency for physicians to concentrate on the physical problems. Failure to do so leads to poorer quality of care, e.g. poor glycaemic control and increased renal/retinal/cardiovascular complications in diabetes mellitus, and worse outcomes such as educational attainment, employment, dependence on welfare, reduced life expectancy.
- Many children and young people with a mental health problem initially consult non mental health specialists about their problem.

Although the overall prevalence of mental health problems in CYPs increased only slightly between 1999 and 2017, there is considerable concern about the effect of the COVID-19 pandemic on CYPs' mental health. A similar national survey of 5–16-year-olds during the first wave of the pandemic in the UK in 2020 showed that the proportion with mental health problems increased from 11.2% in 2017 to 16%; a further increase is anticipated for the second wave. Whilst some older children with mental health problems reported that lockdown had improved their lives, the majority reported that it had made their lives worse. The main problems were anxiety, accompanied by feelings of loneliness and isolation, disrupted sleep with a loss of motivation and hope for the future. This was accompanied by an increase in panic attacks, new or worsening eating disorders, self-harming and maltreatment. They had particular concerns relating to disrupted schooling and its effect on educational attainment and exams, future employment or university places. Whilst the risk for CYPs of developing serious illness from COVID-19 was

low, some were anxious about catching it, or spreading it to their home, especially if a multigenerational household or a member had increased susceptibility. Some had to cope with bereavement of family members or relatives. Children and young people with mental health problems were twice as likely to live in households newly falling behind with bills, rent, or mortgage payments. One in 10 reported that during the pandemic their family did not have enough to eat or had increased reliance on food banks. Socio-economic conditions also markedly affected ability to access home learning and have space for study. There was reduced access and availability of support for mental health problems, especially school counselling services, as well as reluctance to attend hospital emergency departments during the pandemic.

How to ask about emotional and behavioural problems

Effective history taking is open, explorative, non-judgemental and empathic. It allows complex issues to be explored. It is best to interview both parents if possible. Consider the quality of their relationship and the parents' mental state. Ask open questions and where possible ask directly about feelings. Assess the attitudes of the parents to the child or young person.

Obtain examples of the problem and estimate its frequency, severity, duration and the impact it has on the child or young person and family. A good way to approach this is to ask for a description of a normal day or ask what happens between getting up and going to school; this 'grounds' the problem in the actual behaviours and limits judgements and blame. It affords the child or young person an opportunity to challenge or qualify the description. Other situations that can reveal a lot about what is going on include mealtimes and bedtime. It is worth gathering basic information

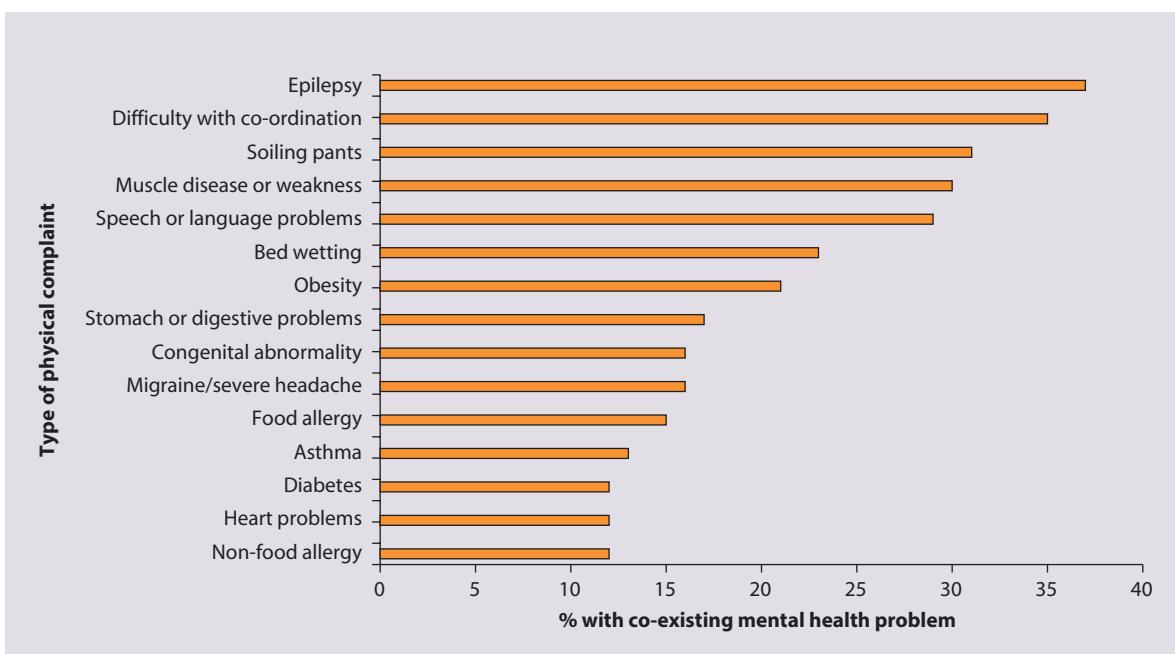


Figure 24.2 Percentage of children with a mental health problem by type of chronic physical condition, showing high rates of mental health problems. These are particularly emotional problems such as anxiety and depression, and increased rates of completed suicide. Some conditions, such as epilepsy, are associated with markedly increased risk. (Source: Melzer H, et al: Mental health of children and young people in Great Britain. ONS, 2000.)

about the household routine, discipline, bedtimes, screen usage, and also leisure and social activities.

Interview the child and ask to see young people alone as part of the assessment. Explain to the parents that you always like to have a few words with young people on their own as they may have things they may feel too embarrassed about to discuss with parents present. Assess the extent of the child or young person's suffering (they may minimize this). Keep your questions simple and specific, making sure the child or young person understands what it is you want to know. This also applies to adolescents, when a HEADS assessment may be indicated to ascertain use of drugs and alcohol, experience of abuse, thoughts of self-harm and suicide. Consider whether reports from school or other involved agencies might help.

When taking a history the following questions may be useful:

- How does the problem affect the child and family?
- Who is in the family? Are there other problems in the family?
- Has the child suffered any adversity?
- How did the current difficulties start?
- What else was happening at the time?

This is standard medical history. However, the next set of questions will reveal more:

- How do people respond to the problem?
- What do you think about the problem? What does the child or young person think?
- What worries everyone most?
- What are you doing about it already?
- Are there any times when it gets better?

When talking to adolescents, asking them to rate their mood (in the last fortnight) on a scale of 1–10 gives a useful baseline. The following approaches may also be helpful:

- Clarifying their thinking – e.g. 'Could you explain that further?'
- Challenging their assumptions – e.g. 'Is this always the case?'
- Requesting evidence – e.g. 'Why do you say that?'
- Exploring implications and consequences – e.g. 'How does... affect...?'
- Questioning the question – e.g. 'Why do you think that I asked that?'

How mental health problems evolve in childhood

Mental health problems are complex and there is seldom a single cause. Factors in their evolution span biological, psychological and social domains. We will describe these factors in turn, then bring them together in a 'biopsychosocial formulation'.

Biological factors

Genetic factors are important in the aetiology of many mental health problems. For autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), genetic factors are important in determining the

Box 24.1 Effect of chronic illness on mental health

- *Biological* – direct effect on neurobiology, either from condition itself (e.g. epilepsy) or treatment (e.g. oral corticosteroids for nephrotic syndrome)
- *Psychological* – often marked by a similar psychological process to bereavement, with both denial and over-acceptance of possible adverse results
- *Social* – effect on family wide-ranging and complex. Difference from peers becomes increasingly important and difficult in adolescence

neurobiology that underpins them. The heritability of ASD is estimated as being in excess of 80% and heritability estimates for ADHD range from 70%–90%. For disorders such as anxiety, which are less clearly of a developmental nature, genetics and family history are still of great importance, but less is known and heritability is lower. Early biological adversity is an important risk factor for developmental conditions and mental health problems. These include:

- prematurity
- exposure to toxins *in utero*, e.g. alcohol
- serious illness in infancy, e.g. meningitis.

Some chronic conditions (e.g. epilepsy) can represent a biological, psychological and social challenge all in one (Box 24.1).

Developmental status is important to ascertain when assessing mental health, whether or not the child has a known specific developmental diagnosis. It may be that a behaviour that is thought to be abnormal is, in a child with developmental delay, normal for their developmental age. Specific problems with communication, interaction, and behavioural inhibition will affect the child's ability to respond in a constructive way to frustration and other challenges (Box 24.2).

Boys are consistently more likely to have a behavioural disorder across the age-groups. In primary school, both boys and girls have similar levels of emotional disorder, but in secondary school and especially in young adulthood, females have higher incidence of emotional problems.

Psychological factors

Self-esteem

Children develop views and make attributions about themselves. Most children experience praise and success

Box 24.2 Developmental problems and behavioural responses

- *Language impairment* – child unable to verbalize feelings, so expresses them in behaviour problem; if this is not appreciated early on, this will escalate
- *Autism spectrum disorder (ASD)* – difficulty by the child understanding and accepting even quite subtle changes can lead to avoidant and often extreme behaviours
- *Attention deficit hyperactivity disorder (ADHD)* – child 'acts before thinking' and so frequently lashes out or shouts when frustrated

in enough areas of their lives to develop a sense of inner self-confidence and self-worth. Those who do not are at increased risk of developing emotional and behavioural disorders, which in turn may breed further shame and failure. Children who do not consider themselves worthwhile and valued by others will play safe and not attempt new activities or explore new situations because of a fear of failure. This restricts the development of coping skills and knowledge of the world generally. It may also be a vulnerability factor for depression and anxiety disorders. Children who lack a belief in their own worth may adopt extraordinary and problematic behaviours in order to attract the attention and acclaim of others. Repeated failure, academically or socially, will undermine self-esteem, as will some disorders themselves (dyspraxia, enuresis and faecal soiling in particular). An important source of low self-esteem, however, is the child's parents, either because of their own low self-esteem or because of abuse (emotional, sexual or physical, and neglect).

Cognitive style

As children grow older, their thinking style evolves from one that is concrete to one that is able to cope with abstract thought. Below the age of about 5 years, thought is fundamentally egocentric, with the child being at the centre of his world (Box 24.3). During middle childhood, the dominant mode of thought is practical and orderly but tied to immediate circumstances and specific experiences rather than hypothetical possibilities or metaphors. Not until the mid-teens does the adult style of abstract thought begin to appear.



Adjust the way you talk to children to be compatible with their thinking style.

Social factors

Early relationships and attachment

In the first 2 months of life, infants are not fussy about who responds to their needs. From 3–6 months of age they become more selective, demanding comfort from one or two caregivers. By age 6–8 months they are particular about who responds to their needs or holds them, especially when distressed, and show tearful *separation anxiety* if their main caregiver is not there. If tired, fearful,

Box 24.3 The quality of preschool thought

- The child is at the centre of his world ('I'm tired so it's getting dark')
- Everything has a purpose ('The sea is there for us to swim in')
- Inanimate objects are alive ('Naughty table hurt me') and have feelings and motives
- Poor categorization (all men are Daddies)
- Use of magical thinking ('If I close my eyes, she'll go away')
- Use of sequences or routines rather than a sense of time
- The use of toys and other aspects of imaginative play as aids to thought (particularly in making sense of experience and social relationships)

unhappy, or in pain, they will cling to them and be comforted by their presence as an *attachment figure*.

At this time, the child learns to crawl, and so is able to leave a primary caregiver and possibly encounter danger. The development of attachment behaviour allows the infant to keep track of their parent's whereabouts and resist separation. This close attachment relationship derives from social interaction and the parent's sensitive responsiveness to the baby's needs, not from any blood tie.

It need not be with a biological parent, although it usually is. Its importance lies in it being:

- a particularly close relationship within which the child's development of trust, empathy, conscience and ideals is promoted, forming a prototype for future close relationships
- the child's primary source of comfort, providing the principal method of coping with stress (fear, anxiety, pain, etc.).

Children who have never had the opportunity of a close, secure attachment relationship in their early years are at risk of growing up as self-centred individuals who seek the affection and attention of others but have difficulty with close personal relationships and with learning to conform with social rules of conduct.

The selective clinging of early attachment behaviour diminishes over time, so that in the second year of life children extend their emotional attachments to other family members and carers. By school age, they can tolerate separations from their parents for several hours. Children vary in their ability to do this depending on their temperament and social circumstances. For example, a child who is constitutionally apprehensive, who has an exceptionally anxious carer, or who has parents who threaten abandonment is likely to continue to cling to his/her main carer for protection and comfort. A series of frightening events will tend to perpetuate clinging, which may persist well into middle childhood (age 5–12 years). This interferes with children's capacity to learn how to cope with anxiety on their own (Fig. 24.3).



Figure 24.3 A 6-year-old with separation anxiety, showing what it feels like to leave her mother to go to school.

With entry into school, the importance of teachers and other children in shaping psychosocial development increases, and their influence must be taken into account in understanding any schoolchild's development.

Summary

Young children's early relationships

- Develop a close attachment relationship with their mother (or main caregiver).
- If separated from their mother, may develop separation anxiety.
- If admitted to hospital, should be able to have a parent stay with them.

Adverse life experiences in the family

Adverse childhood experiences (ACEs) is used to describe a wide range of stressful or traumatic experiences that children and young people can be exposed to while growing up (see Ch. 1, Paediatrics and child health, and Ch. 8, Maltreatment of children and young people). Family relationships are, for most children, the source of their most powerful emotions. Similarly, parents have more effect than anyone else on children's social learning and behaviour. The ecological model of child development indicates that families are generally the most potent environmental influence on a child's mental health. They are not all-powerful, since a predisposition to particular childhood emotional and behavioural problems can be inherited, but family influences interact with this so that overt disorder may or may not emerge.

Not all disorders have their origin in family adversities; some (e.g. ASD and ADHD) arise independently of them. Nevertheless, the non-genetic contribution of family interactions to emotional and behavioural disorders is often substantial, and the mechanisms whereby they produce disorder are various. The following are some of the known risk factors:

- angry discord between family members
- parental mental ill health, especially maternal depression
- bereavement
- divorce and subsequent loss of a parent figure (in some cases)
- intrusive overprotection
- lack of parental authority
- physical and sexual abuse
- emotional rejection or excessive criticism
- inconsistent, unpredictable discipline
- using the child to fulfil the unreasonable personal emotional needs of a parent
- inappropriate responsibilities or expectations for the child's level of maturity.

Parents need to be made aware of changes required to improve the situation, and it is more accurate and constructive to place the difficulties that occur at home into a biopsychosocial context, rather than blame. This is more constructive and accurate, and families are more likely to engage successfully in treatment.

Social disadvantage

Families who are on low income or experience poverty are consistently more likely to have children with poorer mental health. Housing is a particularly important issue. Children in temporary accommodation are 4 times more likely to have a mental health problem. Conversely, engagement in local communities and schools has been shown to be associated with better mental health.

Peer groups and social media

Experiences with other children are increasingly recognized as highly significant in psychosocial development. Bullying is a known adversity, as are other forms of peer-mediated persecution. Conversely, having a number of steady, good-quality peer relationships is a marker for good prognosis in an emotional or behavioural problem which has resulted from environmental influences.

Most older children and adolescents in high-income countries (and increasingly in low- and middle-income countries) have internet access and utilize social media regularly, often using smartphone devices. Social media platforms are transforming the way young people communicate with one another. Whilst there are benefits in the form of online support groups and fora, and promising tools for education and mental health awareness, there is emerging evidence that vulnerable adolescents can be harmed by exposure to social media which may promote eating disordered or addictive behaviour.

There are many online fora where discussions about self-harm and suicide can have a toxic effect on the adolescent. Cyberbullying over the internet is usually carried out by the same people as conventional bullying, but appears to be more damaging.

Excessive use of electronic devices can impact on sleep and reduce interpersonal interactions; however, extensive analysis does not support the widespread belief that the use of social media, and screen time more broadly, is a cause of mental health problems.

Summary

Regarding adversities

- The child's family is the most potent influence on the child's mental health.
- Adversities outside the family, e.g. bullying, may aggravate the situation.

Resilience

Given all the possible adversities that children could suffer, it may seem amazing that mental health problems are not universal! The reason for this is that for every adverse factor there is a corresponding factor that may increase the child's resilience and compensate for any adversity encountered.

Most are simply the converse of the factors listed above (for instance, good social interaction skills), but there are some specific resilience factors that should be enquired about:

- time spent together as a family
- meals eaten as a family
- regular exercise
- regular and sufficient sleep
- absence of bullying.

Putting it together: the biopsychosocial formulation

Once you have a wide-ranging history, the 4p structure (introduced in Ch. 1, Paediatrics and child health, and Ch. 2, History and examination) can be used with biological, psychological and social factors considered under the headings:

- predisposing – which usually cannot be helped
- precipitating – which are useful in explaining the situation
- perpetuating factors – which are ongoing and usually the easiest to target
- protective – which contribute to resilience and can be encouraged.

You can then use the information (Table 24.1) to agree a story with the family about what is happening. This will be more useful than any single explanation of the child's predicament, and it can be used to develop wide-ranging, helpful interventions (see Case history 24.1 for a specific example).

Specific paediatric emotional, behavioural and mental health problems

Common problems of the preschool years

The crying baby

All babies cry to indicate hunger or discomfort or to gain attention, and they usually respond to feeding, comforting or nappy change. Studies have shown that babies fuss or cry for an average of 2 hours a day at 6 weeks and 1 hour at 10 weeks. Some babies in the first few months of life are prone to more prolonged, incessant crying, often called infantile colic (see NICE guidelines). The crying is usually in the late afternoon or evening, is distressing for all concerned, and can engender a feeling of anxiety and helplessness in parents and carers. This applies especially to the mother; it has been shown that mothers are biologically programmed to be particularly sensitive to their own

Table 24.1 The 4p format to assist to develop a biopsychosocial formulation

	Biological/developmental	Psychological	Social
Predisposing factors			
Precipitating factors			
Perpetuating factors			
Protective factors (resilience)			



Case history 24.1

Disruptive behaviour at school

Shane, a 6-year-old child with autism spectrum disorder is being disruptive in school. So far his behaviour has been explained as a result of his autism. However, this is simply the 'backdrop' against which the behaviour is occurring. Enquiry into any other underlying **predisposing** factors (such as ADHD, attention deficit hyperactivity disorder),

precipitating factors (a change of teaching assistant) and **perpetuating** factors (anxiety and negative self-thought about getting in trouble) will yield far more useful information, especially if you also garner factors that **protect** the child's wellbeing (supportive friends and engaging hobby). See Table 24.2.

Table 24.2 Use of 4p framework for Shane

	Biological/ developmental	Psychological	Social
Predisposing	Autism spectrum disorder	Tendency to anxiety/rumination	Repeated home moves due to housing difficulties
Precipitating	Poor sleep due to worries	Anxiety about change / social exclusion	Change of teaching assistant
Perpetuating	Poor sleep, headaches	Anxiety about own behaviour and its effect on people's perceptions of him	Punitive approach from some teachers
Protective	Physically healthy and active	Motivation to continue to engage socially and academically	Supportive group of friends and engaging hobby (board games)

baby's cry. The complaint that a baby is 'always crying' may also be a pointer to a serious level of stress and a warning of potential or actual child maltreatment.

Mothers are often concerned that crying signifies hunger from insufficient milk. If breastfed and the baby is sucking well at the breast, has at least six wet nappies a day and weight is increasing as expected, mothers can be reassured that their baby is getting sufficient milk. If necessary, face-to-face assistance with positioning and attachment and further advice can be obtained from breastfeeding support services. Formula fed infants are often changed to different brands, but without improvement.

Causes

A thorough history, including details about feeding, and examination must be performed, and normal weight gain confirmed, in order to confirm that the baby is healthy and to reassure the family accordingly.

A medical cause is identified in a minority of infants. If of sudden onset, infection or sepsis should be considered, particularly urinary tract, middle ear or meningeal. Other potential causes are obstructed bowel, e.g. from strangulated hernia or torsion of the testis, or an unrecognized fracture. As the baby draws up their knees and arches their back when crying, and the condition is referred to as 'infantile colic', parents often think it is due to abdominal pain, and there is a gastroenterological problem. Gastro-oesophageal reflux may be suspected, but is unlikely in the absence of vomiting. Cows' milk protein allergy (CMPA) is often mentioned (see Ch. 16, Allergy), and breastfeeding mothers advised to avoid dairy products for 2 week or formula fed infants to change to a hydrolyzed formula. However, in the absence of a strong atopic family history and other clinical features of allergy, this is seldom of benefit and has the disadvantage that it medicalizes the problem. Some preterm infants who have spent several weeks in hospital can be difficult to settle, as can infants with evolving neurodisability, e.g. cerebral palsy.

Management

Acknowledging that troublesome crying is extremely distressing is a key part of the management. Manoeuvres often identified to help the baby settle include carrying in a sling, swaddling, talking or singing or white noise, infant massage, rocking or gentle motion by pushing in a baby stroller, or driving in a car, but these are often only partially successful. Kangaroo mother care, with direct skin-to-skin contact for many hours per day, may be helpful. Medicines should be avoided; those used in the past have not been shown to be effective or to be hazardous. There is some evidence that the probiotic *Limosilactobacillus reuteri* may reduce crying time in some breastfed babies. Other family members, such as grandparents, or friends may be brought in to help. Parental or carer stress and anxiety may exacerbate the crying. Maternal depression should be identified. Parental support may also be obtained from health visitors, and self-help support groups specifically for parents of crying babies have been established. In addition to reassurance that their baby is healthy, follow-up is required. By 3 to 4 months of age, the crying has usually markedly reduced.

Meal refusal

A common scenario is a mother complaining that her child refuses to eat any or much of what she provides; mealtimes have become a battleground. Examination

reveals a healthy, well-nourished child whose height and weight are securely within normal limits on a centile growth chart.

An account of what goes on at a typical mealtime may reveal:

- A past history of force-feeding
- Irregular meals so that the child is not predictably hungry
- Unsuitable meals
- Unreasonably large portions
- Multiple opportunities for distraction, e.g. TV.

Most importantly, how much does the child eat between meals? A well-nourished child is getting food from somewhere. Not all parents regard sweets and crisps as being food. Some mothers, while concerned about their child's apparently poor food intake, provide little variety in the child's diet. For strategies for dealing with meal refusal, see Box 24.4.

Sleep-related problems

Difficulty in settling to sleep at bedtime

This is a common problem in the toddler years. The child will not go to sleep unless the parent is present. Most instances are normal expressions of separation anxiety, but there may be other obvious reasons for it which can be explored in taking a history (Box 24.5), supplemented if necessary by the parents keeping a prospective sleep diary.

Box 24.4 Strategies for meal refusal

Mealtimes history

What is the parent most concerned about?

- Nutrition?
 - Refer to growth chart
- Discipline and parenting?
 - Family history of eating problems
 - Parenting style
 - What do others say?
 - Is it part of a broader behavioural problem?

How much food is eaten between meals?

- Food diary to record child's intake over a number of days

Advice

- As long as offered wholesome food with adequate range, children are remarkably good at eating an appropriate quantity of food when allowed a reasonable choice
- As it is impossible to force a child to eat, avoid confrontation at mealtimes
- Develop a relaxed atmosphere
- Use favourite foods as a reward. Introduce other rewards for compliance at mealtimes (e.g. additional privileges such as extra TV time)
- Reduce eating between meals if necessary, although many young children prefer small, frequent snacks

Box 24.5 Reasons for a child not settling at night

- Too much sleep in the late afternoon
- Displaced sleep/wake cycle – not waking child in morning because did not settle until late on the previous night
- Separation anxiety
- Overstimulated or overwrought in the evening
- Kept awake by siblings or noisy neighbours or TV in the bedroom or uncomfortable, e.g. too hot or cold
- Erratic parental practices: no bedtime or routine to cue child into sleep readiness; sudden removal from play to go to bed without prior warning to wind down
- Use of bedroom as punishment
- Dislike of darkness and silence – night light and playing story tapes can be helpful
- Some chronic physical conditions may be associated with sleep problems, e.g. itch, pain, cough.

Many cases will respond to simple advice:

- creating a bedtime routine which cues the child to what is required, e.g. check not thirsty or hungry, bath, pyjamas, teeth, stories, toilet, bed
- telling the child to lie quietly in bed until he/she falls asleep, recognizing that children cannot fall asleep to order (although that is what everyone tells them to do)
- having a period of an hour before sleep time when the child is not involved with screens.

If that advice does not resolve the problem, a more active intervention may be required. This involves parents imposing a graded pattern of lengthening periods between tucking their child up in bed and coming back after a few minutes to visit, but leaving the room before the child falls asleep, even if they are protesting. The object is to provide the opportunity for the child to learn how to fall sleep alone, a skill not yet developed. More refractory cases may require specialist referral.

Waking at night

This is normal, but some children cry because they cannot settle themselves back to sleep without their parent's presence. This is often associated with difficulty settling in the evenings, which should be treated first. Some children who can settle in the evening may be unable to settle when they wake in the night because the circumstances are different – it is quieter, darker, etc. The graded approach described above for evening settling can also be used in the middle of the night. Parents will find it helpful to take alternate nights on duty to share the burden.

Nightmares

These are bad dreams which can be recalled by the child. They are common, rarely requiring professional attention unless they occur frequently or are stereotyped in content, indicating a morbid preoccupation, or are symptomatic of a psychiatric disorder such as posttraumatic stress disorder. Unless a disorder is suspected, reassuring the child and his/her family will usually suffice.

Night (sleep) terrors

These are different from nightmares, typically occurring about 1.5 hours after settling. The parents find the child sitting up in bed, eyes open, seemingly awake but obviously disorientated, confused and distressed, and unresponsive to their questions and reassurances. The child settles back to sleep after a few minutes and has no recollection of the episode in the morning. A night terror is a *parasomnia*, a disturbance of the structure of sleep wherein a very rapid emergence from the first period of deep slow-wave sleep produces a state of high arousal and confusion.

Sleepwalking has similar origins and the two may be combined. Most night terrors need little more than reassurance directed towards the parents. The most important intervention for sleepwalking is to make the environment safe to prevent injury to the child (e.g. not sleeping on the upper bunk of a double-bunk bed, putting gates before the staircase, locking the kitchen, etc.).

Given that a common cause of night terrors and sleepwalking is a poor and erratic sleep schedule, a sleep routine can be helpful in preventing recurrence. Once parents have implemented the safety suggestions highlighted above, they can be reassured, as the natural course of these disorders is to decrease over time.

Disobedience, defiance, and tantrums

Normal toddlers often go through a phase of refusing to comply with parents' demands, sometimes angrily ('the terrible twos'). This is an understandable reaction to the discovery that the world is not organized around them. They also become confused and angered by the fact that the parent who provides them with comfort when they are distressed is also the person who is making them do things they do not wish to do. This seems exceptionally unfair to them. That is one reason why children play their parents up but may be fine with others. All this can exhaust and demoralize parents, not least because many people offer advice or criticism (everyone thinks themselves an expert in the area of children's development and behaviour). The points listed in Box 24.6 can be made.

Temper tantrums are ordinary responses to frustration, especially at not being allowed to have or do something. They are common and normal in young preschool children. If asked for advice, a sensible first move is to take a

Box 24.6 Managing toddler disobedience

- Ensure your demand is reasonable for the developmental stage of the child
- Tell the child what you want him/her to do rather than nagging about what you do not want him/her to do
- Praise for compliance, especially when it is spontaneous (catch doing the right thing)
- Use simple incentives to reward good behaviour
- Use instructions like 'If you (do this or that) ... then we/I can do such and such' (not the other way round)
- Avoid threats that cannot be carried out
- Follow through with any consequences you indicated for non-compliance
- Ignore some episodes of defiance if they are not significant

history, analyzing a couple of tantrums according to the ABC paradigm (Box 24.7). Next, examine the child to identify potential medical or psychological factors. Medical factors include global or language delay, hearing impairment (e.g. glue ear), and medication with bronchodilators or anticonvulsants. If none are present, there are management strategies that can be adopted, some of which are shown in Box 24.8.

The easiest course of action is to distract the child or, if this cannot be done, to let the tantrum burn itself out while the parent leaves the room, returning a few minutes later when things quieten down (provided it is safe to leave the child alone). Obviously this should be done in a calm, neutral manner and certainly not accompanied by threats of abandonment. Tantrums which are essentially coercive (when a child is demanding something from a parent) must be met by a refusal to give in. They can often be forestalled by the simple expedient of making rules which the child can be reminded of before the situation presents itself.

An alternative course is to use 'time out', which is a form of structured ignoring. The child in a tantrum is placed somewhere such as the hallway, where no-one will talk to him for a short time, e.g. 1 min per year of age. During this period they are ignored. Parents often expect this manoeuvre to produce a contrite child, complaining if it does not become so immediately. In fact, when used for tantrums, time out works according to different principles (not as a response to punishment but to the withdrawal of attention) and often takes several weeks to effect a gradual improvement. It may help to ask the parent to keep records to document this.

Disobedience can be dealt with by using a star chart to reward the child for complying with parental requests. The chart needs to be where the child can see it and it must be the case that the child knows what to do in order to get a star. It is wisest not to 'fine' the child by taking stars away once they have been earned. If the parent who is rewarding compliance by the child praises at the same time as

Box 24.7 Analyzing a tantrum

- Antecedents – what happened in the minutes before the episode
- Behaviour – exactly what did the episode consist of
- Consequences – what happened as a result, including what you did and the outcome

Box 24.8 Tantrums: Management strategies

- Affection and attention before the tantrum
- Distraction
- Avoiding antecedents
- Ignoring:
 - effective but can be difficult
 - no surrender (when parents give in, tantrums become harder to deal with over time)
- Time out from positive reinforcement:
 - walk away, returning when quietens down
 - separate from siblings
- Holding firmly if the child is putting themselves or others in danger
- Star chart to prevent future episodes

giving the star, there may not be the need to tie stars with a material reward. However, if a tangible reward had been promised for a certain number of stars, it is important to follow through with this.



For temper tantrums:

- Analyze according to antecedents, behaviour and consequences
- Consider distraction, avoiding antecedents, ignoring and time out.

Aggressive behaviour

Small children can be aggressive for a host of reasons, ranging from spite to exuberance. Much aggressive behaviour is learnt, either by being rewarded (often inadvertently) or by copying parents, siblings or peers. For example, many instances of aggressive, demanding behaviour are provoked or intensified by a parent shouting at or smacking their child. In such cases, it is the parent's behaviour that needs to change. In most instances, the same principles as apply to tantrums are valid: make rules clear, stick to them, keep cool, do not give in, and use time out if necessary. The latter can often be used on a 1–2–3 principle (Fig. 24.4). A tired or stressed child will be irritable and prone to angry outbursts, as will children whose communication skills are compromised by deafness or a developmental language disorder so that they are frustrated and exasperated. Optimistic reassurance that the child will spontaneously grow out of a pattern of aggressive behaviour is mistaken; once established, an aggressive behavioural style is remarkably persistent over a period of years. Thus, aggressive behaviour in children needs to be proactively managed. There are several evidence-based parenting programmes that are effective for teaching parents to manage aggression in their children. Parents should be encouraged to attend such programmes.

Autism spectrum disorder and attention deficit hyperactivity disorder

These are considered in Chapter 4 (Developmental problems and the child with special needs).

Problems of middle childhood

Nocturnal enuresis

Nocturnal enuresis, or bedwetting, is the involuntary passage of urine while asleep at an age after which bladder control has usually been achieved. Infrequent bedwetting is common in children; nocturnal enuresis more than

1 Stop doing that because ...

2 If you don't stop that, you must go to your room (or wherever)

3 Go to your room

Figure 24.4 The 1–2–3 principle for tantrums or aggressive behaviour.

2 nights/week is present in about 6% of 5-year-olds and 1.5% of 10-year-olds. Boys outnumber girls by nearly 2 to 1.

Achievement of night-time dryness is dependent upon the development of two functions:

- the ability of the bladder to increase in functional capacity, aided by the action of antidiuretic hormone (ADH) to reduce nocturnal urine production
- the arousal of the individual to the stimulus provided by a full bladder.

There is a genetically determined delay in acquiring night-time dryness, with two-thirds of children with enuresis having an affected first-degree relative. Young children also need reasonable freedom from stress and a measure of parental approval in order to learn night-time continence. It is well recognized that emotional stress can interfere and cause secondary enuresis (relapse after a period of dryness). Most children with nocturnal enuresis are psychologically normal and treatment still relies mainly on the symptomatic approach described below, although any underlying stress, emotional or physical disorder must be addressed.

Diurnal enuresis (bedwetting with daytime symptoms) is relatively uncommon but causes include:

- urinary tract infection
- constipation with faecal impaction severe enough to reduce bladder volume and cause bladder neck dysfunction
- polyuria from osmotic diuresis, e.g. diabetes mellitus or renal concentrating disorders, e.g. chronic kidney disease
- an overactive bladder
- structural abnormalities, e.g. ectopic ureter or neurological abnormalities.

Investigation for bedwetting is only indicated if the bed wetting follows a significant period of nocturnal dryness, if it occurs during the day, if it is accompanied by symptoms of disruptive urgency and frequency, if there are features of urinary tract infection, diabetes mellitus or ill health. Daytime and secondary enuresis are considered in [Chapter 19](#) (Kidney and urinary tract disorders).

The management of nocturnal enuresis is straightforward but needs to be painstaking to succeed. After the age of 4 years, enuresis resolves spontaneously in only 5% of affected children each year. In practice, treatment of nocturnal enuresis is usually only started in children older than 5 years of age with involuntary wetting during sleep at least twice a week.

Explanation

The first step is to explain to both child and parent that the problem is common and beyond conscious control to avoid the child feeling any degree of blame. The parents should stop punitive procedures, as these are counter-productive. Fluid should be restricted in a period of at least 2 hours leading up to bedtime. The child should be encouraged to fully empty their bladder prior to going to bed. Waking or lifting during the night does not promote long-term dryness.

Star chart

The child earns praise and a star can be awarded for agreed behaviour, helping to change the sheets rather

than dry nights. Wet beds are treated in a matter-of-fact way and the child is not blamed for them. In practice, this behaviour-based system is only occasionally helpful as enuresis is not under voluntary control.

Enuresis alarm

This is a sensor, usually placed in the child's pants or under the child, which sounds an alarm when it becomes wet. In order to be effective, the alarm must wake the child, who gets out of bed, goes to pass urine, returns and helps to remake a wet bed before going back to sleep. It is not necessary to reset the alarm that night. Parental help can be enlisted in the night using a baby alarm to transmit the noise of the alarm to the parents' bedroom.

The alarm method takes several weeks to achieve dryness but is effective in most cases so long as the child is motivated and the procedure is followed fully. About one-third relapse after a few months, in which case repeat treatment with the alarm usually produces lasting dryness.

Desmopressin

Desmopressin, a synthetic analogue of antidiuretic hormone, may be used if treatment with the alarm is unsuccessful or unacceptable, or short-term relief is required, e.g. for holidays or sleepovers. It is taken orally. Fluid intake should be restricted after use. It may need to be continued for 3–6 months.

Self-help groups

These provide advice and assistance to parents and health professionals, e.g. ERIC, The Children's Bowel and Bladder Charity.

Summary

Nocturnal enuresis

- Common, males more than females.
- Most affected children are psychologically and physically normal.
- Treatment usually considered only at >5 years of age.
- Management – explanation, enuresis alarm, desmopressin.

Faecal soiling

This is considered in [Chapter 14](#) (Gastroenterology).

Persistent unexplained physical symptoms (PUS)

These are common in childhood. There is debate about the most appropriate terminology that validates the reality of the symptoms to the sufferer, and some other terms include functional disorders, psychosomatic disorders, somatic symptom disorder, pain disorders. A quarter of children and young people regularly experience unexplained symptoms such as abdominal pain, headaches, musculoskeletal pain, fatigue and dizziness. Most are accepted as normal bodily sensations, but for some the symptoms lead to impairment of daily functioning,

high levels of distress, poor school attendance, isolation from peers and significant use of healthcare, often with a strongly held belief by themselves or their carers that there is underlying physical disease. PUS in childhood predicts PUS in adulthood.

Mind/body link

The presentation and management of PUS is based on an understanding that the mind and body are linked: anatomically (nervous systems), physiologically (hormones, neurotransmitters) and psychologically. The 'mind' is thoughts, feelings, beliefs, attitudes, memories, past experiences and personality. Familiar phrases such as 'pain in the neck', 'gut feeling' or 'heart-broken', recognize that emotional states can be associated with physical sensations. There are also objective physical changes such as increased heart rate with fear/excitement, facial flushing with embarrassment, tears with sadness.

Physical symptoms can present when there is emotional upset, e.g. bullying, performance anxiety, or can start with illness, injury, surgery but continue beyond the expected healing period due to propagating psychosocial factors, e.g. school anxiety, lack of feeling cared for or parental separation. Some painful conditions, e.g. migraine, can be triggered by stress, other disease processes, e.g. eczema or psoriasis, can worsen and/or respond less well to treatment at times of stress. There are also positive effects of the mind–body link, and making time for enjoyable things such as hobbies, seeing friends, fresh air, exercise, mindfulness and relaxation can all influence and improve physical wellbeing.

Common conditions for which there is physical and mental health overlap include:

- chronic pain disorders
- chronic fatigue syndrome
- non-epileptic attack disorder
- postural tachycardia syndrome
- non-specific abdominal pain
- headaches.

Assessment and management

In the history, questions must be asked to identify likely organic illness and address possible sources of emotional distress. The child / young person should be interviewed about school, friends and family, noting the general level of anxiety, ability to communicate, and interaction with parent/carer (see HEADS psychosocial screening tool for adolescents in [Chapter 30](#), Adolescent medicine). This should be an integral part of the interview. Useful routine questions can include 'What is the best thing about school? What is the worst thing?' Both can provoke unexpected responses.

Compiling a timeline can help to identify precipitating factors such as bereavement or divorce, or patterns that indicate contributing factors ([Case history 24.2](#)). Symptoms that are either limited to or much worse on school days or only in the care of one parent suggest a provoking factor.

An interview with the child / young person on their own can reveal sources of stress, especially at school, which may be unrecognized by parents or which the child / young person is wary of mentioning in front of them. A report from the school may be useful. Asking older children/adolescents about their romantic and/or sexual relationships, recreational activities such as drug or alcohol use, and low mood / self harm can be enlightening. Screening questionnaires for depression or anxiety may be helpful.

A thorough physical examination is required to reassure the child / young person and family that there is no underlying organic cause. It also provides an opportunity to gain further information about the nature of the symptoms and the child's / young person's reaction to them. For example, when examining a child / young person with persistent abdominal pain, it is sensible to ask them to point to where the pain is. In general, the further the pain is from the umbilicus, the more likely it is being caused by organic pathology (Apley's rule). Observing the posture, mobility and behaviour of the child / young person in the clinic room, and whether this changes during discussion can also be helpful.



Case history 24.2

Heart attack

Rebecca, an 11-year-old girl, has just started secondary school. Her grandfather recently died suddenly from a heart attack. She is an only child and her parents have separated. Her underlying asthma is normally well controlled apart from occasional exacerbations with exercise. In her first physical education (PE) lesson Rebecca developed some difficulty breathing and mild chest pain. She became frightened that this might be a heart attack, causing further increased heart rate, sweating, shaking, and shortness of breath, such that she had to stop PE. Her mother kept Rebecca off school for the week, allowing Rebecca to rest, and looking after her.

Over the next few weeks every time Rebecca felt slightly short of breath she was afraid a similar 'attack' would happen. She started to avoid physical activity, miss days from school and therefore found it difficult to make friends. Her mother had to take leave to look after her. Rebecca

became more tired, her sleep pattern was disrupted and she developed musculoskeletal pains.

Despite normal blood tests, ECG and chest X ray, she and her mother were worried that there must be an underlying problem and presented repeatedly to their GP asking for further investigations.

Rebecca was referred to a paediatrician, who undertook a detailed history and thorough physical examination, reviewed the investigations, and reassured Rebecca and her mother about the symptoms. It was explained that her problems fitted into the category of 'persistent unexplained physical symptoms'. It was suggested a child psychologist might help her cope with her symptoms when they occurred. Her symptoms began to resolve after the consultation and improved further after input from the child psychologist.

There is often a temptation to undertake some investigations to satisfy an anxious parent or child. Health professionals must be mindful that they may cause secondary harm from unnecessary medical investigations and unhelpful propagation of illness beliefs.

Considerable improvement in severity of symptoms and function can be achieved through the use of good communication skills, including validating their suffering, removing blame, offering explanations which make sense, focusing on the words, ideas, concerns and expectations of the young person, and jointly exploring ways of managing symptoms and improving function. Medications are rarely helpful and have side effects, so should be avoided in favour of self-help strategies such as pain coping skills, distraction, relaxation, regular eating patterns, exercise and good sleep hygiene. Promoting communication within families around emotions can help avoid the tendency for somatic symptoms to replace verbal communication.

Where symptoms are particularly severe or disabling, affecting school and social activities, and/or the contributing psychosocial factors are not easily resolved, the input of other professionals may be needed, such as physiotherapists, occupational therapists, psychologists, family therapists, psychiatrists and social workers, working together as a team.

Summary

Persistent unexplained physical symptoms (PUS)

- These are common in childhood and range from pain to dizziness and/or fatigue.
- When present, a detailed history and physical examination are required to ensure that the child and family believe that their concerns are fully addressed and taken seriously.
- Unwarranted investigation and continued medical reviews can worsen the outcome.
- Where symptoms have become debilitating, may require assistance from other professionals.

Tics

Tics are sudden, repetitive movement or vocalization. They can be simple (brief, non-purposeful, involving one group of muscles) or complex (longer, apparently purposeful, involving a cluster of movements). They are not entirely involuntary as they can be suppressed to some extent, though eventually cannot be resisted.

They are common. About 1 in 10 children develop a tic at some stage, typically around the face and head – blinking, frowning, head-flicking, sniffing, throat clearing and grunting being the most common. Boys are more commonly affected. The average age of onset is 8 years old: the tics tend to peak in intensity aged 11 years, then improve. Tics are most likely to occur when the child is inactive (watching TV or on long car journeys) and often disappear when actively concentrating. They may worsen with anxiety but they are not themselves an emotional reaction. In many cases, there is a family history. Most children do not need treatment. *Transient tic disorders* clear up over the next few months, although they may recur from time to time. They should be treated with reassurance in the first place.

Less commonly, tics may be multiple, although there is fluctuation in the predominance of any particular tic and in overall severity. If the tics continue for more than 12 months they are considered chronic in nature, although most cases still resolve in adulthood. If there are both multiple motor tics and vocal tics such as grunting, coughing, humming or squeaking present for over one year, then the condition is known as *Gilles de la Tourette syndrome* or, more simply, Tourette's. Swearing as a vocal tic (coprolalia), though highly publicized, occurs in only about 10%. The first line of treatment is cognitive behavioural therapy with habit reversal techniques. More serious cases may require medication (such as clonidine or risperidone) under specialist supervision, though there is little evidence for their beneficial effect.

Antisocial behaviour

Children steal, lie, disobey, light fires, destroy things and pick fights for various reasons:

- Failure to learn when to exercise social restraint.
- Lack of social skills, such as the ability to negotiate a disagreement.
- They may be responding to the challenges of their peers in spite of their parents' prohibitions.
- They may be chronically angry and resentful.
- They may find their own notions of good behaviour overwhelmed by emotion such as sadness or temptation.

When serious antisocial behaviour, which infringes the rights of others, is the dominant feature of the clinical picture and is so severe as to represent a handicap to general functioning, a diagnosis of *conduct disorder* is made. Children with conduct disorder may not have necessarily broken the law, although their behaviour excites strong social disapproval. They typically come from homes in which there are considerable discord, coercive relationships, limited boundaries that are inconsistently enforced, and poor supervision by adults. A milder form, characterized by angry, defiant behaviour to authority figures such as parents and teachers, is known as *oppositional-defiant disorder*.

Treating conduct disorder can be difficult. Parent management training programmes (such as Webster-Stratton and Triple P) have an excellent evidence base and are highly recommended as primary interventions. However, poor parental cooperation and motivation can result in minimal benefit. Where parents are unwilling or unable to take up parenting programmes, affected children can be offered individual or group-based interventions focusing on problem-solving skills and anger management. Although these interventions show benefit in research settings, affected children often do not have the level of motivation required to benefit in routine clinic settings. In the absence of a coexisting psychiatric condition responsive to medication, it is not considered standard clinical practice to use medication for conduct disorder in the UK.

Summary

Antisocial behaviour

- It is important to exclude any coexisting psychiatric condition and to treat this directly, e.g. ADHD or depression.
- Parenting groups are an evidence-based treatment for these disorders, but require motivation.

Anxiety

Pathological anxiety exists in two forms: specific and general. In phobias there is fear of a specific object or situation that is excessive and handicapping and cannot be dealt with by reassurance. Most children have a number of irrational fears (e.g. fear of the dark, ghosts, kidnappers, dogs, spiders, bats, snakes) which are common and do not usually handicap the child's ordinary life. Some of these persist into adulthood.

If they are so severe that the child's ability to lead an ordinary life is affected, then treatment by cognitive behavioural therapy with graded exposure to the feared event may be indicated and is usually successful.

More diffuse general anxiety presents indirectly in childhood and it is uncommon for a child to complain directly about anxiety. Often, it is first manifest as physical complaints: nausea, headache or pain. It may take the form of health worries, and the child repeatedly asks for reassurance that he/she is not going to die. Some children with generalized anxiety may develop unusual coping strategies that appear manipulative, in an attempt to gain control over their parents and the world in general. It may be a justifiable reaction to an event or situation, or be disproportionate. If the condition follows a recognizable precipitant such as a parental illness and the parents can be directed to provide comfort and support, prognosis is good. If it arises insidiously, specialist mental health referral is indicated.



Children rarely say spontaneously that they are anxious – instead they tend to complain of aches and pains or behave in apparently manipulative ways to cope with or avoid the feared situation.

School refusal

During the years of compulsory school attendance, a child may be absent from school because of illness, because parents keep the child off school, or because of truancy in which the child chooses to do something else rather than attend school. In truancy, a child leaves to go to school but never arrives or leaves early. It is often accompanied by other behavioural difficulties. A few non-attendees at school suffer from *school refusal*, an inability to attend school on account of overwhelming anxiety. Such children may not complain of anxiety but of its physical concomitants or the consequences of hyperventilation. Anxiety may present as complaints of nausea, headache or otherwise not being well, which are confined to weekday, term-time mornings, clearing up by midday. It may be rational, as when the child is being bullied or there is educational underachievement. If it is disproportionate to stresses at school, it is termed school refusal, an anxiety problem with two common causes – separation anxiety persisting beyond the toddler years and anxiety provoked by some aspect of school, true school phobia. These can coexist.

School refusal based on separation anxiety is typical of children under the age of about 11 years. It may be provoked by an adverse life event such as illness, a death in the family or a move of house. The child is unable to tolerate separation from their attachment figure without whom the child cannot go anywhere, including school. Treatment is aimed at gently promoting increasing separations from the parents (e.g. staying overnight with

Box 24.9 Treatment of school refusal

- Advise and support parents and school about the condition
- Treat any underlying emotional disorder
- Plan and facilitate an early and graded return to school at a pace tolerable for the child and with all involved (child, family, teachers, educational psychologist and educational welfare officers)
- Help the parents make it more rewarding for the child to return to school than stay at home
- Address bullying or educational difficulties if present

relatives or friends), while arranging an early return to school. Some adolescents with school refusal have a depressive disorder, but more usually there is an interaction between an anxiety disorder and long-standing personality issues such as intolerance of uncertainty. True school phobia is seen in slightly older, anxious children who are frequently uncommunicative and stubborn. The management of school refusal is shown in [Box 24.9](#).

Educational underachievement

Children who achieve less well in school than expected are sometimes brought to doctors. It is important to evaluate parents' and teachers' expectations and ensure the child is actually able to rise to them. The services of an educational psychologist are indispensable. Core medical responsibilities include checking sight and hearing and attempting to elicit the cause of underachievement according to the list in [Box 24.10](#). The topic is considered further in [Chapter 4](#).

Problems of adolescence

Although a popular image of adolescence is one of angry, rebellious teenagers, alienated from their parents and embroiled in emotional turmoil, studies show that most

Box 24.10 Causes of underachievement at school

Long-standing problem

- Visual problems
- Hearing problems
- Dyslexia
- Generalized or specific learning problems
- Hyperactivity
- Antieducation family background
- Chaotic family background

Recent onset of problem

- Preoccupations (parental divorce, bullying, etc.)
- Fatigue
- Depression
- Rebellion against teachers, parents, or 'swot' label
- Unsuspected poor attendance at school
- Sexual abuse
- Drug abuse
- Prodromal period of a psychotic illness (rare)
- Degenerative brain condition, rare but important

Box 24.11 Formal operational thought

- The ability to form abstract thoughts
- Comparing implications of hypotheses
- Thinking about one's own thinking
- Testing the logic that links propositions
- Manipulating interactive abstract concepts

adolescents maintain good relationships with their parents. They do, however, tend to bicker with them about minor domestic matters and what they are allowed to do. This is a healthy process involving boundary testing, which precedes the separation phase of leaving home. Minor psychological symptoms such as moodiness or social sensitivity are quite common (as they are in adults), but serious psychiatric problems are no more prevalent than in adult life. Family relationships are often influenced by teenagers' negotiation of their own autonomy, the emergence of their own sense of themselves, and the first moves towards a personal identity. At the same time, their parents may be experiencing midlife crises of confidence in career, physical appearance or sexuality, so that parental and teenage preoccupations coincide, not always helpfully.

Cognitive style

The style of thought specifically associated with adolescence is formal operational (abstract) thought (Box 24.11), but this is acquired at various ages by different individuals during the teenage years, and a substantial minority do not develop it at all. Doctors have been selected for their ability to manipulate abstractions and compare hypothetical predictions so they often find it difficult to think otherwise and may communicate poorly with patients who still think concretely and practically (school-age children, about half of all teenagers, and perhaps 1 in 5 adults). When interviewing adolescents, the skill is to avoid being patronizing, while being sensitive as to whether abstract and reflective thought is solidly achieved. Using practical examples (not metaphors) and checking whether you have been understood will help to avoid the common problem of being faced with an adolescent who responds to questions with a sullen 'don't know'. This is considered further in Chapter 30 (Adolescent medicine).

Anorexia nervosa and other eating disorders

Eating disorders are mental health conditions which lead to persistent abnormal eating behaviours that negatively impact on physical health, emotional wellbeing and ability to function normally. Eating disorders can develop at any age but risk is highest in adolescence, and they are more commonly diagnosed in females than males but occur in both.

The most common types of eating disorder are:

- anorexia nervosa – excessive weight loss is achieved by not eating enough food or exercising excessively
- bulimia nervosa – periods of eating a lot of food quickly ('bingeing') and then trying to get rid of calories in unhealthy ways, e.g. vomiting, laxative abuse, exercise excess, taking medication or using diet supplements
- binge-eating disorder – regularly eating large portions of food all at once (often in secret) and then feeling shameful, upset or guilty

- OSFED – 'other specified feeding or eating disorder', when one of the typical symptom complexes described above are absent.

Features of eating disorders

Features include:

- negative/distorted body image
- preoccupation with, and self-evaluation by, weight and body shape
- desire to lose weight and/or fear of fatness / weight gain
- weight losing and compensatory behaviours such as restricted eating, calorie counting, avoidance of energy-dense foods, exercise, excessive movement, inducing cold, induced vomiting, laxatives, weight losing medications
- eating associated with guilt and upset
- food hidden
- eating in front of others avoided
- preoccupation with food, cooking
- denial or secrecy
- attempts to encourage more 'normal' eating patterns met with conflict/resistance
- binge eating large amounts of calorific foods with sense of loss of control.

In anorexia nervosa, food restriction is extreme and children and young people lose weight, develop low body weight for age (weight and BMI centile charts should be used) and have secondary endocrine disturbance such as amenorrhoea, growth/puberty arrest. In bulimia nervosa, where compensatory induced vomiting is common, weight is often in the normal range for age, whereas in binge-eating disorder, without compensatory behaviours, young people frequently become overweight for age.

Other types of eating disorder

Avoidant restrictive food intake disorder (ARFID) is not driven by body image concerns. It is common in children and young people with neurodevelopmental conditions such as autism where they have a narrow range of foods they will eat and avoid certain colours, textures and smells. Disordered eating may present with specific anxieties, such as fear of vomiting (emetophobia), or with obsessive/compulsive thoughts around germs and food contamination. Newer patterns of disordered eating are also being described such as 'orthorexia', where types of food are restricted because of strongly held beliefs regarding healthy eating or the environment. Muscle-oriented disordered eating is more common in boys, with high levels of protein consumption, restriction of non-protein dietary components, use of protein liquid supplements and rigid eating or exercise regimes in pursuit of muscle development or fitness.

Causes of eating disorders

Eating disorders arise from a complex interaction of genetic, biological, behavioural, psychological, and social factors. There are familial and personality predispositions to developing eating disorders. Abnormal eating behaviours may start as a way of coping with difficult emotions or life circumstances such as anxiety, sadness, loneliness, bereavement, bullying, abuse and parental separation. There are increased social and academic pressures on children and young people, changing societal views on appearance, and an increasing focus in the media on food, health, and the environment. Some activities are associated with increased risk of developing eating disorders such as high-level sport, dance or modelling. They are also more common in medical

Sit Up Squat Stand (SUSS) Test: Description and scoring

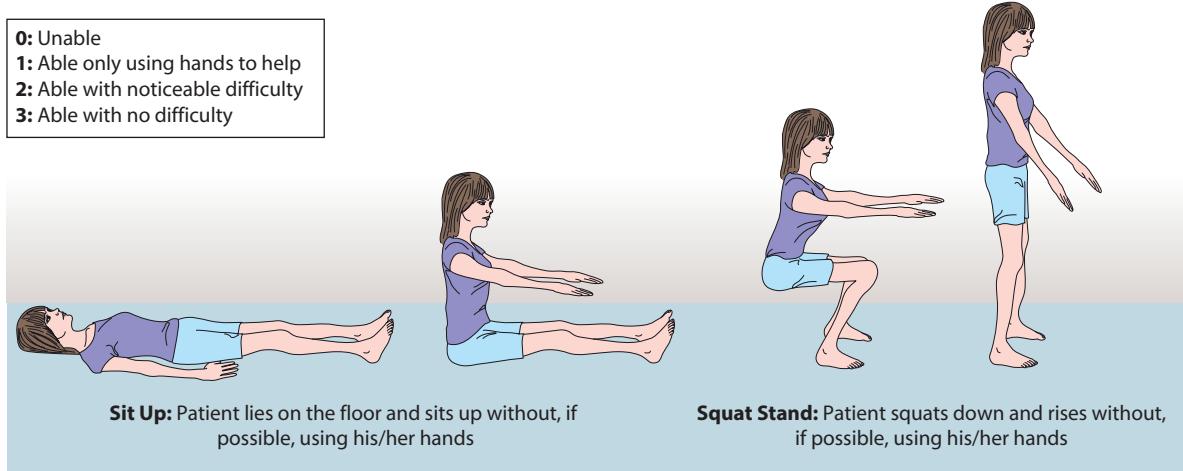


Figure 24.5 SUSS test for muscle weakness in anorexia nervosa. The child or young person is asked to sit up from lying down and to stand from squatting. Their degree of difficulty is assessed.

conditions where there is an emphasis on controlling or monitoring dietary intake, e.g. diabetes, coeliac disease. In diabetes the term 'diabulimia' is used to describe young people who misuse their diet and insulin to achieve changes in body weight and appearance.

How do eating disorders present?

Concerns are often raised by others, e.g. family, friends, teachers, school nurses. Behavioural indicators of an eating disorder, in addition to those above, include reluctant attendance at appointments, resisting weighing and examination, covering the body, being secretive or evasive, and getting angry or distressed when asked about eating problems. Some young people try to falsify their weight by drinking excessively ('water loading'), or hiding weights in their clothing.

Physical risks

Presentation may be with symptoms of malnutrition and low weight or rapid weight loss although these may be strongly denied. Feeling cold, tired, poor concentration, dizzy, faint, and constipated are common. Physical signs include poor peripheral circulation (cold or discoloured hands and feet), fine lanugo hair over the body, bradycardia, postural hypotension, dehydration and muscle weakness, assessed by using the SUSS test (Fig. 24.5). Abnormal investigations include electrolyte disturbances, neutropenia, ECG abnormalities.

Longer term risks to physical health include delayed puberty, secondary amenorrhoea, reduced adult height potential, and low bone density. Mortality in anorexia nervosa is associated with malnutrition, infection and suicide.

Management

Management is two-fold: medical and psychological. Psychoeducation to both the young person and family around energy requirements, normal growth patterns, physical health risks and the mental health aspects of eating disorders is essential. Nutritional rehabilitation (refeeding) is the first step to stabilize the immediate physical risks but as starvation alters cognitive function and propagates abnormal thoughts around food or body image, therapeutic mental health input is not effective until the refeeding process has started. Refeeding can often be achieved through family therapy teams supporting the family to, in turn, support the

young person to re-establish sufficient eating patterns at home. Occasionally, hospital admission for nutritional supplements and nasogastric feeding is required. If a young person resists this, the Mental Health Act can be used to detain them for treatment. Sudden reversal of prolonged starvation can result in a life-threatening metabolic disturbance known as 'refeeding syndrome' which needs careful monitoring. National management guidelines are available.

Later in recovery, individual psychological treatment is introduced to help the young person challenge the cognitions that drive their eating disorder, recognize precipitating and perpetuating factors, and develop ways of managing them to regain independence with eating, and maintain good health and prevent relapse (see Case History 24.3).

Prognosis

The prognosis of eating disorders is changing. Previously many young people had a chronic course into adulthood, but with the introduction over recent years of a more proactive approach to recognition and early intervention in the paediatric age group, recovery rates have improved. Further longitudinal studies are needed to provide data on this.

Summary

Eating disorders

- Include anorexia nervosa, bulimia nervosa, binge-eating disorder and other disorders.
- Presentation is usually from concerns of family or others about low body weight.
- Physical symptoms may include feeling cold, tired, dizzy, poor concentration, constipation and secondary amenorrhoea; signs of low weight, poor peripheral circulation, fine lanugo hair over the body, postural hypotension, muscle weakness and delayed puberty.
- Management involves nutritional rehabilitation followed by psychological treatment.



Case history 24.3

Eating disorder

Ellie, 16 years old, has come to the attention of social services when Youth Offending services noticed that she is unusually thin after an arrest for shoplifting. Her 4p framework is shown in [Table 24.3](#).

The 4p framework provides useful potential avenues for further intervention:

- assessment for possible ADHD

- frank discussion, hopefully including her mother, of risks
- negotiation around how to retain positive aspects of peer group while mitigating risks
- possible use of cognitive behaviour therapy to exploit her good intellectual function.

Table 24.3 4p framework relating to Ellie's eating disorder

	Biological/ developmental	Psychological	Social
Predisposing factors	Possible ADHD	Blames self for father leaving	Chronic conflict with mother
Precipitating factors		Relationship with new boyfriend who uses drugs	Exposure to delinquent peer group
Perpetuating factors	Impulsive, emotionally labile	Identification with 'alternative' lifestyle, distorted body image	Estrangement from family
Protective factors (resilience)	Very bright	Self-worth fairly strong	Many of her peers genuinely supportive

Depression

Low mood can arise secondarily to adverse circumstances or sometimes spontaneously. Depression as a clinical condition is more than sadness and misery; it extends to affect motivation, judgement, and the ability to experience pleasure, and it provokes emotions of guilt and despair. It may disturb sleep, appetite and weight. It leads to social withdrawal, an important sign. Such a state is well recognized among adolescents, particularly girls, but occasionally affects prepubertal children. The general picture is comparable to depression in adults but there are differences ([Box 24.12](#)).

A diagnosis of depression depends crucially upon interviewing the adolescent on his/her own, as well as taking a history from the parents. Teenagers will, out of loyalty, often pretend to their parents that things are all right if interviewed in their presence. It is necessary to ask about feelings directly and to ask specifically about suicidal ideas and plans.

Treatment depends upon severity. Children with mild depression are managed initially in primary care and other non-specialist mental health settings. Many will recover spontaneously; hence a period of watchful waiting for up to 4 weeks may be appropriate. Alternatively, the child or young person could be offered non-directive supportive therapy or guided self-help. However, if mild depression does not respond to these measures in 2–3 months, the child should be referred to specialist mental health services. Similarly, children with moderate and severe depression should be referred to specialist mental health services for more specific psychological intervention such as cognitive behavioural therapy, family therapy, or interpersonal therapy. In all cases, any identified contributing factor such as bullying needs to be addressed. If psychological therapy for moderate or severe depression is insufficient after 6 weeks, then an SSRI (selective

Box 24.12 Features of depression in adolescents

More common than adults

- Apathy, boredom and an inability to enjoy oneself rather than depressed mood
- Separation anxiety which reappears, having resolved in earlier life
- Decline in school performance
- Social withdrawal
- Hypochondriacal ideas and complaints of pain in chest, abdomen, and head
- Irritable mood or frankly antisocial behaviour

Less common than adults

- Loss of appetite and weight
- Loss of sleep
- Loss of libido
- Slowing of thought and movement
- Delusional ideas

serotonin reuptake inhibitor antidepressant), fluoxetine, should be considered. Depressed young people who are suicidal may need admission to an adolescent psychiatric inpatient unit.

Deliberate self-harm

Young people deliberately cause themselves harm for multiple reasons and in multiple ways. Explanations range from a coping technique for dealing with negative feelings (such as low self-esteem) to an expressed wish to punish themselves. Often the young person will describe the positive feeling of control they experience

when harming themselves. The physical pain acts as a distraction from emotional distress.

Self-harm is common and is increasing. Estimates of prevalence find that approximately 22% of 15-year-olds had self-harmed themselves deliberately (32% in females, 11% in males). Many do not present to healthcare professions actively, therefore no assessment of an adolescent with emotional or behavioural difficulties is complete without screening for self-harm.

Common methods of self-harm include cutting, burning, biting, bruising or scratching the skin, or tying ligatures around the neck. Punching of walls should also be considered self-harm (the presentation of a boxer's fracture should raise suspicion).

