Pediatrics Notes

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Preface

Medical knowledge has evolved tremendously over the past century. With the advent of the internet, sharing medical knowledge has become very easy. However, most medical literature available originates from developed countries, thus devoid of the relevant local content for many underdeveloped regions. This is critical for medical education and practice in that these texts often do not consider the cultural relevance of these pathologies, disease patterns and risks, local treatment options and idiosyncrasies of the medical delivery systems. Undoubtedly, these have significant effects on medical education and practice.

This text was birthed out of the need to bridge this gap. Though the content is primarily directed at undergraduate medical teaching, it can be beneficial to postgraduate trainees as well.

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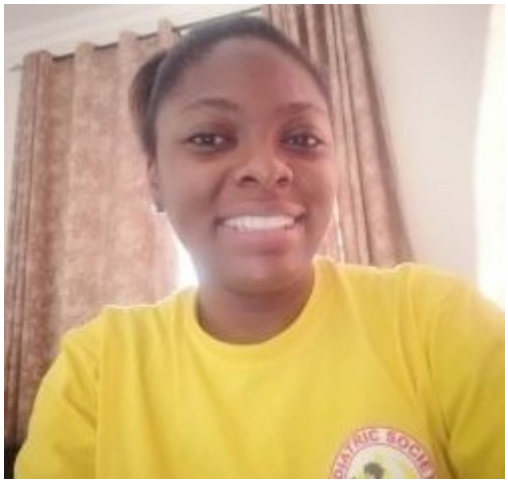

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Part I

Introduction

1 Child History & Examination

1.1 Introduction

To clerk a case is to take a comprehensive **history,** perform a thorough **physical examination**, form an impression about the most plausible diagnosis, known as a provisional diagnosis, order investigations that will confirm this provisional diagnosis, and then plan a **definitive treatment** based on the confirmed diagnosis.

1.2 The Focus of Pediatrics Clerkship

After a complete clerking of a patient, a reasonable Provisional Diagnosis must be arrived at, which can then be confirmed with relevant investigations. The nutritional status of any child should be determined at the end of each pediatric case clerked.

Differential diagnosis: In most patient clerking situations, more than one plausible investigation may be considered after a history and physical examination. In such situations, all the plausible diagnoses are differential diagnoses of each other.

Different, distinctive diagnoses: In some situations, the patient may present with more than one unrelated disease. For example, a patient who presents with pneumonia may also have septic arthritis. Such different and distinct diagnoses are not differentials of each other

History

History-taking is pivotal in all medical encounters, whether in emergencies or in "stable" encounters or consultations.

Paediatric History is essentially the same as adult history, albeit with five additional segments:

1. Informant
2. Pregnancy, Birth & Neonatal History
3. Immunization History
4. Dietary History
5. Developmental History

1.3 The 15 Elements of Pediatrics History

A full history must consist of the following 15 elements:

1. The Informant
2. Demographics
3. Presenting Complaint
4. History of Presenting Complaint (HPC)
5. Direct Question
6. Systemic Enquiry
7. Past Medical History
8. Drug History
9. Pregnancy/Birth & Neonatal History
10. Immunization History
11. Dietary History
12. Developmental History
13. Family History
14. Social History
15. Summary

1.3.1 Informant

The role and importance of an informant in paediatric history are as follows:

- To help with the provision of history. In infants and young children, the history is essentially given by the informant. In older children and adolescents, the sick child could contribute to the history.
- To be reasonably sure whether the history so obtained is reliable or not

The following information should be requested of the informant regarding themselves: their name, relationship to the patient, level of education, and whether they witnessed the current illness from its onset.

1.3.2 Demographics of Patient

This should cover the patient's name, sex, age, residential address, religion, and NHIS enrolment. The importance of patients' demographics is foremost for patient identification. Additionally, the sex & age of a patient may point to certain disease types and rule out others. For example, an infant girl straining at micturition has a form of urethral obstruction, but it cannot be a posterior urethral valve since PUV occurs exclusively in males. Similarly, bronchiolitis is not a usual consideration for a 5-year-old with cough, breathlessness, and wheeze since bronchiolitis occurs almost always in children under 2 years old. The residential address

can help identify the diseases to which the patient is at risk. For example, a patient may be residing in an area where certain diseases are endemic. For patients coming from a slum, the insanitary conditions and congestion predispose them to diarrhoeal and skin diseases.

Note: A family's religion may warn about potential conflicts with certain treatments, such as blood transfusions. Having an active insurance plan ensures the affordability of care to some extent.

1.3.3 Presenting Complaint (PC) or Chief Complaint

This elicits the symptoms the patient is presenting with, together with their duration, in a chronological manner. The importance of the presenting complaint lies in its ability to open up the whole history to the system(s) involved in the disease process and the potential disease under discussion. It serves as the gateway to the disease process under review, as every disease manifests in its unique way. Identifying the system(s) involved allows asking further questions about that system in direct questioning (ODQ).

1.3.4 History of Presenting Complaint(HPC)

This provides detailed accounts of each symptom reported in the PC, presented in chronological order. It also gives details of the characteristics of the symptoms, relieving and aggravating factors, as well as treatments that have been sought so far. The importance of the HPC is to obtain a complete picture of each symptom. The characteristics of the symptoms may provide clues to the disease under review.

1.3.5 On Direct Questioning (ODQ)

This is a focused questioning technique that asks for further symptoms from the system(s) implicated by the presenting complaint, to narrow down to the likely diagnosis. Where no particular system is identified, direct questioning is conducted to identify the likely system of infection or inflammation. For example, if fever is the only symptom presented in the presenting complaint (PC), direct questioning is conducted to identify the likely system of infection or inflammation. For instance, symptoms suggestive of infection in the respiratory, gastrointestinal (GIT), musculoskeletal, central nervous system (CNS), genitourinary, ear, nose, and throat (ENT), etc., should be asked to narrow down to the likely disease. If any positive symptom is elicited in the ODQ, its duration and characteristics should be stated as well.

1.3.6 Systemic Enquiry (Review of Systems)

This section examines the "unaffected systems" to determine if they are involved (through concurrent diseases or as a result of complications from the primary disease). Here, key diagnostic symptoms are asked in each of the systems (GIT, cardiovascular, respiratory, CNS, musculoskeletal, genitourinary, integumentary, endocrine). Review of Systems also allows obtaining all the symptoms the patient has (e.g., in case we did not take note of some symptoms the informant mentioned in the PC, or the informant stopped short of all the symptoms the patient had)

1.3.7 Past Medical History

This section assesses four (4) things:

- Any medical condition the patient is known to have, current or previous, e.g., sickle cell disease, Asthma, Epilepsy, Tuberculosis, hypertension, diabetes, etc.
- Previous hospital admissions, and if so, when and for what condition?
- Previous blood transfusion
- If the condition s/he is currently presenting with has occurred in the past. This is important as the recurrence of a symptom may give a clue to diagnosis. For example, recurrence of bodily swelling may point to relapsing nephrotic syndrome, and recurrence of afebrile seizure may point to epilepsy.

1.3.8 Drug History

This section assesses four (4) things:

1. Medications taken so far for this current illness (usually captured in the HPC)
2. Whether a patient is on long-term medications. This may give a clue to an underlying medical condition, even if the informant failed to mention the condition in the past medical history
3. Any known drug & food allergies. If a patient has known allergies and a doctor fails to extract that information and goes ahead to give that forbidden medication, the practitioner may be liable for disciplinary actions and even prosecution should the patient suffer grave effects of the allergy.
4. Any herbal medications, habitually or acutely, for this illness. The importance is that the herbs may be responsible for the illness under review, since the potential toxic effects of most herbs have not been elucidated and documented, unlike orthodox medicine, whose side effects could easily be elucidated

1.3.9 Pregnancy, Birth & Neonatal History

This section assesses the patient's history during their conception, delivery, and neonatal life. It is not the pregnancy that the mother may be carrying at the time of clerking the sick child. The importance lies in the fact that any disease a mother suffered during pregnancy could affect the offspring of that pregnancy. The same applies to the consequences of labor and delivery, as well as the neonatal life of that child. The following information should be sought for in the pregnancy, labour, and neonatal life:

1.3.9.1 Pregnancy

When booking for antenatal care (ANC) was done, any significant diseases encountered by the mother during that pregnancy (e.g., diabetes, hypertension, rash, febrile illness, jaundice, admissions, and if so, for what condition) should be noted. Febrile illness, rash, and jaundice could all point to a possible TORCH infection in the mother. Whether the pregnancy was carried to term or not should be inquired about.

1.3.9.2 Birth

The gestation of that pregnancy (term or not), the mode of delivery of that child (spontaneous vaginal, induced labor, C/S, etc.), the baby's condition at delivery, whether the baby cried at birth, whether the baby needed resuscitation, and how soon after birth the baby was discharged could all indicate how well or otherwise the baby was at birth. The birth weight should also be asked for.

1.3.9.3 The Neonatal Life

Any neonatal illnesses. In particular, jaundice, febrile illness, or admissions would be important to ask.

1.3.10 Immunization

Immunization is an important tool in preventing infectious diseases in children. A child who is not immunized is at significant risk of acquiring a severe form of infectious disease and of dying within the first few years of life. It is essential to determine whether the child's immunization is up to date or completed, based on the child's age and the national immunization schedule. This information should be cross-checked with the immunization card, if available. The presence of a BCG scar should be checked to ensure that at least some vaccinations have been initiated. Also, a BCG scar failure in those immunized may lead to failure of BCG immunization in a tiny minority. If some immunizations are detected to have been missed, the reasons for the missed

immunizations should be investigated, and if it is still within the appropriate vaccination age, the child should be administered those immunizations.

1.3.11 Dietary History

Since children are growing species that require nutrients for both growth and development, a comprehensive dietary history is a key component of the pediatric history. Information to be sought under this section includes: the breastfeeding history (in all cases) and a typical 24-hour dietary history, with an emphasis on complete meals rather than just the main food type, e.g., rice with tomato stew and fish for lunch, rather than just "rice". The meal should be assessed for both quality (balanced meal) and quantity. For toddlers, types of complementary foods and frequency of feeds, including night feeds, should be sought. Fruits and Snack intake (meals taken in between main meals) should all be assessed. Whether a child was fed breastmilk exclusively or was exposed to cow's milk early in life has implications for diseases in later childhood, e.g., allergic conditions, metabolic conditions, etc, hence the importance of breastfeeding history in all cases.

1.3.12 Developmental History

At any point in a child's life, their level of development must be assessed to determine whether they are progressing at an appropriate rate for their age.

Four areas of development should be assessed, namely:

1. Gross motor development, e.g., sitting, standing, walking
2. Fine motor development (use of hands in coordination with vision)
3. Hearing & Speech development
4. Social development (interactions with parents & others + bladder and bowel control/continence)

Where a developmental abnormality is detected, it is essential to review the pregnancy, birth, neonatal history, as well as nutritional and past medical history, to identify potential insults to the brain that may have occurred during this period.

1.3.13 Family History

The family history assesses for any diseases in the family that could potentially have been transmitted to the patient, either through heredity or environmental factors (common risk factors). In particular, diseases such as sickle cell disease, asthma, epilepsy, tuberculosis, HIV, hypertension, and diabetes in a parent or sibling are important to inquire about. Acute illnesses, such as a runny nose, diarrhea, and febrile convulsions (if a child has a history of

these), would also be important to note from the family. The family tree may be assessed in the family history or under the social history, as given below.

1.3.14 Social History

The family's social status is a significant predictor of risk factors for the child's disease, as well as the family's ability to manage the prescribed treatment effectively.

Information sought for under the social history covers the following six (6) areas:

1. **Parents**: their ages, level of education, and occupation. Whether they are in a stable marriage or not. If a parent has passed, the circumstances of their passing and the likely cause should be sought.
2. **Siblings**: Number, ages, and sexes, as well as their current school status. If a sibling has passed away, the circumstances of their passing should be noted.
3. **Residential facility**: The number of sleeping rooms, the number of people who sleep with the patient, the ventilation of the room (including windows), and the use of mosquito nets.
4. **Water & Sewage**: Source of drinking water, toilet facilities, and means of waste disposal
5. **Financial support** for the child's upkeep
6. **Social habits of parents** like smoking & drinking (Home environmental risk factors for diseases, e.g., a child heavily exposed to smoking will be at risk of respiratory diseases like asthma and pneumonia)

1.3.15 Summary of History

The summary uses not only the symptoms elicited but also any other relevant information obtained from any segment of the history that is worthy of note. Typically, it mentions the patient's name, age, presenting complaint, and all other essential information in a sentence or two.

1.4 Physical Examination

This follows after obtaining the comprehensive history. Always begins the physical examination with **Anthropometry**:

1. Weight, weight-for-age SD score, its interpretation (normal, abnormal, etc)
2. Height, height-for-age SD score, its interpretation (normal, abnormal, etc)
3. Weight-for-height SD score (for children up to 5 years), its interpretation (normal, abnormal, etc)

4. BMI (for children > 5 years), BMI-for-age centile, its interpretation (normal, abnormal, etc)
5. Mid-Upper-Arm-Circumference (MUAC, for 6 months to 5 years), its interpretation
6. Head circumference percentile (for children up to 5 years) and what it means

Of note, WHO simplifies the definitions of anthropometry as follows:

Findings outside the borders of -2SD and +2SD are abnormal, and values -2SD to +2SD are normal. If the values are outside -3SD and +3SD, then they are severely abnormal, e.g., moderate underweight if WFA is < -2SD, severe underweight if WFA <-3SD, overweight if WFA >+2SD, and obese if WFA >+3SD.

Vital Signs: Temperature, Pulse rate, volume & rhythm, Respiratory rate, Oxygen saturation (SPO2), Blood Pressure

1.4.1 General Examination

This assessment evaluates the general state of the patient, including their appearance, distress level, position in bed, nutritional status, state of consciousness, and other relevant factors. It then assesses for pallor, jaundice, lymph node enlargement, pedal edema, hydration status, warmth in the hands, capillary refill, clubbing, or any other stigmata of disease. Additionally, it examines the skin for rashes, pigmentation, and any eruptions.

1.4.2 System-by-System Examination

This should cover at least the four major systems: Cardiovascular, Respiratory, Gastrointestinal/Abdomen, and the central nervous system. Note that all four systems must be examined for every case clerked, regardless of the system affected by the disease. Other systems to note include the musculoskeletal, genitourinary, integumentary (comprising skin and mucous membranes), and endocrine systems.

1.4.2.1 Respiratory System Examination

Inspection: Always begin by assessing the respiratory rate and respiratory effort (quiet or distressful). Then check for cyanosis and the shape of the chest.

Palpation: Palpate the chest wall for tenderness, centrality of the trachea, and lymph nodes (if not already assessed during the general examination). Additionally, assess chest expansion (for older children only) and tactile fremitus (for older children only).

Percussion: The percussion fingers should always be placed horizontally along the intercostal spaces and NEVER across the ribs or scapulae. All chest zones, anteriorly, posteriorly, and

laterally, should be percussed. It is more convenient to finish the anterior and lateral chest examination before moving to the back.

Auscultation: The assessment should report on the volume of air (adequacy of air entering lungs), nature of breath sounds, any additional sounds, and vocal fremitus

1.4.3 Cardiovascular System Examination

A convenient style of cardiovascular examination is to move from the **hands** (for warmth, CRT, clubbing, and cyanosis), wrist (for pulse), arm (for blood pressure), neck (for distended veins), and then settle on the heart or coronary arteries. However, the patient's general position in bed (propped up or not), use of supplementary oxygen, respiratory effort, and mouth for central cyanosis should all be noted, if not already captured during the general examination.

1.4.4 The COR/Heart

Inspection: Inspect for any bulge, precordial pulsations

Palpation: Palpate for the Apex beat, heaves, and thrills

Auscultation: Auscultate over all four areas for quality of the heart sounds 1 & 2, rhythm of the heartbeat, murmurs, and any added sounds. If a murmur is detected, its characteristics must be reported, and the point of maximal sound (which may indicate the valve affected or position of a shunt lesion) as well as its radiation.

Typically, there is no **percussion** in COR examination!

1.4.5 Gastrointestinal System Examination

A typical GIT examination is from mouth to anus, covering the abdomen (liver and intestines).

However, GIT examination may be limited to the Abdomen.

1.4.6 Abdominal Examination

Inspection: Exposure - The abdomen should be reasonably exposed from the nipple level down to both inguinal creases. The genitals must be covered for privacy, but must be inspected. The size of the abdomen (using the chest wall as a reference, both anteroposteriorly and laterolaterally), position of the umbilicus, movement with respiration, presence or absence of distended veins or scars, and the presence of hernia orifices should be commented on. If the patient is edematous, check for edema of the genitals.

Palpation: Perform light palpation to assess tenderness in all nine regions. If masses are detected during this examination, they should be reported. Deep palpation for the Liver, Spleen, kidneys, and any other masses felt during light palpation

Percussion: Percuss for fluid (use shifting dullness if the fluid is judged to be mild to moderate, and use fluid thrill if the fluid is judged to be severe). Always percuss at the level of the umbilicus with the fingers spread out.

If percussion note is tympanitic across the hemi-abdomen to the flank, there is no fluid. If it is dull all through, then the abdomen may be full of fluid, in which case, fluid thrill will be preferred to use. If there is perceived dullness at the flank but the dull note does not change to tympanitic at the shift of the patient to the opposite site, then there is no fluid in the abdomen.

Auscultation: Auscultate for bowel sounds by using the diaphragm of the stethoscope around the umbilicus. Report on the presence or absence of bowel sounds and their pitch. Bowel sound auscultation is typically performed over 2 minutes. If no bowel sounds are heard over this period, the bowel sounds are presumed to be absent. In some cases, bruit can also be auscultated.

1.4.7 Central Nervous System Physical Examination

Here, five (5) areas should be examined and reported on, namely:

1. **The level of Consciousness:** The Blantyre coma scale may be used (for children under 5 years) or the modified Glasgow coma scale.
2. **Signs of meningeal irritation**: Check for Neck stiffness, Kernig's sign, and Brudzinski's sign. Bulging fontanel may be elicited in babies, but this is often a late sign. Fever with irritability is a specific indicator of meningitis in this special group.
3. **Cranial nerves examination:** Examination of the cranial nerves should be performed
4. **Motor system:** Assess for the Tone, Power & Reflexes [TPR])
5. **Sensory system:** Assess fine and deep touch, coordination, gait, and joint position sense

1.5 Provisional Diagnosis & Differential Diagnosis

Information from history and examination is synthesized to arrive at a likely diagnosis [provisionally] + all other potential diagnoses. Notably, if there are two or more separate diagnoses, such as malaria, pneumonia, and otitis, these remain separate diagnoses and not differential diagnoses of one another. Differential diagnoses are usually (but not always) exclusive of one another; for example, is it pneumonia or heart failure?

1.6 Investigations

Main and supportive

Always start with the main investigations that will lead to the confirmation of the diagnosis before coming to the supportive (ancillary) tests. For example, a Chest X-ray is diagnostic for pneumonia, while a full blood count looking for neutrophil leukocytosis is supportive.

1.7 Definitive Diagnosis

Based on the results of investigations, a definitive diagnosis is then made.

1.8 Treatment Plan

Based on the suspected or definitive diagnosis, a treatment plan is formulated:

Main treatment: The specific treatment recommended for the particular disease. For example, antibiotics for infectious diseases

Supportive treatment: Those treatments that relieve symptoms. For example, analgesics for pain, antipyretics for fever

Note on **Empiric Treatment:** At the point of provisional diagnosis, while awaiting confirmation of the disease through appropriate diagnostic investigations, treatment is usually initiated based on the most likely anticipated diagnosis. Such treatment intervention is called empiric treatment. For infectious diseases in which cultures have been taken and the results are waiting, the likely isolate with known antibiotic susceptibility is usually initiated, which will be reviewed either for continuation or discontinuation based on the culture and sensitivity results obtained.

Emergency management:

Where a case is life-threatening and requires emergency intervention, it may not be necessary to wait and go through the details of clerking outlined above. In such emergency cases, a brief history may be taken, and depending on the life-threatening issues identified, emergency interventions may be instituted to stabilize the patient before proceeding with a full clinical review.

USEFUL BOOKS

Clinical Methods by Hutchison and Macleod

2 Growth and Development

2.1 Introduction

Growth and development are fundamental indicators of a child's overall health and well-being. As medical students in Ghana, it is crucial to comprehend the physiological processes of growth and development, their milestones, and how socio-economic and environmental factors specific to Ghana impact these processes.

Growth refers to an increase in physical size (height, weight, head circumference). In contrast, **development** refers to the acquisition of skills and functions such as motor abilities, language, cognition, and social behaviour. Both occur simultaneously and are influenced by genetic, nutritional, hormonal, environmental, and psychosocial factors.

2.2 Principles of Growth and Development

1. **Cephalocaudal progression**: Development proceeds from head to toe. For example, infants gain head control before they can sit or walk.
2. **Proximodistal progression**: Development proceeds from the center of the body outwards. Gross motor skills develop before fine motor skills.
3. **Sequential and Predictable**: Milestones follow a predictable pattern, although the pace may vary.
4. **Critical periods**: There are periods when the child is especially sensitive to environmental stimuli.
5. **Individual variability**: Normal children may achieve milestones at slightly different ages.

2.3 Stages of Growth and Development

1. Neonatal Period (Birth – 28 Days)

Growth:

- **Weight**: Average birth weight is 2.5–4.0 kg. Infants may lose up to 10% of their birth weight in the first week but regain it by day 10.

- **Length**: ~50 cm at birth.
- **Head circumference**: ~35 cm at birth.

Development:

- Primitive reflexes: Rooting, sucking, Moro, palmar grasp, stepping reflex.
- Sensory abilities: Can see up to 20–30 cm, prefer human faces, respond to loud sounds.
- Motor: Moves all limbs symmetrically, exhibits flexed posture.

2. Infancy (1 month – 1 year)

Growth:

- Weight doubles by 5–6 months and triples by 1 year.
- Length increases by 50% in the first year.
- Head circumference increases ~1 cm/month in the first 6 months.

Development:

- **Gross motor**:
  - 3 months: Head control.
  - 6 months: Rolls over.
  - 9 months: Sits without support, crawls.
  - 12 months: Stands, may begin walking
- **Fine motor**
  - 4–6 months: Reaches for objects.
  - 9 months: Pincer grasp begins
  - 12 months: Transfers objects between hands, bangs objects together.
- **Language**:
  - 2 months: Coos.
  - 6 months: Babbles.
  - 9–12 months: Says "mama," "dada" (non-specific), understands "no."
- **Social**:
  - 2 months: Social smile.
  - 6 months: Stranger anxiety.
  - 12 months: Waves "bye-bye," enjoys peek-a-boo.

3. Toddler (1 – 3 years)

Growth:

- Gains 2–3 kg per year.
- Height increases by ~12 cm per year.
- Head growth slows; the anterior fontanelle closes by 18 months.

Development:

- **Gross motor**:
  - 15 months: Walks independently.
  - 18 months: Climbs stairs with help.
  - 2 years: Runs, kicks a ball.
  - 3 years: Rides tricycle, climbs stairs alternating feet.
- **Fine motor**:
  - Builds tower of 3 (18 months) to 9 (3 years) cubes.
  - Can feed themselves with a spoon.
  - Begins to draw lines and circles.
- **Language**:
  - 18 months: 10–20 words.
  - 2 years: 2-word phrases, ~50 words.
  - 3 years: Sentences of 3–4 words.
- **Social**:
  - Parallel play.
  - Temper tantrums, strong desire for independence.
  - Recognizes self in mirror.

4. Preschool (3 – 5 years)

Growth:

- Gains 2 kg/year.
- Height increases ~6–8 cm/year.

Development:

- **Gross motor**: Hops on one foot, skips, throws, and catches a ball.
- **Fine motor**: Copies shapes, uses scissors, dresses self with help.
- **Language**: Clear speech, tells stories, knows names, age, and gender.
- **Cognitive**: Magical thinking, learns numbers, colours.
- **Social**: Cooperative play starts forming friendships.

5. School-Age (6 – 12 years)

Growth:

- Steady growth of ~5–7 cm/year and 2–3 kg/year.
- Permanent teeth begin to erupt around age 6.

Development:

- **Gross motor**: Coordination improves, participates in sports.
- **Fine motor**: Writes well, does crafts, and is independent in dressing and eating.
- **Cognitive**: Concrete operational stage (Piaget) – can think logically about tangible objects.
- **Social**: Peer relationships become central; starts forming moral values.
- **Emotional**: Develops self-esteem; compares self to others.

6. Adolescence (13 – 18 years)

Divided into early (10–13), middle (14–16), and late (17–19) adolescence.

Growth:

- **Pubertal growth spurt**:
  - Girls: Peak at 11–12 years.
  - Boys: Peak at 13–14 years.
- Growth completes by 18–20 years.
- Sexual maturation: Tanner staging is used to assess the progression of puberty.

Tanner Staging Overview:

- **Stage 1**: Prepubertal.
- **Stage 2**: Breast bud (girls); testicular enlargement (boys).
- **Stage 3–5**: Progressive pubic hair growth, breast and genital development.

Development:

- **Cognitive**: Formal operational stage – abstract thinking.
- **Psychosocial** (Erikson): Identity vs. Role Confusion.
- **Emotional**: Self-awareness, mood swings, peer pressure.
- **Social**: Increased independence, interest in opposite sex, development of personal values.

2.4 Factors Influencing Growth and Development in Ghana

1. Nutrition

- Malnutrition remains a significant cause of stunting and wasting in Ghana.
- Exclusive breastfeeding for 6 months followed by appropriate complementary feeding is critical.
- Micronutrient deficiencies (iron, vitamin A, iodine) are common.

2. Health and Disease

- Frequent infections (malaria, diarrheal disease, respiratory infections) affect growth.
- Helminthic infestations (e.g., *Ascaris*, *hookworm*) can cause anemia and malabsorption.
- HIV and chronic illnesses impact weight gain and development.

3. Immunization

- Vaccines under Ghana's EPI (Expanded Programme on Immunization) protect against major childhood illnesses.
- Delays in vaccination can predispose children to infections that impair growth.

4. Socioeconomic Status

- Poverty, poor housing, and low parental education levels contribute to undernutrition and developmental delays.
- Urban-rural disparities exist, with rural children at higher risk of poor outcomes.

5. Environmental Factors

- Poor sanitation increases the risk of repeated infections.
- Environmental toxins (e.g., lead exposure in certain mining communities) can cause neurodevelopmental issues.

6. Parental Care and Stimulation

- Emotional support, play, and verbal interaction are key for early brain development.
- Neglect, abuse, and trauma can lead to delayed speech and cognitive skills

2.5 Clinical Assessment of Growth and Development

Anthropometric Measurements

- **Weight**: Measured at every visit. Weight-for-age is a good screening tool.
- **Height/Length**: Height-for-age assesses linear growth; used to detect stunting.
- **Head circumference**: Measured in children under 2 years; useful in assessing brain growth.
- **Mid-upper arm circumference (MUAC)**: Used in children aged 6–59 months to screen for acute malnutrition.

Growth Charts

- WHO growth standards are used in Ghana.
- Plotted regularly to monitor trends over time.
- Red flags: crossing percentiles downward, weight loss, or faltering height.

2.6 Red Flags in Growth and Development

Medical students should be alert to signs that may indicate problems:

- No head control by 4 months.
- No sitting by 9 months of age.
- No walking by 18 months.
- No single words by 15 months.
- Regression of previously attained milestones.
- Persistent failure to thrive despite nutritional intervention.
- Rapid head growth or microcephaly.
- Poor school performance in school-aged children.

2.7 Role of the Health Worker

In Ghana, health workers play a vital role in promoting optimal growth and development:

1. **Growth monitoring and promotion**: Routine weighing and charting in Child Welfare Clinics (CWC).
2. **Nutrition counseling**: Promote exclusive breastfeeding, weaning practices, and dietary diversity.
3. **Immunization**: Ensuring timely vaccination.
4. **Early identification and referral**: Recognizing signs of developmental delay and making timely referrals.

5. **Parental education**: Encouraging stimulation, responsive parenting, and early learning.
6. **School health services**: Routine screening in schools for hearing, vision, and dental problems.

2.8 Conclusion

Understanding child growth and development is critical in paediatrics and preventive health care. In Ghana, many preventable factors influence a child's trajectory. As future medical practitioners, students must recognize normal patterns, use appropriate tools for assessment, and intervene early where deviations exist. Knowledge of cultural, nutritional, and environmental influences is essential for context-specific care. By prioritizing growth and development, we lay the foundation for healthier futures in Ghana's children.

3 Pediatric Anthropometry

3.1 Introduction

Pediatric anthropometry is the scientific measurement of the physical dimensions and composition of the human body in children. It is a fundamental component of growth monitoring and nutritional assessment, playing a crucial role in evaluating child health. For medical students and healthcare providers in Ghana, mastering anthropometry is essential for identifying malnutrition, developmental issues, and chronic diseases in children. This clinical note will cover the principles, techniques, indicators, interpretation, and clinical application of pediatric anthropometry, with special attention to the Ghanaian context.

3.2 Objectives of Paediatric Anthropometry

1. Assess growth and nutritional status
2. Monitor development over time
3. Detect early signs of undernutrition or overnutrition
4. Evaluate the impact of health and nutrition interventions
5. Assist in diagnosing systemic illnesses
6. Provide evidence for public health surveillance and policy making

3.3 Key Anthropometric Measurements in Children

1. Weight

- **Importance**: Reflects body mass and is sensitive to acute changes in health and nutrition.
- **Equipment**:
  - Infants: Electronic infant scale or beam balance (accurate to ±10g).
  - Older children: Digital or beam scale (accurate to ±100g).
- **Procedure**:
  - Remove clothing and shoes.

  - For infants, weigh naked or with minimal clothing.
  - Ensure the scale is calibrated and on a flat surface.

- **Interpretation**:
  - Compare with WHO growth standards using Weight-for-Age (WFA), Weight-for-Height (WFH), and Body Mass Index (BMI).

2. Length/Height

- **Length (children <2 years)**:
  - Measured using an infantometer.
  - Child lies supine with head held against the fixed headboard and legs fully extended.
- **Height (children 2 years)**:
  - Use a stadiometer or wall-mounted measuring board.
  - The child stands erect without shoes, heels together, and looks straight ahead
- **Accuracy**: ±0.1 cm
- **Interpretation**:
  - Compare with Height-for-Age (HFA) standard.
  - Used to detect stunting (chronic malnutrition)

3. Mid-Upper Arm Circumference (MUAC)

- **Importance**: A rapid screening tool for acute malnutrition in children aged 6–59 months.
- **Equipment**: MUAC tape (color-coded for easy interpretation).
- **Procedure**:
  - Locate the midpoint between the acromion and the olecranon process.
  - Measure the circumference of the left upper arm
- **Interpretation**:
  - MUAC <11.5 cm: Severe Acute Malnutrition (SAM).
  - 11.5–12.5 cm: Moderate Acute Malnutrition (MAM).
  - 12.5 cm: Normal

4. Head Circumference

- **Importance**: Reflects brain growth, especially in the first two years.
- **Equipment**: Non-stretchable measuring tape.

- **Procedure**:
  - Place the tape above the eyebrows and ears, and around the occipital prominence.
- **Interpretation**:
  - Compare with age- and sex-specific World Health Organization (WHO) standards.
  - Used to identify microcephaly or macrocephaly.

5. Chest Circumference

- **Less frequently used**.
- Normally, head circumference exceeds chest circumference at birth; both become equal by 1 year.
- May help in nutritional assessments.

6. Body Mass Index (BMI)

- **Formula**: BMI = Weight (kg) / Height^2 (m^2).
- **Use**: Detects overweight and obesity.
- **Interpretation (children 5 years)**:
  - <5th percentile: Underweight.
  - 5th–85th percentile: Normal.
  - 85th–95th percentile: Overweight.
  - 95th percentile: Obese.

3.4 Anthropometric Indices and Indicators

These indices compare the child's measurement with reference values to classify nutritional status.

1. Weight-for-Age (WFA)

- Detects underweight.
- Sensitive to both acute and chronic malnutrition.
- Limitation: Does not distinguish between stunting and wasting

2. Height-for-Age (HFA)

- Reflects linear growth.
- Low HFA = **Stunting** (chronic malnutrition).
- Not useful for detecting acute malnutrition.

3. Weight-for-Height (WFH)

- Identifies **wasting** (acute malnutrition).
- Independent of age.
- Used in emergencies and hospital settings.

4. BMI-for-Age

- Preferred index for children over 5 years.
- Classifies thinness, normal weight, overweight, and obesity.

5. Head Circumference-for-Age

- Used in infants to assess brain development and detect congenital anomalies or infections (e.g., hydrocephalus, microcephaly).

3.5 WHO Growth Standards

- WHO standards are based on healthy children from multiple countries, including Ghana.
- Charts available for boys and girls separately.
- Include percentiles and **Z-scores** (standard deviations from the median).

Z-Score Interpretation:

Z-score	**Classification**
–1 SD to +1 SD	Normal growth
< –2 SD	Moderate malnutrition
< –3 SD	Severe malnutrition
> +2 SD	Overweight
> +3 SD	Obese

Z-scores are preferred over percentiles for clinical and public health use because they are more statistically robust.

3.6 Anthropometry in Ghana: Local Context

Nutritional Issues in Ghana

- **Undernutrition**: Common in Northern and some rural regions due to food insecurity.
- **Stunting**: Affects ~19% of children under 5 (per recent DHS data).
- **Wasting**: Acute malnutrition is less common but serious in emergencies.
- **Overweight/Obesity**: Emerging problem in urban areas

Common Causes:

- Poverty, food insecurity, and poor weaning practices.
- Frequent infections (e.g., malaria, diarrhea).
- Inadequate maternal education.
- Cultural beliefs affecting feeding.

Public Health Programs:

- Child Welfare Clinics (CWC): Regular growth monitoring, including weight and MUAC measurements.
- Community-Based Management of Acute Malnutrition (CMAM).
- School feeding programs.
- Health education on infant and young child feeding (IYCF).

3.7 Clinical Applications

3.7.1 Case Scenarios:

Case 1: Underweight Child

- **Age**: 18 months
- **Weight**: 6.5 kg
- **WFA Z-score**: –3.2
- **MUAC**: 11.2 cm
- **Diagnosis**: Severe underweight and severe acute malnutrition.
- **Action**: Admit to NRU (Nutritional Rehabilitation Unit); initiate therapeutic feeding

Case 2: Overweight Child

- **Age**: 10 years
- **Weight**: 40 kg
- **Height**: 1.35 m
- **BMI**: 21.9 $\rightarrow$ >95th percentile
- **Diagnosis**: Childhood obesity
- **Action**: Diet and lifestyle counseling; screen for comorbidities like hypertension, type 2 diabetes.

3.8 Challenges in Anthropometric Assessment in Ghana

- **Equipment shortages**: In rural clinics, proper weighing scales or stadiometers may be lacking.
- **Lack of training**: Some healthcare workers and students may not receive adequate training in accurate measurement techniques.
- **Poor record-keeping**: Growth monitoring charts are often incomplete or misinterpreted.
- **Cultural barriers**: Some communities resist exposing children for weighing or measurement.
- **Inconsistent standards**: Some facilities still use outdated or non-standard growth charts.

3.9 Tips for Medical Students

1. **Practice correct technique**: Learn hands-on from skilled clinicians.
2. **Use WHO charts**: Understand how to plot and interpret Z-scores.
3. **Observe growth trends**: One-time measurements are less informative than trends over time.
4. **Correlate with clinical findings**: Anthropometry should complement physical exam and dietary history.
5. **Educate caregivers**: Explain growth status in simple language; encourage regular CWC visits.

Summary Table of Key Measures

Measurement	Age Group	Tool	Indicator	Interpretation
Weight	All	Infant/Beam Scale	WFA, WFH, BMI	Underweight, wasting, obesity
Length	<2 yrs	Infantometer	HFA	Stunting
Height	2 yrs	Stadiometer	HFA, BMI	Stunting, overweight
MUAC	6–59 months	MUAC tape	Acute malnutrition	SAM, MAM
Head Circumference	0–2 yrs	Measuring tape	HC-for-age	Micro/macrocephaly

3.10 Conclusion

Pediatric anthropometry is an indispensable clinical tool for assessing child health and nutrition. In the Ghanaian context, it is vital for early detection of malnutrition and guiding appropriate interventions. As a medical student, mastering these measurements, understanding their interpretation, and applying them in both clinical and public health settings are crucial skills. Consistent, accurate anthropometric assessment can drastically improve child survival and long-term developmental outcomes in Ghana.

Part II

Neonatology

4 Neonatal History & Examination

4.1 Introduction

The newborn period, defined as the first 28 days of life, is a critical phase in human development. It represents a time of rapid physiological adaptation from intrauterine to extrauterine life, with major changes occurring in respiration, circulation, nutrition, and thermoregulation. During this period, morbidity and mortality are highest compared to any other stage of childhood, particularly in low- and middle-income countries such as Ghana.

For clinicians, the neonatal history and examination are essential tools in identifying normal adaptation, detecting abnormalities early, and guiding timely interventions. A detailed assessment requires not only the direct clinical examination of the neonate but also a careful review of maternal, antenatal, intrapartum, and immediate postnatal events.

4.2 Importance of Neonatal History and Examination

- Early diagnosis of congenital anomalies – many conditions can be subtle at birth but become evident on detailed examination.
- Assessment of perinatal risk factors – including maternal illnesses, infections, complications of labour, and prematurity.
- Establishing baseline health status – for growth monitoring and subsequent follow-up.
- Building rapport with the mother and family – ensuring continuity of care.
- Guiding preventive strategies – such as immunisation, exclusive breastfeeding, and infection control.

4.3 Components of Neonatal History

The neonatal history is unique in that it depends heavily on information from the mother and available records, since the newborn cannot communicate symptoms. The history should be systematic and include the following areas:

4.3.1 Maternal History

Demographic and Social Factors

1. Maternal age: Teenage and advanced maternal age pregnancies carry an increased risk.
2. Parity and gravidity: Provide context about reproductive history.
3. Socioeconomic status: influences access to care and nutrition.
4. Occupational exposures: Such as chemicals or radiation.

Maternal Medical History

1. Chronic illnesses: Diabetes, hypertension, renal disease, HIV, tuberculosis, and epilepsy.
2. Medications during pregnancy: Some drugs (e.g., anticonvulsants, ACE inhibitors) are teratogenic.
3. Substance use: Alcohol, tobacco, herbal medications, or recreational drugs.
4. Family history: Genetic disorders, congenital anomalies, consanguinity.

4.3.2 Antenatal History

Antenatal Care

1. Number and timing of visits.
2. Use of supplements (iron, folic acid, tetanus immunisation).

Maternal Illnesses in Pregnancy

1. Infections: TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes, syphilis), malaria, urinary tract infections.
2. Gestational diabetes and pre-eclampsia.
3. Antepartum haemorrhage or polyhydramnios/oligohydramnios.

Fetal Wellbeing

1. Results of ultrasound scans (growth, anomalies, multiple gestation, amniotic fluid volume).
2. Reduced fetal movements.

4.3.3 Intrapartum History

Labour and Delivery

1. Place of delivery (home, health centre, hospital).
2. Duration and course of labour.
3. Prolonged rupture of membranes (risk of infection).
4. Use of intrapartum medications or anaesthesia.
5. Mode of delivery: spontaneous vaginal delivery, assisted delivery, or caesarean section.

Condition of Baby at Birth

1. Apgar scores at 1 and 5 minutes.
2. Need for resuscitation.
3. Cord events (e.g., prolapse, nuchal cord).
4. Meconium-stained amniotic fluid (risk of aspiration).

4.3.4 Immediate Postnatal History

- Cry at birth (immediate and vigorous or delayed).
- Initiation of breastfeeding and feeding adequacy.
- Passage of urine and meconium.
- Neonatal resuscitation or admission to neonatal intensive care unit (NICU).
- Administration of vitamin K, eye prophylaxis, and immunisations (BCG, OPV, Hepatitis B).

4.4 Components of Neonatal Examination

A thorough neonatal examination should ideally be conducted within the first 24 hours and repeated before discharge. It involves general observation, measurement of growth parameters, a head-to-toe physical examination, and a functional systems review.

4.4.1 General Considerations

- Conduct in a warm, well-lit environment to avoid hypothermia.
- Wash hands thoroughly and maintain asepsis.
- Involve the mother to reduce stress and promote bonding.
- Examine systematically from head to toe.

4.4.2 General Observation

- Appearance: alert, active, lethargic, floppy.
- Colour: pink, pale, jaundiced, cyanosed.
- Cry: strong and lusty vs weak or absent.
- Breathing pattern: regular or irregular, presence of grunting, nasal flaring, or retractions.
- Movements: spontaneous, symmetrical, abnormal posturing.

4.4.3 Anthropometric Measurements

- Weight: normal term 2.5–4.0 kg.
- Length: 48–52 cm.
- Head circumference: 33–35 cm.
- Chest circumference: slightly less than head circumference. These values are plotted on neonatal growth charts.

4.4.4 Skin and Subcutaneous Tissue

- Look for vernix caseosa, lanugo hair, birthmarks (Mongolian spots, café-au-lait spots), and congenital anomalies.
- Assess for jaundice, petechiae, cyanosis, or dehydration.
- Palpate for oedema (suggests renal or cardiac disease).

4.4.5 Head and Face

- Shape and size: microcephaly, macrocephaly, cranial swellings (caput succedaneum, cephalohaematoma).
- Fontanelles and sutures: size, tension (bulging may indicate raised intracranial pressure).
- Eyes: red reflex (absent in congenital cataract or retinoblastoma), discharge, conjunctival haemorrhage.
- Ears: position, size, and anomalies (low-set ears suggest chromosomal syndromes).
- Nose: patency (choanal atresia if blocked).
- Mouth: cleft lip/palate, Epstein pearls, ankyloglossia.

4.4.6 Neck

- Masses such as cystic hygroma.
- Neck mobility (torticollis).

4.4.7 Chest

- Inspection: chest shape, symmetry, retractions.
- Auscultation: breath sounds equal? murmurs present?
- Palpation: heart apex position, thrills, or heaves.

4.4.8 Abdomen

- Shape: scaphoid, distended.
- Umbilical cord: number of vessels, infection, hernia.
- Palpation: liver (normally 1–2 cm below costal margin), spleen, kidneys, masses.
- Auscultation: bowel sounds.

4.4.9 Genitalia and Anus

- Male: testicular descent, hypospadias, phimosis.
- Female: labial size, vaginal discharge (may be normal pseudo-menstruation).
- Anus: patency, imperforate anus.

4.4.10 Musculoskeletal System

- Assess posture, limb movements, joint stability.
- Look for polydactyly, syndactyly, clubfoot.
- Check clavicles for fracture.
- Hip stability (Ortolani and Barlow manoeuvres).

4.4.11 Neurological Examination

- Tone: normal flexor tone vs hypotonia or hypertonia.
- Primitive reflexes:
  - Moro reflex
  - Rooting reflex
  - Sucking reflex
  - Palmar grasp
  - Stepping reflex
- Behaviour: alertness, consolability, irritability.

4.5 Special Considerations in Preterm Infants

Preterm babies (<37 weeks) require special attention. History should highlight maternal risk factors for preterm labour, and examination must assess:

- Skin thin and translucent with little subcutaneous fat.
- Lanugo hair more abundant. - Ear cartilage soft, pinna remains folded.
- Breast buds small or absent.
- Genitalia: undescended testes in males, prominent labia minora in females.
- Poor muscle tone and weak reflexes.

4.6 Neonatal Screening and Preventive Measures

In many centres, neonatal assessment is complemented by screening tests:

1. Metabolic screening: for congenital hypothyroidism, phenylketonuria (where available).
2. Hearing screening: Otoacoustic emission tests.
3. Pulse oximetry: to detect critical congenital heart disease.
4. Blood sugar: in infants of diabetic mothers or small/large for gestational age.

4.7 Documentation and Communication

- Findings must be documented systematically in the neonatal record.
- Abnormal findings should be clearly communicated to senior clinicians and to the parents in a sensitive manner.
- Recommendations for follow-up, investigations, or referrals must be made.

4.8 Challenges in Resource-Limited Settings

- Inadequate access to prenatal care records.
- Limited diagnostic facilities for neonatal screening.
- High burden of home deliveries without skilled attendants.
- Cultural practices influencing early care and feeding.

4.9 Conclusion

The neonatal history and examination form the foundation of paediatric practice. They provide critical information about the newborn's adaptation, detect congenital anomalies, and guide early interventions. For medical students and clinicians in Ghana, mastering these skills is essential in reducing neonatal morbidity and mortality. A systematic approach, attention to detail, and sensitivity to family concerns are the cornerstones of effective neonatal assessment.

5 Neonatal Delivery Pathologies

5.1 The health newborn

- Cries / Breathes normally
- Pink all over
- Well-flexed & moves all limbs spontaneously
- Suckles well at the breast
- Birth weight 2.5 – 4.0kg
- Normal vitals signs

5.2 Occurrences at birth

- The fluid in the alveoli is absorbed and replaced by air. If the transition is not smooth, it results in insufficient oxygen delivery to the vital organs…
- Poor muscle tone
- Respiratory distress or depression
- Slow heart rate
- Low BP
- Cyanosis

5.3 Birth Asphyxia

5.3.1 Definition

> **!** World Health Organisation definition
>
> Birth Asphyxia is the medical condition resulting from deprivation of oxygen in the newborn that lasts long enough during the birth process to cause harm, usually to the brain.

5.3.2 Risk factors

Any condition that will lead to impairment of oxygenation or blood flow to the newborn's brain in the perinatal period. These include:

- Prolonged labour (CPD)
- Placental failure
- Cord around the neck
- Problems with oxygenation of maternal blood / maternal disease
- Anaemia and bleeding in the baby
- Congenital heart disease
- Infections
- Deficient medical skills and or knowledge

5.3.3 Presentation

The asphyxiated baby may have any of the following:

- Poor Apgar Scores
- May not cry at birth
- Floppy/spastic
- Breathing problems
- Unresponsive
- Seizures
- Irritable

5.3.4 The APGAR Score

It is an objective method of quantifying the newborn's condition. And is useful for conveying information about the newborn's overall status and response to resuscitation

Table 5.1: The APGAR Score

	0	1	2
Heart Rate	0	<100	>=100
Respiration	0	Weak or Irregular	Good Cry
Reaction	None	Slight	Good
Colour	Blue or Pale	Pink body limbs blue	All pink
Tone	Limp	Some movement	Active movement, limbs well flexed

8-10 = No Asphyxia
5-7 = Mild Asphyxia
3-4 = Moderate Asphyxia
0-2 = Severe Asphyxia

5.3.5 Management

- Largely supportive
- Newborn resuscitation/oxygenation
- Correction of fluid & electrolyte imbalances including shock
- Control of seizures
- Treatment of any underlying infection
- Look out for birth injuries
- Active cooling found to improve neurological outcome
- Temperature maintenance
- Full Blood Count, Culture & Sensitivity, Blood glucose etc
- Serum electrolytes: Na, K, Ca & Mg
- Start empiric 1st line antibiotics according to protocol: / X'pen & Gentamycin
- Start IV Fluids at 50ml/kg (Plain 10% Dextrose).
- Pass a urethral catheter and monitor the baby's urine output.
- The target temperature of the baby is 36.50C – 37.50C

5.3.6 Hypoxemic Ischaemic Encephalopathy

- The most important consequence of birth asphyxia is
- The outcome ranges from complete recovery to death
- 25 - 30% end up with permanent damage like Cerebral palsy & Mental retardation
- Prognosis dependent on gestational age, management of metabolic & cardiopulmonary complications & the severity of the encephalopathy
- Subsequent competent care and available facilities also influence the outcome

5.4 Birth Injuries

A birth injury can simply be referred to as any form of damage incurred by the baby during the birthing process. Injury may occur as a result of inappropriate or deficient medical skill or attention or may occur despite skilled and competent obstetric care.