A full physical examination is an ideal time to look for signs of deliberate self-harm. Cutting to the thighs, for example, can often be missed. The patient wearing long sleeves, reluctant to show their skin, should raise concern. In the upper limbs, signs tend to be on the non-dominant side.

How to ask about self-harm

This involves:

- a history taken with the young person alone. Often a history taken with parents present will result in non-disclosure
- creating a safe environment
- allowing sufficient time to conduct the consultation sensitively, without interruptions
- setting rules about confidentiality clearly
- validating the young person's distress
- giving assurance that they will be supported
- asking questions directly, but sensitively.

There is no single way to ask about self-harm and suicide. Normalization of the problem is key. All clinicians will find a style of asking these questions which suits them, e.g. 'Sometimes if people are feeling particularly stressed, worried or low, they can have thoughts about harming themselves, or ending their lives. Has this ever happened to you?'

A screening tool such as PATHOS (Box 24.13) to assess suicide risk following overdose can be useful alongside a holistic assessment.

Drug misuse

Most teenagers are exposed to illicit drugs at some stage. A number will then experiment with them, some becoming habitual users. Usually, this is for recreational purposes, but a few use them to avoid unpleasant feelings or memories. A very small number become dependent, psychologically or physically. What is taken varies with culture and opportunity, but alcohol and cannabis are common; solvents, LSD, ecstasy and amphetamine derivatives somewhat less so; and cocaine or heroin currently least prevalent. The addictive potential of the last two is the greatest and their dangers are well known.

Abuse implies heavy misuse. The signs vary with the agent but may include:

- intoxication
- unexplained absences from home or school
- mixing with known users
- high rates of spending or stealing money
- possession of the equipment required for drug use
- medical complications associated with use.

Box 24.13 PATHOS instrument to assess suicide risk after adolescent overdose

- **P:** Have you had **P**roblems for longer than a month?
- **A:** Were you **A**lone in the house at the time?
- **T:** Did you plan the overdose for longer than **T**hree hours?
- **HO:** Are you feeling **H**opeless about the future?
- **S:** Were you feeling **S**ad for most of the time before the overdose?

Score 1 for Yes; 0 for No and add together. Child at high risk if score >2. However, the final judgement of suicide risk is a clinical and qualitative decision, not one based on a cut-off score.

From: Kingsbury S, PATHOS: A screening instrument for adolescent overdose: a research note. *Journal of Child Psychology and Psychiatry* 37:609–611, 1996.

Doctors may be approached by parents worried that their adolescent child may be abusing drugs. An assessment will involve interviewing the adolescent, possibly combined with taking a urine sample for drug screening. Most geographical areas have specific services for adolescents with drug and/or alcohol problems. These services usually take self-referrals, so that young people with these difficulties can access them directly. Medical involvement is predominantly focused on users who have other psychopathology including depression or with the physical consequences of intoxication or injection when these threaten health. Solvent abuse (mainly glue and aerosol sniffing) is quite widespread as a group activity of young adolescents in some areas. It can occasionally give rise to cardiac dysrhythmias, bone marrow suppression or renal failure, and any of these can cause death, as may a fall or road traffic accident when intoxicated. Cannabis and LSD use may trigger anxiety or psychotic disorders. Ecstasy taken at dances or raves can cause dangerous hyperthermia, dehydration and death.

Doctors need to ensure that any adolescent known to them who is thought to be using drugs knows the specific risks to health. Dependence is rare among teenagers and most likely to involve alcohol. The few who are using illicit drugs for respite from psychological distress need referral to a psychiatrist.

"Legal highs" are of increasing concern to clinicians. These include chemical substances which produce similar effects to illegal drugs (e.g. cocaine, cannabis, ecstasy). They can have depressant or stimulant, including hallucinogenic, properties. They are easily purchased online, unregulated, and often labelled as incense or salts. They have been associated with a number of deaths, although the association may not be causative. Their long-term effects are uncertain.

Psychosis

Psychosis is a breakdown in the perception and understanding of reality and a lack of awareness that the person is unwell. This can affect ideas and beliefs, resulting in delusional thinking where abnormal beliefs are held with an unshakeable quality and lead to odd behaviour. The connectedness and coherence of thoughts may break down, so that speech is hard to follow, leading to thought disorder. Perceptual abnormalities lead to

hallucinations, where a perception is experienced in the absence of a stimulus.

Psychotic disorders include:

- Schizophrenia, where no specific medical cause is identified and there is generally no major disturbance of mood other than blunting or flattening of affect.
- Bipolar affective disorder, where the psychosis is associated with lowered mood as in depression or elevation in mood as in mania.
- Organic psychosis, which occurs in delirium, substance-induced disorders and dementia.

Both schizophrenia and bipolar affective disorder are rare before puberty, but increase in frequency of presentation during adolescence. In these disorders the psychotic symptoms occur in clear consciousness.

Investigations should include a urine drug screen, exclusion of medication-induced psychosis (e.g. high-dose stimulants or anticholinergic drugs), exclusion of medical causes (i.e. infection, seizures, thyroid abnormalities and sleep disorders) and dementia.

Where schizophrenia and bipolar disorder is suspected, urgent referral to a psychiatrist is needed for comprehensive assessment and treatment with antipsychotic medication, psycho-education, family therapy and, where appropriate, individual therapy. In the case of an organic psychosis the underlying cause needs to be treated promptly by the paediatric team, with help from mental health professionals as appropriate.



Psychosis:

- may present during adolescence
- may be precipitated by or be a consequence of substance abuse.

Management of emotional and behavioural problems

Cultural considerations

Many countries are ethnically diverse in language, religion and culture. This diversity has many important clinical implications for child and adolescent mental health. The first relates to the need to recognize the subgroup of young people who are refugees or asylum seekers. These children and their families have often experienced major traumatic events before arriving in their host country. They are highly vulnerable to mental and socio-economic adversities due to past and ongoing stressful experiences.

Second, culture can alter the presentation of psychiatric symptoms. The content of obsessions in children with obsessive compulsive disorder are often shaped by the child's cultural and religious beliefs. This is also true of some delusions in young people with psychotic disorders, e.g. possession by 'Jinns' (supernatural creatures) in Islamic traditions. Understanding the child's religious and cultural background is essential for making an accurate diagnosis.

Third, there are important cultural differences about normative behaviour in children and thresholds for

help-seeking. Differences in the level of stigma attached to mental illness across cultures also influence parents' help-seeking behaviour and access to child and adolescent mental health services.

Culture and race are not the same thing; education, religion and class all deeply affect the parenting 'culture' of a family. It is essential to avoid making assumptions about the significance of clinical information with cultural or religious meaning but instead to contextualize the information to the patient's culture, e.g. through the use of trained interpreters.

Management

In order to give useful advice, you need to be able to understand the child and family's story, and help them make sense of it. To do this, construct, with the family and child or young person, a story that you all 'own' about how the problem has come about and what is perpetuating it as a biopsychosocial formulation.

Many simple but important intervention opportunities will simply 'fall out' of this formulation, as with the young child Shane in [Case history 24.1](#) and with the young person Ellie in [Case history 24.3](#). You then need to use this understanding to advise them on sources of support and, finally, offer specific advice on dealing with parenting problems, if appropriate.

Coaching parents

The management of many behaviour problems relates to parenting. The key principles are:

- *Positivity – promoting the emotional security of the relationship through shared activities.* 'Catching them being good' and noticing when they have made small positive steps is a powerful tool. Praise should be targeted and specific.
- *Responsivity – promote the time they are available to their children.* Parents must learn to distinguish between listening to the child respectfully and granting the child's every wish. They should demonstrate specific reactions to behaviour, positive and negative, at the time of the behaviour, and this should be clear to the child.
- *Planning – what you are trying to do, what do you want to achieve?* Consider what is meaningful at the child's level. Set realistic objectives, with positive structured rewards. Sanctions should be thought out and achievable.
- *Structure – set rules, binding upon both the adults and children.* Make them simple, unambiguous, and few, which specifically target unwanted behaviours.
- *Consistency – rules and expectations need to be the same across carers, across time and across place,* including where parents have separated. Rules cannot be dependent on parents' moods or energy levels.
- *Patience – this takes time.* Behaviours can become more extreme when these strategies are put in place; things may get worse initially.

As a professional, you can model these principles with the parent as well as the child or young person. You should embody positivity and responsivity without judgement or

Box 24.14 Main psychological treatment interventions employed for emotional and behavioural problems***Explanation and formulation***

Suitable for mild problems with a good prognosis arising in children from supportive families who can work out for themselves a sensible way of managing the problem until it subsides.

Counselling of child or young person or parents

Used to provide non-directive, unstructured supportive therapy for children and young people and families to aid coping with difficulties that are not severe enough to require specialist psychological interventions (e.g. bereavement counselling).

In parental counselling, the aim is to enhance parental coping not by telling the parent what to do but by helping them to find their own solutions, so increasing their confidence and effectiveness.

Parenting groups

Parenting groups have become popular, where a number of parents are seen together and given techniques on how to play with their children and respond effectively to their challenging behaviour. Various approaches are rehearsed using role play and the facilitation of a therapist.

blame. Focus on what has been achieved – not on the final endpoint – will help maintain momentum.

Other treatment interventions

Many general practitioners, paediatricians and other doctors are good generalists in child and adolescent mental health issues, and the mental health specialist should be seen as a specialist extension of their expertise, rather than a completely different sort of person. The main treatment interventions employed are shown in **Box 24.14**, and an approach to managing a child displaying an emotional or behavioural problem is shown in **Figure 24.6**.

In general, the management of children's emotional and behavioural problems:

- should be psychological rather than pharmacological
- does not need the child to be admitted to hospital (unless required as a place of safety for suicidal children or for child protection)
- involves parents as key participants
- may involve a variety of health and social service professionals.

Often more than one intervention is required and treatments are combined, and several professionals become involved.

Medication plays a comparatively small role, although particular instances for which there is evidence for their efficacy are the use of stimulant and non-stimulant drugs in ADHD, neuroleptics in psychosis, and antidepressants for severely depressed adolescents. There is sometimes a temptation to sedate a child who is causing a problem but this is rarely effective and ethically questionable.

Behavioural therapy

A pragmatic approach to problems, which alters the environmental factors that trigger or maintain behaviours. It is particularly effective in the management of behavioural problems in young children.

Family therapy

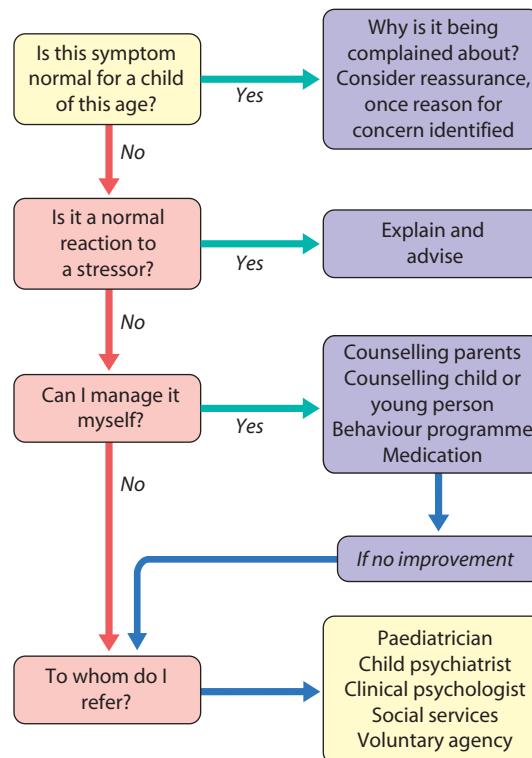
Widely used by child and adolescent mental health professionals. It uses a series of interviews with the entire household to alter dysfunctional patterns of relationships between family members on the basis that many child or young people's problems are perpetuated by the ways in which family members live with and deal with each other.

Cognitive therapy

Used by specialists to explore the way thinking affects feelings and behaviour. It helps the young person to identify and challenge unhelpful thinking styles that perpetuate negative feelings and behaviour. Good evidence for efficacy in a range of disorders including depression.

Individual or group dynamic psychotherapy

More structured and intense extension of counselling, which can help children or young people who, for example, have unconscious conflicts which are manifest as relationship difficulties with a parent. Once the mainstay of child psychiatry, it is now less commonly used.

**Figure 24.6** An approach to children's psychological problems.

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Dermatological disorders

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Features of dermatological disorders in children:

- In the newborn, transient skin disorders are common but need to be distinguished from serious or permanent conditions.
- Atopic eczema affects up to 20% of children.
- Skin infections and infestations, especially viral warts and head lice, are common in school-age children.
- Acne is troublesome for many during adolescence.

Skin complaints are common in children of all ages. The history gives important clues about the possible origin of any lesion. The child's age will often determine the most likely causes. Is it acute or chronic? A recent or ongoing febrile illness suggests that the rash may be one of the exanthema of childhood (see Ch. 15, Infection and immunity). Rashes shared by family members or contacts are frequently infectious or represent infestations (e.g. scabies). Is the child otherwise well or is this part of a systemic illness? Is it itchy or otherwise causing upset? Examination will reveal the distribution and nature of the lesions (Table 25.1).

The newborn

The skin at birth is covered with a chalky-white greasy coat – the vernix caseosa. In the preterm infant, the skin is thin, poorly keratinized, and transepidermal water loss is markedly increased when compared with a term infant. Thermoregulation is also impaired as the preterm infant lacks subcutaneous fat and is unable to sweat until a few weeks old, whereas the term infant can sweat from birth.

Common naevi and rashes in the immediate newborn period are described under the examination of the newborn infant (see Ch. 10, Perinatal medicine). Two common skin lesions which appear in the first few weeks of life, sebaceous gland hyperplasia and miliaria, are described below. The other newborn skin conditions described in this chapter are uncommon.

Sebaceous gland hyperplasia

Presents as multiple tiny yellow papules on the nose, cheeks and upper lip (Fig. 25.1). They are a manifestation

of maternal androgen stimulation. Resolves by a few weeks of age.

Miliaria

Characterised by an erythematous, papulo-vesicular eruption (Fig. 25.2) distributed particularly over face, neck,



Figure 25.1 Sebaceous gland hyperplasia in a 3 week old infant.



Figure 25.2 Miliaria in a 3 week old infant.

Table 25.1 Morphology and description of skin lesions

Morphology (structure)	
Macule	Flat lesion with localized colour change, e.g. freckle
Papule	Solid raised lesion <0.5 cm in diameter
Nodule	Solid raised lesion >0.5 cm in diameter
Plaque	Disc-shaped patch larger than 1 cm in diameter, e.g. psoriasis
Weal	An area of dermal oedema, e.g. urticaria
Vesicle	A raised fluid-containing lesion <0.5 cm in diameter, e.g. varicella
Bulla	A raised fluid-containing skin lesion >0.5 cm in diameter
Pustule	A raised pus-filled lesion, e.g. acne
Descriptive terms	
Atrophy	Depression of the surface due to thinning of the epidermis or dermis
Burrow	Linear papule 3–5 mm long seen in scabies
Comedone (blackhead)	Plug in sebaceous follicle containing altered sebum and cellular material
Crusts	Consist of dried serum and other exudates
Cyst	A cavity lined with epithelium and containing fluid, pus or keratin
Eczema/dermatitis	A pruritic inflammatory condition with papules and vesicles on an erythematous base. Excoriations and secondary infection (impetiginization) are common
Erosion	A break in the skin with partial loss of epidermis
Erythema	Redness
Excoriation	A scratch which removes epidermis and may bleed
Köbner phenomenon	The induction at the site of trauma of skin changes present elsewhere, e.g. psoriasis
Lichenification	Accentuation of the normal skin markings due to rubbing in atopic eczema
Naevus	A localized malformation of tissue structure
Pruritus	Itching
Purpura	Bleeding into the skin or mucosa. Small areas are petechiae, and large areas are ecchymoses. Purpura does not blanch on pressure.
Scales	Are formed by accumulation of excess of normal or abnormal keratin
Ulcer	Full-thickness loss of epidermis and some dermis
Umbilication	Surface depressed in the centre, e.g. molluscum contagiosum

upper chest and back. Caused by eccrine sweat retention and is more common in warmer climates. Management is directed towards avoidance of excessive heat and humidity with lightweight loose clothing.

Bullous impetigo

This is an uncommon but potentially serious blistering form of impetigo, the most superficial form of bacterial infection, seen particularly in the newborn (Fig. 25.3). It is most often caused by *Staphylococcus aureus*. Treatment is with systemic antibiotics, e.g. flucloxacillin (see also Ch. 15).



Figure 25.3 Bullous impetigo in a 12 day old infant showing blisters containing pus.

Congenital moles occur in up to 3% of neonates and any that are present are usually small. Congenital pigmented naevi involving extensive areas of skin (i.e. naevi >9 cm in diameter) are rare but disfiguring (Fig. 25.4) and carry a 4%–6% lifetime risk of subsequent malignant melanoma. They require prompt referral to a paediatric dermatologist and plastic surgeon to assess the necessity for further investigation and/or feasibility of removal.

Melanocytic naevi become increasingly common as children get older and the presence of large numbers in an adult may be indicative of childhood sun exposure.



Figure 25.4 A large (giant) congenital pigmented hairy naevus. Other smaller naevi are also visible.

Prolonged exposure to sunlight should be avoided and sunscreen preparations with a sun protection factor of 30 or higher should be applied liberally to exposed skin in bright weather and reapplied every few hours.

Malignant melanoma is rare before puberty, except in giant naevi. However, in adults, the incidence of malignant melanoma has been increasing for many years. Risk factors for melanoma include a positive family history, having a large number of melanocytic naevi, fair skin, repeated episodes of sunburn, and living in a hot climate with chronic skin exposure to the sun.



Parents should prevent their children becoming sunburnt.

Albinism

This is due to a genetic defect in biosynthesis and distribution of melanin. The albinism may be oculocutaneous, ocular, or partial, depending on the distribution of depigmentation in the skin and eye (Fig. 25.5). The lack of pigment in the iris, retina, eyelids, and eyebrows results in failure to develop a fixation reflex. There is pendular nystagmus and photophobia, which causes constant frowning. Correction of refractive errors and tinted lenses may be helpful. In a few children, the fitting of tinted contact lenses from early infancy allows the development of normal fixation. The disorder is an important cause of severe visual impairment. The pale skin is prone to sunburn and skin cancer. In sunlight, a hat should be worn and high-factor barrier cream applied to the skin.

Epidermolysis bullosa

This is a rare group of genetic conditions with many types, characterized by blistering of the skin and mucous membranes. Autosomal dominant variants tend to be milder; autosomal recessive variants may be severe and even fatal. Blisters occur spontaneously or follow minor trauma (Fig. 25.6a and b). Management is directed at avoiding injury from even minor skin trauma and treating secondary infection. In the severe forms, the fingers and toes may become fused, and contractures of the limbs develop from repeated blistering and healing. Mucous membrane involvement may result in oral ulceration and stenosis from oesophageal erosions. Management, including maintenance of adequate nutrition and analgesia when dressings are changed, should be by a multidisciplinary team including a paediatric dermatologist, paediatrician, plastic surgeon, and dietician.



Figure 25.5 A child with oculocutaneous albinism, with her parents. The hair is silvery white.



(a)



Figure 25.6 (a) Severe, autosomal recessive form of epidermolysis bullosa. There is scarring following recurrent blistering. (b) Milder form of epidermolysis bullosa in a 3-year-old boy. There are blisters over the fingers which healed within a few weeks.

Collodion baby

This is a rare manifestation of the inherited ichthyoses, a group of conditions in which the skin is dry and scaly. Infants are born with a taut, shiny parchment-like or



Figure 25.7 Collodion baby.

collodion-like membrane (Fig. 25.7). There is a risk of dehydration. Emollients are applied to moisturize and soften the skin. The membrane becomes fissured and separates within a few weeks, usually leaving either ichthyotic or, far less commonly, normal skin.

Rashes of infancy

Nappy rashes

Nappy rashes are common. Some causes are listed in Box 25.1.

Irritant dermatitis, the most common nappy rash, is seen less frequently nowadays with the use of modern disposable nappies (diapers) but still occurs if nappies are not changed frequently enough or if the infant has diarrhoea. However, irritant dermatitis can occur even when the nappy area is cleaned regularly. The rash is due to the irritant effect of urine on the skin of susceptible infants. Urea-splitting organisms in faeces increase the alkalinity and likelihood of a rash.

The irritant eruption affects the convex surfaces of the buttocks, perineal region, lower abdomen, and top of the thighs. Characteristically, the flexures are spared, which differentiates it from other causes of nappy rash. The rash is erythematous and may have a scalded appearance. More severe forms are associated with erosions and ulcer formation. Mild cases respond to the use of a protective emollient, whereas more severe cases may require mild topical corticosteroids. While leaving the child without a napkin will accelerate resolution, it is rarely practical at home.

Candida infection may cause and often complicates nappy rashes. The rash is erythematous, includes the skin flexures, and there may be satellite lesions (Fig. 25.8). Treatment is with a topical antifungal agent.

Infantile seborrhoeic dermatitis

This eruption of unknown cause presents in the first 3 months of life. It starts on the scalp as an erythematous scaly eruption. The scales form a thick yellow adherent layer, commonly called cradle cap (Fig. 25.9a). The scaly

Box 25.1 Causes of nappy rashes

Common

- Irritant (contact) dermatitis
- Infantile seborrhoeic dermatitis
- *Candida* infection
- Atopic eczema

Rare

- Acrodermatitis enteropathica (see Fig. 14.13)
- Langerhans cell histiocytosis (see Fig. 22.20)
- Wiskott–Aldrich syndrome (see Fig. 15.28)



Figure 25.8 Napkin rash due to *Candida* infection. The skin flexures are involved and there are satellite pustules visible.



Figure 25.9 Infantile seborrhoeic dermatitis. (a) Cradle cap; and (b) involvement of face, axillae, and napkin area.

rash may spread to the face, behind the ears, and then extend to the flexures and napkin area (Fig. 25.9b). In contrast to atopic eczema, it is not itchy and the child is unperturbed by it. However, it is associated with an increased risk of subsequently developing atopic eczema.

Itching



Figure 25.10 Atopic dermatitis. Inflamed skin worsened by rubbing/scratching. Itch is the key clinical feature in eczema at all ages, leading to an 'itch-scratch-itch' cycle.

Mild cases will resolve with emollients. The scales on the scalp can be cleared with an ointment containing low-concentration sulphur and salicylic acid applied to the scalp daily for a few hours and then washed off. Widespread body eruption will clear with a mild topical corticosteroid, either alone or mixed with an antibacterial and antifungal agent.

Atopic eczema (atopic dermatitis)

The prevalence of atopic eczema in children in the UK is about 20%. A genetic deficiency of skin barrier function is important in the pathogenesis of atopic eczema. Onset of atopic eczema is usually in the first year of life. It is, however, uncommon in the first 2 months, unlike infantile seborrhoeic dermatitis, which is relatively common at this age. There is often a family history of atopic disorders: eczema, asthma, allergic rhinitis (hay fever). Around one-third of children with atopic eczema will develop asthma. Exclusive breastfeeding may delay the onset of eczema in predisposed children but does not appear to have a significant impact on the prevalence of eczema during later childhood. Atopic eczema is mainly a disease of childhood, being most severe and troublesome in the first year of life and resolving in 50% by 12 years of age, and in 75% by age 16 years.

Diagnosis

The diagnosis is made clinically. If the disease is unusually severe, atypical, or associated with unusual infections or faltering growth, an immune deficiency disorder should be excluded. Immunological changes in atopic disease are probably secondary to enhanced antigen penetration through a deficient epidermal barrier.

Clinical features

Rashes may itch in many conditions (Box 25.2), but in atopic eczema, itching (pruritus) is the main symptom at

Box 25.2 Some itchy rashes

- Atopic eczema
- Chickenpox
- Urticaria/allergic reactions
- Contact dermatitis
- Insect bites
- Scabies
- Fungal infections
- Pityriasis rosea



No itch? Then it is not eczema.

all ages, and this results in scratching and exacerbation of the rash (Fig. 25.10). The excoriated areas become erythematous, weeping and crusted. Distribution of the eruption tends to change with age, as indicated in (Fig. 25.11).

Atopic skin is usually dry, and prolonged scratching and rubbing of the skin may lead to lichenification, in which there is accentuation of the normal skin markings (Fig. 25.12).

Complications

Causes of exacerbations of eczema are listed in Box 25.3. However, flare-ups are common, often for no obvious reason. Eczematous skin can readily become infected, usually with *Staphylococcus* or *Streptococcus* (Fig. 25.13). Inflammation increases the avidity of skin for *S. aureus* and reduces the expression of antimicrobial peptides, which are needed to control microbial infections. *S. aureus* thrives on atopic skin and releases superantigens, which seem to maintain and worsen eczema. Herpes simplex virus infection, although less frequent, is potentially very serious as it can spread rapidly on atopic skin, causing an extensive vesicular reaction, eczema herpeticum (see Fig. 15.14). Regional lymphadenopathy is common and often marked in active eczema; it usually resolves when the skin improves.

Management

A number of treatment modalities are available.

Avoiding irritants and precipitants

It is advisable to avoid soap and biological detergents. Clothing next to the skin should be of pure cotton where possible, avoiding nylon and pure woollen garments. Nails need to be cut short to reduce skin damage from scratching, and mittens at night may be helpful in the very young. When an allergen such as cow's milk has been proven to be a precipitant, it should be avoided.

Eczema

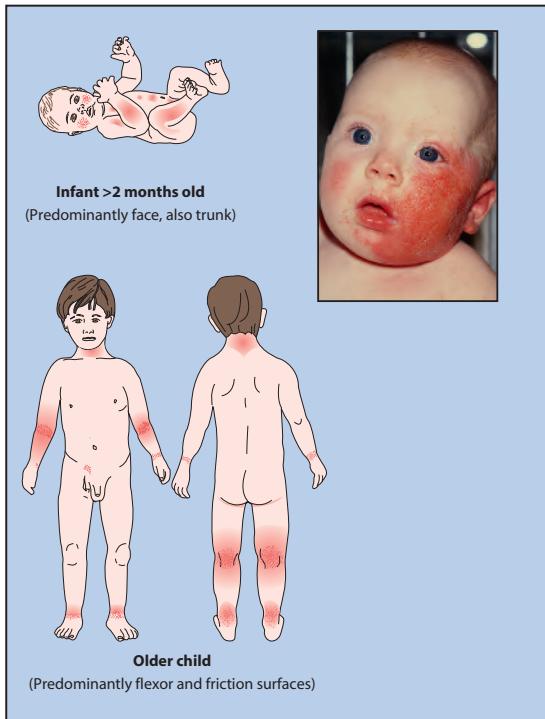


Figure 25.11 Distribution of atopic eczema. The distribution of eczema tends to change with age. In infants, the face and scalp are prominently affected, although the trunk may be involved. In older children, the skin flexures (cubital and popliteal fossae) and frictional areas, such as the neck, wrists, and ankles, are characteristically involved.

Box 25.3 Causes of exacerbation of eczema

- Bacterial infection, e.g. *Staphylococcus*, *Streptococcus* spp.
- Viral infection, e.g. herpes simplex virus
- Ingestion of an allergen, e.g. egg
- Contact with an irritant or allergen
- Environment: heat, humidity
- Change or reduction in medication
- Psychological stress
- Unexplained



Figure 25.12 Lichenification.

Emollients

These are the mainstay of management, moisturizing, and softening the skin. They should be applied liberally two or more times a day and after a bath. They include ointments such as one containing equal parts of white soft paraffin and liquid paraffin. Ointments are preferable to creams when the skin is very dry. A daily or alternate day bath using emollient oil as a soap substitute is also beneficial.

Topical corticosteroids

These are an effective treatment for eczema, but must be used with care. Mildly potent corticosteroids, such as 1% hydrocortisone ointment, can be applied to the eczematous areas once or twice daily. Moderately potent topical steroids play a pivotal role in the management of acute exacerbations, but their use must be kept to a minimum. They should be applied thinly and their use on the face should be generally avoided. Excessive use of topical steroids may cause thinning of the skin as well as systemic side-effects. However, fear of these side-effects should not deter their use in controlling exacerbations.

Immunomodulators

In children over 2 years of age, short-term topical use of tacrolimus ointment or pimecrolimus cream may be indicated for eczema not controlled by topical corticosteroids

and where there is a risk of important adverse effects from further topical steroid use.

Occlusive bandages

These are helpful over limbs when scratching and lichenification are a problem. They may be impregnated with zinc paste or zinc and tar paste. The bandages are worn overnight or for 2–3 days at a time until the skin has improved. For widespread itching in young children, short-term use of wet stockinette wraps may be helpful; diluted topical steroids mixed with emollient are applied to the skin and damp wraps fashioned for trunk and limbs are then applied with overlying dry wraps or clothes.

Antibiotics, antiviral agents, and antihistamines

Antibiotics with hydrocortisone can be applied topically for mildly infected eczema. Systemic antibiotics are indicated for more widespread or severe bacterial infection. Eczema herpeticum is acute and often widespread and is treated with systemic aciclovir.

Itch suppression in eczema is with an oral antihistamine. The second-generation antihistamines are not sedative. Antihistamines can be useful in raising the itching threshold so that scratching is reduced.

Dietary elimination

Food allergy may be suspected if the child reacts consistently to a food, or in infants and young children with

Summary

Assessment of the child with eczema

Condition of the skin

Distribution of the eczema: is the skin excoriated, weeping, crusted, lichenified?
How troublesome is the itching?
Worse or better than usual?
What causes exacerbation – food or other allergens, irritants, medications, stress?
Does it disturb sleep?
Does it interfere with life?
Family knowledgeable about condition and its management?

Check

- Any evidence of infection – bacterial or herpes simplex virus?
- Problems from other allergic disorders?
- Is growth normal?

Management

Avoiding soap, frequently using emollients?
Avoiding nylon and wool clothes?
Is there a need to give or change medications:

- Topical corticosteroids
- Immunomodulators
- Occlusive bandages
- Antibiotics or antiviral agents
- Antihistamines

 Allergy test to egg +/- other foods – is it indicated to identify coexistent IgE-mediated food allergy?
On dietary elimination or is it indicated? If so, dietitian supervision?
Need for psychosocial support?



Figure 25.13 Infected, excoriated atopic eczema.

moderate or severe atopic eczema, particularly if associated with gut dysmotility (colic, vomiting, altered bowel habit) or faltering growth. The most common food allergens resulting in eczema are egg and cow's milk. Allergen-specific IgE antibodies in blood and skin prick testing may be helpful but must be interpreted with caution. Dietary elimination for 4–6 weeks may be required to detect a response.

A trial of an extensively hydrolyzed protein formula or amino acid formula in place of cow's milk formula may be undertaken in formula-fed infants under 6 months of age with severe atopic eczema that cannot be controlled by optimal treatment with emollients and moderately potent topical corticosteroids. Dietary elimination should be carried out with the advice of a dietitian to ensure complete avoidance of specific food constituents and that the diet remains nutritionally adequate. A food challenge is required to be fully objective.

Psychosocial support

Eczema can be sufficiently severe to be disrupting both to the child and to the whole family. The parents and the child need considerable advice, help, and support from health professionals, other affected families, or fellow sufferers. In the UK, the National Eczema Society provides support and education about the disorder.

Viral infections

Viral warts

These are caused by the human papillomavirus, of which there are well over 150 types. Warts are common in children, usually on the fingers and soles (verrucae). Most disappear spontaneously over a few months or years, and treatment is indicated only if the lesions are painful or are a cosmetic problem. They can be difficult to treat, but daily application of a proprietary salicylic acid and lactic acid paint or glutaraldehyde (10%) lotion can be used. Cryotherapy with liquid nitrogen is an effective treatment but can be painful and often needs repeated application, and its use should be reserved for older children.

Molluscum contagiosum

This is caused by a poxvirus. The lesions are small, skin-coloured, pearly papules with central umbilication (**Fig. 25.14**).



Figure 25.14 Molluscum contagiosum. Some of the pearly lesions show characteristic umbilication.

Infections and infestations

Bullous impetigo has been considered earlier in this chapter, and acute bacterial and viral infections of the skin are considered in [Chapter 15](#).



Figure 25.15 Ringworm of the scalp showing hair loss and kerion.

They may be single but are usually multiple. Lesions are often widespread but tend to disappear spontaneously within a year. If necessary, a topical antibacterial can be applied to prevent or treat secondary bacterial infection, and cryotherapy for a few seconds only can be used in older children, away from the face, to hasten the disappearance of more chronic lesions.

Fungal infections

Ringworm

Dermatophyte fungi invade dead keratinous structures, such as the horny layer of skin, nails and hair. The term 'ringworm' is used because of the often ringed (annular) appearance of skin lesions. A severe inflammatory pustular ringworm patch is called a kerion (Fig. 25.15).

Tinea capitis (scalp ringworm), sometimes acquired from dogs and cats, causes scaling and patchy alopecia with broken hairs. Examination under filtered ultraviolet (Wood's) light may show bright greenish/yellow fluorescence of the infected hairs with some fungal species.

Rapid diagnosis can be made by microscopic examination of skin scrapings for fungal hyphae. Definitive identification of the fungus is by culture. Treatment of mild infections is with topical antifungal preparations, but more severe infections require systemic antifungal treatment for several weeks. Any animal source of infection also needs to be treated.

Summary

Tinea capitis (scalp ringworm)

- Annular scaling scalp lesion with patchy alopecia with broken hairs.
- Fungal hyphae on skin scrapings.
- Treated with topical or systemic antifungal.
- Treat the dog or cat, if infected.

Parasitic infestations

Scabies

Scabies is caused by an infestation with the eight-legged mite *Sarcoptes scabiei*, which burrows down the epidermis along the stratum corneum. Severe itching occurs 2–6



Figure 25.16 Scabies. Sole of foot in this 2 month old infant showing burrows (arrows).

weeks after infestation and is worse in warm conditions and at night.

In older children, burrows, papules and vesicles involve the skin between the fingers and toes, axillae, flexor aspects of the wrists, belt line, and around the nipples, penis and buttocks. In infants and young children, the distribution often includes the palms soles (Fig. 25.16), and trunk. The presence of lesions on the soles can be helpful in making the diagnosis. The head, neck, and face can be involved in babies but is uncommon.

Diagnosis is made on clinical grounds with the history of itching and characteristic lesions. Although burrows are considered pathognomonic, they may be hard to identify because of secondary infection due to scratching. Itching in other family members is a helpful clinical indicator. Confirmation can be made by microscopic examination of skin scrapings from the lesions to identify mite, eggs, and mite faeces.

Complications

The skin becomes excoriated due to scratching and there may be a secondary eczematous or urticarial reaction masking the true diagnosis. Secondary bacterial infection is common, giving crusted, pustular lesions. Sometimes slowly resolving nodular lesions are visible.

Treatment

As it is spread by close bodily contact, the child and whole family should be treated, whether or not they have evidence of infestation. Permethrin cream (5%) should be applied below the neck to all areas and washed off after 8–12 hours. In babies, the face and scalp should be included, avoiding the eyes. Benzyl benzoate emulsion (25%) applied below the neck only, in diluted form according to age, and left on for 12 hours, is also effective but smells and has an irritant action. Malathion lotion (0.5% aqueous) is another effective preparation applied below the neck and left on for 12 hours.



If a child and other members of the family are itching, suspect scabies.



Figure 25.17 Head lice. Profuse nits (egg capsules) are visible on scalp hairs. Live lice were visible on the scalp.

Summary

Scabies

- Very itchy burrows, papules, and vesicles – distribution varies with age.
- Scratching leads to excoriation, secondary eczematous, or urticarial reaction often with secondary bacterial infection.
- Not only the child but also the whole family will need treatment.

Pediculosis

Pediculosis capitis (head lice infestation) is the most common form of lice infestation in children. It is widespread and troublesome among primary school children. Presentation may be itching of the scalp and nape or from identifying live lice on the scalp or nits (empty egg cases) on hairs (Fig. 25.17). Louse eggs are cemented to hair close to the scalp and the nits (small whitish oval capsules) remain attached to the hair shaft as the hair grows. There may be secondary bacterial infection, often over the nape of the neck, leading to a misdiagnosis of impetigo. Suboccipital lymphadenopathy is common. Once infestation is confirmed by finding live lice, dimeticone 4% lotion or an aqueous solution of malathion 0.5% is rubbed into the hair and scalp and left on overnight and the hair shampooed the following morning. Treatment should be repeated a week later. Flammability of an alcohol-based lotion should be noted. Wet combing with a fine-tooth comb to remove live lice (bug-busting) every 3–4 days for at least 2 weeks is a useful and safe physical treatment, particularly when parents treat with enthusiasm.

Other childhood skin disorders

Psoriasis

This familial disorder rarely presents before the age of 2 years. The guttate type (Fig. 25.18) is common in children



Figure 25.18 Guttate psoriasis over the back in a 5-year-old.

and often follows a streptococcal or viral sore throat or ear infection. Lesions are small, raindrop-like, round or oval erythematous scaly patches on the trunk and upper limbs, and an attack usually resolves over 3 months to 4 months. However, most get a recurrence of psoriasis within the next 3–5 years. Chronic psoriasis with plaques or annular lesions is less common. Fine pitting of the nails may be seen in chronic disease but is unusual in children. Treatment for guttate psoriasis is with bland ointments. Coal tar preparations are useful for plaque psoriasis and scalp involvement. Calcipotriol, a vitamin D analogue, which does not stain the skin, is useful for plaque psoriasis in those over 6 years of age. Dithranol preparations are very effective in resistant plaque psoriasis. Occasionally, children with chronic psoriasis develop psoriatic arthritis. Chronic psoriasis may have a considerable effect on quality of life. The Psoriasis Association can be helpful in offering support and advice.

Pityriasis rosea

This acute, benign self-limiting condition is thought to be of viral origin. It usually begins with a single round or oval scaly macule, the herald patch, 2–5 cm in diameter, on the trunk, upper arm, neck, or thigh. After a few days, numerous smaller dull pink macules develop on the trunk, upper arms, and thighs. The rash tends to follow the line of the ribs posteriorly, described as the 'fir tree pattern'. Sometimes the lesions are itchy. No treatment is required and the rash resolves within 4–6 weeks.

Alopecia areata

This is a common form of hair loss in children and, understandably, a cause of much family distress. Hairless, single or multiple non-inflamed smooth areas of skin, usually over the scalp, are present (Fig. 25.19); remnants of broken-off hairs, visible as 'exclamation mark' hairs may be seen at the edge of active patches of hair fall. The more extensive the hair loss, the poorer the prognosis, but regrowth often occurs within 6 months to 12 months in localized hair loss. Prognosis should be more guarded in children with atopic disorders.

Granuloma annulare

Lesions (Fig. 25.20) are typically ringed (annular) with a raised flesh-coloured non-scaling edge (unlike ringworm). They may occur anywhere but usually over bony prominences, especially over hands and feet. Lesions may be single or multiple, are usually 1–3 cm in diameter, and tend to disappear spontaneously but may take years to do so. There is also a subcutaneous form.



Figure 25.19 Alopecia areata. Smooth well-defined patch of non-inflamed hair fall.



Figure 25.20 Granuloma annulare. Ringed lesion with a non-inflamed, non-scaling raised edge.

Erythema nodosum



Figure 25.21 Erythema nodosum. There are tender nodules over the legs. She also had fever and arthralgia.

Acne vulgaris

Acne may begin 1–2 years before the onset of puberty following androgenic stimulation of the sebaceous glands and an increased sebum excretion rate. Obstruction to the flow of sebum in the sebaceous follicle initiates the process of acne. Inflammation is also present. There are a variety of lesions, initially open comedones (blackheads) or closed comedones (whiteheads) progressing to papules, pustules, nodules, and cysts. Lesions occur mainly on the face, back, chest, and shoulders. The more severe cystic and nodular lesions often produce scarring. Menstruation and emotional stress may be associated with exacerbations. The condition usually resolves in the late teens, although it may persist.

Topical treatment is directed at encouraging the skin to peel using a keratolytic agent, such as benzoyl peroxide, applied once or twice daily after washing. Sunshine, in moderation, topical antibiotics, or topical retinoids may be helpful. For more severe acne, oral antibiotic therapy with tetracyclines (only when >12 years old, because they may discolour the teeth in younger children) or erythromycin is indicated. The oral retinoid isotretinoin is reserved for severe acne in young people unresponsive to other treatments.

Rashes and systemic disease

Skin rashes may be a sign of systemic disease. Examples are:

- facial rash in systemic lupus erythematosus or dermatomyositis
- purpura over the buttocks, lower limbs, and elbows in Henoch–Schönlein purpura
- erythema nodosum (Fig. 25.21, Box 25.4) and erythema multiforme (Fig. 25.22, Box 25.5) – both can be associated with a systemic disorder, but often no cause is identified
- Stevens–Johnson syndrome – may show limited or extensive skin involvement and involves mucous membranes (Fig. 25.23). It often starts with an upper respiratory tract infection. Eye involvement may include conjunctivitis, corneal ulceration, and uveitis, and ophthalmological assessment is required. It may be caused by drug sensitivity, infection, or both, with morbidity and sometimes even mortality from sepsis or electrolyte imbalance.

Box 25.4 Causes of erythema nodosum

- Streptococcal infection
- Primary tuberculosis
- Inflammatory bowel disease
- Drug reaction
- Idiopathic

(Sarcoidosis, a common association in adults, is rare in children)

Erythema multiforme



Figure 25.22 (a) Erythema multiforme. There are target lesions with a central papule surrounded by an erythematous ring (arrow). Lesions may also be vesicular or bullous. (b) Mucous membranes may be involved, as shown by this boy's lip ulceration.

Box 25.5 Causes of erythema multiforme

- Herpes simplex infection
- *Mycoplasma pneumoniae* infection
- Other infections
- Drug reaction
- Idiopathic



Figure 25.23 Stevens–Johnson syndrome showing severe conjunctivitis and ulceration of the mouth.
(Courtesy of Rob Primhak.)

Urticaria

Urticaria (hives), characterized by flesh-coloured wheals, is described in [Chapter 16](#) (Allergy) and the management of anaphylaxis in [Chapter 6](#) (Paediatric emergencies).

Papular urticaria is a delayed hypersensitivity reaction most commonly seen on the legs, following a bite from a flea, bedbug, animal or bird mite. Irritation, vesicles, papules and wheals appear and secondary infection due to scratching is common. It may last for weeks or months and may be recurrent.

Hereditary angioedema is a rare autosomal dominant disorder caused by a deficiency or dysfunction of C1-esterase inhibitor. There is no urticaria, but subcutaneous swellings occur, often accompanied by abdominal

pain. The trigger is usually physical trauma or psychological stress. Most episodes develop over a few hours and subside over a few days. Angioedema may cause respiratory obstruction.

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Further reading

Chiang NY, Verbov J, Dermatology: A handbook for medical students and junior doctors, ed 3, London, 2020, British Association of Dermatologists. A copy of the online book can be obtained from the British Association of Dermatologists, London (see below).

Website

Chiang NY, Verbov J, Dermatology: A handbook for medical students and junior doctors, ed 3, London, 2020, British Association of Dermatologists. Available at: <https://www.bad.org.uk/shared/get-file.ashx?itemtype=document&id=6595>.

Skin Deep (A Don't Forget the Bubbles project). Available at: <https://dontforgetthebubbles.com/paediatric-dermatology>. Collection of photographs and descriptions of paediatric skin lesions in a range of skin tones to improve diversity of skin images.

DermNetNZ. Available at: <https://dermnetnz.org>. Information and images on wide range of dermatological conditions.



Diabetes mellitus and endocrinology

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Features of diabetes and endocrinology in children:

- In diabetes, keeping blood glucose levels close to the normal range reduces the risk of long-term complications.
- The complications associated with diabetic ketoacidosis can be minimized by following national guidelines.
- The growth, activity and pubertal development of children and adolescents makes it more difficult to maintain blood glucose levels in the normal range.
- Congenital hypothyroidism is identified on neonatal blood spot screening.
- Growth hormone treatment is recommended for growth hormone deficiency and a number of specific conditions where treatment increases final height.
- Adrenal dysfunction may present with hypotension, hypoglycaemia and hyponatraemia and is a medical emergency.

Diabetes mellitus

There are just under 30,000 children and young people under the age of 19 years with diabetes in England and Wales, a prevalence of 2.5 per 1000 (or 1 to 2 per secondary school). Its incidence has increased over the last 30 years, most likely from changes in environmental risk factors, but this is poorly understood. Almost all (95%) children have type 1 diabetes requiring insulin from the outset, although type 2 diabetes due to insulin resistance is increasing in childhood, as obesity becomes more common. The other causes of diabetes are listed in [Box 26.1](#).



Most children have type 1 diabetes (95%), although the number with type 2 diabetes is increasing.

Box 26.1 Classification of diabetes according to aetiology

Type 1 – most childhood diabetes

- Destruction of pancreatic β -cells by an autoimmune process

Type 2 – insulin resistance followed later by β -cell failure

- Usually older children, obesity-related, positive family history, not as prone to ketosis, more common in some ethnic groups (e.g. Black and Asian children)

Other

- Monogenic diabetes:
 - Maturity onset diabetes of the young – various types caused by genetic defects in β -cell function. Strong family history.
 - Neonatal diabetes: transient or permanent secondary to defective β -cell function.
 - Drug-induced, e.g. corticosteroids
 - Pancreatic insufficiency, e.g. cystic fibrosis, iron overload in thalassaemia
 - Endocrine disorders, e.g. Cushing syndrome
 - Gestational diabetes

Aetiology of type 1 diabetes

There is a genetic predisposition to developing type 1 diabetes. Immune activation may trigger an autoimmune response process in susceptible individuals which damages the pancreatic β -cells and leads to increasing insulin deficiency ([Fig. 26.1](#)). Recognized auto-antibodies include glutamic acid decarboxylase (GAD), zinc transporter 8 (ZnT8) and islet antigen 2 (IA-2). Identification of more than one of these auto-antibodies has been shown to be associated with the potential to develop clinical diabetes. Inherited susceptibility is demonstrated by twins have a higher risk of developing diabetes mellitus compared to other siblings

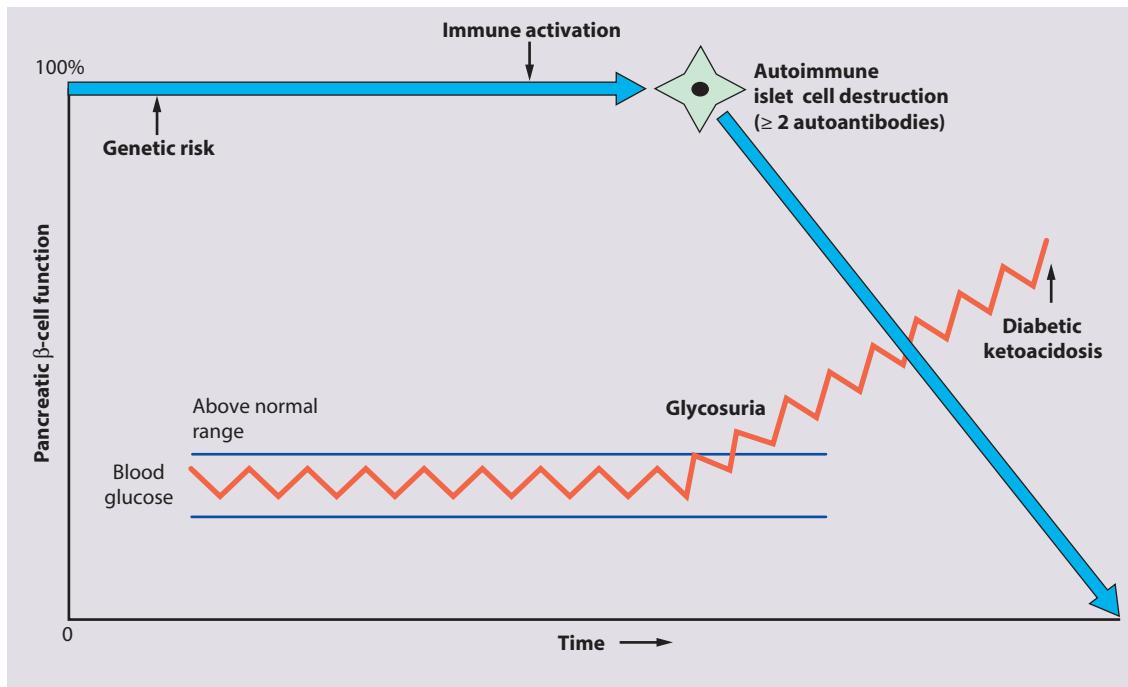


Figure 26.1 Stages in the development of diabetes.

– approximately 70% risk of developing diabetes within 3 years in a twin compared to 15% risk in other siblings. There is an association with other autoimmune disorders such as hypothyroidism, Addison disease, coeliac disease, and rheumatoid arthritis in the patient or family. Diabetes is also more common in children with Down and Turner syndrome.

Clinical features

There are peaks of presentation of type 1 diabetes in spring and autumn months. In contrast to adults, children usually present with only a few weeks of polyuria, excessive thirst (polydipsia) and weight loss (Box 26.2). Diagnosis at an early stage of the illness is important in order to prevent development of diabetic ketoacidosis, so referral to a

Box 26.2 Symptoms and signs of diabetes

Early

Most common – the ‘classical triad’:

- excessive drinking (polydipsia)
- excessive urination (polyuria)
- weight loss

Less common:

- secondary enuresis
- skin infections – e.g. *candidiasis*

Late – diabetic ketoacidosis

- smell of acetone on breath
- vomiting
- dehydration
- abdominal pain
- rapid breathing due to acidosis (Kussmaul breathing)
- hypovolaemic shock
- drowsiness and reduced level of consciousness

specialist team should be done as soon as the diagnosis is suspected. Diabetic ketoacidosis (DKA) requires urgent recognition and treatment as it carries a significant risk of mortality in children and young people. It is easily misdiagnosed if rapid breathing is mistaken for pneumonia or abdominal pain for appendicitis or constipation.

Diagnosis

The diagnosis is usually confirmed in a symptomatic child by finding a markedly raised random blood glucose ($>11.1\text{ mmol/L}$ by the current WHO definition), glycosuria, and ketosis. Where there is any doubt, a fasting blood glucose ($>7\text{ mmol/L}$) or a raised glycosylated haemoglobin (HbA1c) are helpful.

Children and young people with type 2 diabetes may have similar symptoms to those with type 1. However, the diagnosis of type 2 diabetes should be considered if there is a positive family history and in obese children with signs of insulin resistance (acanthosis nigricans – velvety dark skin on the neck or armpits (Fig. 26.2), skin tags or the polycystic ovary phenotype in adolescent females).

Whereas a diagnostic glucose tolerance test is rarely required to diagnose type 1 diabetes in children, it may be necessary for type 2 diabetes.

Initial management of type 1 diabetes

As type 1 diabetes in childhood is uncommon, much of the initial and routine care is delivered by specialist teams (Box 26.3).

The initial management will depend on the child’s clinical condition. Those presenting with diabetic ketoacidosis require intravenous treatment and high dependency care. Most newly presenting children are alert, are able to eat and drink, and can be managed with subcutaneous insulin with a brief hospital admission.



Figure 26.2 Acanthosis nigricans in axilla. A sign of insulin resistance.

Box 26.3 The diabetes team

- Consultant paediatrician(s) with a special interest in diabetes
- Paediatric diabetes specialist nurse(s)
- Paediatric dietitian
- Clinical psychologist
- Social worker / youth worker / play specialist
- Adult diabetes team for transition clinics
- Parent/patient support groups

An intensive educational programme is needed for the parents and child. The information provided must be appropriate for age, including:

- a basic understanding of the pathophysiology of diabetes
- injection of insulin – technique and sites
- blood glucose (finger prick) monitoring to allow insulin adjustment
- blood ketone monitoring when unwell
- healthy diet: same as for a child without diabetes, aiming for a minimum of five portions of fruit and vegetables per day; ‘carbohydrate counting’ should be taught from diagnosis
- encouragement to exercise regularly with adjustments of carbohydrate and insulin for exercise
- ‘sick-day rules’ during intercurrent illness to prevent ketoacidosis

- the recognition and staged treatment of hypoglycaemia
- where to get advice 24 hours a day
- the help available from voluntary groups, e.g. local groups or Diabetes UK
- the psychological impact of a lifelong condition with potentially serious short-term and long-term complications.

A diagnosis of diabetes is life-changing and many families grieve for the loss of their previous life. The specialist nurse should liaise with the school (teachers, those who prepare school meals, physical education supervisors) and the primary care team, so that the child is well supported in all environments.

Insulin

The insulin regimen aims to mimic normal physiological secretion of insulin, where small amounts of insulin are released from the pancreas continuously, with surges when blood glucose rises following carbohydrate ingestion. This requires intensive insulin regimens, which have been shown to reduce the risk of long-term complications.

Therapeutic insulin is produced by recombinant DNA technology to be similar to human insulin, with different types designed to be rapid, short or long acting ([Table 26.1](#)).

Insulin can be given as multiple daily injections ('basal-bolus'), where rapid-acting insulin is given (bolus) before each meal plus a long-acting insulin in the evening and/or before breakfast to provide background insulin (basal) ([Fig. 26.3a](#)). Insulin is injected into the subcutaneous tissue of the anterior and lateral aspects of the thigh, the buttocks, or the abdomen. Rotation of the injection sites is essential to prevent lipohypertrophy. Alternatively, insulin can be given by a continuous subcutaneous insulin pump (CSII); small doses of rapid-acting insulin are delivered continuously, with an additional bolus programmed for each meal or snack ([Fig. 26.3b](#)). These regimens allow flexibility by relating the insulin more closely to food intake and exercise. Patients and families are taught to aim for blood glucose levels between 4 and 7 mmol/L before meals. If the blood glucose is high, additional rapid-acting insulin is given at mealtimes to correct it to the target range. The input required by the child, family and team to initiate and maintain these intensive regimes is high.

Shortly after presentation, when some pancreatic function is preserved, insulin requirements often become minimal, the so-called ‘honeymoon period’. Requirements subsequently increase to 0.5 units/kg/day to 1 unit/kg/day, or even up to 2 units/kg/day during puberty.

Table 26.1 Different types of insulin and their onset, peak and duration of action

Type of insulin	Onset of action	Peak action	Duration of action
Rapid-acting insulin, e.g. lispro (Humalog), aspart (Novorapid), glulisine (Apidra)	15–20 minutes	1–2 hours	3–6 hours
Short-acting, e.g. Actrapid, Humulin S	30–60 minutes	2–4 hours	8 hours
Long-acting insulin analogues, e.g. detemir (Levemir), glargine (Lantus), degludec (Tresiba)	1–2 hours	Minimal	Up to 24 hours

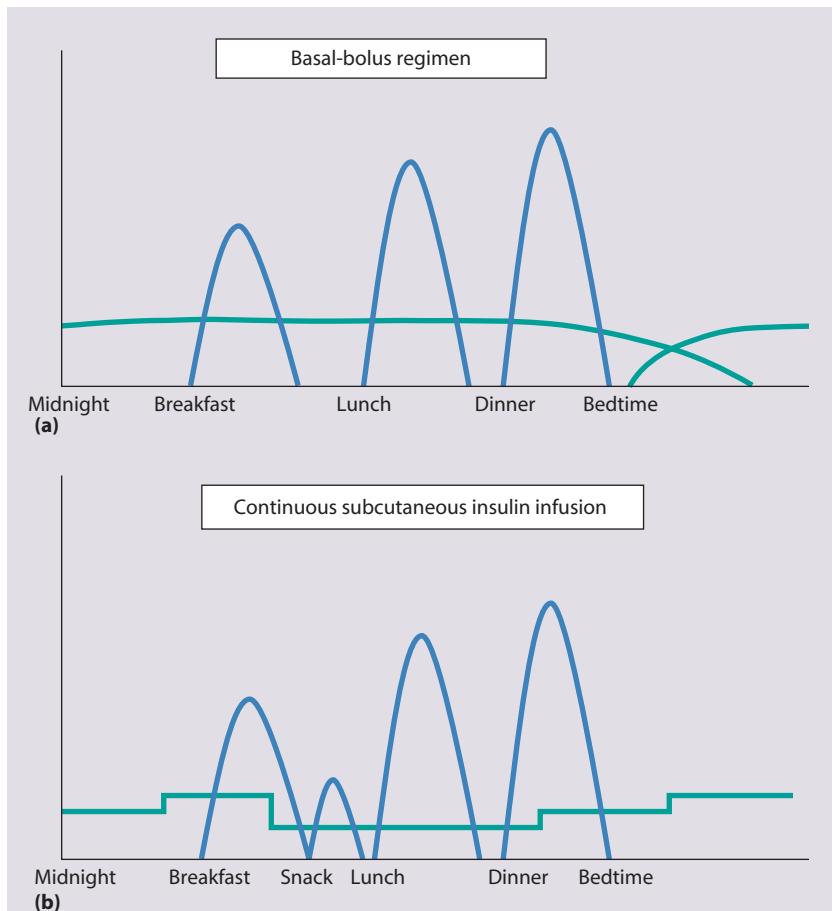


Figure 26.3 (a) Basal-bolus regimen – 3 times daily rapid-acting insulin (blue) and one long-acting insulin (green) by injection each 24 hours. (b) Continuous subcutaneous insulin infusion – quick-acting insulin delivered at a programmed rate (green) depending on requirements, with bolus doses (blue) delivered at mealtimes.

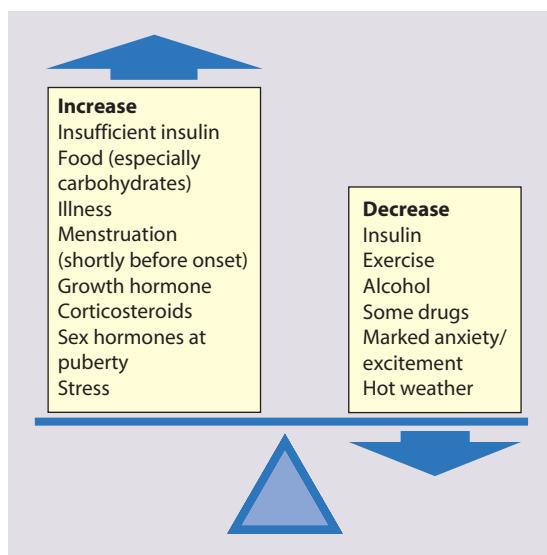


Figure 26.4 Factors affecting blood glucose levels.

Diet

Children and young people with diabetes mellitus are encouraged to eat a healthy diet. The aim is to maintain normal growth, while maintaining normal blood glucose

levels by matching insulin to carbohydrate intake. The diet should be high in fibre, which will provide a sustained release of glucose, rather than refined carbohydrate, which causes rapid swings in glucose levels. 'Carbohydrate counting' allows one to match the insulin dose to the choice of food, also taking into account the premeal glucose level and postmeal exercise pattern.

Blood glucose monitoring

Regular blood glucose measurements are required to adjust the insulin doses and learn how changes in lifestyle, food and exercise affect glucose levels (Fig. 26.4). Learning this balancing act requires considerable educational input followed by refinement in the light of experience. National guidance recommends a minimum of 5 blood glucose tests each day, with some using intensive monitoring of 8 blood glucose tests a day. A record should be kept in a diary or transferred from the memory of the blood glucose meter for ease and accuracy, where data can be displayed in graphic format allowing easier analysis (see *Case history 26.1*). The aim is to maintain blood glucose as near to normal as possible, but this can be extremely difficult and realistic goals need to be agreed with each individual.



Case history 26.1

Blood glucose monitoring

This is the diary of an 8-year-old boy with type 1 diabetes (Fig. 26.5). It shows:

- His parents use carbohydrate counting for all meals, but this can be difficult when eating unfamiliar foods (August 3, blood glucose rises to 11.8 mmol/L).
- He uses correction doses if his blood glucose is high before meals, using 1 unit of Novorapid to bring his blood glucose down by approximately 4 mmol/L (July 29, from 9.3 before breakfast to 6.9 mmol/L before lunch).
- He reduces his rapid-acting insulin before predictable sport to reduce the risk of hypoglycaemia (pre-lunch on August 2).

- He has good recognition of symptoms of hypoglycaemia and treats it with glucose tablets, then a snack. His blood glucose level sometimes ‘overshoots’ after treatment of hypoglycaemia (blood glucose low after physical exercise, high after treatment on August 6).
- When he is unwell or his blood glucose is unexpectedly high, he checks for blood ketones and gives extra Novorapid.
- As keeping a diary is onerous and may be unreliable, they have largely been replaced by blood glucose meter uploads (Fig. 26.5b).

Date	Insulin type and dose (dose in brackets added or subtracted from previous day's dose)				Blood glucose levels (mmol/L)								Comments
	Novorapid 1 unit; 10 g (pre-breakfast)	Novorapid 1 unit; 10 g (pre-lunch)	Novorapid 1 unit; 15 g (pre-tea)	Glargine units (before bed)	Before breakfast	2 hours post	Before lunch	2 hours post	Before tea	2 hours post	Before bed	During night	
29/7	5 (+0.5)	6	5 (+0.5)	7	9.3		6.9		8.7		5.4	6.7 2am	
30/7	4.5	6	5	7	7.2		5.9		6.7		7.1		
31/7	5	6.5	5.5	7	6.2	5.8 10.15am	4.3		3.8/4.7		10.1		Hungry after hypo
1/8	5	7.0 (+0.5)	5	7	7.3		8.8		6.4		6.9		
2/8	4	5 (-2)	4.5	7	5.4		7.2		8.9		5.5		Football match
3/8	4.5	5.5 (+0.5)	5	7	5.0		9.0		6.8		11.8		Out for tea
4/8	4.5	5	5	7	3.5/5.6		5.4		7.3		7.0		
5/8	5	5	7 (+2)	7	6.6		7.1		14.2 Ketones mildly raised	13.3	8.2	7.2 2am	Unwell after school
6/8	5	5.5	4	7	6.3		6.9		5.0		3.4/9.0	4.8 1am	PE afternoon
7/8	4.5	4.5	4	7	4.6		5.4		7.0		7.9		

(a)



(b)

■ <4mmol/L ■ within target range ■ >6.9 mmol/L

Figure 26.5 (a) Blood glucose diary of an 8-year-old boy with type 1 diabetes. As diaries are onerous and sometimes glucose measurements unreliable, they have largely been replaced by read-outs from blood monitors. An example from another child is shown in (b).

Flash glucose monitoring systems are useful for children and young people who require intensive monitoring (Fig. 26.6a,b). Glucose is measured in interstitial fluid by a small sensor which can be scanned to show glucose levels. It warns if the glucose is rapidly decreasing (small quantities of carbohydrate are required) or increasing (extra insulin needed).

Continuous glucose monitors (CGM) use subcutaneous sensors to provide a continuous reading of blood glucose (Fig. 26.6c,d). Sensor data can be viewed remotely, e.g. on a mobile phone, to support younger children at school. Recent technology links CGM to pumps to help control the insulin delivered from a pump, e.g. suspending insulin delivery when anticipating hypoglycaemia or increasing basal delivery when glucose levels are high (hybrid closed

loop pumps). Continuous glucose monitors are particularly useful to detect asymptomatic episodes of hypoglycaemia or high glucose levels after meals as they alarm when approaching low or high levels.

Blood ketone testing (often using the same meter as for blood glucose) is mandatory during illness to recognize and avoid ketoacidosis.

The measurement of glycosylated haemoglobin (HbA1c) is helpful as an indication of diabetes care over the previous 6–12 weeks and should be checked at least four times per year. The risk of developing later complications increases if the level of HbA1c is persistently above target. The HbA1c level may be misleading if the red blood cell lifespan is reduced, such as in sickle cell trait or if the HbA molecule is abnormal, as in thalassaemia.

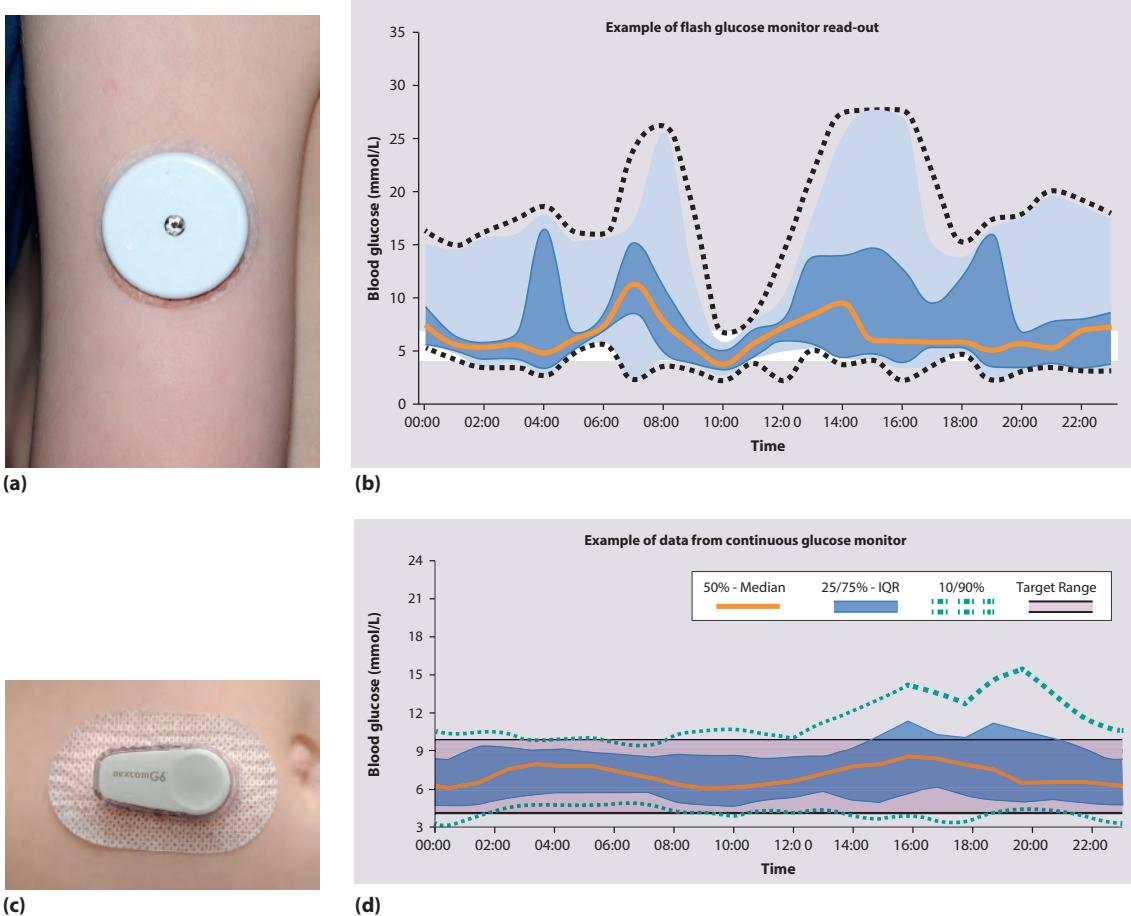


Figure 26.6 Example of a flash glucose meter **(a)** A sensor is inserted subcutaneously and determines the glucose level in the interstitial fluid, which is scanned periodically with a reader (or mobile phone) and shows a glucose reading and trend over a number of hours. **(b)** Example of data from the flash glucose monitor read-out of blood glucose at various times of the day. The orange line shows the average glucose over a two-week period; dark blue shaded area shows 50% of the glucose recordings at that time. There is considerable variability throughout the day, except where the lines are narrow at 10.00. **(c)** Continuous glucose monitors (CGM) send data directly from a sensor to a handheld monitor or pump and can provide alerts for high or low glucose levels. Need to be calibrated regularly and the sensor replaced after several days. **(d)** Example of data from CGM showing average blood glucose levels throughout a 24-hour period. Keeping glucose levels within the target range for >70% of the time is associated with an HbA_{1c} in the target range.

Acute complications

Hypoglycaemia

It is inevitable that children and young people who manage their diabetes well will experience episodes of hypoglycaemia (often called 'hypos'). This is defined for someone with diabetes mellitus as a blood glucose below 4 mmol/L. Symptoms of hypoglycaemia are highly individual and change with age, but most complain of hunger, an unsettled tummy, sweatiness, feeling faint, dizzy or 'wobbly' in their legs. If unrecognized or untreated, symptoms may progress to loss of consciousness and seizures. Parents can often detect hypos in young children by their pallor and a change in behaviour. If suspected, the blood glucose level should be checked. Frequent episodes can be associated with loss of awareness of the symptoms and should be avoided.

Treating a 'hypo' at an early stage requires the administration of easily absorbed glucose in the form of glucose tablets or a sugary drink (e.g. Lucozade). Children should always have easy access to their hypo remedy, although young children may learn to complain of hypo symptoms

in order to leave class or obtain a sweet drink! Oral glucose gels (e.g. Glucogel) are absorbed quickly from the buccal mucosa and are helpful if the child is unable to cooperate. It can be administered by teachers or other helpers. Following treatment, the child usually should have a slowly absorbed carbohydrate (for example fruit or a biscuit) to prevent the blood glucose dropping again.

Parents and school staff should be provided with a glucagon injection kit for the treatment of severe hypos with reduced level of consciousness, and taught how to administer it intramuscularly. If the child is unconscious and brought to hospital, hypoglycaemia is treated with 2 ml/kg of intravenous 10% glucose.

Severe hypoglycaemia can usually be explained by a missed meal, or exercise. The aim is anticipation and prevention, for example by reducing insulin dose prior to planned exercise.

Diabetic ketoacidosis

Presentation is described in **Box 26.2** above, essential investigations in **Box 26.4** and management in **Fig. 26.7**.

Diabetic ketoacidosis

Box 26.4 Essential early investigations in diabetic ketoacidosis

- Blood glucose (>11.0 mmol/L)
- Blood ketones (>3.0 mmol/L)
- Blood gas analysis (metabolic acidosis with pH <7.3 or plasma bicarbonate <15 mmol/L)
- Urea and electrolytes, creatinine (to identify dehydration)
- Evidence of a precipitating cause, e.g. infection (blood and urine cultures performed)
- Cardiac monitor for T-wave changes of hypokalaemia
- Weight (compare with recent clinic weight to ascertain level of dehydration)



(b)



(c)

(a)

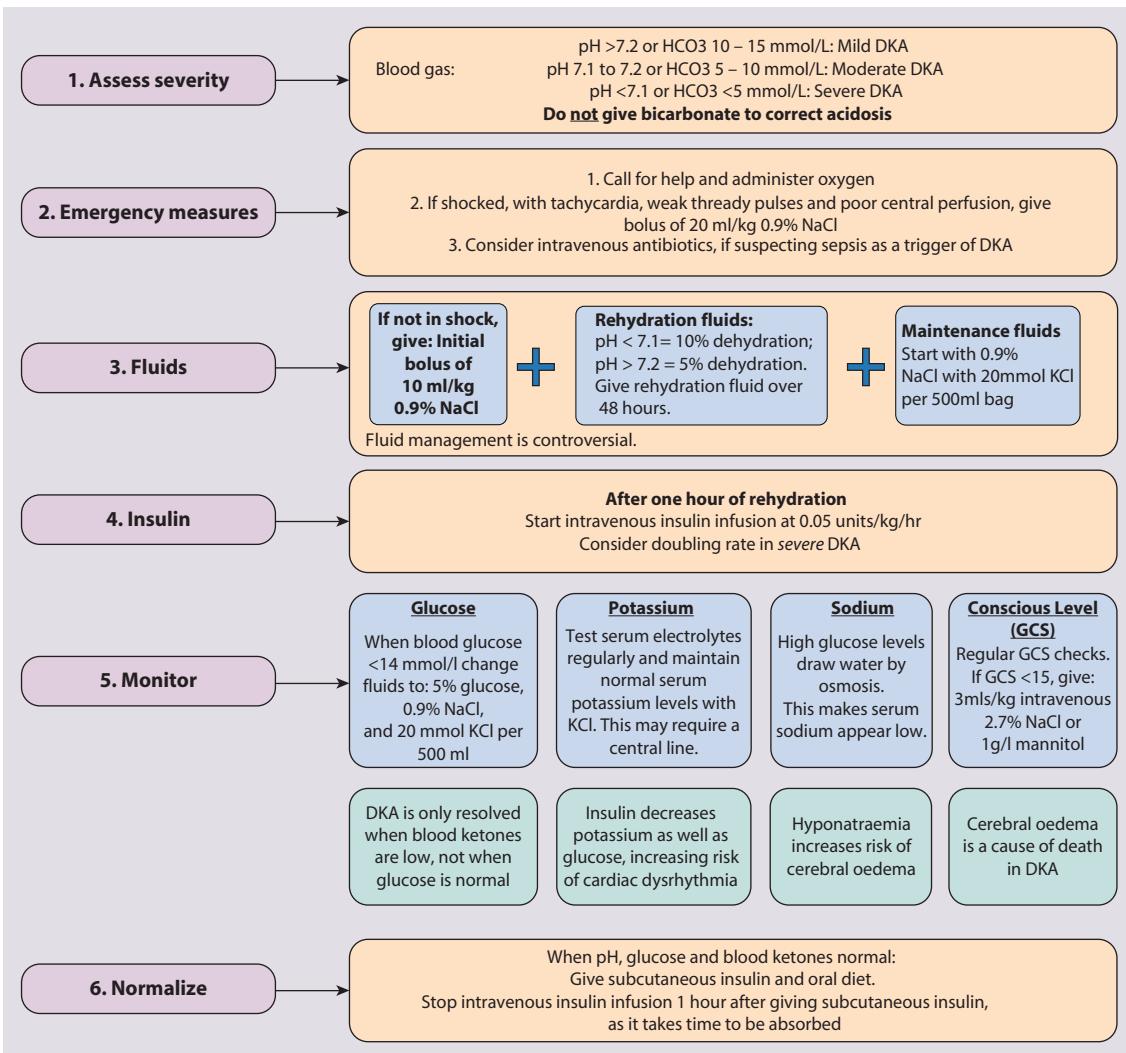


Figure 26.7 (a) Diabetic ketoacidosis management. For detailed management, refer to national guidelines such as NICE or British Society of Paediatric Endocrinology and Diabetes Guidelines, 2020. (b) A boy with severe dehydration and weight loss from diabetic ketoacidosis; and (c) 4 months later. (Photos b and c courtesy of Jill Challener.)

Long-term complications of diabetes

It is unusual for complications to present during childhood, but management of diabetes in children and young people aims at reducing the risk of complications:

- macrovascular – hypertension, coronary heart disease, cerebrovascular disease
- microvascular – retinopathy, nephropathy, neuropathy.

It has been shown that meticulous diabetes care delays or prevents microvascular complications and, if retinopathy occurs, keeping blood glucose levels and HbA1c within the target values can slow its progression. There

is also evidence that having an HbA1c within target early in diabetes reduces the risk of later complications even if the HbA1c deteriorates later in life. Levels of HbA1c above the upper limit of normal (48 mmol/mol [6.5%]) are related to the risk of later complications in an almost exponential fashion, so the ideal is to aim for a level as close to the level of someone without diabetes, as possible.

As these aims are difficult to achieve in all patients at all stages of their condition, children and their families should be reviewed regularly to assess their diabetes care, to monitor the development of complications, to ensure that they have age-appropriate information, and that psychosocial aspects are addressed (Fig. 26.8).

Regular assessment of the child with diabetes

Assessment of diabetes:

- Any episodes of hypoglycaemia, diabetic ketoacidosis, hospital admission?
- Is there still awareness of hypoglycaemia?
- Absence from school? School supportive of diabetes care?
- Interference with normal life?
- HbA1c results – less than 48 mmol/mol (6.5%)?
- Review the diary of blood glucose results or glucose meter uploads– are appropriate actions to results being taken?
- Insulin regimen – appropriate?
- Lipohypertrophy or lipoatrophy (Fig. 26.8b,c) at injection sites?
- Diet – healthy diet, manipulating food intake and insulin to maintain good control?

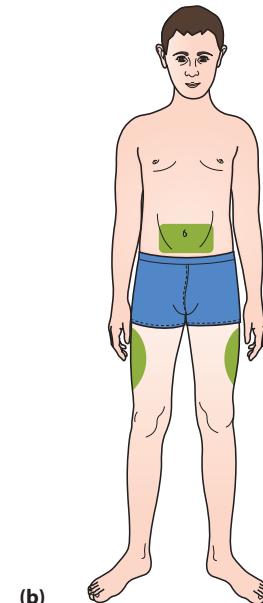
General overview (periodic):

- Normal growth and pubertal development, avoiding obesity – measure height, weight and BMI and plot on growth chart at each clinic visit
- Blood pressure check for hypertension annually from 12 years of age (age-specific centiles)
- Renal disease – screen for microalbuminuria, an early sign of nephropathy, annually from 12 years
- Circulation – check foot pulses and sensation
- Eyes – retinopathy or cataracts are rare in children, but should be monitored annually from 12 years, preferably with retinal photography
- Feet – maintain good care, avoid tight shoes and obtain prompt treatment of infections – annually
- Screening for coeliac and thyroid disease at diagnosis, thyroid screening annually, coeliac again if symptomatic
- Annual reminder to have flu vaccination and see dentist

Knowledge and psychosocial aspects:

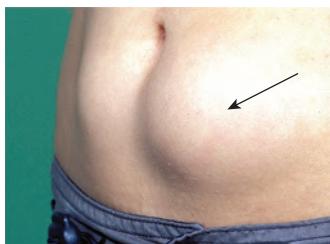
- Good understanding of diabetes, would participation/holidays with other children with diabetes be beneficial? Member of Diabetes UK?
- Becoming self-reliant, but appropriate supervision at home, school, diabetes team?
- Taking exercise, sport? Diabetes not interfering with it?
- Leading as normal life as possible?
- Smoking, alcohol?
- Is 'hypo' treatment readily available? Is stepped approach known?
- What are the main issues for the patient? Are there short-term goals to engage the patient to improve glucose levels?

(a)



(b)

■ Injection sites – check for lipohypertrophy or lipoatrophy



(c)

Figure 26.8 (a) The regular assessment of the child or young person with diabetes. (b) Injection sites. (c) Lipohypertrophy (arrow) of abdomen from insulin injections.

Table 26.2 The impact of diabetes in normal adolescence

Normal adolescence	How diabetes interferes
Biological factors	Insulin resistance secondary to growth and sex hormone secretion Growth and pubertal delay if diabetes not well managed
Psychological factors	Reduced self-esteem, e.g. related to impaired body image, difference from peers
Social factors	Different from peer group, e.g. need for blood tests and injections Hypoglycaemic events – can be frightening and emphasize difference from friends Increased risk from alcohol, smoking, use of recreational drugs Vocational plans restricted, e.g. heavy goods vehicle licence, pilot Separation from parents more complex

Challenges in diabetes management

Diabetes is a devastating diagnosis and the new ‘rules’ of management that children and young people are expected to follow are onerous. Keeping blood glucose levels in target is difficult in the following circumstances:

- illness – viral illnesses usually cause insulin requirements to increase, although less insulin may be required during gastroenteritis. Insulin *must* always be continued during intercurrent illness to prevent ketosis. The dose of insulin should be adjusted according to food intake, results of blood glucose and ketone monitoring. If ketosis is increasing along with a rising blood glucose, the family should know how to increase the rapid-acting insulin dose appropriately or seek medical advice
- exercise – vigorous or prolonged planned exercise (cross-country running, long-distance hiking, cycling, skiing) requires reduction of the insulin dose and increase in carbohydrate intake. Late hypoglycaemia may occur during the night or even the next day, but may be avoided by taking a bedtime ‘recovery meal’, including slow-acting carbohydrate and fat such as cereal with milk. Less vigorous exercise such as sports lessons in school and spontaneous outdoor play can be managed with a reduction in short-acting insulin before the exercise. Regular exercise (and associated ‘fitness’) increases insulin sensitivity, so the insulin requirements of a child who takes up new regular exercise may reduce
- eating too many carbohydrate-containing foods, such as sweets or snacks, without insulin, at parties or on the way home from school
- infrequent or unreliable blood glucose testing. This is apparent if the blood glucose levels recorded are inconsistent with the HbA1c
- family disruption such as divorce or separation
- eating disorders – it is recognized that some young people omit insulin doses to induce weight loss (diabulimia)
- inadequate family motivation, support, or understanding – as children can never have a ‘holiday’ from their diabetes, they need a great deal of encouragement to achieve blood glucose levels in target. Educational programmes for children and families need to be arranged regularly and match their level of development. Children should be encouraged to become self-reliant, but with adult supervision, until they are able to take responsibility. Special courses and holiday camps are available; in the UK they are organized by Diabetes UK and local diabetes teams.

Management at school

An individualized care plan should be developed by the parents, diabetes team and the school to address the specific needs of the child. This will include the child’s dietary needs, management of hypoglycaemia, and exercise. For younger children, support is needed to help test blood glucose, calculate and give the pre-lunch insulin injection or bolus from the pump.

Puberty and adolescence

Diabetes in young people is influenced by biological, psychological, and social factors (Table 26.2). The rapid growth spurt of puberty is governed by a complex interaction of hormonal changes, some of which involve insulin and insulin-like growth factors. Growth hormone, oestrogen and testosterone all oppose insulin action, and there is an increase in the insulin requirement (from the usual 0.5 to 1.0 unit/kg/day of early childhood up to 2 units/kg/day). The increase may be especially marked first thing in the morning due to the peak of growth hormone secretion overnight.

In early adolescence, young people may learn that they are not immediately ill if they eat less healthily or miss an injection. This may discourage them from meticulous self-care. In later adolescence, they may feel indestructible. Some test the degree to which the ‘rules’ can be broken as they ‘feel OK’. It is then important to focus on immediate benefits to good diabetes care and work with the young person to identify the challenges and support them to find solutions (see Ch. 30, Adolescent medicine). With increasing independence, the young person may explore behaviours such as smoking, use of alcohol, and sexual relationships; the diabetes team need to ensure that the young person understands how to manage these safely alongside their diabetes. Conflict with parents (and sometimes professionals) is common during adolescence and may focus on diabetes management. Many parents are very protective and find it difficult to encourage their son/daughter to take more responsibility for their diabetes. Support from the team psychologist may be useful.

Some young people with diabetes, especially girls, have excessive weight gain; height, weight and body mass index should be plotted at each clinic visit. Intensive insulin regimens increase the risk of obesity. The weight gain will increase insulin resistance and may have a major impact on their body image.

It is unhelpful to lecture about the long-term risks to health, as these are likely to be seen as irrelevant by many young people. However, they may be helped if:

- there are clear short-term goals, especially if suggested by themselves

- their efforts to improve their diabetes self-care, e.g. an improving or satisfactory HbA1c level, are communicated promptly and enthusiastically
- there is a united team approach, with unambiguous guidelines for health and diabetes management
- peer group support is used to promote health; activities that allow groups of young people to participate while learning about their diabetes management are encouraged.

After many years in a children and young people's clinic, it can be difficult for the patient and family to move to the adult care environment. This transition is helped by discussing and planning the move well ahead of time, and by the provision of joint clinics with the adult team through to the early twenties or end of tertiary education.

Type 2 diabetes

Children and young people with type 2 diabetes should be offered support to lose weight and increase physical activity. This needs to be done sensitively, with the benefits of improved blood glucose levels and cardiovascular health explained. Metformin should be prescribed if dietary measures do not achieve an HbA1c of less than 48 mmol/mol (6.5%). In addition to the clinical assessment recommended for children with type 1 diabetes, children and young people with type 2 diabetes are at increased risk of reduced cardiovascular health and should be screened for hypertension and dyslipidaemia from diagnosis.

Summary

Diabetes mellitus

- Type 1 diabetes is usually managed by an intensive insulin regimen, matching insulin to the carbohydrate eaten in a balanced diet. Exercise is encouraged.
- Diabetic ketoacidosis is associated with morbidity and mortality and needs meticulous management.
- Long-term complications are reduced if the HbA1c can be maintained at less than 48 mmol/mol (6.5%).

Hypoglycaemia

Hypoglycaemia is a common problem in neonates during the first few days of life (see Ch. 11, Neonatal medicine). Thereafter, it is uncommon unless the child has diabetes or is seriously ill, hence the mnemonic: **ABC** (Airway, Breathing and Circulation), then **DEFG** ('Don't Ever Forget Glucose'). It can also be caused by a number of rare disorders. Severe hypoglycaemia may cause neurodisability or even death unless recognized and treated promptly. It is defined as a blood glucose less than 2.6 mmol/L (in children without diabetes mellitus), although the development of clinical features will depend on whether other energy substrates can be utilized.

Clinical features include:

- sweating
- pallor
- central nervous system signs of irritability, headache, seizures, and coma.

Box 26.5 Causes of hypoglycaemia beyond the immediate neonatal period

Insulin excess

- Excess exogenous insulin, e.g. in diabetes mellitus, maternal diabetes, insulin given surreptitiously
- β-cell disorders – persistent hypoglycaemic hyperinsulism of infancy, insulinoma
- Drug-induced (sulphonylurea)
- Autoimmune (insulin receptor antibodies)
- Beckwith-Wiedemann syndrome

Without hyperinsulinaemia

- Liver disease
- Ketotic hypoglycaemia of childhood
- Inborn errors of metabolism, e.g. glycogen storage disorders, galactosaemia, fatty acid oxidation defects
- Hormonal deficiency: GH↓, ACTH↓, Addison disease, congenital adrenal hyperplasia
- Drugs – alcohol, aspirin, beta blockers
- Sepsis

Neurological sequelae include epilepsy and neurological impairment. Infants are at particular risk as they have high energy requirements and relatively poor reserves of glucose from gluconeogenesis and glycogenesis and brain growth is most rapid. This is why starvation of infants for more than 4 hours, e.g. preoperatively, should be avoided by replacing food with intravenous glucose-containing infusions.

Causes

These are listed in Box 26.5.

- Neonatal hypoglycaemia** – The common, transient neonatal hypoglycaemia in neonates in the first 48 hours of life is due to:
 - exposure to high levels of insulin *in utero* in mothers with diabetes, or
 - insulin resistance in infants born small for gestational age.
- Persistent hypoglycaemic hyperinsulinism of infancy (PHHI)** – In this rare disorder gene mutations cause dysregulation of insulin release by the islet cells of the pancreas, leading to profound non-ketotic hypoglycaemia. Treatment with high-concentration glucose solutions and diazoxide (plus other medications) may be required to maintain safe blood glucose levels pending investigation. Where medical treatment fails, pancreatic surgery may be necessary.
- Ketotic hypoglycaemia** – This is a poorly-defined entity in which young children readily become hypoglycaemic following a short period of starvation, probably due to limited reserves for gluconeogenesis. The child is usually slim, and insulin levels are low. Regular carbohydrate, for example extra glucose drinks, when ill will usually prevent hypoglycaemia. The condition resolves spontaneously in later life.
- Rare endocrine and metabolic disorders** – These may present with hypoglycaemia at almost any age in childhood. Hepatomegaly would suggest the

Box 26.6 Tests to perform when unexplained hypoglycaemia is present

Blood

- Confirm hypoglycaemia with laboratory blood glucose
- Growth hormone, cortisol, insulin, C-peptide, ketones (acetoacetate, 3-hydroxybutyrate), bicarbonate, lactate, ammonia, amino acids, acylcarnitine profile,

First urine after hypoglycaemia

- Organic acids
- Consider saving blood and urine for toxicology, e.g. salicylate, sulphonylurea

possibility of an inherited glycogen storage disorder, in which hypoglycaemia can be profound (see Ch. 27, Inborn errors of metabolism).

Investigations

Blood glucose should be checked and regularly monitored in any child who is seriously unwell with reduced level of consciousness, seizures or septicaemia.

Glucose measurement is often performed using glucose-sensitive strips with a meter. However, this only identifies that the glucose is low and any low reading must be confirmed by laboratory measurement.

If the cause of the hypoglycaemia is unknown, it is vital that blood is collected at the time of the hypoglycaemia and the first available urine sent for analysis, so that a valuable opportunity for making the diagnosis is not missed (Box 26.6) since the results may only be abnormal during hypoglycaemia.

Treatment

Hypoglycaemia can be corrected with an intravenous infusion of glucose (2–5 ml/kg of 10% glucose bolus followed by 10% glucose infusion) or orally (see hypoglycaemia management in diabetes section). Care must be taken to avoid giving an excess volume as the intravenous solution is hypertonic and could cause cerebral oedema. If there is delay in establishing an infusion or failure to respond, glucagon is given intramuscularly. If higher levels of glucose infusion are required in a neonate, the low glucose is highly likely to be secondary to hyperinsulinism.

Summary

Hypoglycaemia

- Should be excluded in any child with septicaemia, who is seriously ill, has a prolonged seizure or has altered state of consciousness ('Don't Ever Forget Glucose').
- Low blood glucose on bedside testing must be confirmed by laboratory measurement.
- If the cause is unknown, diagnostic blood and urine samples must be taken at the time to exclude metabolic or hormonal conditions.

Corticosteroids may also be required if there is a possibility of pituitary or adrenal dysfunction.

Thyroid disorders

The thyroxine hormones produced by the thyroid gland have a crucial role in growth, metabolism and brain development. Only a small quantity of thyroxine is transferred from the mother to the fetus, although severe maternal hypothyroidism, usually from dietary iodine deficiency, can cause congenital hypothyroidism. The fetal thyroid predominantly produces 'reverse T₃', a derivative of T₃ which is largely inactive. After birth, there is a surge in the level of thyroid-stimulating hormone (TSH) which is accompanied by a marked rise in T₄ and T₃ levels. The TSH usually declines to the normal adult range within a week.

Congenital hypothyroidism

Congenital hypothyroidism is included in the universal neonatal blood spot screening programme (Guthrie test), as it is:

- relatively common, occurring in 1 in 3000 births
- a preventable cause of severe learning difficulties.

In the UK, screening identifies a raised TSH when blood is taken at 5 days of age. This will only detect infants with primary hypothyroidism. However, thyroid dysfunction secondary to pituitary abnormalities (which is rare) will not be picked up at neonatal screening as they have a low TSH. In some countries T₄ is also measured.

Causes of congenital hypothyroidism are:

- *thyroid agenesis* – the thyroid gland is absent – the most common cause of sporadic congenital hypothyroidism
- *maldevelopment of the thyroid* – where the thyroid remains as a lingual mass or a unilobular small gland, instead of migrating in early fetal life from a position at the base of the tongue (sublingual) to its normal site below the larynx
- *dyshormonogenesis* – an inborn error of thyroid hormone synthesis, with autosomal recessive inheritance, in about 10% of cases
- *maternal iodine deficiency* – a common cause of congenital hypothyroidism worldwide but rare in the UK; it can be prevented by iodination of salt in the diet
- *hypothyroidism due to TSH deficiency* – isolated TSH deficiency is rare (<1% of cases) and is usually associated with other features of pituitary dysfunction.

The clinical features of congenital hypothyroidism (Box 26.7 and Fig. 26.9) are difficult to differentiate from normal in the first month of life, but become more prominent with age.

Treatment with thyroxine should be started before 2 weeks of age to reduce the risk of impaired neurodevelopment. With neonatal screening, intellectual development and intelligence are in the normal range for the majority of children. Treatment is lifelong with replacement of thyroxine in tablet form, titrating the dose to maintain normal growth, TSH and T₄ levels.

Box 26.7 Clinical features of hypothyroidism

Congenital	Acquired
<ul style="list-style-type: none"> Usually asymptomatic and identified on screening Reduced feeding Faltering growth Prolonged jaundice Constipation Pale, cold, mottled dry skin Coarse facies Large tongue Hoarse cry Goitre (occasionally) Umbilical hernia Delayed development 	<p>Females > males</p> <p>Symptoms:</p> <ul style="list-style-type: none"> Cold intolerance Constipation Delayed puberty/ amenorrhoea Poor concentration Deterioration in school work Learning difficulties <p>Signs:</p> <ul style="list-style-type: none"> Reduced growth rate/ short stature Unexpected weight gain/obesity Goitre Thin, dry hair Pale, puffy eyes with loss of eyebrows Dry skin Cold peripheries Bradycardia Slow-relaxing reflexes Slipped upper femoral epiphysis



Figure 26.9 Untreated congenital hypothyroidism.

Summary

Congenital hypothyroidism

- Is identified on routine neonatal blood spot screening.
- Treatment started soon after birth reduces the risk of impaired intellectual development.

Acquired hypothyroidism

This is usually caused by autoimmune thyroiditis. There is an increased risk in children with Down syndrome or Turner syndrome and in children with other autoimmune disorders, e.g. vitiligo, rheumatoid arthritis, diabetes mellitus. In some families, Addison disease may also occur.

Box 26.8 Clinical features of hyperthyroidism

Systemic	Eye signs (uncommon in children)
Anxiety, restlessness	Exophthalmos
Sweating	Ophthalmoplegia
Diarrhoea	Lid retraction
Weight loss	Lid lag
Rapid growth in height	
Advanced bone maturity	
Tremor	
Tachycardia, wide pulse pressure	
Warm, vasodilated peripheries	
Goitre (with bruit)	
Reduced concentration, learning difficulties / behaviour problems	



Figure 26.10 Exophthalmos in autoimmune thyroiditis (Graves disease).

The clinical features are listed in Box 26.7. It is more common in females. There is a change in growth pattern with reduced height growth, often associated with excessive weight gain. A goitre may be present but may be difficult to differentiate from physiological enlargement in pubertal girls. Thyroid function tests show a high level of TSH, with low levels of T_4 and T_3 . Bone age is delayed. Treatment is with thyroxine.

Hyperthyroidism

This usually results from autoimmune thyroiditis (Graves disease) secondary to the production of thyroid-stimulating hormone receptor antibodies. The clinical features are similar to those in adults (Box 26.8 and Fig. 26.10). It is most often seen in teenage girls. The levels of thyroxine (T_4) and/or tri-iodothyronine (T_3) are elevated and TSH levels are suppressed to very low levels. Antithyroid peroxisomal antibodies may also be present, which may result in spontaneous resolution of the hyperthyroidism but subsequently cause hypothyroidism.

The first-line of treatment is medical, with drugs such as carbimazole or propylthiouracil that block thyroid

hormone synthesis. There is a risk of neutropenia from antithyroid medication, and all families should be warned to seek urgent help and a blood count if sore throat and high fever occur while on treatment. Initially, β -blockers can be added for symptomatic relief of anxiety, tremor, and tachycardia. Medical treatment is given for about 2 years, which should control the thyroid hormone excess, but eye signs may not resolve. When medical treatment is stopped, two thirds of patients relapse. A second course of drugs may be given or permanent remission considered with radioiodine treatment or surgery (thyroidectomy). Follow-up is always required as thyroxine replacement is needed for subsequent hypothyroidism.

Neonatal hyperthyroidism may occur in infants of mothers with hyperthyroidism from the transplacental transfer of thyroid-stimulating hormone receptor antibodies. Treatment of the neonate is required as it is potentially fatal, but it resolves with the regression of maternal antibodies.



Acquired thyroid disorders are less common in children than adults and the diagnosis may be delayed as presentation is with non-specific symptoms.

Pituitary disorders

Pituitary disorders (Box 26.9) are uncommon in childhood and can affect hormones in isolation, e.g. growth hormone deficiency, or a wider pattern of deficiencies across anterior and posterior segments of the pituitary gland. Excess hormone production from an adenoma, e.g. prolactinoma, or acromegaly is much less common than in adulthood.

Growth hormone deficiency

Isolated growth hormone deficiency affects approximately 1 in 4000 children. They are usually asymptomatic and it may only be recognized when the child's measurements are plotted on a growth chart (see Ch. 12, Growth and puberty). Screening investigations show low levels of insulin like growth factors (IGF1 and IGFBP 3) and a delayed bone age, but the diagnosis must be confirmed with a growth hormone provocation test, in which growth hormone levels fail to rise after stimulation with insulin, glucagon, arginine or clonidine.

Clinical assessment should consider potential causes of growth hormone deficiency (see Box 26.9) including detailed examination of the eyes as tumours of or near the pituitary gland may result in abnormal visual fields (characteristically a bitemporal hemianopia as it impinges on the optic chiasm), optic atrophy, or papilloedema on fundoscopy.

Laron syndrome is a rare condition due to defective GH receptors resulting in GH insensitivity. Patients with this condition have high GH levels but low levels of IGF-1, the downstream active product of GH produced at the growth plate and in the liver.

Growth hormone treatment

GH deficiency is treated with recombinant human GH, which is given by daily subcutaneous injection. It is expensive and management must be supervised by a specialist. The best response is seen in children with the most severe hormone deficiency (Case history 26.2). Other indications

Box 26.9 Causes of pituitary disorders

Congenital	Acquired
Structural, e.g. midline pituitary defects including septo-optic dysplasia	Brain tumours affecting hypothalamus or pituitary gland, e.g. craniopharyngioma
Pituitary hypoplasia or aplasia	Cranial irradiation
	Trauma, e.g. affecting pituitary stalk
	Infection, e.g. post meningitis
	Infiltration, e.g. histiocytosis
	Structural, e.g. associated with cerebral malformation, hydrocephalus

where growth hormone has been demonstrated to improve final height include Turner syndrome (see Fig. 9.6), chronic kidney disease, SHOX deficiency, and in children born small for gestational age with failure of catch-up growth. Growth hormone is also indicated in Prader-Willi syndrome (see Fig. 9.13), where it improves muscular strength and body composition as well as a modest increase in final height. The median age for prescription of growth hormone in the UK is 7.6 years, but children with Prader-Willi syndrome are usually started at a younger age (median 2.2 years).

Recently, recombinant IGF-1 has been used to treat children with GH resistance (e.g. Laron syndrome) and IGF-1 deficiency who would have previously not responded to GH treatment. Recombinant IGF-1 therapy is very expensive and confined to a few specialized centres.

Growth hormone excess is extremely rare in childhood.

Gonadotrophin (luteinizing hormone and follicle stimulating hormone) secretion

If reduced, this may cause delayed puberty from hypogonadotropic hypogonadism. Early increase in gonadotrophin secretion results in precocious puberty (see Ch. 12 Growth and puberty).

Diabetes insipidus secondary to antidiuretic hormone insufficiency

This presents with polyuria, although some children are unable to recognize thirst and will present with hyponatraemia (Case history 26.3). The syndrome of inappropriate antidiuretic hormone (SIADH) can be provoked by severe illness or neurosurgery and presents with hyponatraemia.

Adrenocorticotrophin hormone (ACTH) deficiency and excess

These are rare in childhood. Adrenal insufficiency may also be secondary to pituitary dysfunction from hypothalamic-pituitary disease or from hypothalamic-pituitary-adrenal suppression following long-term corticosteroid therapy.



Case history 26.2

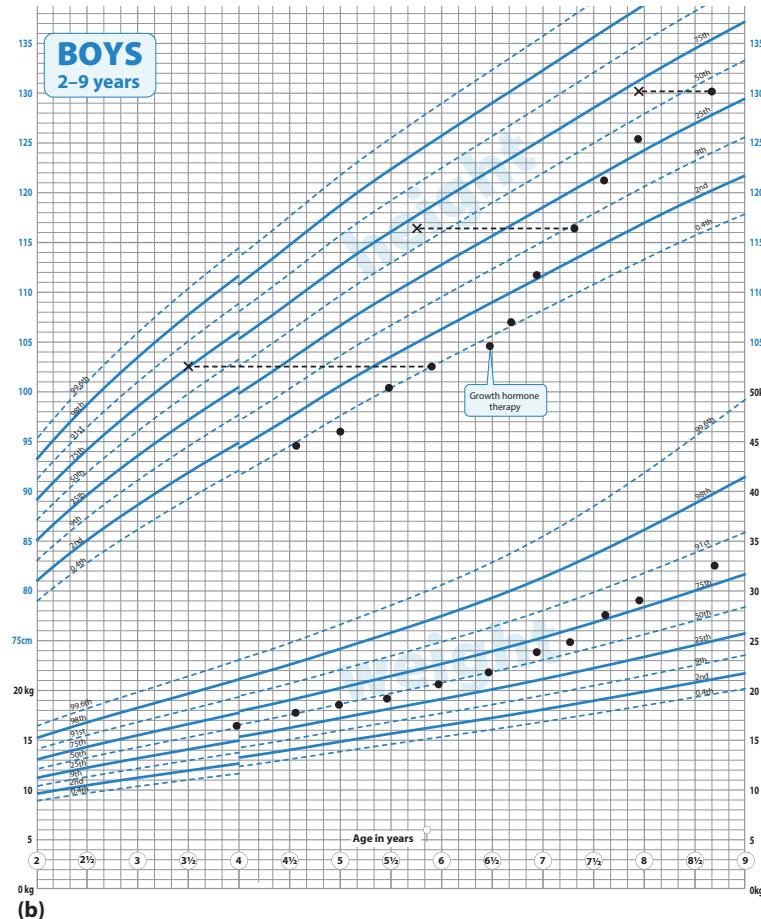
Growth hormone deficiency

This boy presented with short stature at the age of 6 years (Fig. 26.11a). He was small for family size with a height of 102 cm, <0.4th centile. His weight of 17.8 kg was on the 2nd centile. His bone age was delayed 2½ years. He underwent pituitary function tests, including growth hormone provocation using glucagon to provoke rebound hypoglycaemia, to stimulate growth hormone production. His peak growth

hormone level was low (1.7 mcg/L, normal >6.7 mcg/L), other hormones including cortisol showed a good response. This confirmed isolated growth hormone deficiency. He started growth hormone. He responded well to daily subcutaneous injections, reaching a height of 130.3 cm (25th–50th centile) by the age of 8 years and 8 months (Fig. 26.11b).



(a)



(b)

Figure 26.11 (a) Six-year-old boy with short stature showing that he looks well, is slightly overweight and has red cheeks (sometimes a feature). (b) The growth chart shows that this boy was growing below the 0.4th centile for height, with his weight on the 25th centile. Weight centile that is disproportionately high compared to the height centile is characteristic of hormonal deficiencies. His bone age (marked by the cross) is significantly delayed at 6 years of age. After starting growth hormone at 6½ years he grew rapidly over the next two years, and his bone age advanced.

Adrenal disorders

Primary adrenal insufficiency

This is much less common in childhood compared to adulthood and may result from:

- congenital adrenal hyperplasia
- an autoimmune process (Addison disease), sometimes in association with other autoimmune

endocrine disorders, e.g. diabetes mellitus, hypothyroidism, hypoparathyroidism

- haemorrhage/infarction (Waterhouse–Friedrichson disease) – neonatal, meningococcal septicaemia
- X-linked adrenoleukodystrophy, a rare neurodegenerative metabolic disorder
- tuberculosis, now rare.

Adrenal insufficiency can be secondary to long-term use of corticosteroid therapy, for example in the treatment of inflammatory bowel disease or nephrotic syndrome.



Case history 26.3

Diabetes insipidus case study

A 5-year-old boy presented with thirst and a normal blood sugar. He was drinking water excessively both day and night, with recent recurrence of bedwetting. On admission to hospital, his fluid input was 7250 ml and output 7720 ml. He had a raised plasma sodium of 147 mmol/l and serum osmolality of 298 mosmol/kg (normal <295). His urine osmolality of 125 mosmol/kg demonstrated an inability to concentrate

his urine (sometimes a water deprivation test is needed to confirm the diagnosis). Examination, including visual fields, was normal. He responded to a small dose of desmopressin, with immediate reduction in his urine output, confirming a diagnosis of cranial diabetes insipidus. MRI of his pituitary gland showed a small lesion in his pituitary stalk consistent with histiocytosis (Fig. 26.12).



Figure 26.12 MR scan demonstrates a homogenously enhancing infundibular (pituitary stalk) mass after contrast.
(Courtesy of Dr Jonathan Crookdake, University Hospitals of Derby and Burton.)

Presentation

Infants present acutely (Box 26.10) with a salt-losing crisis, hypotension and/or hypoglycaemia. In older children, presentation is usually with non-specific symptoms, such as fatigue, and pigmentation (Fig. 26.13). Postural hypotension can be a clue: check lying and standing blood pressure. The child may present more acutely with hypovolaemic shock and hypoglycaemia during intercurrent illness.

Diagnosis

The diagnosis should be suspected from the typical electrolyte imbalance of hyponatraemia and hyperkalaemia, often associated with a metabolic acidosis and hypoglycaemia. The plasma cortisol is low and the plasma ACTH concentration high (except in pituitary dysfunction). The diagnosis is confirmed with an ACTH (Synacthen) test, where plasma cortisol concentrations remain low

in primary adrenal dysfunction. A normal response excludes adrenal insufficiency.

Management

An adrenal crisis requires urgent treatment with intravenous 0.9% saline, glucose and hydrocortisone. Long-term treatment is with glucocorticoid and mineralocorticoid replacement. Death can occur from adrenal crisis at the time of illness or injury, so the child and family are taught to give 'stress doses' of hydrocortisone during febrile illness, gastroenteritis, major trauma, surgery and endurance sport. Parents are taught how to inject intramuscular hydrocortisone in an emergency. All children at

Box 26.10 Features of adrenal insufficiency

- Vomiting
- Lethargy
- Hyponatraemia
- Hyperkalaemia
- Hypoglycaemia
- Dehydration
- Hypotension
- Pigmentation (gums, scars, skin creases)



Figure 26.13 Buccal pigmentation in adrenal insufficiency (Addison disease). This 9-year-old boy presented with salt craving and pigmentation. (Courtesy of Steven Robinson.)

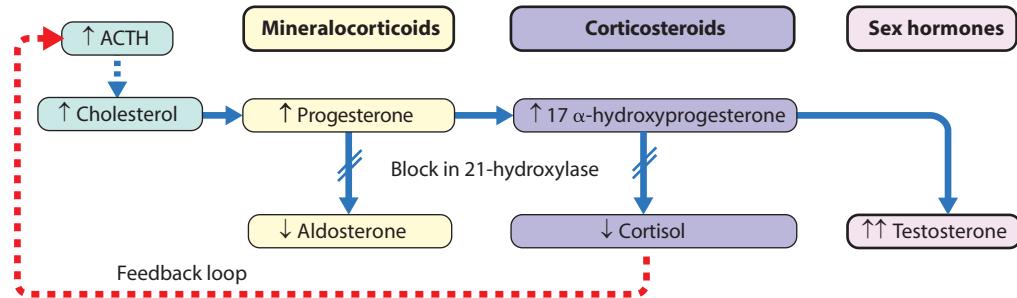


Figure 26.14 Congenital adrenal hyperplasia. Abnormal adrenal steroid biosynthesis from 21-hydroxylase deficiency is the most common form of congenital adrenal hyperplasia. ACTH, adrenocorticotrophic hormone.

risk of an adrenal crisis should wear a MedicAlert bracelet or necklace and carry a steroid card.

Congenital adrenal hyperplasia

Congenital adrenal hyperplasia (CAH) is the most common non-iatrogenic cause of insufficient cortisol and mineralocorticoid secretion. A number of autosomal recessive disorders of adrenal steroid biosynthesis result in congenital adrenal hyperplasia, with an incidence of about 1 in 15,000 births. Over 90% have a deficiency of the enzyme 21-hydroxylase, which is needed for cortisol biosynthesis. The majority of children are also unable to produce aldosterone, leading to salt loss (low sodium and high potassium) (Fig. 26.14). In the fetus, the resulting cortisol deficiency stimulates the pituitary to produce ACTH, which drives overproduction of adrenal androgens.

Presentation is with:

- virilization of the external genitalia in female infants, with clitoral hypertrophy and variable fusion of the labia (see [Case history 26.4](#))
- in the infant male, the penis may be enlarged and the scrotum pigmented, but these changes are often only noted once the diagnosis has been made
- a salt-losing adrenal crisis in males who are salt losers; this occurs at 1 to 3 weeks of age, presenting with vomiting and weight loss, hypotonia and circulatory collapse. A salt-losing crisis is less common in girls as the virilization is noted early and treatment started before salt loss is significant
- tall stature in non-salt losers; both male and female non-salt losers also develop a muscular build, adult body odour, pubic hair, and acne from excess androgen production, leading to pronounced adrenarche or menstrual disorders.

Diagnosis

This is made by finding markedly raised levels of the metabolic precursor 17α -hydroxy-progesterone in the blood. In salt losers, the biochemical abnormalities are:

- low plasma sodium
- high plasma potassium
- metabolic acidosis
- hypoglycaemia.

Management

Infants with a salt-losing crisis require sodium chloride, glucose, and hydrocortisone intravenously.

The long-term management is with:

- lifelong glucocorticoids (e.g. hydrocortisone) to suppress ACTH levels (and hence testosterone) to allow normal growth and maturation
- mineralocorticoids (fludrocortisone) if there is salt loss; infants usually need added sodium chloride until weaned.
- monitoring of growth, skeletal maturity (bone age), plasma androgens and 17α -hydroxy-progesterone – insufficient hormone replacement results in increased ACTH secretion and androgen excess, which will cause rapid initial growth and skeletal maturation at the expense of final height; excessive hormonal replacement will result in skeletal delay and slow growth
- additional hormone replacement to cover illness or surgery, as they are unable to mount a cortisol stress response.

Affected girls may be offered corrective surgery to their external genitalia. Decisions regarding surgery should be considered carefully, aiming for genital appearance compatible with gender and normal adult sexual and reproductive function. This is highly specialized surgery and definitive surgical reconstruction is usually delayed until late puberty.

Prenatal diagnosis is possible when a couple have had a previously affected child. In many countries (but not the UK), identification of congenital adrenal hyperplasia is included the neonatal blood spot screening programme.

Summary

Adrenal insufficiency

- Usually due to withdrawal from long-term corticosteroid therapy, congenital adrenal hyperplasia or, rarely, Addison disease.
- May result in an adrenal crisis requiring urgent treatment.

Cushing syndrome

Glucocorticoid excess in children is usually due to long-term glucocorticoid treatment for conditions such as nephrotic syndrome, asthma or acute lymphoblastic leukaemia ([Box 26.11](#) and [Fig. 26.16](#)). Corticosteroids are potent growth



Case history 26.4

Abnormal genitalia at birth

The appearance of this newborn infant's genitalia is shown in Fig. 26.15.

Investigation revealed:

- a normal female karyotype, 46XX
- the presence of a uterus on ultrasound examination
- a markedly raised plasma 17α -hydroxy-progesterone concentration, confirming congenital adrenal hyperplasia
- a low sodium and a high potassium level
- a low bicarbonate (metabolic acidosis), high urea (dehydration), and low blood glucose (cortisol deficiency).

The low sodium and high potassium indicate that the infant had the salt-losing form of congenital adrenal hyperplasia (CAH). She required correction of her hypoglycaemia with intravenous glucose, then was started on oral hydrocortisone and fludrocortisone replacement therapy. Her growth, biochemistry, and bone age were monitored frequently and she attained normal adult height. Psychological counselling and support were offered around puberty and genital surgery was needed before she became sexually active.

Box 26.11 Clinical features of Cushing syndrome

- Reduced growth rate/short stature
- Face and trunk obesity
- Hypertension
- Psychological/behavioural
- Red cheeks
- Hirsutism
- Striae
- Bruising
- Insulin resistance
- Muscle wasting and weakness
- Osteopenia

suppressors and prolonged use in high dosage will lead to reduced adult height and osteopenia. This unwanted side-effect of systemic corticosteroids is reduced by taking corticosteroid medication in the morning on alternate days.

Non-iatrogenic Cushing syndrome is extremely rare in childhood and may be caused by pituitary or adrenal tumours.

A diagnosis of Cushing syndrome is often questioned in obese children. Most obese children from dietary excess are tall in contrast to children with Cushing syndrome, who are short compared to family size.

If Cushing syndrome is a possibility, the normal diurnal variation of cortisol (high in the morning, low at midnight) may be lost. The 24-hour urine free cortisol is also high. After administration of dexamethasone at night-time, there is failure to suppress the plasma 09.00 hour cortisol levels the following morning (dexamethasone suppression test). If excess cortisol production is confirmed, imaging for adrenal or pituitary tumours is required. Management depends on the source, but is usually surgical resection and/or radiotherapy.



Figure 26.15 Abnormal genitalia at birth. Investigation established that this was a female infant with congenital adrenal hyperplasia causing clitoral hypertrophy with fusion of the labia.



Severe hypospadias and bilateral undescended testes – a male or virilized female? The karyotype and a pelvic ultrasound are required.



Figure 26.16 Facial obesity following prolonged course of high-dose corticosteroids in a preterm infant. Additional oxygen therapy is being given via nasal cannulae.

Disorders of sex development

The fetal gonad is initially bipotential (Fig. 26.17). In the male, a testis-determining gene on the Y chromosome (*SRY*) is responsible for the differentiation of the gonad into a testis. The production of testosterone and its metabolite, dihydrotestosterone, results in the virilization of male genitalia. In the absence of *SRY*, the gonads become ovaries and the genitalia female.

Rarely, newborn infants may be born with a disorder of sex development (DSD) and there may be uncertainty about the infant's sex. A DSD may be secondary to:

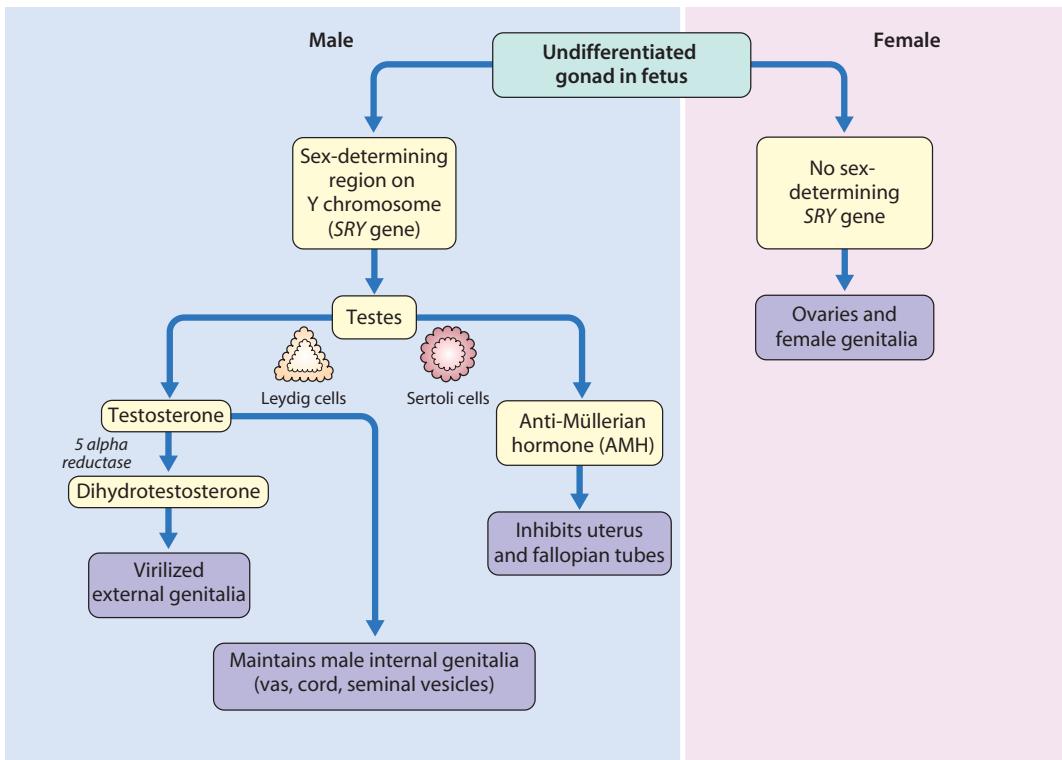


Figure 26.17 Sex development in the fetus.

- excessive androgens producing virilization in a 46XX female – the most common cause of this is congenital adrenal hyperplasia
- gonadotrophin insufficiency – seen in Prader–Willi syndrome and congenital pituitary dysfunction, which results in a small penis and undescended testes in the male
- inadequate androgen action, producing under-virilization in a 46XY male – this can result from:
 - inability to respond to androgens (a receptor problem, such as androgen insensitivity syndrome, which may be complete or partial)
 - inability to convert testosterone to dihydrotestosterone (5α -reductase deficiency) or
 - abnormalities of the synthesis of androgens from cholesterol
- ovotesticular DSD (previously known as true hermaphroditism) – caused by both XX-containing cells and XY-containing cells being present in the fetus, leading to both testicular and ovarian tissue being present and a complex external phenotype; this is extremely rare.

DSD is a medical emergency. All parents are keen to know whether they have a boy or a girl. However, if the genitalia are abnormal, the infant's sex must not be assigned until results are available from a detailed assessment by medical, surgical, and psychological specialists. Where necessary, birth registration must be delayed until this has been completed.

Investigations include:

- urgent microarray or karyotype
- adrenal and sex hormone levels
- ultrasound of the internal structures and gonads
- laparoscopic imaging and biopsy of internal structures if necessary.

It may not be possible to determine the sexual identity of the child from the appearance of the external genitalia alone. Definitive surgery may be delayed to allow the affected individual to give informed consent to any reconstructive procedures, and gender reassignment may be wanted when older. The family may benefit from psychological support throughout childhood. This is a highly complex issue and DSD must be managed by experienced multidisciplinary teams.

 **If there is abnormal sexual differentiation at birth:**

- do not guess the infant's sex
- the most common cause of a disorder of sex development is female virilization from congenital adrenal hyperplasia.

Parathyroid disorders

Parathyroid hormone (PTH) promotes bone formation via bone-forming cells (osteoblasts). However, when calcium levels are low, PTH promotes bone resorption via osteoclasts, increases renal uptake of calcium, and activates metabolism of vitamin D to promote gut absorption of calcium (see Fig. 13.14). In hypoparathyroidism, which is rare in childhood, in addition to a low serum calcium, there is a raised serum phosphate and a normal alkaline phosphatase (Table 26.3). The parathyroid hormone level is very low. Severe hypocalcaemia leads to muscle spasm (tetany), seizures, stridor, and diarrhoea. In vitamin D deficiency, which sometimes causes hypocalcaemia, there may be bone resorption causing rickets (see Ch. 13, Nutrition).

Hypoparathyroidism in infants is usually due to a genetic disorder, DiGeorge syndrome. In older children, hypoparathyroidism is usually an autoimmune disorder and can be associated with Addison disease.

Table 26.3 Bone biochemistry in parathyroid disorders

	Calcium	Phosphate	Alkaline phosphatase	PTH
Vitamin D deficiency	↓ or N	N or ↓	↑	↑
Primary hypoparathyroidism	↓	↑	N	↓↓
Pseudohypoparathyroidism	↓	↑	N	N/↑
Primary hyperparathyroidism	↑	↓	N	↑↑

In *pseudohypoparathyroidism* there is end-organ resistance to the action of parathyroid hormone caused by a mutation in a signalling molecule. Serum calcium and phosphate levels are abnormal but the parathyroid hormone levels are normal or high. Associated abnormalities are short stature, obesity, subcutaneous nodules, short fourth metacarpals, and learning difficulties. There may be teeth enamel hypoplasia and calcification of the basal ganglia. A related state, in which there are the physical characteristics of pseudohypoparathyroidism but the calcium, phosphate and PTH are all normal, is called *pseudopseudohypoparathyroidism*. There may be a positive family history of both disorders in the same family.

Treatment of acute symptomatic hypocalcaemia is with an intravenous infusion of calcium gluconate. PTH cannot easily be replaced, so hypocalcaemia in hypoparathyroidism is usually treated with oral calcium and vitamin D analogues. The doses are adjusted to maintain the plasma calcium concentration just below the normal range as, without PTH, hypercalciuria and nephrocalcinosis are a risk.

Hyperparathyroidism results in a high calcium level, causing constipation, anorexia, lethargy and behavioural effects, polyuria, and polydipsia. Bony erosions of the phalanges may be seen on a hand radiograph. In neonates and young children, it is associated with some rare genetic disorders (e.g. William syndrome), but in later childhood can be secondary to adenomas occurring spontaneously or as part of the multiple endocrine neoplasia syndromes. Severe hypercalcaemia is treated with rehydration, diuretics, and bisphosphonates.

Paul Dimitri (4th, 5th Editions). Tracy Tinklin (5th Edition) We would also like to thank Joanna Walker for her helpful suggestions.

Further reading

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Websites

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International Society for Pediatric and Adolescent Diabetes: Available at: www.ispad.org.

British Society of Paediatric Endocrinology and Diabetes, BSPED, guidelines: Available at: www.bsped.org.uk.

National Institute for Health and Care Excellence (NICE): Diabetes (type 1 and type 2) in children and young people: diagnosis and management. NICE guideline [NG18]. Available at: www.nice.org.uk/guidance/NG18.

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Inborn errors of metabolism

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Features of inborn errors of metabolism:

- Individually rare but collectively numerous.
- Six are included in the UK national newborn bloodspot screening programme.
- There is a wide range of presentations.
- They are unlikely to be diagnosed unless specific investigations are performed.
- Genetic diagnosis is essential for confirmation and to allow genetic counselling.
- With some conditions, delay in diagnosis may result in neurological damage or death.

Families and children with inborn errors of metabolism and other rare conditions often encounter healthcare professionals with little experience or expertise of their condition. To overcome this problem, these conditions are now often grouped together as a specialty of "rare diseases", i.e. diseases that affect fewer than 1 in 2000 of the general population. There are over 6000 known rare diseases. Over 80% have a genetic cause, and genetic testing, particularly with sequencing technologies, is allowing increasing identification of these disorders. The formation of the specialty of rare diseases also allows development and assessment of new treatments, and the opportunity to provide patients and families with the specialist care they require.

Overview

Classification

Inborn errors of metabolism (IEM) represent disorders of the enzymatic reactions that degrade, synthesize, or interconvert molecules within cells. There are three broad pathophysiological groups – disorders of intoxication, energy metabolism, and complex organelles (Table 27.1).

Frequency

They are individually rare (Table 27.2), however, collectively they are not uncommon. Even when familial hypercholesterolaemia is excluded, they affect between 1 in 800 and 1 in 2500 children. Their prevalence varies widely by both country and ethnicity, e.g. fatty acid metabolism disorders are 10 times more common in Saudi Arabia than mitochondrial disorders, although the prevalence of each is similar worldwide.

Table 27.1 Pathophysiological classification

Group	Examples of inborn errors of metabolism
Disorders leading to toxicity due to accumulated metabolite	Aminoacidopathies, e.g. homocystinuria Urea cycle disorders, e.g. citrullinaemia Organic acidaemias, e.g. isovaleric acidaemia Carbohydrate disorders, e.g. galactosaemia Neurotransmitter disorders, e.g. pyridoxine-dependent seizures
Disorders of energy metabolism	Mitochondrial diseases, e.g. MELAS, MERRF Fatty acid oxidation disorders, e.g. carnitine transporter deficiency Glycogen storage disorders, e.g. McArdle disease
Disorders of complex organelles	Lysosomal storage disorders, e.g. mucopolysaccharidoses Peroxisomal disorders, e.g. Zellweger syndrome

Table 27.2 Frequency of some inborn errors of metabolism

Disorder	Type of IEM	Incidence (live births)
Galactosaemia	Carbohydrate disorder	1 in 23,000 to 1 in 44,000
Ornithine transcarbamylase deficiency	Urea cycle disorder	1 in 14,000
Methylmalonic acidaemia	Organic acidaemia	1 in 50,000
Glycogen storage disorder type 1	Carbohydrate metabolism	1 in 100,000
Familial hypercholesterolaemia	Lipid disorder	1 in 250



Rare diseases (prevalence <1 in 2000) are increasingly considered as a single entity. Although each individual condition affects very few children, when considered together, they are actually quite common, as there are over 6000 of them.

Presentation

Can present in a multitude of ways and at any age, although many present in early childhood. They should be considered in all children with:

- an unexpectedly severe presentation of an otherwise common illness
- significant metabolic acidosis
- an unexplained respiratory alkalosis
- hypoglycaemia
- cardiac failure or cardiomyopathy
- hepatomegaly or hepatosplenomegaly or liver dysfunction
- unexpected drowsiness, coma or irritability
- early onset seizures
- dysmorphic features
- developmental regression
- sudden unexplained death.

In the history, specifically ask about:

- a family history of inborn error of metabolism; draw a family tree
- a family history of sudden unexplained death(s), particularly in childhood, epilepsy, or learning difficulties
- consanguinity detailing if first, second, or third cousins.