Predisposing conditions include:

- Cephalopelvic disproportion (CPD) / Small maternal stature / Primiparity

- Macrosomia
- Shoulder Dystocia
- Prematurity
- Prolonged or precipitous labour
- Abnormal presentation
- Instrumentation
- Handling after delivery

5.4.1 Fracture

Generally, the affected limb looks deformed or swollen, and the baby barely moves it on account of pain

5.4.1.1 Clavicle

This is the most fractured bone during delivery; mostly during delivery of the shoulder in vertex and of the extended arms in the breech. Signs of a fracture may include no free arm movement on the affected side, crepitus and bony irregularity, and absent Moro reflex. It has an excellent prognosis, even though it is commonly missed. Treatment, if any, includes immobilization of the arm and shoulder as shown below.

This is the first type of humeral fracture

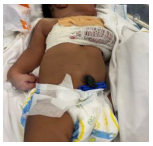

Figure 5.1: Humeral Fracture (immobilised)

5.4.1.2 Humerus

The x-ray below shows another commonly fractured bone, the humerus.

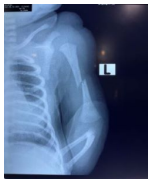

Figure 5.2: X-ray of a humeral fracture

5.4.1.3 Femur

Risk factors: big baby, breech presentation, incompetency. The affected thigh looks deformed, swollen and may be reddened. The main mode of management involves splinting the limb from the waist to below the knee.

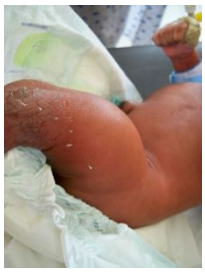

Figure 5.3: Femoral Fracture

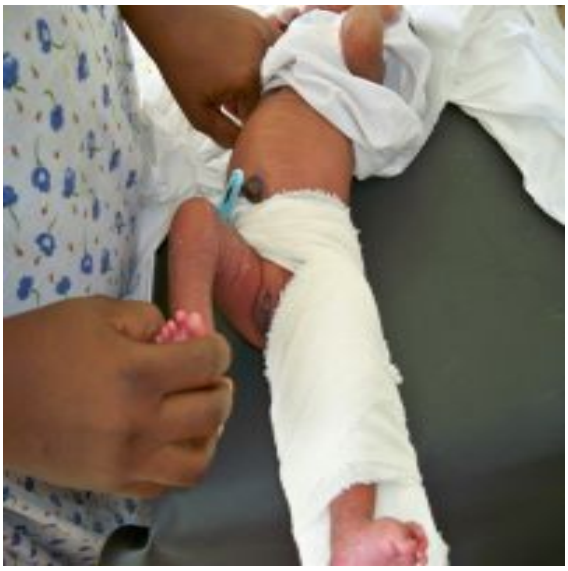

Figure 5.4: Femoral Fracture Splinting

5.5 Nerve injuries

5.5.1 Brachial plexus injuries

The nerves of the brachial plexus may be compressed, stretched or torn in a difficult delivery. Paralysis occurs as a result of nerve compression from either haemorrhage or oedema. Permanent paralysis can occur from the tearing of the nerve or avulsion of the nerve root from the

spinal cord or oedema. Erb's palsy (C5-C6) is the most common type of BPI and is associated with a lack of shoulder motion. The involved extremity lies adducted, prone, and internally rotated. Grasp reflex is usually present and prognosis is generally good. Also described as the Waiter's tip position.

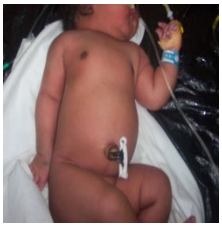

Figure 5.5: Erb's Palsy

5.5.2 Klumpke's paralysis

5.5.3 Facial nerve paralysis

Loss of voluntary muscle movement in the face on account of pressure on the facial nerve during the delivery process. Risk factors include instrumental delivery, poor delivery skills, big baby etc. Usually resolves spontaneously after a few months

5.6 Scalp Injuries

5.6.1 Cephalhematoma

Tearing or disruption of the superficial veins under the periosteum leads to haemorrhage and subsequent swelling. Suture lines confine the cephalhematoma and limit the extent of the bleeding. There could be an underlying linear skull fracture. Prognosis is good with most of them resolving between 2 weeks to 3 months.

5.6.2 Subgaleal Hemorrhage

The subgaleal space is located between the galea aponeurotica & the periosteum. The space extends from the orbital ridges to the nape of the neck and laterally to the ears. Bleeding is caused by damage to the large emissary veins located in the subaponeurotic layer. The bleeding associated with subgaleal haemorrhages can be extensive. Clinically, the baby may present with pallor and lethargy, followed by tachycardia, tachypnea and hypotension. The scalp may appear tight and boggy and complications include anemia, hypovolemic shock and jaundice.

Figure 5.6: Cephalhematoma

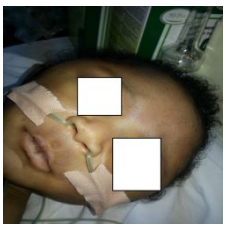

Figure 5.7: Subgaleal Bleed

5.7 Visceral injuries

5.7.1 Liver and spleen

Usually results from pressure on the liver during delivery of the head in breech presentations. Risk factors include macrosomia, intrauterine asphyxia, extreme prematurity, and hepatomegaly

5.8 Respiratory Distress

5.8.1 Meconium aspiration syndrome

Fetuses sometimes pass meconium whilst in utero as a result of some form of stress. If the stress has been going on for a while and the fetus has been passing meconium for a few days, the cord, skin and nails may be stained. Occurs when the fetus passes meconium into the surrounding liquor and then aspirates this into the lungs. Tends to happen in term and post-date babies. Distressed fetuses tend to pass meconium either just before or during the delivery

process. The smaller the amniotic fluid volume, and the more meconium the baby passes, the thicker the fluid and the more dangerous it becomes if aspirated.

History of Pregnancy and delivery looking for predisposing factors such as fetal distress, post-maturity, meconium-stained liquor etc. Physical examination looking for signs of meconium-staining on the baby, and evidence of respiratory distress (fast breathing, chest indrawing, cyanosis etc.). Investigations include FBC, Blood C&S, and sometimes a chest X-ray depending on the severity. Management is mainly supportive. Includes antibiotics, respiratory support, supportive treatment, IVFs and nutrition.

5.8.2 Transient tachypnoea of the newborn

Caused by delay in clearance of fetal lung fluid. Typically resolves within 72 hours. Often associated with Caesarean Section Delivery. Severity varies but is often mild with just tachypnoea. Management involves supportive treatment of the respiratory with oxygen.

6 Neonatal Emergencies

6.1 Introduction

The usual newborn cries on delivery, is pink all over, well flexed and moves all limbs spontaneously, suckles well at the breast, breaths normally and weighs between 2.5 – 4.0kg. Neonatal emergencies are not uncommon and encompass a wide range of conditions occurring in the first 28 days of life. The classical mnemonic for these is **THE MISFITS.**

Trauma/Abuse, **H**eart & Lung, **E**ndocrine, **M**etabolic disturbances, **I**nborn errors of metabolism, **S**epsis, **F**ormula, **I**ntestinal, **T**oxins, **T**risomies, and **S**eizures.

6.2 Approach to newborn emergencies

Presenting features of many serious neonatal disorders are nonspecific. The history and physical examination are essential in the overall approach to the patient. Prenatal, perinatal and postnatal history play a huge role in neonatal assessments They guide and inform the health worker on the most appropriate investigations, which would eventually lead to a correct diagnosis. A complete history may unmask the likely cause of symptoms and guide further questioning, for example, sepsis.

Examination on the other hand involves assessing the Airway, Breathing, Circulation, Random Blood Sugar, provision of Oxygen and checking Oxygen saturation. This can be pre- and postductal. Others include temperature checks and other vital signs. The weight, current weight, head circumference, and length. Intravenous access should be obtained for possible further treatment. Appropriate investigations should also be done.

Requisite investigations should also be done accordingly.

6.3 Respiratory Emergencies

This is one of the most common and includes:

1. Primary pulmonary Hypertension,
2. Meconium Aspiration Syndrome,

3. Congenital Pneumonia
4. Birth Asphyxia and
5. Respiratory Distress Syndrome

6.3.1 Respiratory Distress Syndrome

RDS is due mainly to a lack of surfactant in the lungs. Surfactants are essential for reducing the surface area of the lungs, thus helping in breathing. Incidence and severity increase with decreasing gestational age. Other risk factors include prematurity, male gender, multiple gestations, being born to a mother with diabetes mellitus and hypothermia. Signs of RDS include tachypnea, grunting, recessions and cyanosis. Prevention involves preventing preterm births and administering corticosteroids to the mother of gestation between 24 to 34 weeks before delivery. Treatment however involves the administration of surfactant.

Note that this condition is different from *Respiratory Distress* in a newborn. Respiratory distress is a more generalised term used as a single or a combination of signs as a result of increased work of breathing. It can result from pulmonary as well as non-pulmonary causes. These include cardiac, neurological (eg. Asphyxia), haematological (Anemia) and sepsis. It occurs in both term and preterm children.

6.4 Endocrine Emergencies

Neonatal jaundice is the most prominent endocrine disorder in this section. This is appropriately discussed in Section **??**

6.5 Metabolic Emergencies

6.5.1 Hypoglycemia

Hypoglycemia is common in the stressed neonate and glucose levels should be monitored regularly. In the newborn period, it is defined as a random blood glucose of < 2.6mmol/l. Risk factors include sepsis, Infant of a diabetic mother, prematurity, Intrauterine growth restriction, birth asphyxia and hypothermia. Signs include Lethargy, poor feeding, seizures, and apnea. Neurological damage may result from hypoglycemia in neonates.

Neonatal hypoglycemia is most commonly seen in macrosomic infants and infants of diabetic mothers. For these babies, during pregnancy, maternal glucose crosses the placenta to cause fetal hyperglycaemia. The fetal pancreas responds by increasing insulin production. Following delivery, the hyperglycaemic stimulus is instantly removed but insulin production may take

longer to slow down. This results in an increased risk and incidence of hypoglycemia at the early newborn period.

Management involves initially checking the airway, breathing and circulation. 2ml/kg of IV 10% Dextrose or 5ml/kg of 5% Dextrose may be given PR if IV access is unavailable. Ensure the baby has a normal body temperature (temperature target: 36.50 – 37.50C) as hypothermia prone the baby to hypoglycaemia. Always look for the underlying cause of the hypoglycemia and treat it appropriately.

6.6 Neonatal Sepsis

Sepsis in the neonate kills more than a million babies worldwide every year. It is a clinical syndrome characterized by signs of infection with accompanying bacteremia in the first month of life. It can be categorized into *Early Onset Neonatal Sepsis* (EOS), which refers to the presence of signs of infection accompanied by a positive culture within the first 72 hours of life, and *Late Onset Neonatal Sepsis* (LOS), which signifies the onset of signs of infection with a positive culture after 72 hours of life.

Causative organisms: Early-onset sepsis is typically caused by organisms from the maternal genital tract, whereas late-onset sepsis is caused by organisms in the caregiving environment or community. Common organisms are *Klebsiella pneumoniae,* E. coli, and Coagulase Negative Staphylococcus among others. For many of these organisms, the resistance rate to antibiotics is alarmingly going up.

Antenal risk factors known to be associated with neonatal jaundice include spontaneous rupture of membranes, less than 37 completed weeks of gestation, spontaneous preterm labour, rupture of membranes greater than 18 hours before delivery, maternal chorioamnionitis, maternal fever of 38 degrees Celsius or more, maternal invasive bacterial infection requiring antibiotics, pre-labour rupture of membranes, Group B Streptococcus infection in a previous baby, or current pregnancy, meconium-stained amniotic fluid and foul-smelling liquor.

Postnatally, risk factors for neonatal sepsis include prolonged resuscitation at birth, prematurity, invasive procedures, mechanical ventilation, excessive handling, home delivery, lack of hand washing and inadequate Infection prevention control. Others include overcrowding and prolonged hospital stay.

Signs of neonatal sepsis include

1. Abnormal colour: Pale, cyanotic, mottled appearance, jaundice, grey
2. Temperature instability
3. Abdominal signs: distension, poor feeding, vomiting, diarrhoea
4. Respiratory: Apnea, respiratory distress, gasping (Abnormal breathing)
5. Hypo - or hyperglycemia
6. Cardiovascular: Shock, tachycardia (HR $>$ 180), Bradycardia (HR $<$ 80)

7. Abnormal bleeding
8. Central Nervous System: Excessive crying, irritability, seizures, altered tone, lethargy,

Management of neonatal sepsis should be comprehensive. It should include an initial evaluation for resuscitation of the airway, breathing and circulation. Further, the blood sugar should be measured. Early reversal of the shock state by administering an initial bolus of 10ml/kg of crystalloid or its equivalent should be done in the shock present. Vasopressors or inotropes should be used in septic shock only after appropriate volume resuscitation has been done. The goals of the resuscitation should be Normal Cap refill (less than 2 seconds), normal pulses, warm extremities, and appropriate urine output (greater than 1mL/kg/hr).

Increased successful treatment of neonatal sepsis requires early recognition and urgent administration of appropriate antibiotics.

After resuscitation, ongoing management usually starts with a detailed history to assess risk factors and other presentations. A thorough physical examination will then be performed, looking for and documenting specific signs indicating severity.

Investigations usually include a blood culture. This is considered the gold standard for diagnosis. Ideally, a culture should always be done before the first dose of antibiotics. Other auxiliary investigations include a complete blood count, blood gases, urine culture, and a lumbar puncture. The threshold for performing a lumber puncture in all symptomatic newborns suspected of sepsis should be encouraged. It should however be deferred in neonates considered too unstable to tolerate the procedure, or where there is an absolute contraindication.

Supportive treatment is essential for a good outcome in neonatal sepsis. Antibiotics are not the entire solution to their treatment. Nutrition or breastfeeding should be optimized. The environment should be thermo-neutral and oxygen saturation should be maintained within the normal range (89 – 95%). Intravenous fluids should be used if the infant is hemodynamically unstable. Monitoring of the blood glucose levels should be instituted. Packed red cells and fresh frozen plasma should be used in the event of anaemia or bleeding.

6.7 Gastrointestinal emergencies

Gastrointestinal emergencies in newborns can be broadly divided into the following:

Obstructive: Some of these are Tracheoesophageal fistula, Duodenal Atresia, Hirschsprung's Disease, Biliary Atresia, Pyloric Stenosis, Intestinal Volvulus, Imperforate Anus and Necrotizing enterocolitis.

Abdominal wall defect: The most notable examples here are Omphalocele and Gastroschisis

Figure 6.1: Abdominal distension secondary to intestinal obstruction in a newborn

6.7.1 Gastroschisis

This is an anterior abdominal wall defect, located to the right of the umbilicus, and contains herniated intestines that have no material covering the sac. It occurs in approximately 1 in 10000 births. Rarely, it is associated with other genetic syndromes. However, it may be associated with intestinal atresia, stenosis and malrotation. Other associations include prematurity (50-60%)and cryptochidism (31%). Generally, it has a better prognosis compared to an omphalocele. The prognosis is excellent for small defects. Mortality is expertise and facility-dependent but generally around 5 to 10%. Necrotizing enterocolitis is a well-recognised complication, occurring in as much as 18%.

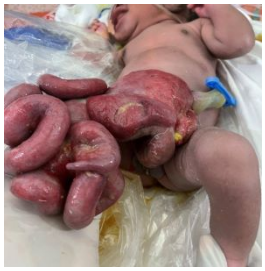

Figure 6.2: Gastroschisis in a newborn

6.7.2 Omphalocele

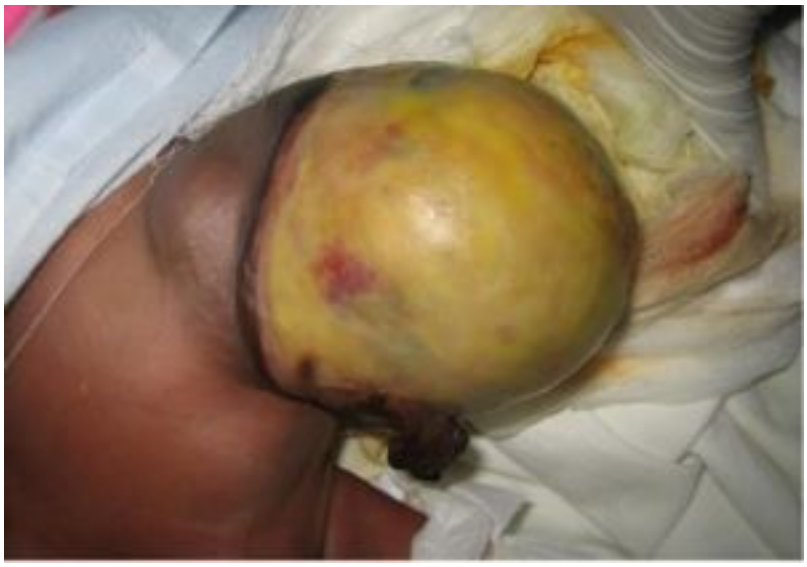

Figure 6.3: Omphalocele in a newborn

7 Neonatal Jaundice

7.1 Introduction

Jaundice is the yellowish discoloration of the skin, eyes and mucous membranes, caused by a pigment called bilirubin in the blood. Out of 10 term and 10 preterm newborns, 6 and 8 will develop jaundice respectively, all in the 1st couple of weeks of life. Universally accepted as one of the commonest causes of admission and readmission in the first month of life. At Komfo Anokye Teaching Hospital Mother Baby Unit, monthly admissions average between 300 and 400 and about 15 to 25% of all these admissions are cases of neonatal jaundice. Whereas the developed world describes kernicterus as a rare condition, unfortunately, the same cannot be said for us in developing countries. On average, cases of severe Neonatal Jaundice have ranged from 2.2% to 30.8% of all jaundice cases, with the monthly mortality ranging from 2.8% to 15.2%(REFERENCE). Remember, kernicterus is the only preventable cause of cerebral palsy!

7.2 Bilirubin metabolism

Humans continuously form bilirubin and the liver is the main organ responsible for the metabolism of bilirubin. For every gram of haemoglobin, 35mg of bilirubin is produced. The bilirubin is conjugated by the UGT enzyme, making it water-soluble, which is then released into the bile before being excreted in the stool (and urine). It can also be broken down in the intestine by bacterial enzymes like E. coli. However, at birth, the newborn has several challenges. The liver is immature, and the levels of bilirubin uridine diphosphate glucuronosyltransferase (bilirubin-UGT) enzyme are low. Newborns have -glucuronidase in the intestinal mucosa/brush border, which deconjugates the conjugated bilirubin found in the meconium. The unconjugated bilirubin can now be reabsorbed through the intestinal wall and recycled back into the circulation. This process is known as the “enterohepatic circulation of bilirubin”. The gut is sterile and, subsequently, infants have far fewer bacteria in the gut, and so very little, if any, bilirubin is reduced to urobilin and stercobilin.

Specifically in newborns, more bilirubin is produced, on account of the short life span of Red Blood Cells and high Hemoglobin levels. The liver is immature. They also have fewer bacteria and low intestinal enzymatic activity in the intestine

7.3 Types of bilirubin

There are two types:

7.3.1 Conjugated (Direct) Bilirubin

This is water soluble, excreted in the urine and stool, and not toxic to the brain. However, high amounts could indicate underlying liver disease or injury.

7.3.2 Unconjugated (Indirect) Bilirubin

This is lipid soluble, can cross the blood-brain barrier and is toxic in high amounts to the brain.

In very high concentrations, unconjugated bilirubin, which is lipid-soluble, is toxic to the developing brain. Once it crosses the blood-brain barrier, it binds to brain tissue and deposits in the developing brain. Since this is an irreversible process, it leads to long-term neurological issues and even death.

7.4 Types of Jaundice

There are two main types of jaundice:

1. Physiological jaundice and
2. Pathological jaundice.

There are three main mechanisms for jaundice:

1. Increased bilirubin production
2. Decreased bilirubin clearance and
3. Increased enterohepatic circulation.

7.4.1 Physiological jaundice

7.4.1.1 Increased bilirubin production

in term newborn infants, bilirubin production is 2 to 3 times higher than in adults. This occurs because newborns have more RBCs and fetal RBCs have a shorter life span than those in adults. Unfortunately, the liver being immature, cannot conjugate and excrete all the bilirubin from the breakdown of all the excess RBCs, thereby resulting in spillover of bilirubin into the blood.

7.4.1.2 Bilirubin clearance or excretion

This is decreased in newborns, mainly due to the low levels of the UGT enzyme in the liver. UGT activity in term infants at day 7 of age is approximately 1% of that of the adult liver and does not reach adult levels until about 14 weeks of age.

7.4.1.3 Enterohepatic circulation

The presence of the ß-glucuronidase results in an increase in the enterohepatic circulation of bilirubin, further increasing the bilirubin load in the infant. This is a diagnosis of exclusion

7.4.2 Pathological jaundice

7.4.2.1 Definition

Neonatal jaundice is said to be pathologic if:

- Jaundice in the 1st 24 - 48 hours of life.
- Rate of SB rise $>$ 0.5 mg/dL (8.5µmol/L) per hour
- Jaundice all over the body (including palms & soles)
- Presence of a danger sign
- History of previous siblings having had jaundice at birth
- Jaundice in a term newborn after 2 weeks of age or in a preterm infant after 3 weeks of age
- Direct (conjugated) bilirubin concentration $>$ 20% of the total

It can be caused by certain pathologic conditions or exaggeration of the mechanisms responsible for physiologic neonatal jaundice. Identification of what is causing the jaundice is useful in guiding management, including counselling of the parents and what to expect for the next pregnancy. Most common cause is increased bilirubin production due to haemolytic disease processes that include the following:

- Isoimmune-mediated haemolysis (e.g., ABO or Rhesus D incompatibility)
- Erythrocyte enzymatic defects, e.g. G6PD deficiency
- Sepsis, especially Urinary Tract Infection
- Polycythaemia
- Birth Injuries resulting in sequestration of blood within a closed space, e.g. cephalohematoma, subgaleal bleed.

7.4.2.2 ABO incompatibility

This is one of the most common causes of isoimmune hemolytic disease during the neonatal period. Infants with blood group A or B, carried by blood group O mother, will have a positive antibody because of maternal anti-A or anti-B transfer into the fetal circulation.

7.4.2.3 Rhesus Incompatibility

Rh incompatibility can occur when an Rh-negative pregnant mother is exposed to Rh-positive fetal red blood cells secondary to feto-maternal haemorrhage during pregnancy/delivery. As a result, the mother's blood gets exposed to the fetal circulation and sensitization occurs leading to maternal antibody production against the foreign Rh antigen. Once produced, maternal Rh (IgG) antibodies may cross freely from the placenta to the fetal circulation, where they form antigen-antibody complexes with Rh- positive fetal RBCs and eventually are destroyed, resulting in a fetal alloimmune-induced hemolytic anaemia and jaundice. The first pregnancy is usually not affected, but more antibodies are produced with each pregnancy making the jaundice worse with each pregnancy.

7.4.2.4 Decreased clearance

Inherited defects in the gene that encodes the UGT liver enzyme (eg, Gilbert Syndrome), decrease bilirubin conjugation (eg Crigglar Najjar). In physiological jaundice, the levels are naturally low, but here, in addition to the low levels the UGT enzyme is either defective, absent or has a reduced function. This reduces hepatic bilirubin metabolism and its clearance thereby increasing the total serum unconjugated bilirubin levels.

7.4.2.5 Increased enterohepatic circulation

The major causes are

- Breastfeeding jaundice
- Breast milk jaundice
- Impaired intestinal motility is caused by functional or anatomic obstruction.
- Congenital hypothyroidism also causes increased enterohepatic circulation on account of reduced gut motility.

7.5 Assessing for Neonatal Jaundice

- Baby should be assessed in natural daylight
- Look for yellow eyes & skin, check the white part of the eyes only if the baby opens the eyes voluntarily.
- You may blanch the skin on the bridge of the nose or the palms/soles of the feet if they turn yellow…
- Remember that the yellowing spreads from head to toe…
- Do not rely on visual inspection alone to estimate the bilirubin level in a baby with jaundice!!! It can be very subjective!!

7.6 Clinical features

The clinical features of neonatal jaundice may include:

- Baby looks yellow! The yellowness appears cephalocaudal.
- May not be as active as he/she used to be
- Lethargic/hypotonic
- Weak cry, irritable
- Poor feeding
- High-pitched cry / poor cry
- Seizures
- Arching of the neck/back

Thus to evaluate a child with jaundice we:

- Determine birth weight, gestation and postnatal age (in hours)
- Assess clinical condition (well or ill)
- Degree of jaundice (visual inspection, SBR etc)
- Look for evidence of kernicterus / BIND

7.7 Management

The general principle of treatment includes

- Encourage frequent exclusive breastfeeding.
- Start Intravenous fluids only when there are signs of dehydration
- Watch out for danger signs
- Pathologic Neonatal jaundice is treated with
  - Phototherapy

- Exchange Blood Transfusion (EBT)
- Antibiotics

Be interested in the cause as this will serve as a guide in the management of the baby and direct your counselling as well as impact on subsequent pregnancies Loads of information in the maternal and child health record book, Gravidity and Parity, G6PD status, maternal Blood group & Rhesus status etc

7.7.1 Investigations

This should include but not be restricted to

- Serum Bilirubin (conjugated, unconjugated and total)
- Full Blood Count
- G6PD screening
- Blood Culture & Sensitivity
- Baby's blood group (only necessary if mother's blood group is O)
- Others include Direct Coomb's test, Urine C & S etc

7.7.2 Phototherapy

Phototherapy is the use of visible light to treat high levels of serum bilirubin in the newborn.

Figure 7.1: Phototherapy Unit

The dose of phototherapy is a key factor in how quickly it works. The dose in turn is determined by:

- The wavelength of the light
- The intensity of the light (irradiance)
- The distance between the light and the baby
- The body's surface area is exposed to the light.

Effective phototherapy lowers serum bilirubin levels by converting the lipid-soluble bilirubin into water-soluble forms that can easily be excreted in the stool and urine Phototherapy also prevents the need for an Exchange Blood Transfusion and prevents bilirubin from depositing in

the brain. The breakdown of bilirubin begins almost instantaneously when the skin is exposed to light, hence, phototherapy should be started as early as possible.

In initiating phototherapy, always note the time the baby's SBR sample is being taken and estimate the age in hours up until that time. Interpret bilirubin levels according to the baby's postnatal age in hours and manage the bilirubin levels according to the threshold table Start phototherapy if the SBR plots on or above the line appropriate for age (in hours) and gestational age If the SBR plots just underneath the line, repeat the SBR after 6 hours or start phototherapy if a repeat is not feasible. Repeat the SBR at least 24 to 48 hours after initiation of phototherapy. Discontinue phototherapy when the SBR plots below the line.

The side effects of phototherapy include:

- Increase insensible water loss
- Loose stools
- Skin rash
- Bronze baby syndrome
- Hypo- or Hyperthermia
- Interruption of mother-baby bonding

7.7.3 Sunlight Therapy

Works for physiological jaundice, however, one can never tell by looking at a baby what kind of jaundice a baby has Err on the side of caution, at least always have the SBR checked first Remember prolonged exposure to UV rays can be harmful to the developing skin Baby cannot be put in the light for more than 30 minutes in a day Even most of the available literature and studies that recommend sunlight still advice that if the jaundice is severe, the baby must be managed in the hospital!! A serum bilirubin high enough to warrant treatment should be managed in the hospital.

7.7.4 Exchange Blood Transfusion

Provides a means of rapid reduction of circulating bilirubin in the blood. Involves manual removal of the baby's blood and simultaneously replacing it with compatible donor blood.

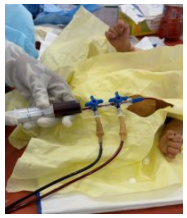

Figure 7.2: Exchange Blood Transfusion

In addition to reducing bilirubin levels, EBT removes partially hemolyzed RBCs, RBCs coated with antibodies and circulating immunoglobulins.

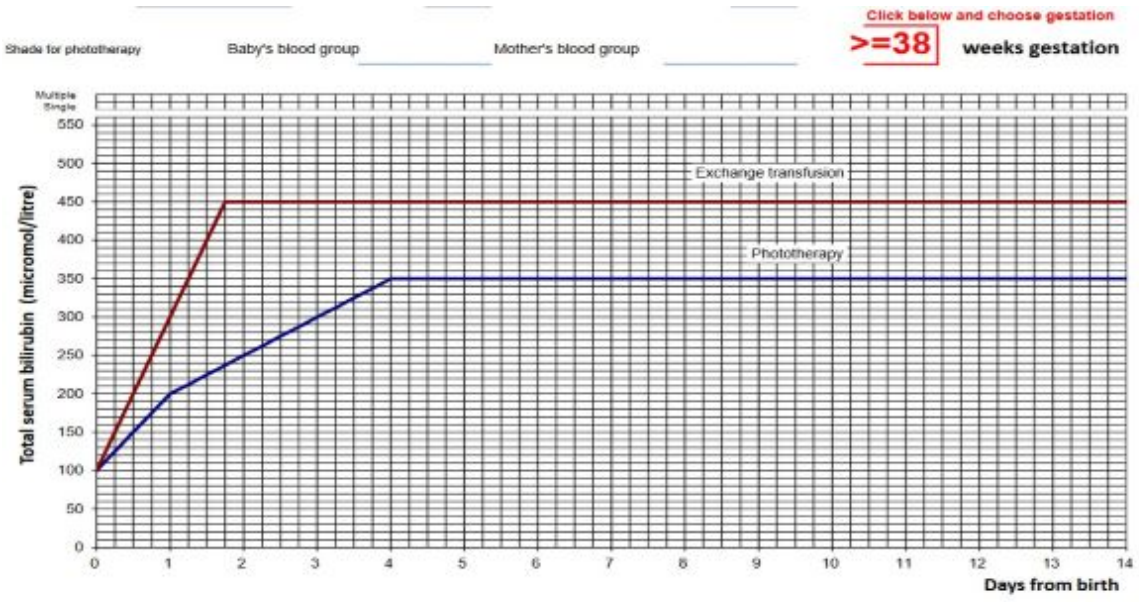

Figure 7.3: Bilirubin Graph (> 38 weeks)

Complications of exchange blood transfusion include:

- Cardiac & respiratory disorders
- Shock due to bleeding or inadequate replacement of blood infection
- Catheter-related complications
- Changes in the composition of the blood (high or low potassium, low calcium, low glucose, changes in pH)
- Thrombocytopenia
- And the rare but serious complications of air embolism, portal hypertension, and necrotizing enterocolitis.

7.7.5 Intravenous Immunoglobins

Treatment with intravenous immunoglobulin (IVIG) has been suggested as an alternative therapy to Exchange Blood Transfusion for isoimmune hemolytic jaundice to reduce the need for Exchange Blood Transfusion and duration of phototherapy and hospitalization in isoimmune hemolytic disease of the newborn. It has been proposed that IVIG blocks the binding of the antibody to the antigen. With this blockade, hemolysis no longer occurs.

7.8 Long term complications

The effects of bilirubin toxicity include

- Hearing loss
- Cerebral palsy
- Mental retardation
- Dental complications
- Delayed developmental milestones
- Seizure and visual disorders

7.9 Recommendations

- Always err on the side of caution
- An SBR is always more objective
- Look out for danger signs
- As much breastmilk as possible by any means necessary
- Sunlight therapy is not recommended, if the baby is yellow enough for you to want to put him/her under the sun, then the baby needs to be brought to the hospital!

8 Newborn Delivery & Resuscitation

8.1 Introduction

The delivery of a newborn is one of the most critical moments in medicine, requiring skill, vigilance, and readiness. The transition from intrauterine to extrauterine life involves complex physiological changes that must occur within seconds. In most deliveries, this transition is smooth and spontaneous. However, about **10% of newborns require some form of assistance**, and approximately **1% need extensive resuscitation**.
Understanding the physiology of transition, preparation for delivery, and the systematic approach to neonatal resuscitation is therefore vital for every healthcare provider involved in childbirth.

8.2 Physiology of Fetal to Neonatal Transition

The fetus depends on the placenta for gas exchange, nutrient delivery, and waste removal. At birth, these functions must shift rapidly to the infant's lungs and other organs.

Key physiological changes: - **Lung expansion**: With the first breaths, alveoli expand and fluid is replaced by air, allowing gas exchange.
- **Circulatory changes**: - Closure of the **foramen ovale**.
- Functional closure of the **ductus arteriosus** as pulmonary resistance drops and oxygen tension rises.
- Closure of the **ductus venosus**, redirecting blood through the liver.
- **Thermoregulation**: The newborn's ability to maintain temperature is limited, necessitating early warmth and drying.

Failure of any of these adaptations can lead to respiratory distress and hypoxia.

8.3 Preparation for Delivery

Every birth, regardless of risk status, must have a **prepared resuscitation team and equipment**.

8.3.1 Personnel

- **At least one skilled person** trained in neonatal resuscitation should be present at every delivery.

- For high-risk deliveries (preterm, meconium-stained liquor, multiple gestation), **two or more trained personnel** should be available.

8.3.2 Equipment and Environment

Preparation should follow the **"warm, clean, ready"** principle: - **Warmth**: Preheat radiant warmer; ensure room temperature 25°C.
- **Cleanliness**: Use sterile instruments and maintain a clean surface.
- **Readiness**: - Functioning **suction device**.
- **Bag and mask** appropriately sized.
- **Oxygen supply** and blender if available.
- **Clock or timer** for monitoring response.
- **Sterile cord clamps**, towels, gloves, and stethoscope.

8.4 Immediate Care at Birth

Immediately after delivery, attention should focus on **rapid assessment and prevention of hypothermia**.

8.4.1 Initial Steps (within 30 seconds)

1. **Provide warmth** – place under radiant warmer.

2. **Position the head** in slight extension ("sniffing position").

3. **Clear the airway** only if obstructed.

4. **Dry and stimulate** – rubbing the back or flicking soles can initiate breathing.

5. **Evaluate breathing and heart rate**.

If the newborn is term, breathing, and with good tone, proceed with **routine care**: - Keep warm, initiate **skin-to-skin contact**, and encourage **early breastfeeding**.

If **not breathing or gasping**, proceed to **resuscitation**.

8.5 Neonatal Resuscitation Algorithm

The process follows the **"Golden Minute" principle**: all interventions up to effective ventilation should occur within the first minute of life.

8.5.1 1. Initial Assessment

Ask three questions: - Is the baby **term**? - Is the baby **breathing or crying**? - Does the baby have **good tone**?

If "yes" to all → Routine care.
If "no" to any → Begin resuscitation steps.

8.5.2 2. Initial Actions

- Warm, position, clear airway (if necessary), dry, and stimulate.
- Reassess after 30 seconds.

If breathing starts → continue observation.
If **not breathing or heart rate <100 bpm**, start **Positive Pressure Ventilation (PPV)**.

8.5.3 3. Ventilation (The Most Critical Step)

- Use **bag and mask ventilation** with room air (21%) initially; increase O if no improvement.
- Deliver 40–60 breaths/min.
- Observe for **chest rise** — if none, check mask seal, airway position, or increase pressure.
- After 30 seconds of effective ventilation, reassess:
  - HR >100 bpm → support spontaneous breathing.
  - HR 60–100 bpm → continue ventilation and reassess.
  - HR <60 bpm → start **chest compressions**.

8.5.4 4. Chest Compressions

- Coordinate with ventilation in a **3:1 ratio** (90 compressions + 30 breaths per minute).
- Compress one-third of the chest depth using **two thumbs** on the lower sternum.
- After 60 seconds, reassess heart rate.

8.5.5 5. Medications

- If HR <60 bpm despite 30 sec of effective ventilation and 60 sec of compressions, administer **epinephrine** (0.01–0.03 mg/kg IV/IO; 1:10,000 dilution).
- **Volume expansion** (normal saline 10 mL/kg IV) if hypovolemia suspected.

8.6 Post-Resuscitation Care

After stabilization: - Maintain **normal temperature** (36.5–37.5°C).
- Provide **oxygen titrated** to maintain saturation (target 90–95% after 10 minutes).
- Monitor **blood glucose** to prevent hypoglycaemia.
- Observe for **respiratory distress, seizures, or shock**.
- If resuscitation was prolonged, consider admission to a **neonatal intensive care unit (NICU)** for ongoing support.

8.7 Common Pitfalls in Neonatal Resuscitation

- **Failure to anticipate risk**.
- **Delay in initiating ventilation** — the most common cause of poor outcome.
- **Ineffective ventilation** due to poor mask seal or incorrect technique.
- **Excessive suctioning**, leading to vagal bradycardia.
- **Overuse of oxygen**, which can cause oxidative injury, especially in preterm infants.

8.8 Special Situations

8.8.1 Meconium-Stained Amniotic Fluid

- If the baby is vigorous (crying, good tone), proceed with routine care.
- If not vigorous, do **not delay ventilation** for suctioning; clear airway only if obstructed.

8.8.2 Preterm Newborn

- Risk of hypothermia and respiratory distress is high.
- Use **polyethylene wrap** or **warm humidified gas**.
- Oxygen titration and **gentle ventilation** to avoid barotrauma.

8.8.3 Multiple Births

- Ensure multiple sets of resuscitation equipment and personnel.

8.8.4 Congenital Anomalies

- Some, such as diaphragmatic hernia, require **intubation without bag-mask ventilation** to prevent gastric distension.

8.9 Equipment Checklist

- Suction device, masks (sizes 0 and 1), self-inflating bag, oxygen source.
- Umbilical venous catheter, syringes, epinephrine, normal saline.
- Radiant warmer, towels, caps, polyethylene wraps.
- Stethoscope, timer, pulse oximeter (if available).

8.10 Documentation and Prognosis

Accurate documentation of time, interventions, and outcomes is essential. Most babies respond promptly to resuscitation; however, prolonged asphyxia may lead to **hypoxic–ischaemic encephalopathy**, **cerebral palsy**, or **neurodevelopmental delay**.

8.11 Summary

Neonatal resuscitation is a time-critical, life-saving skill built on preparation, effective ventilation, and teamwork. In most cases, ensuring a warm environment, clearing the airway only when needed, and establishing effective ventilation within the first minute of life can mean the difference between survival and death.

9 Preterm and Low Birth Weight

9.1 Introduction

Preterm birth and low birth weight are major contributors to neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries such as Ghana. Advances in perinatal care, antenatal monitoring, and neonatal intensive care have improved survival; however, the burden remains high. Both conditions often overlap — most low birth weight (LBW) babies are preterm, but some are born at term and small for gestational age due to intrauterine growth restriction (IUGR). Understanding their causes, physiology, complications, and management is crucial for improving outcomes.

9.2 Definitions

Preterm birth refers to any birth occurring before **37 completed weeks of gestation** (less than 259 days from the first day of the last menstrual period).

Preterm infants are further categorized as: - **Late preterm:** 34 to <37 weeks
- **Moderate preterm:** 32 to <34 weeks
- **Very preterm:** 28 to <32 weeks
- **Extremely preterm:** <28 weeks

Low Birth Weight (LBW) is defined by the World Health Organization as a birth weight **less than 2500 grams**, irrespective of gestational age.

Subcategories include: - **Very Low Birth Weight (VLBW):** <1500 g
- **Extremely Low Birth Weight (ELBW):** <1000 g

9.3 Epidemiology and Global Burden

Globally, about 15 million babies are born preterm every year — roughly 11% of all live births. Over 60% occur in South Asia and sub-Saharan Africa. In Ghana, preterm delivery rates range from 10–15%, with low birth weight accounting for approximately 9–12% of births. Both conditions contribute significantly to neonatal deaths, particularly from respiratory distress, sepsis, and hypothermia.

Factors such as inadequate antenatal care, infections, poor maternal nutrition, multiple pregnancies, and adolescent pregnancy increase the risk. Neonatal care resources — such as incubators, surfactant therapy, and continuous positive airway pressure (CPAP) — are often limited, worsening outcomes in resource-constrained settings.

9.4 Embryological and Physiological Considerations

Normal fetal growth depends on adequate **placental function**, **maternal nutrition**, and **fetal genetic potential**. Disruption of any of these can impair fetal growth or lead to premature birth.

- **Placental development:** The placenta serves as the interface for nutrient and oxygen exchange. Abnormal trophoblastic invasion or uteroplacental insufficiency can limit nutrient delivery, resulting in intrauterine growth restriction.
- **Lung development:** The fetal lungs undergo several stages — embryonic, pseudoglandular, canalicular, saccular, and alveolar. Infants born before 34 weeks have surfactant deficiency, leading to respiratory distress.
- **Thermoregulation:** Preterm infants have a large surface area-to-weight ratio, thin skin, and minimal subcutaneous fat, predisposing them to hypothermia.
- **Metabolic adaptation:** Immature hepatic enzymes, low glycogen stores, and poor feeding contribute to hypoglycaemia and metabolic instability.
- **Neurological immaturity:** Poor reflexes (suck, swallow, gag) and underdeveloped autonomic control affect feeding and cardiorespiratory stability.

9.5 Aetiology and Risk Factors

9.5.1 Maternal Factors

- Poor nutritional status and anaemia
- Infections such as malaria, urinary tract infection, or HIV
- Hypertensive disorders of pregnancy (preeclampsia, eclampsia)
- Smoking, alcohol, or substance abuse
- Short inter-pregnancy intervals
- Low socioeconomic status
- Teenage or advanced maternal age

9.5.2 Fetal Factors

- Multiple gestations (twins, triplets)
- Congenital anomalies or chromosomal abnormalities
- Intrauterine infections (TORCH, syphilis)

9.5.3 Placental Factors

- Placenta previa or abruption
- Placental insufficiency
- Umbilical cord anomalies

9.6 Pathophysiology

The underlying mechanism varies depending on whether the infant is **preterm**, **small for gestational age**, or both.

- **Preterm birth** results from early initiation of labour due to uterine overdistension, infection, or hormonal imbalance.
- **Low birth weight due to IUGR** stems from chronic hypoxia and nutrient deprivation secondary to placental insufficiency.
- **Combined preterm and growth restriction** exacerbate vulnerability to hypoxia, sepsis, and metabolic instability.

Physiologically, the immature organs of a preterm infant — lungs, brain, gut, kidneys, and liver — are unable to perform their functions optimally. The result is a cascade of complications such as respiratory distress, patent ductus arteriosus, necrotizing enterocolitis, and intraventricular haemorrhage.

9.7 Clinical Features

Preterm infants are typically: - Small, thin, with less subcutaneous fat
- Skin reddish and translucent
- Large head relative to body
- Weak cry and poor tone
- Incomplete flexion of limbs
- Absent or weak primitive reflexes (suck, grasp, Moro)

Low birth weight infants (IUGR) may appear: - Small but mature (if term)
- With wasted muscles, loose skin, and relatively large head
- Sometimes meconium-stained due to chronic hypoxia

9.8 Complications

Complications may be **immediate**, **early neonatal**, or **long-term**.

9.8.1 Early Complications

- Respiratory distress syndrome (RDS)
- Apnoea of prematurity
- Hypothermia
- Hypoglycaemia
- Electrolyte imbalance
- Sepsis
- Necrotizing enterocolitis
- Jaundice (due to immature liver conjugation)
- Patent ductus arteriosus
- Intraventricular haemorrhage

9.8.2 Long-Term Complications

- Chronic lung disease (bronchopulmonary dysplasia)
- Retinopathy of prematurity
- Neurodevelopmental delay or cerebral palsy
- Growth failure
- Learning disabilities and visual or hearing impairment

9.9 Diagnosis and Assessment

9.9.1 Determination of Gestational Age

- **Maternal history:** Last menstrual period, early ultrasound
- **New Ballard Score:** Based on neuromuscular and physical maturity
- **Anthropometry:** Weight, length, and head circumference

9.9.2 Investigations

- Blood glucose, electrolytes, calcium
- Full blood count and CRP (if infection suspected)

- Chest X-ray for respiratory distress
- Cranial ultrasound for intraventricular haemorrhage
- Screening for congenital infections if indicated

9.10 Management

Management involves **stabilization, supportive care, and prevention of complications**. The guiding principles are **warmth, feeding, infection prevention, and monitoring**.

9.10.1 1. Immediate Stabilization at Birth

- Dry and wrap the baby immediately to prevent hypothermia
- Assess breathing and initiate resuscitation if necessary
- Maintain airway and oxygenation
- Early cord clamping if stable

9.10.2 2. Temperature Regulation

- Use of incubator or radiant warmer
- Kangaroo mother care (skin-to-skin contact) is highly effective and feasible in low-resource settings

9.10.3 3. Feeding and Nutrition

- Encourage early breastfeeding if the baby can suck
- Expressed breast milk via cup or nasogastric tube for immature infants
- Parenteral nutrition if gut immaturity prevents enteral feeding
- Monitor glucose and electrolytes closely

9.10.4 4. Prevention of Infection

- Strict hand hygiene and aseptic techniques
- Avoid unnecessary invasive procedures
- Antibiotic therapy for suspected or proven sepsis

9.10.5 5. Monitoring

- Regular temperature, respiratory rate, and heart rate
- Daily weight and urine output
- Observation for apnoea or feeding intolerance

9.10.6 6. Management of Specific Complications

- Surfactant replacement and CPAP for RDS
- Phototherapy for jaundice
- Caffeine for apnoea
- Blood transfusion for anaemia if needed

9.11 Discharge Planning and Follow-Up

Discharge Criteria: - Stable temperature in open cot for 24–48 hours
- Feeding well and gaining weight
- No apnoea or cardiorespiratory instability
- Parents trained in home care, including kangaroo care

Follow-Up: - Weekly or biweekly reviews until adequate weight gain
- Monitor for developmental milestones, vision, hearing, and growth
- Immunizations per national schedule (adjusted for weight and age as necessary)

9.12 Prevention

- Adequate **antenatal care** and early detection of high-risk pregnancies
- **Maternal nutrition** and treatment of infections (especially malaria and syphilis)
- **Prevention of teenage pregnancy** and family planning
- **Antenatal corticosteroids** for women at risk of preterm delivery
- **Tocolytic therapy** to delay labour when feasible
- **Facility-based delivery** with neonatal resuscitation readiness

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9.13 Prognosis

Survival depends on gestational age, birth weight, and available neonatal care.
- Infants >32 weeks or >1500 g have good survival with appropriate support.
- Extremely preterm (<28 weeks) and ELBW infants have high mortality and morbidity, especially in low-resource settings.
- Long-term outcomes include growth failure, cognitive delay, and chronic lung disease, emphasizing the need for continuous follow-up.