On examination, there may not be any specific clinical findings. However, examination including the skin, musculoskeletal, and ophthalmological systems is required.



If an inborn error of metabolism is suspected, contact a specialist metabolic centre for advice at an early stage.

Genetics

Inborn errors of metabolism are inherited disorders and display specific inheritance patterns. Although mitochondrial and *de novo* occurrences are seen, the most common mode of inheritance is autosomal recessive, where consanguineous parentage increases the risk.

Investigations

If metabolic disease is not considered within the differential diagnosis, it is unlikely to be identified through standard blood, urine, or cerebral spinal fluid investigations. Early discussion with a specialist centre is vital. If a diagnosis is clear, then specific diagnostic investigations can be performed, including genetic testing. Often the diagnosis is uncertain, as many present with chronic, non-specific signs such as developmental delay, faltering growth, dysmorphism or seizures. Even those presenting acutely with metabolic acidosis or hypoglycaemia will need multiple investigations to elucidate the aetiology. Investigations are often staged. First line investigations are shown in Table 27.3. These are often followed by more specialist testing, such as muscle, skin or liver biopsy, genetic analyses, and specific cerebrospinal fluid testing, e.g. for amino acids or neurotransmitters. These should be guided by specialist advice.

Table 27.3 Typical first line investigations (guided by clinical picture)

Sample	Test	Indication
Blood	Amino acids and acylcarnitines	Suspected urea cycle disorders, organic acidaemia or aminoacidopathy – presenting with developmental delay, seizures, faltering growth, dysmorphism
	Ammonia	Suspected urea cycle disorder
	Beutler screening test or Gal-1-PUT Assay	Suspected galactosaemia
	Very long chain fatty acids	Suspected peroxisomal disorder
	White cell enzymes	Dysmorphism, organomegaly, learning difficulties, developmental regression
	Lactate	Suspected mitochondrial disease, glycogen storage disorders
Urine	Organic acids	Organic acidaemia, fatty acid oxidation disorders
	Amino acids	Tubulopathy, cystinosis
	Glycosaminoglycans and oligosaccharides	Mucopolysaccharidoses or oligosaccharidoses

Management

The two cornerstones of management are:

- day-to-day management of the condition with medications and diet
- emergency plans for times of high metabolic demand (such as intercurrent illness) or metabolic crisis.

If a personal emergency management plan is not available, consult an online resource and contact the metabolic medicine specialist.

The key principles of everyday management are:

1. Medications
 - symptomatic therapies, e.g. anticonvulsants, analgesia
 - specific therapies, e.g. ammonia scavengers
 - enzyme replacement therapy – for a limited number of storage disorders (haemopoietic stem cell transplantation is an option, see mucopolysaccharidoses (MPS) type I below).
2. Dietary manipulation. There are four potential strategies:
 - supplying a deficient product, e.g. regular supply of glucose in hepatic glycogen storage disease type I by regular daytime feeds and continuous overnight feed
 - preventing accumulation of a toxic substrate. In many disorders there is protein restriction, e.g. phenylalanine restriction in phenylketonuria to reduce harmful metabolites. To prevent malnutrition, protein substitutes and vitamin and mineral supplementation is required, guided by a specialist dietician
 - prevention of catabolism. Metabolic demands are increased when ill. If not met, catabolism

occurs and certain groups are at risk of metabolic decompensation, e.g. urea cycle disorder patients are at risk of hyperammonaemia. To prevent this, patients stop their normal diet and commence their emergency regimen. This consists of an oral glucose polymer, e.g. Polycal, which serves to provide a supply of glucose to meet the body's energy demand and reduce catabolism. It can be given at home but must be given regularly during the day and night. Vomiting, refusal to drink the emergency regimen, or deterioration despite taking it require hospital admission for intravenous glucose

- ketogenic diet. Patients with GLUT1 (glucose transporter 1) deficiency are unable to transport glucose into their central nervous system. A ketogenic diet is used to provide ketones as an alternative energy source for the brain.



Children with inborn errors of metabolism can decompensate rapidly. They usually have an established personal emergency management plan.

Newborn blood spot screening

Newborn blood spot screening aims to detect treatable conditions prior to their clinical presentation and allows early treatment to improve outcome. Phenylketonuria was the first IEM to be screened in the 1960s. Screening has been extended in the UK to include five more IEMs. It is offered for all babies on day 5–7 of life with drops of blood from a heelprick collected onto filter paper. The conditions tested for are cystic fibrosis, congenital hypothyroidism, some haemoglobinopathies, and six inborn errors of metabolism (Table 27.4 and Case history 27.1).

Table 27.4 IEM detected on newborn screening in the UK

IEM	Incidence	Presentation if not detected/treated	Management
Phenylketonuria (PKU)	1 in 10,000 Carrier frequency 1 in 50	Learning difficulties, seizures, microcephaly	Phenylalanine restricted diet
MCAD (medium chain acyl-CoA dehydrogenase deficiency)	1 in 10,000	Encephalopathy, often rapidly progressive, collapse after prolonged fast resulting in non-ketotic hypoglycaemia and death if untreated	Avoidance of fasting and provision with an emergency regimen
Glutaric aciduria type 1 (GA1)	1 in 30,000–1 in 40,000	Macrocephaly with encephalopathic crisis aged 6–18 months resulting in dystonic-dyskinetic movement disorder	Specialist diet, avoidance of fasting and daily carnitine
Isovaleric aciduria	1 in 250,000	Metabolic acidosis ± hyperammonaemia	Low protein diet, carnitine and glycine
Homocystinuria	1 in 200,000 to 1 in 335,000, but more common in those with Irish ancestry at 1 in 65,000	Marfanoid appearance, learning difficulties, lens dislocation, osteoporosis, thromboembolism	Low protein diet, pyridoxine and folic acid
Maple syrup urine disease (MSUD)	1 in 185,000	Progressive encephalopathy in first week of life	Low protein diet

(Incidence data from: Genetics Home Reference page (NIH): ghr.nlm.nih.gov, accessed May 2020.)



Case history 27.1

Identification of MCAD (medium chain acyl-CoA dehydrogenase) deficiency on newborn screening

Jack was born at term, birthweight 3.2 kg. On day 5 he had the routine heelprick test for newborn screening. On day 7 it showed he had MCAD deficiency. This was phoned through to the newborn screening nurse who visited the family and checked that Jack was well. She provided them with a 'MCAD deficiency is suspected' leaflet. Jack was seen within 24 hours by the specialist metabolic team, where blood for repeat testing and genetic mutations was taken and urine collected for organic acid analysis. The consultant explained about the condition and that Jack must not go for more than 6 hours without a feed. The specialist dietician provided an emergency regimen for use at times of illness. The family was advised that any future children would have a 1 in 4 risk of also having MCAD deficiency.

Regarding MCAD deficiency:

- Although screening is performed, it can present in the first few days of life (i.e. before screening) with sudden onset of encephalopathy. A few babies die every year prior to screening.
- Any older siblings should be offered testing if they were born prior to newborn screening or in a country where screening does not occur.
- Families require genetic counselling, and future pregnancies should be managed prospectively, ensuring at-risk babies receive regular feeds and early biochemical testing.

Table 27.5 Acid–base disturbance

Abnormality	Primary disturbance	Effect on			
		pH	pCO ₂	Base excess	Compensatory response
Respiratory acidosis	↑ pCO ₂	↓	↑	Negative	↑ [HCO ₃ ⁻]
Metabolic acidosis	↓ [HCO ₃ ⁻]	↓	N or ↓	Negative	↓ pCO ₂
Respiratory alkalosis	↓ pCO ₂	↑	N or ↓	Positive	↓ [HCO ₃ ⁻]
Metabolic alkalosis	↑ [HCO ₃ ⁻]	↑	N or ↑	Positive	↑ pCO ₂

In some countries a wider range of disorders are tested for, as they can be diagnosed by tandem mass spectroscopy.

Metabolic disease and acid–base disturbance

Acid–base balance is essential for correct cellular functioning. Blood gas measurement can help to identify the primary disturbance (Table 27.5). In general:

- Metabolic disturbances are compensated acutely by changes in ventilation and chronically by renal responses.
- Respiratory disturbances are compensated by renal responses.

Metabolic acidosis is common in severely ill children, but may also be the presenting feature of an IEM. A raised respiratory rate reflects the compensatory hyperventilation that occurs to promote removal of carbon dioxide (Kussmaul respiration). An IEM is more likely if:

- there is severe acidosis disproportionate to the usual clinical condition

- abnormalities persist despite standard management
- there is a raised anion gap.

The anion gap

The anion gap is the difference between the commonly measured cations (positively charged ions) and anions (negatively charged ions) in the blood. The anion gap is calculated by:

$$\text{Anion gap} = [\text{Na}^+ + \text{K}^+] - [\text{Cl}^- + \text{HCO}_3^-]$$

Using this equation a normal value is 10–16 mmol/L. This represents the 'unmeasured anions' in the blood. An elevated anion gap most commonly occurs when there is a lactic or ketotic acidosis; but it can occur in the presence of any unmeasured anion such as an organic acid, e.g. methylmalonic or propionic acid (Table 27.6 and Case history 27.2).

Management involves treatment of the underlying aetiology and, if acidosis is severe, administration of sodium bicarbonate (see Case history 27.2).

 **Infection is a common trigger for the presentation of an IEM. Both may require concurrent investigation and treatment.**

Table 27.6 Metabolic acidosis and the anion gap

With normal anion gap	With raised anion gap
Intestinal loss of base, e.g. diarrhoea	Diabetic ketoacidosis
Renal loss of base, e.g. renal tubular acidosis type 1 and type 2	Renal failure Poisoning with: salicylate, ethanol, methanol, or paraldehyde Inborn errors of metabolism



Case history 27.2

An organic acidaemia

Aysha, a 6-day-old girl born at term with a birthweight of 3 kg following an uneventful pregnancy and delivery, presents with reduced feeding and rapid breathing. On examination her respiratory rate is 90 breaths/min and she is unresponsive to stimulation. Blood gas: pH 7.29, pCO_2 2.0 kPa, base excess – 18 mmol/L, HCO_3^- 10 mmol/L, Na^+ 140 mmol/L, K^+ 3.6 mmol/L, Cl^- 110 mmol/L, lactate 8 mmol/L. The anion gap = $(140 + 3.6) - (110 + 10) = 23.6$ mmol/L. Such a large anion gap would not be generated by this level of lactate. The gas normalizes with intravenous 10% dextrose and two half corrections of sodium bicarbonate, and she becomes alert and has a normal respiratory rate. In view of the encephalopathy and raised anion gap, a urine organic acid analysis is performed and shows increased methylmalonic acid. The diagnosis is later genetically confirmed as methylmalonic acidaemia.



- Always consider an inborn error of metabolism if:**
- unexplained encephalopathy and/or markedly raised anion gap
- sudden unexplained death of infancy.

Hyperammonaemia

Ammonia is a highly toxic chemical derived from bodily nitrogen. It is detoxified to urea by the urea cycle, which principally occurs in the liver. An ammonia level should be measured when there is:

- unexplained encephalopathy
- respiratory alkalosis because it is a respiratory stimulant
- recurrent vomiting
- unexplained severe illness in a baby or child
- unexplained seizures as it causes cerebral oedema.

Ammonia can be elevated in severe illness, liver disease, by certain medications, and transiently in the newborn.

Principles of management are to stop feeds, start 10% dextrose, give intravenous ammonia scavenging medications and arginine to support the urea cycle, and arrange urgent transfer to paediatric intensive care for haemofiltration.

Hypoglycaemia

Hypoglycaemia is common in the first day of life in infants who are preterm, growth restricted or ill, and blood glucose measurements are checked routinely in these circumstances. Thereafter, blood glucose should be checked in any child who appears seriously ill, has a prolonged seizure, or develops an altered state of consciousness. It is defined as a blood glucose of less than 2.6 mmol/L. Investigation with a hypoglycaemia screen at the time of hypoglycaemia is required to identify an IEM or endocrine cause (Box 26.6, Ch. 26, Diabetes and endocrinology). The presence or absence of ketones should be specifically sought as their absence is an abnormal response. On physical examination, the presence of hepatomegaly should be sought to identify glycogen storage disorders.

Glycogen storage disorders

The glycogen storage disorders (GSD) are a diverse group and can be divided into hepatic, muscular and cardiac subgroups. The hepatic forms are associated with hypoglycaemia. GSD type 1a exemplifies the hepatic form (Case history 27.3). It is due to deficiency of glucose-6-phosphatase and leads to severe hypoglycaemia because of the inability to mobilize glucose from glycogen or utilize glucose from gluconeogenesis. The most common muscle GSD is GSD V, also called McArdle disease. It is due to deficiency of myophosphorylase. Patients characteristically have exercise intolerance relieved by rest, the 'second wind' phenomena. This reflects the ability of the muscles to 'switch' to using other energy sources, e.g. free fatty acids or free glucose in the blood stream. They are at risk of exercise-induced breakdown of muscle tissue (rhabdomyolysis) and its complications, particularly acute kidney injury.

Lysosomal storage disorders

The lysosome is the recycling centre of the cell and contains a number of enzymes. Deficiency of one of these enzymes results in the inability to break down a specific chemical leading to its accumulation within the cell. This accumulation typically leads to signs of visceral storage (hepatosplenomegaly) and/or central nervous system involvement with developmental regression or seizures or both. There are a number of groups of lysosomal storage disorders, e.g. mucopolysaccharidoses, and sphingolipidoses (Fabry disease). Diagnosis is initially based on urinary glycosaminoglycan and oligosaccharide screening followed by blood testing of the lysosomal enzymes and genetic testing.



Case history 27.3

A glycogen storage disorder

A 4-month-old boy with a normal neonatal and past medical history presents with a 1-day history of cough and fever. He has not fed for 12 hours and has reduced wet nappies. On examination he has a cherubic face, the clinical features of moderately severe bronchiolitis and has a 10-cm soft, enlarged liver. His blood glucose is 1.8 mmol/L. On investigation of his hypoglycaemia, he is found to have a lactic acidosis, his serum is milky, and triglycerides are raised. The nurses note that he becomes sweaty and irritable prior to feeds. Glucose monitoring demonstrates prefeed hypoglycaemia if feeds are more than 2.5 hours apart. GSD type 1a is diagnosed and confirmed on mutation analysis. He is commenced on 2-hourly daytime feeds and a continuous overnight nasogastric feed.

Features of glycogen storage disorders are:

- GSD type 1 often presents when illness prevents feeding or when an infant's feed frequency is reduced.
- The hepatomegaly can be easily missed as it has a soft consistency.
- Lactate is raised because it acts as an alternative fuel.

Mucopolysaccharidoses (MPS)

The mucopolysaccharidoses are the more commonly seen lysosomal disorders. There is defective breakdown of glycosaminoglycans (GAGs). They are progressive multisystem disorders which may affect the neurological, ocular, cardiac, and skeletal systems (Table 27.7).

The different forms of MPS have highly variable clinical features. The characteristics of five of the varieties are shown in Table 27.8. As seen from the table, the majority present with growth faltering, developmental delay, dysmorphism and/or hepatosplenomegaly in the first 6–12 months of life. The dysmorphism is typically a coarsening of the facial features with a prominent forehead due to frontal bossing (Fig. 27.1). Once the diagnosis is suspected the initial test is measuring the excretion in the urine of the major storage substances, the glycosaminoglycans (GAGs). This is followed by lysosomal enzyme testing and genetic testing. Treatment is supportive according to the child's needs and a number of the conditions have enzyme replacement therapies available. Successful enzyme replacement by haemopoietic stem cell transplantation has been performed for MPS type I, but it cannot reverse any established neurological abnormality and has a minimal effect on the skeletal component.

Mitochondrial disease

The Krebs cycle (also known as the tricarboxylic acid cycle) is found in all cells except red blood cells, which lack mitochondria. The primary function of this system is

Table 27.9 Some mitochondrial disorders

Syndrome	Clinical features	Onset
MERRF	Myoclonic epilepsy with ragged red fibres.	5–15 years
MELAS	Mitochondrial encephalopathy, lactic acidosis, stroke-like episodes. Myopathy, migraine, vomiting, seizures, visual and hearing disturbance.	5–15 years
Alpers	Intractable seizures and liver involvement.	Early childhood

the production of ATP (adenosine triphosphate) from the process of oxidative phosphorylation. Mitochondrial disorders are those directly resulting from deficits in energy production by oxidative phosphorylation and therefore affect those organs with the greatest energy demands, i.e. brain, heart, kidney, retina, skeletal muscle. Clinical presentation is very varied (Case history 27.4). Some clinical syndromes are recognized (Table 27.9). Investigation is difficult and often only symptomatic treatment is possible. Mitochondrial disease should be considered when there is:

- multisystem disease
- elevated lactate, though differential diagnosis is wide, and it is not always present
- MRI brain scans showing characteristic features.

Lipid storage disorders

Lipid storage diseases are a group of IEM in which enzyme deficiency causes lipid accumulation in cells and tissues (see Table 27.10). This excessive storage of fats can cause permanent cellular and tissue damage, affecting the brain, nervous system, liver, spleen and bone marrow. The most common lipid storage disorder is Gaucher disease.

Disorders of lipid metabolism

The most common reason for raised cholesterol in childhood is obesity. However, familial hypercholesterolaemia is the most common inherited disorder of lipid metabolism. The majority of children with the familial disease form are detected because a parent has presented with an acute myocardial infarction. However, in the UK, with the implementation of the national familial hypercholesterolemia (FH) screening programme of cascade testing of biological relatives of people with FH, there is likely to be an increase in the number of children diagnosed.

Mucopolysaccharidoses

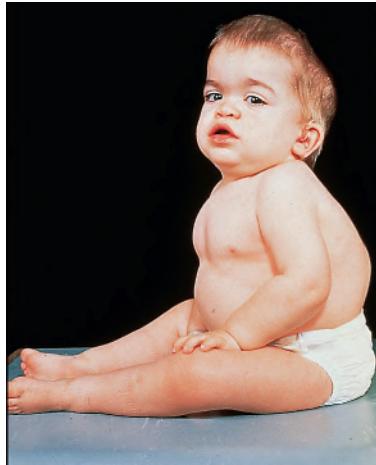


Figure 27.1 Untreated Hurler syndrome showing the characteristic facies and skeletal dysplasia. The prominence of the lower spine is called a 'gibbus'.

Table 27.7 Clinical features of mucopolysaccharidoses

Eyes	Corneal clouding
Skin	Thickened skin
	Coarse facies
Heart	Valvular lesions
	Cardiomyopathy
Neurology	Developmental regression
Skeletal	Thickened skull
	Broad ribs
	Claw hand
	Thoracic kyphosis
Other	Lumbar lordosis
	Hepatosplenomegaly
	Carpal tunnel syndrome
	Conductive deafness
	Umbilical and inguinal hernias

Table 27.8 Types of mucopolysaccharidoses

Type	Inheritance	Cornea	Heart	Brain	Skeletal
MPS I (Hurler)	AR	+++	++	+++	++
MPS II (Hunter)	X-linked	-	+	++	+
MPS III (Sanfilippo)	AR	±	-	+	+
MPS IV (Morquio)	AR	+	+	-	+++
MPS VI (Maroteaux–Lamy)	AR	+++	++	-	++

AR, autosomal recessive.

A few children with homozygous familial hypercholesterolaemia may be the index case. They typically present before 5 years of age to dermatologists with lipid deposits (Fig. 27.3). These deposits classically occur in the natal cleft and the extensor surfaces of the elbows.

Treatment of heterozygotes is with the use of a low fat diet and, from the age of 8 years, a statin. In homozygous patients the risk of myocardial infarction and stroke in

the early teenage years is extremely high. Treatment is started with a low fat diet, a statin and ezetimibe, which lowers cholesterol. If there is a poor response to treatment in homozygous patients, other treatment options include lipid apheresis or liver transplantation. Treatment with PCSK9 inhibitors are being increasingly used for children with the homozygous form.

Abnormally low lipid levels can also be an indicator of metabolic disease, e.g. abetalipoproteinaemia.



Case history 27.4

Mitochondrial disease

Amy is 8 years old and presents with a 3-day history of an upper respiratory tract infection and the sudden onset of seizures and encephalopathy. She was admitted to a paediatric intensive care unit and investigations demonstrated rhinovirus in a nasal pharyngeal aspirate and a raised lactate of 9 mmol/L which failed to normalize once seizure control was obtained. An MRI head scan showed basal ganglia calcification and areas of infarction not confined to vascular territories. On history taking there was a significant family history

(Fig. 27.2). Amy's presentation and family history suggested a mitochondrial disease, specifically MELAS. Genetic mutation analysis confirmed MELAS. Amy recovered from this episode but died 2 years later from recurrent stroke-like episodes and lactic acidosis. Features of mitochondrial disease are:

- There may be marked intra-familial variation.
- The family history and drawing a family tree are helpful.
- Infection is often a trigger for acute decompensation.

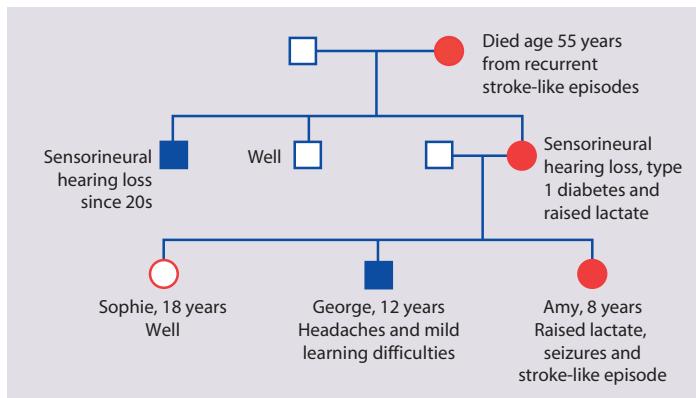


Figure 27.2 Family tree consistent with mitochondrial disease (see Ch. 9, Genetics). Mitochondria are the product of a nuclear and a mitochondrial genome (mtDNA). The mtDNA is inherited exclusively from the mother. The proportion of copies affected by the mtDNA mutation and the severity of the mutation and the tissue response determine the severity of the clinical phenotype. Here, Amy has MELAS as she has a high proportion of mtDNA, whereas others in the family with lower levels only suffer from type 1 diabetes mellitus and sensorineural hearing loss.

Table 27.10 Summary of the features of lipid storage disorders

Disorder	Enzyme defect	Clinical features
Fabry disease	Alpha-galactosidase A	Only X-linked lipid storage disorder Males: present in childhood with recurrent acute pain/paraesthesiae in limbs, diminished sweating, angiokeratomas, normal intelligence Females: 70% asymptomatic. Presentation tends to be from age 15 years onwards Enzyme replacement therapy
Gaucher disease	Beta-glucosidase	Occurs in 1 in 500 Ashkenazi Jews Chronic childhood form – splenomegaly, bone marrow suppression, bone involvement, normal IQ Splenectomy may alleviate hypersplenism Enzyme replacement therapy Acute infantile form – splenomegaly, neurological degeneration with seizures Carrier detection and prenatal diagnosis are possible
Niemann–Pick disease type C	Cholesterol trafficking disorder	Infantile: neonatal liver disease with hepatosplenomegaly. Usually improves but may be fatal Juvenile: age 3–15 years with progressive ataxia, language delay, hepatosplenomegaly, vertical supranuclear gaze palsy, cherry red spot (50%). Death 7 years to adulthood Adult: ataxia, dementia, psychiatric illness Treatment with substrate reduction therapy
Wolman disease	Lysosomal acid lipase	Neonatal presentation with severe growth faltering, steatorrhoea, massive hepatosplenomegaly and X-ray shows adrenal calcification Fatal within first year Newly developed enzyme replacement therapy



Figure 27.3 Severe skin xanthomata. In this child, it was secondary to liver failure, and the condition resolved within weeks of liver transplantation.

Summary

Inborn errors of metabolism

- Are individually rare but collectively not uncommon.
- Neonatal blood spot screening allows the diagnoses of six inborn errors of metabolism.
- Presentation may be at any age with serious unexplained illness, hepatomegaly/splenomegaly, cardiac failure, drowsiness, seizures, dysmorphic features, developmental regression or sudden unexpected death of infancy.
- Should also be considered if there is hypoglycaemia, marked metabolic acidosis and anion gap, or respiratory alkalosis of unknown cause.
- Hyperammonaemia is a time-critical medical emergency: rapid diagnosis is essential to allow early treatment to reduce morbidity and mortality.
- Investigations and management are complex and specialized – consult the specialist metabolic centre early.
- Affected children can deteriorate rapidly during intercurrent illness and may have an advisory emergency management plan.

Acknowledgements

We would like to acknowledge contributors to the section on Inborn Errors of Metabolism in the chapter on Endocrine and Metabolic Disorders in previous editions, whose work we have drawn on: Tony Hulse (1st Edition), Jerry Wales (2nd Edition), Ed Wraith (3rd Edition), Elisabeth Jameson (4th, 5th Editions).

Websites

British Inherited Metabolic Disease Group (BIMDG): www.bimdg.org.uk. Includes emergency guidelines for a range of metabolic diseases.

NHS newborn blood spot screening programme: Available at: www.gov.uk/topic/population-screening-programmes/newborn-blood-spot.

Orphanet: www.orphanet.net. A portal for rare diseases and orphan drugs.

Online Mendelian Inheritance in Man (OMIM): Available at: www.ncbi.nlm.nih.gov/omim. A compendium of human genes and genetic phenotypes.

Rare diseases: <https://www.raredisease.org.uk>. Information about rare diseases.



Musculoskeletal disorders

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Key features of musculoskeletal disorders in children:

- Physical assessment is with pGALS (paediatric Gait, Arms. Legs and Spine) and pREMS (paediatric Regional Examination of the Musculoskeletal System).
- Many, but not all, concerns of parents about their children's posture are variations of normal alignment in the growing skeleton.
- Early management of talipes equinovarus usually avoids the need for surgery.
- Limp has a wide differential diagnosis.
- Juvenile idiopathic arthritis (JIA) is the most common cause of chronic arthritis in children.

Assessment of the musculoskeletal system

This should, as a minimum, include the pGALS assessment (see Ch. 2, History and examination) to identify and localize musculoskeletal problems; any suggestion of a musculoskeletal problem should be followed by more detailed regional musculoskeletal examination (pREMS, see Ch. 2).

Variations of normal posture

Variations are common and may be noticed by parents or on routine developmental surveillance. Most resolve without any treatment but if severe, progressive, painful, functionally limiting or asymmetrical, they should be referred for a specialist opinion.

Bow legs (genu varum) and knock-knees (genu valgum)

Leg alignment in young children may initially include a degree of bowing of the tibiae, causing the knees to be wide apart (genu varum) – best observed while the child

is standing with the feet together (Fig. 28.1). There are pathological causes of bow legs which include nutritional rickets; check for the presence of other clinical features (see Ch. 13, Nutrition), other metabolic bone diseases and skeletal dysplasias such as achondroplasia. Severe progressive and often unilateral bow legs is a feature of Blount disease (infantile tibia vara), an uncommon condition with Black African ethnicity and obesity as risk factors; radiographs are characteristic with beaking of the proximal medial epiphysis.

Genu valgum is when the feet are wide apart when standing with the knees held together (Fig. 28.2). Physiologic genu valgum is the commonest cause, and maximum valgus is reached around 5 years of age and resolves spontaneously. An intermalleolar distance of greater than 8 cm is suggestive of a pathologic cause such as post-trauma (fracture of growth plates) or metabolic bone disorders.

Flat feet (pes planus)

Toddlers learning to walk usually have flat feet due to flatness of the medial longitudinal arch and the presence of a fat pad which disappears as the child gets older (Fig. 28.3). An arch can usually be demonstrated on standing on tiptoe or by passively extending the big toe. Marked flat feet are common in hypermobility. A fixed flat foot (with or without pain) presenting in older children with absence of an arch on tip-toeing may indicate an associated tendo-Achilles contracture, tarsal coalition or inflammatory arthropathy (JIA), and referral to paediatric rheumatology or a paediatric orthopaedic surgeon is indicated. Painful, mobile flat feet are often helped by footwear advice and, occasionally, an arch support may be useful.

In-toeing

There are three main causes of in-toeing:

- metatarsus adductus* (Fig. 28.4a) – an adduction deformity of a highly mobile forefoot, resulting in a kidney bean-shaped foot

Variants of normal

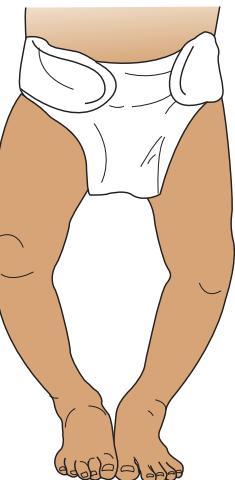


Figure 28.1 Bow legs.
Common in toddlers.

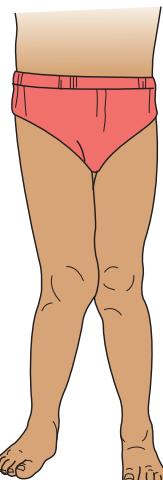


Figure 28.2 Knock-knees.

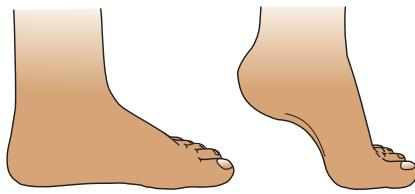
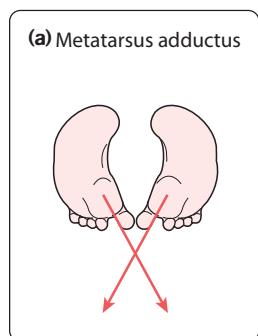
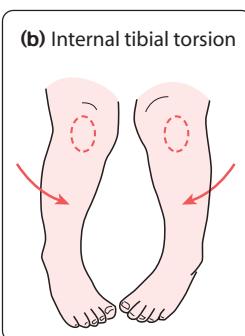


Figure 28.3 Pes planus showing the flat feet of toddlers. The medial longitudinal arch appears on standing on tiptoe.

In-toeing



(a) Metatarsus adductus



(b) Internal tibial torsion

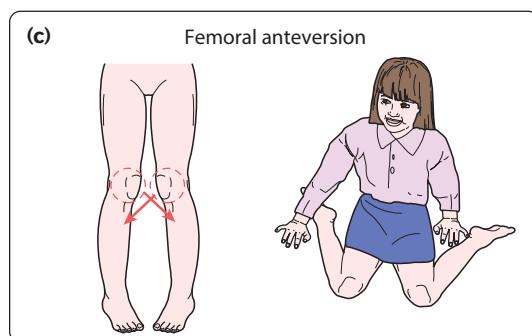


Figure 28.4 In-toeing (a) at the feet; (b) lower leg; and (c) hip, with 'W' sitting.

Box 28.1 Clinical features of in-toeing in children

Metatarsus adductus

- Occurs in infants
- Passively correctable
- Heel is held in the normal position
- No treatment required unless it persists beyond 5 years of age and is symptomatic

Internal tibial torsion

- Occurs in toddlers
- May be associated with bowing of the tibiae
- Self-corrects within about 5 years

Femoral anteversion

- Presents in childhood
- Usually self-corrects by 8 years of age
- May be associated with hypermobility of the joints
- Children sit between their feet with the hips fully internally rotated ('W' sitting)
- Most do not require treatment but femoral osteotomy may be required for persistent anteversion

- *internal tibial torsion* (Fig. 28.4b) – at the lower leg, when the tibia is laterally rotated less than normal in relation to the femur; when standing the feet point inwards while the patella points straight or outwards
- *persistent anteversion of the femoral neck* (Fig. 28.4c) – at the hip, when the femoral neck is twisted forward more than normal; when standing the patella points inwards.

The clinical features are described in Box 28.1.

Toe walking

Common in young children and may become persistent, usually from habit. The child can walk normally on request. Habitual toe walking needs to be distinguished from

Summary

Variations of musculoskeletal normality and differential diagnosis

Perceived disorder	Normal age range	Differential diagnoses to consider
Bow legs	1–3 years	Rickets, osteogenesis imperfecta, Blount disease
Knock-knees	2–7 years	Juvenile idiopathic arthritis (JIA)
Flat feet	1–2 years	Hypermobility, congenital tarsal fusion
In-toeing	1–2 years	Tibial torsion, femoral anteversion
Toe walking	1–3 years	Spastic diplegia, muscular dystrophy, JIA, mucopolysaccharidosis

mild cerebral palsy, tightness of the Achilles tendons, or inflammatory arthritis in the foot or ankle. In older boys, Duchenne muscular dystrophy should be excluded.

Abnormal posture

Talipes equinovarus (clubfoot)

Positional talipes from intrauterine compression is common. The foot is of normal size, the deformity is mild, and it can be corrected to the neutral position with passive manipulation (see Fig. 10.15). Often the baby's intrauterine posture can be recreated. If the positional deformity is marked, parents can be shown passive exercises by the physiotherapist.

Talipes equinovarus is a complex abnormality (Fig. 28.5, Fig. 28.6). The entire foot is inverted and supinated, the forefoot is adducted, and the heel is rotated inwards and in plantar flexion. The affected foot is shorter and the calf muscles thinner than normal. The position of the foot is fixed, cannot be corrected completely and is often bilateral. The birth prevalence is 1 per 1000 live births, affects predominantly males (2:1), can be familial but is usually idiopathic. However, it may also be secondary to oligohydramnios during pregnancy, a feature of a malformation syndrome or of a neuromuscular disorder such as spina bifida. There is an association with developmental dysplasia of the hip (DDH).

Treatment is started promptly with plaster casting and bracing ('Ponsetti method'), which may be required for many months and results in a successful outcome for most infants, with a minority requiring corrective surgery if the changes are severe.

Summary

Regarding talipes equinovarus:

- Needs to be differentiated from positional talipes.
- Check for neuromuscular disorder or spinal lesion and for developmental dysplasia of the hip (DDH).
- Early plaster casting and bracing (Ponsetti method) usually avoids the need for surgery, and has been adopted worldwide.

Talipes

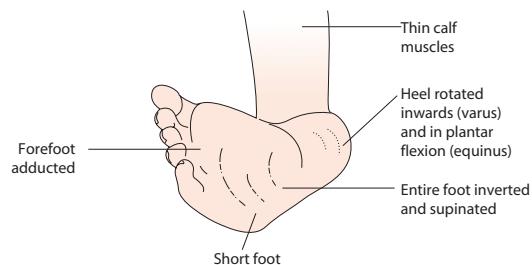


Figure 28.5 Abnormalities in talipes equinovarus.



Figure 28.6 Talipes equinovarus.

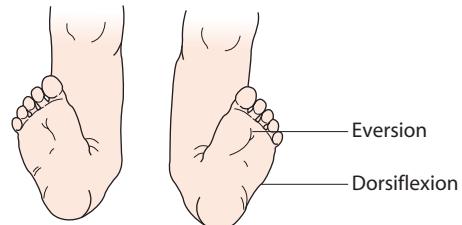


Figure 28.7 Talipes calcaneovalgus.

Vertical talus

Talipes equinovarus needs to be differentiated from the rare congenital vertical talus, where the foot is stiff and rocker-bottom in shape. Many of these infants have neuromuscular and genetic disorders. The diagnosis can be confirmed on X-ray. Surgery is usually required.

Talipes calcaneovalgus

The foot is dorsiflexed and everted (Fig. 28.7). It usually results from intrauterine moulding and self-corrects. Passive foot exercises are sometimes advised. There is an association with DDH (developmental dysplasia of the hip).

Tarsal coalition

This results from lack of segmentation between one or more bones of the foot and coalitions (fibrous or cartilaginous abnormal connections) become symptomatic as they begin to ossify. The foot becomes progressively more rigid with limited foot motion. The feet often become more symptomatic during the preadolescent years. Radiographs may be normal if the coalitions have not yet ossified. Corrective surgery may be required, but treatment is not indicated if coalition is asymptomatic.

Pes cavus

In pes cavus, there is an abnormally elevated longitudinal arch. When it presents in older children, it is often associated with neuromuscular disorders, e.g. Friedreich ataxia and type I hereditary motor sensory neuropathy (peroneal muscular atrophy). Treatment is required if the foot becomes stiff or painful.

Developmental dysplasia of the hip (DDH)

This is a spectrum of disorders ranging from dysplasia to subluxation through to frank dislocation of the hip. Early detection is important as it usually responds to conservative treatment; late diagnosis is usually associated with hip dysplasia, which requires complex treatment often including surgery. It is uncommon for infants and young children with DDH to have any pain or other limitations. Neonatal screening is performed as part of the routine neonatal and infant physical examination (NIPE) (see Fig. 10.19), checking if the hip can be dislocated posteriorly out of the acetabulum (Barlow manoeuvre) or can be relocated back into the acetabulum on abduction (Ortolani manoeuvre), where the sensation of relocation is distinct and usually described as a 'clunk'. These tests are repeated at routine NIPE surveillance at 8 weeks of age. Thereafter, presentation of the condition is usually with a limp or abnormal gait. It may be identified from asymmetry of skinfolds around the hip, limited abduction of the hip or shortening of the affected leg in unilateral cases, but this may not be apparent if the condition is bilateral. In walking children with unilateral DDH, a Trendelenburg pelvic test (when standing on the affected leg, the pelvis drops on the opposite side due to weakness of hip abductors) may be positive.

On neonatal screening, an abnormality of the hip is detected in about 6–10 per 1000 live births. Most will resolve spontaneously. The true birth prevalence of DDH is about 1.3 per 1000 live births. Clinical neonatal screening misses some cases. This may be because of inexperience of the examiner, but in some it is not possible to clinically detect dislocation at this stage, e.g. where there is only a mildly shallow acetabulum. If developmental

dysplasia of the hip is suspected on clinical examination, a specialist orthopaedic opinion should be obtained. An ultrasound is indicated if there is clinical suspicion of hip instability, inconclusive hip examination, or in the presence of risk factors (family history of DDH, breech presentation at ≥ 34 weeks' gestation). It is the main technique to assess the morphology and stability of the hip joint in an infant. In some countries routine ultrasound screening of all babies is performed, but is not recommended in the UK as it is expensive and has a high rate of false positives.

The main goal of treatment is to maintain reduction of the hip to allow development of the femoral head and the acetabulum. If indicated, the infant may be placed in a splint or harness to keep the hip flexed and abducted for several months. Progress is monitored by repeat ultrasound or X-ray. The splintage must be done expertly as necrosis of the femoral head is a potential complication. In most instances, a satisfactory response is obtained. Surgery is required if conservative measures fail.

Scoliosis

Scoliosis is a lateral curvature in the frontal plane of the spine.

In structural scoliosis, there is rotation of the vertebral bodies which causes a prominence in the back from rib asymmetry. In most cases, the changes are mild, pain-free and primarily a cosmetic problem; however, in severe cases, the spinal curvature can lead to cardiopulmonary compromise. Clinical evaluation of scoliosis should include the underlying cause, magnitude of the curvature and determine the risk of progression.

Causes of scoliosis are:

- *Idiopathic* – the most common, either early onset (<5 years old) or, most often, late onset, mainly girls 10–14 years of age during their pubertal growth spurt.
- *Congenital* – from a congenital structural defect of the spine, e.g. hemivertebra, spina bifida, syndromes, e.g. vertebral, anorectal, cardiac, tracheo-oesophageal, renal and limb (VACTERL) anomalies association.
- *Secondary* – related to other disorders such as neuromuscular imbalance (e.g. cerebral palsy, muscular dystrophy); disorders of bone such as neurofibromatosis or of connective tissues such as Marfan syndrome, or leg length discrepancy, e.g. due to arthritis of one knee in juvenile idiopathic arthritis.

Examination should start with inspection of the child's back while standing up straight. In mild scoliosis, there may be irregular skin creases and difference in shoulder height. The scoliosis can be identified on examining the child's back when bent forward (Fig. 28.8). If the scoliosis disappears on forward bending, it is postural although leg lengths should be checked (Fig. 28.9).

Mild scoliosis will resolve spontaneously, or progresses minimally. If more severe, the severity and progression of the curvature of the spine is determined by X-ray. Severe cases are managed in specialist spinal centres where the place of non-medical treatment such as bracing will be considered, with surgery indicated only if severe or there is coexisting pathology such as neuromuscular or respiratory disease.

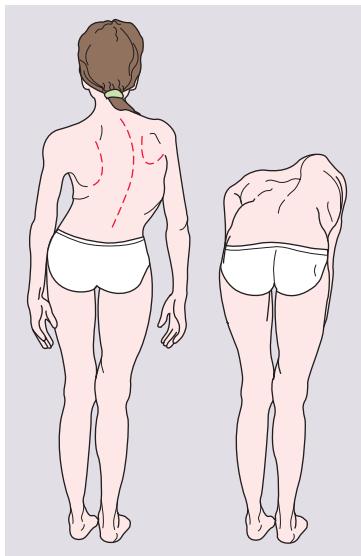


Figure 28.8 Structural scoliosis with vertebral rotation shown by rib rotation on bending forward.

Torticollis

The most common cause of torticollis (wry neck) in infants is a sternomastoid tumour (congenital muscular torticollis). They occur in the first few weeks of life and present with a mobile, non-tender nodule, which can be felt within the body of the sternocleidomastoid muscle. There may be restriction of head turning and tilting of the head. The condition usually resolves in 2–6 months. Passive stretching is advised, but its efficacy is unproven.

The most common acquired cause of torticollis presenting later in childhood is injury or inflammation of the sternocleidomastoid or trapezius muscle groups or acute infections of the ear, nose or throat; other causes include spinal tumour (such as osteoid osteoma), atlanto-axial subluxation and posterior fossa tumour.

The painful limb, knee, and back

Growing pains

Episodes of generalized pain in the lower limbs, referred to as ‘growing pains’ or nocturnal idiopathic pain, are common in preschool and school-age children. The pain often wakes the child from sleep and settles with massage or comforting. There is no consensus for its definition, but the following clinical features are commonly seen and often referred to as the ‘Rules of Growing Pains’:

- age range 3–12 years
- bilateral, symmetrical, mainly in lower limbs and not limited to joints
- pains never present at the start of the day after waking
- physical activities are not limited; no limp
- physical examination normal (including pGALS), with the exception of joint hypermobility in some joints, and otherwise well.

If the presentation ‘does not fit the Rules’, then further assessment is necessary. In addition to massage, heat or



Figure 28.9 Measurement of leg length between the anterior superior iliac spine and the medial malleolus.



Figure 28.10 Hypermobility syndrome, showing ability of a mother and two of her children to hyperextend the thumb onto the forearm.

simple analgesia such as paracetamol may be helpful. Explanation and reassurance are required as well as advice on supportive footwear (e.g. trainer shoes require shoe laces properly fastened).

Hypermobility

Older children or adolescents with hypermobility may complain of musculoskeletal pain, often worse after exercise. Joint swelling is usually absent or is transient. Hypermobility may be generalized or limited to peripheral joints (such as hands and feet). Signs may include symmetrical hyperextension of the thumbs and fingers that can be hyperextended onto the forearms (Fig. 28.10), elbows and knees can be hyperextended beyond 10°, and palms can be placed flat on the floor with knees straight. In addition, flat feet may be seen with normal arches on tiptoe, which are over-pronated secondary to ankle hypermobility.

While mild degrees of hypermobility are a normal finding in younger children, and many children with hypermobility are asymptomatic and find being very flexible an advantage in dancing and gymnastics, some children, young people and adults experience recurrent mechanical joint and muscle pain, which is often activity related. Treatment should be individualized depending on the symptoms. This may include specialist assessment with advice about footwear, exercises and occasionally orthotics. Hypermobility is also a feature of some chromosomal syndromes, e.g. Down syndrome, and some inherited collagen disorders (e.g. Marfan and Ehlers–Danlos syndrome).

Complex regional pain syndromes

The most dramatic musculoskeletal pain is that encountered in complex regional pain syndromes (CRPS), which is a presentation of persistent unexplained physical symptoms (PUS) (see Ch 24, Child and Adolescent Mental Health). It is characterized by severe pain that is out of proportion to the history and physical findings and is often accompanied by one or more autonomic signs. In contrast to adults, an initial physical injury may be absent. It is more common in adolescent females.

Localized forms often present with foot and ankle involvement (typically unilateral); the pain can be extreme and incapacitating, often triggered by minor trauma or without a clear precipitant. Presentation to the clinic may be in a wheelchair. In addition to severe pain, there may be hyperaesthesia (increased sensitivity to stimuli), allodynia (pain from a stimulus that does not normally produce pain), and the affected part (often a foot or hand) may be cool to touch, be swollen and mottled, held in flexion with minimal if any active movement, and bizarre posturing is not uncommon. Typically, with distraction, the normal range of passive movements is possible.

Diffuse forms are characterized by severe widespread pain with disturbed sleep patterns, feeling exhausted during the day, with extreme tenderness over soft tissues. The characteristic tender points that are found in adults with fibromyalgia may be absent or fewer in number in children.

The child or adolescent with complex regional pain is otherwise well and physical examination is otherwise normal.

No laboratory or imaging studies can confirm or exclude the disorder. The aetiology is unknown. The mind/body link in chronic pain is considered in detail in Chapter 24 (Child and adolescent mental health).

A multidisciplinary rehabilitation regimen is required, predominantly physical therapy-based, either community or inpatient. The goal of treatment is to restore function and relieve pain, along with assisting children to develop skills to cope with any residual pain.

Acute-onset limb pain

Limb pain of acute onset has a number of causes. Trauma is the most common, usually accidental from sports injuries or falls, but occasionally non-accidental. Osteomyelitis, bone tumours and septic arthritis are uncommon but need urgent treatment.

Osteomyelitis

In osteomyelitis, there is infection of the metaphysis of long bones. The most common sites are the distal femur and proximal tibia, but any bone may be affected (Fig. 28.11). It is usually due to haematogenous spread of the pathogen, but may arise by direct spread from an infected wound. The skin is swollen directly over the affected site. Where the joint capsule is inserted distal to the epiphyseal plate, as in the hip, osteomyelitis may spread to cause septic arthritis. Most infections are caused by *Staphylococcus aureus*, but other pathogens include *Streptococcus*, *Haemophilus influenzae* and *Kingella kingae*; *Haemophilus influenzae* is now uncommon due to routine vaccination, but some serotypes of streptococcus pneumonia not included in the pneumococcal conjugate vaccine may be a pathogen. Risk factors

include sickle cell anaemia and immunodeficiency. In sickle cell anaemia, there is an increased risk of staphylococcal and salmonella osteomyelitis. Tuberculous and non-tuberculous mycobacteria are uncommon in the UK, but need to be considered, especially in children with immunodeficiency.

Presentation

Initial symptoms are often non-specific, such as low-grade pyrexia or malaise. Once the infection becomes established in a bone, it presents with a markedly painful, immobile limb (*pseudoparesis*) in a child with an acute febrile illness. There may be localized findings of bone inflammation such as tenderness, warmth and swelling. Moving the affected limb usually causes severe pain. There may be a sterile effusion of an adjacent joint. In infants, presentation may be more insidious, and bone infection can spread to the adjacent soft tissues and the limb may be swollen or have reduced movement. If the infection affects the vertebral bodies, children present with dull, constant back pain and tenderness with percussion over the affected vertebrae.

Investigation

Blood cultures should always be taken although they are not always positive. The white blood count, erythrocyte sedimentation rate and C-reactive protein are raised. X-rays may be initially normal, other than showing soft tissue swelling; it takes 7–10 days for a periosteal reaction, from new bone formation or oedema to become visible. Magnetic resonance imaging (MRI) can detect inflammation earlier than plain radiographs, and allows differentiation of bone from soft tissue infection (Fig. 28.12). The X-ray changes of chronic osteomyelitis are shown in Fig. 28.13. Lytic sclerotic lesions are suggestive of a chronic infection.

Treatment

Prompt treatment with parenteral antibiotics based on the most likely pathogen and the child's age is indicated, subsequently adjusted according to antimicrobial sensitivity. Aspiration or surgical decompression of the subperiosteal space may be performed if the presentation is atypical or in immunodeficient children. Clinical improvement should occur in a few days, and reduction in acute phase reactants can be used to monitor progress and change to oral antibiotics. Failure to improve suggests a complication such as a periosteal abscess or antimicrobial resistance, and surgical drainage may be required. The affected limb is initially rested in a splint, especially when bone involvement is extensive, to prevent pathological fractures.

Summary

Osteomyelitis

- Presents with fever, a painful, immobile limb, swelling and extreme tenderness, especially on moving the limb.
- Blood cultures are usually positive, but may be negative.
- Parenteral antibiotics must be given immediately.
- Surgical drainage is indicated if unresponsive to antibiotic therapy.

Osteomyelitis

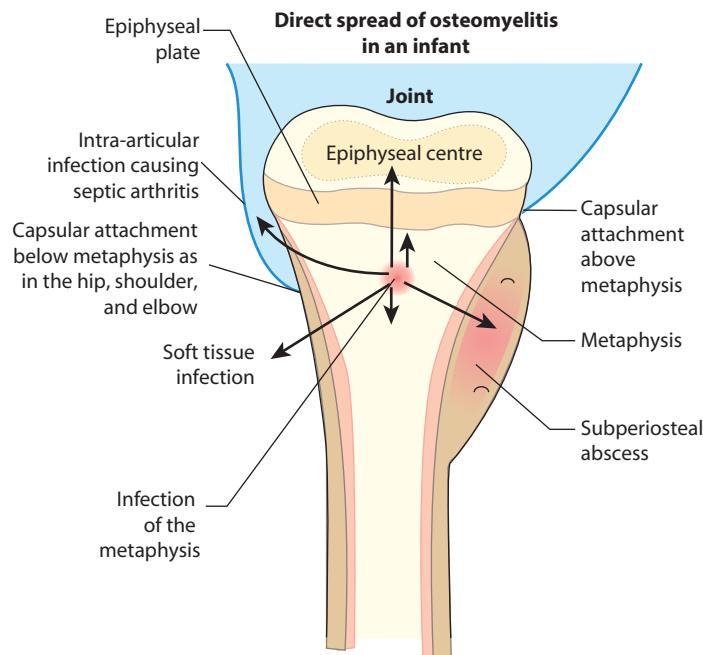


Figure 28.11 Possible spread of osteomyelitis. In children, the epiphyseal growth plate limits the spread of metaphyseal infection. In infants, before there has been maturation of the growth plate, infection can spread directly to cause joint destruction and arrested growth.

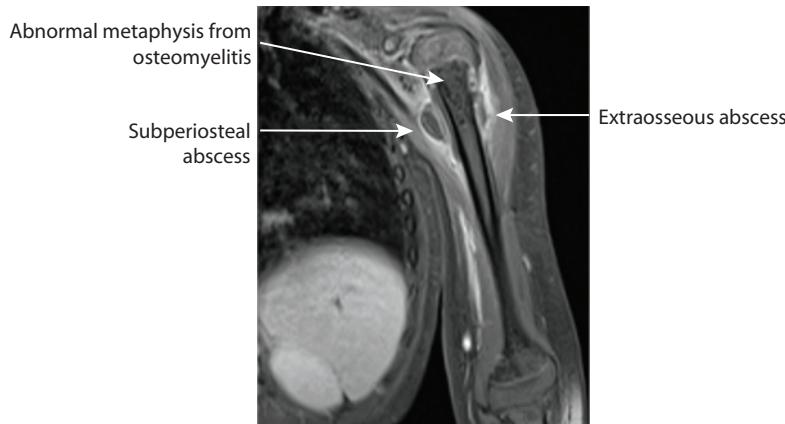


Fig. 28.12 An MRI contrast scan in osteomyelitis at the metaphysis of the proximal humerus showing abnormal metaphysis and a subperiosteal and extraosseous abscess. (Courtesy of Dr Raj Sinha.)



Figure 28.13 Chronic osteomyelitis, showing periosteal reaction along the lateral shaft of the tibia and multiple hypodense areas within the metaphyseal regions.

Malignant disease

Acute lymphoblastic leukaemia may present with bone pain in children (sometimes primarily at night) and even frank arthritis. Neuroblastoma, usually in young children, may present with systemic arthritis or bone pain from metastases which may be difficult to localize.

Bone tumours

Malignant bone tumours – osteogenic sarcoma and Ewing tumour – are rare. They present with pain or swelling, or

occasionally with a pathological fracture. Radiographs of a joint should include the long bone above and below it, especially with knee pain, as distal femur and proximal tibia are the most common sites for malignant bone tumours. Further features are considered in Chapter 22 (Malignant disease).

Osteoid osteoma is a benign tumour affecting adolescents, especially boys, usually involving the femur, tibia, or spine. The pain is progressive and typically worse at night and relieved by nonsteroidal anti-inflammatory drug (NSAID) therapy. There may be some localized tenderness,

The painful knee

When assessing a painful knee, the hip must always be examined, as hip pain is often referred to the knee.

Osgood–Schlatter disease

This is an osteochondritis of the patellar tendon insertion at the tibial tuberosity in the knee, often affecting adolescent males and caused by repetitive strain from overuse in activities such as football or basketball. Presentation is usually with anterior knee pain after exercise, localized tenderness and sometimes swelling over the tibial tuberosity. There is often hamstring tightness. It is bilateral in 25%–50% of cases. This is a self-limiting condition that usually resolves with ossification of the growth plate. Mild analgesics, reduced impact activity, and physiotherapy to strengthen the quadriceps muscles may be helpful.

Chondromalacia patellae

There is softening of the articular cartilage of the patella. It most often affects adolescent females, causing pain when the patella is tightly apposed to the femoral condyles, as in standing up from sitting or on walking up stairs. It is often associated with hypermobility and flat feet, suggesting a biomechanical component to its aetiology. Treatment is with physiotherapy for quadriceps muscle strengthening.

Osteochondritis dissecans (segmental avascular necrosis of the subchondral bone)

This presents with pain in the knee, elbow or ankle made worse with physical activity, often in physically active adolescents. The knee may lock or give way. Pain is caused by separation of a segment of subchondral bone and articular cartilage from the underlying bone, following avascular necrosis. Plain radiographs should be performed. Complete separation of articular fragments may result in loose body formation but radiographs may be normal with small lesions. Treatment is initially with restriction of activities and immobilization followed by physiotherapy. Surgical treatment is recommended for a loose foreign body or if unresponsive to medical treatments.

Subluxation and dislocation of the patella

Subluxation of the patella refers to excessive lateral movements of the patella and produces the feeling of instability or giving way of the knee. It is often associated with generalized hypermobility and a high-riding patella. The patella apprehension test (apprehension and contraction of quadriceps when the examiner pushes the patella laterally) is usually positive. Rarely, dislocation of the patella can occur, usually laterally, suddenly and with severe pain – reduction

occurs spontaneously or on gentle extension of the knee. Treatment is with physiotherapy focusing on quadriceps exercises and orthotics to address biomechanical changes and misalignment. Sometimes surgery is required to realign the pull of the quadriceps on the patellar tendon.

Injuries

Contact sports characteristically result in acute injuries to the knee, while non-contact sports with sustained activity tend to result in chronic injury and overuse syndromes. Sporting injuries to the menisci and ligaments are common in adolescents. MRI scans are helpful to determine the extent of damage. Management is usually conservative. In infants and young children, similar injuries are more likely to result in fractures, as their ligaments are relatively stronger than their bones.

Back pain

Back pain is a symptom of concern in the very young and preadolescent ages as, in contrast to adults, a cause can often be identified. The younger the child, the more likely there will be significant pathology. Red flag clinical features are listed in **Box 28.2**.

- *Mechanical causes* – there may be muscle spasm or soft tissue pain from injury, often sport-related or from poor posture or abnormal loading (such as carrying heavy school bags on one shoulder).
- *Tumours: benign or malignant* – the spine is a common site for osteoid osteoma. It may also be the site of primary tumours or metastases.
- *Vertebral osteomyelitis or discitis* – there is localized tenderness. Plain X-rays are usually normal at start of the illness; further imaging (MRI) is often required. Treatment is with intravenous antibiotics.
- *Spinal cord or nerve root entrapment* – from tumour or prolapsed intervertebral disc – often associated with trauma or heavy lifting.
- *Scheuermann disease* – this is an osteochondrosis affecting the thoraco-lumbar spine in which there is wedging of some vertebral bodies from the posterior part of the vertebrae growing more than the anterior. Presentation is in early adolescence with subacute back pain made worse with activity. Those with kyphosis have a sharp angulation of the spine on bending over. The diagnosis is usually made on

Box 28.2 Red flag clinical features of back pain

- Young age (< 5 years) – pathology more likely
- Fever and malaise – vertebral osteomyelitis
- Night waking, persistent pain – osteoid osteoma or intramedullary/extradural tumours
- Painful scoliosis – infection or malignancy
- Focal neurological signs including asymmetric reflexes, weakness, bowel or bladder dysfunction – nerve root/spinal cord compression, tethered cord
- Morning stiffness – inflammatory arthritis
- Acute trauma and pain radiation to buttocks – intervertebral disc herniation
- Associated weight loss, systemic malaise – malignancy.

- X-ray. In many cases, the radiographic changes are a coincidental finding and the patient is asymptomatic.
- Spondylolysis/spondylolisthesis** – stress fracture of the pars interarticularis of the vertebra. Increased risk with activities that require repetitive flexion/extension or hyperextension of the spine, such as in gymnastics or bowlers in cricket. If bilateral it can result in spondylolisthesis, forward slip of the vertebral body, and potential cord or nerve root compression. Consider in adolescents with low back pain exacerbated on hyperextension of the spine and localized tenderness. May be apparent on X-ray but often further imaging is required.
- Chronic pain syndrome** – diagnosed when no physical cause is found; may be exacerbated by psychological stress.
- Abdominal pathologies** – such as pancreatitis can present with back pain, usually accompanying abdominal symptoms and signs.

Limp

Limp can be divided into acute painful limp and chronic or intermittent limp, where pain may or may not be the presenting feature, and by age (Table 28.1).

Transient synovitis ('irritable hip')

This is the most common cause of acute hip pain in children. It occurs in children aged 2–12 years old. It often follows or is accompanied by a viral infection. Presentation is with sudden onset of pain in the hip or a limp. There is no pain at rest, but there is decreased range of movement, particularly

internal rotation. The pain may be referred to the knee. The child is afebrile or has a mild fever and does not appear ill.

It can be difficult to differentiate transient synovitis from early septic arthritis of the hip joint (Table 28.2), and if there is any suspicion of septic arthritis, joint aspiration and blood cultures are mandatory. The Kocher criteria are a useful tool in differentiating septic arthritis from transient arthritis in a child with painful hip (Box 28.3). Radiological imaging may identify synovitis (Fig. 28.14) and exclude other causes, but is usually not required.

Management of transient synovitis is with bed rest and, rarely, skin traction. It usually improves within a few days.

Legg–Calve–Perthes disease

This is an avascular necrosis of the capital femoral epiphysis of the femoral head due to interruption of the blood supply, followed by revascularization and reossification over 18–36 months. It mainly affects boys (male:female ratio of 4:1) of 5–10 years of age and is associated with obesity. Presentation is insidious, with the onset of a limp, or hip or knee pain. The condition may initially be mistaken for transient synovitis. It is bilateral in 10%–20%. If suspected, X-ray of both hips (including frog views) should be requested, but may be normal early in the disease. MRI may assist with making the diagnosis. In later stages of the disease, X-rays show increased density in the femoral head, which subsequently becomes fragmented and can leave residual deformity (Fig. 28.15).

Treatment involves physiotherapy initially to optimize the range of movement. Sometimes surgery is required. In most children the prognosis is good, particularly in those below 6 years of age with less than half the epiphysis involved. In older children or with more extensive involvement of the epiphysis, deformity of the femoral head and

Table 28.1 Causes of limp

Age	Acute painful limp	Chronic and intermittent limp
1–3 years	Infection – septic arthritis, osteomyelitis of hip or spine Transient synovitis Trauma – accidental/non-accidental Malignant disease – leukaemia, neuroblastoma	Developmental dysplasia of the hip (DDH), talipes Neuromuscular, e.g. cerebral palsy Juvenile idiopathic arthritis (JIA) Perthes disease (chronic)
3–10 years	Transient synovitis Septic arthritis/osteomyelitis Trauma and overuse injuries Perthes disease (acute) Juvenile idiopathic arthritis (JIA) Malignant disease, e.g. leukaemia Complex regional pain syndrome	Neuromuscular disorders, e.g. Duchenne muscular dystrophy Juvenile idiopathic arthritis (JIA) Tarsal coalition
11–16 years	Mechanical – trauma, overuse injuries, sport injuries Slipped capital femoral epiphysis (acute) Avascular necrosis of the femoral head Reactive arthritis Juvenile idiopathic arthritis (JIA) Septic arthritis/osteomyelitis Osteochondritis dissecans of the knee Bone tumours and malignancy Complex regional pain syndrome	Slipped capital femoral epiphysis (chronic) Juvenile idiopathic arthritis (JIA) Tarsal coalition

Transient synovitis

Table 28.2 Contrast in clinical features of transient synovitis and septic arthritis of the hip

	Transient synovitis	Septic arthritis
Onset	Acute limp, non-weight-bearing	Acute onset, non-weight-bearing
Fever	Mild/absent	Moderate/high
Child's appearance	Child often looks well	Child looks ill
Hip movement	Comfortable at rest, limited internal rotation and pain on movement	Hip held flexed; severe pain at rest and worse on any attempt to move joint
White cell count	Normal	Normal/high
Acute-phase reactant/ESR	Slight increase/normal	Raised
Ultrasound	Fluid in joint	Fluid in joint
Radiograph	Normal	Normal/widened joint space
Management	Rest, analgesia	Joint aspiration, usually under ultrasound guidance Prolonged antibiotics, rest and analgesia
Course	Resolves <1 week, approx.	Progressive and severe joint damage if not treated

Box 28.3 Kocher criteria for differentiating septic arthritis from transient synovitis in a child with irritable hip

Score	Likelihood of septic arthritis
1	3%
2	40%
3	93%
4	99%

A point is given for each of the four criteria: non-weight-bearing on affected side; erythrocyte sedimentation rate >40 ; fever $>38.5^{\circ}\text{C}$; and white blood cell count $>12,000$.

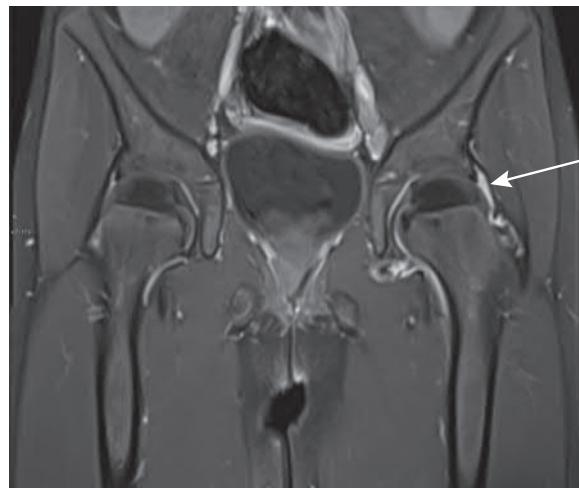


Figure 28.14 MRI scan (post contrast coronal T1 fat saturated) that demonstrates the enhancing synovium in the left hip (arrow) suggesting synovitis. Synovitis can be seen in both transient synovitis and early septic arthritis; they need to be differentiated by clinical examination and blood test results. (Courtesy of Dr Raj Sinha.)



Figure 28.15 Perthes disease, showing flattening with sclerosis and fragmentation of the right femoral capital epiphysis (arrow); the left hip is normal.

metaphyseal damage are more likely, with potential for subsequent degenerative arthritis in adult life.

Slipped capital femoral epiphysis (SCFE)

Displacement of the epiphysis of the femoral head postero-inferiorly requires prompt treatment to prevent avascular necrosis. It is most common at 10–15 years of age during the adolescent growth spurt, particularly in obese boys, and is bilateral in 20%. There is an association with metabolic endocrine abnormalities, e.g. hypothyroidism and hypogonadism. Presentation is with a limp or pain in the hip or referred to the knee. The onset may be acute, following minor trauma, or insidious. Examination shows restricted abduction and internal rotation of the hip. Diagnosis is confirmed on X-ray (Fig. 28.16); a frog lateral view should be requested. If there is high index of suspicion and X-rays are normal, MRI may demonstrate early



Figure 28.16 Slipped capital femoral epiphysis of the right hip.

SCFE and may sometimes detect features consistent with a risk of slipping in the contralateral hip. Management is primarily surgical stabilization – usually with pin fixation *in situ*; prophylactic pinning of contralateral side is performed by some surgeons. Physiotherapy following stabilization is essential to optimize the range of movement and return to normal activities.

Summary

Regarding hip disorders

- Developmental dysplasia of the hip (DDH) – may be identified on neonatal and infant physical examination (NIPE) screening at birth and 8 weeks, thereafter, by detection of asymmetry of skinfolds around the hip, limited abduction of the hip, shortening of the affected leg, or a limp or abnormal gait.
- Transient synovitis – most common cause of acute hip pain or a limp; must be differentiated from septic arthritis.
- Legg–Calve–Perthes disease – usually school-age children with hip pain or limp.
- Slipped capital femoral epiphysis – adolescent with a limp or hip pain.

Arthritis

Acute arthritis presents with pain, swelling, heat, redness and restricted movement in a joint. In a monoarthritis of acute onset, consider septic arthritis or osteomyelitis if the child is systemically unwell with fever, as urgent diagnosis and treatment is required. With infection, more than one joint can be affected, although a single joint is more common. The causes of polyarthritis are listed in [Table 28.3](#).

Reactive arthritis

Reactive arthritis is the most common form of arthritis in childhood. It is characterized by transient joint swelling (usually <6 weeks) often of the ankles or knees. It usually follows (or rarely accompanies) evidence of extra-articular infection. The enteric bacteria (*Salmonella*, *Shigella*,

Table 28.3 Causes of polyarthritis

Infection	Bacterial – septicaemia/septic arthritis, TB Viral – rubella, mumps, adenovirus, coxsackie B, herpes, hepatitis, parvovirus Other – <i>Mycoplasma</i> , Lyme disease, rickettsia Reactive – gastrointestinal infection, streptococcal infection Rheumatic fever Crohn disease, ulcerative colitis
Inflammatory bowel disease	
Vasculitis	Henoch–Schönlein purpura, Kawasaki disease
Haematological disorders	Haemophilia, sickle cell disease
Malignant disorders	Leukaemia, neuroblastoma
Connective tissue disorders	Juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), dermatomyositis, mixed connective tissue disease (MCTD), polyarteritis nodosa (PAN)
Other	Cystic fibrosis

Campylobacter and *Yersinia*) are often the cause in children, but viral infections, sexually transmitted infections in adolescents (chlamydia, gonococcus), *Mycoplasma* and *Borrelia burgdorferi* (Lyme disease) and post-streptococcal reactive arthritis are other causes. Fever is low grade, acute-phase reactants are normal or mildly elevated, and X-rays are normal. Analgesics and NSAIDs are required, and complete recovery can usually be anticipated. Rheumatic fever is uncommon in high-income countries but frequent in many low- and middle-income countries and is described in [Chapter 18](#) (Cardiac disorders).

Septic arthritis

This is a serious infection of the joint space by bacteria or fungi, as it can lead to bone destruction. It is most common in children less than 4 years old. It usually results from haematogenous spread but may also occur following a puncture wound or infected skin lesions, e.g. chickenpox. In young children, it may result from spread from adjacent osteomyelitis into joints where the capsule inserts below the epiphyseal growth plate. Usually only one joint is affected, particularly the hip, but also the knee and ankle. Beyond the neonatal period, the most common organism is *Staphylococcus aureus*. Other microbes include *Streptococci* and *Kingella kingae*; *H. influenzae* was an important cause in young children prior to immunization, and it often affected multiple sites. Underlying and predisposing illnesses such as immunodeficiency and sickle cell disease should be considered.

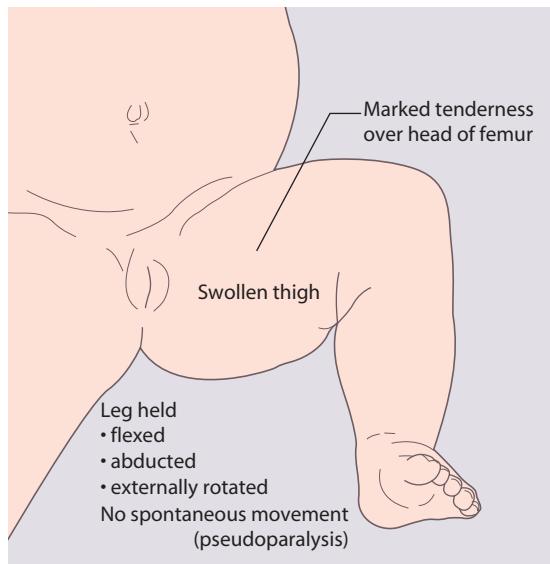


Figure 28.17 Septic arthritis of the hip in infants, showing the characteristic posture to reduce intracapsular pressure. Any leg movement is painful and is resisted.

Presentation

This is usually with an erythematous, warm, acutely tender joint, with a reduced range of movement, in an acutely unwell, febrile child. Infants often hold the limb still (pseudoparesis, pseudoparalysis) and cry if it is moved. A joint effusion may be detectable in peripheral joints. Although a sympathetic joint effusion may be present in osteomyelitis, in osteomyelitis it is accompanied by marked tenderness over the bone. However, in up to 15% of cases of osteomyelitis, there is co-existent septic arthritis. The diagnosis of septic arthritis of the hip can be particularly difficult in toddlers, as the joint is well covered by subcutaneous fat (Fig. 28.17). Initial presentation may be with a limp or pain referred to the knee.

Investigation and management

There is an increased white cell count and acute phase reactants. Blood cultures must be taken. Ultrasound of deep joints, such as the hip, is helpful to identify an effusion. X-rays are used to exclude trauma and other bony lesions. However, in septic arthritis, the X-rays are initially normal, apart from widening of the joint space and soft tissue swelling. Further imaging options include MRI scanning or a radioisotope bone scan may be indicated if the site of infection is unclear. Aspiration of synovial fluid should be done as soon as possible to identify the organisms and culture as the definitive investigation; this also decompresses the joint and provides symptom relief. Antibiotics should be started promptly and subsequently adjusted according to culture results; a prolonged course of antibiotics is required, initially intravenously. Washing out of the joint or surgical drainage may be required if resolution does not occur rapidly or if the joint is deep-seated, such as the hip. The joint is initially immobilized in a functional position, but subsequently must be mobilized to prevent permanent deformity.



Early treatment of septic arthritis is essential to prevent destruction of the articular cartilage and bone.

Juvenile idiopathic arthritis (JIA)

This is the commonest chronic inflammatory rheumatic condition in children and adolescents. It is defined as persistent joint swelling (of >6 weeks duration) presenting before 16 years of age in the absence of infection or any other defined cause. Most children have a disease that is clinically and immunogenetically distinct from rheumatoid arthritis in adults. It has a prevalence of approximately 1 in 1000 children (i.e. similar to epilepsy), with over 12,000 affected children in the UK and estimated over 2 million worldwide.

There are seven different subtypes of JIA. Each subtype and its clinical features are shown in Fig. 28.18. Classification is clinical and based on the number of joints affected in the first 6 months:

- oligoarthritis – up to and including four joints
- polyarthritis – more than four joints (Fig. 28.19)
- systemic – with fever and rash (see Case history 28.1).

Psoriatic arthritis and enthesitis (localized inflammation at insertion of tendons or ligaments into bone, often in feet) are further subtypes. Subtyping is further classified according to the presence of rheumatoid factor and HLA B27 tissue type.

Features in the history are gelling (stiffness after periods of rest, such as long car rides), morning joint stiffness, and pain. In the young child, it may present with intermittent limp or deterioration in behaviour or mood, or avoidance of previously enjoyed activities, rather than complaining of pain.

Initially, there may be only minimal evidence of joint swelling, but subsequently there may be swelling of the joint due to fluid within it, inflammation, chronic arthritis, proliferation (thickening) of the synovium and swelling of the periarticular soft tissues.

As the presentation can be indolent, especially in young children, and in the most common forms the baseline investigations are often initially normal (i.e. normal full blood count and inflammatory markers, negative rheumatoid factor and radiographs), diagnosis can be difficult (see Case history 28.2). Antinuclear factor may be present in children with JIA, but can also be present in healthy children or during transient illness. However, in any child with widespread joint pain, fatigue or multisystem involvement, the possibility of a connective tissue disorder (e.g. JIA or systemic lupus erythematosus) needs to be considered. Long term, with uncontrolled disease activity, there may be bone expansion from overgrowth, which in the knee may cause leg lengthening or valgus deformity; in the hands, discrepancy in digit length; and in the wrist, advancement of bone age.

If systemic features are present, sepsis and malignancy must always be considered.



If JIA is suspected, even if joint abnormality is not clear, referral to paediatric rheumatology is indicated as early treatment radically improves outcome.

Complications

Chronic anterior uveitis

This is common but usually asymptomatic in the early stages and, if not detected and treated, can lead to severe visual impairment due to cataract and glaucoma. Oligoarticular subtype, the presence of HLA-B27, and positive antinuclear antibody (ANA) are risk factors for

Subtype, typical age of onset and sex ratio (F:M)	Articular pattern	Extra-articular features	Laboratory abnormalities
Oligoarthritis (persistent) (49%) 1–6 years; F:M, 5:1	1–4 (max) joints involved Knee, ankle or wrist	Chronic anterior uveitis – 20% Leg length discrepancy Prognosis: excellent	ANA+/-
Oligoarthritis (extended) (8%) 1–6 years; F:M, 5:1	>4 joints involved after first 6 months. Asymmetrical distribution of large and small joints	Chronic anterior uveitis – 20% Asymmetrical growth Prognosis: moderate	ANA+/-
Polyarthritis (RF negative) (16%) 1–6 years; F:M, 5:1	Symmetrical large and small joint arthritis, often marked finger involvement Cervical spine and temporomandibular joint may be involved	Low-grade fever Chronic anterior uveitis – 5% Late reduction of growth Prognosis: moderate	
Polyarthritis (RF positive) (3%) 10–16 years; F:M, 5:1	Symmetrical large and small joint arthritis, often marked finger involvement	Rheumatoid nodules – 10% Similar to adult rheumatoid arthritis Prognosis: poor	RF+ (long term)
Systemic arthritis (9%) 1–10 years; M:F, 1:1	Oligoarthritis or polyarthritis. May have aches and pains in joints and muscles (arthralgia/myalgia) but initially no arthritis	Acute illness, malaise, high daily fever initially, with salmon-pink macular rash, lymphadenopathy, hepatosplenomegaly, serositis Prognosis: variable to poor	Anaemia, raised neutrophils and platelets, high acute-phase reactants
Psoriatic arthritis (7%) 1–16 years; M:F 1:1	Usually asymmetrical distribution of large and small joints, dactylitis	Psoriasis, nail pitting or dystrophy Chronic anterior uveitis – 20% Prognosis: moderate	
Enthesitis-related arthritis (7%) 6–16 years; M:F, 1:4	Lower limb, large joint arthritis initially Mild lumbar spine or sacroiliac involvement later	Enthesitis Occasional acute uveitis Prognosis moderate	HLAB27+

Fig. 28.18 Classification and clinical features of juvenile idiopathic arthritis (JIA). (ANF: Anti-Nuclear Factor; RF: Rheumatoid Factor. Enthesitis – localized inflammation at insertion of tendons or ligaments into bone, often in feet.)



Figure 28.19 Polyarticular juvenile idiopathic arthritis, showing swelling of the wrists, metacarpal, and interphalangeal joints, and early swan-neck deformities of the fingers.

JIA-associated uveitis. Regular ophthalmological screening using a slit lamp is indicated (Fig. 28.20).

Joint contractures and erosions

Chronic uncontrolled joint inflammation can lead to erosion of the articular cartilage which contributes to limitation of joint movement and functional impairment; joint destruction can lead to the need for joint replacement. Joint contracture (Fig. 28.21) is preventable with early diagnosis and treatment.

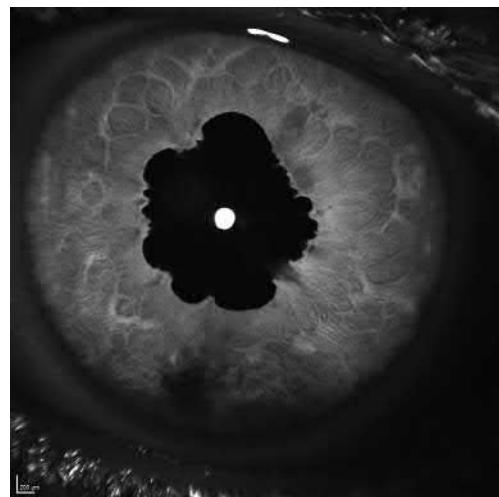


Figure 28.20 Chronic anterior uveitis associated with juvenile idiopathic arthritis. Near infrared light photograph showing extensive posterior synechiae resulting in small and irregular pupil. (Courtesy of Mr Alan Connor.)

Growth faltering

Uncontrolled joint inflammation can cause abnormal skeletal growth (Fig. 28.22). Overgrowth of the affected limb may occur due to increased blood flow accompanying inflammation. Joint inflammation can also lead to early



Figure 28.21 Swollen left knee in juvenile idiopathic arthritis. There is also flexion contracture of the knee.



Figure 28.22 Growth failure and marked genu valgum (knock-knees) in an 8-year-old girl with juvenile idiopathic arthritis. For comparison, her sister on the left is 4 years old. This can be prevented with early optimal management.

fusion of the growth plates in the affected limb resulting in undergrowth. Both processes can lead to limb-length discrepancies which can result in mechanical problems such as scoliosis. Systemic inflammation disease and steroids may also be associated with a generalized reduction in linear growth. Growth problems are largely preventable with early diagnosis and treatment.

Macrophage activation syndrome

The most serious complication of systemic JIA is macrophage activation syndrome (MAS), which occurs in 4%–13%. Presentation is acute, with continuous fever,

reduction in erythrocytes, leukocytes and platelets, abnormal clotting and multiple organ failure. Without early recognition and prompt treatment, it is life-threatening.

Constitutional problems

Anaemia of chronic disease, delayed puberty.

Osteoporosis

Multifactorial aetiology, including diet, reduced weight-bearing, systemic corticosteroids and delayed menarche. Reduce risk by dietary supplements of calcium and vitamin D; regular weight-bearing exercise; and minimize oral corticosteroid use. Sometimes bisphosphonate therapy is indicated.

Amyloidosis

Rare with modern treatment, but can present with proteinuria and subsequent renal failure and has a high mortality.

Management

The management of JIA has radically changed in the last decade and improvement in outcome is evident as long as children access appropriate care. Although JIA cannot be cured, early, aggressive control of joint inflammation improves long-term outcome. Deformity and disability are much less common with current treatment approaches and early diagnosis.

Medical management includes:

- *NSAIDs and analgesics* – do not modify disease but help relieve symptoms during flares.
- *Joint injections* – effective, first-line treatment for oligoarticular JIA; in polyarticular disease multiple joint injections are used as a bridging agent when starting methotrexate. Often requires sedation or inhaled anaesthesia (Entonox). Depending on the joint, guidance with ultrasound or X-rays may be needed.
- *Methotrexate* – early use reduces joint damage. Effective in approximately 70% with polyarthritis, less effective in systemic features of JIA. It is given as weekly dose (tablet, liquid, or injection) and regular blood monitoring is required (for abnormal liver function and bone-marrow suppression). Nausea is common.
- *Systemic corticosteroids* – avoided if possible, to minimize risk of growth suppression and osteoporosis. Pulsed intravenous methylprednisolone often used for severe polyarthritis as an induction agent. May be life-saving for severe systemic arthritis or macrophage activation syndrome.
- *Cytokine modulators ('biologics') and other immunotherapies* – many agents (e.g. anti-TNF alpha, IL-1, CTLA-4, or IL-6) are now available and useful in severe disease refractory to methotrexate. They are expensive and given under strict national guidance with registries for long-term surveillance. T-cell depletion coupled with autologous haematopoietic stem cell rescue (bone marrow transplant) is an option for refractory disease. Selecting the most suitable medication remains problematic.



Case history 28.1

Systemic-onset juvenile idiopathic arthritis

A 2-year-old boy presented with a high fever (Fig. 28.23a) and malaise. A salmon-coloured rash was present at times of fever (Fig. 28.23b). Investigation showed markedly raised acute-phase reactants. Shortly afterwards, he developed severe polyarticular joint disease. A diagnosis of systemic-onset juvenile idiopathic arthritis was made on the basis of the clinical presentation and exclusion of other disorders (Table 28.3).

He was treated with high-dose intravenous corticosteroids with rapid improvement. This was followed by low-dose oral corticosteroids and weekly methotrexate given by subcutaneous injection. The family were taught

about giving his injections and treatment, and physiotherapy and exercises and stretches to improve his joint range and muscle strength. He had further flares of his disease and was started on a biological therapy (tocilizumab) given by monthly intravenous infusion on the paediatric day unit. Within 4 months from diagnosis he had excellent disease control, and a year later he was well but still on weekly methotrexate and monthly biological treatment. He will require long-term follow-up including regular blood tests and review by the paediatric rheumatology team.

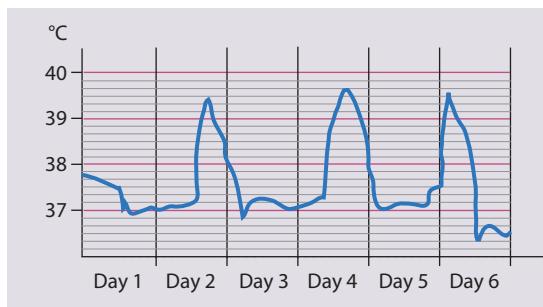


Figure 28.23a Temperature chart showing spikes, often in the evenings, but normal in between times.



Figure 28.23b Salmon-pink rash.



Case history 28.2

Oligoarticular onset juvenile idiopathic arthritis

A 4-year-old girl was noted by her parents to be limping intermittently for several weeks. Her teacher at school commented that she was quieter, less keen to play, and was not able to sit on the floor in story time. Her general practitioner performed a pGALS assessment and observed she had a limp and her right knee was swollen and restricted (Fig. 28.24). She was referred to the paediatric department and then paediatric rheumatology.

Investigations showed that her basic blood tests (full blood count, acute phase reactants) were normal but her ANA (antinuclear antibody) test was positive. She had evidence of chronic anterior uveitis on slit-lamp examination, although she had no visual symptoms. Her uveitis was treated with topical corticosteroids. Her knee was injected with corticosteroids under general anaesthesia. She had physiotherapy to improve her joint movement and function. The family received information and support from the paediatric rheumatology multidisciplinary team. Her mobility, mood and energy improved and she returned to normal activities at home and school. Her prognosis is excellent, although further flares of her arthritis and/or uveitis are possible and she needs regular review. This case history demonstrates how prompt diagnosis and early specialist management reduces long-term morbidity.



Figure 28.24 Swollen right knee in 4-year-old girl with oligoarticular onset juvenile idiopathic arthritis.

Multidisciplinary team

A multidisciplinary team, usually consisting of a paediatric rheumatologist, specialist nurse, ophthalmologist, physical and occupational therapist, and psychologist, and links to other specialities including dentistry and orthopaedics, is required to deliver optimal care. Physical therapy delivered by a specialist therapist is required to restore muscle and bone strength and to maintain the range of joint movement. The child is encouraged to take part in all activities except contact sports during active flares. With optimal care, most children are managed as outpatients.

Prognosis

The prognosis has markedly improved and most children, and families can expect good disease control and quality of life. If good disease control is not achieved, there can be significant morbidity from previous inflammation, such as joint damage requiring joint replacement surgery, visual impairment from uveitis, or fractures from osteoporosis. Joint replacements are now rarely needed in childhood, but are still needed in some adults with JIA. Long-term outcome studies have shown that at least one in three children will need ongoing treatment into adult years to maintain remission. There is also significant psychosocial morbidity with impact on schooling and employment outcomes.

Transitional care programmes are increasingly provided to facilitate the changes through adolescence and young adulthood and to help young people learn how to self-manage their chronic disease, live independently, and engage in shared decision-making.

Summary

Juvenile idiopathic arthritis (JIA)

- JIA is a group of disorders causing arthritis of 6 weeks or more in a child or young person 16 years of age or younger with no identifiable cause.
- Classification is clinical – oligoarthritis (≤ 4 joints), polyarthritis (> 4 joints) affected in first 6 months, systemic (fever and rash), psoriatic arthritis and enthesitis. Subclassified according to the presence of rheumatoid factor and HLA B27 tissue type.
- Early aggressive treatment improves outcomes and prevents complications such as joint damage or contracture, limb length discrepancy, and blindness from uveitis.
- In spite of immunomodulatory medications, more than half have active disease into adulthood.

Summary

Diagnostic clues regarding musculoskeletal disorders

'Typical' symptom combinations	Pivotal clinical features	Possible diagnoses
Nocturnal wakening with leg pain	Normal child	'Growing pains' Osteoid osteoma
'Clunk' on hip movement on neonatal and early infant screening, limp in an older infant	Anaemia, bruising, irritability, infections Older infant: asymmetrical upper leg skin folds, limited hip abduction	Leukaemia, lymphoma, neuroblastoma (young child) Developmental dysplasia of the hip (DDH)
Febrile, toxic-looking infant, irritability with nappy changing	Restricted joint range (especially hip) or limb movement	Septic arthritis Osteomyelitis
Sudden limp in an otherwise well young child	Unilateral restricted hip movement	Transient synovitis of the hip Perthes disease
Fever, erythematous rash, red eyes, irritability in infant or young child	Erythema/oedema of hands and feet, oral mucositis, cervical lymphadenopathy	Kawasaki disease
Irritability, fever, reluctance to move in an infant or young child	Stiff back, 'tripod' sitting	Discitis Vertebral osteomyelitis
Joint pain, stiffness, and restriction	Persistent joint swelling	Juvenile idiopathic arthritis
Loss of joint function	Loss of joint range	
Hip pain in an obese adolescent boy	Unilateral hip restriction	Slipped capital femoral epiphysis
Lethargy, unwilling to do physical activities, irritability, rash	Eyelid erythema Proximal muscle weakness	Juvenile dermatomyositis
Constitutional symptoms, lethargy, arthralgia in an adolescent female	Multisystem abnormalities, haematuria, facial erythema	Juvenile-onset systemic lupus erythematosus

Henoch–Schönlein purpura

This is the most common vasculitis of childhood and presents with a purpuric rash over the lower legs and buttocks, usually associated with arthritis of the ankles or knees. Other features are abdominal pain, haematuria and proteinuria (see Ch. 19, Kidney and urinary tract disorders).

Juvenile-onset systemic lupus erythematosus (JSLE)

JSLE is a rare chronic autoimmune inflammatory condition that can involve any organ. Children of Asian and Black African and Black Caribbean ethnicity are affected more severely than Caucasians. Usually presents in adolescent females with malaise, arthralgia and malar rash (often photosensitive); haematological involvement is also common. Organ involvement (kidneys, lung, or central nervous system) are serious complications. Blood tests show low white cell count, low complement, presence of antinuclear antibodies and anti-double-stranded antibodies. Treatment depends on the severity of the disease and ranges from corticosteroids to disease-modifying anti-rheumatic drugs (DMARDs), including cyclophosphamide.

Juvenile dermatomyositis

Juvenile dermatomyositis (JDMS) is rare. It usually begins insidiously with malaise, progressive weakness (often difficulty climbing stairs), facial rash with erythema over the bridge of the nose and malar areas, and a violaceous (heliotropic) discolouration of the eyelids (see Fig. 29.10). The skin over the metacarpal and proximal interphalangeal joints may be hypertrophic and pink, and the nailfold capillaries may be dilated and tortuous. Muscle pain is a common, if non-specific, symptom, and arthritis is present in 30% of cases. Respiratory failure and aspiration pneumonia may be life threatening. The condition is described further in Chapter 29 (Neurological disorders).

Auto-inflammatory syndromes

These conditions are characterized by activation of inflammatory pathways and most have definable underlying genetic mutations usually involving the inflammasome pathways. Clues that point towards auto-inflammatory disorders include recurrent episodes of systemic inflammation, onset in early childhood, family members with similar symptoms, elevated inflammatory markers during the episode, negative infection screens and absent autoantibodies. Malignant disease needs to be excluded. Clinical manifestations include fever, rash, serositis (presenting as abdominal or chest pain), arthritis and sterile meningitis. The major auto-inflammatory disorders include familial Mediterranean fever (FMF), tumor necrosis factor receptor-1 associated periodic fever syndromes (TRAPS), cryopyrin-associated periodic fever syndromes (CAPS), hyperimmunoglobulinemia D syndrome (HIDS) and periodic fever with aphthous stomatitis, pharyngitis and adenitis (PFAPA). When the diagnosis is suspected, referral to a specialist centre is needed to establish the diagnosis and provide treatment, monitoring for development of secondary amyloidosis and for genetic counselling if necessary.

Genetic skeletal conditions

These are inherited abnormalities resulting in generalized developmental disorders of the bone, of which there are several hundred types. They usually result in reduced growth and abnormality of bone shape rather than impaired strength, except for osteogenesis imperfecta. The bones of the limbs and spine are often affected, resulting in short stature. Intelligence is usually normal. Genetic testing is allowing better delineation of some of these disorders.

Achondroplasia

This is due to mutations in the fibroblast growth factor receptor 3 gene. It is an autosomal dominant disorder, but about 50% are new mutations. Clinical features are short stature from marked shortening of the limbs, a large head, frontal bossing, and depression of the nasal bridge (see Fig. 12.9). The hands are short and broad. A marked lumbar lordosis develops. Hydrocephalus sometimes occurs.

Thanatophoric dysplasia

There are more severe findings than achondroplasia. The infants have a large head, extremely short limbs and a small chest; severe cervical medullary compression leads to early death. The appearance of the bones on X-ray is characteristic. The importance of the correct diagnosis of this disorder is that, in contrast to achondroplasia, its inheritance is sporadic. It may be identified on antenatal ultrasound.

Cleidocranial dysostosis

In this autosomal dominant disorder, there is absence of part or all of the clavicles, and delay in closure of the anterior fontanelle and of ossification of the skull. The child is often able to bring the shoulders together in front of the chest to touch each other as a 'party trick'. Short stature is usually present. Intelligence is normal.

Arthrogryposis

This is a heterogeneous group of congenital disorders in which there is stiffness and contracture of multiple joints. There may be an underlying neurological abnormality or primary muscle disease. It is usually sporadic. Marked flexion contractures of the knees, elbows and wrists, dislocation of the hips and other joints, talipes equinovarus, and scoliosis are common, but the disorder may be localized to the upper or lower limbs. The skin is thin, subcutaneous tissue is reduced, and there is marked muscle atrophy around the affected joints. Intelligence is usually unaffected. Management is with physiotherapy and correction of deformities, where possible, by splints, plaster casts, or surgery. Walking is impaired in the more severe forms of the disorder.

Osteogenesis imperfecta (brittle bone disease)

This is a group of rare inherited disorders of type 1 collagen, causing bone fragility, with bowing and frequent fractures.

Osteogenesis imperfecta



(a)



(b)

Figure 28.25 Osteogenesis imperfecta type I, showing (a) fracture of the humerus and osteoporotic bones; and (b) blue sclerae.



Osteogenesis imperfecta is often considered in the evaluation of unexplained fractures in suspected child abuse.



Figure 28.26 Osteogenesis imperfecta (type II) showing shortened, deformed lower limbs from gross deformity of the bones with multiple fractures.

In the most common form (type I), which is autosomal dominant, there are fractures during childhood (Fig. 28.25a) and a blue appearance to the sclerae (Fig. 28.25b), and some develop hearing loss. This condition is often considered in children with fractures in relation to non-accidental injury. Treatment with bisphosphonates reduces fracture rates. The prognosis is variable. Fractures require splinting to minimize joint deformity.

There is a severe, lethal form (type II) with multiple fractures already present before birth (Fig. 28.26). Many affected infants are stillborn. Inheritance is variable but mostly autosomal dominant or due to new mutations. In other types, scleral discolouration may be minimal.

Osteopetrosis (marble bone disease)

In this rare disorder, the bones are dense but brittle. The severe autosomal recessive disorder presents with faltering growth, recurrent infection, hypocalcaemia, anaemia and thrombocytopenia. Prognosis is poor, but bone marrow transplantation can be curative. A less severe autosomal dominant form may present during childhood with fractures.

Marfan syndrome

This is an autosomal dominant disorder of connective tissue associated with tall stature, long thin digits (arachnodactyly), hyperextensible joints, a high arched palate, dislocation (usually upwards) of the lenses of the eyes, and severe myopia. The body proportions are altered, with long, thin limbs resulting in a greater distance between the pubis and soles (lower segment) than from the crown to the pubis (upper segment). The arm span, measured from the extended fingers, is greater than the height. There may be chest deformity and scoliosis. The major problems are cardiovascular, due to degeneration of the media of vessel walls resulting in a dilated, incompetent aortic root with valvular incompetence and mitral valve prolapse and regurgitation. Aneurysms of the aorta may dissect or rupture. Monitoring by echocardiography is required.

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Further reading

- Petty RE, Laxer RM, Lindsey CB, Wedderburn LR: Textbook of pediatric rheumatology, ed 8, Edinburgh, 2020, Elsevier.
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Ravelli A: Handbook of juvenile idiopathic arthritis, ed 1, 2016, Springer.

Websites

Clinical assessment of the musculoskeletal system: A guide for medical students and healthcare professionals. Available free at: www.versusarthritis.org/media/3080/student-handbook-11-2.pdf.

Free educational materials including pGALS, pREMS, interactive cases, and notes on common and significant musculoskeletal conditions relevant to paediatric rheumatology can be freely accessed at www.pmmonline.org; pGALS app is available to download from Google Play and Apple stores.

Current guidance related to paediatric rheumatology for clinicians are available at the British Society of Rheumatology website: www.rheumatology.org.uk/practice-quality/guidelines/paediatric-adolescent-guidance.

E-modules: (1) Introduction to Paediatric Musculoskeletal Clinical Skills – pGALS, (2) Paediatric Musculoskeletal Medicine in Primary Care – A Guide for GPs and (3) The Child with Fever – Infection or not? Available via Newcastle University at: cpd.ncl.ac.uk/courses.



Neurological disorders

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Features of neurological disorders in children:

- Recurrent headaches are most often caused by migraine and tension-type headache.
- Febrile seizures are common and usually have a good prognosis, but any treatable cause of the febrile illness needs to be identified.
- The diagnosis of an epilepsy is primarily based on a detailed history and is often substantiated by a video.
- Epilepsy syndromes present at different ages, e.g. infantile spasms at 4–6 months, childhood absence epilepsy at 4–12 years.
- Motor disorders may be central (involving the corticospinal (pyramidal) tract, basal ganglia or cerebellum) or peripheral (neuromuscular disorders).
- The number of babies born with neural tube defects has declined markedly over the last 50 years.

The central nervous system comprises 100,000 million neurones and when it malfunctions it has the potential to generate a wide spectrum of clinical problems. The site of the dysfunctional neurones determines the nature of the problem, which may involve impaired movement, vision, hearing, sensory perception, learning, memory, consciousness or sleep. They generate ‘neurological’, as well as ‘emotional’ (affective) disorders, e.g. anxiety and depression, and other ‘mental health’ disorders, and some ‘functional’ or ‘medically unexplained’ illnesses. The division of brain disorders into ‘neurological’ and ‘mental health’ is artificial, and although based historically on morbid pathology, is nowadays more based on the therapies offered than on biology. Classifying this wide range of symptom complexes can be problematic.

Headache

Headache is a frequent reason for older children and adolescents to consult a doctor. The International Headache Society has devised a classification, as shown in [Box 29.1](#), which defines:

- *primary headaches* – four main groups, comprising migraine, tension-type headache, cluster headache, and other primary headaches (such as primary stabbing headache). They are thought to be due to a primary malfunction of neurones and their networks
- *secondary headaches* – symptomatic of some underlying pathology, e.g. from raised intracranial pressure or space-occupying lesions
- *trigeminal and other cranial neuralgias and other headaches* – including root pain from herpes zoster.

Primary headaches

Tension-type headache

This is a symmetrical headache of gradual onset, often described as tightness, a band or pressure. There are usually no other symptoms.

Migraine

Migraine without aura

This accounts for 90% of migraine. In children, episodes may last 1–72 hours; the headache is commonly bilateral but may be unilateral. Characteristically pulsatile, over the temporal or frontal area, it is often accompanied by unpleasant gastrointestinal disturbance such

Box 29.1 The classification of headache disorders

Primary headaches	Secondary headaches	Cranial neuralgias, central and primary facial pain, and other headaches (rare in children)
<ul style="list-style-type: none"> • Migraine • Tension-type headache • Cluster headache and other trigeminal autonomic cephalgias • Other primary headaches 	<p>Headache attributed to:</p> <ul style="list-style-type: none"> • Non-vascular intracranial disorder – raised intracranial pressure, idiopathic intracranial hypertension • Medication overuse • Head and/or neck trauma • Cranial or cervical vascular disorder – vascular malformation or intracranial haemorrhage • A substance or its withdrawal – alcohol, solvent or drug abuse • Infection – meningitis, encephalitis, abscess • Disorder of homeostasis – hypercapnia or hypertension • Disorder of facial or cranial structures – acute sinusitis • Associated with emotional disorders 	<p>Trigeminal and other cranial neuralgias and central causes of facial pain</p> <ul style="list-style-type: none"> • Other headaches

as nausea, vomiting, abdominal pain, photophobia and phonophobia (sensitivity to sounds). It is typically aggravated by physical activity and relieved by sleep.

Migraine with aura

This accounts for 10% of migraine. The headache is preceded by a unilateral aura (visual, sensory, or motor impairment), although the aura may occur without a headache. Features are the absence of problems between episodes and the frequent presence of premonitory symptoms (tiredness, difficulty concentrating, autonomic features, etc.).

The most common aura comprises visual disturbance, which may include:

- negative phenomena, such as hemianopia (loss of half the visual field) or scotoma (small areas of visual loss)
- positive phenomena such as fortification spectra (seeing zigzag lines).

Rarely, there are unilateral sensory or motor symptoms (e.g. hemiplegic migraine).

Symptoms of *tension-type headache* or a *migraine* often overlap. They are probably part of the same pathophysiological continuum, with evidence that both result from primary neuronal dysfunction, including channelopathies, with vascular phenomena as secondary events. There is a genetic predisposition, with first-degree and second-degree relatives often also affected. Bouts are often triggered by a disturbance of inherent biorhythms, such as late nights or early rises, stress, or winding down after stress at home or school. Certain foods, e.g. cheese, chocolate, and caffeine, are only rarely a reliable trigger. In females, headaches can be related to menstruation and the oral contraceptive pill.

Uncommon forms of migraine

These include:

- *familial hemiplegic migraine* – caused by a calcium channel defect, dominantly inherited
- *sporadic hemiplegic migraine*
- *migraine with brainstem aura* – vomiting with nystagmus and/or cerebellar signs
- *periodic syndromes* – often precursors of migraine and include:
 - *cyclical vomiting* – recurrent stereotyped episodes of vomiting and intense nausea associated with pallor and lethargy. The child is well in between episodes
 - *abdominal migraine* – an idiopathic recurrent disorder characterized by episodic midline abdominal pain in bouts lasting 1–72 hours. Pain is moderate to severe in intensity and associated with vasomotor symptoms, nausea, and vomiting. The child is well in between episodes
 - *benign paroxysmal vertigo of childhood* – is characterized by recurrent brief episodes of vertigo occurring without warning and resolving spontaneously in otherwise healthy children. Between episodes, neurological examination, audiometric and vestibular function tests are normal.

Secondary headaches

Raised intracranial pressure and space-occupying lesions

Headaches often raise the fear of brain tumours; this may well be the reason for parents to consult a doctor. Headaches due to a space-occupying lesion are worse when lying down, and morning vomiting is characteristic. The headaches may also cause night-time waking. There is often a change in mood, personality, or educational

performance. Other features suggestive of a space-occupying lesion are:

- visual field defects – from lesions pressing on the optic pathways, e.g. craniopharyngioma (a pituitary tumour)
- cranial nerve abnormalities causing diplopia, new-onset squint or facial nerve palsy. The VIth (abducens) cranial nerve has a long intracranial course and is often affected when there is raised pressure, resulting in a squint with diplopia and inability to abduct the eye beyond the midline. It is a false localizing sign. Other nerves are affected depending on the site of lesion, e.g. pontine lesions may affect the VIIth (facial) cranial nerve and cause a facial nerve palsy
- abnormal gait
- torticollis (tilting of the head)
- growth failure, e.g. craniopharyngioma or hypothalamic lesion

- papilloedema – a late feature
- cranial bruits – may be heard in arteriovenous malformations but these lesions are rare
- early or late puberty
- change in personality or academic ability.

Medication overuse headache

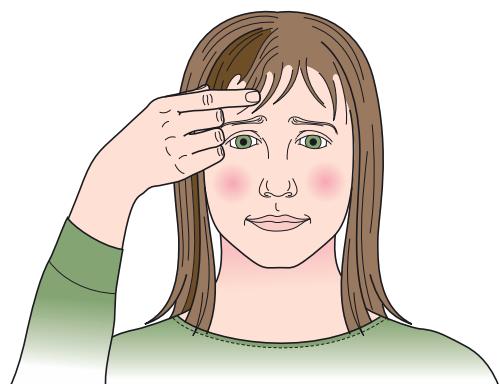
Patients with primary headaches, especially migraine, are at risk of developing a rebound “chronic daily headache” (technically, headache on 15 or more days a month) if they have a bad patch and use acute analgesics or triptans on more than 2 days a week. Withdrawing the offending medication will resolve this in about 2 weeks.

Other causes

These are listed in [Box 29.1](#).

Summary

Headaches



Headaches history

Premonitory symptoms, aura, character, position, radiation, frequency, duration, relieving and exacerbating factors?
Special consideration:
Triggers – stress, relaxation, food, menstruation?
Emotional or behavioural problems at home or school?
Vision checked – refractive error?
Head trauma?
Alcohol, solvent, or drug abuse?
Analgesia over-use?

Headache type

Tension-type headache – constriction band
Migraine without aura – bilateral or unilateral, pulsatile, nausea, vomiting, abdominal pain, photophobia, phonophobia. Lies in quiet, dark place. Relieved by sleep
Migraine with aura – preceded by aura (visual, sensory or motor transient impairments). Both tension-type and migraine headaches – common

Red flag symptoms – space-occupying lesion

Headache – worse lying down or with coughing or straining
Headache – wakes up child or young person (different from headache on awakening, not uncommon in migraine)
Associated confusion, and/or morning or persistent nausea or vomiting
Recent change in personality, behaviour or educational performance

Red flag physical signs – space-occupying lesion

- Growth failure
- Visual field defects – craniopharyngioma
- Squint
- Cranial nerve abnormality
- Torticollis
- Abnormal coordination – for cerebellar lesions
- Gait – upper motor neurone or cerebellar signs
- Fundi – papilloedema
- Bradycardia
- Cranial bruits – arteriovenous malformation

Other physical signs

Visual acuity – for refractive errors
Sinus tenderness – for sinusitis
Pain on chewing – temporomandibular joint malocclusion
Blood pressure – for hypertension

Investigations

Only consider these if ‘red flag’ features

Management

The mainstay of management is a thorough history and examination with detailed explanation and advice. Imaging is unnecessary in the absence of any 'red flag' features (see summary).

Efforts should be made to make a specific headache diagnosis. Children or young people and parents should be informed that recurrent headaches are common, that for most there are good and bad spells, with periods of months or even years in between the bad spells, and that they cause no long-term harm. Written child-friendly information for the family to take home is helpful. Children and young people should be advised on how to live with and control the headaches, rather than allowing the headaches to dominate their lives. There is nothing medicine can do to cure this problem but there is much it can offer to make the bad spells more bearable.

Rescue treatments

- analgesia – paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs), taken as early as possible in an individual troublesome episode
- antiemetics – prochlorperazine or cyclizine, for nausea
- triptans (serotonin (5-HT₁) agonists), e.g. sumatriptan. A nasal preparation of this is particularly useful in children and young people, early in a migraine attack, together with an NSAID or paracetamol
- physical treatments such as cold compresses, warm pads, topical forehead balms.

Prophylactic treatments

Where headaches are frequent and intrusive:

- sodium channel blockers – topiramate or valproate
- beta-blockers – propranolol (contraindicated in asthma)
- tricyclics: pizotifen (5-HT₂ antagonist) – can cause weight gain and sleepiness, or amitriptyline – can cause dangerous arrhythmias in overdose
- acupuncture.

Psychosocial support

- psychological support – is there a manageable stressor, e.g. bullying, anxiety over exams, or illness in friends or family?
- relaxation and other self-regulating techniques, addressing lifestyle issues: ensuring adequate and regular rest, play, sleep, water, and food
- acknowledge that primary headaches can be extremely painful and incapacitating even though there is no tissue damage or incipient tissue injury.

Seizures

A seizure is a paroxysmal abnormality of motor, sensory, autonomic, and/or cognitive function, due to transient brain dysfunction. The term includes epileptic, syncopal (anoxic), brainstem (hydrocephalic, coning), emotional or functional (psychogenic non-epileptic seizures, dissociative states), and as yet undetermined. Regarding seizures as epileptic or non-epileptic will guard against the misdiagnosis of epilepsy, which is common.

Epileptic seizures

What makes a seizure epileptic is the nature of the underlying electrical activity in the brain, especially in the cerebral cortex, so it can sometimes be difficult to tell from a non-epileptic (especially a syncopal) seizure clinically. Epileptic seizures are due to excessive and hypersynchronous electrical activity, typically in neural networks in all or part of the cerebral cortex.

Convulsions

A convulsion is a seizure (epileptic or non-epileptic) with motor components, particularly stiff (tonic), a massive jerk (myoclonic), jerking (clonic), trembling (vibratory), thrashing about (hypermotor); as opposed to a non-convulsive seizure with motor arrest, e.g. an unresponsive stare (as in generalized epileptic absence seizures and some focal epileptic seizures), or drop attack (as in an epileptic atonic seizure).

Causes of seizures

These are listed in [Box 29.2](#).

Epilepsies

An epilepsy is a brain disorder that predisposes the patient to have unprovoked epileptic seizures. Generally, an epilepsy can be recognized after two or more unprovoked epileptic seizures have occurred.

Acute symptomatic epileptic seizures

When epileptic seizures are provoked by an acute brain injury – e.g. from acute cortical ischaemia during arterial ischaemic stroke, from a cerebral contusion during a traumatic brain injury, or from cortical inflammation during meningitis – they do not constitute an epilepsy, even if there were recurrent injuries. These are called acute symptomatic epileptic seizures. The causes of these seizures are listed in [Box 29.2](#).

Febrile seizures

A 'febrile seizure' or 'febrile convulsion' is an epileptic seizure accompanied by a fever in the absence of intracranial infection. These occur in 3% of children between the ages of 6 months and 6 years. There is a genetic predisposition, with a 10% risk if the child has a first-degree relative with febrile seizures. The seizure usually occurs early in a viral infection when the temperature is rising rapidly. They are usually brief generalized tonic-clonic seizures. About 30%–40% will have further febrile seizures. This is more likely the younger the child, the shorter the duration of illness before the seizure, the lower the temperature at the time of seizure and if there is a positive family history.

Simple febrile seizures do not cause brain damage; the child's subsequent intellectual performance is the same as in children who did not experience a febrile seizure. There is a 1%–2% chance of subsequently developing an epilepsy, similar to the risk for all children.

However, complex febrile seizures, i.e. those which are focal, prolonged, or repeated in the same illness, have an increased risk of 4%–12% of subsequent epilepsy.

The acute management of seizures is described in [Chapter 6](#) (Paediatric emergencies). Examination should

Box 29.2 Causes of seizures**Epilepsies**

- **Genetic** (70%–80%) – also called ‘idiopathic’, caused by alleles at several loci together rather than a single gene, so inheritance is ‘complex’
- **Structural, metabolic:**
 - Cerebral dysgenesis/malformation
 - Cerebral vascular occlusion
 - Cerebral damage, e.g. congenital infection, hypoxic–ischaemic encephalopathy, intraventricular haemorrhage/ischaemia
 - Cerebral tumour
 - Neurodegenerative disorders
 - Neurocutaneous syndromes, e.g. tuberous sclerosis

Acute symptomatic seizures

- **Due to any cortical brain injury or insult, at the time of the trauma or illness:**
 - Stroke, traumatic brain injury, intracranial infection
 - Hypoglycaemia, hypocalcaemia, hypomagnesaemia, hyponatraemia/hypernatraemia
 - Poisons/toxins

Febrile seizures**Non-epileptic seizures (paroxysmal disorders)**

- **Convulsive syncope:**
 - Expiratory apnoea syncope ('blue breath-holding spells')
 - Vasovagal syncope: often predominantly vasodepressor, but can be predominantly cardioinhibitory (reflex asystolic syncope), or mixed.
 - Hypovolaemic syncope, e.g. with haemorrhage, dehydration or anaphylaxis
 - Cardiac syncope, e.g. prolonged Q-T syndrome
- **See Fig. 29.1 for other causes**

focus on the cause of the fever, which is usually a viral illness, but a bacterial infection including meningitis should always be considered. The classical features of meningitis such as neck stiffness and photophobia may not be as apparent in children less than 18 months of age, so an infection screen (including blood cultures, urine culture, and lumbar puncture for cerebrospinal fluid) may be necessary. If the child is unconscious or has cardiovascular instability, lumbar puncture is contraindicated and antibiotics should be started immediately.

Parents need reassurance and information. Advice sheets are usually given to parents. Antipyretics may be given but have not been shown to prevent febrile seizures. The family should be taught the first aid management of seizures. If there is a history of prolonged seizures (>5 min), rescue therapy with buccal midazolam can be supplied. Oral prophylactic antiepileptic drugs are not used as they do not reliably reduce the recurrence rate of seizures, and have a relatively high risk of adverse effects. An EEG is not indicated as it does not predict seizure recurrence.

Summary**Febrile seizures**

- Affect 3% of children; have a genetic predisposition.
- Occur between 6 months and 6 years of age.
- Are usually brief, generalized tonic–clonic seizures occurring with a rapid rise in fever.
- If a bacterial infection, especially meningitis, is present, it needs to be identified and treated.
- Advise family about management of seizures, consider rescue therapy.
- If simple, does not affect intellectual performance or risk of developing epilepsy.
- If complex, 4%–12% risk of subsequent epilepsy.

Non-epileptic seizures (Paroxysmal disorders)

There is a broad differential diagnosis for children with paroxysmal disorders ('funny turns'). Epilepsy is a clinical diagnosis based on the history from eyewitnesses and the child's own account. If available, videos of the seizures can be of great help. The diagnostic questions are: was it an epileptic seizure, and if so does the child have an epilepsy? Epilepsies can be further delineated as outlined below. If non-epileptic or uncertain, further delineation of the nature of the seizure or paroxysmal event is required (Fig. 29.1). The most common pitfall is that of syncope leading to an anoxic (non-epileptic) convulsive seizure.

The key to the diagnosis lies in a detailed history, review of video if available, which, together with the past history and clinical examination, will lead to a diagnosis of 'epilepsy', acute symptomatic or febrile seizure, or non-epileptic seizure. Inter-ictal EEG is useful in categorizing an epilepsy once diagnosed. Ictal EEG can be helpful in difficult to diagnose cases when seizures are frequent enough to capture or can be triggered.

Transient loss of consciousness is most commonly due to syncope, which is caused by a transient impairment of brain oxygen delivery, generally due to impaired cerebral perfusion (see Ch. 18, Cardiac disorders).

Summary**Non-epileptic seizures (paroxysmal disorders) in toddlers**

- 'Blue breath-holding' spells (expiratory apnoea syncope) – precipitated by anger or crying and cannot catch his/her breath which is stuck in expiration, goes blue, stiff then limp, with rapid recovery.
- Reflex asystolic syncope (reflex anoxic seizures) – precipitated by sudden surprising pain, stops breathing, goes pale, stiff with brief convolution sometimes, rapid recovery, or if severe sleeps for an hour or more.
- Other non-epileptic paroxysmal disorders – see Fig. 29.1.

Causes of paroxysmal disorders ('funny turns')

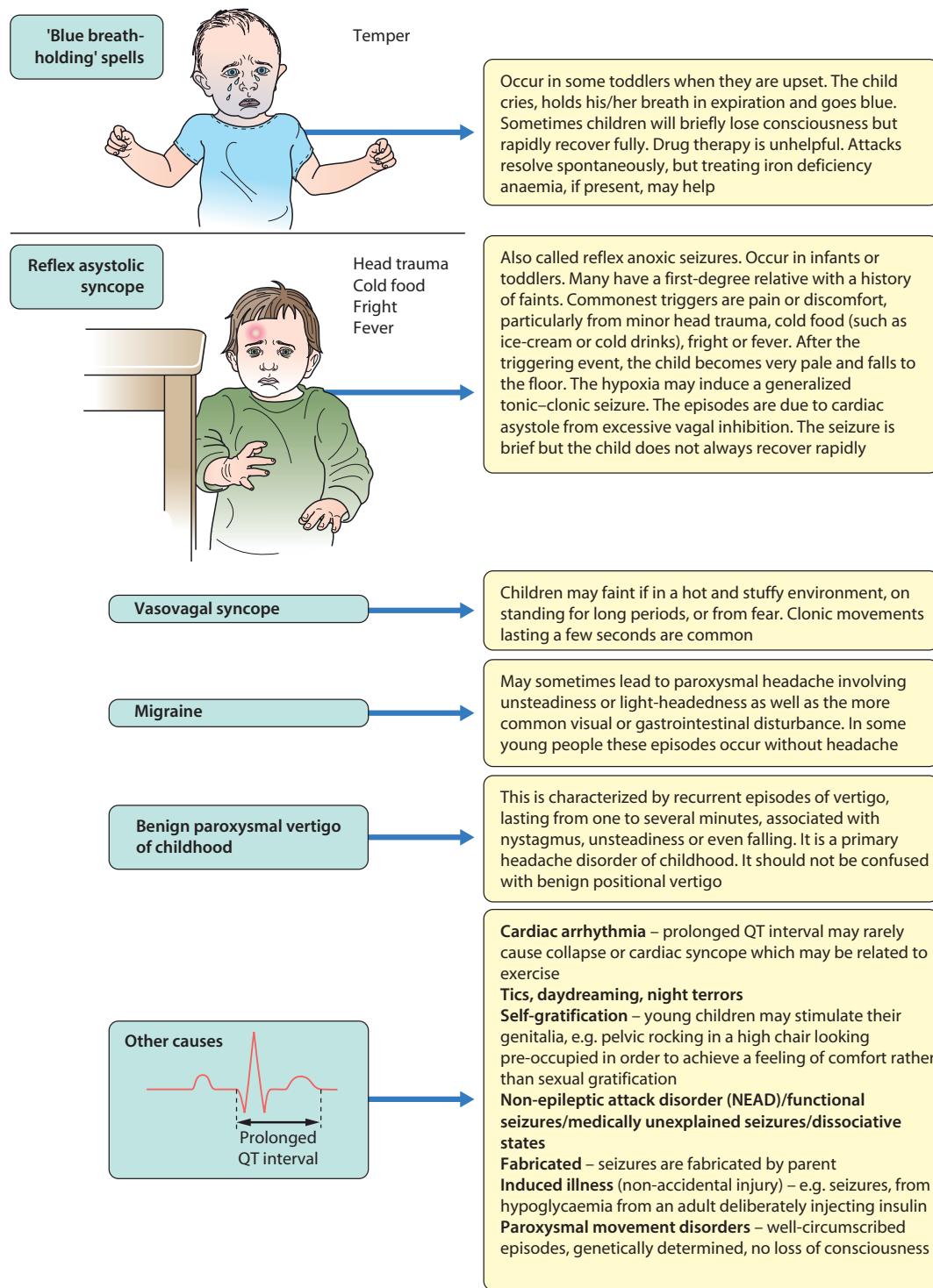


Figure 29.1 Causes of paroxysmal disorders ('funny turns').

Epilepsies of childhood

Epilepsy has an incidence of about 0.05% (less common during first year of life) and a prevalence of 0.5%. This means that most large secondary schools will have about six children with an epilepsy. Most epilepsy is 'genetic' (i.e. 'idiopathic') with complex inheritance, but other causes of recurrent unprovoked epileptic seizures are listed in Box 29.2.

An international classification of epileptic seizures and epilepsies is used (International League Against Epilepsy (ILAE) 2011–2017 Classifications). This broadly classifies seizures as either:

- **generalized** – discharge arises from both hemispheres, includes absence, myoclonic, tonic, spasms, tonic-clonic, atonic; may be in combination or in sequence
- **focal** – where seizures arise from one or part of one hemisphere.

Focal seizure manifestations will depend on the part of the brain where the discharge originates and moves to:

- *frontal seizures* – involve the motor or pre-motor cortex. May lead to clonic movements, which may travel proximally (Jacksonian march), or a tonic seizure with both upper limbs raised high for several seconds. Asymmetrical tonic seizures can be seen, which may be bizarre and hypermotor and can be mistaken for non-epileptic seizures
- *temporal lobe seizures* – may result in strange warning feelings or aura with smell and taste abnormalities and distortions of sound and shape. Lip-smacking, plucking at one's clothing, and walking in a non-purposeful manner (automatisms) may be seen, following spread to the pre-motor cortex. Déjà-vu feelings are described (intense feelings of having

been in the same situation before). Consciousness can be impaired and the seizures are usually longer than absence seizures

- *occipital seizures* – cause stereotyped visual hallucinations
- *parietal lobe seizures* – cause contralateral dysaesthesia (altered sensation), or distorted body image.

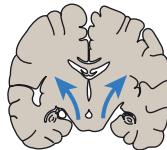
In focal seizures, the level of consciousness may be retained, consciousness may be lost, or the seizure may spread to both hemispheres and become a secondarily generalized tonic-clonic seizure.

In many children, especially under 5 years old, it may be unclear whether an epileptic seizure is generalized or focal. The main seizure types are summarized in Fig. 29.2 and the epilepsies in Table 29.1.

Epileptic seizure types

Generalized seizures

Onset in both hemisphere



In generalized seizures, there is:

- loss of consciousness if > 3 seconds duration
- no warning
- symmetrical seizure
- bilaterally synchronous seizure discharge on EEG

Absence seizures

Transient loss of consciousness, with an abrupt onset and termination, unaccompanied by motor phenomena except for some flickering of the eyelids and minor alteration in muscle tone. Absences can often be precipitated by hyperventilation

Myoclonic seizures

Brief, often repetitive, jerking movements of the limbs, neck or trunk
Non-epileptic myoclonic movements are also seen physiologically in hiccoughs (myoclonus of the diaphragm) or on passing through stage II sleep (sleep myoclonus)

Tonic seizures

Generalized increase in tone

Tonic-clonic seizures

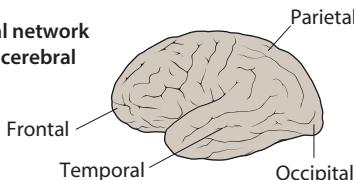
Rhythmic contraction of muscle groups following the tonic phase.
In the rigid tonic phase, children may fall to the ground, sometimes injuring themselves. They do not breathe and become cyanosed. This is followed by the clonic phase, with jerking of the limbs. Breathing is irregular, cyanosis persists and saliva may accumulate in the mouth. There may be biting of the tongue and incontinence of urine. The seizure usually lasts from a few seconds to minutes, followed by unconsciousness or deep sleep for up to several hours

Atonic seizures

Often combined with a myoclonic jerk, followed by a transient loss of muscle tone causing a sudden fall to the floor or drop of the head

Focal seizures

Onset in neural network limited to one cerebral hemisphere



Focal seizures:

- originate in a relatively small group of dysfunctional neurones in one of the cerebral hemispheres
- may be heralded by an aura (the sensory epileptic seizure) which reflects the site of origin
- may or may not be associated with change in consciousness or evolve to generalized tonic-clonic seizure

Focal seizures

Frontal seizures – motor phenomena
Temporal lobe seizures – auditory or sensory (smell or taste) phenomena
Occipital – positive or negative visual phenomena
Parietal lobe seizures – contralateral altered sensation (dysaesthesia)

Table 29.1 Some epilepsy syndromes – arranged by age of onset

Name	Age of onset	Seizure pattern	Comments
Infantile spasms (West syndrome)	3–12 months	Violent flexor spasms of the head, trunk, and limbs followed by extension of the arms, last 1–2 s, often multiple bursts of 20–30, often on waking or many times a day. May be misinterpreted as colic. Social interaction often deteriorates – a useful marker in the history.	Most have underlying neurological cause. EEG – hypsarrhythmia (Fig. 29.3). Treatment is vigabatrin and/or corticosteroids; good initial response in 70%, but unwanted side effects of therapy, and relapses common. Most will lose skills and develop learning disability and continuing epilepsy.
Lennox–Gastaut syndrome	1–3 years	Multiple seizure types, but mostly atonic, atypical (subtle) absences, and tonic seizures in sleep. Also neurodevelopmental arrest or regression and behaviour disorder.	Many causes, and often other complex neurological problems or history of infantile spasms. EEG shows slow generalized spike and wave (1–2.5 Hz). Prognosis is poor.
Childhood absence epilepsy	4–12 years	Momentary unresponsive stare with motor arrest, may twitch their eyelids or a hand or mouth minimally. Sudden onset, lasts only a few seconds (<30 s). Child has no recall except realizes they have missed something and may look puzzled or say 'pardon' on regaining consciousness. Developmentally normal but can interfere with schooling. Accounts for only 2% of childhood epilepsy.	Two-thirds are female. Episodes can be induced by hyperventilation – blowing on a piece of paper or windmill for 2–3 min; useful during EEG. The EEG shows fast generalized spike and wave (3–4 Hz) discharges, bilaterally synchronous during and sometimes between absences (Fig. 29.4). Prognosis good with 80% remission in adolescence; a few evolve into juvenile absence or juvenile myoclonic epilepsy.
Epilepsy with centro-temporal spikes (childhood rolandic epilepsy)	4–10 years	Tonic–clonic seizures in sleep, or simple focal seizures with awareness of abnormal feelings in the tongue and distortion of the face (supplied by the rolandic (centro-temporal) area of the brain).	15% of all childhood epilepsies. EEG shows focal sharp waves from the rolandic area. Important to recognize as relatively benign and may not require AEDs. Remits in adolescence.
Panayiotopoulos syndrome (early- onset benign occipital epilepsy)	1–5 years	Autonomic features with vomiting and unresponsive staring in sleep, with head and eye deviation, progressing sometimes to a convulsive seizure.	Comprises 5% of childhood epilepsies. EEG shows posterior focal sharp waves and occipital discharges when eyes are shut. Remits in childhood. Some have specific learning difficulties.
Juvenile absence epilepsy	10–20 years	Absences, and generalized tonic–clonic seizures, often with photosensitivity. Learning is unimpaired.	Characteristic EEG. Response to treatment is usually good but lifelong. Remission unlikely.
Juvenile myoclonic epilepsy	10–20 years	Myoclonic seizures, generalized tonic–clonic seizures, and absences may occur, mostly shortly after waking. A typical history is throwing drinks or cereal about in the morning as myoclonus occurs at this time. Learning is unimpaired.	Characteristic EEG. Response to treatment is usually good but lifelong. Remission unlikely.

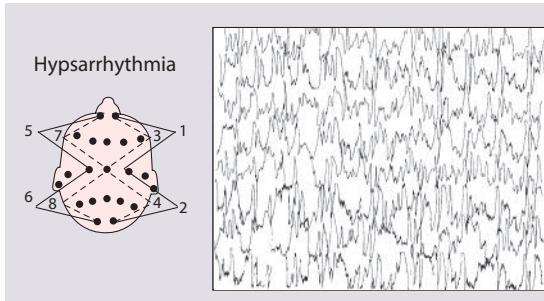


Figure 29.3 EEG of hypsarrhythmia in infantile spasms (West syndrome). There is a chaotic background of slow-wave activity with sharp multifocal components.