9.14 Conclusion

Preterm birth and low birth weight remain major challenges in neonatal care, particularly in resource-limited settings such as Ghana. A comprehensive approach — involving antenatal prevention, skilled perinatal care, thermal protection, infection control, nutritional support, and long-term follow-up — is essential. With improved maternal health programs, wider adoption of kangaroo mother care, and enhanced neonatal intensive care capacity, the survival and quality of life of these vulnerable infants can continue to improve.

10 Breastfeeding – Theory and Practice

10.1 Introduction

Breastfeeding is more than just a method of feeding infants; it is a sophisticated biological process that nurtures, protects, and connects both mother and child. Over recent decades, scientific discoveries have deepened our understanding of breastmilk's dynamic nature and its systemic benefits. This chapter examines the theoretical foundations and practical applications of breastfeeding, focusing on its physiological, immunological, nutritional, and psychosocial aspects. It also outlines strategies to overcome common challenges, ensuring healthcare workers can support mothers effectively.

10.2 Learning Objectives

By the end of this chapter, students should be able to:

- State Ghana's National Breastfeeding Policy.
- Describe the protective systems in breastmilk and their mechanisms.
- Explain the physiology of breastfeeding and how it supports maternal and infant health.
- Identify common breastfeeding challenges and outline appropriate management strategies.

10.3 The National Breastfeeding Policy

Ghana's policy promotes optimal breastfeeding practices, which include:

- Early Initiation of Breastfeeding (EIB) with early skin-to-skin contact and initiation of breastfeeding within the first hour of life.
- Exclusive Breastfeeding for the first six months, with no other foods or liquids, not even water.
- Appropriate Complementary Feeding by introducing nutrient-dense foods at six months, while continuing to breastfeed.
- Continue breastfeeding for up to two years or even beyond, if this is desirable for both mother and baby

This policy is grounded in evidence that links breastfeeding to improved neonatal, childhood, and even long-term health outcomes.

10.4 The Dynamic Nature of Breastmilk

Breast milk is an amazing, living, and dynamic fluid. Its composition adapts:

- From one feed to the next (foremilk vs. hindmilk),
- From day to night,
- Depending on the baby's gestational age (preterm vs. term),
- In response to the mother's health and environmental exposures.
- With the age of the baby

These adaptations ensure optimal nutrition, immune protection, and developmental support for the infant.

10.5 Some biological systems in Breastmilk that promote the health of the newborn.

10.5.1 Infection Prevention

Breastmilk contains secretory IgA (SIgA), critical for mucosal immunity. Unlike formula, breastmilk actively defends the infant against bacterial, viral, and other infections such as:

- **HIV:** Transmission risk is reduced significantly with exclusive breastfeeding under antiretroviral therapy.
- **Hepatitis B:** Not transmitted via breastmilk; vaccination prevents perinatal transmission

During the COVID-19 pandemic, breastmilk was shown to contain antibodies against SARS-CoV-2, with no evidence of viral transmission, further reinforcing its immunological role.

10.5.2 Gut Microbiota and Disease Prevention

Human milk oligosaccharides (HMOs) act as prebiotics, fostering healthy gut flora that:

- Shapes immunity,
- Reduces the risk of allergies, asthma, and dermatitis,
- Contributes to neurodevelopment and emotional regulation via the gut-brain axis.

10.5.3 Brain Development

Breastmilk supports brain growth through components such as:

- **Sphingomyelin:** Vital for myelination,
- **Sialic acid:** Enhances cognitive function,
- **Myo-inositol:** Boosts neuronal connectivity

Studies using MRI have shown that breastfed infants demonstrate superior white matter development and cognitive outcomes compared to formula-fed peers.

10.5.4 4. Support for Preterm Infants

Breastmilk of mothers of preterm babies contains:

- Higher energy content,
- Increased lactoferrin for iron absorption,
- HMOs and glycosaminoglycans that prevent necrotizing enterocolitis (NEC),
- More bioactive molecules for immune support.

10.6 The Physiology of Breastfeeding

Breastfeeding involves the coordinated action of:

- **Prolactin:** Stimulates milk production in the mammary gland
- **Oxytocin:** Facilitates milk ejection by causing contraction of the smooth muscle surrounding the milk ducts. (the "let-down" reflex).

Early Initiation of Breastfeeding (EIB) serves as a crucial step in initiating and establishing effective lactation. Efficient breast emptying is the key to sustaining milk production.

10.7 Some benefits of Breastfeeding

10.7.1 For Infants:

- Reduced incidence of infections (e.g., Pneumonia, otitis media),
- Lower risk of chronic conditions in adulthood (e.g., Diabetes, Leukemia, obesity),
- Enhanced cognitive development.

10.7.2 For Mothers:

- Reduced postpartum bleeding,
- Delayed return of fertility,
- Lower risks of breast and ovarian cancer,
- Decreased risk of type 2 Diabetes and cardiovascular disease.

10.8 Practical Challenges and Solutions

10.8.1 EARLY INITIATION OF BREASTFEEDING (EIB)

Early Initiation of Breastfeeding is essential, as it significantly decreases the risk of neonatal mortality. Unless there is a complication with the mother or the baby that prevents early initiation of breastfeeding (EIB), the baby should be delivered directly onto the mother's abdomen and allowed to "crawl" to the breast and start suckling. This process is like a light switch that kicks start the process of establishing successful breastfeeding.

10.8.2 Bottle Feeding

Health workers must be cautious about recommending feeding bottles, as mothers may not always be able to clean them due to inadequate water supplies and facilities for boiling and sterilizing. Feeding bottles and teats may also lead to nipple confusion, causing difficulties with latching.

10.8.3 Prematurity

Feeding methods vary (tube, cup, cup and spoon) based on gestational age and coordination of the suck-swallow reflex. Expressed breast milk is the food of choice for every preterm baby, unless there is a genuine contraindication, such as an inborn error of metabolism, in which case breastmilk is contraindicated.

10.8.4 Mouth Abnormalities

Mouth conditions, such as cleft lip and/or palate, or severe oral thrush, may necessitate expressed milk and alternative feeding methods.

10.8.5 Multiple Births

Frequent feeding stimulates supply. Twins and triplets can be exclusively breastfed with proper support for the mother. Higher multiples should also start with exclusive breastfeeding, but are likely to outgrow a mother's milk supply rapidly and require supplementation. Support for the mother, making sure she is relieved of as many other chores as possible, is key to successful breastfeeding in multiple pregnancies.

10.8.6 Perceived or Real Milk Insufficiency

It is common for mothers, especially first-time mothers, to lack confidence in their ability to breastfeed and to feel they do not have enough breast milk. Once the baby is gaining weight and is generally well, support and counseling are essential and are often all that is needed. True breastmilk insufficiency is rare but distressing when it occurs. Good expression techniques can help maintain a sufficient milk supply.

10.8.7 Maternal Illness

Most conditions, including maternal tuberculosis and HIV (with precautions), are not necessarily contraindications to breastfeeding. Support and education are critical. When a mother is ill, it is important not to assume that she cannot breastfeed, but rather to objectively assess the risk to the baby as against the many benefits the baby will receive from breastfeeding. National guidelines, where available, should be consulted, and each mother and baby dyad assessed carefully. The decision not to breastfeed should never be made lightly, as even where the family can afford and correctly prepare infant formula, the risk of illnesses such as asthma and allergies may be increased. Where the ability to sustain adequate formula feeding is a challenge to the family, the effect on the child's health can be disastrous.

10.8.8 Mothers in Formal Employment

Supportive workplaces (Baby Friendly Workplaces), extended paid maternity leave, effective use of hand expression, and good-quality breast pumps are some of the ways to help mothers who work outside the home to continue breastfeeding. Breast pump technology has evolved over the years so that there are, for example, wearable hands-free breast pumps which can discreetly pump breast milk whilst the mother is at work. However simple, correctly done hand expression of breast milk is very effective. Breast milk can then be stored at room temperature for 6 hours, in a good fridge with a temperature of 6-7^{o}C for 24 hours, and in a deep freezer or fridge freezer at a temperature of -17^{o}C and below for 6 months. The milk can then be fed to the baby by cup by whoever is caring for the child.

10.9 Counteracting Challenges to Breastfeeding

Barriers to breastfeeding in Ghana include:

- Aggressive and inappropriate marketing and promotion of Infant Formula by companies that manufacture and sell Infant Formula.
- Negative cultural attitudes to breastfeeding.
- Lack of support from health professionals or family.

10.9.1 Solutions

- Community education,
- Health worker training,
- Advocacy for breastfeeding-friendly policies.

10.10 Conclusion

Breastfeeding is a public health priority with far-reaching benefits for infants, mothers, and society. Despite its challenges, successful breastfeeding is achievable with informed support, early initiation, and continued advocacy. As science reveals more about the biology of breastmilk, our responsibility to protect and promote breastfeeding becomes ever more urgent.

10.11 Recommended Reading and Viewing

- The Ghana National Breastfeeding Policy
- The Lancet Breastfeeding Series (2016 and 2023)
- Global Health Media videos on breastfeeding
- Human Milk and Brain Development in Infants
- The Ghana National Policy on PMTCT of HIV

Part III

Pulmonology

11 Basics

11.1 Introduction

Pediatric pulmonology is a vital subspecialty of pediatrics that focuses on the structure and function of the lungs and respiratory tract in infants, children, and adolescents. To understand pediatric respiratory diseases and their clinical manifestations, a solid grasp of the **anatomical**, **physiological**, **embryological**, **biochemical**, and **pathophysiological** underpinnings of the pediatric respiratory system is essential.

This foundational knowledge enables clinicians to recognize what is normal, anticipate how and why diseases develop, and determine appropriate investigations and interventions. This write-up provides a focused introduction to these aspects, tailored to the context of medical education in Ghana.

11.2 Anatomy of the Pediatric Respiratory System

The pediatric respiratory system consists of the **upper airway**, **lower airway**, and **lungs**, with supporting structures including the thoracic cage and diaphragm.

11.2.1 Upper Airway:

Includes:

- **Nasal cavity** – filters, humidifies, and warms inspired air
- **Nasopharynx, oropharynx, and laryngopharynx** – direct airflow toward the larynx
- **Larynx** – houses the vocal cords; functions in phonation and protection during swallowing

Clinical relevance: Infants are obligate nose breathers. Even mild nasal congestion can lead to significant respiratory distress.

11.2.2 Lower Airway:

Includes:

- **Trachea** – extends from the cricoid cartilage to the carina
- **Bronchi** – right main bronchus is shorter and more vertical
- **Bronchioles** – terminal and respiratory
- **Alveolar ducts and alveoli** – site of gas exchange

Age-related note: The airway diameter in neonates is narrow, which increases resistance and the risk of obstruction.

11.2.3 Lungs:

- Right lung has **three lobes**, left lung has **two lobes**
- Lungs are surrounded by a pleural membrane
- Richly supplied with blood vessels and lymphatics

11.2.4 Thoracic Cage and Diaphragm:

- Ribs are more horizontal in infants
- Diaphragm is the main muscle of respiration; intercostal muscles assist with increasing age

11.3 Physiology of the Pediatric Respiratory System

Respiratory physiology involves **ventilation**, **perfusion**, and **gas exchange**, as well as **control of breathing** and **defense mechanisms**.

11.3.1 Ventilation:

The process of moving air into and out of the lungs.

- **Tidal volume (VT):** Volume of air moved in and out per breath (~6–8 mL/kg in children)
- **Minute ventilation:** VT × respiratory rate
- **Compliance:** Children have **high chest wall compliance**, meaning it deforms easily, but **low lung compliance**, especially in neonates

Clinical note: High compliance of the chest wall predisposes neonates to respiratory fatigue.

11.4 Gas Exchange:

Occurs at the alveolar-capillary interface:

- **Oxygen (O)** diffuses from alveoli to blood
- **Carbon dioxide (CO)** diffuses from blood to alveoli

Dependent on:

- Surface area of alveoli
- Thickness of the alveolar-capillary membrane
- Adequate ventilation-perfusion (V/Q) matching

11.5 Control of Breathing:

Controlled by centers in the **medulla** and **pons**, modulated by:

- **Chemoreceptors** (central: respond to CO ; peripheral: respond to O)
- **Stretch receptors** in the lungs
- Voluntary control is limited in neonates

Age-specific physiology:

- Infants have periodic breathing and are prone to apneas
- Immature respiratory drive increases risk of hypoventilation

11.5.1 Defense Mechanisms:

- **Nasal hairs and mucosa** trap particles
- **Mucociliary clearance** moves mucus upward toward the oropharynx
- **Cough reflex** clears lower airways
- **Immune defense:** IgA in secretions, macrophages in alveoli

11.6 Embryology of the Respiratory System

11.6.1 Development Timeline:

- **Week 4**: Respiratory diverticulum (lung bud) arises from foregut endoderm
- **Week 5–7**: Formation of primary, secondary, and tertiary bronchi
- **Week 16**: Terminal bronchioles formed
- **Week 24**: Respiratory bronchioles begin to develop

- **Week 28–36**: Alveolar ducts and primitive alveoli form
- **Birth to 8 years**: Postnatal alveolar multiplication (from ~20 million at birth to ~300 million)

11.6.2 Embryological Germ Layers:

- **Endoderm**: Forms the epithelium of the airways and alveoli
- **Mesoderm**: Forms connective tissue, cartilage, smooth muscle, and blood vessels

11.6.3 Lung Maturation Stages:

1. **Pseudoglandular (weeks 5–17):** Branching of airways; no gas exchange possible
2. **Canalicular (weeks 16–25):** Formation of airspaces; capillary network appears
3. **Saccular (weeks 24–36):** Terminal sacs form; beginning of surfactant production
4. **Alveolar (week 36 to 8 years):** Alveoli mature and multiply

11.6.4 Surfactant:

Produced by **type II pneumocytes** from ~week 24, with sufficient amounts by ~week 34.

Function: Reduces surface tension in alveoli, preventing collapse during expiration

Clinical relevance: Premature infants often lack surfactant, a substance that can lead to respiratory distress.

11.7 Biochemistry of the Respiratory System

11.7.1 Gas Transport:

- **Oxygen Transport:**
  - 98% carried by hemoglobin
  - Oxyhemoglobin dissociation curve describes the relation between PaO and SaO
  - Fetal hemoglobin (HbF) has a **higher affinity** for oxygen than adult hemoglobin
- **Carbon Dioxide Transport:**
  - Dissolved in plasma (~10%)
  - Bound to hemoglobin as carbaminohemoglobin (~20%)
  - As **bicarbonate ions** (~70%) via carbonic anhydrase reaction:

11.8 Acid-Base Balance:

- **Lungs regulate pH** by excreting CO
- **Respiratory acidosis**: from hypoventilation (↑CO)
- **Respiratory alkalosis**: from hyperventilation (↓CO)

Maintaining proper ventilation is crucial to acid-base homeostasis in children.

11.9 Surfactant Biochemistry:

- Composed mainly of **phospholipids** (especially **dipalmitoylphosphatidylcholine - DPPC**)
- Also contains **surfactant proteins (SP-A, SP-B, SP-C, SP-D)** that help spread and regulate surfactant

Synthesis is cortisol-dependent, which is why maternal corticosteroids are given antenatally in preterm labor.

11.10 Pathophysiology of the Pediatric Respiratory System

Pathophysiology describes the **functional changes** that occur in response to disease or injury. Understanding these responses helps to explain signs such as **wheezing**, **cough**, **hypoxia**, and **tachypnea**.

11.10.1 Airway Obstruction:

- Can occur **extrathoracically** (e.g., larynx) or **intrathoracically** (e.g., bronchioles)
- Narrow pediatric airways mean even minor swelling or secretions cause significant resistance
- Leads to increased work of breathing, wheezing, or stridor

11.10.2 Ventilation-Perfusion (V/Q) Mismatch:

- Ideal: ventilation matches perfusion
- In disease (e.g., mucus plugging, consolidation), mismatch occurs
  - **Low V/Q**: alveoli are perfused but not ventilated → hypoxemia
  - **High V/Q**: alveoli are ventilated but not perfused → wasted ventilation

11.10.3 Hypoventilation:

- Due to fatigue, CNS depression, or neuromuscular disease
- Leads to **hypercapnia** and **respiratory acidosis**

11.10.4 Surfactant Deficiency:

- Causes alveolar collapse (atelectasis)
- Reduces lung compliance
- Seen in premature infants or inactivation by infection/inflammation

11.10.5 Immature Immune System:

- Neonates have limited production of IgA, poor neutrophil function
- Makes them vulnerable to respiratory infections

11.11 Conclusion

The pediatric respiratory system is uniquely structured and regulated, necessitating a comprehensive understanding of its **anatomy**, **development**, **biochemistry**, **physiology**, and **response to disease**. Medical students should appreciate how these fundamental sciences interact in the context of health and disease. This understanding lays the groundwork for clinical reasoning, diagnosis, and management of respiratory illnesses in children.

In Ghana, where pediatric respiratory conditions are prevalent, this foundational knowledge becomes particularly crucial. As a future clinician, you are encouraged to integrate basic science with clinical practice to improve child health outcomes.

12 Respiratory Failure in Children

12.1 Introduction

Respiratory failure is a life-threatening condition in which the respiratory system fails to maintain adequate oxygenation and/or carbon dioxide elimination. In paediatrics it is a frequent final common pathway of many severe illnesses — particularly pneumonia, bronchiolitis, severe asthma, and sepsis — and is a major contributor to childhood mortality in low- and middle-income countries including Ghana. Recognition of early signs, understanding the underlying pathophysiology, and prompt institution of supportive measures are essential skills for the medical student and junior clinician.

Children differ from adults in airway anatomy, chest wall compliance, metabolic rate and reserve, which makes them prone to rapid deterioration. Where resources are limited, timely clinical assessment, oxygen therapy, and basic respiratory support often determine outcome.

12.2 Classification and Basic Concepts

Respiratory failure is commonly classified by the dominant gas-exchange abnormality:

- **Hypoxaemic (Type I)** respiratory failure — impaired oxygenation (PaO $<$ 60 mmHg) with normal or low PaCO . Typical causes include pneumonia, acute respiratory distress syndrome (ARDS), pulmonary oedema and large shunts.
- **Hypercapnic (Type II)** respiratory failure — inadequate alveolar ventilation resulting in raised PaCO (>50 mmHg). Causes include severe airway obstruction (status asthmaticus), respiratory muscle fatigue, central depression of respiration, and neuromuscular disease.
- **Mixed respiratory failure** combines both elements and is common in advanced respiratory disease or severe sepsis.

Understanding the difference is practical: hypoxaemia requires restoration of oxygenation (oxygen and recruitment of alveoli), while hypercapnia indicates a need to improve ventilation (support minute ventilation).

12.3 Pathophysiology — how failure develops

Effective respiration requires airway patency, adequate ventilatory drive and muscle function, properly functioning lung units for diffusion, and coordinated perfusion. Disruption to any of these leads to failure.

In **ventilatory failure**, the work of breathing exceeds the capacity of respiratory muscles; progressive fatigue causes hypoventilation and CO retention. Children with severe asthma, upper airway obstruction, or neuromuscular weakness may decompensate rapidly.

In **oxygenation failure**, processes such as alveolar consolidation (pneumonia), surfactant deficiency (preterm infants), pulmonary oedema, or widespread inflammation (ARDS) reduce the effective surface area for oxygen diffusion. Ventilation-perfusion mismatch and intrapulmonary shunting contribute to refractory hypoxaemia.

Neonates and infants are particularly vulnerable because of small functional residual capacity, high oxygen consumption, and immature control of breathing — they desaturate quickly once compromise begins.

12.4 Aetiology — common causes in Ghana

The spectrum of causes varies with age and setting. In Ghanaian paediatric practice, the most frequent precipitants are:

- **Infectious lower respiratory disease:** severe community-acquired pneumonia, TB in older children, and bronchiolitis in infants.
- **Asthma exacerbations:** poorly controlled asthma presenting with severe bronchospasm.
- **Sepsis and severe malaria:** systemic illness that increases oxygen demand and may cause ARDS or metabolic acidosis.
- **Upper airway obstruction:** foreign body aspiration, croup, or deep neck infections.
- **Neonatal causes:** surfactant deficiency, meconium aspiration, congenital pneumonia, and persistent pulmonary hypertension.
- **Neuromuscular disease or central depression:** e.g., head injury, meningitis, or drug overdose.

Resource constraints, delayed presentation, and coexisting malnutrition or anaemia often worsen the clinical picture.

12.5 Clinical presentation and early recognition

Respiratory failure may present subtly. Early identification hinges on careful observation and monitoring. Important clinical features are:

- **Increased work of breathing:** tachypnoea, nasal flaring, intercostal/subcostal retractions, tracheal tug, and use of accessory muscles.
- **Abnormal breathing patterns:** grunting (infants), prolonged expiratory phase (asthma), or shallow irregular respirations.
- **Hypoxia signs:** central cyanosis (late), restlessness, agitation, poor perfusion, and tachycardia progressing to bradycardia.
- **Hypercapnia signs:** headache and drowsiness in older children; in infants, poor feeding and lethargy are common.
- **Failure to feed, pallor, and altered consciousness** indicate severe or advanced disease.

Because children compensate well until late, a sudden collapse may occur. Routine use of pulse oximetry at triage helps detect hypoxaemia before clinical cyanosis appears.

12.6 Investigations — practical approach

Confirmatory investigation is an arterial blood gas (ABG), which defines oxygenation and ventilation status and reveals acid-base disturbance. In many settings, ABG may be unavailable, so clinical assessment and pulse oximetry guide most initial decisions.

Additional useful tests:

- **Pulse oximetry:** continuous SpO monitoring.
- **Chest X-ray:** identifies consolidation, pneumothorax, pleural effusion or cardiomegaly.
- **Blood tests:** full blood count, blood cultures, electrolytes, lactate and blood glucose.
- **Viral testing** or nasopharyngeal aspirate for bronchiolitis where available.
- **Point-of-care tests:** malaria rapid tests and HIV testing as clinically indicated.
- **Ultrasound:** lung ultrasound can detect consolidation and effusion at the bedside.

Interpret findings in the clinical context: a high PaCO points to ventilatory failure and need for ventilatory support; severe hypoxaemia with low PaCO suggests shunt physiology and oxygenation failure.

12.7 Management principles

Management aims to reverse hypoxaemia and/or hypercapnia, treat the underlying cause, and prevent complications. Interventions should be guided by severity and available resources.

12.7.1 Immediate actions

Apply the ABC approach. Ensure airway patency, give supplemental oxygen early, and support ventilation if there are signs of respiratory compromise. Keep the child warm, monitor glucose, and establish IV access (or IO in emergencies). Treat reversible causes such as severe asthma with bronchodilators and steroids, or sepsis with timely antibiotics.

12.7.2 Oxygen therapy

Oxygen is the cornerstone for hypoxaemic children. Start with low-flow oxygen via nasal prongs or face mask, titrating to target SpO levels appropriate for age (generally 92% in older children; lower targets may apply for certain neonates/conditions). Where available, high-flow nasal cannula (HFNC) or CPAP provides effective respiratory support in moderate distress, reducing the need for intubation in many cases.

12.7.3 Non-invasive and invasive ventilation

When oxygen alone is insufficient (persistent hypoxaemia on high FiO , rising PaCO , or respiratory fatigue), provide ventilatory support. Non-invasive options such as CPAP and BiPAP are useful for selected patients. Intubation and mechanical ventilation become necessary for respiratory arrest, severe hypercapnia, or inability to protect the airway. Mechanical ventilation requires skilled staff and monitoring to avoid complications such as barotrauma and ventilator-associated pneumonia.

12.7.4 Specific therapies

Treat the underlying pathology: antibiotics for bacterial pneumonia, bronchodilators and systemic steroids for asthma, surfactant for neonatal respiratory distress syndrome (where indicated), diuretics for cardiogenic pulmonary oedema, and bronchoscopy for airway foreign bodies.

12.7.5 Supportive care

Adequate hydration, nutritional support, correction of anaemia, and seizure control (if present) are vital. Prevent and manage complications like pneumothorax promptly. Keep meticulous infection control practices and consider early transfer to higher-level care when advanced ventilation or paediatric intensive care is needed.

12.8 Monitoring and escalation

Continuous monitoring of oxygen saturation, heart rate and respiratory rate is essential. Frequent reassessment of work of breathing, mental state, and perfusion identifies deterioration. ABG monitoring guides ventilatory adjustments where available. Escalate care promptly if hypoxaemia persists despite maximal non-invasive support, or if CO retention or acidosis worsens.

12.9 Complications and long-term outcomes

Untreated or prolonged respiratory failure can cause hypoxic brain injury, multi-organ dysfunction, and death. Survivors may develop chronic lung disease, neurodevelopmental impairment (especially after neonatal respiratory failure), or recurrent respiratory morbidity. Prevention of complications, early protective ventilation strategies and rehabilitation improve long-term outcomes.

12.10 Prevention and public health considerations

Reducing the burden of respiratory failure in Ghana requires both clinical and public health measures. Strengthening immunisation (pneumococcal, Haemophilus influenzae type b, measles, pertussis, and influenza), improving indoor air quality, promoting exclusive breastfeeding, and early care-seeking for respiratory symptoms reduce disease incidence. At the facility level, training in paediatric emergency care, widespread availability of pulse oximetry, oxygen concentrators, and basic CPAP devices have high impact even in resource-limited hospitals.

12.11 Practical tips for the Ghanaian setting

Simple interventions save lives: triage with pulse oximetry, give oxygen early to any child with respiratory distress, use CPAP for neonates and infants when available, and ensure rapid antibiotic administration for suspected severe pneumonia. Implementing standardised early warning signs, training in paediatric airway management, and protocols for escalation of care greatly improve outcomes.

12.12 Conclusion

Respiratory failure in children is a medical emergency that demands prompt recognition and decisive action. Familiarity with the physiological differences of children, common causes in the local context, and a stepwise approach to oxygenation and ventilation are essential competencies for medical students and clinicians. While advanced therapies exist, many deaths from respiratory failure are preventable with timely basic interventions, improved public health measures, and strengthened paediatric acute care capacity across Ghana.

13 Asthma

13.1 Introduction

Asthma is a chronic inflammatory disorder of the airways, characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation. It is one of the most common chronic diseases in children worldwide, including in Ghana. Effective management is essential in pediatric care, especially due to its impact on the quality of life, school attendance, and healthcare utilization.

Understanding asthma in children is crucial for early diagnosis, effective management, and the prevention of complications. This note outlines the epidemiology, pathophysiology, clinical features, diagnosis, differential diagnoses, management, and public health implications of childhood asthma, with a focus on the context of Ghanaian healthcare.

13.2 Epidemiology

Asthma affects an estimated 10-15% of children in Ghana, although its prevalence varies by region, urbanization, and environmental factors. Urban areas such as Accra and Kumasi report higher cases due to increased pollution, lifestyle changes, and indoor allergens.

Risk Factors:

- **Genetics:** Family history of asthma or atopy (eczema, allergic rhinitis).
- **Environmental exposures:** Dust, smoke (including biomass fuel), pollution, and cockroach or mould allergens.
- **Infections:** Respiratory syncytial virus (RSV), influenza.
- **Socioeconomic status:** Overcrowded housing, poor ventilation.
- **Early weaning or formula feeding.**

13.3 Pathophysiology

Asthma is mainly an inflammatory disease that affects the airways. In children, this airway inflammation is often eosinophilic and results in:

1. **Airway Hyperresponsiveness:** Increased sensitivity to triggers such as cold air, dust, or exercise.
2. **Bronchoconstriction:** Constriction of bronchial smooth muscles causes narrowing of airways.
3. **Airway Remodelling (in chronic cases):** Thickening of the basement membrane, increased mucus secretion, and smooth muscle hypertrophy.

These changes contribute to the classic symptoms: wheezing, cough, chest tightness, and shortness of breath.

13.4 Clinical Features

The presentation of asthma in children may vary based on age and severity. Key symptoms include:

- **Wheezing:** High-pitched whistling sound, often during expiration.
- **Coughing:** Worse at night, early morning, or after exercise.
- **Shortness of breath:** This is especially noticeable during exertion or with infections.
- **Chest tightness or pain.**

Patterns of Childhood Asthma:

- **Intermittent asthma:** Symptoms occur less than twice a week.
- **Persistent asthma:** Symptoms occur more frequently and may impact daily activities.
- **Exercise-induced asthma:** Triggered by physical activity.
- **Nocturnal asthma:** Symptoms worsen at night.
- **Viral-induced wheeze:** Common in toddlers; often resolves with age.

In Ghana, children may also present late or with severe symptoms due to poor access to healthcare or misdiagnosis.

13.5 Diagnosis

Asthma is primarily a clinical diagnosis in children, especially those under 5 years of age.

1. History:

- Recurrent episodes of cough, wheeze, and breathlessness.
- Family or personal history of allergies.
- Symptoms triggered by cold, dust, exercise, or smoke.

2. Physical Examination:

- Wheezing on auscultation.
- Use of accessory muscles in severe cases.
- Hyperresonance on percussion in chronic cases.

3. Investigations:

- **Spirometry (in children >5 years):** Shows reversible airway obstruction (FEV1/FVC ratio $< 80\%$).
- **Peak Expiratory Flow Rate (PEFR):** Helps monitor asthma control.
- **Chest X-ray:** To exclude other conditions (e.g., foreign body, pneumonia).
- **Allergy testing:** Useful in atopic children (skin prick or serum IgE)

Diagnostic Challenge in Ghana:

- Limited access to spirometry in rural settings.
- Reliance on clinical judgment.
- Misdiagnosis as pneumonia or bronchitis is common.

13.6 Differential Diagnosis

- **Bronchiolitis:** Common in infants; usually due to viral infections.
- **Foreign body aspiration:** Sudden onset of wheeze with localized findings.
- **Pneumonia:** Fever with cough; may have focal crepitations or consolidation.
- **Congenital anomalies:** E.g., tracheomalacia or vascular rings.
- **Tuberculosis:** Chronic cough, weight loss, and a history of contact.

13.7 Management

1. Education and Self-Management

- Educate caregivers and older children on:
  - Nature of asthma.
  - Avoidance of triggers.
  - Proper inhaler technique.
  - Recognition of early warning signs.
  - Importance of medication adherence

2. Pharmacologic Management

a. Reliever Medications:

- **Short-acting beta2-agonists (SABA):** e.g., *Salbutamol.*

  - First-line for acute symptoms.
  - Delivered via metered-dose inhaler (MDI) with a spacer.

b. Controller Medications

- **Inhaled corticosteroids (ICS):** e.g., *Beclomethasone, Budesonide*
  - First-line for persistent asthma.
- **Leukotriene receptor antagonists (LTRA):** e.g., *Montelukast.*
  - Useful for allergic or exercise-induced asthma.
- **Long-acting beta2-agonists (LABA):** Used in combination with ICS in older children with poor control.

c. Systemic corticosteroids:

- *Prednisolone* for acute exacerbations (short course).

3. Non-Pharmacological Measures

- Avoid known allergens (dust, cockroach, pet dander).
- Reduce exposure to cigarette smoke and biomass fuel.
- Immunization (including flu vaccine where available).
- Treatment of comorbidities (e.g., allergic rhinitis).

13.8 Acute Exacerbations

Signs:

- Rapid breathing, use of accessory muscles.
- Inability to speak in full sentences.
- Cyanosis or drowsiness (life-threatening).

Management:

1. **Assess severity (mild, moderate, severe, life-threatening).**
2. **Oxygen therapy:** Maintain SpO $> 92\%$.
3. **Nebulized SABA:** e.g., Salbutamol every 20 minutes for 1 hour.
4. **Oral corticosteroids:** Prednisolone 1–2 mg/kg/day for 3–5 days.
5. **Ipratropium bromide:** In severe cases, combined with SABA.
6. **Magnesium sulphate IV:** In very severe or unresponsive cases.
7. **Referral:** If there is a poor response or worsening symptoms

13.9 Monitoring and Follow-up

- Review asthma control every 1–3 months.
- Monitor growth in children on long-term corticosteroids.
- PEFR monitoring for older children.
- Step-up or step-down therapy based on control.

13.10 Asthma Control Criteria (based on GINA):

- Daytime symptoms 2 times/week.
- No night waking.
- No limitation of activity.
- Minimal reliever use.
- No exacerbations.

13.11 Challenges in the Ghanaian Context

- **Limited diagnostic tools:** Lack of spirometry or PEFR in rural facilities.
- **Access to medication:** Inhalers may be expensive or unavailable.
- **Cultural beliefs:** Asthma is often attributed to spiritual causes.
- **Poor adherence** Due to a lack of understanding or medication side effects.
- **Stigma:** Especially among school children using inhalers.
- **Environmental triggers:** Open burning, indoor smoke, and dust.

13.12 Public Health Interventions

- **Health education:** Community sensitization on asthma and triggers.
- **School health programs:** Identification and management of asthma in schools.
- **Policy support:** Include essential asthma medications in the National Health Insurance Scheme (NHIS).
- **Training healthcare providers:** On asthma diagnosis and management.

13.13 Conclusion

Asthma in children is a significant public health issue in Ghana. Early recognition, accurate diagnosis, and comprehensive management can greatly enhance outcomes. Medical students need to be prepared to address asthma in both urban and rural environments, understand the

unique challenges in Ghana, and advocate for improved care across all levels of the healthcare system.

Key Takeaways for Medical Students**:**

- Always consider asthma in a child with recurrent cough or wheeze.
- A detailed history and clinical examination are often sufficient for diagnosis.
- Use inhale corticosteroids for long-term control and SABAs for quick relief.
- Educate families and monitor regularly.
- Advocate for improved access to asthma care in Ghana.

14 Bronchiolitis

14.1 Introduction

Bronchiolitis is a common viral infection of the lower respiratory tract that primarily affects infants and young children. It is the leading cause of hospitalization for children under 2 years of age worldwide. In Ghana and other sub-Saharan African countries, bronchiolitis significantly contributes to infant morbidity and mortality, especially during the harmattan season when respiratory infections are more prevalent.

Understanding bronchiolitis is essential for medical students, particularly in environments where diagnostic tools are scarce and treatment depends largely on clinical skills and supportive care.

14.2 Definition

Bronchiolitis is defined as an **acute viral infection of the lower respiratory tract**, primarily affecting the **bronchioles**. It leads to inflammation, edema, and increased mucus production, resulting in **airway obstruction**, **wheezing**, and **respiratory distress**.

14.3 Epidemiology

- **Age group**: Primarily affects children **under 2 years**, most commonly **under 6 months**
- **Peak incidence**: During the **cold and dry months** (November to February in Ghana)
- **Transmission**: Highly contagious; spread via **respiratory droplets**, **direct contact**, or **contaminated surfaces**
- **High-risk groups**:
  - Premature infants
  - Infants with congenital heart disease
  - Children with chronic lung disease
  - Immunocompromised children
  - Children exposed to tobacco smoke or indoor air pollution

14.4 Etiology (Causative Agents)

The most common cause is **Respiratory Syncytial Virus (RSV)**, responsible for 50–80% of cases.

Other viruses:

- Human metapneumovirus
- Parainfluenza virus
- Influenza virus
- Rhinovirus
- Adenovirus
- Coronavirus

14.5 Pathophysiology

1. **Viral infection** of the **nasal and lower respiratory epithelium**
2. Inflammation and edema of the bronchioles
3. Necrosis and sloughing of epithelial cells
4. Increased mucus production and plugging of small airways
5. Air trapping and **hyperinflation**, leading to:
    - Increased work of breathing
    - Impaired gas exchange
    - **Hypoxia** and, in severe cases, **respiratory failure**

14.6 Clinical Features

History

- Starts as an **upper respiratory tract infection** (e.g., runny nose, mild cough)
- Progresses over 2–3 days to:
    - **Cough**
    - **Tachypnea**
    - **Wheezing**
    - **Poor feeding**
    - **Apnea** (especially in premature or very young infants)
    - **Fever** (may or may not be present

Examination

- **Tachypnea**
- **Nasal flaring**
- **Chest retractions** (intercostal, subcostal, suprasternal)
- **Wheezing** and **crackles** on auscultation
- **Hypoxia** (low oxygen saturation)
- **Dehydration**
- **Cyanosis** in severe cases

14.7 Differential Diagnosis

Condition	**Key Features**
Asthma	Older children (>2 years), recurrent episodes, personal/family history of atopy
Pneumonia	Fever, focal crackles, lobar consolidation on chest X-ray
Foreign body aspiration	Sudden onset, localized wheeze, asymmetric breath sounds
Congenital heart disease	Cyanosis, poor weight gain, murmur
Pertussis	Paroxysmal cough, whoop, post-tussive vomiting

14.8 Diagnosis

Clinical diagnosis is key in most settings, especially where investigations are limited.

Investigations (if available)

- **Pulse oximetry**: Assess oxygen saturation
- **Chest X-ray** (not routinely indicated): May show hyperinflation, peribronchial thickening, patchy atelectasis
- **Nasopharyngeal swab** for viral testing (e.g., RSV) – rarely available in Ghana
- **Complete blood count**: To rule out bacterial infection if fever is high or toxic appearance
- **Serum electrolytes**: In severely ill or dehydrated children

14.9 Severity Assessment

Mild

- Normal feeding
- Mild tachypnea, minimal retractions
- Oxygen saturation 92%

Moderate

- Poor feeding
- Moderate tachypnea and retractions
- Wheezing or crackles
- Oxygen saturation 90–92%

Severe

- Marked retractions, grunting, nasal flaring
- Apnea
- Cyanosis
- Oxygen saturation $< 90\%$
- Lethargy or altered mental status

14.10 Management

14.10.1 General Principles

- Most cases are **self-limiting** and can be managed with **supportive care**
- Hospitalization is required for:
  - Moderate to severe disease
  - Apnea
  - Inability to feed
  - Oxygen saturation $< 90\%$
  - High-risk infants

14.10.2 Outpatient (Home-Based) Management

- Ensure **adequate hydration** and feeding
- Educate caregivers on danger signs:
  - Rapid breathing
  - Chest in-drawing

  - Inability to feed
  - Cyanosis
  - Lethargy

- Clear nasal secretions with saline drops/suction
- Follow-up in 24–48 hours

14.10.3 Inpatient (Hospital) Management

1. Supportive Care

- **Oxygen therapy**:
  - Give oxygen if SpO $< 90\%$
  - Via nasal prongs or face mask
- **Hydration and nutrition**:
  - Encourage breastfeeding or oral feeds
  - NG tube feeding or IV fluids if unable to feed orally
- **Monitoring**:
  - Respiratory rate
  - Oxygen saturation
  - Fluid status
  - Level of consciousness

14.10.4 Medications (Avoid routine use)

Medication	Recommendation
Bronchodilators (e.g., salbutamol)	Not routinely recommended; trial may be considered in wheezing children >12 months
Steroids	Not beneficial in uncomplicated bronchiolitis
Antibiotics	Not indicated unless bacterial co-infection suspected (e.g., pneumonia, otitis media)
Nebulized hypertonic saline	Limited evidence; not routinely used in Ghana
Antiviral agents	Not routinely available or used in Ghana

14.11 Complications

- **Apnea**
- **Respiratory failure**
- **Dehydration and poor nutrition**
- **Secondary bacterial infections**
- **Recurrent wheezing or asthma-like episodes** later in life
- **Death** (in severe, untreated cases, particularly in high-risk infants)

14.12 Prevention

1. Infection Control

- **Hand hygiene**
- **Avoid crowding**, especially in daycares and nurseries
- Educate caregivers on **cough etiquette**

2. Breastfeeding

- Exclusive breastfeeding for the first **6 months** provides protective antibodies

3. Avoid Smoke Exposure

- Avoid smoking near infants
- Reduce indoor air pollution (e.g., smoke from firewood)

4. Immunization

- Ensure up-to-date **vaccination**, especially:
  - **Influenza vaccine**
  - **Pneumococcal vaccine**
  - **Pertussis vaccine**

5. Prophylaxis (Palivizumab)

- A monoclonal antibody used for **RSV prophylaxis**
- Expensive and not readily available in Ghana
- Considered only for **very high-risk infants** in specialized centers

14.13 Prognosis

- Most children **recover fully within 7–10 days**
- **Cough** may persist for 2–3 weeks
- Infants with severe disease may have **recurrent wheezing or asthma**

14.14 Special Considerations in Ghana

- **Overcrowded homes** and **poor air quality** increase risk
- Health-seeking behavior may be delayed due to cultural beliefs or access issues
- Resource limitations often mean:
  - Reliance on clinical diagnosis
  - Limited access to oxygen and pulse oximetry
- Need for **education of caregivers** about early signs of respiratory distress
- Emphasize **community-based health interventions** (e.g., CHPS compounds)

14.15 Case Scenario

Case: 4-month-old male infant

Presentation:

- 3-day history of cough, runny nose, and poor feeding
- Developed fast breathing and wheezing today
- No fever
- No significant past medical history

On examination:

- RR: 68 breaths/min
- Chest retractions present
- O saturation: 88% on room air
- Nasal flaring, scattered wheeze

Diagnosis:

- Likely **moderate to severe bronchiolitis**

Management:

- Admit for supportive care

- Oxygen via nasal prongs
- NG tube feeding due to poor suck
- Monitor vitals and oxygen saturation
- Educate mother on hand hygiene and signs of deterioration

14.16 Summary Table

Feature	**Bronchiolitis**
Age group	< 2 years (commonest < 6 months)
Onset	Gradual, following URTI
Common virus	RSV
Main symptoms	Cough, wheeze, tachypnea, and feeding difficulty
Diagnosis	Clinical
Mainstay of treatment	Supportive care
Antibiotics	Not routinely indicated
Oxygen	If SpO $< 90\%$
Prognosis	Excellent in most cases

14.17 Conclusion

Bronchiolitis is a common and potentially severe illness affecting infants and young children in Ghana. Early recognition and supportive management are essential to preventing complications. Medical students need to be familiar with its presentation, clinical evaluation, and evidence-based treatment, especially in resource-limited healthcare settings where advanced diagnostics may not be available.

15 Croup

15.1 Introduction

Croup, medically known as laryngotracheobronchitis, is a common acute upper respiratory illness in children, characterized by inspiratory stridor, a barking cough, and hoarseness. It typically results from a viral infection that causes inflammation of the larynx, trachea, and bronchi. Though it is usually self-limiting, it can occasionally lead to life-threatening airway obstruction. Croup is particularly important for medical students and healthcare providers in Ghana, where respiratory infections are a leading cause of childhood morbidity, particularly during the rainy season when viral infections peak.

15.2 Epidemiology

- **Age group**: Primarily affects children between **6 months and 5 years**. The peak incidence occurs around **2 years of age**.
- **Gender**: Males are slightly more affected than females.
- **Seasonality**: Most cases occur during the rainy or cold seasons (June to October in Ghana), coinciding with an increase in viral respiratory infections.
- **Prevalence**: Although there is limited Ghana-specific data, studies across sub-Saharan Africa indicate that viral croup accounts for a significant proportion of paediatric respiratory admissions, particularly in urban areas such as Accra and Kumasi.

15.3 Etiology

Viral infections most commonly cause croup. The **Parainfluenza virus type 1** is the most frequent cause globally and in Ghana.

Common viral agents:

- **Parainfluenza viruses** (types 1, 2, 3)
- **Respiratory syncytial virus (RSV)**
- **Influenza A and B**
- **Adenoviruses**

- **Rhinoviruses**
- **Coronavirus (including some SARS-CoV-2 variants)**

These viruses infect and inflame the epithelial lining of the **upper airway**, leading to swelling, increased mucus, and narrowed air passages, especially in the subglottic region.

15.4 Pathophysiology

The hallmark of croup is **subglottic inflammation**. In the paediatric airway, the narrowest part is the **subglottic space**, located just below the vocal cords. Viral infection triggers:

- Mucosal oedema
- Cellular infiltration
- Increased mucus production

These changes reduce airway diameter, particularly during **inspiration**, leading to:

- **Stridor** (turbulent airflow)
- **Barking cough** (from irritated vocal cords)
- **Respiratory distress** in severe cases

Young children are especially vulnerable due to their **smaller airway diameter** and less developed respiratory musculature.

15.5 Clinical Features

The classic presentation involves:

Prodromal Phase:

- Begins with **non-specific upper respiratory symptoms**:
  - Nasal congestion
  - Rhinorrhoea
  - Low-grade fever
  - Mild cough

Croup Syndrome:

- **Barking cough** (seal-like)
- **Hoarseness**
- **Inspiratory stridor** (worse with agitation or crying)
- **Respiratory distress** (tachypnoea, nasal flaring, retractions)

- **Fever** (low to moderate)

Symptoms often **worsen at night**, leading to sudden parental concern.

Severity Classification:

1. **Mild**:
    - Occasional barking cough
    - No stridor at rest
    - No retractions
2. **Moderate**:
    - Frequent cough
    - Stridor at rest
    - Mild to moderate chest wall retractions
3. **Severe**
    - Marked stridor at rest
    - Severe retractions
    - Agitation or lethargy
    - Hypoxia (SpO $< 92\%$)
4. **Impending respiratory failure**:
    - Decreased level of consciousness
    - Fatigue
    - Cyanosis
    - Silent chest

15.6 Differential Diagnoses

Croup must be differentiated from other **causes of upper airway obstruction**:

Condition	**Key Differences**
Epiglottitis	Sudden onset, high fever, toxic appearance, drooling, "tripod" posture
Foreign body aspiration	Sudden choking episode, unilateral breath sounds
Bacterial tracheitis	High fever, purulent secretions, toxic look
Peritonsillar abscess	Older children, muffled voice, difficulty opening mouth
Retropharyngeal abscess	Neck stiffness, drooling, visible swelling on imaging

15.7 Diagnosis

Croup is primarily a **clinical diagnosis**, especially in resource-limited settings like many areas in Ghana.

Clinical Evaluation:

- Vital signs: look for tachypnoea, fever
- Oxygen saturation (pulse oximetry)
- General appearance: level of alertness, work of breathing

Investigations

- **Neck X-ray (AP view)**: May reveal the classic "steeple sign" (subglottic narrowing), although it is not routinely needed.
- **CBC, CRP**: Not usually necessary unless bacterial superinfection is suspected.
- **Nasopharyngeal swabs**: Can confirm viral aetiology, but are rarely done due to cost and availability.

15.8 Management

Management depends on **severity**. The key principles are:

- Relieve airway obstruction
- Reduce inflammation
- Minimize agitation
- Monitor for deterioration

15.8.1 General Measures:

- **Keep the child calm**: Crying worsens stridor.
- **Humidified air**: Traditionally used, though evidence is weak.
- **Supplemental oxygen**: For SpO $< 92\%$ or signs of hypoxia.

15.8.2 Pharmacologic Treatment

1. Corticosteroids

Mainstay of treatment, regardless of severity.

- **Dexamethasone** (preferred):

  - Dose: 0.15–0.6 mg/kg PO/IM/IV (max 10 mg)
  - Long half-life (~36–72 hours), a single dose is often enough

- **Prednisolone** (if dexamethasone unavailable):
  - Dose: 1 mg/kg/day PO for 3–5 days

Corticosteroids reduce airway inflammation, decrease hospital admissions, and shorten the duration of illness.

2. Nebulized Epinephrine (Racemic or L-epinephrine)

- Used for moderate to severe croup:
- Dose: 0.5 mL of 2.25% racemic epinephrine or 5 mL of 1:1000 L-epinephrine via nebulizer.
- Acts quickly but temporarily (1–2 hours), often used while waiting for the corticosteroid effect.
- Observe the child for 3–4 hours after administration for any rebound symptoms.

3. Antibiotics

Not indicated unless there is a suspicion of bacterial tracheitis or a secondary infection (high fever, toxic appearance, purulent secretions).

Monitoring and Admission Criteria

Admit if:

- Persistent stridor at rest following epinephrine
- Hypoxia (SpO $< 92\%$ on room air)
- Severe work of breathing
- Inadequate oral intake
- Age under 6 months
- Pre-existing comorbidities (e.g., sickle cell disease, malnutrition)

In Ghana, **admission should also be considered if reliable follow-up is uncertain**, especially in rural or underserved areas.

15.9 Complications

- Respiratory failure
- Secondary bacterial tracheitis
- Dehydration
- Rarely, death (usually in severe, untreated cases)

15.10 Prevention

- **Routine immunization**: Influenza and measles vaccines reduce incidence
- **Hand hygiene and cough etiquette**
- **Avoid exposure to sick contacts**, especially during viral seasons

15.11 Public Health Considerations in Ghana

- **Limited access to nebulizers or corticosteroids** in rural facilities may delay treatment.
- **Overcrowding and poor ventilation** increase the transmission of respiratory viruses.
- **Training community health workers** in the recognition and referral of severecases is crucial.
- Integration of **Integrated Management of Childhood Illness (IMCI)** strategies can help guide early treatment at the primary care level.

15.12 Conclusion

Croup is a common, self-limiting pediatric illness that can become life-threatening without prompt recognition and management. Medical students and practitioners in Ghana should be proficient in diagnosing croup based on clinical features and effectively managing it with corticosteroids and supportive care. Knowing when to escalate care is crucial, particularly in resource-constrained settings.

16 Pneumonia

16.1 Introduction

Pneumonia is an acute infection of the lung parenchyma, leading to inflammation and consolidation of the alveoli. It remains a major cause of childhood morbidity and mortality worldwide and is especially significant in low- and middle-income countries such as Ghana. Despite progress in immunization and child health services, pneumonia continues to account for a large proportion of paediatric hospital admissions and deaths, particularly among children under five years of age.

Understanding its causes, clinical presentation, and management is essential for medical students and young clinicians. The disease spectrum ranges from mild, self-limiting illness to severe, life-threatening conditions requiring intensive care.

16.2 Epidemiology and Burden

Globally, pneumonia is responsible for approximately 14% of all deaths in children under five. In sub-Saharan Africa, the burden is disproportionately high due to limited access to healthcare, malnutrition, and environmental risk factors such as indoor air pollution.

In Ghana, pneumonia is among the top five causes of under-five mortality. Both viral and bacterial pneumonias are common, and coinfections such as malaria, tuberculosis, or HIV-associated infections complicate the picture. The disease shows a seasonal pattern, often peaking during the rainy seasons when respiratory viruses are more prevalent. Neonates and young infants, malnourished children, and those with underlying chronic conditions such as congenital heart disease or HIV are at greater risk.

16.3 Aetiology

The causes of pneumonia vary with age, immune status, and environment.

16.3.1 In Neonates:

- *Bacterial:* Group B Streptococcus, Escherichia coli, Klebsiella species, Listeria monocytogenes.
- *Viral:* Respiratory syncytial virus (RSV) and cytomegalovirus (in congenital infection).

16.3.2 In Infants and Young Children:

- *Bacterial:* **Streptococcus pneumoniae** (pneumococcus) is the most common; **Haemophilus influenzae type b (Hib)** is important where vaccination coverage is low. **Staphylococcus aureus** causes severe, necrotizing pneumonia with empyema.
- *Viral:* RSV, parainfluenza, influenza, adenovirus, and human metapneumovirus are frequent, especially in the first two years of life.
- *Atypical: Mycoplasma pneumoniae* and *Chlamydia pneumoniae* appear more often in older children and adolescents.

16.3.3 In Immunocompromised Children:

- Opportunistic infections such as *Pneumocystis jirovecii*, cytomegalovirus, and fungal pneumonias may occur, particularly in HIV-positive children.

Environmental exposures, malnutrition, passive smoking, and crowded living conditions amplify susceptibility.

16.4 Pathophysiology

The lungs normally maintain sterility through effective mucociliary clearance, immune defenses, and cough reflexes. Pneumonia develops when these defenses are breached — by overwhelming microbial inoculation, impaired clearance, or immune compromise.

Microorganisms reach the alveoli by inhalation, aspiration, or via the bloodstream. The host immune response leads to inflammation, exudation of fluid and cells into the alveolar spaces, and impaired gas exchange.

Typical bacterial pneumonia leads to alveolar consolidation — a process in which alveoli are filled with exudate containing neutrophils and fibrin. This impedes oxygen diffusion and causes hypoxaemia.

Viral pneumonia, in contrast, causes interstitial inflammation, airway oedema, and epithelial necrosis, predisposing to secondary bacterial infection.

The degree of impairment depends on the virulence of the organism and host factors such as nutritional status, immunization history, and presence of comorbidities.

16.5 Clinical Features

The presentation of pneumonia varies with age and severity.

General symptoms include:

- Fever, often high-grade.
- Cough, which may be dry or productive in older children.
- Difficulty in breathing, nasal flaring, and grunting in infants.
- Poor feeding, irritability, or lethargy.

Physical findings:

- Tachypnoea is the most sensitive clinical sign. The WHO defines tachypnoea as:
  - >60 breaths/min in infants <2 months
  - >50 breaths/min in 2–12 months
  - >40 breaths/min in 1–5 years
- Chest indrawing, nasal flaring, or grunting indicate severe disease.
- Auscultation may reveal crackles, bronchial breath sounds, or decreased air entry.
- Cyanosis, hypoxia, and altered sensorium are signs of respiratory failure.

Infants and neonates may have nonspecific presentations; temperature instability, apnea, or poor feeding, making a high index of suspicion essential.

16.6 Differential Diagnosis

Several other conditions can mimic pneumonia, and distinguishing them is crucial for correct management:

- **Bronchiolitis** (in infants under 2 years) — wheezing and diffuse crackles rather than localized findings.
- **Asthma or viral-induced wheeze** — recurrent episodes with reversible airway obstruction.
- **Pulmonary tuberculosis** — chronic cough, weight loss, and failure to thrive, often with contact history.
- **Severe malaria** — fever and respiratory distress due to metabolic acidosis.
- **Congestive heart failure** — history of cardiac disease and signs of cardiomegaly or murmurs.

Clinical judgement, aided by investigations, guides differentiation.

16.7 Investigations

Diagnosis is often clinical, especially in resource-limited settings. However, investigations help confirm and classify pneumonia, identify complications, and guide therapy.

Basic Investigations:

1. **Pulse oximetry** — to assess oxygen saturation; hypoxaemia (<92%) indicates severe disease.
2. **Chest X-ray** — shows lobar consolidation, interstitial infiltrates, or pleural effusion.
3. **Full blood count** — leukocytosis with neutrophilia suggests bacterial infection; lymphocytosis may indicate viral infection.
4. **Blood culture** — useful for identifying pathogens but often low yield.
5. **Nasopharyngeal aspirate or PCR testing** — for viral pathogens where available.

Further investigations in selected cases:

1. **Sputum culture or tracheal aspirate** (in ventilated patients).
2. **HIV testing** in children with recurrent or severe pneumonia.
3. **Ultrasound or CT scan** if empyema, abscess, or foreign body is suspected.

In Ghana, reliance is often on clinical diagnosis supported by simple tests due to cost and availability limitations.

16.8 Treatment

The management of pneumonia involves supportive care, antimicrobial therapy, and treatment of complications.

16.8.1 1. Supportive Management

- **Oxygen therapy** for hypoxaemia using nasal prongs or face mask.
- **Hydration:** maintain fluid balance; overhydration may worsen pulmonary oedema.
- **Antipyretics** (e.g., paracetamol) for fever.
- **Nutritional support** to prevent catabolism.
- **Monitoring** of respiratory rate, SpO , and consciousness level.

16.8.2 2. Antibiotic Therapy

Empiric treatment is based on the likely pathogen and local resistance patterns:

- **Neonates:** Ampicillin plus gentamicin for 7–10 days.
- **Infants and older children:**
  - Outpatient: Oral amoxicillin for 5–7 days for mild pneumonia.
  - Inpatient (severe): IV ampicillin (or penicillin) plus gentamicin; add cloxacillin or ceftriaxone if *S. aureus* or Gram-negative sepsis is suspected.
  - Macrolides (e.g., azithromycin) for atypical infections.

Treatment is modified based on clinical response or culture results.

16.8.3 3. Management of Complications

- **Pleural effusion/empyema:** chest tube drainage and antibiotics.
- **Lung abscess:** prolonged antibiotic therapy; drainage if necessary.
- **Septicemia:** aggressive IV antibiotics and supportive care.
- **Respiratory failure:** CPAP or mechanical ventilation as indicated.

16.8.4 4. Discharge and Follow-up

Discharge once afebrile, feeding well, and maintaining oxygen saturation in room air. Follow-up in 1–2 weeks ensures full recovery and detects post-pneumonia complications such as bronchiectasis.

16.9 Complications

Complications occur more commonly with delayed treatment or virulent organisms. They include:

- Parapneumonic effusion or empyema
- Lung abscess
- Pneumatocele formation
- Septicemia and metastatic abscesses
- Bronchiectasis or chronic lung disease
- Acute respiratory failure and death

Prompt recognition and intervention are vital to prevent long-term morbidity.

16.10 Prevention

Preventive measures are among the most cost-effective interventions in child health.

Immunization plays a key role:

1. Pneumococcal conjugate vaccine (PCV13)
2. Haemophilus influenzae type b (Hib) vaccine
3. Measles and pertussis vaccines
4. Annual influenza vaccination in at-risk groups

Nutrition: Exclusive breastfeeding for the first six months, adequate complementary feeding, and vitamin A supplementation strengthen immunity.

Environmental control: Reducing exposure to tobacco smoke and indoor air pollution from biomass fuels.

Early treatment of illnesses such as malaria, HIV, and malnutrition decreases susceptibility to pneumonia.

Community education on danger signs and early health-seeking behavior significantly reduces mortality.

16.11 Prognosis

The outcome depends on the child's age, nutritional status, immune function, causative agent, and timeliness of treatment.

Most children with uncomplicated pneumonia recover fully with appropriate therapy. However, mortality remains high among neonates, severely malnourished children, and those with HIV or delayed presentation.

Recurrent or chronic infections may lead to lasting lung damage. Strengthening preventive strategies and early intervention are therefore crucial to reducing the burden of pneumonia in Ghana.

16.12 Conclusion

Pneumonia remains one of the most important paediatric health challenges in Ghana and across Africa. Understanding its pathophysiology, timely diagnosis, and appropriate management are fundamental skills for every medical student.

While antibiotics and supportive care remain the mainstay of treatment, prevention through vaccination, nutrition, and improved living conditions offers the greatest hope for sustainable

reduction in disease burden. A holistic approach that integrates clinical excellence with strong public health measures is the surest way to protect Ghana's children from this preventable killer.

17 Bronchopulmonary Dysplasia

17.1 Definition

Bronchopulmonary dysplasia (BPD) is a chronic lung disease that affects newborns, especially those born prematurely and requiring oxygen therapy. It damages the lungs and airways, causing tissue destruction in the lung's tiny air sacs. While most infants recover from BPD, some may have long-term breathing difficulties.

17.2 Incidence

Globally, the incidence in extremely preterm infants(< 28 weeks) ranges between 10-89%, while 40% of extremely low birth weight infants (<1000g) will develop BPD. At the Komfo Anokye Teaching Hospital, 44 out of 171 preterm babies admitted from January to April 2024 had Respiratory Distress Syndrome.

17.3 Aetiology

The causes of BPD vary and can be divided into:

Pre-natal - These include lack of maternal steroids, maternal smoking, Pregnancy-induced hypertension, preeclampsia, chorioamnionitis, hypoxia, congenital anomaly causing pulmonary hypoplasia, and genetic susceptibility.

Post-natal - These include prematurity, immature lungs, apnea, sepsis, need for mechanical ventilation and a Patent Ductus Arteriosus

17.4 Pathogenesis

BPD is a multifactorial process and is linked to immature lung tissue, prenatal factors and postnatal factors. Injury from mechanical ventilation and reactive oxygen species to the premature lungs in the presence of antenatal factors predisposing the lung to BPD forms the basis of the pathogenesis in preterm infants. This leads to an inflammatory response with

an increase in pro-inflammatory cytokines like IL-6 IL-8, and TNF alpha, along with growth factors (Transforming growth factors,), angiogenic factors (vascular endothelial growth factors, angiopoietin 2), which result in aberrant tissue repair and arrest in lung development. Dysregulated vascular and arrested alveolar development form the basis of the pathology seen in the new BPD. Histologically, BPD occurs when lung development arrests in the late canaliculi to the saccular stage of lung development. The pathology characteristically demonstrates decreased septation and alveoli hypoplasia resulting in simplified large alveoli and reduced availability for gaseous exchange.

17.5 Signs and symptoms

Initial findings in BPD are consistent with Respiratory Distress Syndrome. These include respiratory distress, tachypnea, chest retractions, tachycardia, and paradoxical breathing. Others include intermittent expiratory wheezing, crackles and frequent desaturations. There might be significant weight loss during the first 10 days of life.

17.6 Investigations

A Chest radiograph is often the first investigative modality employed The lung field may show a sponginess and decreased lung volumes. Others include areas of hyperventilation, atelectasis, pulmonary oedema, and pulmonary interstitial emphysema. A high-resolution CT Scan demonstrates abnormalities not readily seen with routine chest radiography. Infants with moderate or severe BPD must be screened for pulmonary hypertension at 36 post-menstrual age using an echocardiogram. In the intensive care unit, arterial blood gases may reveal the extent of hypoxia, hypercarbia or acidosis.

17.7 Treatment

Treatment is generally divided into two phases:

Acute phase - As previously mentioned, most cases of BPD present as Respiratory Distress Syndrome. Hence its management starts from this stage. This requires surfactant replacement with oxygen supplementation, Continuous Positive Airway Pressure, and mechanical ventilation when necessary. Antibiotics are initiated if chronic chorioamnionitis or an infective process is suspected. Others may insert an indwelling arterial line for treatment administration and parenteral nutrition

Long-term - Attention should be paid to the nutrition of the infant. When necessary, a fluid restriction may be required. Also, clinicians will need to minimise ventilator-associated

and oxygen-associated lung injury. Some pharmacological interventions may include steroids, diuretics and bronchodilators.

17.8 Complications

Recognised complications include decreased pulmonary function and defence, chronic reflux and microaspiration with a risk of aspiration pneumonia and chronic inflammation. Others develop asthma-like symptoms, exercise intolerance, pulmonary artery hypertension, systemic hypertension, poor neurodevelopmental outcomes, left ventricular hypertrophy and dysfunction.

17.9 Prognosis

Most babies with BPD recover completely but mortality ranges between 1% to 20% during the first year of life.

17.10 Differential diagnosis

These include pulmonary atelectasis, pneumonia, pulmonary hypertension, tracheomalacia and pulmonary interstitial emphysema.

18 Bronchiectasis

18.1 Introduction

Bronchiectasis is a chronic pulmonary disorder characterised by irreversible dilatation and distortion of the bronchi, associated with chronic inflammation, impaired mucociliary clearance, and recurrent respiratory infections. Although once thought to be rare, bronchiectasis remains a significant cause of childhood morbidity in many low- and middle-income countries, including Ghana.

In West Africa, persistent respiratory infections, tuberculosis, post-measles complications, and poorly treated severe pneumonias contribute substantially to the burden of disease. For clinicians, early recognition is crucial because timely treatment improves quality of life and reduces long-term lung damage.

This chapter provides a comprehensive overview of bronchiectasis in children, tailored to the realities of clinical practice in Ghana and neighbouring countries.

18.2 Epidemiology

- Bronchiectasis prevalence is under-reported in Africa due to limited diagnostic capacity, especially the low availability of CT scans.
- Higher prevalence occurs in areas with:
  - High rates of **severe pneumonia**, **tuberculosis**, and **HIV**.
  - Delayed access to quality healthcare.
  - Malnutrition and environmental exposures such as indoor air pollution.
- In Ghana, common antecedents include:
  - Recurrent pneumonia
  - Post-TB lung disease
  - Severe measles
  - Foreign body aspiration
  - Chronic aspiration from neurological impairment

Worldwide, non–cystic fibrosis (non-CF) bronchiectasis is more common in LMICs than CF-related bronchiectasis.

18.3 Pathophysiology

Bronchiectasis develops through a "vicious cycle" (or "vicious vortex") of:

18.3.1 Infection

Recurrent or severe infections initiate inflammation and disrupt mucociliary clearance.

18.3.2 Inflammation

Neutrophil-dominated inflammation leads to the release of proteases and oxidative stress, damaging bronchial walls.

18.3.3 Impaired Mucociliary Clearance

Damaged cilia and thick mucus impair clearance, predisposing to persistent infection.

18.3.4 Structural Damage

Bronchial dilatation becomes irreversible, leading to airflow obstruction, mucus plugging, and parenchymal destruction.

Factors contributing in Ghana include:

- Delayed treatment of pneumonia and TB
- Inadequate immunisation (especially measles)
- Chronic aspiration from gastro-oesophageal reflux

18.4 Aetiology

Common causes in children:

18.4.1 Post-Infectious (Most Common in Ghana)

- **Severe bacterial pneumonia**
- **Tuberculosis**
- **Post-viral infections**: measles, pertussis, adenovirus

18.4.2 Congenital and Genetic

- Cystic fibrosis (rare in West Africa)
- Primary ciliary dyskinesia
- Primary immunodeficiency

18.4.3 Obstruction

- Retained foreign body
- Tumours (rare)

18.4.4 Aspiration-Related

- Neuromuscular disorders
- Severe GERD
- Recurrent aspiration syndromes

18.4.5 Immunodeficiency

- HIV
- Antibody deficiency (e.g., IgG subclass deficiency)

18.5 Clinical Features

Symptoms often begin after a severe pneumonia or gradually over months to years.

18.5.1 Respiratory Symptoms

- Chronic wet or productive cough (hallmark)
- Sputum that is:
  - Mucoid or purulent
  - Persistent despite antibiotic use
- Recurrent or persistent pneumonia
- Wheezing or breathlessness
- Exercise intolerance

18.5.2 Systemic Features

- Failure to thrive
- Fatigue
- Digital clubbing in advanced disease

18.5.3 Physical Examination

- Crackles (coarse, persistent)
- Wheezing
- Signs of hyperinflation
- Chest deformities (in chronic severe disease)

18.6 Investigations

18.6.1 Imaging

Chest X-ray (CXR)

- May show:
  - Tram-track lines
  - Peribronchial thickening
  - Atelectasis
  - Hyperinflation
- Limited sensitivity; a normal CXR does not exclude disease.

High-Resolution CT Scan (Gold Standard)

- Confirms diagnosis
- Shows bronchial dilatation (broncho-arterial ratio >1), lack of tapering, signet-ring sign
- Not always accessible in rural Ghana.

18.6.2 Laboratory Tests

- Full blood count (leucocytosis in infections)
- Sputum culture (including TB workup)
- HIV testing where indicated
- Immunoglobulin levels if immunodeficiency is suspected

18.6.3 Other Tests

- Spirometry (for children 5 years): obstructive pattern
- Bronchoscopy:
  - Suspected foreign body
  - Localised bronchiectasis

18.7 Differential Diagnosis

- Uncontrolled asthma
- Recurrent pneumonia due to underlying immunodeficiency
- Cystic fibrosis (rare locally, but consider in persistent cases)
- Post-TB lung disease
- Chronic aspiration syndromes

18.8 Management

Management goals:

1. Reduce symptoms
2. Prevent exacerbations
3. Improve lung function
4. Prevent further lung damage.

18.8.1 Airway Clearance Techniques (Core Treatment)

- Chest physiotherapy
- Postural drainage
- Percussion and vibration
- Oscillatory PEP devices (e.g., Flutter valve) if available

Parents should be trained to perform airway clearance at home.

18.8.2 Antibiotics

18.8.2.1 Acute Exacerbations

- Amoxicillin–clavulanate (first-line)
- Alternatives: cefuroxime, macrolides (if atypical pathogens suspected)
- Duration: **10–14 days**

18.8.2.2 Chronic Colonisation

- Long-term macrolide therapy can reduce exacerbations, but requires specialist oversight.

18.8.3 Bronchodilators

- Useful in children with coexisting wheeze
- Consider a salbutamol trial.

18.8.4 Anti-inflammatory Therapy

- Inhaled corticosteroids are *not routinely indicated* unless asthma overlaps.

18.8.5 Management of Underlying Causes

- Remove foreign body
- Treat TB
- Manage GERD and aspiration.
- Treat immunodeficiency

18.8.6 Vaccinations

- Ensure full immunisation
- Annual influenza vaccination, where available
- Pneumococcal vaccine

18.8.7 Nutritional Support

- High-calorie diet for children with chronic disease
- Treat malnutrition aggressively

18.8.8 Surgical Intervention

- Consider **lobectomy** in children with:
  - Localised bronchiectasis
  - Recurrent severe infections
  - Failure to respond to medical therapy
- Only after thorough evaluation

18.9 Complications

- Recurrent pneumonia
- Haemoptysis
- Lung abscess
- Respiratory failure
- Pulmonary hypertension (rare but serious)
- Reduced quality of life and growth failure

18.10 Prognosis

- Good if diagnosed early and managed appropriately
- Poorer outcomes in:
  - Delayed diagnosis
  - Severe post-infectious disease
  - Associated immunodeficiency
- Lifelong follow-up may be needed.

18.11 Prevention

- Early and adequate treatment of pneumonia
- Prevention and early treatment of TB
- Prompt immunisation (especially measles, pertussis)
- Reduce indoor air pollution (charcoal and biomass exposure)
- Train caregivers in early recognition of respiratory symptoms
- Improve access to child health services

18.12 Key Points

- Bronchiectasis is underdiagnosed in Ghana due to limited access to imaging.
- A chronic productive cough should prompt evaluation for bronchiectasis.
- Airway clearance is the cornerstone of therapy.
- Antibiotics are essential for the treatment of exacerbations and for controlling chronic infections.
- Preventive strategies—especially vaccination and pneumonia control are critical.

18.13 Further Reading

1. Chang AB, Bush A. *Paediatric bronchiectasis: modern management.*
2. Ghana Health Service. **Standard Treatment Guidelines**.
3. WHO. *Pocket Book of Hospital Care for Children.*
4. Singleton RJ et al. *Bronchiectasis in childhood.* Lancet.
5. Al-Saleh S, et al. *Non-CF bronchiectasis in Africa and LMICs.*

Part IV

Cardiology

19 Basics

19.1 Anatomy

The heart is located in the mediastinum of the chest, bounded anteriorly by the sternum, posteriorly by the spine and laterally by the lungs. Externally, the right ventricle is anterior. Most of the left ventricle, left atrium and right atrium are posterior. Internally, the right and left atria are separated by the tricuspid and mitral valves from the right and left ventricles respectively. The arterial supply of the heart is through the coronary arteries while venous drainage is through the coronary sinus. The aorta and pulmonary arteries arise from the left and right ventricles. The heart has three layers:

1. Endocardium: Inner epithelial layer of the heart
2. Myocardium: Muscular part of the heart
3. Pericardium: Outer layers of the heart. Divided into the visceral and parietal pericardium.

Venous blood enters the right atrium through the inferior and superior vena cavae. It empties in atrial systole into the right ventricle through the tricuspid valve. It then moves on through the pulmonary valve in ventricular systole, to the pulmonary artery and then the lungs. Blood returning from the lungs enters the left atrium through the four pulmonary veins. In atrial systole, it moves into the left ventricle through the mitral valve. Finally, it empties into the aorta through the aortic valve.

19.2 Conduction system

The heart has an inherent electrical system that automatically paces and conducts depolarization throughout it. The parts are:

1. *Sinoatrial (SA) node*: This is the pacemaker of the heart and depolarizes the two atria.
2. *Atrioventricular (AV) node*: Receives impulses from the SA node, and delays a bit before propagating it further.
3. *His-purkinje fibre* system: Responsible for the spread of electrical impulses to the ventricles

19.3 Heart as a pump

There is a difference in the pumping action of the heart in utero and after birth.

1. Fetal
    - Most work is done by the right ventricle
    - The right Ventricle is therefore relatively hypertrophic
    - Only 15% of the cardiac output is pumped into the lungs
2. After birth
    - Gradual transition to Left ventricle dominance
    - Gradual fall in pulmonary pressure (over 6 weeks)
    - The left ventricle does most of the work and becomes more hypertrophic than the right

19.4 Systolic and diastolic functions

Systole: This is the contractile phase of the heart. It starts after the atria is filled with blood. The atria then contract, emptying its content into the ventricles. At this stage, the ventricle also undergoes systole, which further empties the blood into the aorta and pulmonary arteries.

Diastole: This is the relaxation phase where the heart relaxes and lets in blood. It also starts with the atrium and then the ventricles.

Compliance: This describes how easily the heart chamber relaxes in response to the inflow of blood.

19.5 Intracardiac Pressures

The pressures in the heart vary for different ages and individuals. Generally, the pressures in the atria are lower than the ventricles. Also, the peak systolic pressure in the left ventricle is higher than in the right. The diastolic pressure in the left ventricle is however lower than the right ventricle. Also, both systolic and diastolic pressures in the aorta are higher than that in the pulmonary artery.

Systolic pressure in general is generated by the ventricles. In conditions such as coarctation of the aorta, aortic stenosis and pulmonary hypertension, the ventricles increase their workload to generate enough pressure. The diastolic pressure on the other hand is maintained by the closure of the aortic and pulmonary valves. Thus, an incompetent pulmonary or aortic valve leads to a decrease in diastolic pressure in the two vessels respectively.

19.6 Fetal circulation

The heart begins developing in the fetus as the cardiogenic area and primitive blood vessels as early as 18 days old. By 20 days the paired endocardial tubes are formed. By day 35 the heart would have completed its looping with blood already flowing through.

Three main shunts exist in the fetal circulation. These are adaptations to using the placenta rather than the lungs for oxygenation. These shunts are the ductus venosus, ductus arteriosus and patent foramen. At birth, these shunts regress. The ductus venosus regresses quickly to form the ligamentum arteriosus. The foramen ovale closes at birth physiologically but may take years to close anatomically. The patent ductus arteriosus closes soon after birth but can physiologically stay open for 72 hours. Beyond this period it is considered to be pathologic if it continues to stay open. Patent ductus arteriosus are quite common in preterm newborns.

19.7 Pathologic classification

The pathology of pediatric cardiac disorders varies. Broadly, they can be divided into these:

1. ***Congenital heart disorders***: These are cardiac conditions that a child is born with. Thus they are present at birth. They form about 85% of all pediatric heart diseases seen in the Komfo Anokye Teaching Hospital (KATH). It is further divided into:
    - *Acyanotic*: These are congenital heart diseases that are traditionally not known to be associated with cyanosis. Examples include ventricular septal defect (VSD), Atrial Septal Defect (ASD) and Patent Ductus Arteriosus (PDA)
    - *Cyanotic*: These on the other hand are associated with cyanosis and include Tetralogy of Fallot (ToF), Truncus Arteriosus and Tricuspid Atresia.
2. ***Acquired heart disorders***: These are heart conditions that are not present at birth but develop afterwards. They include Infective Endocarditis (IE), Rheumatic Heart Disease (RHD) and Endomyocardial Fibrosis (EMF)
3. ***Rhythm disorders***: This set of disorders can present as either congenital or acquired. They affect the electrical system of the heart leading to an increase in heart rate (tachyarrhythmia), decrease in heart rate (bradyarrhythmia) or even normal heart rate.
4. ***Secondary cardiac disorders***: Some pathologies tend to affect the heart as a complication. Such conditions include some glycogen storage disorders resulting in cardiomyopathy and Rheumatoid arthritis resulting in pericardial effusion.

20 Evaluating Heart Diseases

To fully evaluate a child with a suspected cardiac condition, one needs to go through the regular steps applicable in medicine. These are outlined below:

20.1 History

The history is traditionally divided into:

20.1.1 Prenatal

Prenatally, the history should delve into but not be limited to the following:

1. ***Infections***: Some infections are the well-known TORCHES. They include Toxoplasmosis, HIV, syphilis, parvovirus B19 (fifth disease), varicella (chickenpox) and (Zika), Rubella, Cytomegalovirus, and Herpes simplex virus. Rubella, when acquired in the first trimester of pregnancy, is very well known to be associated with PDAs.
2. ***Medications:*** The use of some medications, including herbs, predisposes to heart disease in newborns. Anticonvulsant such as phenytoin, carbamazepine, and valproic acid are highly teratogenic.(Kalisch-Smith, Ved, and Sparrow 2019)
3. ***Recreational drugs***: Excessive smoking, cocaine, and alcohol use in early pregnancy are all associated with teratogenic effects on the heart.
4. ***Maternal illnesses:*** Maternal medical conditions during pregnancy may be associated with heart diseases in their fetuses. Diabetes mellitus is particularly well known, predisposing to hypertrophic cardiomyopathy, d-Transposition of the Great Arteries, etc. Autoimmune conditions such as Systemic Lupus Erythematosus may also predispose to rhythm disturbances in the fetus and child, even when the mother is not symptomatic.
5. ***Family history of CHD***: The recurrence of CHD in first-degree relatives varies but is almost always higher than in the rest of the population. For instance, having a first-degree relation with a cornoventricular defect is associated with a recurrence risk ratio of 24.3 (95% CI,12.2 to 48.7), 7.1 (95% CI, 4.5 to 11.1) for isolated Atrial Septal Defect, and 3.4 (95% CI, 2.2 to 5.3) for isolated Ventricular Septal Defect.(Øyen et al. 2009)

20.1.2 Perinatal

Perinatal history associated with heart disease may include the following:

1. ***Birth weight***: A high birth weight, often associated with a child of a diabetic mother, is also associated with an increased incidence of CHDs. Conversely, a low birth weight may also be associated with fetal alcohol syndrome or congenital rubella syndrome, both of which are associated with CHDs.
2. ***Newborn resuscitation***: Some critical CHDs can be similar to neonatal asphyxia in a newborn, thus requiring resuscitation.

20.1.3 After birth

Ascertaining history after birth is the most extensive. Many of these are directed to the features of heart failure. These include:

1. ***Growth failure***: Poor weight gain is a very prominent feature of CHDs in children. Many clinically significant CHDs result in poor feeding, chronic metabolic demand on the patient and poor oxygenation in cyanotic CHDs. All these result in increased caloric demand, resulting in poor growth.
2. ***Cyanotic spells***: Some cyanotic CHDs are associated with recurrent periods where the child has increasing cyanosis, sometimes associated with weakness, fast breathing and even unconsciousness. The presence of these spells may be a pointer to a CHD.
3. ***Squatting and exercise intolerance***: Exercise intolerance is a common presentation of heart disease in children. However, for some cyanotic congenital heart diseases, most notably Tetralogy of Fallot, the added feature is frequent squatting when the child becomes fatigued.
4. ***Delayed milestones***: Growth failure, easy fatiguability, and other genetic syndromes may delay motor milestones in children.
5. ***Others***: *Fast* and sometimes *difficult breathing* are also common presentations of CHDs. Some children develop *oedema.*(Figure **??**) This is predominantly seen in younger children's faces and older children's feet. Frequent *lower respiratory infection* is also seen in children with heart diseases, especially those associated with heart failure.
6. ***Uncommon symptoms***: Uncommon presentation of heart disease in children include:
    - *Chest pain* is a rather feared symptom in adults but usually portends another diagnosis rather than heart disease in children.
    - *Syncope* can be observed in children with an arrhythmia or left or right ventricular obstruction. However, this is still not a common presentation in pediatric heart diseases.
    - Older children report *palpitations.*
    - *Joint swelling* does occur in Rheumatic Heart Disease, but again, it is not a common presentation in children with heart pathology.

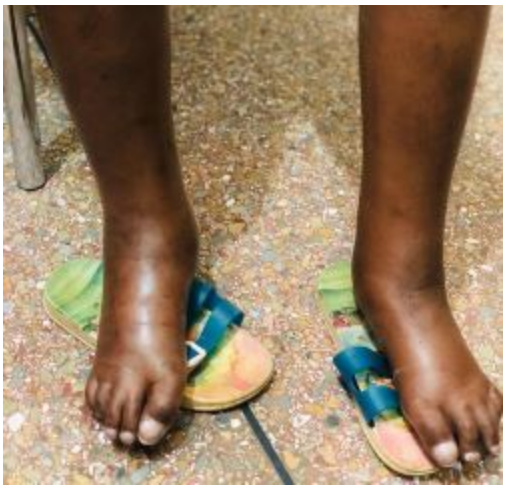

Figure 20.1: Pedal oedema in a child with heart failure

20.2 Clinical examination

20.2.1 General

Clinical examination for a child with a suspected heart disease should always start as general. One should first look out for life-threatening signs and intervene quickly. Subsequent steps could include:

1. ***Nutritional status*** is vital as many children with chronic heart conditions with significant heart failure present with malnutrition. The growth pattern of the patient should always be evaluated.
2. ***Dysmorphism*** is very critical in pediatric heart diseases. As much as 23% of all children with CHD will have a chromosomal abnormality.(Wang et al. 2023) There are many genetic syndromes with well-documented recognisable heart defects. Below are just a few adapted from Ko (2015):

Table 20.1: Common genetic syndromes associated with congenital heart diseases

Genetic syndrome	% with CHD	Cardiac anomalies
Down Syndrome	40 to 50	Atrial Septal Defect, Ventricular Septal Defect, Atrioventricular Canal Defect, Patent Ductus Arteriosus, Tetralogy of Fallot

Genetic syndrome	% with CHD	Cardiac anomalies
Turner's syndrome	25 to 45	Coarctation of the Aorta. Bicuspid Aortic Valve, Aortic Stenosis, Hypoplastic left heart syndrome
DiGeorge syndrome	70 to 75	Aortic arch anomalies, Truncus arteriosus, Tetralogy of Fallot
William's syndrome	75 to 80	Supravalvar Aortic Stenosis, Peripheral Pulmonary Stenosis
Noonan syndrome	70 to 80	Pulmonary Stenosis, Hypertrophic Cardiomyopathy, Atrial Septal Defect
Kabuki syndrome	31 to 55	Coarctation of the Aorta, Atrial Septal Defect, Aortic Stenosis, Mitral Stenosis, Hypoplastic left heart syndrome
Alagille syndrome	90	Peripheral Pulmonary Stenosis, Pulmonary Stenosis, Tetralogy of Fallot

3. ***Colour***: The skin colour of a child with a CHD could hold signs of its presence. *Cyanosis*, the blueish duskiness of the skin and mucous membranes can be seen in children with cyanotic congenital heart disease. This may not be easy on black skin and can only be observed in the mouth and tongue (Figure **??**). Mild cyanosis is often not visible and may require pulse oximetry. *Pallor* can be observed in patients with heart diseases, such as Infective Endocarditis. *Jaundice* can be observed in patients with Infective Endocarditis or those with hepatic injury secondary to chronic heart failure.

4. ***Clubbing***: All four stages of digital clubbing are seen in children with cyanotic CHD or Infective Endocarditis. (Figure **??**) Note that some cases of finger clubbing may be familial.

5. ***Respiratory signs***: Respiratory signs commonly associated with heart diseases in children are *tachypnoea*, *dyspnoea*, *chest recessions,* and *increased work of breathing*. These are especially true when there is associated heart failure, which worsens with exercise or breastfeeding infants.
6. ***Circulation***: The circulation in a child with a suspected heart disease is critical. Reduced circulation can be assessed with the warmth of the extremities, capillary refill time,

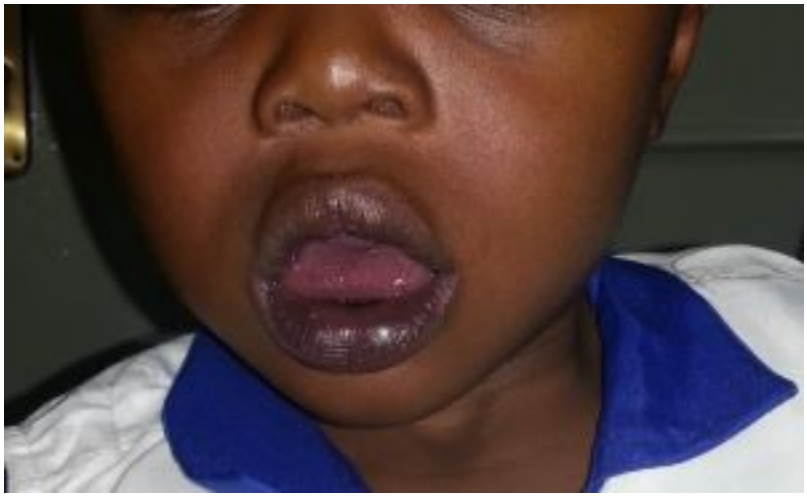

Figure 20.2: Cyanosis in the tongue of a child

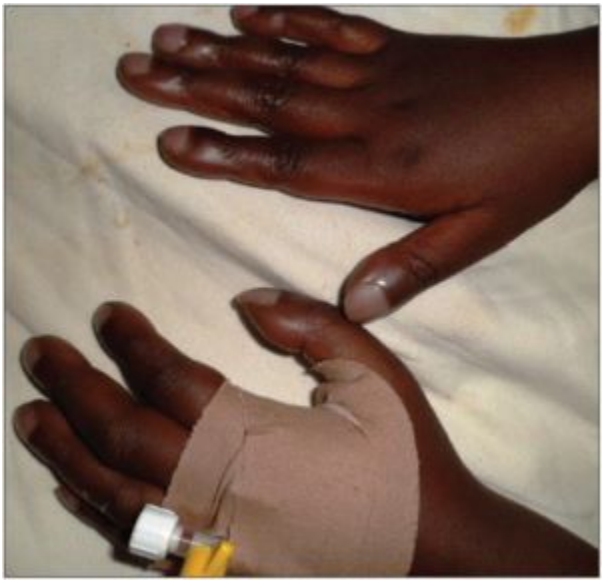

Figure 20.3: Finger clubbing

and blood pressure.

7. ***Blood pressure***: Low blood pressure is a late sign of circulatory failure and cardiogenic shock. Conversely, weak pulse may be associated with hypertensive heart disease as well. Wide pulse pressure, an abnormally wide difference between the systolic and diastolic blood pressures, may indicate a patent ductus arteriosus, aortic insufficiency or an aorticopulmonary window. Blood pressure should be checked in the upper and lower limbs as a higher BP in the upper limbs compared to the lower may indicate the presence of a Coarctation of the Aorta.
8. ***Pulses***: The radial pulse is the most routinely examined in cardiovascular examination. It should be checked for the rate, rhythm, volume and character. If they are difficult to examine, especially in young infants, the brachial pulsus can be used. Other pulses should be examined, including the brachial femoral and dorsalis pedis. Next, the synchronisation of the radio-femoral pulse should be determined for a delay. This happens in the coarctation of the aorta. Pulses that are challenging to palpate or inconsistent could be caused by large artery arteritis, such as Taksyasu's arteritis.

20.2.2 Precordial

1. ***Inspection***: Inspection of the precordium yields a wealth of information in a child with a suspected heart disease. A midline bulge or left-sided bulge will often indicate a right or left-sided heart chamber dilatation. Visible precordial pulsation should be noted. Scars, especially from previous surgeries, are useful. Scarification, the usually small "medicinal" scars done on the chest as a means of treatment, should also be noted. A Harrison sulcus, depression of the lower part of the chest, is common in children with chronic heart failure and, thus, dyspnoea. Figure **??**

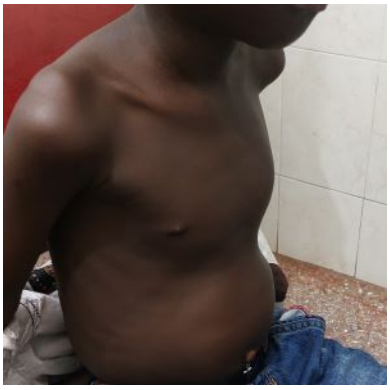

Figure 20.4: Chest bulge and Harrison's sulcus in child

2. ***Palpation***: Palpation should be directed toward determining the presence of a thrill (a palpable murmur) heave at the apex or middle of the precordium. Also, a palpable

Table 20.2: Grades of murmurs

Grade	Description
Grade I	Barely perceptible
Grade II	Soft, but easily audible
Grade III	Moderately loud but has not thrill
Grade IV	Loud and associated with a thrill
Grade V	Audible with stethoscope partially of the chest
Grade VI	Audible with stethoscope off the chest

heart sound, especially the second at the upper left sternal edge, may indicate pulmonary hypertension.

3. ***Percussion***: This is of very little relevance in examining the heart in children.

4. ***Auscultation***: Auscultation of the heart can yield a wealth of information. It should be done in a quiet environment, with the child as calm as possible. Auscultating can be performed with both bell and diaphragm. All four auscultatory areas need to be auscultated. Auscultating the back (between the scapulae) and over the carotids is always prudent. First, the regular two heart sounds should be determined. If muffled, they could indicate a pericardial effusion or sometimes obesity. Pulmonary hypertension and an Atrial Septal Defect, for instance could result in a loud or split-second heart sound. The presence of a third heart sound (S3) is not always pathologic in children, but an S4 is. The presence of a murmur needs to be determined. If present, it should be determined if it is systolic or diastolic and the point of maximal intensity. It needs to be graded (Table **??**), and the presence of radiation must be ascertained. Table **??** indicates types of murmurs, their location and likely heart diseases. Diastolic murmurs are difficult to appreciate for the average medical student but may be present in aortic regurgitation, pulmonary regurgitation, and at the cardiac apex in cases of heart failure secondary to a large left-to-right shunt. Notably, approximately 80% of murmurs in children can be categorised as "innocent murmurs" as they are not associated with cardiac pathology.

   Other sounds need to be evaluated as well. These may include a pericardial rub, which occurs in pericarditis, an ejection click heart in early systole and cases of aortic or pulmonary stenosis.

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Table 20.3: Heart diseases and their murmur characteristics

Murmur	Location	Condition
Pansystolic	LLSB	VSD, Tricuspid regurgitation
Pansystolic	Apex	Rheumatic Heart Disease, Mitral valve prolapse
Ejection systolic	URSB	Aortic stenosis
Ejection systolic	ULSB	ASD, Pulmonary stenosis, Tetralogy of Fallot, Coarctation of the aort
Continuous	2nd left ICS	Patent Dutus Arteriosus

20.3 Investigation

Various investigations used in the diagnosis and management of heart diseases are:

1. ***Pulse Oximetry***: Pulse oximetry helps determine heart rate and oxygen saturation. An oxygen saturation lower than expected (<95% outside the early neonatal period) is considered abnormal and a strong indication of cyanotic heart disease in the presence of a non-pathologic lung.

2. ***Electrocardiogram***: The electrocardiogram is a common modality for the bedside investigation of heart diseases in all age groups. It indicates the heart rate, rhythm, chamber dilatation, wall thickness, laterality of the chambers, electrolyte abnormalities and even the presence of a head injury. It is often not conclusive in many heart conditions but serves as a good auxiliary test in children, especially post-surgery. There are various types: The routine ECG takes just a few minutes to perform on a resting patient, usually lying supine. On the other hand, the stress ECG is traditionally done with the heart under stress, as may happen during an aerobic exercise. The Holter ECG, on the other hand, is attached to the patient and continuously monitors the heart for 24 to 48 hours. This usually gives a better reflection of the heart's electrical activity over a prolonged period instead of just a brief period.