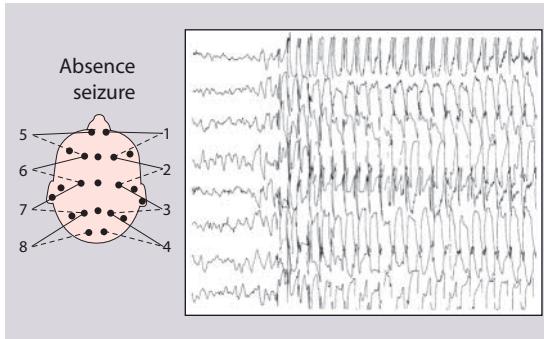


Figure 29.4 EEG in a typical absence seizure in childhood absence epilepsy. There is a three per second spike and wave discharge which is bilaterally synchronous during, and sometimes between, attacks.

Diagnosis

The diagnosis of an epilepsy is primarily based on a detailed history from the child and eyewitnesses, substantiated by a video if available. This is increasingly provided on mobile phones. Particular attention is focused on any specific triggers and if the child has any impairments, as there may be educational, psychological, or social problems. Clinical examination should include checking for skin markers for a neurocutaneous syndrome or neurological abnormalities. Although epilepsy is usually genetic (idiopathic), it may be the presentation or a complication of an underlying neurological disorder.

Investigation

Remember not all seizures are epileptic!

ECG

It is recommended that a 12-lead standard ECG is done in all children with seizures, especially convulsive seizures, even when an epilepsy seems most likely, as the consequences of missing convulsive syncope due to an arrhythmia, e.g. long-QT syndrome, can be an avoidable fatality (see Ch. 18).

EEG (electroencephalogram)

An inter-ictal EEG is indicated whenever an epilepsy is diagnosed. It can help categorize the epilepsy type and severity. If seizures are frequent then an ictal EEG can make the diagnosis, e.g. in suspected childhood absence epilepsy and suspected infantile spasms (West syndrome).

If the standard inter-ictal EEG is normal, a sleep or sleep-deprived record can be helpful. Additional techniques are 24 hour ambulatory EEG or a 5-day video-telemetry EEG. For assessment prior to surgery, more invasive techniques such as intracranial electrodes can be used.

Brain imaging

- **Structural** – MRI and CT brain scans are generally required routinely for childhood epilepsies unless there is a characteristic history of childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, or childhood rolandic epilepsy. MRI fluid-attenuated inversion recovery (FLAIR) sequences are better at detecting mesial temporal sclerosis in temporal lobe epilepsy, which can sometimes be surgically cured.
- **Functional** – While it is not always possible to see structural lesions, techniques have advanced to allow functional imaging to detect areas of abnormal metabolism suggestive of epileptogenic zones. These include PET (positron emission tomography) and SPECT (single photon emission computed tomography), which use isotopes and ligands injected and taken up by metabolically active cells. Both can be used between seizures to detect areas of hypometabolism in epileptogenic lesions. Ictal SPECT can locate areas of hypermetabolism during epileptic seizures. They are used in the work-up of patients for possible epilepsy surgery.

Other investigations

Metabolic investigations will be indicated if there is developmental arrest or regression, or seizures are related to feeds or fasting, and should be considered in epilepsies (i.e. not including febrile seizures) starting in the first two years of life. Genetic tests are becoming increasingly useful, especially in intractable epilepsies with developmental arrest or delay ('epileptic and developmental encephalopathies').

Management

Management begins with diagnosis, but this is often uncertain initially. So the uncertainty needs explaining and a plan put in place to ensure the child's safety until more information, e.g. from investigations or parental video clips, is available. Once diagnosed, a clear explanation of the diagnosis and advice to help adjustment to the condition is needed. A specialist epilepsy nurse may assist families by providing education and continuing advice on lifestyle issues. The decision whether to treat or not is related to the risk of recurrence, how dangerous or impairing, and how upsetting further seizures would be, in the context of the child or young person's life. It is common practice not to institute treatment for typical childhood rolandic epilepsy, and treatment of childhood absence epilepsy is aimed at maximizing their educational potential and supporting their social development.

Antiepileptic drug therapy

Principles governing use:

- Not all children with epileptic seizures require antiepileptic drug (AED) therapy. The decision should be based on the seizure type, epilepsy type, frequency, and the social and educational

- consequences of the seizures set against the possibility of unwanted effects of the AED.
- Choose an appropriate AED for the seizure and epilepsy. Inappropriate AEDs may be detrimental, e.g. carbamazepine can make absence and myoclonic seizures worse.
 - Monotherapy at the minimum dosage to prevent the seizures without adverse effects is the desired goal, although in practice more than one AED may be required.
 - All AEDs have potential unwanted effects and these should be discussed with the child and parent.
 - AED levels are not measured routinely, but may be useful to check for concordance (adherence) or to see if a dose increase could be considered if a high dose is not working.
 - Children with prolonged epileptic seizures (convulsive epileptic seizures with loss of consciousness >5 min) are given rescue therapy to keep with them. This is usually buccal midazolam.
 - AED therapy may be discontinued after 2 years free of seizures, but should usually be continued indefinitely in young people with juvenile absence epilepsy or juvenile myoclonic epilepsy.

Guidance regarding treatment options for different seizure types and epilepsies are shown in **Table 29.2**. Common unwanted effects of AEDs are shown in **Table 29.3**.

Other treatment options

In children with intractable epilepsies, there are a number of other treatment options.

- Ketogenic (low-carb, fat-based) diets* may be helpful in some children.
- Vagal nerve stimulation*, delivered using externally programmable stimulation of a wire implanted around the afferent (left) vagus nerve, may be helpful in some children.
- Epilepsy surgery*. Cessation of seizures and AED therapy may be achieved in some children whose epilepsy has a well-localized structural cause or epileptogenic zone, as demonstrated by good concordance between ictal EEG, MRI, and functional imaging findings. The main procedure is temporal lobectomy for mesial temporal sclerosis, but other procedures include hemispherotomy (disconnection of the hemisphere) and other focal resections.

Advice and prognosis

The aim is to promote independence and confidence. Some children with epilepsy and their families need psychological help to adjust to the condition. The school needs to be aware of the child's problem and teachers advised on the management of seizures. Unrecognized absences may interfere with learning, which is an indication for being vigilant about 'odd episodes' which may be epileptic seizures. Relatively few restrictions are required, but situations where having a seizure could lead to injury or death should be avoided. This includes avoiding deep baths (showers are preferable) and not swimming unsupervised.

For adolescents, there will be issues to discuss around driving (only after 1 year free of seizures), contraception and pregnancy. There may also be issues with concordance (adherence) and the precipitation of seizures by alcohol and poor sleep routines.

Table 29.2 Choice of antiepileptic drugs

Seizure type	First-line	Second-line
Generalized		
Tonic-clonic	Valproate [†] , carbamazepine*	Clobazam, levetiracetam, topiramate
Absence	Valproate [†] , ethosuximide	Clobazam, levetiracetam, topiramate
Myoclonic	Valproate [†] , levetiracetam	Clobazam, piracetam, clonazepam
Focal		
	Carbamazepine, valproate [†] , levetiracetam, lamotrigine	Clobazam, topiramate, lacosamide, gabapentin*

*Avoid with absence seizures, myoclonic seizures e.g. in juvenile myoclonic epilepsy.

†Avoid in females of child-bearing potential, if possible.

Table 29.3 Common or important unwanted effects of antiepileptic drugs

Drug	Adverse-effects
Valproate	Weight gain, hair loss, teratogenic, rare idiosyncratic liver failure
Carbamazepine	Rash, ataxia, liver enzyme induction can reduce effect of oral contraception
Lamotrigine	Rash, insomnia, ataxia
Ethosuximide	Nausea and vomiting
Levetiracetam	Irritability
Gabapentin	Insomnia
Topiramate	Weight loss, depression, paraesthesia
Vigabatrin	Irritability, visual field restriction limits its use mainly to infantile spasms

All the above drugs may cause drowsiness.

Sudden unexpected death in epilepsy (SUDEP) is very rare in childhood, but may be discussed and its rarity emphasized. Information is available from self-help groups and organizations such as Epilepsy Action.

Children with epilepsy do less well educationally, with social outcomes and with future employment than those with other chronic illnesses such as diabetes.

Two-thirds of children with epilepsy go to a mainstream school, but some require educational help for associated learning difficulties. One-third attend a special school, but they often have multiple disabilities and their epilepsy is part of a severe brain disorder. A few children require residential schooling where there are facilities and expertise in monitoring and treating intractable seizures.



Valproate should not be prescribed for females of child-bearing potential as it is teratogenic.

Status epilepticus

Established status epilepticus is an epileptic seizure lasting 30 minutes or repeated epileptic seizures for 30 minutes without recovery of consciousness. It is described in [Chapter 6](#). Emergency treatment is best given after about 5 minutes of a convulsive epileptic seizure (incipient convulsive status epilepticus).

Summary

Epilepsy

- Affects 1 in 200 children.
- Classified according to seizure type, epilepsy type, and underlying aetiology.
- An inter-ictal EEG is performed whenever an epilepsy is diagnosed to help categorize the epilepsy type. An ictal EEG may make the diagnosis.
- Antiepileptic drug therapy should be considered where the seizures are intrusive, and selected according to seizure and epilepsy type. Monotherapy is given if possible and chosen for the least potential adverse effects.
- Requires liaison with the school about how to manage a seizure and avoiding situations which could lead to injury.

Motor disorders

Movement is governed by cerebral control centres. Patterns of information, modulated by afferent sensory information (joint position, crude touch, visual, auditory and vestibular), pass down the brainstem and spinal cord, through synapses in the anterior horns and along peripheral nerves to the target muscles. In clinical practice the first question to ask when seeing a child with a motor disorder is whether this is a central or a peripheral nervous system disorder. The pattern of movement usually gives the answer.

Central motor disorders

The three central movement control centres are:

- *Motor cortex* – lying along the precentral gyrus (the homunculus reflects the body upside down, legs superiorly and face inferiorly, just above the Sylvian fissure, with large areas to govern fine movements of the tongue, fingers and thumb). Information from here passes down the corticospinal (pyramidal) tracts and links with the basal ganglia.
- *Basal ganglia* – deep grey matter structures, store patterns of movement so that we need not put conscious effort into every movement we make.
- *Cerebellum* – controls posture, balance, coordination and speech.

Disorders of these central movement control centres are:

- *Corticospinal (pyramidal) tract disorders* – there is weakness with a pattern of adduction at the shoulder, flexion at the elbow and pronation of the forearm; adduction and internal rotation at the hip, extension at hip and knee, and plantar flexion at the ankle with brisk hyperreflexia and extensor plantar reflexes. Fine finger movement will be lost.
- *Basal ganglia disorders* – will lead either to difficulty initiating movement, with fluctuating (largely increased) tone – a ‘dystonia’ or a ‘dyskinesia’ where packets of movement information are released to give jerky movement (chorea) or writhing movement (athetosis).
- *Cerebellar disorders* – will lead to difficulty holding a posture; past-pointing (dysmetria); poor alternating movements (dysdiadochokinesis). The gait is wide-based and ataxic. Posterior-column sensory pathway problems may give a similar clinical picture (but with even worse ataxia when the eyes are closed), but are much rarer in childhood. Associated nystagmus and a characteristic scanning dysarthria may be seen. Causes of these disorders are listed in [Table 29.4](#).

Cerebral palsy

This is described in [Chapter 4](#) (Developmental problems and the child with special needs).

Table 29.4 Causes of movement disorders

Corticospinal (pyramidal) tract disorders	Basal ganglia disorders	Cerebellar disorders
Acquired brain injury Cerebral dysgenesis, e.g. neuronal migration disorder Global hypoxia-ischaemia Arterial ischaemic stroke Cerebral tumour Acute disseminated encephalo-myelitis (ADEM) Postictal Todd's paresis Hemiplegic migraine	Acquired brain injury: <ul style="list-style-type: none"> • Acute and profound hypoxia-ischaemia • Carbon monoxide • Post-bypass surgery chorea Post-streptococcal chorea (rheumatic fever) Mitochondrial disease Wilson disease Huntington disease	Acute intoxication, e.g. alcohol, carbamazepine Post-viral, e.g. varicella Posterior fossa lesions, e.g. medulloblastoma Genetic disorders, e.g. Friedreich ataxia and ataxia telangiectasia

Peripheral motor disorders: the neuromuscular disorders

Any part of the lower motor neurone pathway can be affected in a neuromuscular disorder, including anterior horn cell disorders, peripheral neuropathies, disorders of neuromuscular transmission, and primary muscle diseases. The causes of neuromuscular disorders are shown in Fig. 29.5. The key clinical feature of a neuromuscular disorder is weakness, which may be progressive or static. Affected children may present with:

- hypotonia (floppiness)
- delayed motor milestones
- muscle weakness
- unsteady/abnormal gait
- fatigability
- muscle cramps (suggesting a metabolic myopathy).

History and examination may provide useful clues. Children with myopathy often show a waddling gait or positive Gowers' sign suggestive of proximal muscle weakness. Gowers' sign is the need to turn prone to rise to a standing from a supine position. This is normal until the age of 3 years. It is only when children have become very weak that they 'climb up the legs with the hands' to gain the standing position (Fig. 29.6).

A pattern of more distal wasting and weakness, particularly in the presence of pes cavus, suggests a hereditary motor sensory neuropathy. Increasing fatigability through the day, often with ophthalmoplegia and ptosis, suggests a disorder of the motor end-plate/neuromuscular junction, e.g. myasthenia gravis.

It is usually difficult to differentiate a myopathy from a neuropathy on clinical grounds but there are some broad points to look for:

- anterior horn cell – there are signs of denervation: weakness, loss of reflexes, fasciculation and wasting as the nerve supply to the muscle fails
- neuropathy – often longer nerves affected. Motor neuropathy will give weakness, sensory neuropathy will give impaired perception of pain and temperature or touch, with a loss of reflexes in both
- myopathy – there is weakness (often proximal), wasting, and gait disturbance
- neuromuscular junction – as end-plate acetylcholine stores become depleted, there is diurnal worsening through the day, leading to fatigability.

Investigations

Myopathy

- Plasma creatine kinase – markedly elevated in Duchenne and Becker muscular dystrophy, congenital muscular dystrophy, many limb girdle muscular dystrophies and inflammatory myopathies
- DNA testing – for abnormal genes
- Ultrasound and MRI of muscles – used to diagnose and monitor progress
- Muscle biopsy – modern histochemical techniques often enable a definitive diagnosis.

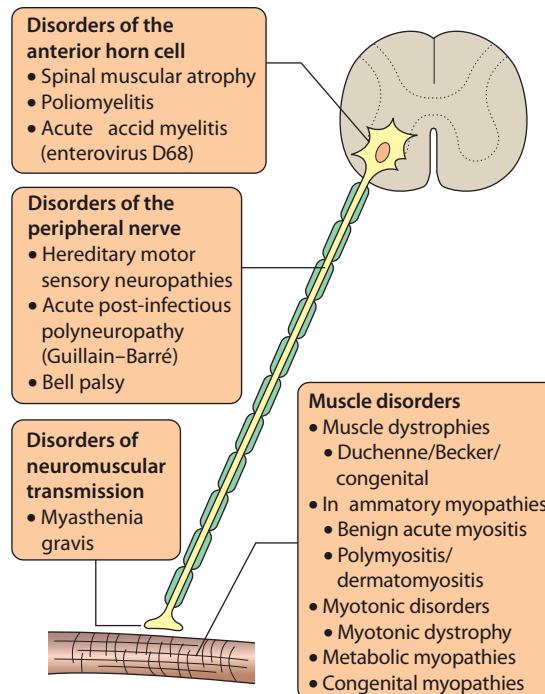


Figure 29.5 Neuromuscular disorders.

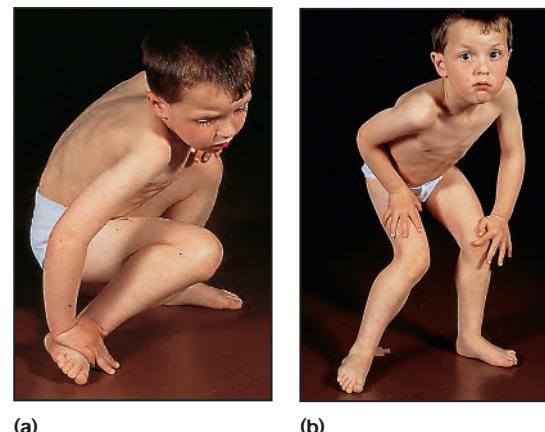


Figure 29.6 (a, b) Gowers' sign. The child needs to turn prone to rise (the key, early feature of Gowers' sign), then uses his hands to climb up on his knees before standing (late feature), because of poor hip girdle fixation and/or proximal muscle weakness. Any child continuing to turn prone to rise after 3 years of age is likely to have a neuromuscular condition.

Neuropathy

- DNA testing – for abnormal genes
- Nerve conduction studies – to identify delayed and/or diminished motor and sensory nerve conduction velocities seen in neuropathy
- EMG (electromyography) helps in differentiating myopathic from neuropathic disorders, e.g. fatigability on repetitive nerve stimulation in myasthenia
- Nerve biopsy – occasionally performed by removing a segment of sural nerve in the calf.

Diagnosis of neuromuscular disorders has been made easier by advances in genetic (DNA) testing, e.g. for spinal muscular atrophy (SMA), Duchenne muscular dystrophy, myotonic dystrophy, the congenital muscular dystrophies, limb girdle muscular dystrophies, and hereditary neuropathies.

Disorders of the anterior horn cell

Presentation is with weakness, wasting and absent reflexes. Poliomyelitis has almost been eradicated globally by immunization.

Spinal muscular atrophy

SMA is an autosomal recessive degeneration of the anterior horn cells, leading to progressive weakness and wasting of skeletal muscles due to mutations in the survival motor neurone (*SMN1*) gene. This is the second most common cause of neuromuscular disease in the UK after Duchenne muscular dystrophy, and affects 1 in 6000–10,000 live births. A number of phenotypes are recognized.

Spinal muscular atrophy type 1 (Werdnig-Hoffmann disease)

A very severe progressive disorder presenting from birth to 3 months of age (Fig. 29.7). Diminished fetal movements are often noticed during pregnancy and there may be arthrogryposis (positional deformities of the limbs with contractures of at least two joints) at birth. Typical signs include:

- alert expression
- fasciculation of the tongue
- symmetrical flaccid paralysis
- absent deep tendon reflexes
- intercostal recession
- weakness of bulbar muscles causing weak cry and poor suck with pooling of secretions.



Figure 29.7 Spinal muscular atrophy type 1 (Werdnig-Hoffmann disease) showing proximal muscle wasting, chest deformity from weakness of the intercostal muscles and thighs held abducted because of hypotonia.

Untreated, the natural history comprises death from respiratory failure within about 12 months of age. However recent innovative treatments affecting gene expression have been shown to be effective and are now available in countries that can afford them. The first of these treatments (Nusinersen) targeted a closely related but partially functioning gene, *SMN2*. By preventing exon-skipping it increases the production of the *SMN2* protein and this ameliorates the clinical expression of SMA in some children. Gene therapy has recently proved successful in very young children but all these new treatments are very expensive.

There are milder forms of the disorder with a later onset. Children with type 2 spinal muscular atrophy present at age 3 months to 15 months and can sit but never walk independently. Those with the milder type 3 present after 1 year of age and do learn to walk. The most severe form is SMA type 0 and is diagnosed in newborn infants that are born so weak that their survival has been limited to only a few weeks. The place of the treatments described above is yet to be established.

Peripheral neuropathies

Charcot-Marie-Tooth disease (the hereditary motor sensory neuropathies)

There are many forms of Charcot-Marie-Tooth (CMT) disease, which typically lead to symmetrical, slowly progressive distal muscular wasting. They are caused by mutations in myelin genes. CMT1A accounts for 70%–80% and is inherited in an autosomal dominant manner in two thirds, one third developing the mutation *de novo*. The other types of CMT disease can be inherited by autosomal dominant, recessive or X-linked modes.

Children may present preschool with tripping from bilateral foot drop. Examination shows loss of ankle reflexes progressing to loss of knee reflexes. Pes cavus may be present, the lower limbs being affected more than the upper. Nerve conduction studies show a motor and sensory neuropathy. Affected nerves may be hypertrophic due to demyelination followed by attempts at remyelination. The disease is chronic but only rarely do those affected lose the ability to walk. The initial presentation of Friedreich ataxia can be similar.

Guillain–Barré syndrome (acute post-infectious polyneuropathy)

Can occur at any age, and typically presents 2–3 weeks after an upper respiratory tract infection or campylobacter gastroenteritis, with an ascending, progressive, symmetrical weakness over a few days to 2 weeks. There is loss of tendon reflexes and autonomic involvement. Sensory symptoms, usually in the distal limbs or trunk, are less striking than the weakness but can be unpleasant. When present, a bilateral facial weakness is easily missed in young children. Involvement of bulbar muscles leads to difficulty with chewing and swallowing and the risk of aspiration.

Dysautonomia occurs in 70% and manifests as tachycardia, bradycardia and other arrhythmias, hypertension and orthostatic hypotension, urinary retention, ileus, and loss of sweating. Hypoventilation can require artificial ventilation, best started before established respiratory failure. The maximum muscle weakness may occur only 2–4 weeks after

the onset of illness. Although full recovery can be expected in 90% of cases, this may take up to 2 years.

MRI of the spinal cord (or brain and spinal cord) is the most useful acute investigation, to identify or exclude a spinal cord lesion, e.g. a bleed, tumour, or inflammatory transverse myelitis. The CSF white count is not raised, but CSF protein is characteristically markedly raised; however this may not be seen until the second week of illness. Nerve conduction studies typically show reduced velocities but this may not be evident until after the second week.

Management is supportive, particularly of respiration. The disorder is probably due to the formation of antibody attaching itself to protein components of myelin. Corticosteroids have no beneficial effect and may delay recovery. Controlled trials indicate that recovery is more rapid with intravenous immunoglobulin infusion or plasma exchange.

Bell palsy and facial nerve palsies

Bell palsy is an isolated lower motor neurone paresis of the VIIth cranial nerve leading to facial weakness (Fig. 29.8). The aetiology is often unclear, although it is sometimes caused by post-infectious inflammation associated with herpes simplex virus or Lyme disease. Herpes virus infection of the geniculate ganglion can cause painful vesicles on the tonsillar fauces and external ear, with a facial nerve paresis. If herpes is suspected, treat with aciclovir.

Corticosteroids can reduce any facial nerve inflammation and swelling in the facial canal, if given during the first week, and speed full recovery. Recovery is complete in the majority of cases but may take several months. The main complication is conjunctival infection due to incomplete eye closure on blinking. This may require the eye to be protected with lubricating drops or ointment, a patch, or even tarsorrhaphy.

There are important differential diagnoses. If there is also a recent VIth nerve paresis, or ipsilateral cerebellar signs, or contralateral upper motor neurone signs, suspect



Figure 29.8 Bell palsy. There is left facial weakness of both the upper and lower face.

a brain stem lesion. If there are symptoms of a recent VIIth nerve paresis, the most likely diagnosis is a compressive lesion in the cerebellopontine angle. Hypertension should be excluded, as there is an association between Bell palsy and coarctation of the aorta and renal failure.

Disorders of neuromuscular transmission

Myasthenia gravis

This presents as abnormal muscle fatigability which improves with rest or anticholinesterase drugs.

Juvenile myasthenia

This is similar to adult autoimmune myasthenia gravis and is due to binding of antibody to acetylcholine receptors on the postsynaptic membrane of the neuromuscular junction. This reduces the number of functional receptors. Presentation is usually after 10 years of age with ophthalmoplegia and ptosis, loss of facial expression, and difficulty chewing (Fig. 29.9). Generalized, especially proximal, weakness may be seen.

Diagnosis is made by observing improvement following the administration of intravenous edrophonium over a few minutes or oral pyridostigmine or neostigmine over days. Identifying acetylcholine receptor antibodies (seen in 60%–80%) or, more rarely, anti-MuSK (antimuscle-specific kinase) antibodies will confirm the diagnosis and direct treatment decisions. Treatment is with the choline esterase inhibitors pyridostigmine or neostigmine and immunosuppressive therapy. Immune-modulating drugs such as prednisolone, azathioprine or mycophenolate mofetil, or even monoclonal antibodies ('biologicals'), e.g. rituximab are of value. Thymectomy is indicated if a thymoma is present or in young antibody-positive patients with a very acute, severe presentation affecting more than just ocular muscles. Plasma exchange is used for crises.

Congenital myasthenic syndromes

These are rare genetic syndromes which cause neuromuscular junction failure in newborn infants. Features may include ptosis, ophthalmoplegia and bulbar and respiratory muscle weakness and arthrogryposis. These disorders do not always respond to anticholinesterase inhibitors.



Figure 29.9 Myasthenia gravis showing ptosis from ocular muscle fatigue which improved with edrophonium.

Muscle disorders

The muscular dystrophies

This is a group of inherited disorders with progressive muscle degeneration.

Duchenne muscular dystrophy (DMD)

Affects 1 in 3000–6000 male infants. It is an X-linked recessive disorder, although about a third of boys have *de novo* mutations. It results from a deletion of the gene for dystrophin, which connects the cytoskeleton of a muscle fibre to the surrounding extracellular matrix through the cell membrane. Where it is deficient, there is gradual, progressive myofibre necrosis. Some countries (but not the UK) have neonatal screening programmes; affected children are detected by an elevated plasma creatine kinase (CK).

In countries without screening, presentation is often with a waddling gait and/or language delay; they have to mount stairs one by one and run slowly compared with their peers. Although the average age of clinical diagnosis remains 5 years, children often have symptoms and signs much earlier. They will show Gowers' sign (the need to turn prone to rise over the age of 3 years). There is pseudohypertrophy (enlargement) of the calves because of replacement of muscle fibres by fat and fibrous tissue.

In the early school years, affected boys tend to be slower and clumsier than their peers. The progressive muscle atrophy and weakness means that they typically are no longer able to walk by the age of about 10–14 years. Life expectancy is reduced to the late twenties from respiratory failure or the associated cardiomyopathy. About one-third of affected children have learning difficulties. Scoliosis is a common complication.

Management

Physiotherapy and splinting of the ankles helps to prevent contractures. Achilles tendon lengthening and scoliosis surgery may be required. Weakness of respiratory and upper airway muscles may lead to sleep disordered breathing. If undetected and untreated this may cause daytime headache, irritability and loss of appetite. Symptoms are highly variable; boys who are no longer able to walk should have regular sleep studies. Overnight CPAP (continuous positive airway pressure) or non-invasive positive pressure ventilation may be provided to improve the quality of life.

Corticosteroids may help to preserve mobility and prevent scoliosis. The precise mechanism by which glucocorticoids help is not known. Innovative molecular genetic therapies are becoming available, including exon-skipping drugs, which can bypass the effect of some mutations leading to the production of a small amount of dystrophin, and a milder phenotype.

Becker muscular dystrophy

Becker dystrophy is allelic with Duchenne muscular dystrophy (i.e. caused by different mutations in the same gene), but some functional dystrophin is produced. The features are similar to those of Duchenne muscular dystrophy but clinically the disease is milder and progresses more slowly. The average age of onset is 11 years, loss of independent ambulation is in the late twenties, with life expectancy well into middle or old age.

Limb girdle muscular dystrophies

These conditions present with proximal upper and lower limb weakness. Cardiomyopathy and difficulty with breathing may be associated with some. These conditions can have different modes of inheritance. Plasma creatine kinase is usually raised.

Congenital muscular dystrophies

These have autosomal recessive inheritance, and most present at birth or in early infancy with weakness, hypotonia or contractures. Typically the proximal weakness is slowly progressive with a tendency to contracture when the ability to walk is lost. Feeding difficulties and breathing difficulties may occur in some cases. Some may run a more static course. Muscle biopsy shows dystrophic features with a reduction of one of the extracellular matrix proteins such as laminin (most common); or one of several glycosyltransferases. Some congenital muscular dystrophies have associated central nervous abnormalities, which cause intellectual disability.

Congenital myopathies

These conditions present at birth or in infancy with defects primarily affecting skeletal muscle fibres, causing muscle weakness and/or hypotonia. They are static or slowly progressive. They are named according to the changes seen on muscle biopsy or electron microscopy. Plasma creatine kinase is normal or only mildly elevated.

Metabolic myopathies

Metabolic conditions can affect muscles, due either to the deposition of storage material or to energy-depleting enzyme deficiencies. Presentation is as a floppy infant or, in older children, with muscle weakness or cramps on exercise. The main causes are:

- glycogen storage disorders (see Ch. 27, Inborn errors of metabolism)
- disorders of lipid metabolism. Fatty acids are important muscle fuel. Fatty acid oxidation occurs in the mitochondria and defects in this pathway can result in weakness. Carnitine palmitoyltransferase II (CPT II) deficiency is the most frequent disorder of lipid metabolism. Defects of fatty acid oxidation can cause a secondary deficiency in carnitine
- mitochondrial cytopathies (see Ch. 9, Genetics, and Ch. 27). Rare disorders caused by mutations in the genes for mitochondrial proteins involved in respiratory chain function can be caused by mitochondrial DNA mutations (which are maternally inherited), or nuclear DNA mutations (mostly recessive or X-linked). Myopathy may be the major manifestation or the disorder may be multisystem, with lactic acidosis and encephalopathy. The mutation responsible and mode of inheritance should be determined.

The inflammatory myopathies

Benign acute myositis

This is assumed to be post-viral, and runs a self-limiting course. Pain and weakness occur in affected muscles. Plasma creatine kinase is usually raised.



Figure 29.10 Pink-purple rash in dermatomyositis.

Dermatomyositis

This is a systemic illness, probably due to an angiopathy. Onset is usually between 5–10 years of age. This can be acute, but more typically is insidious with fever, misery, and eventually symmetrical muscle weakness, which is mainly proximal. Sometimes pharyngeal muscle involvement affects swallowing. Muscle pain is common and arthritis may occur. There is also a characteristic violaceous (pink-purple) rash on the eyelids, and periorbital oedema (Fig. 29.10). The rash may also affect the extensor surfaces of joints, e.g. elbow, and with time subcutaneous calcification (calcinosis) can appear. Inflammatory markers (CRP (C-reactive protein), ESR) are sometimes raised, and CK is usually raised. Muscle biopsy shows an inflammatory cell infiltrate and atrophy. Physiotherapy is needed to prevent contractures. Corticosteroids and other immunosuppressants, e.g. methotrexate, ciclosporin (cyclosporine), may be needed. Mortality is 5%–10%.

Myotonic disorders

Myotonia is delayed relaxation after sustained muscle contraction. It can be identified clinically and by EMG.

Dystrophia myotonica type I

This relatively common illness is dominantly inherited and caused by a nucleotide triplet repeat expansion, CTG in the *DMPK* gene, so this means there can be anticipation through generations, especially when maternally transmitted (see Ch. 9). Newborns with congenital myotonic dystrophy can present with hypotonia and feeding and respiratory difficulties due to muscle weakness. They can have thin ribs, talipes at birth, together with oligohydramnios and reduced fetal movements during pregnancy. It is then useful to examine the mother for myotonia. This manifests as slow release of handshake or difficulty releasing the tightly clasped fist. This may be mild and not previously noticed. Sensitivity is required as diagnosis in a neonate may have repercussions for the family. However, making the diagnosis in family members can help to reduce the risk of potential complications, such as cardiac dysrhythmia and anaesthetic complications. Older children can present with a myopathic facial appearance (Fig. 29.11), learning difficulties and myotonia. Adults develop cataracts and males develop baldness, testicular atrophy and type 2 diabetes. Death is usually due to cardiac conduction defects.

The hypotonic or 'floppy' infant

Persisting hypotonia can be readily felt on picking up the infant, who tends to slip through the fingers (Fig. 29.12a), hang like a rag doll when suspended prone (Fig. 29.12b), and there is marked head lag when the infant is pulled forward by the arms from supine (Fig. 29.12c). The causes



Figure 29.11 Myotonic dystrophy in an 8-year-old who has marked facial weakness and moderately severe learning difficulties.

are listed in Fig. 29.13. The clinical examination may help determine the site of the lesion, whether cerebral or neuromuscular. Central hypotonia is associated with poor truncal tone but preserved limb tone. Dysmorphic features suggest a genetic cause. Lower motor neurone lesions are suggested by a frog-like posture (see Fig. 29.7), poor antigravity movements and absent tendon reflexes.

Ataxia

The causes of cerebellar ataxia are listed in Box 29.3. But unsteadiness of posture and movement can also be caused by disorders of the inner ear labyrinth, sensory nerves and dorsal columns of the spinal cord, muscle weakness, or seen in someone with functional neurological symptoms and signs.

Friedreich ataxia

This is an autosomal recessive condition. It is due to a triplet repeat in the *FXN* gene causing a lack of the frataxin protein. It presents with worsening ataxia and dysarthria, distal wasting in the lower limbs with absent reflexes and pes cavus. It is similar to Charcot–Marie–Tooth disease, but in Friedreich ataxia there is impairment of joint position and vibration sense (posterior-columns affected), extensor plantars (indicating pyramidal involvement) and typically optic atrophy. The cerebellar component becomes more apparent with age. Evolving kyphoscoliosis, diabetes mellitus and cardiomyopathy can cause cardiorespiratory compromise and death at age 40–50 years.

Ataxia telangiectasia

This disorder of DNA repair is autosomal recessive. The gene codes for a protein kinase mutation which, among other things, is involved in repairing double-stranded DNA breaks. There is mild delay in motor development in toddlers and incoordination of eye movements with delay in ocular pursuits and saccades (moving eyes to a target). Difficulty with balance, coordination, and speech become evident in primary school. There is subsequent deterioration, with many children requiring a wheelchair



Figure 29.12 Clinical features of hypotonia. (a) On vertical suspension when held upright under the arms, the hypotonic infant slides through one's hands. (b) On 'ventral suspension', the infant flops like a rag doll. (c) On 'pulling to sit' by traction of the arms, there is marked head lag. From: Lissauer T, Fanaroff AA, Mial L, Fanaroff J (eds), *Neonatology at a Glance*, ed 4, Chichester, 2020, John Wiley.

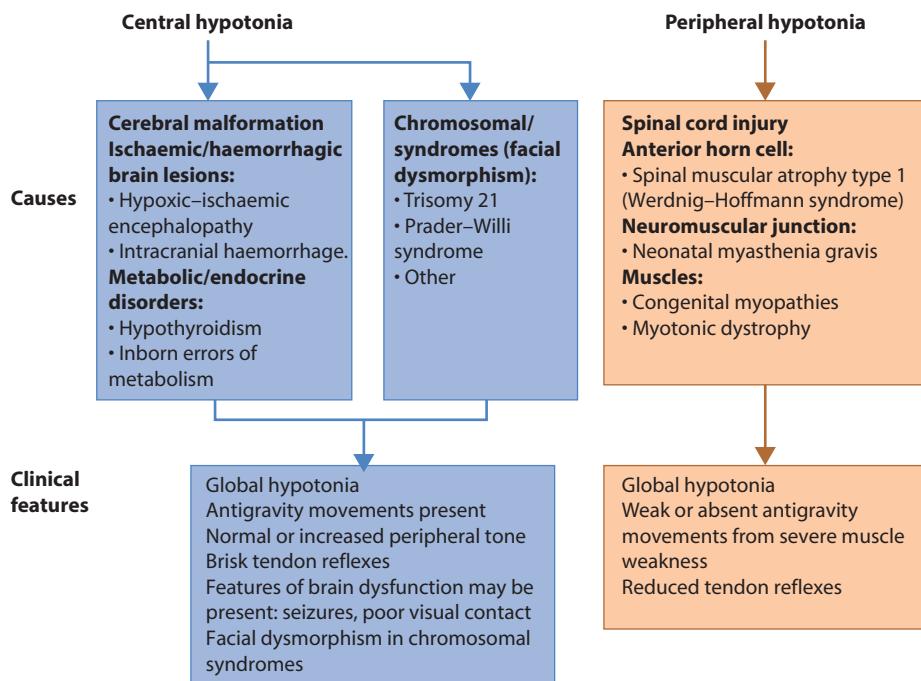


Figure 29.13 Causes of a hypotonic ('floppy') infant.



Figure 29.14 Telangiectasia of the conjunctiva are present from about 4 years of age in ataxia telangiectasia

Box 29.3 Causes of cerebellar ataxia

- Toxins, e.g. ethanol
- Drugs, e.g. carbamazepine, lamotrigine
- Post-infectious cerebellitis – varicella
- Posterior fossa tumours
- Cerebellar agenesis/dysgenesis
- Friedreich ataxia
- Ataxia telangiectasia
- Mitochondrial disease
- Other hereditary cerebellar ataxias
- Miller Fisher syndrome (a variant of Guillain–Barré syndrome)

in their teens. Telangiectasia develop in the conjunctiva ([Fig. 29.14](#)), and may occur in the neck and shoulders from about 4 years of age. These children:

- have an increased susceptibility to infection, and deficiencies of IgA and IgE
- develop malignant disorders, such as lymphomas and acute leukemias
- develop progressive pulmonary disease with bronchiectasis
- have a raised serum alpha-fetoprotein
- have sensitivity to ionizing radiation.

Most will die of malignancy or chronic lung disease in their twenties.

Cerebrovascular disease

Intracranial haemorrhage

Extradural haemorrhage

This usually follows direct head trauma (see [Fig. 7.5](#)), often associated with skull fracture (tearing of middle meningeal artery as it passes through the foramen spinosum of the sphenoid bone). It results from arterial or venous bleeding into the extradural space. There is often a lucid interval until the conscious level deteriorates, and sometimes epileptic seizures, secondary to the expanding haematoma. There may be focal neurological signs with dilatation of the ipsilateral pupil, paresis of the contralateral limbs, and a false localizing unilateral or bilateral VIth nerve paresis. In young children, initial presentation may

be with anaemia and shock. The diagnosis is confirmed with a CT scan. Management is to correct hypovolaemia, urgent evacuation of the haematoma and arrest of the bleeding.

Subdural haematoma

This results from tearing of the bridging veins as they cross the subdural space. It is a characteristic lesion in non-accidental injury caused by shaking and/or direct trauma in infants and toddlers. Retinal haemorrhages are typical of shaking injury. Subdural haematomas are occasionally seen following a fall from a considerable height, and rarely in association with brain shrinkage through atrophy or overdrainage of hydrocephalus.

Subarachnoid haemorrhage

This is much more common in adults. Presentation is usually with a severe headache with rapid onset ('thunderclap headache'), vomiting, confusion or a decreased level of consciousness, and sometimes epileptic seizures, and coma. A CT scan of the head usually identifies blood in the CSF. Occasionally a lumbar puncture is required. The cause is often an aneurysm or arteriovenous malformation. It can be identified on MR angiography, CT, or conventional angiography. Treatment can be neurosurgical or with interventional radiology.

Summary

Intracranial haemorrhage

- History of significant head injury – an extradural haemorrhage may be present even if lucid immediately afterwards.
- Subdural haematoma and retinal haemorrhages in an infant – consider non-accidental injury caused by shaking and/or direct trauma.

Stroke

Perinatal stroke is described in [Chapter 11](#) (Neonatal medicine). Childhood stroke may be due to vascular, thromboembolic or haemorrhagic disease. The clinical presentation is determined by the vascular territory involved. In arterial ischaemic stroke there is commonly compromise of the anterior circulation (internal carotid, anterior cerebral arteries and middle cerebral arteries), which leads to contralateral hemiparesis with or without hemianopia, and speech disturbance. Less common is compromise of the posterior circulation (vertebrobasilar arteries) with associated visual and/or cerebellar signs.

Causes of stroke include:

- Cardiac – congenital cyanotic heart disease, e.g. Fallot tetralogy, endocarditis.
- Haematological – sickle cell disease; deficiencies of antithrombotic factors, e.g. protein S.
- Postinfective – following varicella or other viral infections.
- Inflammatory – damage to vessels in autoimmune disease, e.g. SLE (systemic lupus erythematosus).

- Metabolic/genetic – homocystinuria, mitochondrial disorders, e.g. myoclonic epilepsy, lactic acidosis, and stroke (MELAS); cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
- Vascular malformations – arteriovenous malformation or moyamoya disease, in which there is a progressive involution of cerebral arteries. Moyamoya comes from the Japanese for ‘puff of smoke’, similar to the blurred appearance seen on angiography
- Trauma – dissection of carotid or vertebral arteries.

Investigations should include an assessment of cerebral and external carotid vasculature with MRI, MR angiogram and, when indicated, MR venography; echocardiography to detect a source of embolism, along with a thrombophilia and vasculitis screen, and metabolic tests for homocysteine and mitochondrial cytopathy. Often no cause can be identified. Rehabilitation requires the involvement of the multidisciplinary therapy team. Low-dose aspirin prophylaxis is recommended after arterial ischaemic stroke.

Summary

Strokes

- Occur in infants and children.
- In infants, occur in the perinatal period, and may present in late infancy with a hemiplegia or with epileptic seizures.
- In children, are seen in association with cardiac or sickle cell disease, following varicella infection or neck trauma. However, often no cause is evident.

Microcephaly and macrocephaly

These are described in [Chapter 12](#) (Growth and puberty).

Neural tube defects and hydrocephalus

Neural tube defects

Neural tube defects result from failure of normal fusion of the neural plate to form the neural tube during the first 28 days following conception. Mothers of a fetus with a neural tube defect have a 10-fold increase in risk of having a second affected fetus. The risk is also increased 10–20 fold in mothers taking the antiepileptic drug sodium valproate. Maternal folic acid supplementation during early pregnancy has been shown to reduce prevalence by 25%–50%. In many countries, but not in the UK or most countries in Western Europe, cereal grain products are fortified with folic acid.

The birth prevalence of neural tube defects in the UK has fallen dramatically from 4/1000 live births in the 1970s to 0.1/1000 live births in 2018 ([Fig. 29.15](#)). The reason for the decline is uncertain, but may be associated with improved maternal nutrition, mothers taking folate supplements pre and during pregnancy, and avoiding sodium valproate in pregnancy, together with antenatal diagnosis and the option of termination of pregnancy.

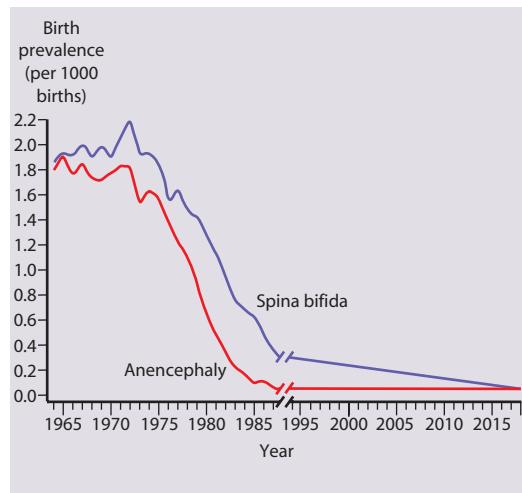


Figure 29.15 The decline in the number of babies born with neural tube defects. This has resulted from a natural decrease together with antenatal diagnosis and termination of pregnancy.

Anencephaly

This is failure of development of most of the cranium and brain. Affected infants are stillborn or die shortly after birth. It is detected on antenatal ultrasound screening and termination of pregnancy is usually offered.

Encephalocele

There is extrusion of brain and meninges through a midline skull defect, which can be corrected surgically. However, there are often underlying associated cerebral malformations.

Spina bifida occulta

This failure of fusion of the vertebral arch ([Fig. 29.16a](#)) is often an incidental finding on X-ray, but there may be an associated overlying skin lesion such as a tuft of hair, lipoma, birth mark or small dermal sinus, usually in the lumbar region. There may be underlying tethering of the cord (diastematomyelia), which, with growth, may cause impairments in bladder and lower limb function. The extent of the underlying lesion can be delineated by ultrasound and/or MRI. Neurosurgical division of the tethering is usually indicated.

Meningocele and myelomeningocele

Meningoceles ([Fig. 29.16b](#)) usually have a good prognosis following surgical repair.

Myelomeningoceles ([Figs. 29.16c, 29.17](#)) may be associated with:

- variable paresis of the lower limbs with hypotonia
- muscle imbalance, which may cause dislocation of the hip and talipes
- sensory loss
- bladder denervation (neuropathic bladder)
- bowel denervation (neuropathic bowel)
- scoliosis
- hydrocephalus from the associated Chiari type 2 malformation (herniation of the cerebellar tonsils and brainstem tissue through the foramen magnum), leading to disruption of CSF flow.

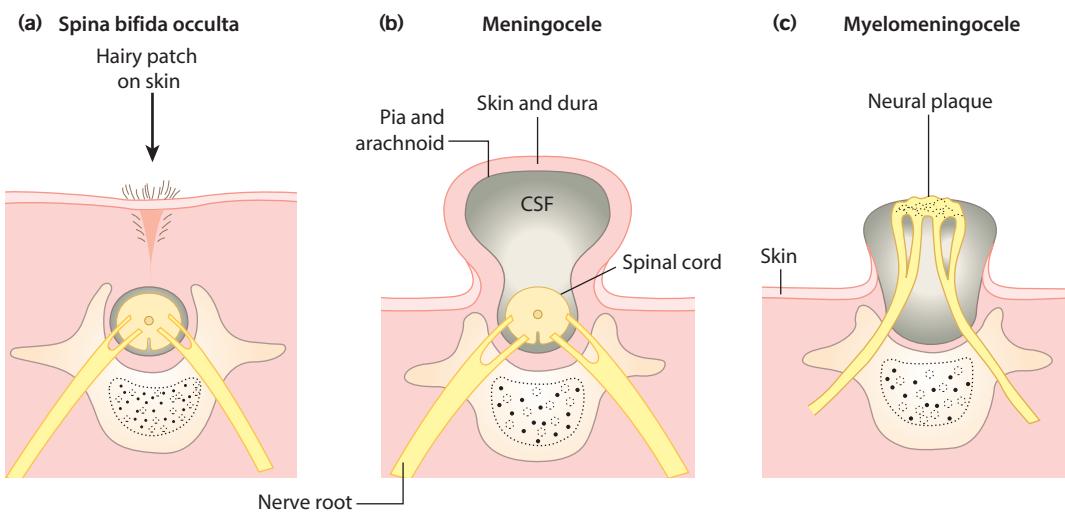


Figure 29.16 Neural tube defects: (a) spina bifida occulta; (b) meningocele; and (c) myelomeningocele.



Figure 29.17 Myelomeningocele showing the exposed neural tissue and the patulous anus from neuropathic bowel.

Management

The back lesion is usually closed soon after birth. Paralysis and muscle imbalance requires physiotherapy to prevent joint contractures. Walking aids or a wheelchair help mobility. Because of the sensory loss, skin care is required to avoid the development of skin damage and ulcers.

The neuropathic bladder is managed with an indwelling catheter or intermittent urinary catheterization by parents or by older children themselves. There should be regular checks for hypertension, renal function and urinary infection. Prophylactic antibiotics may be necessary. Medication (such as ephedrine or oxybutynin) may improve bladder function and improve urinary dribbling.

Bowel denervation requires regular toileting, and laxatives and suppositories are likely to be necessary with a low roughage diet for lesions above L3.

Scoliosis is monitored and may require surgical treatment. Ventricular dilatation associated with a Chiari 2 malformation is often present at birth, and 80% of affected infants require a ventriculoperitoneal shunt for progressive hydrocephalus during the first few weeks of life.

The most severely disabled have a spinal lesion above L3 at birth. They are unable to walk, have a scoliosis, neuropathic bladder, hydronephrosis and frequently develop hydrocephalus.

Modern medical care has improved the quality of life for severely affected children. Their care is best managed by a specialist multidisciplinary team.

Recently, fetoscopic surgery to repair the myelomeningocele *in utero* in the late mid-trimester of pregnancy has been performed on selected fetuses in a few specialist centres. This may reduce the need for ventricular shunting and improve neurodevelopmental outcome, but carries a risk of preterm delivery.

Summary

Neural tube defects

- Include anencephaly, encephalocele, spina bifida occulta, meningocele, myelomeningocele.
- The UK birth prevalence has fallen recently, due to a natural decline and antenatal screening.
- The birth prevalence is reduced by periconceptual folic acid.
- Myelomeningocele may cause lower limb sensory loss and paralysis, dislocation of hips, talipes equinovarus, neuropathic bladder and bowel, scoliosis, and hydrocephalus from the Chiari 2 malformation.

Hydrocephalus

In hydrocephalus, there is an accumulation of cerebrospinal fluid (CSF) in the brain. In infants and children this can be congenital, associated with cerebral anomalies, or obstruction to the flow of CSF leading to dilatation of the ventricular system proximal to the site of obstruction. The obstruction may be within the ventricular system or aqueduct (obstructive hydrocephalus), or at the arachnoid villi, the site of absorption of CSF (communicating hydrocephalus), or both (Box 29.4).

Box 29.4 Causes of hydrocephalus***Obstructive hydrocephalus (obstruction in the ventricular system)***

Congenital anomaly:

- Aqueduct stenosis
- Chiari malformation (cerebellar tonsils herniation through foramen magnum)

Posterior fossa neoplasm or vascular malformation

Intraventricular haemorrhage in preterm infant

Communicating hydrocephalus (failure to reabsorb CSF)

Subarachnoid haemorrhage

Meningitis, e.g. pneumococcal, tuberculous

Combined hydrocephalus***Clinical features***

In infants with hydrocephalus, as their skull sutures have not fused, the head circumference will be disproportionately large or show an excessive rate of growth. The skull sutures separate, the anterior fontanelle bulges, and the scalp veins become engorged.

An advanced sign is fixed downward gaze or 'sun setting' of the eyes (Fig. 29.18). Older children will develop signs and symptoms of raised intracranial pressure.

Hydrocephalus may be diagnosed on antenatal ultrasound screening or in preterm infants on routine cranial ultrasound scanning. For suspected hydrocephalus, initial assessment is with cranial ultrasound (in infants) or head MRI. The head circumference should be monitored over time and plotted on a centile chart.

Treatment is required for symptomatic relief of raised intracranial pressure and to minimize the risk of neurological damage. The mainstay is the insertion of a ventriculoperitoneal shunt (Fig. 29.19), but endoscopic treatment to create a ventriculostomy is sometimes performed. Shunts can malfunction due to blockage or infection (usually with coagulase-negative staphylococci). They then need replacing or revising. Over-drainage of fluid can cause low-pressure headaches but the insertion of programmable valves can help avoid this.

Summary**Hydrocephalus**

- In infants, presents with excessive increase in head circumference, separation of skull sutures, bulging of the anterior fontanelle, distension of scalp veins and sun-setting of the eyes.
- Older children present with symptoms of raised intracranial pressure.
- Treatment is usually with a ventriculo-peritoneal shunt.



Figure 29.18 Grossly enlarged head and downward deviation of the eyes (setting-sun sign) from untreated hydrocephalus.

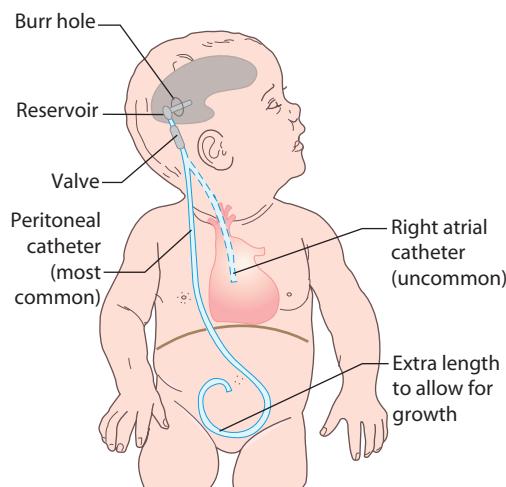


Figure 29.19 Ventriculoperitoneal shunt for drainage of symptomatic hydrocephalus. A sufficient length of shunt tubing is left in the peritoneal cavity to allow for the child's growth. Right atrial catheters require revision with growth and have more complications.

Neurocutaneous syndromes

The nervous system and the skin have a common ectodermal origin. Embryological disruption causes syndromes involving abnormalities to both systems – the neurocutaneous syndromes.

Neurofibromatosis

Neurofibromatosis type 1 (NF-1) affects 1 in 3000 live births. It is an autosomal dominant, highly penetrant condition, with variable expression. It is caused by a mutation in the neurofibromin-1 (*NF1*) gene, which arises in about 50% as a *de novo* mutation.

To make the diagnosis, two or more of these criteria need to be present:

- six or more café-au-lait spots greater than 5 mm in size before puberty, greater than 15 mm after puberty (Fig. 29.20)
- more than one neurofibroma, a firm nodular overgrowth of any peripheral nerve



Figure 29.20 Café-au-lait patches and axillary freckling in neurofibromatosis.

- axillary freckling (Fig. 29.20)
- optic glioma which may cause visual impairment
- one Lisch nodule: a hamartoma of the iris seen on slit-lamp examination
- bony lesions from sphenoid dysplasia, which can cause eye protrusion
- a first-degree relative with NF-1.

The cutaneous features tend to become more evident after puberty, and there is a wide spectrum of involvement from mild to severe. Neurofibromata appear in the course of any peripheral nerve, including cranial nerves. They may look unsightly or cause neurological signs if they occur at a site where a peripheral nerve passes through a bony foramen. Visual or auditory impairment may result if there is compression of the IInd or VIIIth cranial nerve. Megalencephaly with learning difficulties and epilepsy are sometimes seen.

Neurofibromatosis type 2 (NF-2; multiple inherited schwannomas, meningiomas, and ependymomas) is less common. It is an autosomal dominant syndrome caused by a mutation in the NF2 gene, usually presenting in adolescence. About 50% are due to *de novo* mutations. Bilateral acoustic neuromata are the predominant feature and present with deafness and sometimes a cerebello-pontine angle syndrome with a facial (VIIth) nerve paresis and cerebellar ataxia.

Both NF-1 and NF-2 can be associated with endocrine disorders, the multiple endocrine neoplasia syndromes.

Other associations are phaeochromocytoma, pulmonary hypertension, renal artery stenosis with hypertension. Rarely, the benign tumours undergo sarcomatous change. However, most people with the disorders carry no features other than the cutaneous stigmata.

Tuberous sclerosis

The prevalence of tuberous sclerosis is 1 in 9000 live births. It is autosomal dominant, with variable penetrance, and up to 70% of mutations arise *de novo*. The cause is a mutation in the *TSC1* or *TSC2* genes.



Figure 29.21 Facial angiofibromas in tuberous sclerosis.

The cutaneous features consist of:

- depigmented 'ash leaf'-shaped patches or amelanotic naevi which fluoresce under ultraviolet light (Wood's light)
- roughened patches of skin (shagreen patches) usually over the lumbar spine
- angiofibromata ('adenoma sebaceum') in a butterfly distribution over the bridge of the nose and cheeks, which are unusual before the age of 3 years (Fig. 29.21).

Neurological features are seen in 50%, including:

- epilepsy with infantile spasms and/or focal seizures, usually associated with intellectual disability, and autism.

Other features include:

- fibromata beneath the nails (subungual fibromata)
- dense white areas on the retina (phakomata) from local degeneration
- rhabdomyomata of the heart which are identifiable in the early weeks of life on echocardiography but usually resolve in infancy
- angiomyolipomas and polycystic kidneys
- cysts in the lungs.

In the brain, even if asymptomatic, there are subependymal nodules and cortical tubers. The subependymal nodules may enlarge over time and form subependymal giant cell astrocytomas which sometimes block the flow of CSF causing headache, vomiting, and hydrocephalus.

Many people who carry the gene have no stigmata other than the cutaneous features and no associated neurological features. CT scans will detect the calcified subependymal nodules and tubers from the second year of life. MRI is more sensitive and more clearly identifies the lesions.

Sturge–Weber syndrome

This is a sporadic disorder with a haemangiomatous facial lesion (a port-wine stain) in the distribution of the trigeminal nerve associated with a similar lesion intracranially

(ipsilateral leptomeningeal angioma). In the most severe form, it may present with epilepsy, intellectual disability, and a contralateral hemiplegia.

The ophthalmic division of the trigeminal nerve is always involved (Fig. 29.22). MRI is the imaging modality of choice. Children presenting with intractable epilepsy in



Figure 29.22 Sturge–Weber syndrome. There is a port-wine stain in the distribution of the trigeminal nerve.

early infancy benefit from hemispherectomy. Laser treatment may be used to lighten or remove the port-wine stain. For children who are less severely affected, deterioration is unusual after the age of 5 years, although there may still be seizures and learning difficulties. There is a high risk of ipsilateral glaucoma in 50% of children, which should be assessed in the neonatal period.

Neurodegenerative disorders

These are disorders that cause a deterioration in motor and intellectual function (Table 29.5). Abnormal neurological features develop, including seizures, spasticity, abnormal head circumference (macrocephaly or microcephaly), involuntary movement disorders, visual and hearing loss, and behaviour change. While individually rare, they are numerous and include many inborn errors of metabolism. These are discussed in more detail in Chapter 27.

Developmental regression or reported loss of previously acquired skills should prompt investigation of the cause. The most commonly encountered neurodegenerative conditions are:

- lysosomal storage disorders, e.g. mucopolysaccharidosis type III, in which absence of an enzyme leads to accumulation of harmful metabolites within the lysosomes. These disorders often have organomegaly associated with them

Table 29.5 Some examples of neurodegenerative disorders seen in children, for reference

	Presentation	Diagnostic investigations
Age 0–2 years		
Infantile neuronal ceroid lipofuscinosis (NCL)	Developmental arrest by end of first year, seizures and blindness	Skin biopsy, blood enzyme analysis, DNA testing
Krabbe leukodystrophy	Irritability, hypertonia, myoclonus	White cell enzymes
Rett syndrome	Regression by 6–18 months, with characteristic hand wringing	DNA testing
Tay Sachs	Hypotonia, seizures, and blindness.	White cell enzymes
Age 2–5 years		
Mucopolysaccharidosis type III	Developmental delay, behavioural disturbances, dysmorphism	Urinary glycosaminoglycans
Late infantile NCL	Myoclonus, motor difficulties, blindness	White cell enzymes
Alpers	Seizures, developmental regression, hypotonia and hepatic derangement	Skin biopsy, enzymes analysis, DNA testing
Age 5–12 years		
Juvenile NCL	Cognitive and motor decline. Visual deterioration. Seizures later	DNA testing
Adrenoleukodystrophy	Cognitive development slowed, visual impairment, seizures	Vacuolated lymphocytes on light microscopy, fingerprinting on electron microscopy, DNA testing
Niemann–Pick type C	Seizures, vertical gaze palsy	VLCFA (very long chain fatty acids), DNA testing
Friedreich ataxia	Ataxia, pyramidal signs, and peripheral neuropathy	Oxysterols, DNA testing
Age 12+years		
Wilson disease	Liver disease, extrapyramidal movement disorder and tremor	DNA testing
Juvenile Huntington	Progressive dystonia, dementia, seizures, corticospinal tract signs	Plasma copper and caeruloplasmin, DNA testing

- peroxisomal enzyme defects, e.g. X-linked adrenoleukodystrophy (see below). Peroxisomes are catalase- and oxidase-containing organelles involved in long-chain fatty acid oxidation. Enzyme deficiencies can lead to accumulation of very long-chain fatty acids (VLCFAs)
- Wilson disease, from the accumulation of copper, may cause changes in behaviour and additional involuntary movements or a mixture of neurological and hepatic symptoms (see Ch. 21, Liver disorders).

Leukodystrophies

MRI can identify many degenerative, often life-limiting (shortening), genetic diseases affecting predominantly the myelination of white matter in the brain. Once suspected, some can be diagnosed by white cell enzyme assay or other biochemical tests, but increasing reliance is placed on DNA testing. Krabbes and adrenoleukodystrophy (ALD) are just two examples.

Poliodystrophies

MRI can also assist in diagnosing some degenerative diseases affecting predominantly the grey matter in the brain. These include the neuronal ceroid lipofuscinoses (NCLs), Alpers, and the fatal complication of measles, subacute sclerosing panencephalitis (SSPE). This was almost eradicated in many countries by immunization, but has reemerged in some countries following reduced uptake of the measles vaccine. SSPE presents 6–8 years after measles in preschool childhood with progressive dementia, dystonia and visual impairment, and characteristic periodic jerks best identified on EEG.

Acknowledgements

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Further reading

Forsyth R, Newton R: *Paediatric neurology: Oxford specialist handbook in paediatrics*, ed 3, Oxford, 2017, Oxford University Press.

Websites

British Paediatric Neurology Association: www_bpna.org.uk.

International Headache Society classification: www_ihs-headache.org/ichd-guidelines.

International League Against Epilepsy (ILAE): www_ilae.org.

Neuromuscular Disease Center (Washington University School of Medicine, St Louis, MO): neuromuscular.wustl.edu.

NICE Epilepsies: Diagnosis and Management 2020:
Available at: www_nice.org.uk/guidance/cg137.

Systematic reviews of migraine treatment in children, epilepsy, steroids for facial palsy and treatment of Guillain–Barré syndrome can be found in the Cochrane Library.
Available via: www.thecochanelibrary.com.

Adolescent medicine

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Features of adolescent medicine:

- The adolescent consultation differs from the paediatric consultation.
- The HEADS acronym assists in taking a psychosocial history.
- Chronic illness may impact on adolescent development, which in turn may impact on the chronic illness, e.g. adherence.
- Prominent mental health problems are eating disorders and self-harm.

Adolescence is the transition from childhood to adulthood. There is no clearly defined age range, but it is usually considered to be from puberty to 19 years of age, although development to adulthood continues into the third decade. There are 7.4 million adolescents in the UK, 12% of the population, with increased proportions observed in ethnic minority groups.