3. ***X-ray***: A chest x-ray is very useful in diagnosing and managing heart diseases in children. Fortunately, it is readily available in many parts of Ghana. Both posteroanterior and lateral chest X-rays can be useful in assessing the individual chamber and overall heart sizes. Cardiomegaly, assessed with a cardiothoracic ratio > 60% in children, is seen in many cases of heart disease. Chest X-rays also indicate ling pathologies, often showing as opacification or silhouetting. Increased lung markings, for instance, can be found in patients with VSD and ASD, while decreased lung markings are often seen in the Tetralogy of Fallot and pulmonary stenosis. The shape of the heart is often an indicator of the underlying cardiac pathology. A Boot-shaped heart may indicate a Tetraloy of Fallot (Figure **??**), while a globular-shaped heart points to dilated cardiomyopathy or pericardial effusion. Figure **??**

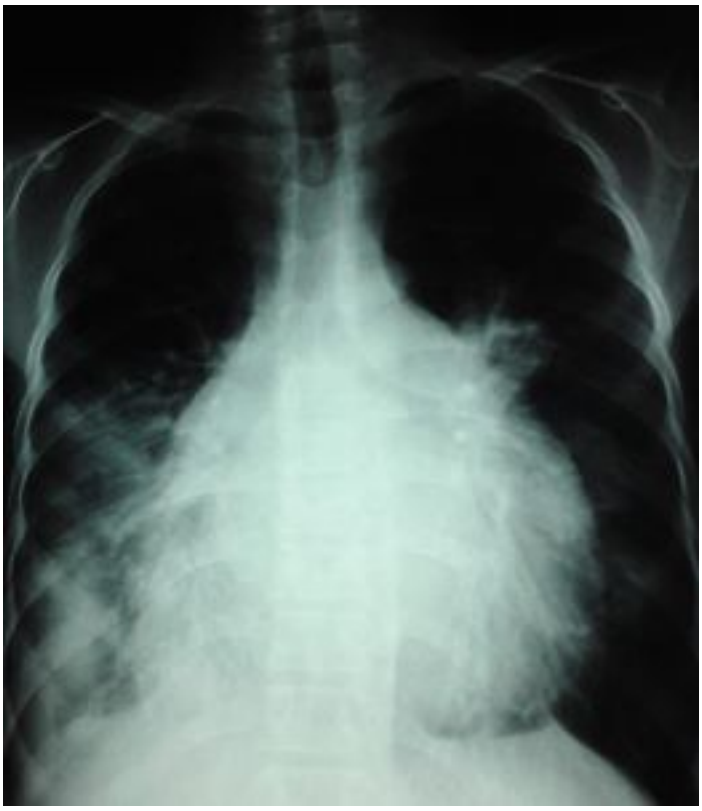

Figure 20.5: Chest x-ray showing cardiomegaly and lung shadowing

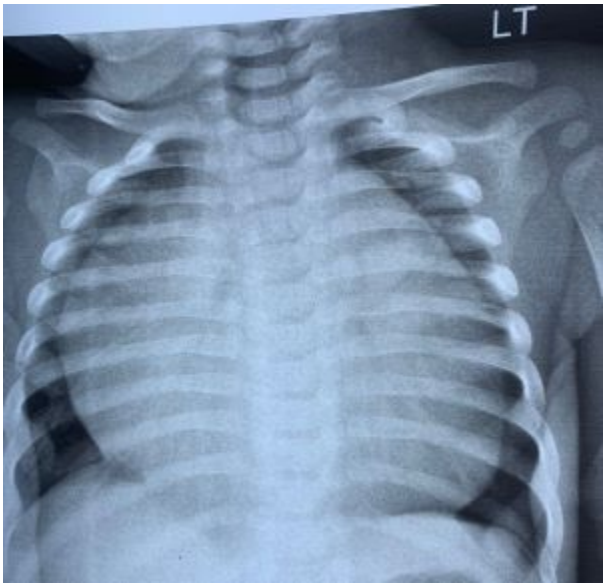

Figure 20.6: Chest x-ray showing a globular heart

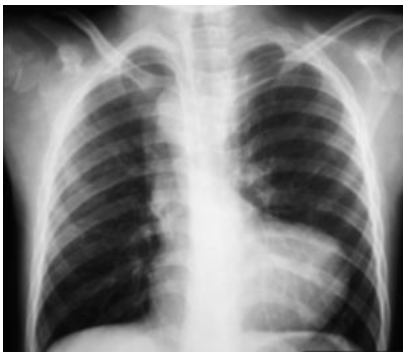

Figure 20.7: Boot-shaped heart of Chest X-X-ray

4. ***Echocardiogram***: This is a rather old but new investigatory modality. It is old because it has been around since the 1960s and new because it is relatively new in Ghana. It is, however, a beneficial modality of investigation. An echocardiogram is essentially an ultrasound of the heart and great vessels. Its most significant advantage is its ability to visualise the heart in real-time, assess systolic and diastolic functions, measure chamber sizes and wall thickness, detect defects such as ventricular septal defect, determine valvular abnormalities such as stenosis and regurgitation, and even assess all these under stressful situation (stress echocardiogram). The video below illustrates the various echocardiographic views used in children. Unfortunately, since it is very user-dependent, it is not commonly available in Ghana, with pediatric echocardiography only currently available in Accra, Kumasi, Cape Coast and Tamale.

   https://www.youtube.com/watch?v=WpJuARIoR6s&t=39s

5. ***Computerised tomography (CT) scan and Magnetic resonance Imaging (MRI)***: These are more advanced modalities available for use, especially when an echocardiogram is inconclusive or further study of the patient is necessary. A CT scan generates the image using a series of X-rays taken at different angles without the complication of significant X-ray radiation exposure. Both modalities can employ contrast to delineate vessels.

6. ***Others***: Other specialised investigatory modalities are used as required, including cardiac catheterisation in a specialised catheter laboratory.

21 Heart Failure

21.1 Definition

The inability of the heat to provide enough output to the body.

21.2 Causes

Varies, especially in children. They can occur in both structurally normal hearts and in congenital cardiac malformations. There are three main groups of causes:

1. **Ventricular dysfunction** results from either systolic or diastolic dysfunction of the ventricles. Systolic dysfunction is more commonly encountered compared to diastolic ones. Examples are:

    - Cardiomyopathy (dilated, restrictive and hypertrophic)
    - Myocarditis
    - Arrhythmias
    - Coronary artery anomalies
    - Post-op cardiac dysfunction

2. **Volume overload** occurs in conditions associated with increased volume (preload) in the heart, especially the ventricles. The ventricle must, therefore, eject an increased blood volume, leading to tachycardia. It may or may not be associated with ventricular dysfunction. Examples include:

    - Ventricular septal defect (left to right shunt)
    - Atrial septal defect
    - Patent ductus arteriosus
    - Aortic regurgitation (left ventricle)
    - Mitral regurgitation (Left atrium)

3. **Pressure overload** is when heart failure is caused by an increased pressure (afterload) in the heart. Ventricles must, therefore, contract against higher pressures. It may or may not be associated with ventricular dysfunction. These include:

    - Hypertension

- Aortic valve stenosis
- Pulmonary stenosis
- Coarctation of the aorta

In all these, the result is decreased cardiac output and pulmonary oedema.

21.3 Classification

The symptoms of heart failure vary significantly, with infants and young children having different presentations compared to older children. The classification of heart failure there is not uniform. The most well-known classification is the NYHA, which is appropriate for older children. It is shown below:

Table 21.1: NYHA Classification

Class	Patient Symptoms
Class I (Mild)	No limitation on physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest but ordinary physical activity results in fatigue, palpitation or dyspnoea
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest but less than ordinary physical activity causes fatigue, palpitation or dyspnoea
Class IV (Severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken discomfort is increased

On the other hand, the Ross classification shown below is more suited for infants and young children.

Table 21.2: Modified Ross Classification

Class	Symptoms
Class I	Asymptomatic

Class	Symptoms
Class II	Mild tachypnoea or diaphoresis in feeding in infants Dyspnoea on exertion in older children
Class III	Marked tachypnoea or sweating with feeding in infants Marked dyspnoea on exertion Prolonged feeding times with growth failure
Class IV	Symptoms such as tachycardia, retraction, grunting, or diaphoresis at rest

21.4 Pathophysiology

A schematic drawing of the various processes involved is shown below:

21.5 Signs and symptoms

The symptoms of heart failure are variable and age-dependent. For infants, the symptoms include poor feeding, sweating with breastfeeding, prolonged feeding time, tachypnoea, poor weight gain and dyspnoea. For young children symptoms include recurrent respiratory tract infection, recurrent wheezing, fatigue, exercise intolerance, facial and recurrent cough. Older children have symptoms that more resemble those of adults. These include tachypnoea, tachycardia, recurrent wheezing, pedal swelling, palpitations, and vomiting.

Signs of heart failure also vary with age. These include for infants, failure to thrive, tachycardia, tachypnoea, hepatomegaly, displaced apex (cardiomegaly), S3 gallop, oedema (pedal in older children and facial or abdominal distension in older children).

21.6 Investigation

The investigations required are generally towards the likely underlying pathology. Some of them would include:

Chest x-ray: This may show cardiomegaly, increased pulmonary lung markings, pulmonary oedema, pleural effusion and heart shape.

Electrocardiogram: This helps to identify chamber enlargement and dysrhythmias that may be the cause or consequent to the heart failure

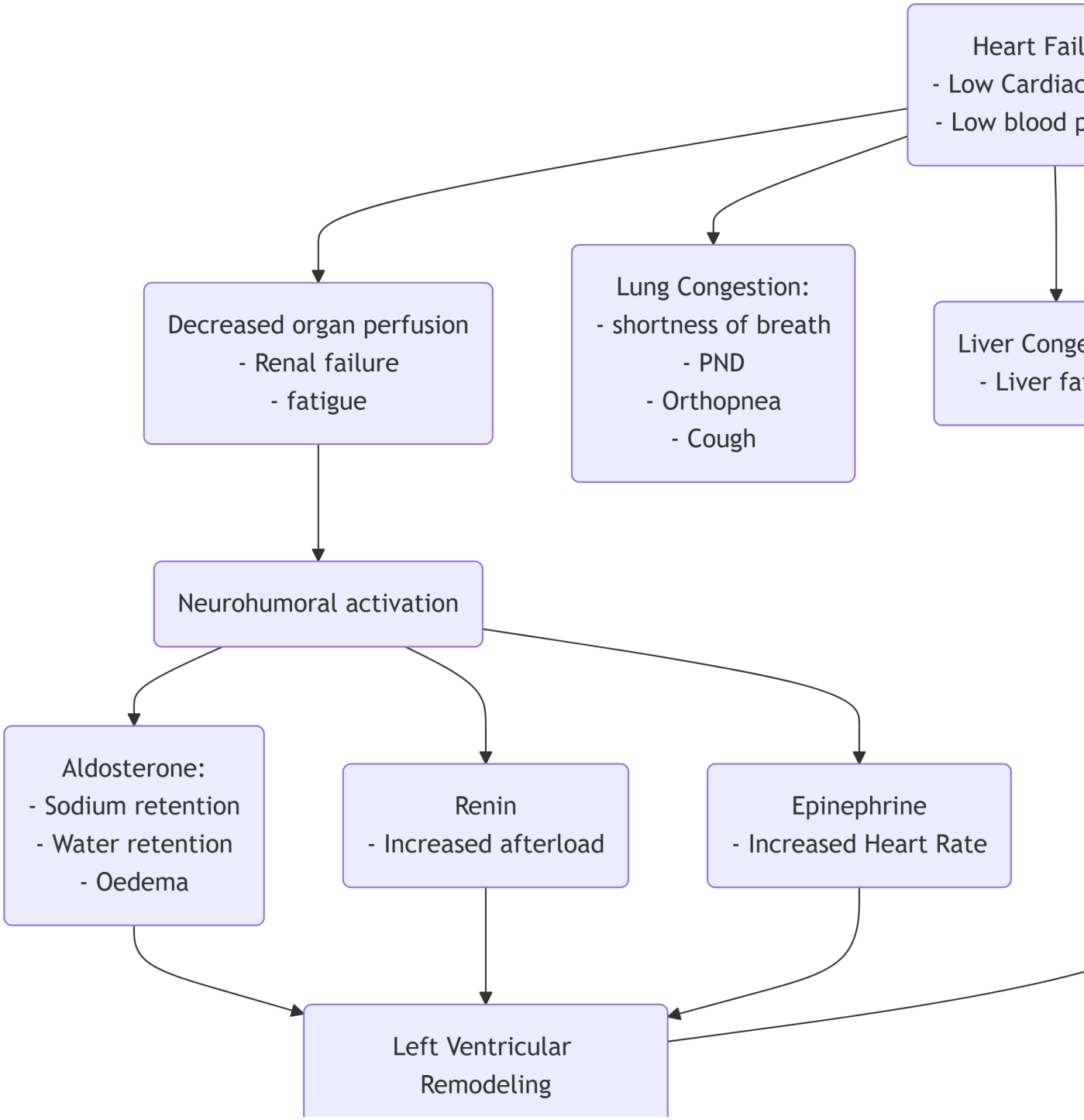

Figure 21.1: Pathophysiology of heart failure

Echocardiogram: This identifies and quantifies the function of the ventricle as well as the chamber sizes

Blood test: The complete blood count helps to identify anaemia or polycethemia. The serum urea and creatinine identify possible renal dysfunction. Other tests include BNP (Brain Naturetic Peptide) and Troponin both of which are elevated in heart failure.

Other investigatory modalities: These include Magnetic Resonance Imaging, Cardiac catheterization,

21.7 Treatment of Heart Failure

This is done with some goals:

1. Improve the quality of life
2. Arrest and possibly reverse the heart failure
3. Sustain till other definitive therapeutic interventions are employed, including surgery.

The treatment for heart failure is dependent on the pathophysiology, clinical features and stage of the disease.

21.7.1 Non-pharmacological treatment

This includes fluid restriction in case of congestion and fluid overload, intubation and mechanical ventilation to help support breathing and reduce the workload on the heart and patient. Others include cardiac Resynchronization Therapy, Ventricular Assisted Devices and Extracorporeal Membrane Oxygenation. Heart transplantation is the last option in some cases of heart failure.

21.7.2 Pharmacological treatment

Treatment depends on the clinical presentation and cause of the heart failure. There are 2 main groups to be considered:

21.7.3 Acute decompensated heart failure

Table 21.3: Drugs used in acute decompensated heart failure

Drug	Action
Diuretics	Notable here is furosemide. The aim is to help decongest the lungs, reduce preload by vasodilatation and improve heart failure symptoms.
Inotropes	These include adrenaline, noradrenaline, dopamine and dobutamine. They help improve the contractility of the heart, increase heart rate, and increase peripheral vascular resistance, thus maintaining the blood pressure and cardiac output. They are usually Intravenous medications.

21.7.4 Chronic heart failure

These are usually oral medications given to treat heart failure on an outpatient basis

Table 21.4: Drugs for chronic heart failure treatment

Group	Action
Diuretics	These are given to decongest the lungs, liver and other edematous organs. The most commonly used is furosemide.
Aldosterone antagonists	These counteract the aldosterone effect of water and sodium retention. They decrease afterload while helping in reversing cardiac remodelling.
ACE-I/ARB	Angiotensin-converting enzyme inhibitors and Angiotensin II receptor blockers counteract the renin effects of increasing afterload. They thus decrease the afterload and help reverse and prevent cardiac remodelling
Digoxin	This is probably the oldest anti-heart failure medication. It has negative chronotropic and positive inotropic effects. Thus increasing contractility and reducing heart rate.

Group	Action
β -adrenergic blocking	These are adrenergic-blocking agents that work by decreasing sympathetic activity to the heart, decreasing heart rate, and thus decreasing oxygen demand. Examples are Propranolol, Atenolol and Carvedilol.

21.8 Complications

Complications of heart failure include renal failure, hepatic failure, pulmonary hypertension, arrhythmia, and thromboembolic effects.

22 Atrial Septal Defect

22.1 Introduction

An Atrial Septal Defect (ASD) is a defect in the wall separating the left and right atria.

22.2 Incidence/Prevalence

It is the second most common congenital heart disease and may occur in as much as 25% of all congenital heart disease patients. It is thought to have a small female preponderance. Still, in a compilation of all electrocardiogram cases in Kumasi, it formed 26% of the patients and showed no difference in incidence between sexes. There are four main types: Secundum ASD (50-70%), Primum ASD (~30%), Sinus Venosus ASD and Coronary sinus ASD. Figure **??**

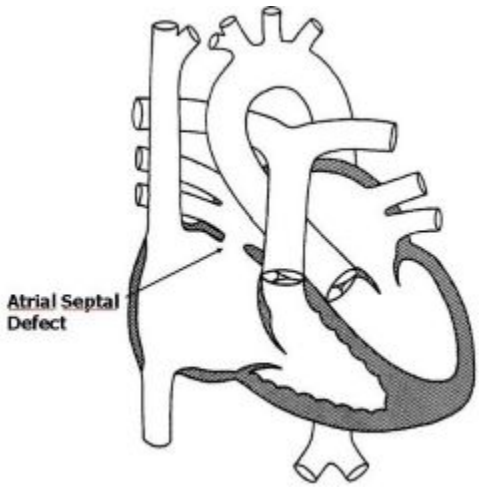

Figure 22.1: Schematic drawing of an Atrial Septal Defect

22.3 Aetiology

Most ASDs are thought to occur sporadically, but there are recorded associations with some genetic defects and syndromes. (Caputo et al. 2005) Among these are Holt-Oram, Noonan,

Down, and Budd-Chiari syndrome.

22.4 Pathophysiology

Since the pressure in the left atrium is higher than that of the right, the high oxygen-content blood shunts from the left atrium to the low oxygen-content right atrium. Thus an uncomplicated ASD is **acyanotic**. The shunting also leads to volume overload of the right atrium, right ventricle, pulmonary artery and lungs. This consequently results in dilatation of the right atrium, right ventricle and pulmonary artery, and pulmonary oedema. The low pressure in the atria implies low pressure in the right ventricle, pulmonary artery and lungs. This reduces the extent of pulmonary oedema and, subsequently, overt heart failure in a child with ASD, compared to other congenital heart defects such as ventricular septal defects. However, longstanding long-standing lesions or relatively large ones, especially those with a pulmonary-to-systemic flow ratio of 2 or more, could lead to heart failure and pulmonary hypertension after about 15 to 20 years with subsequent reversal of the shunt.

22.5 Signs and symptoms

Most children with an atrial septal defect are without overt symptoms. However, those with relatively large defects with a high Qp:Qs may result in heart failure. Therefore, many of these patients have been diagnosed incidentally when they, for instance, report to the health institution for another complaint. They tend to have slender bodies and reduced exercise tolerance.

Auscultation usually reveals a widely fixed-split second heart sound and an ejection systolic murmur of grade 2/3 to 3/6, loudest at the left upper sternal border. Unfortunately, many ASDs are silent as well. These properties lead to many undiagnosed ASD that are subsequently seen in adulthood.

22.6 Investigations

- At the bedside, pulse oximetry would likely reveal a normal SpO_2 as this is an acyanotic congenital heart disease.
- A chest X-ray could show cardiomegaly with dilatation of the right side of the heart. Prominence of the pulmonary artery and an increase in vascular markings may also be present.
- The electrocardiogram will likely show a right axis deviation due to the dilated right ventricle and a right atrial enlargement.

- An echocardiogram is diagnostic as it visualises the defect, quantifies the shunt and other chamber sizes, and identifies possible complications.
- Cardiac catheterisation is often done in long-standing cases to detect complications, possibly pulmonary hypertension, and quantify the shunt volume.

22.7 Treatment

Treatment depends on the age at diagnosis and the size of the defect. For a small defect with no signs of heart failure, and in a child less than 3 years, counselling and regular review may be what is required. The echocardiogram should be repeated at 4 years, and surgical or device closure should be considered if the defect persists. For large defects, heart failure medications can be started as planning of immediate surgical closure is being made. Closure of the ASD is by use of a device or, as may occur more often in Ghana, by open heart surgery. There is no need for exercise restriction or prophylaxis for endocarditis.

22.8 Prevention

There is no known mode of prevention of ASDs. However, early and appropriate treatment of the associated symptoms and complications go a long way in improving quality of life.

22.9 Complication

- Many patients with ASDs may not grow appropriately and instead become thin.
- Arrhythmias may arise because of the dilated right atrium.
- Though there are reported cases of paradoxical strokes in patients with ASDs, it remains an uncommon occurrence.
- Infective endocarditis is rare in ASDs.

22.10 Prognosis

Most ASDs will close spontaneously by 4 years, with smaller ones having a higher closure rate than bigger ones. A long-standing large defect, however, leads to chronic heart failure and pulmonary hypertension in early adulthood. Prognosis is generally good, with many living into adulthood, even without corrective surgery. Post-surgical mortality is currently less than 0.5%. The patient will need little long-term follow-up after the corrective surgery.

22.11 Differential diagnosis

Differential diagnosis includes pulmonary stenosis and a pink Tetralogy of Fallot.

23 Ventricular Septal Defect

23.1 Introduction

This is the most common Congenital Heart Disease (CHD), being seen in about 15-20% of all CHDs. VSD occurs in different anatomical locations. The most common is the peri-membranous. Others are inlet, outlet, muscular and infundibular. They also appear in different shapes and sizes as well.

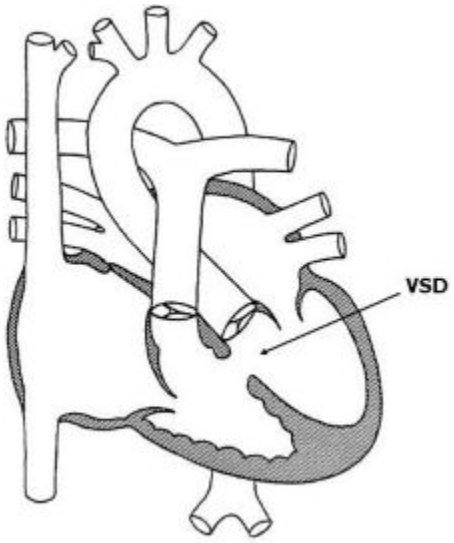

Figure 23.1: Ventricular Septal Defect

23.2 Pathophysiology

Typically VSD without the presence of another congenital heart malformation results in a left to right ventricle shunting lesion because of the pressure difference. Thus, a VSD is usually an acyanotic congenital heart lesion. This leads to a volume overload of the pulmonary artery, lungs, left atrium and left ventricle. These chambers subsequently dilated. Pulmonary edema develops from lung congestion leading to signs of heart failure.

Secondly, depending on the size of the defect the pressure in the left ventricle will get transmitted to the right. How much pressure is transmitted depends on the size of the defect with bigger defects transmitting more than smaller ones. This can result in increased right ventricular pressure, and hypertrophy. It also worsens the pulmonary oedema already mentioned above.

Persistent pressure and volume overload cause remodelling of the pulmonary vasculature, resulting in permanent changes and pulmonary hypertension. When the pulmonary pressure rises significantly higher than the systemic pressure, a reversal of the shunt results, leading to decreased oxygen saturation.

23.3 Clinical presentation

The clinical presentation of VSDs is variable and depends on the size and position.

Position: A perimembranous VSD of comparable size may exhibit more signs of heart failure than one that is mid-muscular or apical.

Size: Generally, the sizes of VSDs determine the extent of the volume and pressure overload of the right heart and lungs. Larger ones result in relatively higher pressure and volume. Small VSDs are usually asymptomatic with no volume or pressure overload of the lung, pulmonary artery and right heart. Some volume and pressure overload usually accompanies moderate-sized VSDs. They are thus often accompanied by some heart failure and recurrent lower respiratory infections. Large defects are accompanied by severe volume and pressure overload. They present with persistent heart failure and failure to thrive, exercise intolerance. When longstanding, they often end up with significant pulmonary hypertension.

Newborns with VSD may not have a murmur at birth. This is due to relatively high pulmonary pressure in the first weeks of life. The intensity of the murmur may increase as the pulmonary pressure decreases, usually over 4 weeks. The patient then becomes more symptomatic with a louder pansystolic murmur loudest at the lower left sternal border. Patients with a large defect may present with an apical diastolic rumble. Cyanosis may present in a long-standing large VSD with pulmonary hypertension.

23.4 Investigations

- At the bedside pulse oximetry would likely reveal a normal SpO_2 as this is an acyanotic congenital heart disease.
- A chest X-ray could show cardiomegaly with dilatation of the left side of the heart. Increased vascular markings may also be present.
- The electrocardiogram will likely show features of left ventricular dilatation and left atrial enlargement.

- An echocardiogram is diagnostic as it visualises the defect, quantifies the shunt and other chamber sizes, and identifies possible complications.
- Cardiac catheterisation is often done in cases of moderate to large defects. to detect complications such as possibly pulmonary hypertension, and quantify the shunt volume.

23.5 Treatment

Treatment modalities depend on the patient's age, defect size and location, associated symptoms and complications. Small defects in the very young, without signs of heart failure, can be treated by watchful waiting as some may close spontaneously. Defects accompanied by heart failure symptoms should be treated for heart failure while planning for possible surgical ligation is being done. Large defects are treated the same but with more aggressive heart failure management and urgent surgical therapy. This is because these are often accompanied by a failure to thrive, poor feeding and generally poor health.

Current surgical treatment involves device closure, but some centers such as Ghana still close the defects with an open heart surgery. Also, there are certain circumstances where a device closure cannot be done, thus open heart surgery becomes the only option.

23.6 Prognosis

In many developed countries, the prognosis of VSDs has become excellent with surgical and device treatment. (Jortveit et al. 2016) However, in Ghana, most patients do not realistically have the chance of early surgical correction. Thus the prognosis of VSDs with significant symptoms tends to be poor.

23.7 Differential diagnosis

Differential diagnosis of a ventricular septal defect is mitral regurgitation and tricuspid regurgitation.

23.8 Complications

Notable complications of VSDs include Infective Endocarditis, aortic regurgitation, pulmonary hypertension, left ventricular outflow tract obstruction and growth failure.

24 Patent Ductus Arteriosus

24.1 Definition

Patent Ductus Arteriosus (PDA) is an acyanotic congenital heart disease. that results from the persistence into the post-natal life of the normal fetal vascular conduit between the pulmonary and systemic arterial systems. Figure **??** Normally, the ductus arteriosus functionally closes within the first 1-3 days after birth. Structural closure is usually completed by the 3rd week of birth.

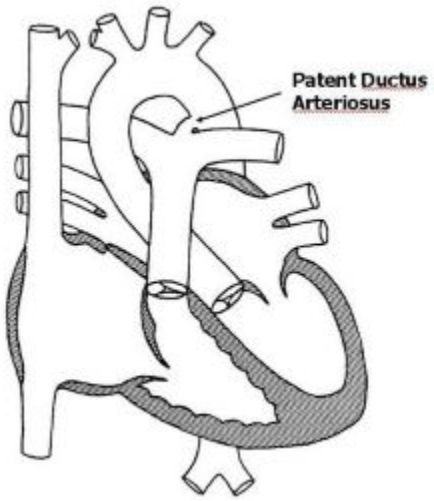

Figure 24.1: Patent Ductus Arteriosus

24.2 Incidence/prevalence

PDAs represent about 5-10% of all congenital heart defects, with an equal male-to-female ratio.(Borges-Lujan et al. 2022) It made up 23% of all electrocardiograph diagnoses of heart diseases seen in Kumasi, with a male-female-ratio of 1:0.9. This high proportion of PDAs in this cohort could be because a significant proportion of the children scanned were preterm infants.

24.3 Aetiology

Although there are no recognized etiological factors, PDAs are associated with a few recognisable conditions. These include:

1. **Prematurity** - The more premature a baby is the higher the incidence of PDA. it is seen in as much as 80% of babies born from 24 to 28 weeks.
2. **Teratogenic agents** such as Congenital Rubella, fetal alcohol syndrome, fetal hydantoin syndrome and maternal phenylketonuria
3. **Genetic or familial** factors such as Trisomy 21, Trisomy 18, Trisomy 13, Noonan syndrome, CHARGE association, VATER association, Holt-Oram syndrome, Treacher Collins syndrome, PHACE Syndrome, Smith-Lemli-Opitz syndrome, Cri du chat syndrome
4. **Living at high altitudes** has long been associated with a higher incidence of PDAs
5. **Idiopathic** - Many patients with a PDA have no identifiable risk factors.

24.4 Pathophysiology

Ductus arteriosus in fetal circulation is indispensable to allow right-to-left shunting of nutrient-rich oxygenated blood from the placenta to the fetal systemic circulation, bypassing the fetal pulmonary circuit. At birth, the rise in PaO_2 and decline in prostaglandin concentration cause closure of the ductus arteriosus, typically beginning within the first 10 to 15 hours of life. If this normal process does not occur, the ductus arteriosus will remain patent. The PDA then results in excess blood shunting from the aorta, across the duct and into the pulmonary artery. This shunting causes volume overload. There is therefore a circuit of excess blood volume in the pulmonary arteries, lungs, left atrium, left ventricle, and aorta. This subsequently leads to dilatation of the left pulmonary artery, left atrium and left ventricle as well as pulmonary edema and heart failure.

24.5 Signs and symptoms

Symptoms vary based on the volume of additional blood flow to the lungs.

1. The degree of the shunt depends on:
    - The size of the PDA (including diameter, length, and tortuosity). Bigger ducts with shorter lengths often result in worse symptoms. Conversely, patients with small PDAs are often asymptomatic.
    - Pulmonary vascular resistance when high does not encourage shunting across the duct. However, as the resistance drops the shunt gets worse, with worsening symptoms.

- Moderate to larger shunts produce the symptoms of congestive heart failure as the pulmonary vascular resistance decreases over the first 6 to 8 weeks of life.

2. The physical examination depends on the size of the shunt, and to a lesser extent the age and maturity of the patient.
   - Premature infants may present with:
     - Tachypnoea, crackles, tachycardia
     - Hyperdynamic precordium and bounding pulses with wide pulse pressure
     - ***Pansystolic*** murmur loudest at the left upper or mid-sternal border.
     - With a large PDA and equalization of pressure between the main pulmonary artery and the aorta, no murmur may be heard.
     - Soft tender hepatomegaly
   - Infants and older children with small PDAs may present with:
     - A pansystolic murmur loudest in the 2^{nd} left intercostal space
     - Murmur becomes continuous as the pulmonary vascular resistance decreases over the first months of life.
   - Infants and older children with moderate to large PDA may present with:
     - Louder murmur with a harsh quality and acquires a ***machine-like*** quality often being heard posteriorly. A systolic thrill may be felt at the left upper sternal border.
     - Tachycardia, bounding pulses with a wide pulse pressure, and a mid-diastolic low-frequency rumbling murmur may be audible at the apex with a large PDA
     - With severe left ventricular failure the classic PDA signs may disappear, but there will be findings consistent with congestive heart failure (tachycardia, S3 gallop at the apex, tachypnoea, soft tender hepatomegaly, bi-basal crackles)
     - Pulmonary hypertension may occur in long-standing cases. In advanced cases of irreversible pulmonary vascular disease, cyanosis occurs with the reversal of shunting.

24.6 Investigations

1. **Chest X-ray:** Varies from normal (small PDAs) to prominence of main and peripheral pulmonary arteries and vasculature. Findings are more pronounced with moderate to large PDAs and may show cardiomegaly, and increased pulmonary vascular markings proportional to the left-to-right shunt. A dilated pulmonary artery may be seen on the chest x-ray in long-standing cases. Figure **??** Pulmonary oedema can be seen with congestive heart failure.
2. **Electrocardiogram:** Findings vary from normal (small PDAs) to evidence of left atrial dilatation and left ventricular hypertrophy with moderate to large PDA. Evidence of bi-ventricular hypertrophy in long-standing cases. If pulmonary hypertension is present, evidence of right ventricular hypertrophy may be seen.

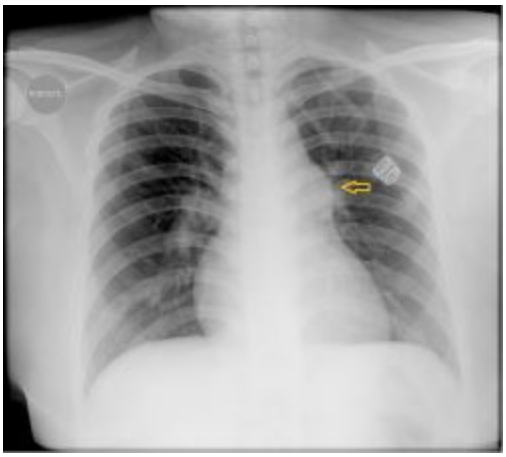

Figure 24.2: Chest X-ray showing dilated pulmonary artery in a child with PDA

3. **Echocardiogram:** This delineates the PDA and assesses the size of the left atrium and ventricle. Useful for evaluating pulmonary hypertension. Doppler for determining the flow pattern.
4. **Cardiac catheterisation:** most often not essential for diagnosis. Can be performed for treatment using transcatheter closure techniques

24.7 Treatment

1. Supportive treatment including careful use of oxygen and respiratory assistance
2. Management of CHF with diuretics commonly furosemide and spironolactone, digoxin and afterload reduction on a case-by-case basis
3. Pharmacologic closure of PDA: Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) such as indomethacin or ibuprofen; are not usually effective in infants or older children but are in the early neonatal period. Contraindications to pharmacologic closure include co-existing congenital heart defects that are duct-dependent, renal impairment, thrombocytopenia and associated conditions such as NEC and IVH.
4. Surgical closure is indicated in symptomatic or haemodynamically significant PDA. Surgical closure is achieved by open surgical ligation and division, video-assisted thoracoscopic ligation or transcatheter occlusion with coils or other devices.

24.8 Complications

The recognised complication of PDA includes infectious endocarditis, pulmonary hypertension and heart failure.

24.9 Prognosis

1. The chance of spontaneous closure in a preterm baby is about 95%, while the likelihood of spontaneous closure in a term baby is more than 90% by age 1.(Yuan et al. 2021) This is because PDA in term infants results from a structural abnormality of the ductal smooth muscles rather than a decrease in responsiveness of the ductal smooth muscles to oxygen.
2. Heart failure and risk of recurrent chest infections develop for large shunts
3. Large shunts are also a risk for the development of pulmonary hypertension
4. Surgical treatment now has an almost 100% success rate in many centres.

24.10 Differential diagnosis

Other acyanotic congenital heart diseases are possible differentials. These include a large atrial septal defect and a coarctation of the aorta.

25 Coarctation of the Aorta

25.1 Definition

Coarctation of the aorta (CoA) is a congenital heart defect characterized by the narrowing of the aorta, the major artery responsible for carrying oxygen-rich blood from the heart to the rest of the body. This condition accounts for approximately 5-8% of all congenital heart defects in children and is more prevalent in males than females. CoA can present with varying degrees of severity and may occur as an isolated defect or associated with other cardiac anomalies, such as bicuspid aortic valve, ventricular septal defect (VSD), or complex syndromes like Turner syndrome.

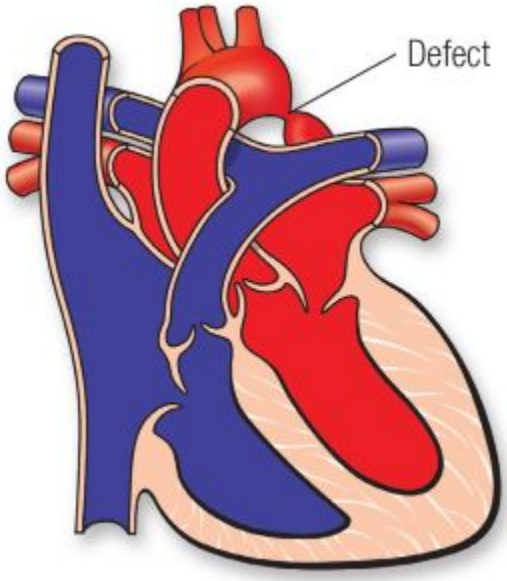

Figure 25.1: Coarctation of the aorta

25.2 Anatomy and Pathophysiology

The aorta plays a crucial role in distributing oxygenated blood from the heart's left ventricle to the systemic circulation. In CoA, the narrowing typically occurs at the isthmus of the aorta, which is located distal to the left subclavian artery and near the ductus arteriosus, a fetal blood vessel that normally closes after birth. The severity of CoA depends on the degree of narrowing, which can obstruct blood flow and increase the heart's afterload.

The left ventricle must work harder in children to pump blood through the narrowed segment, leading to left ventricular hypertrophy. Prolonged obstruction may result in high blood pressure (hypertension) in the upper body and diminished blood flow to the lower body. Collateral circulation often develops as the body compensates using smaller vessels to bypass the narrowing, but this is not always sufficient to normalize blood flow.

25.3 Clinical Presentation

The clinical manifestations of CoA in children vary based on the severity of the narrowing. Severe cases may present in infancy, while milder forms might remain undetected until adolescence or adulthood.

25.3.1 Infants:

- Severe CoA may cause critical illness within the first few weeks of life, especially after the ductus arteriosus closes.
- Symptoms include poor feeding, failure to thrive, lethargy, respiratory distress, and signs of heart failure.
- Pulses in the lower extremities may be weak or absent, and blood pressure measurements reveal significant upper-to-lower extremity discrepancies.

25.3.2 Older Children:

- Milder CoA might be asymptomatic or present with less obvious symptoms, such as fatigue, leg pain during exercise (claudication), headaches, or nosebleeds.
- Hypertension is common in older children and may be detected incidentally during routine health check-ups.
- Physical examination often reveals a systolic murmur heard best over the back, diminished or delayed femoral pulses, and upper extremity hypertension relative to the lower extremities.

25.4 Diagnostic Evaluation

Timely diagnosis of CoA is critical to prevent complications and ensure appropriate management. Several diagnostic tools are employed to confirm the condition and assess its severity.

1. **Physical Examination:**

    - Blood pressure measurements in all four extremities to identify discrepancies.
    - Palpation of pulses to detect reduced or absent femoral pulses.
    - Auscultation for murmurs and other abnormal heart sounds.

2. **Imaging Studies:**

    - **Chest X-ray:** May show rib notching (caused by collateral vessels) and a characteristic "3 sign" of the aorta.
    - **Echocardiography:** The primary diagnostic tool for visualizing the narrowed segment of the aorta and assessing associated anomalies.
    - **Magnetic Resonance Imaging (MRI) or Computed Tomography (CT):** Provides detailed anatomical information, especially in older children or when planning surgical interventions.

3. **Cardiac Catheterization:**

    - Invasive procedures are used for definitive diagnosis in certain cases and for interventional treatment.
    - Measures pressure gradients across the narrowed segment and evaluates the severity of obstruction.

25.5 Management

The treatment of CoA depends on the child's age, the severity of the condition, and the presence of associated cardiac defects. The primary goal is to relieve the obstruction, restore normal blood flow, and prevent complications.

1. **Medical Management:**

    - In neonates with severe CoA and ductal-dependent circulation, prostaglandin E1 infusion maintains ductus arteriosus patency and ensures adequate lower body perfusion.
    - Medications such as inotropes and diuretics may be administered to manage heart failure symptoms before definitive treatment.

2. **Surgical Repair:**

- Surgical correction is often the preferred treatment for infants and young children with severe CoA.
- Techniques include resection of the narrowed segment with end-to-end anastomosis, subclavian flap aortoplasty, or patch augmentation.
- Surgery is typically performed during infancy or early childhood to minimize long-term complications and avoid the development of significant collateral circulation.

3. **Catheter-Based Interventions:**
    - Balloon angioplasty and stent placement are minimally invasive alternatives, particularly in older children and adolescents.
    - These procedures are often used for coarctation after initial surgical repair or in cases where surgery is not feasible

25.6 Complications

Untreated or inadequately treated CoA can lead to significant complications, including:

- Persistent hypertension, even after successful repair.
- Aortic aneurysm or dissection, particularly in cases of long-standing hypertension.
- Heart failure due to left ventricular strain.
- Premature coronary artery disease and cerebrovascular events, such as stroke.
- Infective endocarditis, especially in cases with associated valvular abnormalities.

25.7 Long-Term Outcomes

With advancements in diagnostic techniques and treatment modalities, the prognosis for children with CoA has improved significantly. However, long-term follow-up is essential to monitor for residual or recurrent narrowing, hypertension, and other complications. Lifelong care under a cardiologist familiar with congenital heart defects is recommended.

25.8 Prognosis

The long-term outlook for children with CoA largely depends on the timing and success of treatment. Early intervention typically results in good outcomes, with most children leading normal or near-normal lives. However, ongoing surveillance is crucial to address potential issues such as:

- Residual or recurrent coarctation.
- Systemic hypertension.
- Associated cardiac or vascular anomalies.

25.9 Prevention and Genetic Considerations

Since CoA is a congenital defect, prevention strategies focus on early detection and management. Prenatal ultrasounds can sometimes identify CoA in utero, especially in high-risk pregnancies. Genetic counseling may be beneficial for families with a history of congenital heart defects or syndromes like Turner syndrome, which are associated with a higher risk of CoA.

25.10 Conclusion

Coarctation of the aorta is a significant congenital heart defect that poses challenges in diagnosis and management, particularly in infants and young children. Advances in medical and surgical interventions have greatly improved outcomes, but timely recognition and treatment remain critical. Long-term follow-up and a multidisciplinary approach involving pediatric cardiologists, surgeons, and primary care providers are essential to optimize the health and well-being of affected children.

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26 Tetralogy of Fallot

26.1 Definition

Tetralogy of Fallot (ToF) is a conotruncal defect resulting from anterior misalignment of the infundibular septum, giving rise to four components:

- Large, nonrestrictive Ventricular Septal Defect
- The aorta overriding the interventricular septum
- Right ventricular outflow tract obstruction, including at the infundibulum, main and branch pulmonary arteries
- Right ventricular hypertrophy

26.2 Incidence/prevalence

It is the most common cyanotic congenital heart disease. About 1 in 3500 babies born in the US are born with ToF. Accounts for 7–10% of all congenital cardiac malformations. More common in Males. In a series of echocardiograms done in Kumasi, Ghana, ToF was the most common cyanotic congenital heart disease seen in 13% of all heart diseases. There was a significant male preponderance with a female vs male prevalence of 10% vs 15%, respectively.

26.3 Aetiology

Although there is no known definite cause as to why some babies develop ToF in utero, certain environmental and biological factors are known to increase the risk:

- **Genetic**: CHARGE syndrome, chromosome 22q11 microdeletion (Di George syndrome), Down syndrome, Edward's syndrome, or Patau syndrome, VACTERL association
- **Teratogens**: maternal diabetes mellitus, retinoic acid exposure, maternal phenylketonuria (PKU), Alcohol (fetal alcohol syndrome), Warfarin (fetal warfarin syndrome), Trimethadione: antiepileptic drug

26.4 Pathophysiology

- The severity of clinical signs and symptoms depends on the proportion of the cardiac output going through the pulmonary artery, the relative pressures in the right and left ventricles, and the proportion of the aorta overriding the VSD.
- The VSD is normally of a significant size, which causes the systolic pressures between the ventricles to equalize. In mild ToF, the left ventricular pressures remain higher than the right ventricle, thus, blood shunts from left to right through the VSD. These patients are normally acyanotic. In more severe diseases, due to increased right ventricular pressure (secondary to Pulmonary Stenosis), the shunt direction reverses from right to left, allowing the mixing of deoxygenated and oxygenated blood. This results in lower oxygenated blood in the systemic circulation, making patients cyanotic.
- Pulmonary stenosis can be classified according to its location. The commonest site is the infundibular septum (50%). The stenosis may also be valvular (10%) or a combination (30%). This results in impaired flow of deoxygenated blood into the main pulmonary artery. It may be severe enough to cause intermittent right ventricular outflow tract obstruction. This forms the basis of hypercyanotic episodes (tet spells).
- Hypertrophy of the right ventricle occurs in response to the high pressures it must overcome to force deoxygenated blood through the right ventricular outflow tract obstruction. Compared to the normal heart, the aorta in ToF is dilated and displaced over the interventricular septum. Aortic dilatation is caused by an increase in blood flow through the aorta as it receives blood from both ventricles via the Ventricular Septal Defect.

26.5 Signs and symptoms

Patients with Tof are often not born with cyanosis. This may lead to the diagnosis being missed at birth. However, progressive cyanosis occurs in the first year of life. They usually have little or no signs of heart failure. Most will present with poor exercise tolerance, which worsens as the child ages. In children who can walk, frequent squatting is observed in unrepaired ToF. Other features include poor feeding and poor weight gain.

Physical examination of children with ToF may reveal digital clubbing of varying stages, central cyanosis, and plethora, usually seen in the hands and eyes. Auscultation classically reveals the first and second heart sounds with an ejection systolic murmur loudest at the upper to middle left sternal edge.

26.6 Investigations

Bedside pulse oximetry often reveals an oxygen saturation of less than 90%. A chest X-ray shows a normal-sized heart with a classical boot shape and decreased pulmonary vascular

markings. In about 30% of the cases, a right arch is present.

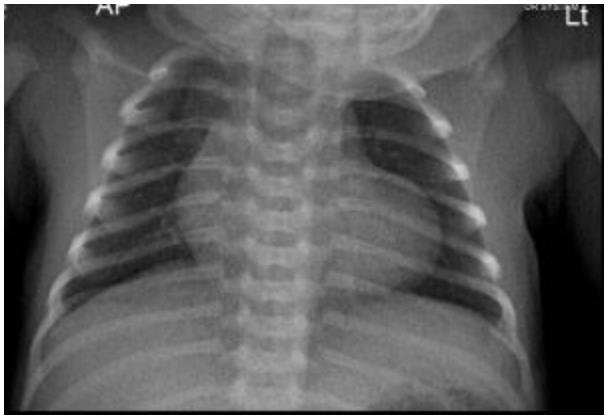

Figure 26.1: Boot-shaped heart of Tetralogy of Fallot

An electrocardiogram, though non-specific, may show right axis deviation, right ventricular hypertrophy, and right atrial enlargement.

An echocardiogram is the most useful diagnostic modality. It delineates the defect by showing the anterior malalignment Ventricular Septal Defect, degree of infundibular stenosis, state of the pulmonary artery and/or branches, and the overriding aortic arch sidedness. Other anatomical abnormalities that may co-exist, eg, Atrioventricular Canal Defects, Atrial Septal Defect, and coronary artery abnormalities can also be obtained. A CT angiogram and Magnetic Resonance Angiography can be done in complex cases and in preparation for surgery.

26.7 Treatment

Since patients with ToF hardly experience heart failure, antifailure medications are not the mainstay of treatment.

Untreated cyanotic congenital heart disease is associated with a chronic hypoxic state, which leads to polycythemia. This leads to a high demand for iron and increases susceptibility to iron deficiency. Furthermore, it is well documented that iron deficiency increases the chance of a hypercyanotic spell and stroke. Iron treatment in ToF is therefore key in its outpatient management. Nutritional rehabilitation is done for chronically malnourished patients.

Surgical therapy is the definitive treatment. A Blalock-Taussig shunt can be done to improve oxygenation. A stand can also be inserted in younger children when deemed necessary. Definitive corrective surgery should be done for all children with ToF.

26.8 Natural history

Features of ToF are progressive if not corrected surgically. There is usually progressive dyspnoea on exertion and cyanosis as the child ages. However, some "pink tets" can live very well into adulthood. Untreated, approximately 50% will live to their 6th birthday.

26.9 Complications

A feared presentation in untreated children with a ToF is the hypercyanotic spell (Tet spell). This is treated further below. Other complications can result from the embolus effect, leading to stroke and cerebral abscess. High hematocrit may lead to hyperviscosity, headache, and dizziness. Infective endocarditis is another known complication. Long-term complications include right ventricular dysfunction, coagulopathy, and arrhythmias.

26.10 Prognosis

Repaired, the 25-year survival is about 95%.(Smith et al. 2019) Unrepaired, most will die by their 10th birthday. This is especially so for those with other genetic syndromes and associated malformations.

26.11 Differential diagnosis

Cyanosed ToF patients have a differential diagnosis of Transposition of the great arteries, Tricuspid atresia, pulmonary atresia, etc. Pink ToFs will have a differential diagnosis of a Ventricular Septal Defect

26.12 Prevention

There is no known prevention for ToF. However, it is always prudent for prospective mothers and those in the first trimester to avoid recreational drugs, alcohol, and some over-the-counter medications. Also, folic acid supplementation should be encouraged.

26.13 Hypercyanotic spell

A hypercyanotic spell (tet spell) is an emergency in children with ToF and, to a lesser extent, other cyanotic congenital heart diseases. It presents most commonly in children less than 2 years old.

26.13.1 Presentation

Children with hypercyanotic spells present with paroxysms of increased and deep breathing, irritability, prolonged, unsettled crying, increasing cyanosis, seizures, and decreased intensity of the heart murmur. In untreated cases, this might lead to brain damage or death.

26.13.2 Pathophysiology

A hypercyanitic spell can have many precipitating factors. These may include fever, anemia, dehydration, prolonged crying, and eating. These precipitants lead to decreased lung blood flow and progressively increase right-to-left shunting. This leads to increasing cyanosis, tachycardia, and reduced systemic vascular resistance. Carbon dioxide accumulation stimulates the central respiratory center, leading to increased and deep breathing. All these unfortunately cause further right-to-left shunting, thus perpetuating the hypoxia.

26.13.3 Treatment

The treatment goal is to increase preload and promote pulmonary blood flow.

- First, the child should be placed in a knee-chest position. This increases systemic vascular resistance, temporarily raises the systemic pressure, and reduces the right-to-left shunting.
- Oxygen can be administered, though it is of limited value and should not be forced on the patient if he is combative.
- Next volume expansion with intravenous fluids should be administered. This raises the preload and increases systemic pressure, thus reducing right-to-left shunting.
- Intramuscular or subcutaneous morphine can be administered. This aids in relaxing the infundibular muscle and thus promotes pulmonary blood flow. It also sedates the child, thus making him/her less acidotic. Acidosis perpetuates the hyperchaotic spell
- Intravenous propranolol, esmolol, or metoprolol is administered to reduce the right ventricular outflow tract obstruction.
- Some alpha-agonists, such as Phenylephrine, can be given to improve blood pressure in severe cases
- Long-term treatment may include oral propranolol for prophylaxis, iron supplementation, and surgical correction.

27 Rheumatic Heart Disease

27.1 Introduction

Rheumatic heart disease (RHD) is a chronic condition resulting from acute rheumatic fever (ARF), an autoimmune response to group A beta-hemolytic streptococcal (GAS) pharyngitis. It is characterized by permanent damage to the heart valves, particularly the mitral and aortic valves, due to repeated episodes of inflammation and scarring. RHD remains a significant cause of morbidity and mortality among children and young adults in low- and middle-income countries. Early diagnosis and management of ARF and RHD are critical to prevent severe complications and improve outcomes.

27.2 Incidence and Prevalence

RHD affects approximately **40 million people worldwide**, with the highest burden in sub-Saharan Africa, South Asia, the Pacific Islands, and parts of Latin America. The global prevalence in children aged 5–15 years is estimated at **1–3 per 1,000**, but it can exceed **10 per 1,000** in high-risk populations. ARF, the precursor to RHD, occurs most commonly between **5 and 15 years** of age, with peak incidence following untreated or inadequately treated GAS pharyngitis.

27.3 Etiology

The primary etiology of RHD is **recurrent ARF episodes** triggered by an **immune response to GAS infection**. The following factors contribute to its development:

1. **Infectious Agent**: GAS infection, particularly of the throat, is necessary to initiate the autoimmune process. Certain GAS strains (M-protein serotypes) are more rheumatogenic.
2. **Host Susceptibility**: Genetic predisposition plays a role, with family clustering observed in affected individuals.
3. **Environmental Factors**: Overcrowding, poor hygiene, and limited access to healthcare increase the risk of GAS infections and progression to ARF and RHD.

RHD develops through the following sequence:

1. **GAS Pharyngitis**: GAS infection elicits an immune response involving antibodies and T-cells targeting streptococcal antigens.
2. **Molecular Mimicry**: Cross-reactivity occurs between streptococcal antigens (e.g., M protein) and human proteins in the heart, joints, brain, and skin. Autoimmune inflammation leads to tissue damage.
3. **Acute Rheumatic Fever**: Pancarditis (endocarditis, myocarditis, and pericarditis) is the hallmark of ARF. The endocardium is most affected, leading to valvulitis.
4. **Chronic RHD**: Recurrent inflammation and scarring cause permanent valvular damage, predominantly affecting the mitral and aortic valves. Mitral stenosis is the most common lesion, followed by mitral regurgitation and aortic regurgitation.

27.4 Signs and Symptoms

The clinical presentation of RHD varies based on the severity of valvular involvement and associated complications.

1. **Symptoms**:
    - Fatigue and exercise intolerance
    - Dyspnea, initially on exertion and later at rest
    - Palpitations due to arrhythmias (e.g., atrial fibrillation)
    - Cough and hemoptysis (in severe mitral stenosis)
    - Edema and signs of heart failure in advanced cases
2. **Signs**:
    - **Cardiac Murmurs**:
        - Mitral stenosis: Low-pitched diastolic murmur with an opening snap.
        - Mitral regurgitation: holosystolic murmur at the apex
        - Aortic regurgitation: High-pitched diastolic murmur.
    - Cardiomegaly with a displaced apex beat
    - Signs of pulmonary hypertension (e.g., loud pulmonary component of S2)
    - Peripheral edema, hepatomegaly, and ascites in heart failure
3. **History of ARF**:
    - Clinical features such as migratory polyarthritis, carditis, chorea, subcutaneous nodules, or erythema marginatum support prior episodes of ARF.

27.5 Investigations

The diagnosis of RHD involves clinical assessment, laboratory tests, and imaging studies.

1. **Laboratory Tests**:
    - **Throat Culture or Rapid Antigen Test**: To confirm GAS infection if suspected.
    - **Anti-Streptolysin O (ASO) Titer**: Elevated in recent GAS infections.
    - **C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR)**: Markers of inflammation during ARF episodes.
2. **Imaging**:
    - **Echocardiography**:
        - Key diagnostic tool for detecting valvular lesions and assessing severity.
        - Common findings include leaflet thickening, restricted mobility, and regurgitation or stenosis
    - **Chest X-Ray**:
        - Cardiomegaly and pulmonary congestion in advanced disease.
    - **Electrocardiogram (ECG)**:
        - Prolonged PR interval (first-degree heart block) in ARF.
        - Atrial fibrillation or other arrhythmias in chronic RHD
3. **Other Tests**:
    - Cardiac MRI in selected cases for detailed assessment of myocardial and valvular involvement.

27.6 Treatment

Management of RHD aims to reduce symptoms, prevent disease progression, and address complications.

1. **Medical Management**:
    - **Antibiotic Prophylaxis**: Long-term benzathine penicillin G intramuscular injections every 3–4 weeks to prevent recurrent ARF episodes.
    - **Heart Failure Management**: Diuretics, ACE inhibitors, and beta-blockers for symptomatic relief.
    - **Anticoagulation**: Warfarin for patients with atrial fibrillation or mechanical valve replacement.
    - **Anti-Inflammatory Therapy**: Aspirin or corticosteroids for active carditis.
2. **Surgical and Interventional Treatment**:

- **Valvuloplasty**:
  - Percutaneous balloon mitral valvotomy for mitral stenosis in suitable candidates
- **Valve Repair or Replacement**:
  - Required for severe valvular dysfunction or when medical management fails.

27.7 Prevention

The cornerstone of RHD prevention is the timely diagnosis and treatment of GAS pharyngitis and ARF.

1. **Primary Prevention**:
   - Early recognition and antibiotic treatment of streptococcal pharyngitis with penicillin or amoxicillin.
   - Improved hygiene and reduced overcrowding to lower transmission risk.
2. **Secondary Prevention**:
   - Long-term antibiotic prophylaxis to prevent recurrent ARF.
   - Duration of prophylaxis:
     - At least 10 years after the last episode of ARF or until the patient is 21 years old, whichever is longer.
     - Life-long prophylaxis for severe valvular disease or post-surgical cases
3. **Community Interventions**
   - Public health programs to increase awareness and access to healthcare in high-burden regions.

27.8 Complications

RHD can lead to severe complications if not adequately managed:

1. **Heart Failure**: Due to progressive valvular dysfunction and increased cardiac workload.
2. **Atrial Fibrillation**: Common in mitral stenosis, leading to thromboembolic events like stroke.
3. **Pulmonary Hypertension**: Resulting from chronic left-sided valvular disease.
4. **Infective Endocarditis**: Increased risk in patients with damaged valves.
5. **Pregnancy Complications**: Significant maternal and fetal risks due to increased hemodynamic demands.

27.9 Prognosis

The prognosis of RHD depends on the severity of valvular involvement, the effectiveness of secondary prophylaxis, and access to medical and surgical care. Without intervention, severe RHD can result in progressive heart failure, significant morbidity, and premature death. With timely diagnosis and appropriate management, many children can experience improved quality of life and survival.

27.10 Differential Diagnosis

Several conditions can mimic the clinical presentation of RHD and should be considered:

1. **Congenital Heart Disease**: Examples include atrial septal defect, ventricular septal defect, and patent ductus arteriosus.
2. **Infective Endocarditis**: Characterized by fever, new murmur, and signs of embolization.
3. **Kawasaki Disease**: Vasculitis with coronary artery involvement, fever, and mucocutaneous inflammation.
4. **Myocarditis**: Viral or autoimmune causes leading to cardiac inflammation.
5. **Mitral Valve Prolapse**:
    - Can mimic mitral regurgitation murmurs

27.11 Conclusion

Rheumatic heart disease remains a major public health challenge in developing countries, disproportionately affecting children and young adults. Early recognition and treatment of GAS pharyngitis and consistent secondary prophylaxis are essential to prevent the progression to RHD. Multidisciplinary care, including medical, surgical, and public health interventions, is crucial to improving outcomes and reducing the global burden of this preventable disease.

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28 Infective Endocarditis

28.1 Definition

Infective endocarditis (IE) is an infection of the endocardial surface of the heart, typically involving one or more heart valves. It can be caused by bacteria, fungi, or other pathogens, leading to the formation of vegetation on the heart valves or endocardium. A serious condition that can result in significant morbidity and mortality without prompt diagnosis and treatment.

28.2 Incidence/Prevalence

Rare in children, with an estimated incidence of 0.05–0.12 cases per 1,000 pediatric hospital admissions. More common in children with underlying congenital heart disease (CHD), accounting for up to 80% of cases. Increasing prevalence due to improved survival rates of children with CHD and the use of indwelling central venous catheters. Higher incidence in children with prosthetic heart valves or those who have undergone cardiac surgery.

Aetiology

- **Microorganisms**:
  - Bacteria: Most common cause, including *Streptococcus viridans*, *Staphylococcus aureus*, and *Enterococcus* species.
  - Fungi: Less common, but *Candida* and *Aspergillus* can cause IE, particularly in immunocompromised patients
- **Risk Factors**:
  - Congenital heart defects, particularly cyanotic lesions.
  - Prosthetic heart valves.
  - Indwelling devices (e.g., pacemakers, central venous catheters).
  - Rheumatic heart disease (rare in developed countries).
  - Immunosuppression or intravenous drug use (less common in pediatrics).

Pathophysiology

- Initial endothelial damage due to turbulent blood flow or direct trauma (e.g., from catheters).
- Formation of sterile thrombotic vegetations at the site of damage.
- Colonization of vegetations by microorganisms during transient bacteremia.
- Vegetations grow, consisting of microorganisms, fibrin, and platelets.
- Can result in local destruction of heart structures, systemic embolization, and immune-mediated complications (e.g., glomerulonephritis).

Signs and Symptoms

- **Non-specific symptoms**:
  - Fever (most common presenting symptom).
  - Fatigue, malaise, anorexia, weight loss
- **Cardiac manifestations**:
  - New or changing heart murmur.
  - Signs of heart failure (e.g., dyspnea, tachypnea, peripheral edema)
- **Systemic features**:
  - Petechiae, splinter hemorrhages.
  - Osler nodes (painful nodules on fingers/toes).
  - Janeway lesions (painless macules on palms/soles).
  - Roth spots (retinal hemorrhages with central clearing).
- **Embolic phenomena**:
  - Stroke or other neurologic deficits.
  - Splenic or renal infarction.
  - Pulmonary emboli in right-sided IE.
- Symptoms may be less pronounced in children, particularly in chronic or subacute presentations.

Investigations

- **Blood cultures**:
  - Essential for diagnosis; obtain at least three sets before starting antibiotics.
  - May reveal causative organism in >90% of cases if appropriately timed.
- **Echocardiography**:
  - Transthoracic echocardiography (TTE): Initial investigation; non-invasive.
  - Transesophageal echocardiography (TEE): Higher sensitivity, especially for prosthetic valves or difficult-to-image cases

- **Laboratory tests**:
  - Full blood count: May show anemia, leukocytosis, or thrombocytopenia.
  - Inflammatory markers: Elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)
  - Renal function and urinalysis: May detect embolic phenomena or immune-mediated injury.
- **Imaging**:
  - Chest X-ray: Evaluate for heart failure or pulmonary embolism in right-sided IE
  - CT or MRI: Assess embolic complications (e.g., stroke, abscess).

Treatment

- **Antimicrobial therapy**:
  - Empiric treatment with broad-spectrum antibiotics after blood cultures are drawn.
  - Tailor therapy based on culture results and sensitivity testing.
  - Prolonged intravenous antibiotics (typically 4–6 weeks).
- **Surgical intervention**:
  - Indicated for severe valvular damage, heart failure, abscess formation, or persistent infection despite antibiotics.
  - Often required for prosthetic valve endocarditis.
- **Supportive care**:
  - Management of heart failure or other complications.
  - Anticoagulation generally avoided due to risk of embolization from vegetations

Complications

- **Cardiac complications**:
  - Valvular dysfunction (regurgitation or stenosis).
  - Heart failure.
  - Perivalvular abscess.
  - Conduction disturbances (e.g., heart block).
- **Embolic events**:
  - Stroke, myocardial infarction, or organ infarctions.
  - Septic emboli causing abscesses.
- **Systemic complications**:
  - Immune complex-mediated glomerulonephritis.
  - Disseminated infection or sepsis

- **Prosthetic valve complications**:
  - Dehiscence or dysfunction requiring reoperation

Prognosis

- Depends on the underlying cause, diagnosis timeliness, and treatment appropriateness.
- Mortality rates in children range from 10% to 25%, higher in fungal infections or prosthetic valve IE.
- Early surgical intervention improves outcomes in high-risk cases.
- Long-term follow-up necessary for valve function and detection of late complications.

Differential Diagnosis

- **Non-infective causes of endocarditis-like features**:
  - Non-bacterial thrombotic endocarditis (marantic endocarditis).
  - Libman-Sacks endocarditis (associated with systemic lupus erythematosus)
- **Conditions with overlapping symptoms**:
  - Rheumatic fever.
  - Systemic vasculitis (e.g., Kawasaki disease, polyarteritis nodosa).
  - Malignancy (e.g., leukemia).
  - Infectious diseases (e.g., osteomyelitis, septic arthritis, tuberculosis)
- **Other cardiac conditions**:
  - Myocarditis.
  - Pericarditis.
  - Congenital heart disease exacerbations.

This outline provides a structured approach for understanding infective endocarditis in children and serves as a foundation for deeper study. Let me know if you need any sections expanded or clarified.

29 Endomyocardial Fibrosis

29.1 Definition

Endomyocardial fibrosis (EMF) is a progressive, restrictive cardiomyopathy characterized by fibrotic thickening of the endocardium, predominantly affecting the inflow tracts of the right and/or left ventricles. This leads to impaired diastolic filling, atrioventricular valve regurgitation, and ultimately heart failure. EMF is most commonly seen in tropical and subtropical regions, and it remains an important cause of pediatric heart failure in these areas.

29.2 Incidence/Prevalence

- EMF is primarily seen in tropical and subtropical regions, particularly in sub-Saharan Africa, India, and parts of South America.
- It is estimated to affect 10 million people worldwide, with the highest burden in children and young adults.
- The prevalence in endemic areas ranges from 10% to 20% of all heart diseases.
- The condition is more common in socioeconomically disadvantaged populations and is associated with malnutrition and infections.
- While rare in developed countries, cases have been reported in immigrants from endemic regions.

29.3 Aetiology

The exact cause of endomyocardial fibrosis remains unknown, but several contributing factors have been proposed, including:

1. **Infectious Causes:**
    - Parasitic infections such as *Plasmodium falciparum* (malaria) and *Schistosoma* species have been implicated in the pathogenesis.
    - Viral infections, including Epstein-Barr virus and Coxsackie virus, have also been suggested.
2. **Autoimmune Mechanisms**

- Immune system dysregulation leading to chronic inflammation and fibrosis.
- Presence of eosinophilia in many patients suggests an allergic or immune-mediated response.

3. **Nutritional Deficiencies:**
    - Chronic malnutrition, specifically deficiencies in magnesium, selenium, and protein, may predispose individuals to EMF.
    - Exposure to toxic dietary substances such as cassava, which contains cyanogenic glycosides, is considered a potential factor
4. **Genetic Predisposition:**
    - Familial clustering has been noted in some endemic areas, suggesting a genetic susceptibility to the disease.
5. **Environmental Factors:**
    - Living in rural, low-income areas with high exposure to infections and dietary toxins.

Pathophysiology

- EMF predominantly affects the ventricular endocardium, leading to fibrosis that extends from the apex toward the atrioventricular valves.
- **Right ventricular involvement** is more common than left, but both can be affected (biventricular disease).
- Fibrosis results in:
    1. **Diastolic dysfunction:** The stiff ventricle cannot fill adequately, leading to elevated atrial pressures.
    2. **Atrioventricular valve regurgitation:** Fibrosis and restriction of valve movement lead to tricuspid or mitral regurgitation.
    3. **Thrombus formation:** The fibrotic endocardium is prone to thrombus development, which can embolize systemically or to the lungs.
    4. **Myocardial dysfunction:** Though the myocardium is often spared early in the disease, late-stage fibrosis can affect contractility and lead to heart failure.

Signs and Symptoms

The clinical presentation of EMF in children varies depending on the extent of cardiac involvement and which ventricle is affected.

Right Ventricular EMF (Most Common Presentation):

- Signs of right heart failure:
    - Hepatomegaly
    - Ascites

  - Peripheral edema
  - Elevated jugular venous pressure
- Fatigue and exercise intolerance
- Right upper quadrant pain due to liver congestion

Left Ventricular EMF:

- Signs of left heart failure:
  - Pulmonary congestion (dyspnea, orthopnea)
  - Cough, hemoptysis (in advanced cases)
  - Fatigue and poor growth in children
- Systemic embolization (e.g., stroke) from left-sided thrombus formation

Biventricular Disease:

- Severe heart failure with a combination of right- and left-sided symptoms
- Anasarca (generalized edema)
- Reduced cardiac output leading to shock in advanced case

General Symptoms:

- Failure to thrive
- Recurrent respiratory infections
- Cyanosis (in severe cases)

Investigations

1. Blood Tests:

- Eosinophilia: Found in a subset of patients.
- Elevated inflammatory markers (CRP, ESR).
- Liver function tests: Abnormal in cases with severe right heart failure.
- Pro-BNP: Elevated in cases of heart failure.

2. Electrocardiogram (ECG):

- Low voltage QRS complexes.
- Right or left atrial enlargement.
- Conduction abnormalities (e.g., atrioventricular block)

3. Echocardiography (Key Diagnostic Tool):

- Thickened endocardium, especially in the apical region.
- Atrioventricular valve regurgitation.
- Restricted ventricular filling pattern.

- Intracardiac thrombus formation.
- Diastolic dysfunction with preserved systolic function in early stages.

4. **Cardiac MRI:**

- Provides detailed imaging of fibrotic areas.
- Helps differentiate EMF from other restrictive cardiomyopathies.

5. **Cardiac Catheterization:**

- Confirms restrictive physiology with elevated end-diastolic pressure

6. **Endomyocardial Biopsy:**

- Rarely performed but can confirm fibrosis histologically.

Treatment

Treatment of endomyocardial fibrosis in children is primarily supportive and aimed at symptom relief.

1. **Medical Management:**

- **Diuretics:** Reduce fluid overload and symptoms of heart failure.
- **Anticoagulation:** Indicated for patients with atrial fibrillation or intracardiac thrombi.
- **ACE inhibitors/ARBs:** Help reduce afterload and improve heart function.
- **Nutritional support:** Address malnutrition with appropriate supplementation.

2. **Surgical Management:**

- Endocardial resection and valve repair or replacement in selected cases.
- High surgical risk with variable outcomes in children.

3. **Symptomatic Care:**

- Management of complications such as arrhythmias and infections.
- Regular follow-up for disease progression and heart failure management.

Complications

- **Heart Failure:** Progressive and refractory to medical therapy.
- **Thromboembolism:** Stroke, mesenteric ischemia, or pulmonary embolism.
- **Arrhythmias:** Atrial fibrillation or heart block leading to sudden cardiac death.
- **Growth retardation:** Due to chronic illness and malnutrition.
- **Infective endocarditis:** Due to damaged endocardial surfaces.

Prognosis

- EMF is a chronic, progressive condition with a poor long-term prognosis.
- Early diagnosis and medical management can improve quality of life.
- In children, the prognosis is worse if diagnosed late or if biventricular involvement is present.
- Surgical intervention provides limited benefit and carries high perioperative risks.

Differential Diagnosis

- **Restrictive Cardiomyopathy:** Similar presentation but without endocardial fibrosis on imaging.
- **Constrictive Pericarditis:** Presents with similar right heart failure symptoms but is distinguished by pericardial thickening on imaging.
- **Rheumatic Heart Disease:** Can cause valvular regurgitation and heart failure but lacks endocardial thickening.
- **Hypereosinophilic Syndrome:** Can mimic EMF but includes systemic involvement (e.g., skin, lungs).

Figure 29.1: Endomyocardial Fibrosis showing classical Egg-on-Stick appearance

30 Miscellaneous Cardiac Conditions

30.1 Introduction

Beyond the commonly discussed congenital and acquired heart diseases such as septal defects, ductal anomalies, coarctation, and rheumatic disease, children may present with a variety of other cardiac conditions that, although less frequent, are clinically significant. These disorders encompass abnormalities of rhythm, cardiomyopathies, pericardial disease, pulmonary hypertension, and conditions secondary to systemic illness.

In the Ghanaian context, where diagnostic resources are limited and late presentations are common, awareness of these miscellaneous cardiac conditions is vital for timely recognition, appropriate referral, and improved outcomes. This chapter explores these diverse entities, emphasising their pathophysiology, clinical features, diagnostic approach, and management principles.

30.2 Arrhythmias in Children

30.2.1 Overview

Arrhythmias refer to disturbances in the heart's rhythm, either too slow, too fast, or irregular. They can occur in structurally normal hearts or as complications of congenital heart disease, myocarditis, or postoperative states.

30.2.2 Common Types

- **Sinus bradycardia:** Often physiological in athletes or during sleep, but may occur with raised intracranial pressure or hypothyroidism.
- **Sinus tachycardia:** Commonly secondary to fever, anaemia, or dehydration.
- **Supraventricular tachycardia (SVT):** The most common pathological tachyarrhythmia in children, often due to re-entry mechanisms.
- **Ventricular tachycardia (VT):** Rare but life-threatening, seen in myocarditis or cardiomyopathy.
- **Heart block:** May be congenital or secondary to maternal lupus, cardiac surgery, or myocarditis.

30.2.3 Clinical Features

- Palpitations, dizziness, syncope, or chest discomfort
- Cyanosis or heart failure in sustained tachyarrhythmia
- Irregular pulse or variable heart rate on auscultation

30.2.4 Diagnosis and Management

Diagnosis is made via **ECG**, **Holter monitoring**, or **event recorders**.
Management includes:

- **Vagal manoeuvres** and **adenosine** for SVT
- **Amiodarone** or **procainamide** for VT
- **Pacemaker insertion** for complete heart block
- Long-term follow-up with paediatric cardiology is essential.

30.3 Myocarditis

30.3.1 Definition and Aetiology

Myocarditis is inflammation of the myocardium that impairs contractility. It may be viral, bacterial, autoimmune, or toxin-induced.

Common causes include:

- **Viral:** Coxsackie B, adenovirus, enterovirus, parvovirus B19
- **Bacterial:** Diphtheria, Staphylococcus, Mycoplasma
- **Others:** Kawasaki disease, autoimmune disorders, drug reactions

30.3.2 Pathophysiology

Infectious agents cause direct myocyte injury or immune-mediated destruction, leading to myocardial oedema, necrosis, and fibrosis. This results in reduced systolic function and may progress to **dilated cardiomyopathy**.

30.3.3 Clinical Features

- Fatigue, feeding difficulties, dyspnoea
- Tachycardia disproportionate to fever
- Gallop rhythm, hepatomegaly, or heart failure signs
- In severe cases, **cardiogenic shock**

30.3.4 Diagnosis

- **Elevated cardiac enzymes (CK-MB, troponin)**
- **ECG:** ST-T changes, arrhythmias
- **Echocardiogram:** Global hypokinesia, chamber dilation, reduced ejection fraction
- **Viral studies** where available

30.3.5 Management

- Supportive: oxygen, diuretics, inotropes
- **Avoid excessive fluid loading.**
- **IV immunoglobulin (IVIG)** or **steroids** may be considered in selected cases.
- Long-term follow-up for ventricular function recovery

30.4 Cardiomyopathies

Cardiomyopathies are diseases of the heart muscle not explained by abnormal loading or coronary artery disease. They are classified based on ventricular morphology and function.

30.4.1 Dilated Cardiomyopathy (DCM)

- Most common in children; can follow viral myocarditis, genetic mutations, or nutritional deficiencies (e.g., selenium deficiency).
- **Pathophysiology:** Progressive ventricular dilation and systolic dysfunction.
- **Clinical features:** Fatigue, failure to thrive, dyspnoea, hepatomegaly, and heart failure.
- **Management:** Standard heart failure therapy: ACE inhibitors, beta-blockers, diuretics, and occasionally anticoagulation.
- **Prognosis:** Variable; some recover, others progress to chronic failure or require transplantation.

30.4.2 Hypertrophic Cardiomyopathy (HCM)

- A genetic disorder characterized by asymmetric septal hypertrophy and diastolic dysfunction.
- **May present with:** Syncope, exertional dyspnoea, or sudden cardiac death, particularly during exercise.
- **Diagnosis:** ECG showing LV hypertrophy; echocardiography reveals a thickened septum and a small LV cavity.

- **Management:** Beta-blockers or calcium channel blockers; avoid dehydration and strenuous activity.

30.4.3 Restrictive Cardiomyopathy (RCM)

- Characterized by impaired ventricular filling with normal systolic function.
- Rare in children, sometimes secondary to infiltrative diseases.
- **Features:** Hepatomegaly, ascites, elevated jugular venous pressure.
- **Management:** Diuretics for congestion; poor prognosis without transplant.

30.5 Pericardial Diseases

30.5.1 Pericarditis

Inflammation of the pericardium often secondary to viral infection, rheumatologic disease, or post-surgical states.

Clinical features:

- Sharp chest pain relieved by sitting forward
- Pericardial rub on auscultation
- Low-grade fever

Diagnosis: ECG showing diffuse ST elevation; echocardiogram may reveal effusion.
Management: NSAIDs, rest, and treatment of underlying infection.

30.5.2 Pericardial Effusion and Cardiac Tamponade

Fluid accumulation within the pericardial sac impedes cardiac filling, leading to tamponade.
Causes: Tuberculosis (common in Ghana), malignancy, uremia, trauma.
Clinical features: Dyspnoea, tachycardia, muffled heart sounds, distended neck veins, pulsus paradoxus.
Management: Pericardiocentesis (urgent in tamponade), antituberculous therapy if indicated.

30.6 Pulmonary Hypertension (PH)

30.6.1 Definition and Classification

Pulmonary hypertension is a sustained elevation of pulmonary artery pressure >25 mmHg at rest. It may be:

- **Primary (idiopathic)**: rare in children
- **Secondary**: Due to chronic hypoxia, congenital heart disease, or pulmonary disorders

30.6.2 Pathophysiology

Chronic elevation of pulmonary vascular resistance leads to right ventricular hypertrophy and eventual right heart failure.

30.6.3 Clinical Features

- Exertional dyspnoea, fatigue, syncope
- Loud pulmonary component of the second heart sound
- Right ventricular heave and signs of failure

30.6.4 Diagnosis

- **Echocardiography:** Estimates pulmonary pressures
- **Cardiac catheterization:** Gold standard
- **CXR:** Enlarged pulmonary arteries
- **ECG:** Right axis deviation, RV hypertrophy

30.6.5 Management

- Treat underlying cause (e.g., repair of shunt lesions)
- **Oxygen therapy** for hypoxia
- **Vasodilators:** Sildenafil, calcium channel blockers
- **Anticoagulation** in selected patients
- **Avoid dehydration and high altitude** exposure

Prognosis depends on the cause and reversibility of vascular changes.

30.7 Kawasaki Disease

An acute, self-limiting vasculitis of childhood, predominantly affecting the coronary arteries. Most common in children under 5 years.

30.7.1 Clinical Features

- Persistent high fever >5 days
- Conjunctival injection, strawberry tongue, cracked lips
- Rash, cervical lymphadenopathy
- Desquamation of fingers and toes
- Coronary artery aneurysms may develop in untreated cases.

30.7.2 Diagnosis and Management

Clinical diagnosis: Elevated ESR, CRP, and platelets support inflammation.
Echocardiogram to detect coronary aneurysms.

Treatment includes:

- **IVIG (2 g/kg single dose)** within 10 days of onset
- **High-dose aspirin** during acute phase, then low-dose for 6–8 weeks
- Long-term cardiology follow-up for aneurysm surveillance

30.8 Cardiac Tumours

30.8.1 Types

- **Rhabdomyoma:** Most common; often associated with **tuberous sclerosis**
- **Fibroma, Teratoma, Myxoma, Hemangioma:** Less common

30.8.2 Clinical Manifestations

- Obstructive symptoms (outflow tract obstruction)
- Arrhythmias
- Heart failure or sudden death

Diagnosis: Echocardiography reveals intracardiac mass; MRI provides further characterization.
Management: Rhabdomyomas often regress; others may require surgical excision.

30.9 Systemic Diseases with Cardiac Involvement

Certain systemic illnesses have important cardiac manifestations.

30.9.1 Anaemia and Malnutrition

Chronic anaemia leads to **high-output cardiac failure**, while severe malnutrition can cause cardiac atrophy and reduced contractility.

30.9.2 Sickle Cell Disease

Recurrent anaemia, iron overload, and pulmonary hypertension contribute to **cardiomegaly** and **diastolic dysfunction**.

30.9.3 Sepsis

Severe sepsis may cause **myocardial depression** secondary to cytokine release, which is reversible with recovery.

30.9.4 Thyroid Disorders

- **Hyperthyroidism:** Tachyarrhythmias and high-output failure
- **Hypothyroidism:** Bradycardia and pericardial effusion

30.9.5 HIV-Associated Cardiac Disease

In resource-limited settings like Ghana, HIV-infected children may develop:

- **Dilated cardiomyopathy**
- **Pericardial effusion** (often tuberculous)
- **Pulmonary hypertension**
- **Drug-related cardiotoxicity**

Early ART initiation and cardiac monitoring are essential to reduce morbidity.

30.10 Drug-Induced Cardiotoxicity

Several medications used in paediatrics can cause cardiac dysfunction.

Examples:

- **Anthracyclines (e.g., doxorubicin):** Dose-dependent cardiomyopathy
- **Cyclophosphamide:** Myocardial necrosis
- **Antimalarials (chloroquine):** QT prolongation

Prevention: Regular ECG, echocardiography, and adherence to cumulative dose limits.

30.11 Prognosis and Long-Term Care

The outcome of miscellaneous paediatric cardiac conditions varies widely. Transient viral myocarditis may resolve completely, while genetic cardiomyopathies often progress despite optimal therapy. Chronic conditions such as pulmonary hypertension and postoperative arrhythmias require ongoing multidisciplinary follow-up.

Early detection through echocardiography, routine screening in high-risk children, and integration of paediatric cardiology into tertiary care systems in Ghana are crucial to improving survival and quality of life.

30.12 Conclusion

Miscellaneous paediatric cardiac conditions represent a heterogeneous group that collectively contribute significantly to cardiac morbidity in children. While individually less frequent than septal defects or rheumatic disease, they often carry substantial diagnostic and therapeutic challenges. For medical students and practitioners in Ghana, a high index of suspicion, thorough clinical evaluation, and appropriate use of echocardiography can facilitate early recognition and management. Strengthening diagnostic infrastructure and ensuring access to paediatric cardiology services remain essential priorities in improving outcomes for these children.

Part V

Infectious Diseases

31 ID Basics

31.1 Introduction

Infectious diseases remain a leading cause of morbidity and mortality among children in Ghana and across sub-Saharan Africa. Understanding the pathological basis of these infections is essential for accurate diagnosis, rational treatment, and prevention. The pathology of infectious diseases encompasses the mechanisms by which microorganisms invade, disseminate, cause tissue injury, and interact with the host's immune system. Children, particularly infants, are uniquely susceptible due to immature immunity, high exposure, nutritional vulnerabilities, and environmental factors that enhance transmission.

This chapter focuses on the fundamental pathological processes underlying infectious diseases in children, highlighting local epidemiology, pathogen–host interactions, immune responses, mechanisms of tissue injury, and the pathological features of major infectious syndromes encountered in West African paediatric practice.

31.2 Epidemiological Context in Ghana and West Africa

Several factors influence infectious disease patterns in children in the subregion:

- **High burden of communicable diseases** due to tropical climate, poor sanitation, and limited access to healthcare.
- **Malnutrition**, especially protein–energy malnutrition, weakens immunity.
- **Lower vaccination coverage** in rural areas.
- **Prevalence of HIV**, tuberculosis, and endemic bacterial and parasitic infections.
- **Exposure to contaminated water**, leading to gastrointestinal pathogens.
- **Overcrowding and poor ventilation**, contributing to respiratory infections.

These factors shape the pathological landscape of paediatric infectious diseases, often resulting in severe forms of otherwise mild illnesses.

31.3 Host–Pathogen Interactions

The pathological basis of infections is rooted in the dynamic relationship between pathogens and the host.

31.3.1 Entry and Colonisation

Pathogens enter the body through:

- Respiratory tract (viruses, bacteria)
- Gastrointestinal tract (enteric pathogens)
- Skin (injuries, insect bites)
- Mucous membranes
- Transplacental (e.g., congenital infections)
- Blood (transfusion-associated or vector-borne)

Successful colonisation depends on:

- Adhesins and surface molecules
- Ability to evade mucosal defences
- Overcoming gastric acidity (in GI infections)

31.3.2 Invasion and Spread

Pathogens may:

- Remain localised (e.g., streptococcal pharyngitis)
- Spread via lymphatics (e.g., TB)
- Disseminate haematogenously (sepsis, meningitis)
- Spread along anatomical planes (e.g., necrotising fasciitis)

31.3.3 Evasion of Host Defences

Microorganisms avoid immune elimination through:

- Capsule formation (e.g., *S. pneumoniae*)
- Antigenic variation
- Inhibition of phagolysosome fusion (e.g., *Mycobacterium tuberculosis*)
- Destruction of immune cells (HIV)
- Formation of biofilms

31.3.4 Host Immune Response

The immune response determines disease expression:

31.3.4.1 Innate Immunity

- First line of defence
- Involves neutrophils, macrophages, NK cells, complement
- Critical in infant immunity

31.3.4.2 Adaptive Immunity

- Humoral (B-cell mediated)
- Cellular (T-cell mediated)

Pathology occurs when:

- The immune response is excessive (cytokine storm)
- Host immunity is insufficient (malnutrition, HIV)
- There is immune-mediated tissue destruction (post-infectious sequelae)

31.4 Mechanisms of Tissue Injury

Pathogens cause tissue injury through:

31.4.1 Direct Mechanisms

- **Toxin production**
  - Exotoxins (e.g., *Corynebacterium diphtheriae*)
  - Enterotoxins (e.g., cholera toxin)
  - Neurotoxins (e.g., tetanus toxin)
- **Direct cellular invasion and lysis**
  - Viruses hijack host machinery, causing cytopathic effects
- **Obstruction**
  - Worm burden (e.g., intestinal obstruction by *Ascaris*)

31.4.2 Indirect Mechanisms

- **Inflammation and immune-mediated damage**
  - Immune complexes (e.g., post-streptococcal glomerulonephritis)
  - Hypersensitivity reactions
- **Septic shock**
  - Endotoxins trigger cytokine storm → multi-organ failure
- **Fibrosis and scarring**
  - Chronic infections (e.g., TB)
- **Nutritional derangements**
  - Prolonged infection leads to wasting and malnutrition

31.5 Pathology of Major Infectious Syndromes

31.5.1 1. Respiratory Tract Infections

Common pathogens include RSV, influenza, rhinoviruses, *S. pneumoniae*, *H. influenzae*, and TB.

Pathological basis:

- Viral infections → necrosis of epithelium, mucus plugging, bronchiolitis
- Bacterial pneumonia → alveolar exudates, consolidation
- TB → granuloma formation, caseous necrosis, cavity formation

Infants are prone to severe bronchiolitis due to small airway calibre.

31.5.2 2. Gastrointestinal Infections

Pathogens: rotavirus, norovirus, *Shigella*, *Salmonella*, enterotoxigenic *E. coli*, *Giardia.*

Pathology:

- Viruses → villous atrophy → malabsorption → diarrhoea
- Invasive bacteria → mucosal ulceration, bloody diarrhoea
- Toxin-mediated diarrhoea → water and electrolyte loss without mucosal injury

Malnutrition exacerbates enteropathy, leading to persistent diarrhoea.

31.5.3 3. Central Nervous System Infections

Meningitis and encephalitis commonly result from *S. pneumoniae*, *N. meningitidis*, viral agents.

Pathology:

- Purulent meningitis → neutrophilic exudate in subarachnoid space
- Cerebral oedema → raised ICP
- Vasculitis → infarctions
- Chronic infections (TB) → granulomas, basal exudates

Delayed treatment results in long-term neurological sequelae (hearing loss, developmental delay).

31.5.4 4. Sepsis and Septic Shock

Sepsis is a dysregulated host response to infection leading to organ dysfunction.

Pathology:

- Widespread endothelial dysfunction
- Capillary leak
- Microthrombi (DIC)
- Multi-organ failure

Children progress from sepsis to shock rapidly due to limited physiological reserves.

31.5.5 5. Skin and Soft Tissue Infections

Pathogens: *Staph aureus*, *Strep pyogenes*, fungi.

Pathological features:

- Superficial infections (impetigo) → epidermal vesicles
- Deep infections (cellulitis) → dermal inflammation
- Necrotising fasciitis → fascial destruction, systemic toxicity

In West Africa, poor hygiene and delayed presentation contribute to severe forms.

31.5.6 6. Bone and Joint Infections

Osteomyelitis and septic arthritis arise from: - Haematogenous spread (common in children) - Contiguous spread - Trauma

Pathology:

- Suppurative inflammation
- Bone necrosis (sequestrum)
- Periosteal elevation
- Joint cartilage destruction (in septic arthritis)

Sickle cell disease predisposes to *Salmonella* osteomyelitis.

31.5.7 7. Congenital and Perinatal Infections

TORCH infections cause:

- Microcephaly
- Hepatosplenomegaly
- Jaundice
- Chorioretinitis

Pathology involves viral invasion of neural tissue, destructive brain lesions, and immune-mediated damage.

31.6 Influence of Immunodeficiency and Malnutrition

Conditions common in Ghana modulate pathological responses:

31.6.1 HIV Infection

- Chronic immune activation
- Loss of CD4 cells
- Susceptibility to opportunistic infections (PCP, CMV, TB)

31.6.2 Malnutrition

- Thymic atrophy → impaired T-cell responses
- Reduced complement activity
- Poor mucosal immunity

These factors lead to severe, atypical, or persistent infections.

31.7 Diagnostic Pathology in Resource-Limited Settings

In Ghana, pathological diagnosis relies on:

- Basic blood tests
- Microscopy and culture
- Chest and abdominal radiographs
- GeneXpert for TB
- Histopathology (available in teaching hospitals)

Limitations include:

- Inadequate laboratory capacity in district hospitals
- Delays in sample transport
- Limited access to advanced diagnostics (PCR, immunohistochemistry)

Despite this, clinical pathology remains essential for patient care.

31.8 Prevention and Control

Understanding pathology informs prevention:

- **Vaccination** (pneumococcal, Hib, measles, rotavirus)
- **Improved sanitation and hygiene**
- **Prompt treatment of infections**
- **Nutritional rehabilitation**
- **Early detection of immunodeficiency**
- **Strengthening health systems** at community and district levels

31.9 Key Points

- Infectious disease pathology in children is shaped by pathogen factors, host immunity, and environmental context.
- Tissue injury may result from direct microbial effects or host immune responses.
- Immature immunity and high exposure make infants highly vulnerable.
- Common infectious syndromes have characteristic pathological features that guide clinical diagnosis.
- Malnutrition and immunodeficiency significantly modify disease patterns and severity.
- Understanding pathology is essential for rational diagnosis, treatment, and prevention strategies in Ghana and West Africa.

31.10 Further Reading

- Nelson Textbook of Pediatrics – Infectious Diseases Section
- Kumar & Clark: Clinical Medicine (Pathology chapters)
- WHO Child Health Guidelines
- Ghana Standard Treatment Guidelines (latest edition)
- Global Infectious Diseases Pathology (Elsevier)

32 Immunodeficiency

32.1 Introduction

Immunodeficiency in children refers to a group of disorders in which components of the immune system are absent, defective, or functionally impaired, resulting in increased susceptibility to infections, poor response to treatment, unusual infection patterns, and immune dysregulation. These conditions may be **primary (genetic)** or **secondary (acquired)**. Early recognition is essential because timely diagnosis and treatment can prevent severe morbidity and mortality, especially in low- and middle-income settings such as Ghana and West Africa, where infectious disease burden is already high.

32.2 Classification of Immunodeficiency

Immunodeficiencies are broadly classified as:

32.2.1 Primary Immunodeficiency Disorders (PIDs)

Genetically determined, usually presenting in infancy or early childhood. Over 450 PIDs have been described, grouped into: - **Combined immunodeficiencies**
(e.g., Severe Combined Immunodeficiency—SCID) - **Predominantly antibody deficiencies**
(e.g., X-linked agammaglobulinemia, CVID) - **Phagocytic defects**
(e.g., Chronic Granulomatous Disease) - **Complement deficiencies** - **Immune dysregulation disorders** - **Innate immune defects**

32.2.2 Secondary (Acquired) Immunodeficiency

More common globally, especially in sub-Saharan Africa. Causes include:

- **HIV infection** (most common)
- **Severe malnutrition** (major contributor to immunosuppression in children)
- **Malignancy**
- **Immunosuppressive drugs**
- **Protein-losing enteropathy or nephrotic syndrome**

- **Chronic renal or liver disease**

32.3 Epidemiology

True prevalence of PIDs in Ghana and West Africa is unknown due to:

- Limited diagnostic capacity (genetic testing, flow cytometry)
- Misdiagnosis as recurrent infections without further evaluation
- High competing burden of infectious diseases masking underlying immune defects

However, increased awareness has led to rising recognition of conditions like SCID and agammaglobulinemia.

Secondary immunodeficiencies are far more common, particularly due to:

- HIV
- Severe acute malnutrition
- Sickle cell disease
- Tuberculosis
- Chemotherapy-related immunosuppression

32.4 Normal Immune Development in Children

Understanding immunodeficiency requires familiarity with the developing immune system:

- Newborns rely on **maternal IgG** transferred transplacentally.
- Endogenous IgG production rises after 3–6 months.
- IgA and IgM levels are low in infancy, predisposing young children to respiratory and gastrointestinal infections.
- Complement system matures over the first few years of life.
- T-cell immunity is robust at birth but may be impaired by prematurity or congenital defects.

This developmental process explains why certain age groups show characteristic vulnerability patterns.

32.5 Clinical Features of Immunodeficiency

Children with immunodeficiency may present with varied symptoms, but several "warning signs" should raise suspicion.

32.5.1 Recurrent Infections

- 4 ear infections in one year
- 2 serious sinus infections in one year
- 2 pneumonias in one year
- Persistent diarrhoea
- Infections with unusual or opportunistic organisms (e.g., *Pneumocystis jirovecii*)

32.5.2 Severe, Persistent, or Unusual Presentations

- Severe sepsis or meningitis
- Failure to thrive
- Delayed wound healing
- Poor response to standard antibiotics
- Deep-seated infections (liver abscess, osteomyelitis)
- Persistent oral thrush or fungal skin infections

32.5.3 Non-infectious Manifestations

- Autoimmune cytopenias
- Eczema (e.g., Wiskott–Aldrich syndrome)
- Lymphoproliferation
- Chronic diarrhoea ± malabsorption

32.6 Common Primary Immunodeficiencies in Children

32.6.1 Severe Combined Immunodeficiency (SCID)

- Absence of T-cell immunity, with or without B/NK cell defects
- Presents in early infancy:
  - Recurrent or severe infections
  - Persistent diarrhoea
  - Failure to thrive
- Fatal without immune reconstitution (HSCT)

32.6.2 X-linked Agammaglobulinemia (XLA)

- Mutation in *BTK* gene → absent B cells
- Recurrent respiratory infections starting after 6 months
- Low IgG, IgA, and IgM

32.6.3 Common Variable Immune Deficiency (CVID)

- Later childhood onset
- Low IgG and IgA, recurrent sinopulmonary infections
- Risk of autoimmunity

32.6.4 Chronic Granulomatous Disease (CGD)

- Phagocytic defect due to NADPH oxidase deficiency
- Recurrent abscesses, lymphadenitis, osteomyelitis
- Catalase-positive organisms (e.g., *Staph aureus*)

32.6.5 Complement Deficiencies

- Recurrent meningococcal or pneumococcal infections
- Terminal complement defects → *Neisseria* infections

32.7 Secondary Immunodeficiency: Context of Ghana and West Africa

32.7.1 HIV Infection

- Most common cause of immunodeficiency in children
- Presents with:
  - Opportunistic infections
  - Failure to thrive
  - Lymphadenopathy
  - Chronic diarrhoea
- Diagnosis via PCR in infants and serology after 18 months

32.7.2 Severe Acute Malnutrition (SAM)

- Suppresses both innate and adaptive immunity
- Increased risk of pneumonia, sepsis, skin infections
- Restoring nutrition is essential for immune recovery

32.7.3 Sickle Cell Disease (SCD)

- Functional asplenia → susceptibility to encapsulated organisms (e.g., *Strep pneumoniae*, *H. influenzae*)
- Need for routine prophylaxis

32.7.4 Tuberculosis and Chronic Diseases

- TB leads to chronic immune exhaustion
- Renal and liver failure also impact immunity

32.8 Investigations

Evaluation depends on the suspected type of immunodeficiency.

32.8.1 First-line Tests (available in many Ghanaian hospitals)

- Complete blood count with differential
- ESR/CRP
- HIV test
- Blood film for parasites (if indicated)
- Chest X-ray
- Serum immunoglobulin levels (IgG, IgA, IgM)
- Culture studies for recurrent infections

32.8.2 Second-line Tests (limited availability)

- Lymphocyte subset analysis (CD3, CD4, CD8, CD19, NK cells)
- Specific antibody titers (response to vaccines)
- Complement levels (CH50, C3, C4)
- Neutrophil oxidative burst test (for CGD)
- Genetic testing (send-out)

In many West African settings, diagnosis is often clinical plus basic laboratory support due to cost and availability constraints.

32.9 Management

32.9.1 Treat Acute Infections Promptly

- Early, aggressive antibiotics for bacterial infections
- Antifungals or antivirals as needed

32.9.2 Long-term Management Strategies

- **Immunoglobulin replacement therapy**
  For antibody deficiencies (XLA, CVID)
- **Prophylactic antibiotics**
  e.g., Cotrimoxazole prophylaxis for HIV-exposed/infected infants or SCID
- **Stem cell transplantation**
  Curative option for SCID and some PIDs (availability limited in West Africa)
- **Nutritional rehabilitation**
  Essential for children with SAM
- **Vaccination considerations**
  - Avoid live vaccines in severe T-cell immunodeficiency
  - Prioritize pneumococcal, Hib, and meningococcal vaccines
  - Ensure annual influenza vaccination where available

32.9.3 Family Screening

- Important for hereditary conditions
- Genetic counselling (where available)

32.10 Complications

- Recurrent lung infections → bronchiectasis
- Growth failure
- Chronic diarrhoea and malabsorption
- Autoimmune diseases
- Increased risk of lymphoma (e.g., CVID)

32.11 Prognosis

Varies widely:

- Early diagnosis → excellent outcomes in many PIDs
- Delayed diagnosis → high morbidity, irreversible organ damage
- Secondary immunodeficiency often improves with treatment of underlying cause (e.g., nutritional recovery, ART in HIV)

Resource constraints in West Africa impact prognosis, making early suspicion vital.