The transition from being a child to an adult involves many biological, psychological, and social changes ([Table 30.1](#)), with adolescent brain development continuing into the third decade. Pubertal development is considered in [Chapter 12](#) (Growth and puberty). Difficulties may arise if the pubertal changes are early or delayed. While general practitioners will see all adolescent medical problems, difficulties may arise when obtaining specialist medical care. Those less than 16 years old are generally looked after by paediatricians; over 16 years old, by either paediatricians or more often by adult physicians and surgeons. However, paediatric facilities, e.g. children's wards, are often geared to the needs of young children rather than adolescents, whilst older adolescents may be overwhelmed by the medical conditions encountered on adult wards and the independence expected of them. Adolescent females with gynaecological problems are often cared for by gynaecologists, usually in adult facilities. Some paediatricians in the UK are now

specializing in adolescent medicine in a similar way to North America and Australia, and the number of facilities focusing on the special needs of adolescents is increasing.

Communicating with adolescents

The adolescent consultation differs from the paediatric consultation for young children, in that the adolescent has a potentially greater active role in the consultation, although the health professional may need to advocate for the young person and their evolving autonomy.

As well as seeing adolescents with their parents, an integral component of adolescent healthcare is offering young people the opportunity to be seen independently of their parents for at least part of the visit. They, however, still have the right to a chaperone but it should not be assumed the latter should be a parent. Another principle is that the parents should ideally not be seen alone after the adolescent has spent time with the doctor, so that the adolescent can trust that whatever confidences have been disclosed to the doctor have been kept.

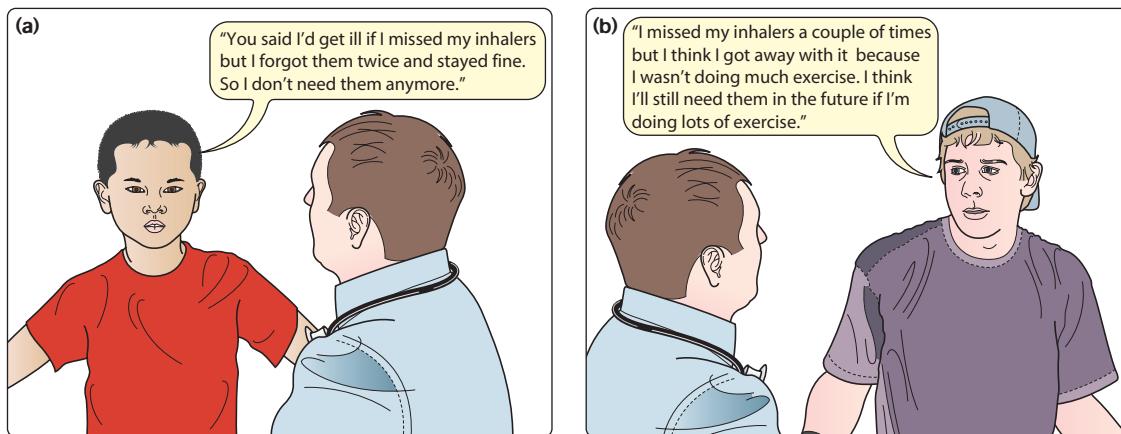
Some practical points about communicating and working with adolescents are:

- Make the adolescent the central person in the consultation.
- Be yourself. When establishing rapport, it may be appropriate to engage the adolescent by talking about his/her interests, e.g. football, clothes, or music, but do not try to be cool, false, or patronizing; your relationship should be as his/her doctor, not his/her friend.
- Consider the family dynamics. Is the mother or father answering for the adolescent? Does the adolescent seem to want this or resent being interrupted?

Table 30.1 Developmental changes of adolescence

	Biological	Psychological	Social
Early adolescence	Early stages of puberty: Females – breast bud, pubic hair development, start of growth spurt Males – testicular enlargement, start of genital growth	Concrete thinking (Fig. 30.1a), but begin to develop moral concepts and awareness of their sexual identity	The early emotional separation from parents, start of a strong peer identification, early exploratory behaviours, e.g. may start smoking
Mid-adolescence	Females – end of growth spurt, menarche, change in body shape Males – sperm production, voice breaks, start of growth spurt Acne Blushing Need for more sleep	Abstract thinking, but still seen as ‘bulletproof’, increasing verbal dexterity, may develop a fervent ideology (religious, political)	Continuing emotional separation from parents, strong peer group identification, development of sexual identity and orientation, early vocational plans
Late adolescence	Males – end of puberty, continued growth in height until growth plate fusion (usually 15–18 years in females, 18–22 years in males), and in strength, and body hair	Complex abstract thinking (Fig. 30.1b), identification of difference between law and morality, increased impulse control, further development of personal identity, further development or rejection of ideologies	Social autonomy, may develop intimate relationships, further education or employment, may begin or develop financial independence

(From: Christie D, Viner R. Adolescent Development. BMJ 330:301–304, 2005, with permission.)

**Figure 30.1** Example showing the difference between (a) concrete and (b) abstract thinking in the management of asthma in an older child and an adolescent.

- Avoid being judgemental or lecturing. Avoid ‘You ...’ statements and use ‘I ...’ statements in preference, e.g. ‘I am concerned that you ...’. A frank and direct approach works best. Your role should be that of a knowledgeable, trusted adult from whom they can get advice if they so choose.
- An authoritarian approach is likely to result in a rebellious stance. Working things out together in a practical way has the best chance of success.
- Frame difficult questions so they are less threatening and judgemental, e.g. ‘some teenagers drink alcohol, do any of your friends drink? How much do they drink in a week? Do you drink alcohol – how much do you drink compared with them?’ Likewise, when

asking sensitive questions on, for example, sexual health, always give young people warning and explain the rationale of why such questions need to be asked.

- Do not perpetuate myths in your questions to the young person, e.g. ‘Lots of young people smoke – do you?’ Only 3% of 11–15-year-olds in the UK currently smoke regularly although this increases to one in five in the 16–24-year-old age group.
- Confidentiality is particularly important to this age group and must be respected. Explain that you will keep everything you are told confidential, unless they or somebody else is at risk of serious harm. Always assess the adolescent’s understanding of confidentiality and correct any misunderstanding.

Table 30.2 HEADS acronym for psychosocial history taking in adolescents

H	Home life	Relationships, social support, household chores
E	Education	School, exams, work experience, career, university, financial issues
A	Activities	Exercise, sport, other leisure activities Social relationships, friends, peers, who can they rely on? Bullying?
D	Drugs	Drug use, cigarettes, alcohol. How much? How often?
	Diet	Weight, caffeine (diet drinks), binges/vomits
S	Sexual health	Concerns, periods, contraception (and in relation to medication)
	Sleep	How much? Hard to get to sleep? Wake often?
	Suicide/affect	Early waking? Depression, self-harm, body image
	Safety	Safety issues around substance use, sexual activity, internet use, etc.
	Social Media	Which platforms; duration of use in a typical day; impact on self-confidence; cyberbullying/sexting

- Bear in mind proxy presentations, e.g. abdominal pain, when the real reason is anxiety about the possibility of pregnancy, or sexually transmitted infection (STI), or the result of recreational drug use.
- A full adolescent psychosocial history is useful to engage the young person, to assess the level of risk, as well as identifying protective or resilient factors and provide information that will aid the formulation of effective interventions. The HEADS acronym may be helpful in this regard (**Table 30.2**), although questions must always be tailored to stage of development and the right of the young person to not answer should be respected.
- Communicate and explain concepts appropriate to their cognitive development. For young adolescents, use concrete examples (here and now) rather than abstract concepts (if ... then).
- History-taking should avoid making the assumption of heterosexuality, with questions about romantic and sexual partners asked in a gender neutral way.
- If they need to have a physical examination, consider their privacy and personal integrity. Who do they want present? Also, find out if they would prefer a doctor of the same sex, if this is an option.

Summary

Talking and listening with young people

- Always give them the opportunity to be seen independently of their parents.
- Explain and assure confidentiality.
- Psychosocial screening is useful to:
 - engage young people
 - assess risk
 - identify protective/resilient factors: they assist formulation of interventions.
- Always give time for the young person to answer.

Consent and confidentiality

Consent

In the UK, young people can give consent if they are sufficiently informed and either over 16 years old or under 16 years of age and competent to make decisions for themselves. This is known as Gillick competent. Conflict rarely arises about a treatment, as usually the adolescent, his/her parents and doctors agree that it is necessary. Handling of disagreement over consent is considered in [Chapter 5](#) (Care of the ill child and young person).

Confidentiality

Confidentiality is regarded by adolescents as of crucial importance in their medical care. They want to know that information they have disclosed to their doctor is not revealed to others, whether parents, school, or police, without their permission. In most circumstances, their confidentiality should be kept unless there is a risk of serious harm, either to themselves from physical or sexual abuse, from suicidal thoughts, or to others from homicidal intent. Difficulties relating to confidentiality for adolescents are usually about contraception, abortion, STIs, substance abuse, or mental health. It is usually desirable for the parents to be informed and involved in the management of these situations, and the adolescent should be encouraged to tell them or allow the doctor to do so. However, if the young person is competent to make these decisions for himself/herself, the courts have supported medical management of these situations without parental knowledge or consent.

Range of health problems

Adolescence is considered a healthy stage of life compared with early childhood or old age. In spite of this, the majority of young people will consult their general practitioner more than once in a year, and 23% of 11–15-year-olds report a long-term illness or disability. The range of health problems affecting adolescents include:

- common acute illnesses – respiratory disorders, skin conditions, musculoskeletal problems including sports injuries, and somatic complaints. Acute serious illness has become rare, with mortality predominantly from trauma
- chronic illness and disability – e.g. asthma, epilepsy, diabetes, cerebral palsy, juvenile idiopathic arthritis,

sickle cell disease. There is also a range of uncommon disorders with serious chronic morbidity such as malignant disease and connective tissue disorders. In addition, children with many congenital disorders which often used to be fatal in childhood now survive into adolescence or adult life, e.g. cystic fibrosis, Duchenne muscular dystrophy, complex congenital heart disease, metabolic disorders

- high prevalence of somatic symptoms – e.g. fatigue, headaches, backache, chronic musculoskeletal pain
- mental health problems including anxiety, depression, suicide and deliberate self-harm
- eating disorders and weight problems
- those associated with health-risk behaviours, such as smoking, drinking, drug misuse and sexual health, contraception, and teenage pregnancy.

Mortality

The dramatic improvement in the mortality of young children seen since the 1960s has not been matched in adolescents, who now have a higher mortality rate than that of 1–4-year-old age group (Fig. 30.2). Although deaths in adolescents from communicable diseases have declined markedly, this has not been matched by mortality from road traffic accidents, other injuries and suicide, and these now predominate (Fig. 30.3). Alcohol is thought to be a contributing factor in one-third of these deaths.



Mortality rate in UK for 15–19-year-olds is now greater than for 1–4-year-olds.

Impact of chronic illness

Chronic illness may disrupt biological, psychological, and social development. In addition, these developmental changes may affect the control and management of the disorder (Table 30.3). The impact of chronic illness on children, young people and their families is considered in Chapter 24 (Child adolescent mental health).

Adherence

Suboptimal adherence is a problem for many people, including adolescents, as they are beginning to take over

management of their health, wish to avoid parental supervision, and may give the management of their illness a lower priority than social and recreational activities. They may not believe, due in part to the developmental status of their brain, that taking the medication really matters, especially if it is preventative or of long-term rather than short-term benefit.

Aspects of social and psychological adolescent development, such as peer relationships, body image and self-identity, are very important when considering adherence. For example, it may be more important for an adolescent with diabetes to lunch promptly, so he/she can sit with his/her friends rather than go to the school nurse first for his insulin injection. Side-effects are also important, particularly those that affect wellbeing or appearance. They may assess risk differently from adults, so that the risk of not being one of their crowd because of having to adhere to a certain treatment may appear to be more important than the risks attached to not taking any medication.

Adherence may be influenced by lack of knowledge and/or poor recall of previous disease education. The disorder may have presented when the child was much younger, so that the original consultation will have taken place primarily between the doctor and parents. If this communication has not been updated with increasing age, the adolescent's knowledge may be poor, with little understanding about his/her illness, what medications he/she is taking and why. As the responsibility for management moves to the young person, information needs to be provided about medications, and treatment needs to

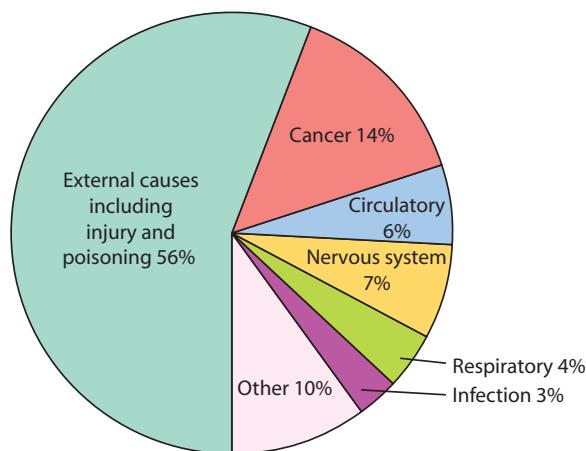


Figure 30.3 Causes of death, 15 years to 19 years of age, in England and Wales, 2017. Total number 752. (Data from: ONS, 2018.)

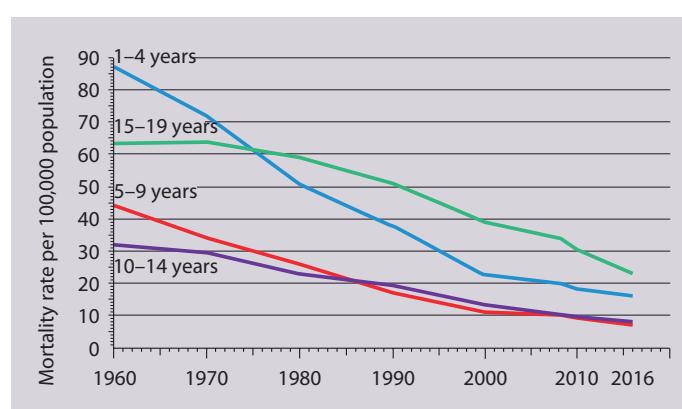


Figure 30.2 Mortality by age group in England and Wales 1960–2016. The graph shows that the mortality rate is now greater at age 15 years to 19 years than at 1 year to 4 years of age. (Data from: ONS, 2019.)

Table 30.3 Some of the ways in which chronic illness and development interact with each other

	Effect of chronic illness on development	Effect of development on chronic illness
Biological	Delayed puberty Short stature Reduced bone mass accretion Malnutrition secondary to inadequate intake due to increased caloric requirement of disease or anorexia Localized growth abnormalities in inflammatory joint disease, e.g. premature fusion of epiphyses	Pubertal hormones may impact on disease, e.g. growth hormone worsens diabetes and increases insulin requirements; females with cystic fibrosis may have deterioration in lung function; corticosteroid toxicity worse in the peripubertal phase Increased caloric requirement may worsen disease control or result in undernutrition – may need dietary supplements or overnight feeding with nasogastric tube or gastrostomy Growth may cause scoliosis
Psychological	Regression to less mature behaviour Adopt sick role Impaired development of sense of attractive/sexual self Parental stress, depression, financial problems in providing care; siblings may suffer	Deny that their health may suffer from their actions Poor adherence and disease control Reject medics like parents
Social	Reduced independence when should be separating Failure of peer relationships Social isolation – unable to participate in sports or social events School absence and decline in school performance, may lower self-esteem Vocational failure	Risk behaviour may adversely affect disease, e.g. smoking and asthma or cystic fibrosis; alcohol and diabetic control; sleep deprivation and epilepsy Chaotic eating habits lead to malnutrition or obesity

be appropriate for his/her development. Other ways to maximize adherence are summarized in [Table 30.4](#).

The implications of their condition on the rest of their health and their life needs to be considered. This may include sexual health, future vocational development, including the need for disclosure and their rights (under the Equality Act 2010). Similarly, the implications of other health-risk behaviours such as substance use, tattoos, and piercing may need to be discussed.

Summary

Chronic conditions during adolescence

- Chronic illness and/or disability may disrupt adolescent development (biological/physical, psychological, social and/or vocational).
- Consideration should be made of the impact of the chronic condition on the rest of health (including sexual and reproductive health) as well as education and leisure.

Fatigue, headache, and other somatic symptoms

Fatigue, headache, abdominal pain, backache, and dizziness are common in adolescence. In large school-based surveys of young people in the UK, 65% (59% of boys and 71% of girls) report experiencing at least one health

complaint on a weekly basis. Such reports are more common in girls and also increase with age, with 24% of 15-year-old boys and 48% of girls reporting headache, 12% and 28% stomach ache, 22% and 30% backache, and 30% and 49% reporting sleep problems more than once a week, respectively. In many, these symptoms appear to be a feature of adolescent development, although organic disease must be excluded by history, examination and, occasionally, investigation. For a minority, they may be a physical manifestation of psychological problems, and are precipitated by or maintained by factors such as bullying or parental discord. This is considered further under persistent unexplained physical symptoms (PUS) in [Chapter 24](#).

Occasionally, the symptoms are so severe and persistent that they considerably affect quality of life, with impairment of school attendance, academic results, and peer relationships. Multidisciplinary rehabilitation within the family and cognitive behavioural therapy may be beneficial.

Mental health problems

The prevalence of mental health problems in adolescents has been reported to be 14.4% of 11–16-year-olds and 16.9% of 17–19-year-olds. The main problems are listed in [Table 30.5](#). Although adolescents are at much less risk of serious illness from COVID-19 than adults, the pandemic has had a major impact on the lives of adolescents in terms of mental health and on their social, educational and vocational development. This is considered further in [Chapter 24](#).

Table 30.4 Ways to maximize adherence

Assess the size of the problem and be non-judgemental	Ask: 'Some people have trouble taking their medication. When was the last time you forgot?'
Take time to explore practicalities	Try to put yourself in the adolescent's shoes and think through the detail of their regimen with them. 'Which is the most difficult dose to remember?' 'How do you fit in taking your tablets into your daily routine?' Make regimen as simple as possible. Do not forget practical issues – poor adherence may be as simple as not having any private space at school to take the treatment
Explore beliefs	May harbour strange or incorrect beliefs about medications, e.g. falsely attribute a side-effect, and therefore refuse to take the medication
Use daily routines to 'anchor' adherence	Find daily activities to anchor taking the medication, e.g. brushing teeth, or 'with breakfast and dinner' instead of 'twice a day'. Find the least chaotic time of day: may be morning or evening! Use alarms on phones. Let the suggestions come from the adolescent
Motivation	Negotiate short-term treatment goals. Search for factors that motivate the young person. Ask three questions: 'Out of 10, how important / what priority / how confident are you that you take your medications?'
Involve and contract	Plan the regimen with the adolescent. Some may respond to a written contract that both sides agree to stick to
Written instructions	Most of what is said has been shown to be forgotten once they leave the room! Get them to take a photo of any instructions on their phone
Take time to explain	Check level of knowledge on each occasion
Solution-focused approach	Find out what has been going well and why. Use this information, e.g. 'How have you managed to remain out of hospital for 3 weeks this month?'

Table 30.5 Prevalence (%) of main mental health problems and disorders in 11–16-year-olds by gender, England 2017

Problem or disorder	Females	Males
Depression	3.6	3.3
Anxiety	8.3	6.1
Attention deficit hyperactivity disorder	0.8	3.3
Behavioural disorder	4.8	7.8
Other less common disorders	1.6	2.3
Any disorder	13	14.2

From: NHS Digital 2018: Mental health of children and young people in England, 2017.

Self-harm varies from little actual harm, where there is a wish to communicate distress or escape from an interpersonal crisis, to suicide. About 32% of 15-year-old girls and 11% of 15-year-old boys report self-harming behaviour.

Abnormal eating behaviour including eating disorders are common during adolescence. About 50% of 15-year-old girls and 24% of boys report feeling their body is 'too fat'. A quarter of girls and 9% of boys in this age group report being on a diet or doing something to try and lose weight. In anorexia nervosa and bulimia, there is a morbid preoccupation with weight and body shape. This is discussed in more detail in [Chapter 24](#).

Health-risk behaviour

During adolescence, young people begin to explore 'adult' behaviours, including smoking, drinking, drug use, and sex. These experimentation behaviours, often referred to as 'risk-taking' behaviours, are part of adolescent development and reflect the adolescent's search for pleasure and excitement by participating in new and enjoyable experiences, as well as exerting independence from parents or rebelling against parents' wishes and lifestyle. There is also considerable pressure to fit in with peers. However, they have significant health implications when they become risky behaviours.

During adolescent development, young people may not always understand the risks involved, particularly if long term, and may behave as if they are immune from harm. Participating in these activities may also deflect attention away from themselves to mask shyness or anxiety. Unfortunately, health-risk behaviours started in adolescence tend to continue into adult life.

Sexual health

The average age for first sexual intercourse in the UK is 16 years, with a quarter of boys and a fifth of girls reporting having had sexual intercourse by age 15. Having sexual intercourse at an early age is often associated with unsafe sex. This may be because of a lack of knowledge, lack of access to contraception, inability to negotiate obtaining contraception, being drunk or high on drugs, or unable to resist being pressurized by his/her partner.

Risk-taking behaviour in adolescents can result in STIs or unplanned pregnancy. STIs may present with urethral or vaginal discharge, urinary symptoms, pain on micturition, abdominal or loin pain, or postcoital vaginal bleeding. Chlamydia is asymptomatic in 50% of cases and can lead to later infertility. In young teenagers, it is more likely to present with a vaginal discharge. Studies have shown that up to one-third of sexually active teenage girls have an STI. They are also at risk of human immunodeficiency virus (HIV) infection.

Management of sexually transmitted infections

Taking a sexual history from an adolescent should be approached sensitively, in a developmentally appropriate manner, giving the young person warning of the topic, as well as why the questions are being asked. Relevant questions include those related to the risk of STIs: number of partners; any partners during travel abroad; contraception used; whether vaginal, oral, or anal sex; any discharge, lower abdominal pain, urinary symptoms; and last menstrual period. However, many STIs are asymptomatic, especially in younger teenagers, male and female.

If indicated, swabs should be taken for virology and microbiology (to look for human papillomavirus [HPV], herpes simplex virus, chlamydia, and gonorrhoea). HIV testing may be indicated. In England, in response to the high rates of chlamydia in the under-25-year-old age group, there is a national chlamydia screening programme enabling them to test themselves with easy-to-use kits.

Treatment regimens vary, depending on prevalent antibiotic resistance. Chlamydia can be treated with azithromycin or doxycycline, gonorrhoea with a cephalosporin. Metronidazole can be added for pelvic inflammatory disease. It is advisable to inform and treat partners.

The National HPV Vaccination programme for girls and more recently for boys in the UK is an excellent opportunity for conversations about sexual health in early adolescence and has probably been a factor in the reduction in new diagnoses of genital warts.

Contraception

Most adolescents who are sexually active are using contraception, albeit sometimes haphazardly. In the UK, contraception is used by only half at first intercourse. Condoms, followed by the oral contraceptive pill, are the most common forms of contraception used. As adolescents have a relatively high failure rate in their ability to use condoms correctly and with the oral contraceptive pill having irregular use, the 'double Dutch' method of condom and oral contraception is advocated to protect against both STIs and pregnancy.

Adolescents with chronic disease, e.g. diabetes, even without microvascular complications, are generally started on lower doses of the contraceptive pill. Some medications prescribed in adolescents are potentially teratogenic (e.g. retinoids for acne, methotrexate for juvenile idiopathic arthritis or other disorders) and may therefore need to be combined with an oral contraceptive pill or depot hormonal implant. Discussions,

however, must also reinforce condom use to prevent STIs. An alternative to the anti-epileptic drug valproate should be prescribed for adolescent females who may become pregnant as it is teratogenic. Finally, young people's accessibility to youth-friendly contraception services needs to be checked as over half have been reported to be unaware of such services in their local area.

Emergency contraception

Emergency contraception (in the past misleadingly known as the 'morning after pill') can provide significant protection from pregnancy for up to 72 hours after unprotected intercourse. Emergency contraception is available from a pharmacist without prescription for those 16 years and over, and on prescription for those under 16 years. If taken within 72 hours, it has a 2% failure rate. Side-effects include nausea and lethargy. However, knowledge of emergency contraception is poor among many young people.

Teenage parenthood

The UK has the highest rate of teenage pregnancy in Western Europe, though encouragingly with a downward time trend. Teenage girls may present with complaints such as abdominal pain, fatigue, breast tenderness, or appetite changes rather than late or missed menstrual period.

Becoming a teenage parent can be a positive life choice and is influenced by culture. There may be considerable support from the extended family, and this may work well. However, in those where the pregnancy was unintended or who are emotionally deprived themselves, or who are unsupported and live in poverty, there may be many adverse consequences for the mother and child. Children of teenage mothers have a higher infant mortality, a higher rate of childhood accidents, illness, and admission to hospital, being taken into care, low educational achievement, sexual abuse, and mental health problems. Deprivation, from the mother's lack of financial and emotional support and the paucity of her own education and life experiences, is the strongest risk factor. Protective factors are having a supportive family, religious belief, and a stable, long-term relationship with the partner.

Health promotion

Reasons to undertake health promotion in adolescents:

- It is the period for starting health-risk behaviours (smoking, alcohol, drug misuse, unsafe sexual activity) as well as health-promoting behaviours (regular physical exercise, nutrition).
- Health-risk behaviours started in adolescence often continue into adult life.
- Health behaviours may have a direct effect on their lives, e.g. teenage pregnancy, road traffic accidents
- Increasing morbidity, e.g. obesity and diabetes.

The main areas for health promotion are:

- health-risk behaviours
- mental health

- violent behaviour
- physical activity, nutrition, and obesity
- parent-adolescent communication.

There are a number of approaches to health promotion for adolescents:

- provide suitable information in a user-friendly and developmentally appropriate way for young people. There are several websites and apps that provide this
- health promotion by society as a whole, e.g. banning cigarette advertising, making emergency contraception available in pharmacies. These can be very effective. However, there is increasing evidence that improving the socio-economic circumstances of young people would be the most effective intervention for health promotion. Also, as adolescents often embark on more than one risk behaviour, tackling the underlying problem may reduce other risk-taking behaviours; e.g. a programme to reduce bullying in a whole school may also reduce other behaviour, such as drug misuse
- training programmes to improve adolescents' ability to accept or reject certain courses of behaviour can be effective for the individual, but is time-consuming and expensive
- health promotion by professionals. Exhorting adolescents not to smoke, to eat a balanced diet, use contraception, etc., has not been found to be effective, and may be counterproductive. Health professionals do have a role in health promotion at

an individual level. It is likely to be most effective if targeted at those who are receptive or contemplating change in their health-risk behaviour. However, motivational interviewing techniques (which do not assume that they are ready to change their behaviour, but aim to increase their intrinsic motivation to change) have also been shown to be useful with this age group.

Transition to adult services

Adolescence and young adulthood encompass many transitions – pubertal, social, educational to name but a few. Another one is health transitions, and all young people will need to learn how to navigate health services as adults and know who to contact, where and when for different health-related issues. The young person with a chronic childhood-onset condition must leave paediatric and adolescent services (with which they may have long-term relationships) for adult services. This often involves changing from a treatment model based around close contact between the adolescent and healthcare professionals (e.g. unlimited telephone advice from clinical nurse specialists, possibly home visits, frequent appointments) and involvement with parents and other family members, to one where they are likely to be seen less frequently in a busy adult clinic where parental involvement may be minimal or discouraged.

Summary

The main health problems of adolescents



Common acute illness

- respiratory disorders, skin conditions, musculoskeletal problems

Chronic illness and disability, including previously fatal congenital disorders

Somatic symptoms

- Fatigue, headache, backache and abdominal pain (see Ch. 24, Child adolescent mental health)

Mental health problems (see Ch. 24)

Health-risk behaviours

- Smoking, drinking, drug abuse, road traffic accidents (see Ch. 1, Paediatrics and child health, Ch. 7, Accidents and poisoning, and Ch. 24)

Sexual health

- Sexually transmitted infections, contraception, teenage pregnancy

Eating disorders (see Ch. 24) and obesity (see Ch. 13, Nutrition)

Young people and their parents need both information about the transfer process and time to prepare, including the necessary skills to negotiate the adult healthcare system. Transitional care encompasses this preparation which, by definition, addresses the medical, psychosocial, and educational/vocational needs as a young person moves from child- to adult-centred services. Parents are often concerned that the adult team will not address their child's healthcare needs. It is helpful if an identified healthcare professional, often a nurse specialist, is responsible for coordinating transition arrangements.

Whereas transitional care starts in early adolescence, some flexibility in age of transfer is desirable, so that it can occur when the young person is developmentally ready and has the necessary maturity to cope with adult services. Transitional care should ideally continue in adult care until the young person is successfully engaged and navigating adult services effectively, i.e. transition is triphasic and does not end at the point of transfer.

Transfer may be via an adolescent or young adult service with clinics run by both adolescent and adult teams together. Such bridging arrangements have many advantages, but require a sufficient number of patients and medical staff able and willing to provide this service. These clinics are usually for specialist conditions, e.g. diabetes, juvenile idiopathic arthritis, cystic fibrosis, or congenital heart disease. Alternatively, transfer may be successfully accomplished if there is good communication between teams, although it usually involves a radical change in ethos for the adolescent and family. The general practitioner ideally is the source of continuity between changing specialty practitioners and should be actively involved during the whole transition process.

Summary

Transition to adult services

- Transitional care aims to address medical, psychosocial, and educational/vocational issues as young people move from child- to adult-centred services.

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Global child health

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Features of global child health:

- Great progress has been made in improving the survival of children and young people <15 years globally over the last 3 decades.
- There are wide regional, intercountry and intracountry disparities in mortality rates.
- Poverty, poor maternal education, conflict, undernutrition, inadequate access to safe water, food, sanitation and healthcare are the main causes of child mortality.
- The number of children dying from infectious diseases has declined markedly.
- Neonatal mortality accounts for an increasing proportion of child deaths, but could be markedly reduced by implementing basic neonatal care.

Child mortality

There has been a remarkable reduction in the number of deaths globally among children and young people <15 years since 1990, with a 56% reduction from 14.2 million to 6.2 million in 2018. Of these child deaths, 85% (5.3 million) were children under 5 years of age. Neonatal mortality (first 4 weeks of life) accounts for 47% of all under-5-year-old deaths (2.5 million) (Fig. 31.1). Infectious diseases remain an important cause of under-5 mortality with pneumonia, diarrhoea and malaria accounting for nearly a third of under-5 deaths (Fig. 31.2). Undernutrition is also a contributing factor to over one-third of child deaths.

Where deaths occur

Although only about 52% of the world's under-5-year-olds live in sub-Saharan Africa and Central/South Asia, more than 80% of child deaths occur in these two regions.

Over half of all child deaths occur in just five countries: India, Nigeria, Democratic Republic of Congo, Pakistan, and Ethiopia. Mortality rates are a useful measure of the quality of child health outcomes between regions and countries. For example, the <5 years mortality rate of sub-Saharan Africa compared to the UK is shown in Table 31.1. The major discrepancy in mortality between different countries of the world is shown in Figure 31.3. All six countries with an under-5-year-old mortality rate above 100 deaths per 1000 live births are in sub-Saharan Africa; this means that the risk of dying before the fifth birthday for a child born in one of these countries, e.g. Sierra Leone with a mortality rate 105/1000 live births, is about 72 times higher than in the lowest mortality country.

Determining child mortality rates and health outcomes in different countries

In order to determine child mortality and health outcomes and monitor change, accurate data need to be collected. There has been considerable effort to improve data collection, but many obstacles remain; even deaths, particularly of newborn infants, are often unreported in countries with poor vital registration systems.

Table 31.1 Mortality rates in sub-Saharan Africa compared with the UK, 2018.

Mortality rate (per 1000 live births)	Sub-Saharan Africa	UK
Under 5 years old	78	4
Infant (<1 year old)	53	4
Neonatal (<28 days old)	28	3

(Data from: www.unicef.org/media/60561/file/UN-IGME-child-mortality-report-2019.pdf.)

Deaths of children <5 years old

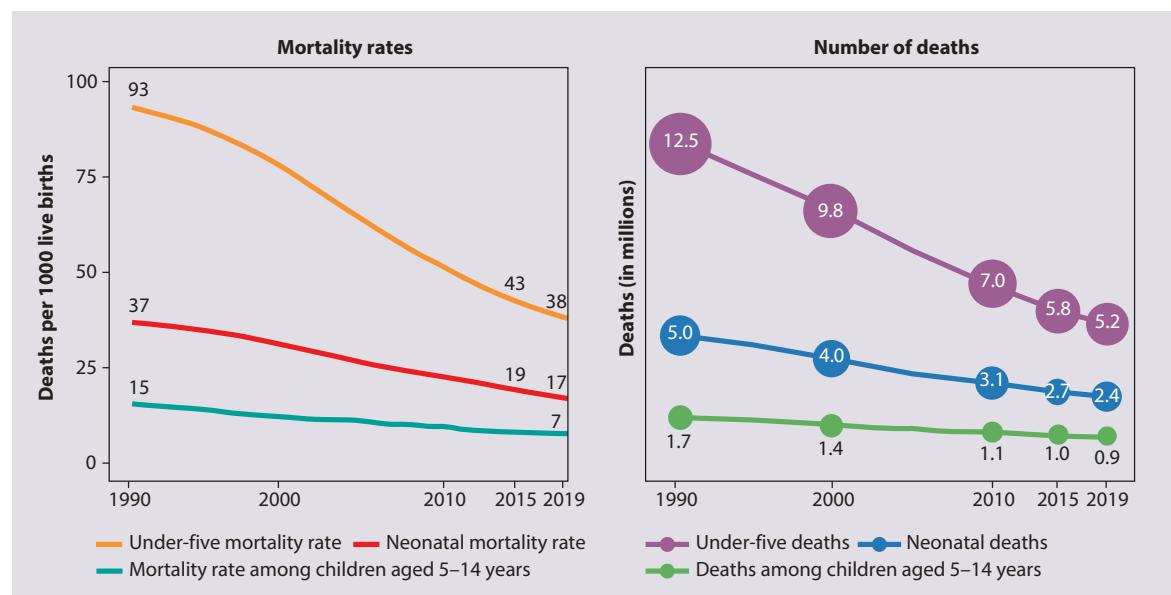


Figure 31.1 Reduction in global mortality rates and deaths from 1990 to 2019 in children under 5 years, neonates, and children aged 5–14 years. The under-5-year-old mortality rate fell from 93 per 1000 in 1990 to 38 per 1000 in 2019; neonatal mortality rate fell from 37 to 17 per 1000 live births in 2019. (Adapted from: United Nations Inter-agency Group for Child Mortality Estimation (UN IGME): Levels and Trends in Child Mortality: Report 2019, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. New York, 2019, United Nations Children's Fund.)

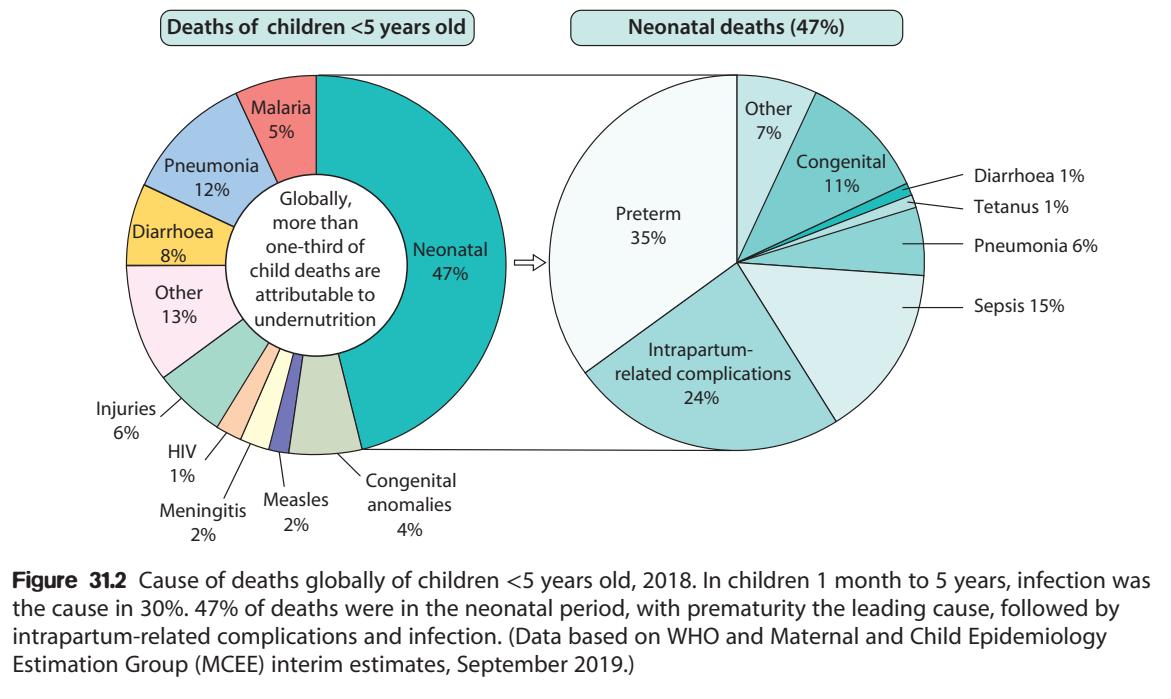


Figure 31.2 Cause of deaths globally of children <5 years old, 2018. In children 1 month to 5 years, infection was the cause in 30%. 47% of deaths were in the neonatal period, with prematurity the leading cause, followed by intrapartum-related complications and infection. (Data based on WHO and Maternal and Child Epidemiology Estimation Group (MCEE) interim estimates, September 2019.)

Why is child mortality so high?

Children depend on their environment as well as the provision of healthcare for their survival, as described in Chapter 1 (Paediatrics and child health). The environment can have major detrimental effects on their chances of survival:

- poverty and social determinants – pervade almost all aspects of health and healthcare. In almost all low-resource countries, there is a marked difference in health outcomes between high-income and low-income groups (Fig. 31.4)

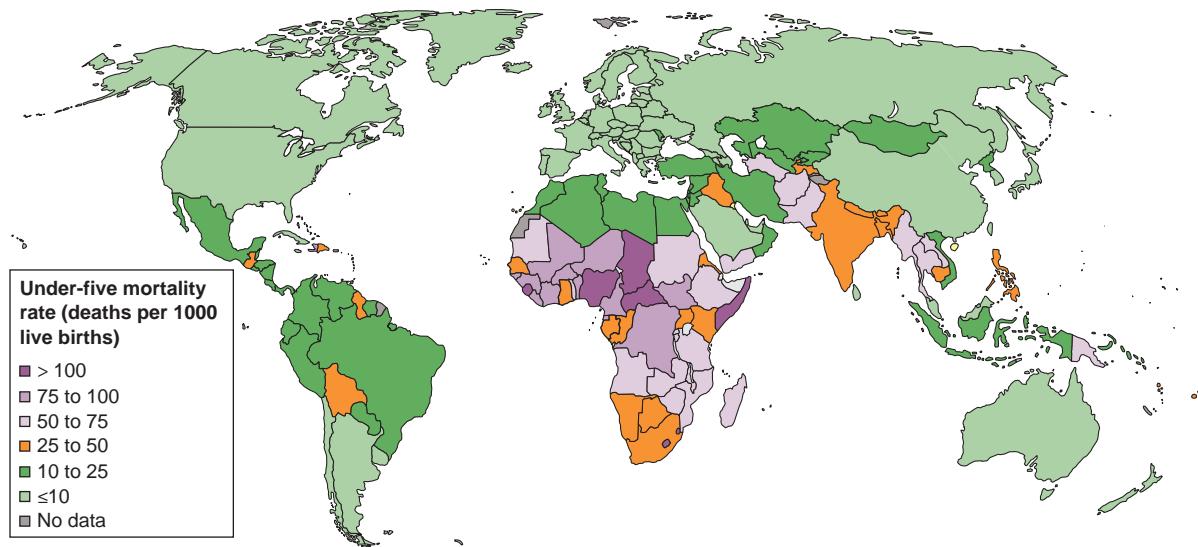


Figure 31.3 Under-five mortality rate (deaths per 1000 live births) by country, 2019. (Source: <https://childmortality.org/wp-content/uploads/2020/09/UNICEF-2020-Child-Mortality-Report.pdf>, with permission from UNICEF)

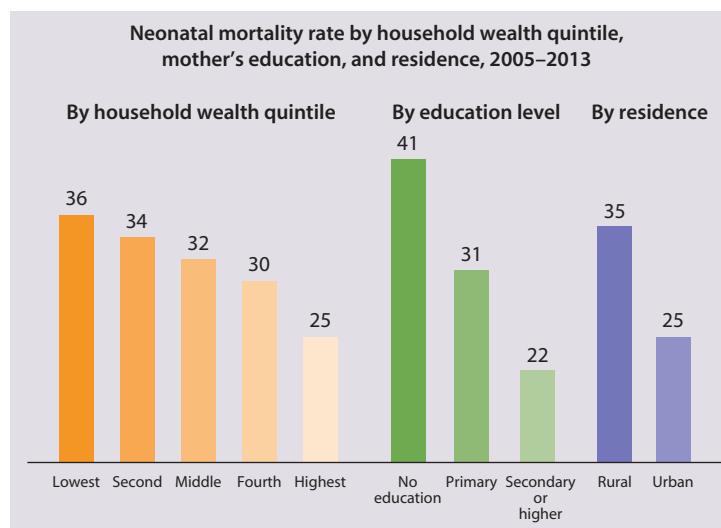


Figure 31.4 Children born to poorer households, to mothers with no formal education, and living in rural areas face a higher risk of dying in the first 28 days of life. (Data from Committing to Child Survival: a promise renewed. Progress report 2014, UNICEF.)

- maternal education – the higher the level of maternal education, the higher the chance of her child's survival (see Fig. 31.4)
- poor sanitation and unclean water – increase in diarrhoea and infection
- poor food security – malnutrition increases vulnerability and severity of illness, especially infection (see Ch. 13, Nutrition). Chronic malnutrition is reflected in stunting of children
- inadequate housing, air pollution, and urban overcrowding – promotes the spread of respiratory pathogens (see Fig. 31.4)
- conflict – see the 'Children affected by conflict' section below
- geographical variation in diseases – large intercountry and inter-regional differences, e.g. children under 5 years accounted for 61% of malaria deaths worldwide in 2017 but the rate was much higher in sub-Saharan Africa compared with South-East Asia (WHO 2018).

The provision of healthcare in many low- and middle-income countries is poor and adversely affects survival:

- limited finance available for healthcare – whereas Sweden spends US\$5500/person per year on health (11% of gross domestic product), in 24 low-resource countries it is less than US\$50/person per year (WHO 2016)
- disease prevention, e.g. vaccination, insecticide-treated net distribution for protection from malaria – lower coverage in poor areas of the country or conflict
- access – may be difficult to get to health facilities; increased cost and therefore affordability may be major limiting factors
- community care – limited by lack of trained community health workers
- health centres and hospitals – care compromised by lack of trained healthcare professionals, equipment, drugs, suitable buildings, etc.

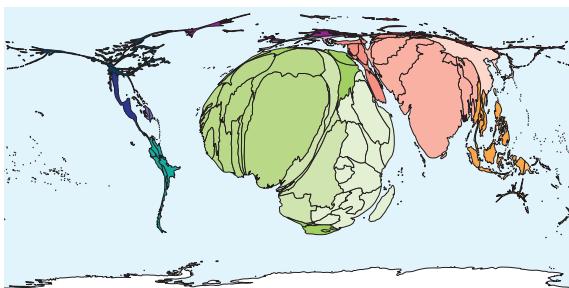


Figure 31.5 Territory size shows the proportion of all deaths of children aged 1 year to 5 years. (From: worldmapper.org/maps/age-under5-deaths-2015/?sf_action=get_data&sf_data=results&sft_product_cat=death&sf_paged=2, copyright worldmapper.org.)

- medical care – lack of trained doctors is a serious problem in almost all these countries. The contrast between the proportion of doctors compared with deaths in children is shown in Figures 31.5 and 31.6.

Reducing child mortality

There has been a major effort by many low- and middle-income countries to improve child health. This has been done in conjunction with the international community, with programmes of aid (United States Agency for International Development [USAID], Department for International Development [DfID], etc.), charities (Gates Foundation, etc.), and non-governmental organizations (UNICEF, Save the Children, etc.). Some of the major international initiatives are listed in Box 31.1.

The publication of the Integrated Management of Childhood Illness (IMCI) in 1992 was an important step in promoting the comprehensive and holistic management of children attending primary and secondary health facilities. It recognized that an integrated approach to childhood illness is required, including nutrition and preventative care in families and communities. In health facilities, sick children are triaged according to the presence of specific danger signs and management is planned according to algorithms.

A major advance in global child health was the adoption of the Millennium Development Goals (MDGs), which have served as a focus for the international community's commitment to reduce child mortality. The specific target for MDG 4 was to reduce child mortality in children under 5 years of age by two-thirds between the years 1990 and 2015. In 1990 there were 12.7 million deaths of children under 5 years of age compared with the 5.9 million in 2015, a 54% reduction (see Fig. 31.1). Contributions were also made by other MDGs, which included reducing maternal mortality (MDG 5) and reducing the burden of HIV (human immunodeficiency virus), malaria, and tuberculosis (MDG 6). Progress in improving global child health has continued and accelerated further with the adoption of the Sustainable Development Goals (Fig. 31.7).

Sustainable Development Goals

These were approved by all 193 United Nations Member States in 2015. The eight MDGs (Millennium Development

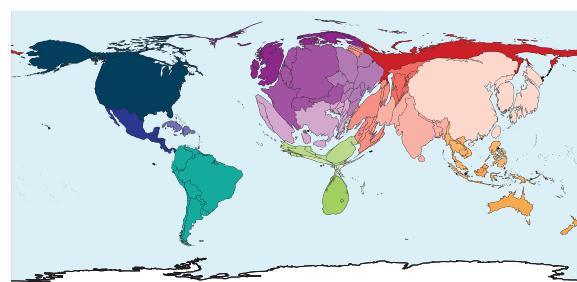


Figure 31.6 Territory size shows the proportion of doctors (anaesthetists) who work in that territory. (From: worldmapper.org/maps/anaesthesiologists-2015/?sf_action=get_data&sf_data=results&sft_product_cat=medical-workforce, copyright worldmapper.org.)

Box 31.1 Key international developments in maternal and child health

- 1946: United Nations Children's Emergency Fund (UNICEF) established
- 1948: World Health Organization (WHO) formed
- 1974: Extended Programme of Immunization (EPI) – included diphtheria, pertussis, tetanus, polio, tuberculosis, and measles
- 1980s: GOBI-FFF – Key primary care strategies: growth monitoring, oral rehydration therapy, breastfeeding, immunization, family spacing, female education, and food supplementation
- 1989: UN Convention on the Rights of the Child
- 1992: World Summit for Children – Child-to-Child strategy, Baby Friendly Initiative, Integrated Management of Childhood Illness
- 2000: United Nations endorses Millennium Development Goals
- 2013: Global Action Plan for Pneumonia and Diarrhoea
- 2015: Sustainable Development Goals adopted by all United Nations Member States

Goals) were replaced by 17 Sustainable Development Goals (SDGs), which have broad aspirations (see Fig. 31.7). One SDG specifically focuses on health, to 'ensure healthy lives and promote wellbeing for all at all ages'. This includes ending preventable deaths of newborns and children under 5 years of age, and sets a target mortality rate of <12 per 1000 live births for neonatal mortality and <25 for children aged under 5 years by 2030. In addition, other SDGs, with relevance to health are focused on ending poverty and hunger, combating climate change, and improving education. An example of how SDGs may overlap are school-based programmes, which include: school feeding, micronutrient supplementation, treatment of soil-transmitted helminths, protection from malaria, and improved water, sanitation, and hygiene. Whilst many countries have already achieved child health mortality targets set out in the SDGs (121 out of 195 countries) and a number more are on target to do so by 2030 (21 countries), 53 countries (two thirds of which are in sub-Saharan Africa) are projected to fail to achieve the targets; major additional support will be required to avoid this from happening.

SUSTAINABLE DEVELOPMENT GOALS



Figure 31.7 The 17 Sustainable Development Goals. (© United Nations. United Nations Sustainable Development Goals, <https://www.un.org/sustainabledevelopment>. The content of this publication has not been approved by the United Nations and does not reflect the views of the United Nations or its officials or Member States.)

Table 31.2 Maternal health and obstetric care that improve neonatal morbidity and mortality

Before conception	Pregnancy	Labour and delivery
<ul style="list-style-type: none"> Family planning (encourage delay of first pregnancy to age 18 years and 3-yearly birth interval) Maternal nutrition optimized, including folic acid to prevent neural tube defects Chronic conditions stabilized – hypertension, diabetes Infection prevention and treatment – malaria, tetanus, sexually transmitted infections, HIV (human immunodeficiency virus) 	<ul style="list-style-type: none"> Complications of pregnancy managed – pre-eclampsia, etc. 	<ul style="list-style-type: none"> Antenatal steroids for preterm labour Skilled birth attendant at all births, with newborn resuscitation training Timely and skilled management of complications, e.g. caesarean section to prevent perinatal asphyxia Clean delivery practices

Improving neonatal survival

There were 2.4 million neonatal deaths (deaths in the first month of life) in 2019. Progress in reducing neonatal mortality has been strikingly slower than in reducing under-5-year-old mortality (see Fig. 31.1). Whereas the birth of a baby should be a joyous occasion, globally every year some 295,000 mothers die during or following pregnancy and childbirth, and about a third of all neonatal mortality occurs during or in the first day after birth. There are also around 2.6 million stillbirths.

The main causes of neonatal death are:

- preterm birth
- intrapartum-related complications, e.g. perinatal asphyxia
- infections, e.g. sepsis and pneumonia.

Neonatal tetanus is an important cause of death in many countries, though this has been markedly reduced by

maternal immunization and hygiene at delivery, especially clean cord-care. Intrauterine growth restriction is a significant comorbidity in many neonatal deaths. Around 20 million infants are born with low birth weight (<2.5 kg) each year (a global prevalence of 15.5%) with over 95% of these in low-income countries. Low birth weight contributes to 60% to 80% of neonatal deaths.

Maternal health and obstetric care

Maternal health and obstetric care are major determinants of neonatal morbidity and mortality. Factors are listed in Table 31.2. About 70% of deliveries worldwide are now by a skilled birth attendant, but their obstetric skills are variable, and rapid referral to health facilities able to deal with obstetric emergencies remains problematic. Participatory women's groups, where mothers meet for peer counseling to deal with their local issues, have been shown to markedly reduce both maternal and neonatal mortality.

Saving newborn lives

It has been estimated that over 1 million newborns could be saved by the provision of essential newborn care (Fig. 31.8).

While, in some settings, provision of more advanced neonatal care or even neonatal intensive care including mechanical ventilation may be appropriate, the lives of the largest number of babies could be saved if essential neonatal care was available.

Key interventions in the neonatal period

	Essential newborn care	Hospital-level interventions
Neonatal resuscitation	Skilled birth attendants can provide basic neonatal resuscitation (Helping Babies Breathe programme) and identify infants needing additional care	Appropriately trained healthcare professionals (Helping Babies Breathe programme)
Infection prevention	Hand hygiene, clean cord cutting/ligature, chlorhexidine to cord	Hand hygiene, clean equipment
Hypothermia prevention	Drying of baby, skin to skin contact of mother and baby, covering the baby including head, delay bathing the baby	If significantly preterm, place in plastic bag/wrap immediately after birth, then radiant heater or incubator or warming mattress, or kangaroo mother care if condition is stable (Case History 31.1)
Feeding	Early and exclusive breastfeeding within 1 hour of birth	Supplemental feeding if required (expressed breast milk given via cup or nasogastric tube)
Sick, preterm, or low-birth-weight babies	Transfer these infants to a neonatal unit	Antibiotic treatment if at increased risk or signs of infection Supplemental oxygen, non-invasive respiratory support and intravenous fluids if required

Figure 31.8 Key interventions in the neonatal period.



Case history 31.1

Preterm birth

A baby boy was born with a birthweight of 1.9 kg at estimated gestational age of 32 weeks in Malawi. The mother was transferred to a district hospital to deliver her baby after the spontaneous onset of preterm labour. Following delivery, the infant received oxygen for mild respiratory distress, intravenous antibiotics, and expressed breast milk via a nasogastric tube. Oxygen therapy was monitored with an oxygen saturation monitor. After 3 days in an incubator, he was nursed by kangaroo mother care, where the mother provides continuous care for her baby on her chest (Fig. 31.9). This provides better thermal care and lower infection rates than incubator care, and promotes breastfeeding and maternal bonding to her baby. Breastfeeding was successfully established over a period of 2 weeks.



Figure 31.9 Kangaroo mother care of preterm infants. This is widely promoted and practised in many low- and middle-income countries, and is gaining popularity in high-income countries.

Improving the survival and quality of life of children

Nutrition – undernutrition and obesity

Exclusive breastfeeding for the first 6 months of life is strongly advocated by the World Health Organization as it is the ideal milk for babies and there is less risk of gastro-enteritis and other infections. The Baby-Friendly Hospital Initiative comprises 10 steps for maternity departments to promote breastfeeding and exclude any other feeds unless medically indicated.

Undernutrition remains a major problem in many countries, both as acute and chronic malnutrition (Ch. 13). It is estimated that 52 million children under 5 years of age are wasted (low weight-for-height), 17 million are severely wasted, and 155 million are stunted (low height-for-age). Over 90% are in Africa and Asia, the majority in South Asia.

As well as undernutrition, malnutrition in the form of obesity is becoming an increasing problem in low- and middle-income countries and has become a major global public health problem. Globally, over 41 million children under the age of 5 years are overweight, but over half

of these live in Asia and a quarter in Africa. Being overweight (above one standard deviation body mass index for age and sex) or obese (above two standard deviations body mass index for age and sex) is predominantly seen in middle-class families, where energy-dense food and drinks are popular, and children do much less exercise than those in poorer communities.

Infection

A major component of the reduction in child mortality has been reduced mortality from infectious diseases. The strategies adopted to reduce infection are shown in Figure 31.10.

Vaccination is a key contributor; it is estimated to prevent 2–3 million deaths a year. During 2018, 86% of infants worldwide (116 million) received 3 doses of diphtheria-tetanus-pertussis (DTP3) vaccine, with over 90% coverage in 129 countries. In addition, 86% of children received one dose of the measles vaccine, 69% two doses; global measles mortality has declined by 73%. However, about 19 million children had not received even their DTP vaccine. Inadequate coverage is threatening the continued contribution of vaccination to reduce child mortality, and there is inequity in the vaccines offered

Strategies to reduce infection and malnutrition

	Prevention	Community management	Hospital management
Pneumonia	Expanded programme for immunization (EPI), including pertussis, Hib, PCV, measles	Detection of severe pneumonia, antibiotic therapy and hospital referral	Antibiotic and oxygen therapy
Diarrhoea	Water, Sanitation, and Hygiene (WASH)	Oral rehydration therapy (ORS) and continued feeding	ORS or IV fluids if shock
Malnutrition	Household food security School feeding programmes Deworming Breastfeeding promotion Zinc supplementation	Ambulatory management of mild or moderate malnutrition with ready-to-use therapeutic food (RTUF)	WHO Ten Steps to Recovery for inpatient management of severe acute malnutrition
Malaria	Insecticide-treated bed nets Vector control, indoor residual spraying	Near-patient Rapid Diagnostic Testing (RDT) for malaria Artemisinin Combination Therapy (ACT)	
TB	Effective adult TB control programme BCG immunization Contact tracing and isoniazid preventative treatment	Effective childhood TB case detection and access to suitable laboratory services Child-friendly TB treatment programmes	
HIV	Prevention of Mother-To-Child Transmission (PMTCT)	Access to HIV serological (antibody) and virological (antigen) testing Child-friendly antiretroviral therapy (ART) treatment programmes	
Guidelines	Integrated management of childhood illness (IMCI)	Training courses e.g. Emergency Triage, Assessment and Treatment (ETAT)	

Figure 31.10 Strategies to reduce infection and malnutrition showing prevention and community and hospital management. Hib, *Haemophilus influenzae* type b vaccination; PCV, pneumococcal conjugate vaccine; IV, intravenous; WHO, World Health Organization.

in different countries as well as in the coverage of vaccination schedules within countries. The WHO Global Vaccine Action Plan aims to ensure universal access to vaccination, but uptake has stagnated in recent years and has been further adversely affected by the COVID-19 pandemic. Reasons include difficulty in delivering vaccines because of poor infrastructure, exacerbated by the need to keep vaccines cool. A major issue is vaccine hesitancy, which may be fueled by the spread of misinformation about vaccines via highly connected social media networks, as well as distrust of governments or health systems. Decline in uptake of measles vaccine has resulted in measles outbreaks in Europe and the USA, as vaccine acceptance has been insufficient to provide herd immunity.

Injuries

Globally, injuries are responsible for more than 700,000 deaths of children and young people under the age of 20 years each year. The five major causes of global child injury are road traffic incidents, burns, drowning, poisoning, and falls. Road traffic injuries were responsible for around 185,000 child deaths with 93% of these deaths occurring in low- and middle-income countries. They are the leading cause of deaths among 15- to 19-year-olds. Injury from road traffic incidents is one of the few causes of child mortality that is predicted to increase by 2030. Mortality and morbidity are exacerbated by limited access to good surgical care.

Non-communicable diseases (NCDs)

Non-communicable diseases, predominantly cancer, cardiovascular disease, chronic respiratory disease and diabetes, have markedly increased in low- and middle-income countries, such that they now constitute 80% of the global burden. Five key risk factors are an unhealthy diet predisposing to obesity, tobacco use, alcohol abuse, physical inactivity and air pollution, which accompany increasing affluence in low- and middle-income countries and often have their origins in childhood. Undernutrition in early childhood followed by overnutrition appears to be a particular risk for subsequent cardiovascular disease and diabetes. Household air pollution from smoke in homes using solid fuels, such as wood or charcoal for cooking and heating, predisposes children to lower respiratory infections and asthma and the women to chronic obstructive airways disease and other NCDs. This can be prevented by the use of cleaner fuels, which also helps reduce forest degradation and slows climate change.

Mental health disorders

Globally, 10%–20% of children and adolescents have mental health disorders that impact negatively on their health and wellbeing. The epidemiology of child mental health is poorly described, and access to services is scarce, even in middle-income countries. Suicide is a major cause of death in young male adolescents.

Coexisting multiple pathologies: a major threat to child survival

In low- and middle-income countries children often have multiple coexisting pathologies as well as multiple adversities relating to the background in which they live. This combination contributes to poor outcomes. Examples are shown in [Case histories 31.2 and 31.3](#).



Case history 31.2

Burns to the face

This girl in rural Niger sustained facial burns ([Fig. 31.11](#)). She fell into the open kitchen fire when she had a seizure. Although her epilepsy had initially responded well to phenobarbital, regular supplies were unavailable. Difficulty in finding affordable transport from the village to the health clinic delayed presentation by 4 days, by which time there was secondary infection and increased risk of cataract from conjunctival injury. This simple example highlights the influence of environment on children's health. Although her illness was readily treatable and her injuries were preventable with a fireguard, delayed treatment resulted in complications and only basic medical care was available at the clinic.



Figure 31.11 Facial burns in a rural Nigerian girl.

Children affected by conflict

Conflicts in a number of countries in the Middle East, Africa and South-East Asia, mean that there are large numbers of internally displaced people (41.3 million) and refugees (25.9 million), over half of whom are under the age of 18 years old. Children and women are disproportionately affected physically and psychologically by conflict.

As well as the threat to life, children living in conflict may suffer in a wide variety of ways. They may lack shelter and endure exposure to harsh weather such as freezing



Case history 31.3

Malnutrition

This 10-month-old girl in Kenya presented to an urban health clinic with cough and diarrhoea, and was found to be severely malnourished, with a mid-upper-arm circumference less than 115 mm and weight for length more than 3 standard deviations below the median (Fig. 31.12). She was referred to hospital for inpatient management of her severe acute malnutrition (see Ch. 13). In the weeks after her birth, she had moved from a rural area to the city as her 17-year-old mother needed to find work. After exclusively breastfeeding for 3 months, the baby had been fed predominantly on *ugali* (maize flour cooked to thick porridge consistency). Her mother had struggled to maintain breastfeeding as she had two manual jobs and could not afford artificial milk. This example shows how poverty can affect infant health. The combination of her mother's conflicting demands between home and work, coupled with the isolation of moving to a new urban environment and her poverty, resulted in her daughter developing severe acute malnutrition before seeking help.



Figure 31.12 A 10-month-old in urban Kenya with malnutrition because of poor socio-economic circumstances. She has oedema of the feet and lower limbs and redness of the hair from kwashiorkor.

winters. There may be lack of clean water and sanitation and fragile food security and hunger. They may not be able to access education as no schooling is available. There may be a lack of safe birthing facilities and neonatal care. Healthcare is likely to be compromised by poor

uptake of vaccinations, limited access to poorly staffed and equipped health facilities, and also low supplies of essential medicines. The direct threat posed to health facilities and healthcare workers combines to undermine the health of children in conflict. The mental health of children and young people may be severely affected by deep-rooted fear, unrelenting anxiety and exposure to violence that undermines normal social development and psychological growth. Family members may have been injured or killed. Feelings of hopelessness and lack of a future as well as witnessed trauma and the direct psychological impact of conflict or civil unrest may lead to post-traumatic stress disorder. There may be a continual fear of physical or sexual violence. Providing even basic healthcare under these conditions is often extremely difficult; it requires innovative strategies adapted to particular circumstances.

Climate change

Rising temperatures and extreme weather patterns are likely to have direct and indirect consequences for child health. The direct effects on children are from events such as floods, mudslides, cyclones, heatwaves and wildfires; the indirect health effects are through displacement as a consequence of drought and flooding affecting food security through the effects of climate change on agriculture and ecosystems.