32.12 Summary

Immunodeficiency in children represents a spectrum of disorders that increase susceptibility to infections and immune dysregulation. Primary immunodeficiencies, though less common, are serious and often present early. Secondary causes, notably HIV and malnutrition, are far more prevalent in Ghana and West Africa. Early diagnosis through careful clinical assessment, basic laboratory tests, and timely management—including prompt treatment of infections, immunoglobulin replacement where indicated, and supportive care—is essential to improving outcomes.

32.13 Further Reading

- Nelson Textbook of Paediatrics – Immunodeficiency Chapters
- WHO Guidelines on HIV and Paediatric Care
- Jeffrey Modell Foundation: Warning Signs of Primary Immunodeficiency
- African Society for Immunodeficiencies (ASID) Resources

33 Enteric Fever

Typhoid and Paratyphoid Fevers

33.1 Definition

Typhoid fever is a life-threatening infection caused by the bacterium *Salmonella Typh*i. It is usually spread through contaminated food or water. Once Salmonella Typhi bacteria are ingested, they multiply and spread into the bloodstream. It causes an acute generalised infection of the reticuloendothelial system, intestinal lymphoid tissue, and the gall bladder.

33.2 Incidence/prevalence

As of 2019 estimates, there were 9 million cases of typhoid fever annually, resulting in about 110,000 deaths annually.(WHO 2023) In 2023, information from LHIMS, Komfo Anokye Teaching Hospital, Kumasi indicated a rate of 0.4% or 4/1000 admissions through the Paediatric Emergency Unit (PEU) were diagnosed as enteric fever.

33.3 Aetiology

An infectious feverish disease caused by the bacterium Salmonella typhi (Salmonella enterica Serovar Typhi) and less commonly by Salmonella paratyphi.

33.4 Pathogenesis

S. typhi and S. paratyphi are transmitted through ingestion of fecally contaminated food or water, improper hygiene, and unsafe food/water handling practices. Individual-level risk factors include contaminated water supply, patronizing food vendors, ingestion of raw fruits and

vegetables and a history of contact with a case or a chronic carrier. The risk of environmental transmission of typhoid fever is higher in the rainy season, proximity to open sewers and highly contaminated water bodies and residing in areas of low elevation.(Adesegun et al. 2020) Ingested organisms survive exposure to gastric acid before gaining access to the small bowel, where they penetrate the epithelium, enter the lymphoid tissue, and disseminate via the lymphatic or hematogenous route. A chronic carrier state is established in an estimated 1 to 5 per cent of cases.(Andrews and Charles 2023)

33.5 Signs and symptoms

The incubation period ranges from 7-14 days on average but can range from 3 days to two months. Symptoms include prolonged high fever, fatigue, headache, nausea, abdominal pain, constipation or diarrhoea, and in some cases a rash. Typhoid can affect every system of the body. Other manifestations include drowsiness, seizures, coma, psychosis, meningitis, acute renal failure, osteomyelitis, and septic arthritis. Severe cases may lead to serious complications including terminal ileal perforation or even death.

33.6 Investigations

In the first and second weeks of the presentation, blood culture and sensitivity are recommended. Stool culture is also relevant more in the first week as compared to the second week. Bone marrow aspirate and culture are important after the second week. Recently, antibodies (IgM) have been used as a diagnostic tool. Local studies are needed to validate these antibody tests. Depending on the system involved, other tests must be requested.

33.7 Treatment

Treatment is supportive (Antipyretics, hydration, nutrition, transfusion) and specific (antibiotics are given starting with the empiric regimen: Third generation cephalosporin or quinolone eg. Ciprofloxacin). The choice of antibiotics should be changed to a narrower spectrum when culture and sensitivity results are available. Where there is poor response attributed to a focus e.g. abscess formation, source control should be pursued. Safe water, sanitation, and hygiene (WASH) interventions are critical to preventing the spread of typhoid. Typhoid is spread via the faecal-oral route when bacteria pass into people's mouths through food, water, hands, or objects contaminated with faecal matter. Solutions such as water treatment or filtration, installation and management of toilets and sanitation systems, and education about proper handwashing and food-handling practices can save lives and protect people from typhoid infection. Three types of typhoid vaccines of demonstrated safety and efficacy are available on the international market:-

1. A conjugated vaccine in which the Vi polysaccharide vaccine is bound to a carrier protein,
2. A non-conjugated Vi polysaccharide vaccine, and
3. A live attenuated Ty21a vaccine.

33.8 Complications

These include anicteric hepatitis, bone marrow suppression, paralytic ileus, myocarditis, psychosis, cholecystitis, osteomyelitis, peritonitis, pneumonia, haemolysis, and syndrome of inappropriate release of antidiuretic hormone (SIADH)

33.9 Prognosis

The prognosis among persons with typhoid fever depends primarily on the speed of diagnosis and initiation of correct treatment. Generally, untreated typhoid fever carries a mortality rate of 15%-30%. In properly treated diseases, the mortality rate is less than 1%. (emedicine 2024)

33.10 Differential diagnosis

Differential diagnosis will depend on the types of presentation. The most common are malaria, liver abscesses, tuberculosis, and meningitis.

33.11 Sample questions

1. A 5-year-old boy complained of general body weakness, abdominal pain and a fever of two weeks duration. He had 2 courses of antimalarial treatment even though the RDT was negative. On examination, he was lethargic and had a body temperature of 39.9^{o}C. If you suspect enteric fever, what will be the best test to perform?

    a. Urine culture

    b. Stool culture

    c. Blood culture

    d. Widal test

    All the options are feasible but with the duration of illness, blood culture with sensitivity testing will provide the best yield. Widal tests are widely used in some facilities but have a high tendency of false positive results.

2. A 10-year-old known sickle cell disease patient genotype SS presented with severe pain in the right leg of 3-week duration. She is on her routine medications but has yet to be initiated on hydroxyurea. On examination, there was tenderness in the right leg, especially at the knee joint with evidence of inflammation. Blood culture isolated Salmonella typhi. What is your best management approach?

   A more detailed history and examination is warranted. Before the blood culture results came out, the child would have been on empiric antibiotics. This must be changed to a narrower spectrum based on the sensitivity results. Remember to request for ultrasound of the inflamed knee for possible effusion. If there is fluid collection, this must be drained to achieve source control. This will optimize antibiotic response.

33.12 Practice question

Concerning question 2 (above) if the child was started on ceftriaxone, discuss what must be done after microbiology provides the sensitivity results as shown in the table below.

Sensitive	Resistant
Meropenem Ciprofloxacin Amikacin	Ceftriaxone, Linezolid

34 HIV

34.1 Definition

Human immunodeficiency virus (HIV) is an infection that attacks the body's immune system, specifically the white blood cells called CD4 cells. HIV destroys these CD4 cells, weakening a person's immunity against opportunistic infections, such as tuberculosis, fungal infections, severe bacterial infections, and some cancers.(World Health Organization (WHO) 2023)

34.2 Incidence/prevalence

Globally, 39 million people were living with HIV in 2022 out of which 1.5 million were children below 15 years. In Ghana, out of 354,927 people living with HIV in 2022, 7% (24,845) were children below 15 years. There were 16,574 new HIV infections in 2022 out of which 17% (2,818) were children. Mother-to-child transmission of HIV at 6 weeks in 2022 was 9.12% while the final MTCT rate at 18 months was 17.75%. In 2022, there were 21,439 adolescents (10-19 years) living with HIV out of which 1,791 were newly infected.(Ghana Health Service 2023)

34.3 Aetiology

HIV is a retrovirus with two main subtypes namely HIV 1 and HIV 2. HIV-1 is the most common type of HIV and accounts for 99% of all infections in Ghana, whereas HIV-2 is relatively uncommon (0.08%) and less infectious. Ghanaians co-infected with HIV 1 and HIV 2 form 0.02% of total infections. HIV-2 is mainly concentrated in West Africa and the surrounding countries. HIV-2 is less fatal and progresses more slowly than HIV-1. Modes of HIV transmission are sexual (80% in Ghana) mainly heterosexual but also same-sex; parenteral transmission (5%) examples include blood transmission, shared needles, and needle stick accidents, and mother-to-child transmission (15%) of which in-utero, intrapartum and postpartum accounts for 10-25%, 60-75%, and 10-20% respectively.

34.4 Pathogenesis

HIV entry, the first phase of the viral replication cycle, begins with the adhesion of the virus to the host cell and ends with the fusion of the cell and viral membranes with subsequent delivery of the viral core into the cytoplasm. The intricate series of protein-protein interactions that ultimately result in virus infection can be divided into several phases, some of which are essential and others that may modulate the efficiency of the process.(Wilen, Tilton, and Doms 2012)

Infection with HIV starts without symptoms or ill-feeling and is accompanied by slight changes in the immune system. This stage spans up to three months after infection until seroconversion where HIV-specific antibodies can be detected in individuals following recent exposure. The outcome of infection and duration of disease progression with clinical symptoms may vary greatly between individuals, but often it progresses fairly slowly. It takes several years from primary infection to the development of symptoms of advanced HIV diseases and immunosuppression.(Cunningham et al. 2000) Although individuals may look healthy during primary infection, the virus replicates in infected individuals' lymph nodes and bloodstream. As a result, the immune system may get slowly damaged by the burst of viral load in their bodies.(Moir, Chun, and Fauci 2011)

34.5 Signs and symptoms

Signs and symptoms develop when the immune system's ability to fight the disease is compromised due to viral replication and reduced CD4 cells.

34.5.1 Early/ acute HIV

Acute HIV infection, also known as primary HIV infection, can cause a range of symptoms that can begin a few days after exposure to the virus and last for a few days to several months

34.5.2 Late chronic HIV

The late stage of HIV infection is AIDS (acquired immunodeficiency syndrome), which occurs when the virus weakens the immune system.

34.5.3 Staging of HIV

Table 34.1: HIV Staging

-

Stage 1
Asymptomatic
Generalised lymphadenopathy

Stage 2
Unexplained persistent hepato-splenomegaly
Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
Herpes zoster
Linear gingival erythema
Recurrent oral ulceration
Papular pruritic eruption
Fungal nail infections
Extensive wart virus infection
Extensive Molluscum contangiosum
Unexplained persistent parotid enlargement

Stage 3
Unexplained moderate malnutrition and not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one 1 month)
Persistent oral candidiasis (after first 6 weeks of life)
Oral hairy leukoplakia
Lymph node tuberculosis

Stage 3
Pulmonary tuberculosis
Severe recurrent bacterial pneumonia
Acute necrotising ulcerative gingivitis or periodontitis
Unexplained anaemia (<8g/dl), neutropenia (<0.5x 10^9/l) and chronic thrombocytopenia (<50 x 10^9/l).
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease, including
bronchiectasis

Table 34.1: HIV Staging

Stage 4	**Stage 4**
Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy	HIV encephalopathy
Pneumocystis (jiroveci) pneumonia	Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month)
Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, and meningitis, but excluding pneumonia)	Extrapulmonary Cryptococcosis, including meningitis
Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or	Disseminated non-tuberculous mycobacterial infection
visceral at any site)	Progressive multifocal leukoencephalopathy
Oesophageal candidiasis (or candidiasis of the trachea, bronchi or lungs)	Chronic cryptosporidiosis (with diarrhoea)
Extrapulmonary tuberculosis	Chronic Isosporiasis
Kaposi sarcoma	Disseminated endemic mycosis
Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month)	(Extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)
Central nervous system toxoplasmosis (after the neonatal period)	Cerebral or B-cell non-Hodgkin lymphoma
	HIV-associated nephropathy or cardiomyopathy

34.6 Investigations

Depending on signs and symptoms, a patient could be suspected of HIV infection and AIDS. Children are then tested for HIV depending on their age.

34.6.1 Newborn to <18 months

Younger children (< 18 months) who are exposed to HIV or are suspected of HIV should be tested at any time they have symptoms of HIV disease. The preferred test is the DNA PCR which is done using dried blood spots (DBS) taken from pricking the heel of a child onto filter paper. If the test is positive, the child should be started on treatment, but a second confirmatory test must be done. Infants born to HIV-positive mothers without symptoms are routinely tested within 6 weeks of birth, at 9 months of age using DNA PCR. At 18 months such children are tested with antibody tests using a "triple algorithm" as detailed below.

Table 34.2: Baseline investigations for HIV

Test	Types
Haematological	Full blood count
Biochemistry	Blood Urea Electrolytes and Creatinine
	Liver Function tests
	Fasting Blood Sugar
	Cholesterol and lipid profile
Routine	Urinalysis (Urine R/E)
	Stool R/E
Respiratory	TB screening
	GeneXpert
	Chest X-ray
Serological	Hepatitis B Surface antigen
Immunological	CD4
Optional (Patient dependent)	Histology on skin and lymph node biopsy
	Kidney biopsy
	Screening for STIs
	Pap smear, HPV DNA
	Abdominal Ultrasound

34.6.2 18 months and above

Should be tested using the "triple algorithm" when a patient is sequentially tested using first response, Oraquick, and SD biofilm test. ALL three tests must be positive before a child is confirmed HIV positive. Figure **??** below gives further information

Baseline investigations are needed before initiating antiretroviral treatment/ monitoring of the disease. These are listed in Table **??**

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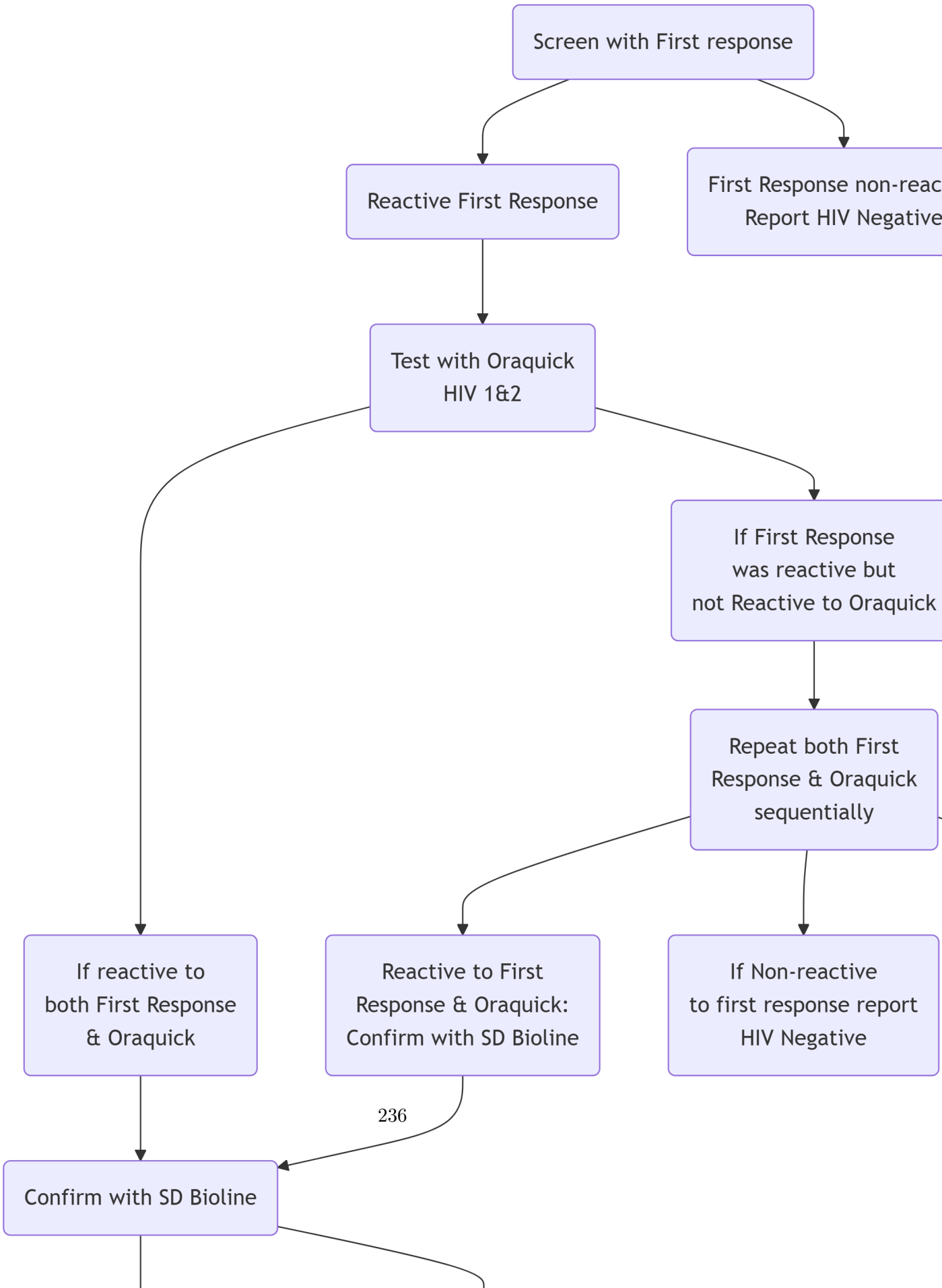
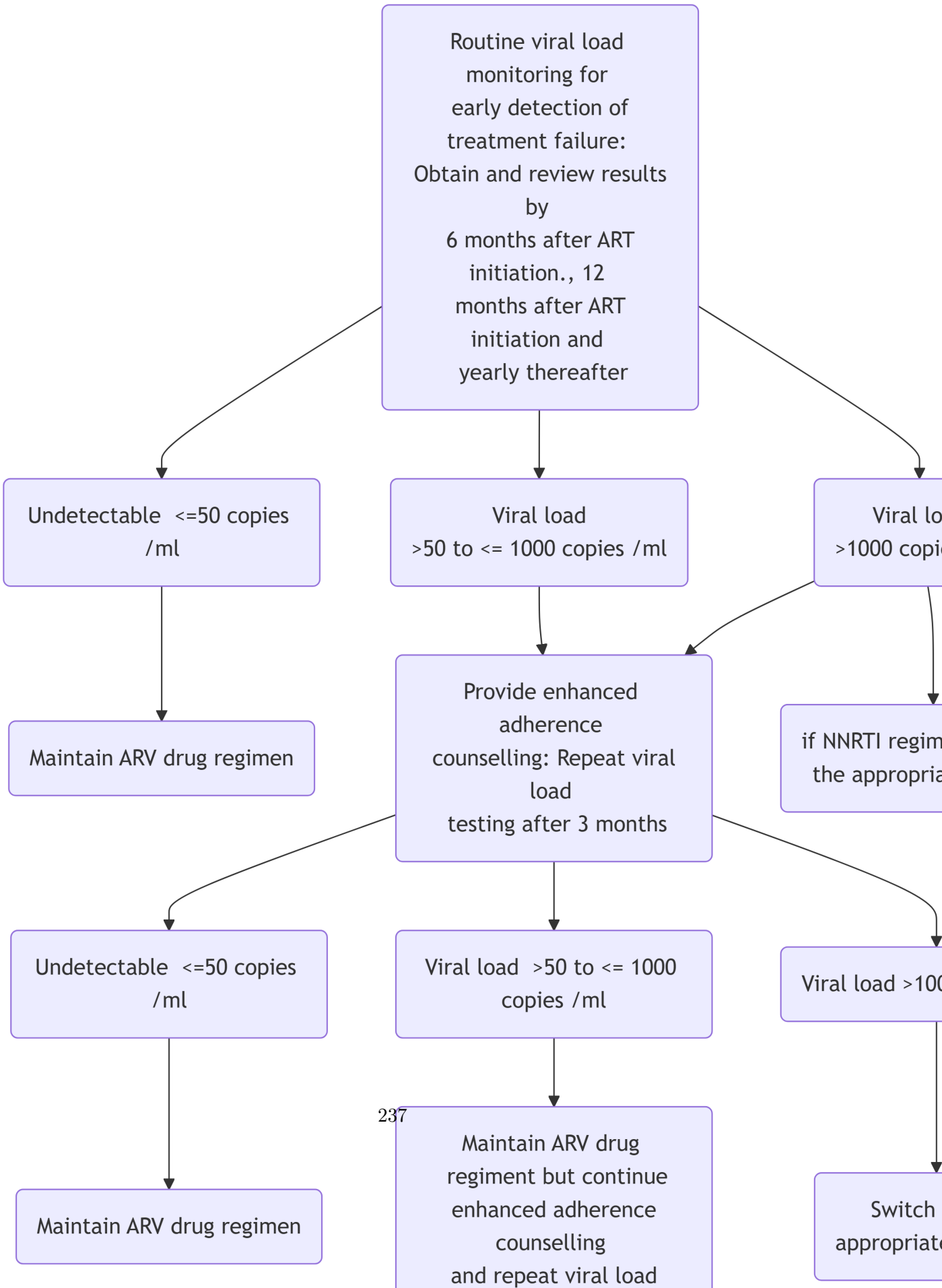
When children are on treatment viral load tests are done regularly. This is done to detect early virological failure. When highly active antiretroviral therapy (HAART) is started, the first viral load test is done at 6 and 12 months. If there is virological suppression, then monitoring is done yearly. The table below outlines what to do with various viral load cut-offs and actions to take


Screen with First response
Reactive First Response
First Response non-reac
Report HIV Negative
Test with Oraquick
HIV 1&2
If First Response
was reactive but
not Reactive to Oraquick
Repeat both First
Response & Oraquick
sequentially
If reactive to
both First Response
& Oraquick
Reactive to First
Response & Oraquick:
Confirm with SD Bioline
If Non-reactive
to first response report
HIV Negative
Confirm with SD Bioline


Routine viral load monitoring for early detection of treatment failure: Obtain and review results by 6 months after ART initiation., 12 months after ART initiation and yearly thereafter
Undetectable <=50 copies /ml
Viral load >50 to <= 1000 copies /ml
Viral lo >1000 copi
Maintain ARV drug regimen
Provide enhanced adherence counselling: Repeat viral load testing after 3 months
if NNRTI regim the appropria
Undetectable <=50 copies /ml
Viral load >50 to <= 1000 copies /ml
Viral load >100
Maintain ARV drug regimen
Maintain ARV drug regiment but continue enhanced adherence counselling and repeat viral load
Switch appropriat

34.7 Treatment

Before commencing HAART for any child or adolescent, counsel the caregiver and the child if old enough to appreciate the counselling

34.7.1 Infants born to HIV-positive mothers (post-exposure prophylaxis)

All newborns of HIV-positive mothers are called HIV-exposed babies. These babies should be given antiretroviral prophylaxis namely nevirapine and zidovudine daily starting from birth (within 24 hours) for 3 months. At week 6, infants should be started on cotrimoxazole daily till HIV infection is ruled out at 18 months. At any point in time when a child tests positive for HIV, treatment with cotrimoxazole should be continued for a longer duration till the child's immune system is fully re-constituted and appropriate for age. The best marker is appropriate CD4 for age. In the absence of CD4 testing, the child should be virologically suppressed with no evidence of clinical disease.@borges-lujan2022

34.7.2 Treatment of HIV infection

Counselling caregivers and children is a must before initiating HAART. Emphasise should be on HAART being a lifelong treatment. Adherence counselling should be integrated into clinical care. The HAART consist of 2 Nucleos(t)ide Reverse Transcriptase Inhibitor (N(t)RTI plus Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) or Integrase Strand Transfer Inhibitor (INSTI) or Protease Inhibitor (PI). HAART regimen should have a minimum of three ARVs. The table below shows the types of ARVs available in Ghana

Table 34.3: Antiretroviral Groups

Group 1	**Group 2**	**Group 3**		
N(t)RTI	**NRTI**	**NNRTI**	**INSTI**	**PI**
Abacavir (ABC)	Lamivudine (3TC)	Efavirenz (EFV) Weight > 10 kg	Dolutegravir (DTG) Weight >3 kg	Ritonavir boosted Lopinavir (LPV/r)
Zidovudine (AZT) (Hb> 8 g/dl)	Emtricitabine (FTC)	Nevirapine (NVP)	Raltegravir (RAL)	Ritonavir boosted Atazanavir (ATV/r)
Tenofovir (TDF) (Renal disease) Weight=>30 kg	**Read around the main side effects/contraindications of each ARV**			Ritonavir boosted Darunavir (DRV/r)

HAART combination can be made easy by choosing one ARV from each group.

Table 34.4: Preferred and alternative first-line ART regimens for adolescents, children and neonates

Populations	**Preferred first-line regimen**	**Alternative first-line regimen**	**Special circumstances**
Adolescents	TDF + 3TC (or FTC) + DTG	TDF + 3TC + EFV 400mg	TDF + 3TC (or FTC) + EFV600mg AZT + 3TC + EFV 600 mg TDF + 3TC (or FTC) + PI/r TDF + 3TC (or FTC) + RAL ABC + 3TC + DTG TDF + 3TC (or FTC) + PI/r
Children	ABC + 3TC + DTG	ABC + 3TC + LPV/r TDF+ 3TC (or FTC) + DTG	ABC + 3TC + EFV ABC + 3TC + RAL AZT + 3TC + EFV AZT + 3TC + LPV/r (or RAL)
Neonates	AZT (or ABC) + 3TC + RAL(or DTG)	AZT + 3TC + NVP	AZT + 3TC + LPV/r

34.7.3 Side effects of main ARVS

Depending on the type of HAART, children may experience different side effects. Regular clinical and laboratory monitoring will be needed to identify side effects early. There are alternative ARVs in each group to substitute if a child on HAART experiences a major side effect.

Table 34.5: Common ARV toxicities

Haematological toxicity	Drug-induced bone marrow suppression is most commonly seen with AZT (anaemia, neutropenia).

Mitochondrial Dysfunction	Primarily seen with the NRTI drugs, including lactic acidosis, hepatic toxicity, pancreatitis, peripheral neuropathy, lipoatrophy, myopathy
Renal Toxicity	Renal tubular dysfunction is associated with Tenofovir (TDF). ATV/r can also cause nephrolithiasis.
Other Metabolic Abnormalities	More common with PIs and INSTIs. Include hyperlipidaemia, fat accumulation, insulin resistance, diabetes and osteopenia. Lipodystrophy is also associated with Zidovudine. The risk of cardiovascular events with Abacavir (ABC) is still debatable.
Allergic Reactions	Skin rashes and hypersensitivity reactions, are more common with the NNRTI drugs but also seen with certain NRTI drugs, such as ABC and some PIs.
Hepatic Toxicity	Liver enzyme elevation with DTG especially in patients with HBV or HCV co-infection. DRV/r also causes liver enzyme elevation
Muscular Toxicity	Muscle weakness and sometimes rhabdomyolysis are seen with RAL

34.8 Complications

The main complication of HIV infection is the progression to AIDS when HAART is not initiated. Those children on treatment with non-adherence or poor adherence to HAART can ultimately develop AIDS. This will be the consequence of reduced CD4 cell count and increased viral load

34.9 Prognosis

Patients who start treatment early before immune dysgenesis and are virologically controlled have a life expectancy like an HIV-negative individual

34.10 Differential diagnosis

Acute HIV infection may be asymptomatic or may cause a mononucleosis-like syndrome. It should be differentiated from similar diseases that cause fever, fatigue, sore throat, myalgia, and lymphadenopathy such as acute toxoplasmosis, acute CMV/EBV infections, and acute viral hepatitis

34.11 Further reading

Consolidated Guidelines for HIV care in Ghana

34.12 Sample case scenarios

1. A 10-year-old boy presented to your facility with skin rashes, weight loss, fever, and cough of 3 months duration. On examination, he was semi-conscious. Chest X-ray was suggestive of pulmonary tuberculosis. CSF from Lumber puncture was positive on GeneXpert

    a. How would you confirm HIV in this child?
    b. What is the appropriate WHO clinical staging

2. A 5-year-old boy has recently been diagnosed with HIV. You intend to start antiretrovirals. He weighs 25 kg with Hemoglobin of 6 gm/dl. His renal and liver function is normal. Which option will be your best HAART?

    a. ABC/3TC/EFV
    b. ABC/3TC/DTG
    c. AZT/3TC/LPV/r
    d. TDF/3TC/EFV

3. A 15-year-old male drug addict, newly diagnosed with HIV. He weighs 35 kg. The renal and liver functions are normal. Based on the history, what additional questions will you ask? What additional test would you do?

    a. Propose ARVs

4. A 6-month-old was admitted to your facility with a fever, poor weight gain and oral thrush. HIV antibody test came up positive in both mother and infant

    a. Does this HIV antibody test confirm HIV in the child?
    b. What other tests are required in this child?

5. A 2-month-old newly diagnosed with HIV. Weight 5kg, Hb=12 g/dl normal renal and kidney function.

a. Suggest ARVs for treatment

34.13 Answers to sample questions

1. It is important to know the duration of the other symptoms if they are beyond 3 months. Ask about interventions, facilities visited and what was done for the patient. The top three possibilities are HIV/AIDS, Malignancy and tuberculosis. Malignancy should be ruled out (REFER TO ONCOLOGY LECTURES). Tuberculosis is confirmed in this child. Since HIV is a risk factor for developing TB, it is right to think of HIV in this child. Remember HIV is a family disease. Parents and other siblings MUST also be screened if they exist.

   To diagnose HIV test, this child must have positive tests on all tests using the "triple algorithm" namely first response, Oraquick, and SD bioline.

   This child has confirmed Pulmonary TB. PTB is airborne and therefore there is the need to screen close contacts. This will help identify the index case and put in necessary screening tests. Those who have the disease are treated while those exposed without the disease will need TB preventive therapy.

   This child's HIV test was positive. He has both pulmonary TB and TB meningitis. Referring to the notes on WHO clinical staging, PTB is stage 3 while TB Meningitis (TBM) is stage 4. This child therefore has clinical stage 4

   Remember that this child has an opportunist infection (TB). To prevent Immune Reconstitutive Inflammatory Syndrome (IRIS), this child has to start TB treatment before starting HAART, for PTB HAART is started preferably 2 weeks after TB medication. For TBM, HAART should be started 4-6 weeks after initiating TB medications.

   Note: Drug-drug interaction occurs between some ARVs and rifampicin. Dolutegravir, lopinavir/ritonavir, and nevirapine should be doubled when administered simultaneously with rifampicin. When TB treatment ends, extend the duration of the double dose of the ARVs for 2 weeks before reducing the dose to the expected age and weight of the children.

2. In deciding on the best HAART, an ARV should each be selected from groups 1,2 and 3. From group 1, the only feasible option is abacavir because HB is < 8g/dl and weight is < 30 kg(AZT and TCF cannot be used). Under group 2, either 3TC or FTC are possible but 3TC is readily available. Under group 3, DTG will be the best option because EFV has a lower resistance barrier and high community resistance. LPV/r is plausible but twice daily regimen makes compliance more difficult. The best option will be ABC/3TC/DTG (option b is the best choice)

3. Being a drug addict, he may be using intravenous injection which increases his risk of being infected with hepatitis B or hepatitis C. Again, he may be having sexual partners exposing him to STI. He, therefore, has to be investigated for hepatitis B/C, full blood count, and screened for other STIs. The choice of HAART will have to factor in hepatitis B status. TDF can be given because he weighs more than 30 kg and renal function is normal. Based on the previous explanation, TDF/3TC/DTG is the best choice. This option comes as a Fixed dose combination so he will take just 1 tablet daily, improving compliance among adolescents. Should the adolescent be Hepatitis B positive, TDF/3TC are also active against hepatitis B. Adolescents should be referred for appropriate services if there are other co-morbidities. Referral to a clinical psychologist will also be needed because he is addicted to drugs

4. Antibodies are IgG and cross the placental to the baby. Newborns testing positive using antibody tests might be maternally transmitted. Antibody tests do not confirm HIV in children below 18 months. These antibodies are expected to disappear by 18 months. The recommended test for a 6-month-old baby is a DNA PCR test (refer to above). Other tests and timelines if the baby is negative at 6 months, are at 9 months (DNA PCR) and 18 months (antibody test)

5. For a 2-month-old, an Hb of 12 is low; therefore, AZT will not be a good option. The HAART of choice is ABC/3TC/DTG

34.14 Self-assessment questions

1. A 15-year-old takes HAART which he thinks are vitamins for SCD. How would you disclose his true status to him?
2. A 17-year-old adolescent girl is about to start HAART. Explain the content of your counselling.

35 Sepsis in Children

35.1 Definition

Sepsis is a life-threatening condition characterized by organ dysfunction resulting from a dysregulated host response to infection. In children, it presents a range of disorders caused by bacterial, viral, fungal, or parasitic infections. Septic shock, a severe form of sepsis, is defined by persistent hypotension that requires vasopressors to maintain a mean arterial pressure (MAP) of 65 mmHg and a serum lactate level greater than 2 mmol/L, despite adequate fluid resuscitation.

35.2 Incidence and Prevalence

Sepsis continues to be a major cause of morbidity and mortality in children around the globe. As stated by the World Health Organization (WHO), sepsis plays a significant role in childhood mortality, especially in low-resource environments. The incidence varies by region, with higher rates observed in neonates and infants due to their immature immune systems.

35.3 Aetiology

Sepsis can result from infections caused by bacteria, viruses, fungi, and parasites. The most common bacterial pathogens vary by age:

- Early-Onset Neonatal Sepsis: *Streptococcus agalactiae*, *Escherichia coli*, *Haemophilus influenzae*, *Listeria monocytogenes*.
- Infant Sepsis: *Haemophilus influenzae type b (Hib)*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Salmonella* species.
- Late-Onset Neonatal Sepsis: *Staphylococcus aureus*, *E. coli*, *Klebsiella* species, *Pseudomonas aeruginosa*, *Candida* species.

35.4 Pathogenesis

Sepsis results from a dysregulated immune response to infection, leading to widespread tissue injury. The process involves:

1. **Immune Dysregulation:** Excessive release of pro-inflammatory and anti-inflammatory mediators.
2. **Microcirculatory Derangements:** Increased vascular permeability, leading to hypotension and organ dysfunction.
3. **End-Organ Damage:** Progression to multi-organ failure due to poor perfusion.

35.5 Signs and Symptoms

Early recognition is crucial, as sepsis can progress rapidly. Symptoms include:

- Fever or Hypothermia
- Tachycardia and Tachypnea
- Altered Mental Status
- Hypotension
- Cool Extremities
- Petechial or Purpuric Rash (suggestive of meningococcal sepsis)
- Oliguria or Anuria (kidney dysfunction).

35.6 Investigations

A thorough **laboratory workup** is essential for diagnosis:

- **Blood Tests:** Complete Blood Count (CBC), Blood Culture, Blood Gas Analysis (including lactate levels).
- **Urine Analysis:** Dipstick, Routine Examination, Culture.
- **Cerebrospinal Fluid (CSF) Analysis:** Culture and Sensitivity.
- **Coagulation Studies:** To assess disseminated intravascular coagulation (DIC).
- **Inflammatory Markers:** C-Reactive Protein (CRP), Procalcitonin (PCT), Interleukins (IL-1b, IL-6, IL-8), Tumor Necrosis Factor-alpha.

35.7 Treatment

Early antibiotic therapy and fluid resuscitation are critical:

- **Empirical Broad-Spectrum Antibiotics:** Based on suspected pathogens.
- **Fluid Resuscitation:** Crystalloids (e.g., normal saline or Ringer's lactate).
- **Vasopressors:** If hypotension persists despite fluids.
- **Supportive Care:** Oxygen therapy, mechanical ventilation, renal replacement therapy if needed.

35.8 Complications

Sepsis can lead to multi-organ failure and death if untreated. Common complications include:

- Acute Respiratory Distress Syndrome (ARDS)
- Disseminated Intravascular Coagulation (DIC)
- Renal Failure
- Cardiac Dysfunction
- Neurological Sequelae (e.g., cognitive impairment post-sepsis).

35.9 Prognosis

The mortality rate varies based on early recognition and intervention. Neonatal sepsis has a higher fatality rate, especially in low-resource settings. Survivors may experience long-term complications, including neurodevelopmental delays.

35.10 Differential Diagnosis

Sepsis must be distinguished from other conditions with similar presentations:

- Meningitis
- Severe Pneumonia
- Hemorrhagic Shock
- Metabolic Disorders
- Autoimmune Diseases.

35.11 References

1. Bone RC. The sepsis syndrome: definition and general approach to management. Clin Chest Med. 1996 Jun;17(2):175-81. Available here.
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35.11.1 Clinical Scenario 1: Neonatal Sepsis

A 5-day-old male infant presents with lethargy, poor feeding, respiratory distress, and a fever of 38.5°C. On examination, the infant appears jaundiced, with cool extremities and tachypnea. The mother had a prolonged rupture of membranes (>18 hours) before delivery, and the infant had meconium-stained amniotic fluid.

Key Considerations:

- **Etiology:** Early-onset neonatal sepsis, likely *Streptococcus agalactiae* (Group B Strep) or *Escherichia coli*.
- **Investigations:** Blood cultures, CBC, CRP, procalcitonin, serum lactate, and lumbar puncture for CSF culture.
- **Management: Empirical IV antibiotics** (Ampicillin + Gentamicin), fluid resuscitation, oxygen therapy, and supportive care.
- **Complications:** Risk of meningitis and multi-organ failure if untreated.

35.11.2 Clinical Scenario 2: Pediatric Septic Shock

A 6-year-old girl presents with a history of fever (40°C) for 3 days, altered mental status, and poor urine output. She is tachycardic (HR: 150 bpm), hypotensive (BP: 75/50 mmHg), and has delayed capillary refill (>3 seconds). A petechial rash is noted on the lower extremities.

Key Considerations:

- **Etiology:** Meningococcal sepsis (*Neisseria meningitidis*) suspected.
- **Investigations:** Blood culture, CBC, coagulation studies, lactate, kidney function tests, and inflammatory markers.
- **Management: IV Ceftriaxone**, aggressive fluid resuscitation, vasopressors if needed, and close monitoring in ICU.
- **Complications:** Disseminated Intravascular Coagulation (DIC), Acute Respiratory Distress Syndrome (ARDS), multi-organ failure

36 Paediatric Tuberculosis

36.1 Definitions

Infection with Mycobacterium tuberculosis usually results from inhaling infected droplets produced by someone who has Pulmonary Tuberculosis (TB) and is coughing. The most infectious source cases are those with sputum smear-positive disease. The closer the contact with this source case, the greater the exposure and the greater the risk of getting infected with tuberculosis.

TB infection occurs when a person carries the Mycobacterium tuberculosis bacteria inside the body. Many people have TB but are well. A positive tuberculin skin test (TST) suggests infection but a negative TST does not exclude the possibility of infection.

TB disease occurs in someone with TB infection when the bacteria inside the body start to multiply and become numerous enough to damage one or more organs of the body. This damage causes clinical symptoms and signs. This is referred to as "tuberculosis" or active disease.

Close contact is defined as living in the same household as, or in frequent contact with (e.g. caregiver, school staff), a source case with PTB.

Multidrug-resistant TB (MDR-TB) is caused by M. tuberculosis strains that are resistant to both *isoniazid* and rifa*mpicin*.

Pre-extensively drug-resistant TB (Pre-XDR): TB caused by M. tuberculosis strains that fulfil the definition of multidrug-resistant TB (MDR-TB) or rifampicin-resistant TB (RR-TB) and that are also resistant to any fluoroquinolone.

Extensively drug-resistant TB (XDR-TB): TB caused by M. tuberculosis strains that fulfil the definition of MDR/RR-TB and that are also resistant to any fluoroquinolone and at least one additional Group A medicine. (bedaquiline and linezolid)

36.2 Incidence/prevalence

According to the 2023 WHO global TB report; globally, a total of 10.6 million people fell ill with TB in 2022 of which children less than 15 years accounted for 12%. According to WHO estimates for 2022, there were 44,000 estimated incident cases in Ghana. Of this number,

Ghana notified 16,526 cases of which 10% were expected to be paediatric (0-14yrs). However, 5% of paediatric cases were notified.

36.3 Aetiology

The Mycobacterium tuberculosis complex (MTBC) constitutes a significantly genetically similar group of bacteria that cause tuberculosis in various hosts. They are rod-shaped, acid-base-fast, aerobic, slow-growing intracellular pathogens that destroy phagosomal cells to maintain and evade the immune system. The major MTBC pathogenic mycobacteria species include M. tuberculosis, M. bovis, M. africanum, and M. microti.(Zhang et al. 2022)

36.4 Pathogenesis

Following the M. tuberculosis transmission to a new host, the bacilli enter the lung and get ingested by macrophages. Further, immune cells are recruited to wall off the infected macrophages, forming granuloma, the hallmark of TB. Healthy individuals remain latently infected, and the infection is kept at bay at this stage, but it is prone to the risk of reactivation. As the granuloma develops, the bacilli emerge from the macrophages. When the reactivation occurs, M. tb proliferates, the bacterial load becomes overwhelmingly high, and the granuloma ruptures, disseminating the bacteria to the airways. The bacilli are then expectorated as contagious aerosol droplets, restarting the cycle, and infecting other individuals.(Alsayed and Gunosewoyo 2023)

36.5 Signs and symptoms

It is important to understand the risk for TB infection and TB disease. Taking the history from children and caregivers must include questions on risk factors.

For an infection to occur, there are certain factors:

1. Contact with source case (Close contact and duration of contact)
2. Source case (Smear positivity: smear positive is more infectious; Cavitation on Chest X-ray: more infectious)
3. Increased exposure (Living in high TB endemic areas; children of families living with HIV)

Factors affecting TB disease:

1. Young age (2 years and below)
2. HIV infection

3. Other immunosuppression (Malnutrition, Post-measles)
4. Not BCG vaccinated (Risk of disseminated TB or severe TB disease)

Pulmonary Tuberculosis

History –The major considerations

Make every effort to look for the close contact or the household contact who is the source of the infection. It is helpful to note that close contact may be at school in a classroom, dormitory/ school bus, or church. Sometimes, it may be someone who frequently visits the child's home or a caregiver. In childhood, it may take between 3 months to 2 years from the time of exposure to develop TB disease.

History of symptoms suggestive of TB

More commonly children with TB will present with the following symptoms:

1. Cough of any duration or progressive non-remitting cough which may be dry or wet.
2. Fever (persistent or unexplained)
3. Lethargy/reduced playfulness/less active
4. Poor weight gain or weight loss or very low weight (failure to thrive), flattened growth curve is a very sensitive marker of disease. More specifically it is important to plot the measurement and compare it to previous charts on the growth charts in the child health record booklet
5. Night sweat. Since most children sweat at night, it is usually difficult to establish this symptom.

Physical Examination (Some clinical findings suggestive of PTB)

General Examination

1. Fever- Temperature that remains persistently high or irregular >37.5 (fever)
2. Weight- (confirm poor weight gain, recent weight loss): the weight should be plotted on the child's growth curve, and any child who "falls off" or is unable to maintain their usual line of growth should be considered as having possible TB
3. Length/Height is needed to determine the weight-for-length/height Z-scores (<-3 Z indicates severe wasting)
4. MUAC -Middle upper arm circumference of < 12.5 cm
5. Respiratory rate - (fast breathing) depends on the patient's age. (Children 0-2 months above 60cpm, 3 months to 12 months more than 50 CPM and 1-5 years more than 40 CPM)
6. Signs of respiratory distress are not specific to TB but must raise the index of suspicion e.g Low oxygen saturation, stridor, and wheezes

Physical signs suggestive of Extra Pulmonary TB (EPTB) include:

1. Enlarged cervical lymph nodes which are not painful with or without fistula formation – TB lymphadenopathy;
2. Presence of spinal kyphosis (angular swelling) – spinal TB ("gibbous");
3. Signs of non-acute meningitis with poor response to antibiotic treatment and/or with raised intracranial pressure – TB Meningitis;
4. Pleural effusion, especially one-sided dullness with pleuritic pain in a child who is not acutely ill – pleural TB;
5. Pericardial effusion, distant or muffled heart sounds or signs of new-onset heart failure – pericardial TB;
6. Non-acute distended abdomen with or without ascites – abdominal TB;
7. Non-tender swollen joints with painful or abnormal gait – osteoarticular TB.

36.6 Investigations

In addition to a detailed history and careful physical examination, all children suspected to have TB will require additional investigations. Investigations commonly used are grouped into the following categories.

1. Bacteriological investigations
2. Radiologic investigations and
3. Immunologic investigations.

36.6.1 Bacteriological investigations

Xpert MTB/RIF Assay is the recommended first-line investigation for diagnosing TB in children. Results are rapid and determine if the patient has a drug-sensitive or resistant organism. Various specimens may be collected, including expectorated sputum, induced sputum, gastric aspirate, bronchoalveolar lavage, transbronchial biopsies, pleural aspirate urine, blood, cerebrospinal fluid tissue and, more recently, stool. Other modalities for confirming TB are smear microscopy and TB cultures.

36.6.2 Radiologic investigations

Children often have paucibacillary TB and therefore bacteriological yields are low. Various imaging modalities can be suggestive of TB. Chest X-ray is the most frequently used radiological imaging. The presence of hilar lymphadenopathy (Figure **??**), effusions, and cavitations could all support the diagnosis of TB in children. Ultrasound, CT scan, and MRI all have roles in suspected extrapulmonary TB.

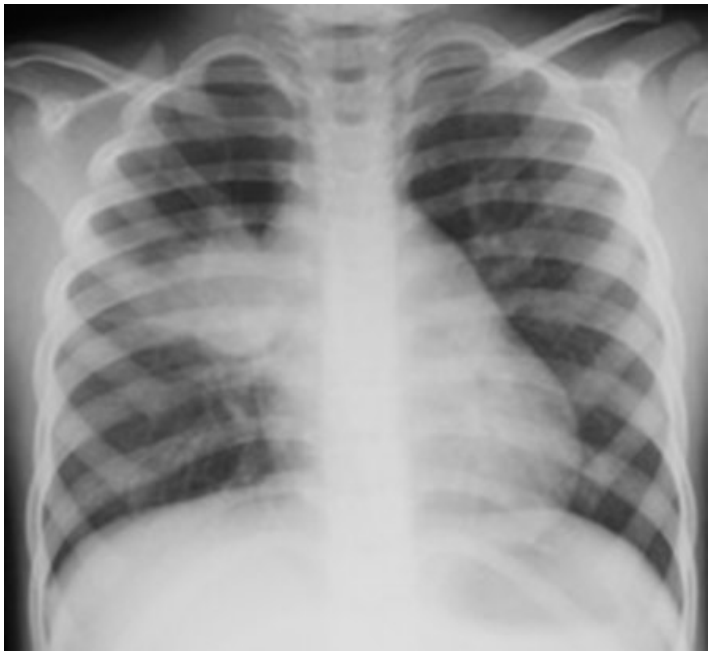

Figure 36.1: Chest X-ray showing perihilar lymphadenopathy suggestive of TB

36.6.3 Immunologic investigations

Immunological tests provide evidence for TB infection but not TB disease. Two tests are widely used namely the *Tuberculin skin test* and the *interferon-gamma release assay.*

36.7 Treatment

36.7.1 Antituberculous medications

There are two types of treatment namely *TB disease treatment* and *TB preventive therapy.* The Paediatric TB Medicines comprises of 3 different formulations as follows:

1. Rifampicin + Isoniazid + Pyrazinamide (RHZ) 75/50/150 mg
2. Ethambutol (E) 100 mg 3. Rifampicin + Isoniazid (RH) 75/50 mg

Every child receives 2RHZE (2 months intensive phase)/4RH (4 months continuation phase) for all forms of TB except TB meningitis and osteoarticular TB where the continuation phase is extended for 10 months (10 RH). For non-severe TB (refer to further reading) 2RHZE/2RH regimen can be applied.