Outbreaks and emerging infections

The last 20 years has seen a marked increase in the number of global infectious disease outbreaks and emerging infections. Reasons include transmission by international travel as well as the effect of warming temperatures from climate change on vector-borne diseases such as the dengue virus spread by *Aedes* mosquito species. The incidence of dengue fever has increased 30-fold over the past 50 years. Other infectious disease outbreaks include chikungunya, yellow fever and Zika virus. The Ebola virus outbreaks have been associated with a high mortality not only from the intrinsic lethality of the virus, but also the difficulties in implementing infection control when healthcare systems are poorly developed. These outbreaks had already highlighted the global health dangers of inadequate health system infrastructure, and the need for international collaboration prior to the most significant recent global pandemic. Cases of Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 were first described in Wuhan, China in December 2019. By the end of April 2021 more than 145 million infections had been recorded globally with more than 3 million deaths. For poorly understood reasons case fatality in children for this virus has been very low, although a small number (about 1 in 5000 infected children) have developed the serious paediatric multisystem inflammatory syndrome (PMIS). However, the indirect impact of the pandemic on child health across the globe is far reaching. It has resulted in worrying loss of schooling and education, and an increase in concerns about mental health. Many children have missed immunizations and

experienced reduced access healthcare. There may have been difficulty on obtaining food. Many families have experienced loss of income from local and international trade and travel restrictions and family life may have been adversely affected by death of family members. Restriction of social interaction and outdoor activities have created concern about maltreatment and on child development. Epidemics highlight the importance of strengthening health systems in all countries throughout the world.

Summary

Global child health

- The number of child deaths globally has decreased markedly over the last 30 years, but there are still 5.2 million under-5-year-old deaths per year.
- Neonatal deaths are responsible for 47% of all under-5-year-old deaths; its main causes are preterm birth, intrapartum-related conditions and infection.
- The main causes of postneonatal mortality in children <5 years old are infections – pneumonia, diarrhea and malaria, followed by injuries.
- Undernutrition contributes to one-third of child deaths, but overnutrition resulting in obesity is a rapidly increasing problem in many low- and middle-income countries.
- The Sustainable Development Goals are setting the agenda for improving global child health until 2030.

Acknowledgements

We would like to acknowledge contributors to the section or chapter on global child health in previous editions, whose work we have drawn on: Tom Lissauer (3rd Edition), Mitch Blair (3rd Edition); Stephen Allen, Ike Lagunju and Raúl Pardíñaz-Solís (4th Edition); Dan Magnus, Anu Goenka, Bhanu Williams (5th Edition). We would also like to thank Anu Goenka for reviewing this chapter.

Further reading

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Appendix



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Growth charts

Examples of growth charts used in the UK for:

- Preterm infants: males ([Fig. A.1a](#)) and females ([Fig. A.1b](#))
- 0–1-year-old boys ([Fig. A.1c](#)) and girls ([Fig. A.1d](#))
- 1–4-year-old boys ([Fig. A.1e](#)) and girls ([Fig. A.1f](#))
- 2–9-year-old boys ([Fig. A.1g](#)) and 2–8-year-old girls ([Fig. A.1h](#))
- 9–18-year-old boys ([Fig. A.1i](#)) and 8–18-year-old girls ([Fig. A.1j](#)).

In the nine-centile UK charts, the interval between each pair of centile lines is the same (two-thirds standard deviation). They show the 0.4 and 99.6 centile lines, which are two and two-thirds standard deviations below and above the median, respectively. The charts for older children also show the timing of the stages of puberty.

Appendix

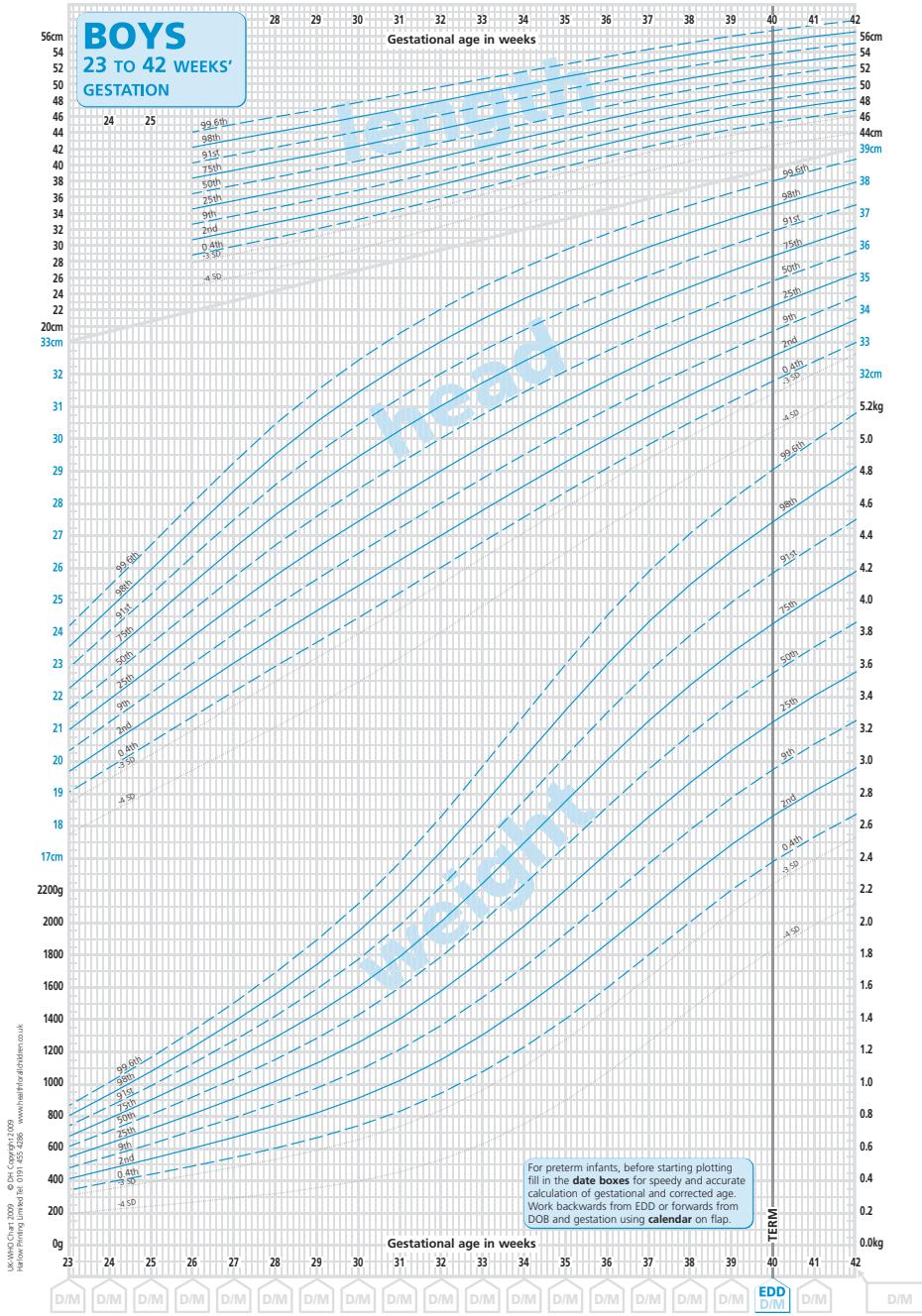


Figure A.1 Growth chart for preterm infants: (a) Boys. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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Appendix

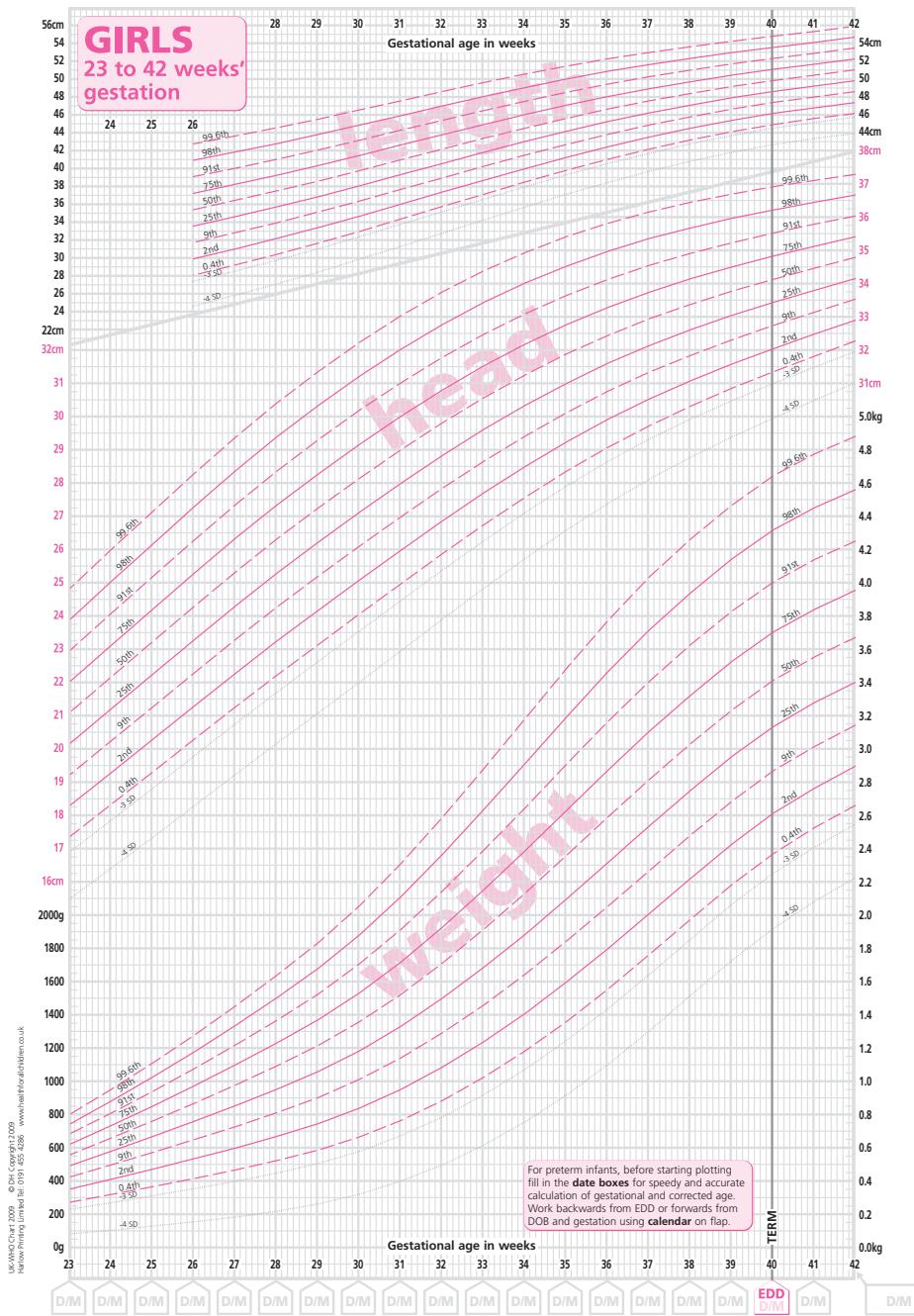


Figure A.1, continued Growth chart for preterm infants: (b) Girls. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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Appendix

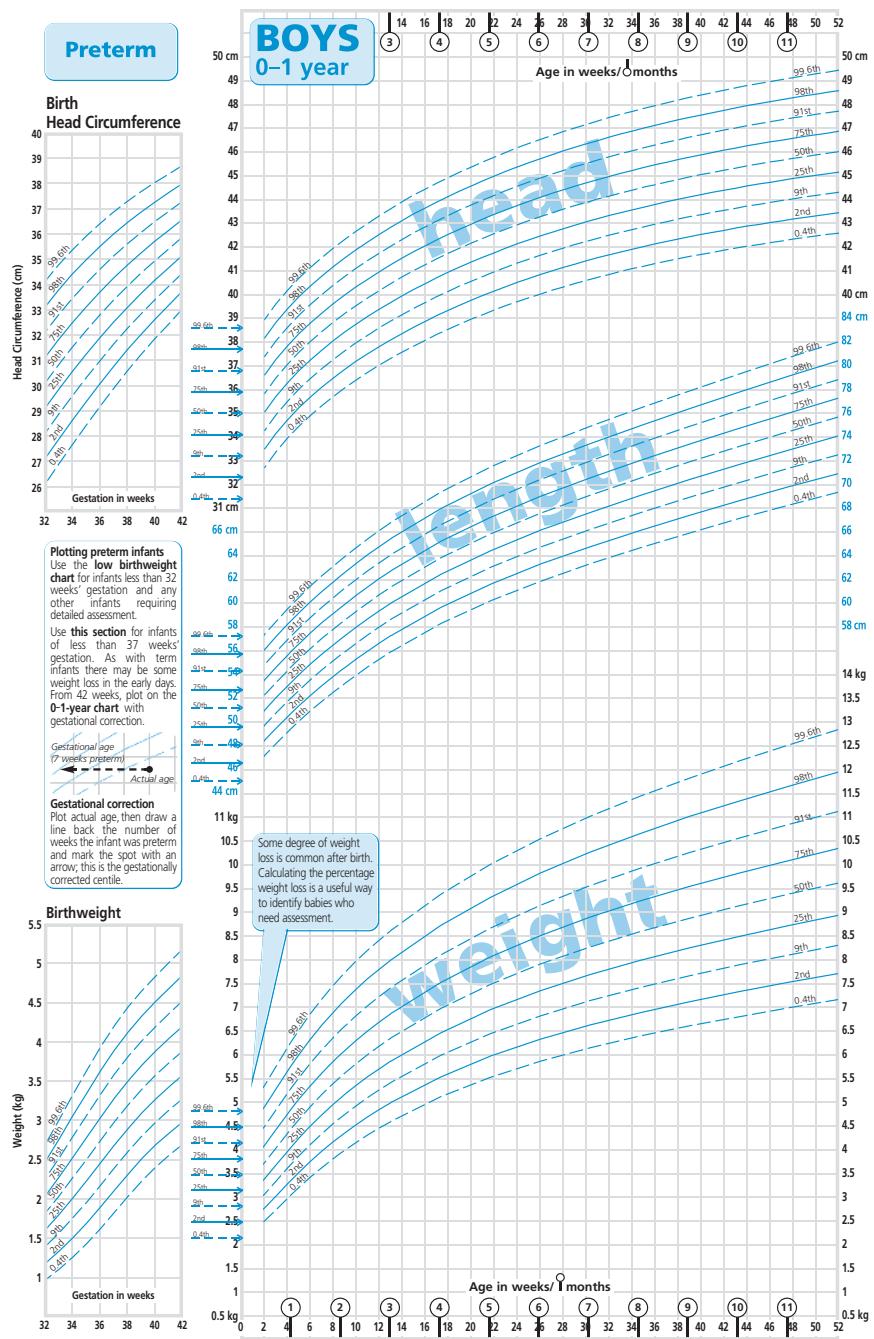


Figure A.1, continued Growth chart ages 0-1 year: (c) Boys. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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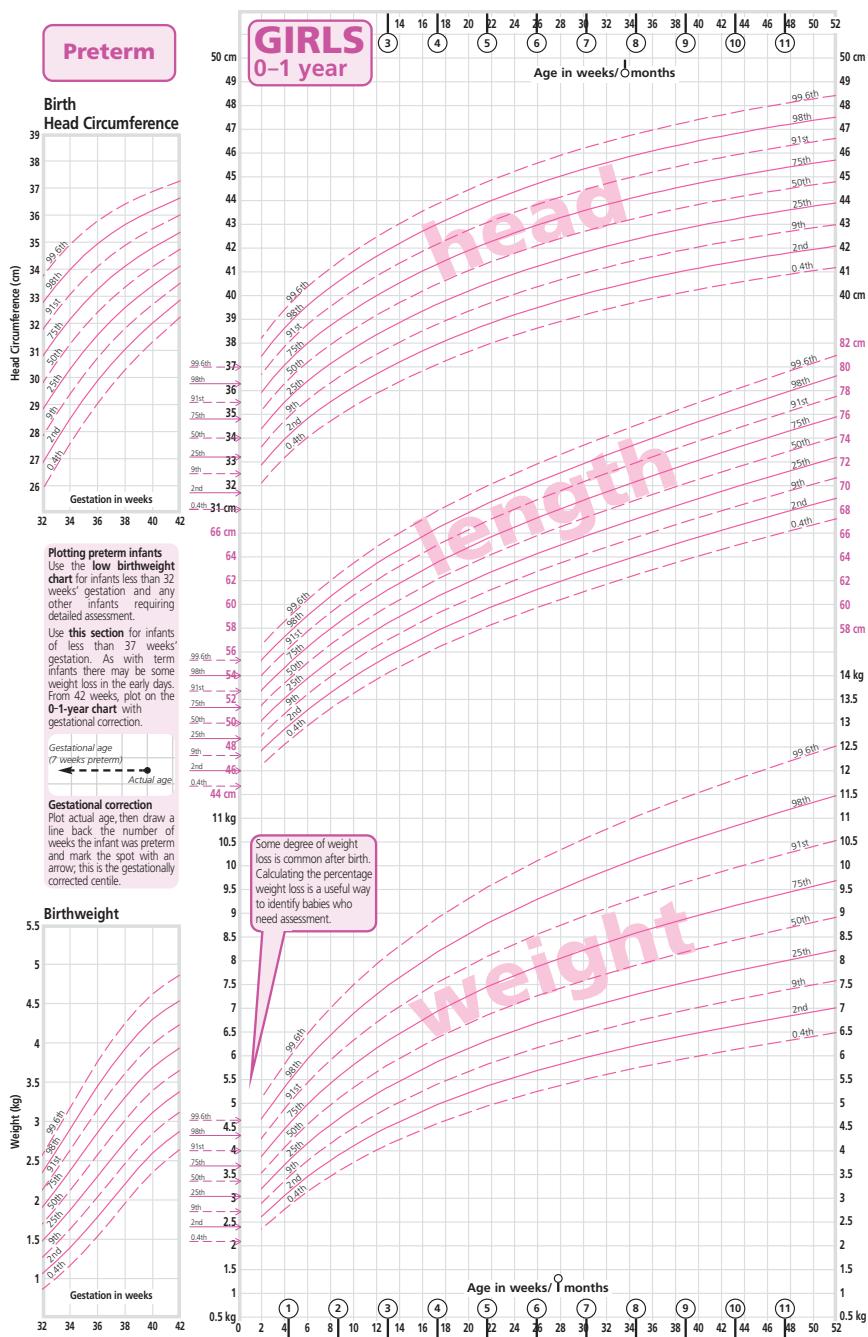


Figure A.1, continued Growth chart ages 0–1 year: (d) Girls. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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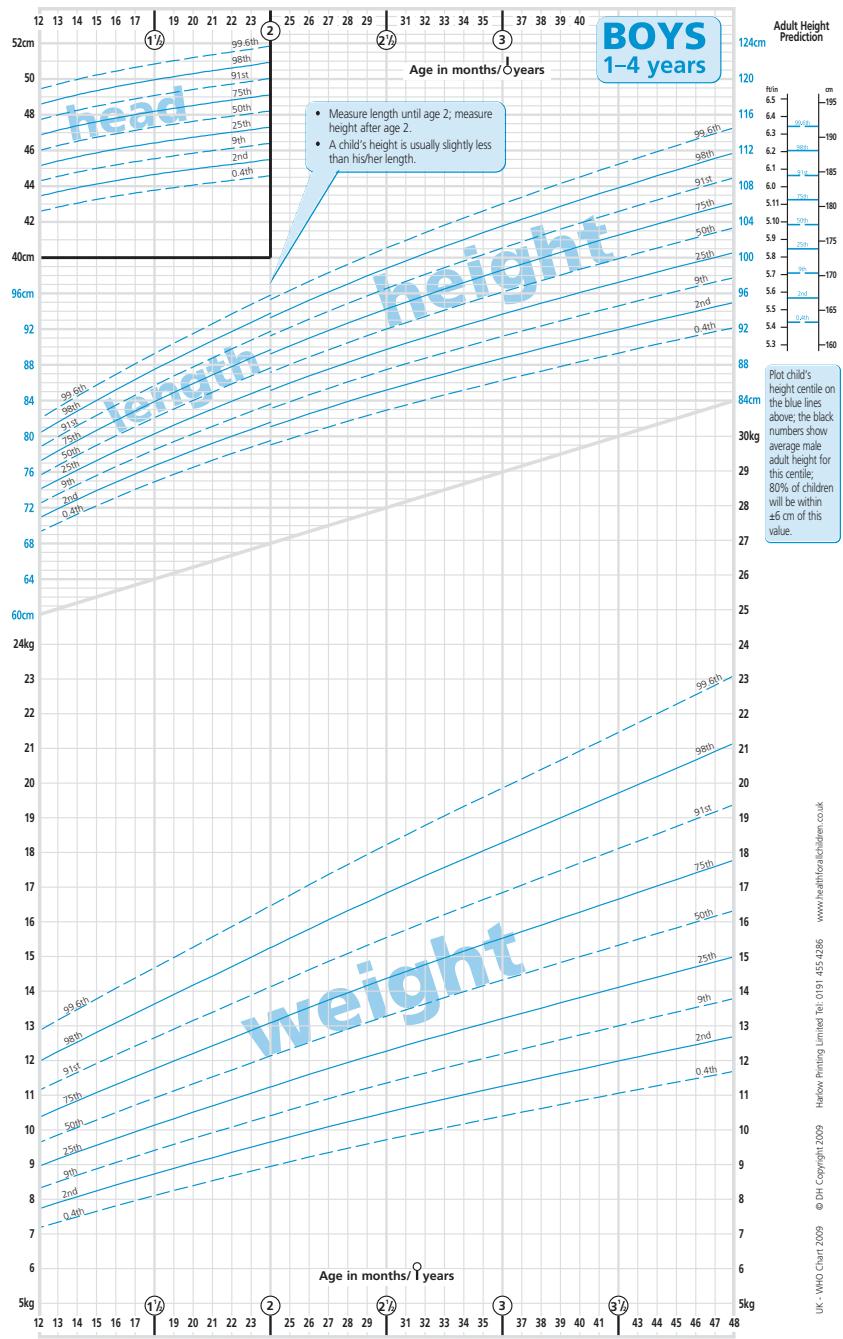


Figure A.1, continued Growth chart ages 1–4 years: (e) Boys. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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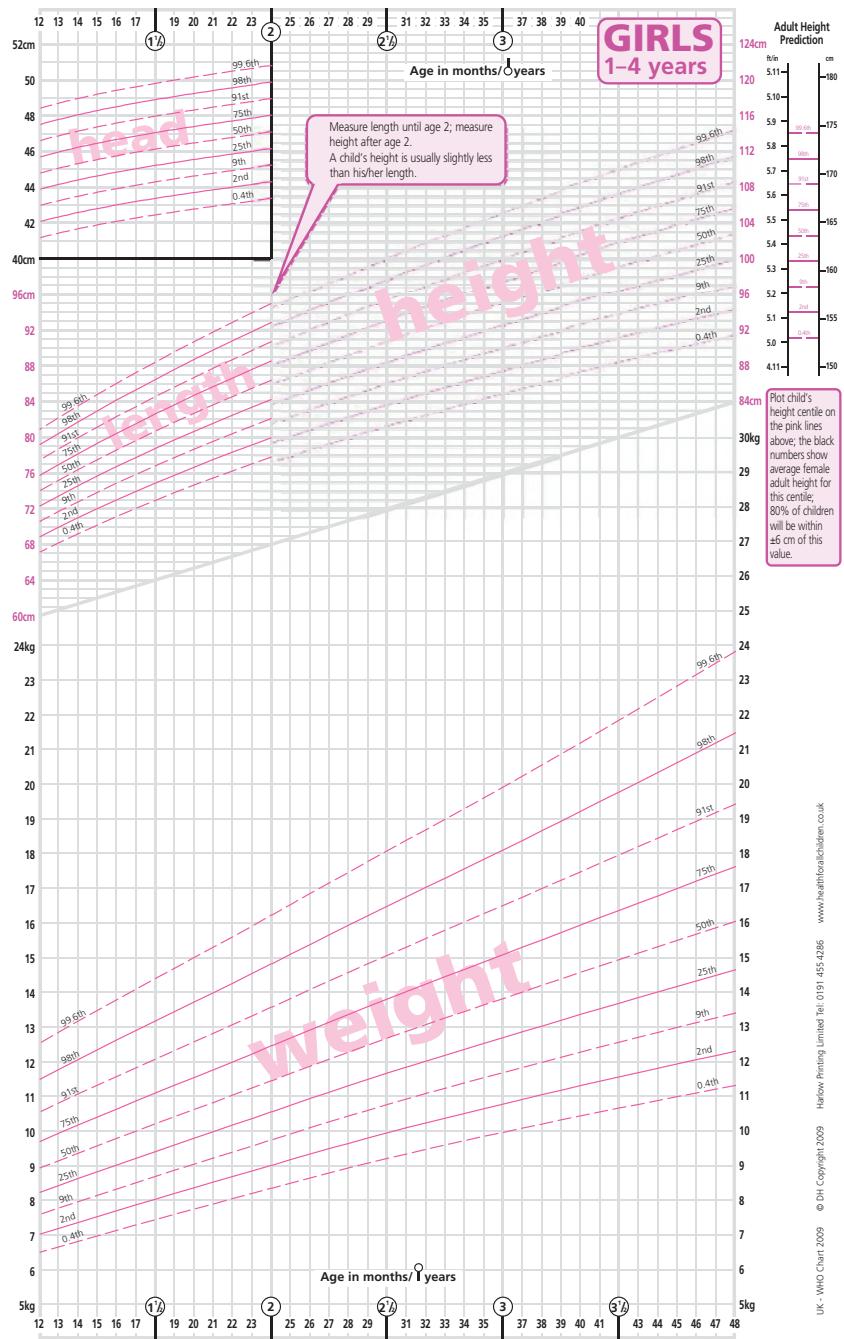


Figure A.1, continued Growth chart ages 1–4 years: (f) Girls. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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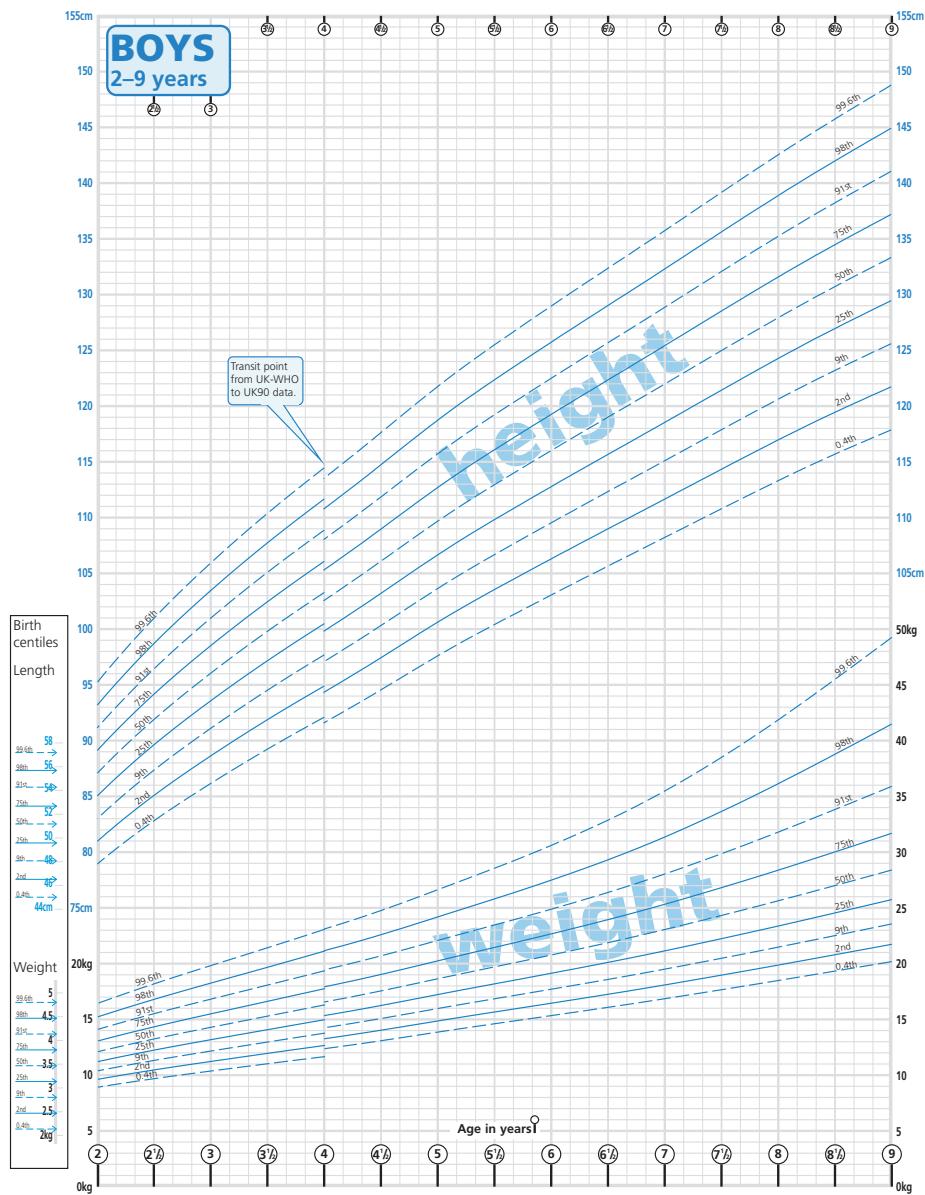


Figure A.1, continued Growth chart ages 2–9 years: (g) Boys. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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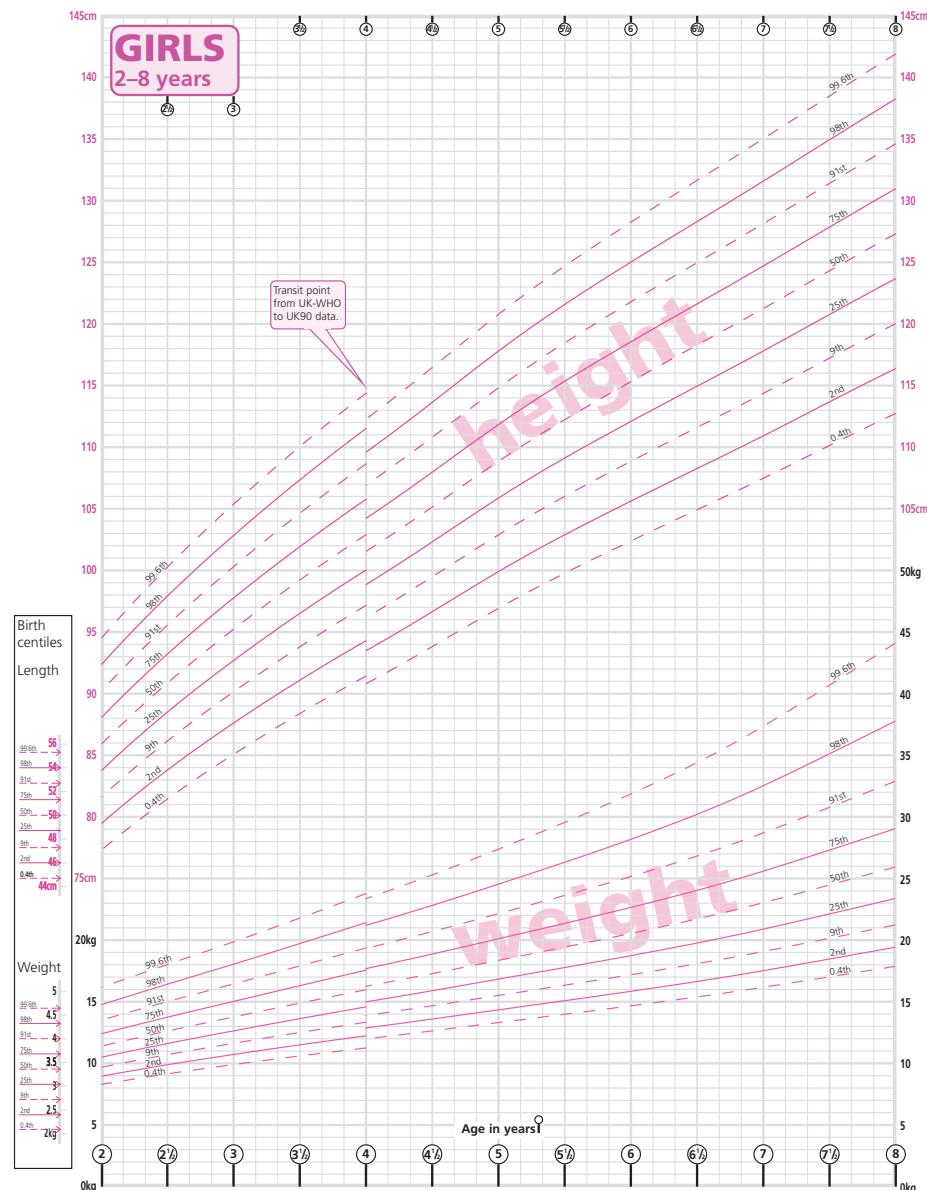


Figure A.1, continued Growth chart ages 2–8 years: (h) Girls. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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Appendix

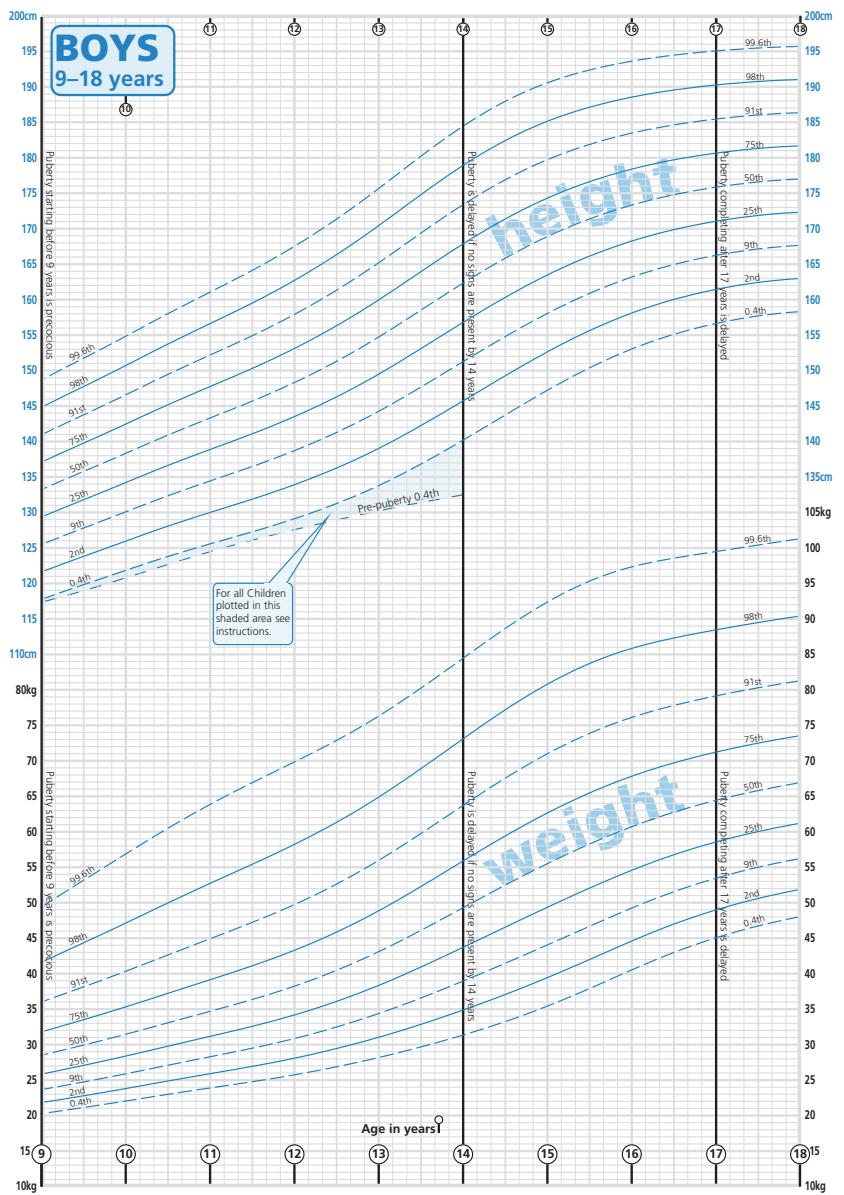


Figure A.1, continued Growth chart ages 9–18 years: (i) Boys. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

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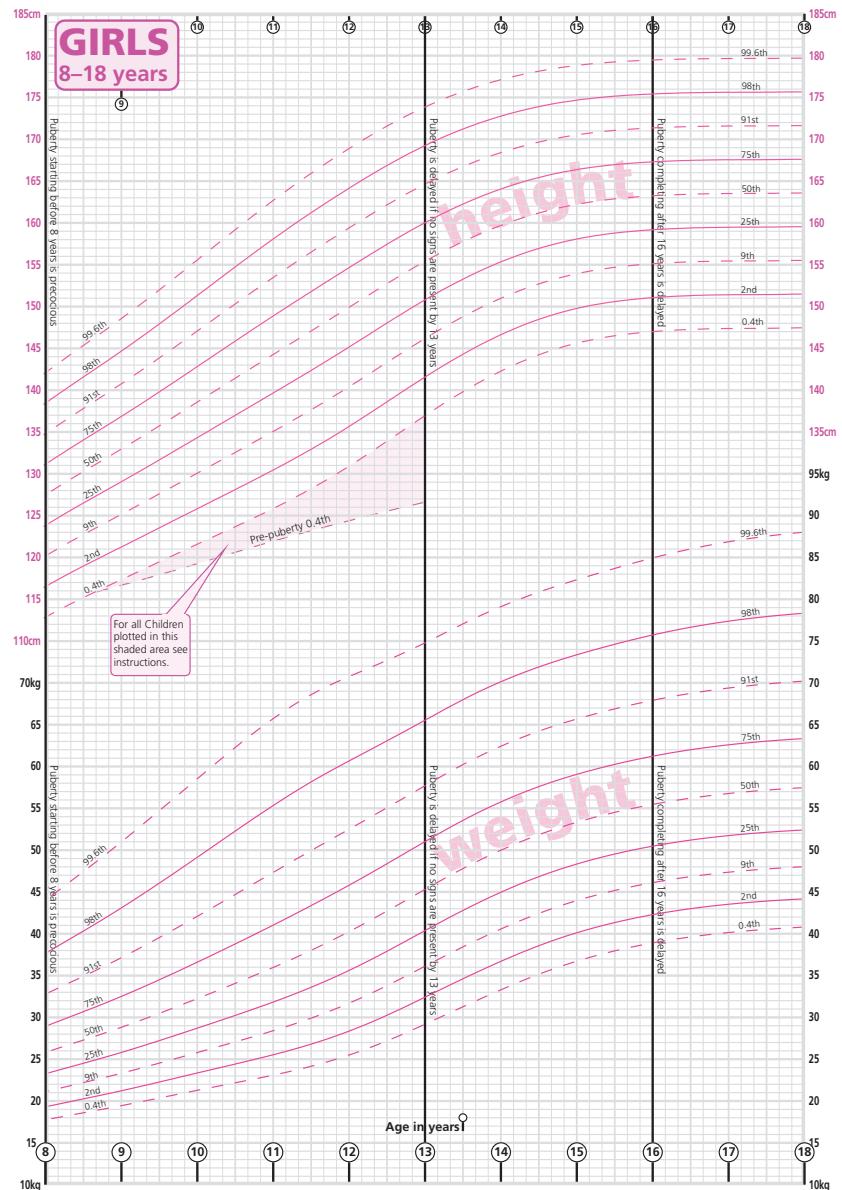


Figure A.1, continued Growth chart ages 8–18 years: (j) Girls. (Chart © Child Growth Foundation. Further supplies and information from www.healthforallchildren.co.uk. Reproduced with permission.)

Gestational age assessment of newborn infants

(a) Neuromuscular maturity

	-1	0	1	2	3	4	5
Posture							
Square window (wrist)							
Arm recoil							
Popliteal angle							
Scarf sign							
Heel to ear							

(b) Physical maturity

	Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth pink, visible veins	Superficial peeling and/or rash, few veins	Cracking pale areas rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald		
Plantar surface	Heel-toe 40–50 mm: -1 <40 mm: -2	>50 mm no crease	Faint red marks	Anterior transverse crease only	Creases ant. 2/3	Creases over entire sole		
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola 1–2-mm bud	Raised areola 3–4-mm bud	Full areola 5–10-mm bud		
Eye/ear	Lids fused loosely: -1 tightly: -2	Lids open Pinna flat, stays folded	Sl. curved pinna; soft; slow recoil	Well-curved pinna; soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff		
Genitalia male	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal; rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae		
Genitalia female	Clitoris prominent, labia flat	Prominent clitoris, small labia minora	Prominent clitoris, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora		

(c) Maturity rating

Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Figure A.2 Scoring system for assessment of gestational age in newborn infants (New Ballard score). This is a method of estimating gestational age according to neuromuscular (a) and physical maturity (b). The infant's gestation or age (± 2 weeks) is determined from the total score using the conversion chart (c). (Adapted from: Ballard JL, Khoury JC, Wedig K, et al: New Ballard score, expanded to include extremely premature infants. *Journal of Pediatrics* 119:417–423, 1991.)

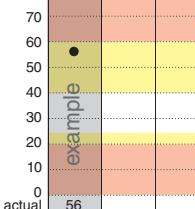
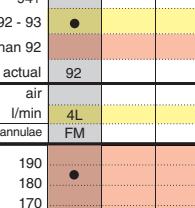
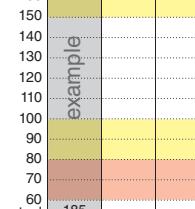
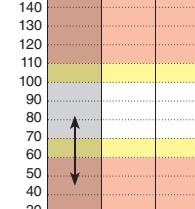
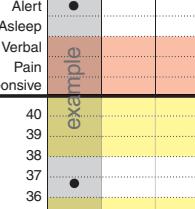
Appendix

Paediatric Early Warning Score (PEWS)

NAME:

CHI NO:

Date:							
Time:	0800						
Location	Ward						
Prescribed frequency of observations:	15 min						

Respiratory Rate example actual 56		70 60 50 40 30 20 10 0 actual RR
SpO₂ 94+ 92 - 93 less than 92 actual 92		94+ 92 - 93 less than 92 actual SpO ₂
Oxygen air l/min 4L FM		190 180 170 160 150 140 130 120 110 100 90 80 70 60 actual O ₂
Heart Rate example actual 185		190 180 170 160 150 140 130 120 110 100 90 80 70 60 actual HR
Blood Pressure (Plot systolic and diastolic but score SYSTOLIC only) BP cuff size: 82/46		140 130 120 110 100 90 80 70 60 50 40 30 actual BP
Capillary return less than 2 secs 2 - 4 secs more than 4 secs		less than 2 secs 2 - 4 secs more than 4 secs CRT
Conscious level Alert Asleep Verbal Pain Unresponsive		Alert AVPU Asleep (if V / P / U) Verbal complete GCS chart Pain GCS chart Unresponsive AVPU
Temperature °C example actual 36.8		40 39 38 37 36 35 34 actual Temp °C
Staff or Carer Concerns (Staff = S, Carer = C, None = N)	C	(Staff= S, Carer = C, None = N)
PEWS Initials Time of medical review if score elevated 08.15	PEWS Initials Time of medical review if score elevated 08.15	
Pain Score Blood Glucose	Pain Score Blood Glucose	

12-23
MONTHS



Figure A.3 An example of a Paediatric Early Warning Score (PEWS) in children 12–23 months to identify children whose clinical condition has deteriorated and may require escalation of care (NHS Scotland). (Source: Health Improvement Scotland iHub (Creative Commons licence) – ihub.scot/improvement-programmes/scottish-patient-safety-programme-spssp/maternity-and-children-quality-improvement-collaborative-mcqic/paediatric-care/pews.)

Continued



PAEDIATRIC EARLY WARNING SCORE (PEWS) 12 – 23 MONTHS

(To be used from 12 months until day before 2nd birthday)

PEWS is a tool to aid recognition of sick and deteriorating children.

PEWS should be calculated every time observations are recorded.

How to calculate score:

- Record observations at intervals as prescribed
- Record observations in black pen with a dot
- Score as per the colour key

0	1	3
---	---	---

- Add total points scored
- Record total score in PEWS box at bottom of chart
- Action should be taken as below

Name.....
DOB.....
CHI	Affix Patient ID label
Ward..... Consultant	
Chart Number	
Date	

PEWS	Level of escalation	Action to be taken	Concerns include, but are not restricted to;
Regardless of PEWS always escalate if concerned about a patient's condition			
0	0		→
1-2	1		
3-4 or any in red zone	2		
5 or more	3		
Bradycardia, cardiac or respiratory arrest			

If observations are as expected for patient's clinical condition, please note below accepted parameters for future calls					
Acceptable parameters	RR	O ₂ saturation	HR	BP	Temperature°C
Upper acceptable					
Normal range					
Lower acceptable					
Doctor's signature	Date & Time				

PAEDIATRIC SEPSIS 6 Recognition: Suspected or proven infection + 2 of: <ul style="list-style-type: none">Core temperature < 36°C >38°CInappropriate TachycardiaAltered mental state: sleepy / irritable / floppyPeripheral perfusion, CRT >2 sec, cool, mottled	Lower threshold in vulnerable groups Think could this be sepsis? IF NOT then why is this child unwell?	If YES respond with Paediatric Sepsis 6 within 1 hour: <ul style="list-style-type: none">Give high flow oxygenIV or IO access and blood cultures, glucose, lactateGive IV or IO antibioticsConsider fluid resuscitationConsider inotropic support earlyInvolve senior clinicians/ specialists EARLY
---	--	---

Figure A.3, continued

Asthma action plan

<p>Green zone – GO</p> <p>Your asthma is under control if:</p> <ul style="list-style-type: none"> • your breathing feels good • you do not have a cough or wheeze • you can take part in normal activities and play games / sport. • you are sleeping through the night • you are not missing school because of your asthma <p>Peak flows are between:</p> <p>.....</p> <p>Green zone action – Your normal medicines are: Preventer</p> <p>.....</p> <p>Other medicines</p> <p>.....</p> <p>Reliever</p> <p>..... as required. Remember: If necessary take this before exercise or if you have cold-like symptoms. Take 2–4 puffs every 4 hours if you need it. If there is no improvement, move to the Amber zone.</p>	<p>Amber zone – WARNING</p> <p>Your asthma is getting worse if you:</p> <ul style="list-style-type: none"> • wake at night with asthma symptoms • have a cough, wheeze, or ‘tight’ chest • need to use the reliever inhaler once a day, more than usual or, it is not lasting for 4 h. <p>Peak flows are between:</p> <p>.....</p> <p>Amber zone action – Take all medicines as normal.</p> <p>Take 4–10 puffs of reliever – one puff at a time as taught. Use a spacer if you have one and shake the MDI in between puffs. Take every 4 hours if needed.</p> <ul style="list-style-type: none"> • If no improvement – make an appointment to see your doctor for that day. • If you have a Symptom/Peak flow Diary – start filling it in and take it with you to the doctor. <p>Or Start your home prednisolonemg daily, if you have it. See your doctor if you are not better after 12 hours.</p> <p>Remember: If no better after 10 puffs of reliever, move to Red zone.</p>	<p>Red zone – DANGER</p> <p>Your asthma is severe if after taking 10 puffs of reliever you:</p> <ul style="list-style-type: none"> • are still breathing hard and fast • cannot talk or feed easily • are exhausted • are frightened and look anxious • are very pale/grey/blue in colour <p>Peak flow reading (if able) below:</p> <p>.....</p> <p>Red zone action – Call an ambulance now</p> <ul style="list-style-type: none"> • Keep taking one puff of reliever every 20–30 s or four slow breaths or, if you have one, nebulized reliever with oxygen until the ambulance arrives. • Take a dose of oral steroids if not already taken. • Do not move about • Keep calm
--	--	--

Figure A.4 Example of personalized asthma action plan for patients.

Blood pressure

Table A.1 Systolic blood pressure for males and females by age and height centile. In children 1–13 years: elevated BP is >90th centile, hypertension (HTN) is ≥95th centile or ≥130/80 (whichever is lower). In young people ≥ 13 years: elevated BP is ≥120/80, HTN is ≥ 130/80.

		Systolic BP (mm Hg)					
Age (years)	Height centile	50th height centile		90th height centile		95th height centile	
		Males	Females	Males	Females	Males	Females
1	50th	86	86	88	88	88	88
	90th	100	100	101	102	101	102
	95th	103	103	105	105	105	105
5	50th	94	93	96	96	96	96
	90th	106	107	108	110	108	110
	95th	109	110	112	113	112	113
10	50th	100	99	102	102	103	103
	90th	112	112	115	115	116	116
	95th	116	116	120	119	121	120
12	50th	104	105	108	108	109	108
	90th	117	118	121	122	122	122
	95th	121	122	126	125	128	126
15	50th	113	108	114	109	114	109
	90th	128	122	130	123	130	124
	95th	132	126	135	127	135	128

(Adapted from: Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics* 2017;140(3):e20171904.) Blood pressure centile can be obtained electronically at <https://www.mdcalc.com/aap-pediatric-hypertension-guidelines>.

Peak expiratory flow rate (PEFR)

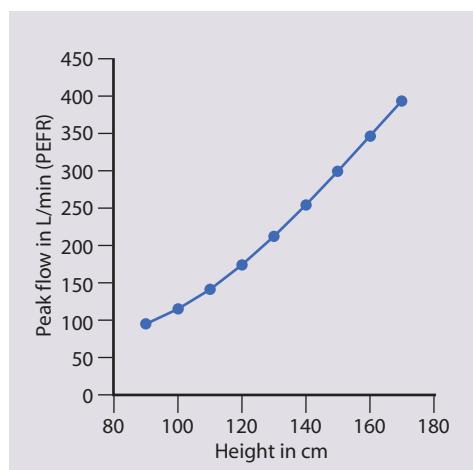


Figure A.5 The normal range of peak flow measurements according to height.

Forced expiratory volume in 1 second (FEV₁)

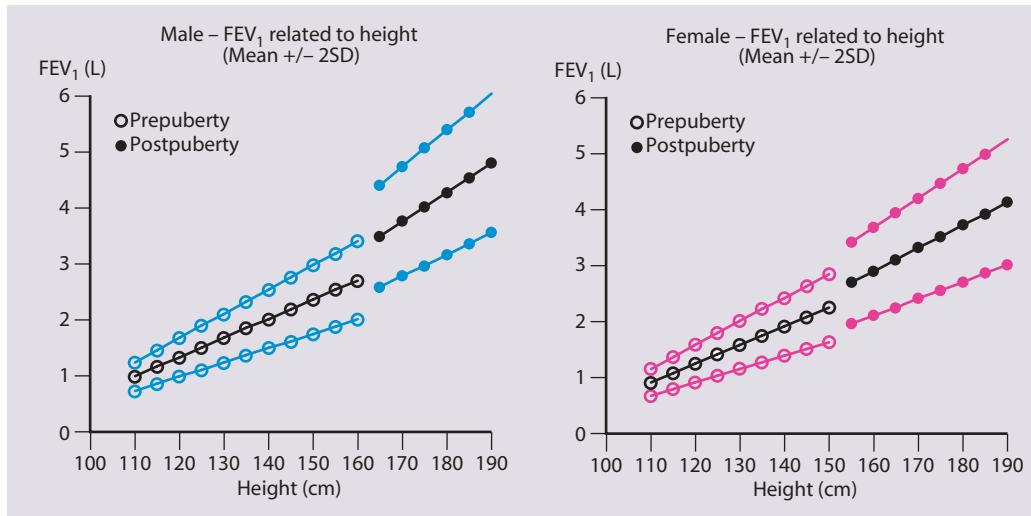


Figure A.6 The normal range of forced expiratory volume in 1 second (FEV₁). It varies with height, sex, and before and after puberty. It is the change over time that is most important in determining the effectiveness of treatment.

Imaging in children

Principles relating to the use of imaging are:

- X-rays – use is minimized to avoid the risk of ionizing radiation. If used, the minimum number of exposures with the lowest radiation dose is used.
- Ultrasound – is good at identifying structures where there is a fluid/solid interface, but images are not obtained through bone. It is highly operator dependent, and paediatric expertise is required.
- MRI (magnetic resonance imaging) scans – provide detailed images but the child has to lie still. This may require co-operation, assistance of a play therapist, immobilizers, sedation, or even a general anaesthetic.
- CT (computerized tomography) scans – can usually be obtained quickly and are less distorted by movement artefact, but involve ionizing radiation. They are useful for acute head injury (where time is crucial) and for chest imaging.

Blood tests

All children dislike needles. It is also time-consuming. Before requesting a blood test, consider 'Can I get this information in another way?' and 'Is this essential – will it alter management and benefit the child?' Some investigations are required when a child is seriously ill.

Taking blood from children

If a blood test is necessary, consider the kindest and safest way to do it. Be patient whenever possible. Local anaesthetic cream reduces the pain of venepuncture, but requires at least 30 minutes to be effective; cold spray/ice can also be effective if time is limited. Distraction can be very helpful for some children, but needs to be tailored to the child's age and the

procedure. Experience in performing the procedure helps reduce pain and upset. Capillary heel-prick or finger-prick methods are useful ways to obtain small volumes of blood without venepuncture, but the blood

samples are prone to haemolysis and insufficient volume for analysis. The most common blood tests undertaken in paediatric clinical practice are summarized in [Tables A.2–A.4](#).

Table A.2 Common blood tests and their interpretation

Blood test		Normal value	Interpretation
Urea and electrolytes	Sodium	130–150 mmol/L	Low in relative water excess (or sodium loss). High in water loss (i.e. dehydration)
	Potassium	3.5–4.7 mmol/L	Elevated in renal failure/dysfunction. Low in recurrent vomiting
	Urea		Elevated in dehydration but also in gastrointestinal bleeding
Full blood count	Creatinine		Elevated in renal disease (and dehydration)
	Haemoglobin	Varies with age	See Table A.4 . If low haemoglobin, suggests either iron deficiency or haemoglobinopathy. High in polycythaemia
	Mean cell volume		
	White cell count		High count in infection, low in severe infection. Very high or low in malignancy
Blood gas (capillary)	Platelet count	150–450 × 10 ⁹ /L	High in infection. Low if consumed, i.e. DIC (disseminated intravascular coagulation), ITP (immune thrombocytopenic purpura)
	pH	pH 7.31–7.41	Low is acidosis, high is alkalosis
	Partial pressure of carbon dioxide	4.5–6 kPa	High values suggest respiratory cause for any acidosis (see Table A.3 and Table 27.5 for further details)
Blood glucose	Glucose	2.6–6.0 mmol/L	High in diabetes, elevated by stress. Low in children with metabolic diseases
Inflammatory markers	C-reactive protein (CRP)	<5 mg/L (laboratory values vary)	Elevated in infection or proinflammatory states. Rises and falls more quickly than ESR
	Erythrocyte sedimentation rate (ESR)	<10 mm/h (laboratory values vary)	
Blood culture	Bacteraemia		Will identify bacteria in the blood if sufficient volume. Typically takes 48 h to achieve growth in culture
Thyroid function tests	Thyroid stimulating hormone (TSH)	0.3–5.5 mIU/L	Elevated in hypothyroidism (unless due to hypopituitarism, when thyroid-stimulating hormone will remain low and measurement of free T3/T4 is required)
	Free T3/T4		

Table A.3 Capillary blood gas interpretation. Sometimes used to measure blood pH and blood carbon dioxide (CO_2) on very small volumes of blood. Digit must be warm and free flowing blood sample. Bicarbonate (HCO_3) and base excess values are calculated. Abnormal results should always be repeated.

(a) General guide				
	Parameters	Normal	Acidosis	Alkalosis
Acidotic or alkalotic?	pH	7.31–7.41	<7.31	>7.41
Respiratory cause?	CO_2	4.6–6 kPa	↑	↓
Metabolic cause?	HCO_3	22–26 mmol/L	↓	↑
	Base excess	–2 to +2		

(b) More detailed analysis				
pH	CO_2	HCO_3	Interpretation	
Normal	Normal	Normal	Normal	
<7.31	↑	Normal	Respiratory acidosis	
<7.31	Normal	↓	Metabolic acidosis	
<7.31	↑	↓	Mixed respiratory and metabolic acidosis	
Normal	↑	↑	Compensated respiratory acidosis	
Normal	↓	↓	Compensated metabolic acidosis	
>7.41	↓	Normal	Respiratory alkalosis	
>7.41	Normal	↑	Metabolic alkalosis	
>7.41	↓	↑	Mixed respiratory and metabolic alkalosis	

Table A.4 Normal ranges: haematology

Age	Haemoglobin (g/L)	Mean corpuscular volume (fl)	White blood cells ($\times 10^9/\text{L}$)	Platelets ($\times 10^9/\text{L}$)
Birth	145–215	100–135	10–26	150–450 at all ages
2 weeks	134–198	88–120	6–21	
2 months	94–130	84–105	6–18	
1 year	113–141	71–85	6–17.5	
2–6 years	115–135	75–87	5–17	
6–12 years	115–135	77–95	4.5–14.5	
12–18 years:				
Male	130–160	78–95	4.5–13	
Female	120–160	78–95	4.5–13	

WETFLAG emergency management of resuscitation

Table A.5 WETFLAG emergency management of resuscitation. This is used to guide resuscitation based on estimation of a child's weight based on age.

WETFLAG		
W	Weight (kg)	Age <1 year = (Age in months/2) + 4; Age 1–5 years = (2 × Age in years) + 8; Age 6–12 years = (3 × Age in years) + 7. Alternatively, simpler but even less accurate formula is used: $2 \times (\text{Age (years)} + 4)$
E	Energy for defibrillation (J)	4J per kg
T	Tube size for endotracheal intubation (internal diameter)	$4 + \frac{\text{Age (years)}}{4}$
F	Fluid bolus volume IV 0.9% saline	Trauma: 10ml per kg Medical: 10–20ml per kg
L	Lorazepam dose	0.1 mg per kg
A	Adrenaline dose for cardiac arrest	0.1 ml/kg of 1:10,000 IV adrenaline
G	Glucose dose for hypoglycaemia	2 ml per kg of IV 10% dextrose

Initial fluid management of dehydration and shock

This is summarized in [Fig. A.7](#), and an example is shown in [Case History A.1](#).

Initial fluid management of dehydration and shock in children

1. Resuscitation:
Intravenous fluid boluses of 0.9% crystalloid (usually 0.9% NaCl) should be used to restore circulatory volume. Use 10 or 20 ml/kg bodyweight, then reassess; 10 ml/kg bodyweight initial bolus following trauma.

2. Fluid deficit replacement:
Assessment of the volume of fluid needed to restore circulating volume (after resuscitation) is based on either:

- Estimation of percentage dehydration based on clinical features (clinical dehydration, i.e. moderately severe dehydration – 5% deficit; shock, i.e. severe dehydration – 10% deficit)
- Change in weight (where an accurate premorbid weight measurement is available).

Fluid replacement is based on the premise that:

- 1 kg of body weight loss is equivalent to 1 litre of fluid loss and % deficit is calculated as a proportion of body weight.

Fluid boluses given during resuscitation are deducted from the fluid deficit.

3. Maintenance fluids
This formula calculates the fluid requirements for a child over 24 hours

100 ml/kg body weight for first 10 kg	A
50 ml/kg body weight for second 10 kg	B
20 ml/kg body weight for every 1 kg thereafter	C
Total fluid requirement in 24 hours	A + B + C

For intravenous fluids, use 0.9% NaCl with 5% dextrose and consider 20 mmol KCl per 500-ml bag according to serum levels.

4. Adjusting fluids

Fluids are adjusted according to clinical situation:

- When there is a risk of SIADH, for example in pneumonia two thirds of standard maintenance should be given, enterally or intravenously.
- Maintenance fluid may need to be increased to take account of ongoing losses, e.g. due to profuse diarrhoea or the diuretic phase following acute tubular necrosis.
- Maintenance fluids are reduced to take account of oral intake.
- Fluid replacement time is increased to 48 hours to avoid rapid changes in osmolarity, as with hypernatraemic dehydration or diabetic ketoacidosis.

Figure A.7 Initial fluid management of dehydration and shock in children (SIADH – Syndrome of inappropriate antidiuretic hormone).



Case history A.1

Initial fluid management of dehydration and shock

Darpana is 18 months old and has had a mild fever, a runny nose, and lacks interest in playing. She has been refusing almost all oral fluid for 48 hours and, over the last 24 hours, has developed severe vomiting. She has not passed urine all day. On examination, she is drowsy but responds to her mother's voice, and has a temperature of 37.8°C. She is tachycardic and mottled, with reduced skin turgor. Her capillary refill time is 4 seconds, despite a normal blood pressure. Her weight is 11kg. Intravascular access is established. Blood samples are sent for culture, urea, creatinine and electrolytes, CRP and full blood count. A capillary blood gas is taken, which shows a metabolic acidosis and

raised lactate. Antibiotics are administered in case she is has sepsis.

Darpana meets the clinical criteria for shock. A bolus of 20ml/kg is given, with good effect. Based on her clinical assessment, she is estimated to be 10% dehydrated.

She is admitted to the paediatric ward to receive intravenous fluid as shown in [Table A.6](#). Sodium and potassium concentrations were in the normal range.

Overnight Darpana's vomiting settles and her intravenous treatment continues while she sleeps. The following day she is much better and is drinking a little. Her intravenous fluids are reduced according to her oral intake.

Table A.6 Calculation of fluid requirement of Darpana for first 24 hours, weight 11 kg

Fluid	Fluid requirement	Fluid volume
Dehydration	10% of 11 kg	1100 ml
Maintenance fluid per 24 hrs	100 ml/kg for first 10kg 50 ml/kg for second 10kg	1000 ml 50 ml Total: 1050 ml
Total requirement over 24 hrs		2150 ml
Less resuscitation bolus given – 20 ml/kg		220 ml
Remaining fluid requirement over 24 hrs		1930 mls, i.e. 80 ml/hr

Parkland formula for burns

The Parkland formula is used to calculate the *additional* 24-hour fluid requirement for children with burns >10% body surface area owing to increased insensible losses from burned skin.

Parkland formula:

$$P = \text{Body weight kg} \times 4 \text{ ml} \times \% \text{ Burned body surface area}$$

Give half of this amount over 8 hours in addition to the normal fluid maintenance. Give the remaining half over 16 hours in addition to the normal fluid maintenance. Preferred fluid – Plasma-lyte, as it does not contain calcium and has higher pH than Hartmann's solution (Ringer's lactate), the alternative fluid.