Note:

Corticosteroids are often used as an adjunct in the treatment of these forms of TB to prevent complications. These include TB Meningitis; TB Pericarditis; and Pott disease/ TB Spondylitis. Pleural diseases, and Endobronchial TB
Pyridoxine (Vitamin B6) supplement is necessary in some patients to prevent peripheral neuropathy but recommended in ALL HIV-infected persons and severely acute malnourished patients on isoniazid

36.7.2 Major side effects

Potential side effects of TB medications are:

1. Rifampicin: Orange-colored urine, saliva or tears, jaundice
2. Pyrazinamide: GI disturbances, hepatotoxicity
3. Ethambutol: GI disturbances, blurred vision
4. Isoniazid: numbness and tingling in the extremities, GI disturbances, rash

36.7.3 TB Preventive Therapy

Every person living with HIV should be given TB preventive therapy (TPT) after screening and ruling out active TB disease. Other categories of children requiring TPT after ruling out TB disease are:

1. Newborns of mothers with TB,
2. All Children exposed to an index case with sputum-positive TB,
3. Long-term steroids, and immunocompromised children.

If a patient develops TB disease, the patient should be investigated, and treatment changed from TPT to full treatment. There are four(4) options for TPT in children:

1. Rifapentine + Isoniazid- weekly for 3 months
2. Rifampicin + isoniazid – daily for 3 months
3. Rifampicin- daily for 4 months
4. Isoniazid only – daily for 6 months

36.8 Complications

The most common complication is chronic lung disease. TB can affect any part of the body including the brain, spine and therefore can cause other complications such as stroke, abscesses, impaired growth and so forth.

36.9 Prognosis

With early identification and treatment, the prognosis is good.

36.10 Differential diagnosis

Common differentials are bacterial pneumonia, atypical pneumonia, brucellosis, bronchogenic carcinoma, HIV, and Hodgkin lymphoma

36.11 Further readings

WHO consolidated guidelines on tuberculosis: module 5: management of tuberculosis in children and adolescents

WHO operational handbook on tuberculosis: module 5: management of tuberculosis in children and adolescents

36.12 Sample case scenarios

Question

1. A mother delivers a newborn at 40 weeks gestation. Within the last 4 weeks of pregnancy, she started coughing. She bought cough syrup and amoxicillin at a dispensary. Her coughing got severe and she noted weight loss. At week 39, she visited the hospital and was diagnosed with TB (GeneXpert MTB positive and RIF sensitive). She was started on treatment immediately. She lives in a single room with her 3 other children who are 2 years, 8 years, and 10 years respectively who were all clinically well except the 2 years old who weighed 8 kgs.

    1. Identify risks of infection for the children
    2. Identify risks of disease in children
    3. How would you approach the management of the children

Answers

a. The risks of infection in the above scenario are sputum-positive MTB on GeneXpert tests and the single room is occupied by a single mother and her children.
b. The risk of TB disease will be in the newborn and the 2-year-old sibling who is already failing to thrive. If the mother has HIV or the children are not immunised with BCG, that would also be a risk factors for disease.

c. All the children have been exposed to TB through a close contact, who happens to be their mother. The mother has to be tested for HIV. If she is positive, all the children should also be tested. All the children would have to be screened for TB. The newborn should ideally not be given BCG vaccine but put on TPT if TB disease is excluded. The recommended TPT will depend on the HIV status of the newborn, but Isoniazid is an option for 6 months. After 6 months of INH, if there is no evidence that the newborn has been exposed to TB (Mantoux testing), the child can be given BCG vaccine. If the newborn has the disease, then full TB treatment should be given. The 2-year-old weighs 8 kg which is evidence of weight faltering. Plot the weight for age on the Z-score. Do other investigations such as Chest X-ray, stool for Xpert, and HIV testing. If the clinical, bacteriological, and imaging are suggestive of TB, treat the 2-year-old. If HIV is positive, remember to adjust the dose of ARVs that interact with rifampicin during TB treatment. If the screening of the 8 and 10 years is normal, then put them on TPT, otherwise treat them

Self-assessment questions

1. A 5-year-old boy diagnosed with TB and started on RHZE complained to his mother that he finds it difficult to see clearly what his school teacher has projected in class. Which of the following medications is likely responsible?

    a. Isoniazid
    b. Pyrazinamide
    c. Ethambutol
    d. Rifampicin

2. Explain why bacteriological yield from children with suspected PTB is often very low.

37 Childhood Immunization

37.1 Introduction

Childhood immunization is a cornerstone of public health, offering lifesaving protection against infectious diseases. It is one of the most cost-effective strategies for reducing morbidity and mortality in children worldwide. Immunization is vital in achieving Sustainable Development Goal (SDG) 3, which aims to reduce neonatal mortality to 12 per 1000 live births and under-five mortality to 25 per 1000 live births by 2030. Despite its effectiveness, challenges such as parental misconceptions, healthcare accessibility, vaccine hesitancy, and logistical issues persist.

37.2 Key Immunization Concepts

- **Immunization**: The process of artificially conferring immunity against infectious diseases.
- **Vaccination**: The act of introducing an antigenic material into the body to stimulate an immune response, leading to future protection upon exposure.
- **Vaccine**: A biological preparation that enhances active acquired immunity against specific pathogens. Vaccines can be live-attenuated, inactivated, subunit, toxoid-based, or nucleic acid-based.

37.3 Types of Vaccines

Vaccines are classified based on their composition and mechanism:

1. **Live Attenuated Vaccines**: Contain weakened pathogens (e.g., Measles, Mumps, Rubella, BCG, Yellow Fever, OPV).
2. **Killed/Inactivated Vaccines:** Pathogens are killed but retain their immunogenic properties (e.g., Hepatitis A, Rabies, IPV).
3. **Toxoid-Based Vaccines**: Contain inactivated toxins to generate immunity (e.g., Tetanus, Diphtheria).
4. **Subunit/Conjugate Vaccines**: Use fragments of pathogens for immunity (e.g., Pneumococcal, Hib, Hepatitis B).

5. **Nucleic Acid-Based Vaccines**: Utilize mRNA or DNA to instruct cells to produce an immune response (e.g., SARS-CoV-2 vaccines).

37.4 Expanded Programme on Immunization (EPI) in Ghana

Ghana's routine immunization schedule includes:

- **Birth:** BCG, OPV (0)
- **6 Weeks:** Pentavalent (DTwP/HepB/Hib), OPV (1), PCV (1), Rotavirus (1)
- **10 Weeks:** Pentavalent (2), OPV (2), PCV (2), Rotavirus (2)
- **14 Weeks:** Pentavalent (3), OPV (3), IPV, PCV (3), Rotavirus (3)
- **6-7 Months:** RTS,S (Malaria vaccine)
- **9 Months:** Measles-Rubella (MR), Yellow Fever, RTS,S (3)
- **18 Months:** MR Booster, Meningococcal A, RTS,S (4)
- **Adolescents:** HPV vaccine for girls aged 10-13.

37.5 Principles of Immunization

- **Herd Immunity:** High vaccination coverage reduces disease transmission.
- **Cold Chain Management:** Essential for vaccine potency.
- **Missed Opportunities:** Ensuring timely vaccination enhances community protection.
- **Vaccine Safety:** Strict protocols ensure vaccines are safe and effective.

37.6 Contraindications to Vaccination

While vaccines are generally safe, contraindications exist:

- **Live vaccines** should be avoided in **immunocompromised individuals**.
- **Severe allergic reactions** (anaphylaxis) to vaccine components.
- **Pregnancy** – Certain live vaccines (e.g., Yellow Fever, Measles) are contraindicated.

37.7 Vaccine-Preventable Diseases & Control Programs

Immunization programs target several infectious diseases:

- **Tuberculosis (BCG):** Protects against severe TB forms in infants.
- **Polio:** Eradication efforts involve IPV and OPV.
- **Pneumococcal Disease (PCV13):** Prevents pneumonia, meningitis.

- **Rotavirus:** Reduces childhood diarrheal deaths.
- **Measles, Rubella, Mumps (MR/MMR):** Prevents severe complications.
- **Meningococcal Disease (Men A):** Prevents outbreaks.
- **Yellow Fever:** Essential for endemic regions.
- **HPV:** Prevents cervical cancer.

37.8 Challenges & Future Directions

- **Vaccine Hesitancy:** Addressing misinformation.
- **New Vaccine Development:** Ongoing innovations like mRNA vaccines.
- **Policy & Surveillance:** Strengthening disease monitoring to prevent outbreaks.

37.9 Specific vaccines

37.9.1 BCG Vaccine (Tuberculosis)

- **Pathogen:** *Mycobacterium tuberculosis* or *M. bovis* (Non-sporing, rod-shaped, acid-fast bacillus)
- **Type:** Live attenuated, freeze-dried
- **Storage:** 2°C - 8°C (Never frozen)
- **Administration:** Intradermal (deltoid)
- **Shelf Life:** 12 - 18 months
- **Usage:** Do not shake to mix; use within 2 hours
- **Efficacy:**
  - 0–80% for Pulmonary TB (PTB)
  - 75–86% for Miliary TB & TB Meningitis
- **Indications:**
  - Infants, health personnel, and contacts with sputum-positive cases.
  - Suspected exposure? Perform a tuberculin test before immunization.
  - In cases of contact: Tuberculin test, repeat after 6 months. If positive Chemoprophylaxis.
- **Notes:**
  - Duration of immunity is uncertain; it wanes over time.
  - Protects children against meningitis & disseminated TB but does not prevent primary infection or reactivation.
  - Scar confirms vaccination but not protection. Absence of a scar may indicate the need for testing and revaccination.

  - Up to 10% scar failure rate is acceptable in properly vaccinated individuals.
  - Tuberculin test: Uses Purified Protein Derivative (PPD) for Mantoux/Heaf test.

37.9.2 Polio Vaccines

- **Pathogen:** Poliovirus Types I, II, III.
- **Adults:** More prone to **inapparent paralytic infections**.
- **Virus Survival:** Inactivated at 55°C for 30 minutes (but inhibited by Mg++, milk, ice cream)
- **Types of Vaccines:**
  - **Inactivated Polio Vaccine (IPV)** – Salk (1956)
  - **Live Attenuated Oral Polio Vaccine (OPV)** – Sabin (1962)
  - **Variants:**
  - **tOPV (Trivalent OPV):** Contains live strains of all three virus types.
  - **bOPV (Bivalent OPV):** Contains live strains of Types I & III.
  - **nOPV (Novel OPV):** A modified strain of Type II with enhanced stability.
- **Efficacy:**
  - 90% in industrialized nations.
  - 72–98% in hot climates (**lower protection against Type III**).
- **Duration of Immunity:**
  - Lifelong if boosted by wild virus, otherwise shorter.
- **Vaccine-Associated Paralytic Poliomyelitis (VAPP):**
- Polio Type II in tOPV linked to **VAPP**, undermining eradication efforts.
- **Solution:** Withdraw Type II from OPV Introduce bOPV + at least one IPV dose in routine schedules.
- **Ghana (since June 2018):** bOPV + IPV at 14 weeks.
- nOPV introduced as a **more antigenically stable** next-gen Type II vaccine.

37.9.3 Pentavalent Vaccine ("PENTA")

- **Components:** Diphtheria, Whole-cell Pertussis, Hepatitis B, Hib (Haemophilus influenzae type
- **Introduced:** 2001; used in Ghana since March 2002.
- **Storage:**
  - Liquid DPT-HepB: Refrigerated at 2°C - 8°C (**not frozen**).
  - Lyophilized Hib: Stored at -20°C or refrigerated at +2 - 8°C.
- **Preservation:** Contains preservatives, allowing reconstitution for extended use.

37.9.4 Tetanus Vaccine

- **Pathogen:** *Clostridium tetani* (Toxin-producing)
- **Vaccine Type:** Toxoid (inactivated toxin)
- **Schedule:**
  - **Children & Adults:** 3 doses (one month apart); reinforced every 10 years with two doses for lifelong immunity.
  - **Boosters:** Recommended at time of injury.
  - **Maternal immunization:** Protects against neonatal tetanus.

37.9.5 Hepatitis B Vaccine

- **Pathogen:** Hepadnavirus (Double-stranded DNA virus)
- **Carrier Rate:** 2 - 10% (higher in perinatal infections).
- **Transmission:** Highly infectious among carriers with **HBeAg**.
- **Vaccine:**
  - HBsAg adsorbed onto alum (adjuvant).
  - Produced via recombinant DNA in yeast cells.
- **Pre-exposure Immunization**
  - Universal infant immunization.
  - Catch-up vaccination for adolescents.
  - Healthcare workers, hemodialysis patients, blood recipients, drug abusers, transplant candidates.
- **Post-exposure Prophylaxis:**
  - **HBIG (Hepatitis B Immunoglobulin):** Provides passive immunity (3-6 months).
  - Best protection: **HBIG + Hep B vaccine** within **24 hours** after exposure.
  - **Routine infant vaccination:** HB vaccine alone is sufficient.
  - Not needed for pre-transfusion prophylaxis due to modern blood screening.

37.9.6 Yellow Fever Vaccine

- **Pathogen:** *Flavivirus* (RNA virus); spread by *Aedes aegypti* mosquitoes.
- **Vaccine:** Live attenuated, freeze-dried (17D strain, grown in chick embryo).
- **Contains:** Neomycin, polymyxin.
- **Contraindications:** Allergy to components.

37.9.7 Measles-Rubella (MR) & MMR Vaccine

- **Viruses:**
  - Measles, Mumps (*Paramyxoviruses*, RNA)
  - Rubella (*Togavirus*, single-stranded RNA)
- **Purpose:** Prevent congenital rubella infection.
- **Variants**
  - MR (Measles-Rubella) – Used in Ghana.
  - MMR (Measles-Mumps-Rubella).
- **Presentation:** Freeze-dried.
- **Administration:** Subcutaneous injection.

37.9.8 Pneumococcal Disease & Vaccines

- **Pathogen:** *Streptococcus pneumoniae* (Gram-positive diplococcus).
- **Common Diseases:**
  - **Non-Invasive:** Otitis media, sinusitis, bronchitis.
  - **Invasive (IPD):** Pneumonia, Bacteraemia, Meningitis.
- **Vaccines**
  - **Polysaccharide (PPV23):** Short-lived immunity, recommended for high-risk individuals 2 years.
  - **Conjugate (PCV13):** Provides longer-lasting immunity and is effective against pneumonia. Ghana uses PCV13 ("Prevenar")

37.9.9 Rotavirus Vaccine

- **Disease Impact:** Severe diarrheal illness in young children; major cause of dehydration.
- **Transmission:** Ubiquitous (water and sanitation improvements do not prevent infection).
- **Vaccine Options in Ghana:**
- **Rotavac (May 2021):** 3 doses (6, 10, 14 weeks).
- **Rotarix (GSK):** Monovalent, given orally in **two doses** (by 16 weeks, no later than 24 weeks).
- **Rotateq:** Bovine-human reassortant vaccine; **three doses** at 2, 4, 6 months.
- **RotaShield (Wyeth):** Withdrawn due to risk of **intussusception**.

37.9.10 Human Papillomavirus (HPV) Vaccine

- **Virus Type:** Small, double-stranded DNA virus.
- **High-Risk Oncogenic Strains:** Types **16 & 18** (cause 70% of cervical cancers).
- **Vaccines:**
  - **Quadrivalent (HPV 6, 11, 16, 18)** – Produced in yeast.
  - **Bivalent (HPV 16, 18).**
- **Target Age Group:** 10-13-year-old girls (not a standard vaccination group).
- **Catch-up Vaccination:** Not recommended in public health programs.

37.9.11 Malaria Vaccines and Immunization Strategy

Malaria remains a significant global health challenge, particularly in endemic regions. The **Plasmodium falciparum life cycle** involves two distinct stages:

1. **Asexual Stage (Human Host)** – Sporozoites enter the bloodstream through mosquito bites, travel to the liver, and mature into merozoites before infecting red blood cells.
2. **Sexual Stage (Mosquito Vector)** – Gametocytes ingested by mosquitoes undergo development, enabling transmission.

RTS,S/AS01 Malaria Vaccine

The RTS,S/AS01 malaria vaccine provides partial protection against **Plasmodium falciparum** infection.

- **Mechanism of Action**:
  - Induces **antibody production** to block sporozoite entry into liver cells.
  - Activates **T-cell responses** to eliminate sporozoites that reach the liver.
- **Administration**:
  - **Four-dose series**:
    - **1st dose** at **5 months** (not recommended for infants
    - **2nd and 3rd doses** administered at **4-week intervals**.
    - **4th dose** given between **15–18 months**
  - Can be co-administered with other vaccines in **national immunization programs**
- **Efficacy**: Less than **50%**, but beneficial for reducing severe cases and mortality.
- **Recommendations**: Targeted for **high-malaria-burden African countries** with existing control programs.

37.9.12 Rabies Vaccines and Post-Exposure Prophylaxis

Rabies is a fatal viral zoonosis transmitted through the bite of infected animals (mainly carnivores and bats).

- **Disease Determinants**:
  - Severity of wound and viral inoculation.
  - Proximity of bite to central nervous system (higher risk if near head).
  - Timeliness of post-exposure prophylaxis (PEP).
- **Rabies Virus (RABV) Presence in Humans**:
  - Found in saliva, tears, urine, and nervous tissues.
  - Not detected in blood.
- **Incubation Period**: 1-3 months, but may extend up to 1 year

Post-Exposure Prophylaxis (PEP)

- **Immediate wound cleansing**.
- **Rabies vaccine series initiation**.
- **Rabies immunoglobulin (Rabies IG)** infiltration around the wound (if indicated).

Rabies Vaccine Types

- Cell Culture or Embryonated Egg Vaccines (CCEECV):
  - Live attenuated, freeze-dried (propagated in human diploid or chick embryo).
  - Administered intramuscularly (IM) or intradermally (ID) on Days 0, 3, 7, 14, and 28.
  - Preferred site of administration: Deltoid (adults) or anterolateral thigh (children)
- Nerve Tissue Vaccines (NTV) (Obsolete):
- Derived from animal brain tissue.
- Associated with Guillain-Barré Syndrome, encephalitis.
- Not recommended by WHO.

Note: Chloroquine prophylaxis suppresses rabies vaccine antibody response, particularly when given intradermally.

37.9.13 Influenza and COVID-19 Vaccines

37.9.13.1 Influenza Virus and Vaccine Development

Influenza viruses undergo continuous genetic variations, requiring annual vaccine updates.

- Antigenic Drift – Small mutations producing minor variants (Influenza A, B) → epidemics.
- Antigenic Shift – Major genetic reassortments (Influenza A only) → pandemics.

37.9.13.2 COVID-19 Vaccine Technologies

- **Inactivated or Weakened Virus** – Uses killed virus components.
- **Protein-Based Vaccines** – Uses harmless protein fragments to generate immunity.
- **Viral Vector Vaccines** – Genetically engineered virus produces spike proteins.
- **RNA/DNA Vaccines** – Uses mRNA/DNA encoding spike proteins (e.g., Moderna, Pfizer).

37.10 Vaccine Reactions and Adverse Events Following Immunization (AEFI)

37.10.1 Minor Vaccine Reactions

- Common reactions occur as part of the immune response:
  - Fever, injection-site swelling/pain, malaise.
  - Most frequent with DPT vaccines.
  - Symptoms self-resolve.
- Parents should be educated on symptom management.

37.10.2 Severe Reactions (Rare)

- Anaphylaxis (1 per million doses) – Requires urgent medical intervention (e.g., adrenaline).
- BCG Osteitis – Rare, vaccine-specific reaction.
- Vaccine-Induced Fainting – Common in adolescents, often misinterpreted as anaphylaxis.

37.10.3 AEFI Classification

1. **Vaccine Reaction** – Direct response to vaccine components.
2. **Program Error** – Due to improper vaccine handling/administration
3. **Coincidental** – Occurs post-immunization but is unrelated to vaccination.
4. **Injection Reaction** – Pain/anxiety linked to the injection process.
5. **Unknown Cause** – Unresolved cases

37.11 Vaccine Storage and Multidose Vial Policy

- **Cold Chain Maintenance**: Essential for vaccine efficacy and stability.
- **Heat Sensitivity**:
  - BCG, Measles, Polio can be frozen.
  - Diluent-containing vaccines (DPT, TT, HepB) must NOT be frozen.
  - Frozen vaccines may cause reduced immune response
- **Shelf Life**: Max 2 years under ideal storage.
- **Vaccine Vial Monitors (VVM)**:
- Monitor vaccine exposure to heat.
- Discard if VVM reaches critical stages.

37.11.1 Multidose Vial Policy (Current Guidelines)

- Vaccines usable for up to 4 weeks if:
  - Stored at 2–8°C.
  - Aseptic techniques are used for administration.
  - VVM remains intact.
- Reconstituted vaccines (BCG, Measles, Yellow Fever):
- Must be discarded after 6 hours or at the end of the session.

Contraindications to Vaccination

- **Live vaccines contraindicated in**:
  - Immunocompromised individuals (HIV, malignancies).
  - Pregnant women (risk of teratogenicity).
  - Neurological disorders (avoid DPT in uncontrolled epilepsy).
- **Egg allergy**: Avoid Yellow Fever, Influenza, but alternative fibroblast-derived vaccines may be used.

37.12 Vaccination in Special Populations

37.12.1 Preterm Infant Immunization

- Immunization response similar to term infants.
- Start immunization at 2 months, irrespective of prematurity.
- OPV delayed until discharge (reduces nursery transmission risks).

37.12.2 Adolescent Immunization

- HPV vaccine for girls aged 10–13.
- Booster doses for waning childhood immunity (e.g., Tetanus).
- Catch-up vaccination for missed/incomplete schedules.

37.12.3 Pregnancy and Vaccination

- Live viral vaccines generally avoided due to potential fetal risks.
- Tdap recommended in the third trimester to protect against pertussis.

37.13 Conclusion

Immunization remains a cornerstone of preventive healthcare, reducing the infectious disease burden globally. Maintaining vaccine quality, storage protocols, and surveillance systems enhances safety and efficacy. Addressing vaccine hesitancy, logistical challenges, and misinformation remains crucial for improving immunization coverage. Future advancements, including next-generation vaccines, aim to strengthen global disease prevention efforts. This detailed narrative is tailored for a professional audience and integrates key immunization strategies, vaccine science, and best practices in public health. Let me know if you need further elaboration on any aspect!

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37.14 Practical work

37.14.1 Question

A 4-month-old baby is presented with fever, cough, and rhinorrhoea of 2 days duration. O/E: Active, healthy-looking child with occasional smiles; axillary temp 37.8 °C. The baby is treated for the common cold. Baby has no scar over the Left deltoid area and on enquiry has visited the immunization clinic two times since birth, but has misplaced the weighing card.

- Which vaccinations will the child require at that age?
- Which vaccinations are contraindicated?
- Which ones should the child receive before going home?
- When should the child be returned for follow-up vaccinations? And for which vaccines?
- What if the baby's mother is HIV-positive?
- What if there is a parental history of SCD?

37.14.2 Answers

The baby should have received several routine vaccinations at four months old according to Ghana's Expanded Programme on Immunisation (EPI). Based on the standard schedule, the following vaccines are typically required at this age:

Vaccinations Required at Four Months

- Oral Polio Vaccine (OPV) – Third dose
- Pentavalent Vaccine (DPT/HiB/HepB) – Third dose (protects against diphtheria, pertussis, tetanus, Haemophilus influenzae type B, and hepatitis B)
- Pneumococcal Conjugate Vaccine (PCV) – Third dose
- Rotavirus Vaccine – Second dose

Contraindicated Vaccines

- Live vaccines such as BCG (for tuberculosis) and Measles-Rubella (MR) may be contraindicated if the child has certain immunodeficiencies, such as HIV/AIDS, or other medical conditions. However, specific contraindications should be assessed by a healthcare provider.

Vaccines to Receive Before Going Home

- Since the baby has visited the immunization clinic only twice and has no visible BCG scar, verifying which vaccines have been missed is crucial. Before discharge, the baby should receive any missed doses of the routine vaccines, particularly BCG if it was not previously administered.

Follow-up Vaccinations and Schedule

The baby should return for the next scheduled vaccinations:

- **At 6 months** – Vitamin A supplementation
- **At 9 months** – Measles-Rubella (MR) and Yellow Fever vaccines
- **At 12 months** – Meningococcal vaccine (Men A) and second dose of Measles-Rubella (MR)

Considerations for Special Cases

- If the mother is HIV-positive: The baby may require additional monitoring and possible adjustments to the vaccination schedule. BCG may be contraindicated if the baby is symptomatic or severely immunocompromised.
- If there is a parental history of Sickle Cell Disease (SCD): The baby should be screened for sickle cell status. Additional precautions may be needed if diagnosed with SCD, including early pneumococcal and meningococcal vaccines to prevent infections.

38 Meningitis (bacterial)

38.1 Definition

Inflammation of the meninges due to bacterial infection. The onset of symptoms is classified as acute (symptoms evolving rapidly over 1-24hrs), sub-acute (1-7 days), and Chronic ($>$ 1 week). Infants, children, and young adults are most likely to suffer from bacterial meningitis.

38.2 Incidence/prevalence

An estimated 2.5 million cases of meningitis occur globally each year, with approximately 250,000 deaths.(PATH 2021) In 2023, information from LHIMS, Komfo Anokye Teaching Hospital, Kumasi indicated a rate of 1.5% or 15/1000 admissions through the Paediatric Emergency Unit (PEU) were diagnosed as meningitis. Most of the KATH cases were not confirmed.

38.3 Aetiology

Several different bacteria can cause meningitis. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* are the most frequent ones. N. meningitidis, causing meningococcal meningitis, has the potential to produce large epidemics. 12 serogroups of N. meningitidis have been identified, 6 of which (A, B, C, W, X and Y) can cause epidemics.(Organization 2021) Viral, fungi and Mycobacterium species can also cause meningitis. This write-up is limited to bacteria.

38.4 Pathogenesis

The bacterial gain access to the central nervous system through

i. Invasion of mucosal surface (respiratory tract) then, hematogenous to the brain;
ii. Spread from Para meningeal focus(otitis media, sinusitis); penetrating head trauma, and previous neurosurgical procedure.

Bacterial meningitis is distinguished by the introduction of bacteria into the cerebrospinal fluid (CSF) and the subsequent proliferation of bacteria in this compartment, leading to inflammation both within the CSF and in the brain tissue next to it. By production and/or release of virulence factors into and stimulating the formation of inflammatory cytokines within the central nervous system, meningeal pathogens increase the permeability of the blood-brain barrier, thus allowing protein and neutrophils to move into the subarachnoid space.(Hoffman and Weber 2009)

38.5 Signs and symptoms

Infants: Temperature instability, convulsions, meningeal irritation (stiff neck, positive Kernig's sign, Positive Brudzinski's sign), bulging fontanelles and increased head circumference are common and may be late signs. Signs are very non-specific. Examine for spinal or cranial abnormalities

Older children: Fever, headache, photophobia, Changes in mental status (Irritability, lethargy, coma, and confusion), and End organ dysfunction (Heart, Lung, Kidney, Liver). Meningeal irritation (neck stiffness, positive Kernig's sign), cranial nerve palsies, and purpuric rash – meningococcal meningitis.

38.6 Investigations

Lumbar puncture: White Blood Cells, Red Blood Cells, protein content, Glucose content (2/3 blood glucose), Culture and sensitivity, Serology (latex agglutination test), PCR

Table 38.1: Lumbar puncture findings in different meningitis

Item	Bacterial	Viral	Fungal	Tuberculous
Opening pressure	Elevated	Slightly elevated	Normal or high	Unusually high
Appearance	Turbid	clear	Turbid	Cob-web
Proteins	Very high	Normal	High	High
Glucose	Low	Normal	Low	Low
RBCs	Few	None	None	None
WBCs	>200	<200	<50	20-30
Differential	Polymorphonuclear cells	Monocytes	Monocytes	Monocytes

Blood: Glucose, culture and sensitivity

Imaging: (CT Scan/MRI) helps identify: brain abscesses, meningeal inflammation, infarction, haemorrhages, subdural effusion, focal infections (sinusitis)

38.7 Contraindications

Focal neurologic deficit or signs of increased intracranial pressure, deep coma, protracted seizures, cranial nerve palsy, pupillary dilatation, bleeding disorders, septic lesion at the site of LP.

38.8 Treatment

38.8.1 General and supportive measures

Close cardio-respiratory monitoring, frequent neurologic assessment, strict fluid balance, frequent urine specific gravity assessment, nil per os until neurologically stable, isolate until the organism is known, daily weighing, and frequent BP monitoring may be needed, monitor and treat for (hypoglycaemia, hyponatraemia, Acidosis, Septic shock, DIC, Seizures, Increased intracranial pressure)

38.8.2 Definitive treatment

Ceftriaxone is the drug of empiric choice beyond the neonatal period (cefotaxime is preferred in the first 2 weeks of life). Modify after culture and sensitivity results are available. Look out for focus if the response to antibiotics is sub-optimal. Steroids such as dexamethasone may be used depending on the organism isolated. Anticonvulsants (phenobarbitone, diazepam, and midazolam) and analgesics may also be required.

38.8.3 Prophylaxis

Close contacts especially for patients with Neisseria meningitidis meningitis will need post-exposure prophylaxis preferably within 48 hours. Options are ciprofloxacin or rifampicin.

38.8.4 Vaccines

Vaccines are available for use, especially during outbreaks

38.9 Complications

These include seizures, persistent focal seizures, neurological deficits, cerebral oedema, visual impairment, ataxia, hearing loss, hydrocephalus, cranial nerve palsy, mental retardation, severe behavioural problems, syndrome of the inappropriate release of antidiuretic hormone (SIADH), and vegetative state.

38.10 Prognosis

Even with timely, appropriate treatment, bacterial meningitis can be fatal in 5 to 20% of newborns and 5 to 15% of older infants and children.(Skar et al. 2024)

38.11 Differential diagnosis

Differential diagnoses include cerebral malaria, liver failure, brain abscess, encephalitis, brain tumour, and subarachnoid haemorrhage.

38.12 Sample questions

1. A neonate presented at 24 hours post-delivery with fever, floppiness, and poor feeding. These were your CSF chemistry report

Appearance	Proteins	Glucose	WBCs	Differentials
Turbid	High	low	<50	Monocytes

Which of the following diagnoses is most likely?

a. Bacterial
b. **Fungal**
c. Tuberculosis
d. Viral

This CSF characteristic is more consistent with the fungal cause of meningitis. There will be a need to investigate immunosuppression.

2. You suspect a 10-year-old presenting with focal seizures and febrile illness had meningitis. You were not able to do a Lumbar puncture. You started treatment with ceftriaxone. Three days into treatment, the child still had a fever (39.7°C) and focal seizures. What will be your best next step?

    a. Increase the ceftriaxone dose
    b. Modify antipyretic dose
    c. Immediate lumbar puncture
    d. **Imaging of the head**

    Imaging (CT scan /MRI) will be the best option to help identify the focus of infection especially abscesses.

Practice question

3. You worked as Director of Public Health in a rural facility. There was a sudden increase in the number of students admitted to your facility from a particular secondary school with meningitis. Enumerate the steps you will take to stop the outbreak.

39 Osteomyeliltis

39.1 Introduction

Osteomyelitis is an infection of the bone and bone marrow, most commonly caused by bacteria. In children, it is an important cause of morbidity, frequently presenting with fever, bone pain, and reduced limb use. Early diagnosis and prompt initiation of antimicrobial therapy are essential to prevent permanent complications such as growth disturbances, chronic osteomyelitis, limb deformities, and disability.

In Ghana and other parts of sub-Saharan Africa, osteomyelitis remains a relatively common paediatric condition due to a combination of factors, including high rates of **Staphylococcus aureus carriage**, delays in seeking care, limitations in imaging availability, malnutrition, and the burden of conditions such as sickle cell disease. Both acute and chronic osteomyelitis are frequently encountered in clinical practice, with chronic cases sometimes presenting late with draining sinuses or sequestration.

This chapter provides a comprehensive overview of the epidemiology, pathogenesis, clinical features, diagnosis, and management of osteomyelitis in children, with attention to resource-appropriate recommendations for Ghanaian settings.

39.2 Definitions

Osteomyelitis:
An infectious process involving the bone, including marrow, cortical bone, and periosteum.

Acute osteomyelitis:
Symptoms present for less than 2 weeks.

Subacute osteomyelitis:
Symptoms persist for 2–6 weeks, often with milder systemic signs. Brodie abscess is a classic form.

Chronic osteomyelitis:
Symptoms lasting 6 weeks, often with sequestrum formation, involucrum, or draining sinuses.

39.3 Epidemiology

- Most common in **children <5 years**, due to rich metaphyseal blood supply.
- Highest incidence in:
  - **Staphylococcus aureus** carriers
  - Children with **sickle cell disease** (especially Salmonella species)
  - Children with malnutrition or immunosuppression
  - Post-traumatic injuries and open fractures
  - Neonates, who may also have septic arthritis
- Seasonal peaks sometimes correspond with increases in skin infections and bacteraemia.

39.3.1 Local Context: Ghana

- S. aureus is the **leading cause**, with emerging reports of MRSA in teaching hospitals.
- Salmonella osteomyelitis is common in **sickle cell disease**, which has a high prevalence in Ghana (up to 2% of newborns).
- Late presentation is common due to:
  - Delayed referral from lower-level facilities
  - Use of herbal treatments
  - Limited access to early imaging (MRI rarely available outside regional/teaching hospitals)
  - Financial constraints.

39.4 Aetiology

39.4.1 Common Organisms

Staphylococcus aureus

- Most frequent causative organism.
- Can be MSSA or MRSA.

Streptococcus species

- Group A Streptococcus (GAS)

- Streptococcus pneumoniae

Gram-negative bacilli

- *Salmonella* spp (common in sickle cell disease)
- *Escherichia coli* (neonates)
- *Klebsiella* spp
- *Pseudomonas aeruginosa* (puncture wounds, burns)

Neonatal organisms

- GBS
- Enteric bacteria
- S. aureus

39.4.2 Routes of Infection

1. **Haematogenous spread** – most common in children.
2. **Contiguous spread** – from adjacent soft tissue infection.
3. **Direct inoculation** – trauma or surgery.

39.5 Pathophysiology

Children have a unique bone blood supply, especially in the **metaphysis of long bones**, predisposing them to haematogenous infection. Slow blood flow through metaphyseal vessels facilitates bacterial seeding. Infection leads to:

1. **Inflammatory response** → swelling within rigid bone → increased intramedullary pressure.
2. **Vascular compromise** → bone necrosis.
3. **Formation of sequestrum** (dead bone).
4. **Involucrum** formation (new bone surrounding necrosis).
5. Chronic draining sinuses may develop if untreated.

In neonates, transphyseal vessels allow infection to spread easily to the epiphysis and joint space, leading to **concomitant septic arthritis**.

39.6 Clinical Features

39.6.1 General Symptoms

- Fever (often high-grade)
- Irritability, poor feeding (infants)
- Malaise

39.6.2 Local Symptoms

- Localised bone pain (often severe)
- Swelling, warmth, and tenderness
- Refusal to bear weight / pseudoparalysis
- Reduced limb movement
- Overlying cellulitis

39.6.3 Common Sites in Children

- Long bones: femur, tibia, humerus
- Neonates: multiple bones may be affected
- Vertebral osteomyelitis occurs but is less common

39.6.4 Special Populations

Sickle cell disease:

- Salmonella species more likely
- Multifocal osteomyelitis possible
- Bone infarction can mimic osteomyelitis

Neonates:

- Subtle signs
- Often concomitant septic arthritis
- High risk of growth plate destruction

39.7 Differential Diagnosis

- Bone infarction (especially in SCD)
- Septic arthritis
- Cellulitis or deep soft tissue infection
- Trauma/fracture
- Malignancy (Ewing sarcoma, leukaemia)

- Langerhans cell histiocytosis

39.8 Investigations

39.8.1 Laboratory Tests

- **Full blood count:** leucocytosis may be present.
- **ESR and CRP:** usually elevated; useful for monitoring treatment response.
- **Blood cultures:** positive in 30–60% of cases.
- **Bone aspirate or biopsy:** gold standard for pathogen identification.
- **U&E and creatinine:** baseline before prolonged antibiotic therapy.

39.8.2 Imaging

39.8.2.1 Plain X-ray

- Often normal in early stages (<7 days).

- Later findings:
  - Periosteal elevation
  - Lytic lesions
  - Sequestrum formation

39.8.2.2 Ultrasound

- Useful in resource-limited settings.

- Detects:

- Subperiosteal collections
- Adjacent soft tissue abscess
- Joint effusions (septic arthritis)

39.8.2.3 MRI (if available)

- Most sensitive and specific modality.
- Detects early marrow oedema.
- Identifies complications (abscess, physis involvement).

39.8.2.4 CT Scan

- Helpful for detecting sequestrum in chronic osteomyelitis.

39.8.3 Ghana-Specific Considerations

- MRI is often unavailable outside tertiary centres.
- Ultrasound is more readily available and should be used early.
- Plain X-rays may be delayed in very rural settings.

39.9 Diagnosis

Diagnosis is based on:

1. Clinical features (fever, severe localized bone pain)
2. Elevated inflammatory markers
3. Blood cultures
4. Imaging findings

In resource-limited settings, **clinical diagnosis + raised ESR/CRP** is often sufficient to begin treatment.

39.10 Management

Management goals include eradication of infection, preventing complications, and preserving limb function.

39.10.1 Initial Steps

- Assess for sepsis; stabilize ABCs.
- Begin **empiric IV antibiotics immediately** after obtaining cultures.
- Provide adequate analgesia.
- Immobilise affected limb with splinting.

39.10.2 Antibiotic Therapy

39.10.2.1 Empiric Choices

Standard acute osteomyelitis

- **Cloxacillin IV** (or flucloxacillin)
- If MRSA suspected: **Vancomycin** or **Linezolid**

Sickle cell disease

- Add coverage for Salmonella:
  - **Ceftriaxone**
  - OR **Cefotaxime**

Neonates

- **Cloxacillin + Gentamicin**
- Consider cefotaxime for Gram-negative coverage.

39.10.2.2 Directed Therapy

Adjust based on culture and sensitivity results.

39.10.2.3 Duration

- Total of **4–6 weeks** of antibiotics.
- Typically IV for 1–2 weeks → switch to oral once improving.

39.11 Surgical Management

Indications:

- Lack of response to antibiotics after 48–72 hours
- Subperiosteal abscess
- Sequestrum (chronic cases)
- Draining sinus tract
- Joint involvement requiring drainage

Procedures:

- Incision and drainage
- Debridement
- Sequestrectomy
- Placement of antibiotic beads (where available)

39.11.1 Supportive Management

- Adequate nutrition
- Analgesia
- Physiotherapy after acute phase
- Monitoring ESR/CRP weekly

39.12 Chronic Osteomyelitis

Chronic cases present with:

- Draining sinuses
- Sequestrum/involucrum
- Persistent pain

Management requires:

- Extended antibiotics (6–12 weeks)
- Surgical debridement and sequestrectomy
- Reconstruction of bone defects (rarely available outside tertiary centres)

Challenges in Ghana include:

- Late presentation
- Recurrent infections
- Antibiotic resistance
- Limited access to orthopaedic surgery in district facilities

39.13 Complications

- Chronic osteomyelitis
- Pathological fractures
- Growth plate damage → limb length discrepancies or angular deformities
- Septic arthritis
- Sinus tract carcinoma (very rare; seen in long-standing disease)
- Sepsis

39.14 Prognosis

- Good if diagnosis is early and antibiotics started promptly.
- Poorer outcomes associated with:
  - Delayed presentation
  - Chronic osteomyelitis
  - Sickle cell disease
  - Neonatal infection
  - Lack of surgical intervention when indicated

39.15 Special Considerations in Ghana

- **Delayed care-seeking** is common; many patients first go to herbal centres.
- **Radiology access** is limited in rural districts; reliance on ultrasound is pragmatic.
- **Referral systems** sometimes lead to prolonged pre-hospital delays.
- **Sickle cell population** requires targeted awareness due to increased risk.
- **Antibiotic resistance patterns** vary; MRSA prevalence should be monitored.

Strengthening primary care recognition and prompt referral can significantly improve outcomes.

39.16 Conclusion

Osteomyelitis remains a significant cause of morbidity in Ghanaian children. Early recognition, appropriate antimicrobial therapy, and surgical intervention when necessary can prevent long-term disability. Resource limitations require clinicians to be pragmatic while adhering to fundamental principles of management. A high index of suspicion is crucial, especially in infants, children with sickle cell disease, and those presenting with persistent limb pain and fever.

39.17 Further Reading

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40 Septic Arthritis

40.1 Introduction

Septic arthritis is an acute infection of the joint space, usually caused by bacteria, resulting in inflammation, joint destruction, and potential long-term disability if not promptly treated. It is a paediatric emergency, with younger children—especially infants and toddlers—being at the highest risk due to their unique vascular anatomy and developing immune systems.

Septic arthritis may occur via haematogenous spread (most common), direct inoculation from trauma, or contiguous extension from adjacent infections such as osteomyelitis. Quick recognition and early treatment are crucial to prevent irreversible cartilage destruction.

40.2 Epidemiology

Septic arthritis occurs worldwide but is especially important in low- and middle-income countries (LMICs) where delays in diagnosis and limited access to advanced diagnostics may worsen outcomes. In Ghana and West Africa, it remains a significant cause of morbidity among children due to late presentation, limited imaging availability in some settings, and high burden of invasive bacterial diseases.

Peak incidence:

- Neonates and infants
- Children <5 years
- Teenagers with high-risk behaviours or sports-related injuries

40.3 Aetiology

40.3.1 Common Pathogens

The causative organisms vary by age group:

- **Neonates**

  - *Staphylococcus aureus*
  - Group B Streptococcus (*Streptococcus agalactiae*)
  - Gram-negative bacilli (e.g., *E. coli*, *Klebsiella*)
- **Infants and Young Children**
  - *Staphylococcus aureus* (most common overall)
  - *Streptococcus pyogenes*
  - *Streptococcus pneumoniae*
  - *Kingella kingae* (increasingly recognised, but less frequently detected in West Africa due to limited PCR use)
- **Adolescents**
  - *Staphylococcus aureus*
  - *Neisseria gonorrhoeae* (sexually active teenagers)

40.3.2 Risk Factors

- Haematogenous spread from distant infection (URTI, skin infection, pneumonia)
- Immunosuppression (malnutrition, HIV, long-term steroids)
- Sickle cell disease (may predispose to *Salmonella*)
- Trauma or intra-articular injections
- Neonatal risk factors (prematurity, invasive procedures)

40.4 Pathophysiology

Septic arthritis begins when bacteria seed the synovial membrane. The joint is particularly vulnerable because:

- Synovial tissue lacks a basement membrane → bacteria easily invade the joint space.
- Rapid inflammatory response leads to:
  - Purulent effusion
  - Increased intra-articular pressure → impaired cartilage perfusion
  - Chondrocyte death within hours to days

In young children, blood vessels penetrate the metaphysis and epiphysis, facilitating spread between joint and adjacent bone, hence frequent coexistence of osteomyelitis.

40.5 Clinical Features

Septic arthritis typically presents acutely, with symptoms varying by age.

40.5.1 General Symptoms

- Acute onset fever (often >38.5°C)
- Severe joint pain (non–weight-bearing is a strong predictor)
- Swelling, warmth, and erythema over the joint
- Limited range of motion (PROM > AROM due to pain)
- Irritability in infants

40.5.2 Joint-specific Findings

- **Hip and knee** are the most commonly affected joints.
- **Infants** may present subtly:
  - Pseudoparalysis (not moving limb)
  - Feeding difficulties
  - Fever may be absent
- **Shoulder involvement** seen in neonates and may be associated with obstetric trauma or sepsis.

40.5.3 Red Flags (Emergency Indicators)

- Child refusing to bear weight
- High-grade fever + acute joint swelling
- Severe pain with any movement
- Toxic appearance

40.6 Differential Diagnosis

- Transient synovitis
- Osteomyelitis
- Juvenile idiopathic arthritis
- Trauma/haemarthrosis
- Sickle cell bone crisis
- Reactive arthritis
- Lyme arthritis (not endemic in West Africa)

40.7 Investigations

Diagnosis is clinical, supported by laboratory and imaging studies. Urgent arthrocentesis is often necessary.

40.7.1 Laboratory Tests

- Full blood count (elevated WBC)
- ESR, CRP markedly elevated (CRP >20 mg/L supports diagnosis)
- Blood cultures (positive in 30–50%)

40.7.2 Synovial Fluid Analysis (gold standard)

Obtain via urgent arthrocentesis **before antibiotics**, if possible.

- Gross appearance: turbid, purulent
- WBC: usually >50,000/mm³, with >75% neutrophils
- Gram stain and culture
- PCR for *Kingella* where available (rare in West Africa)

40.7.3 Imaging

- **Ultrasound**: detect effusion, especially in the hip
- **X-ray**: rule out trauma; late changes only
- **MRI**: detects adjacent osteomyelitis when accessible

40.8 Management

Septic arthritis is a **medical and surgical emergency** requiring early antibiotics and joint drainage.

40.8.1 1. Empiric Antibiotic Therapy

Initiate immediately after cultures are taken.

- **Neonates**
  - IV cloxacillin + gentamicin

  - Consider cefotaxime if gram-negative concern

- **Infants/children**
  - IV cloxacillin (or cefazolin)
  - Add ceftriaxone/cefotaxime if GNB suspected

- **MRSA-prevalent areas**
  - Use vancomycin or clindamycin (if local susceptibility permits)

- **Sickle cell disease**
  - Cover *Salmonella* (ceftriaxone)

Duration:
- IV for 1–2 weeks → Oral to complete 3–4 weeks, depending on organism and clinical response.

40.8.2 2. Joint Drainage

Drainage reduces intra-articular pressure and prevents cartilage necrosis.

Options:

- Needle aspiration (often adequate for superficial joints)
- Arthroscopic drainage
- Open surgical drainage (hip, shoulder, delayed cases)

40.8.3 3. Supportive Care

- Analgesia
- Immobilization initially, then early mobilization after 48–72 hours of improvement
- Treatment of underlying sepsis

40.8.4 4. Monitor Response

- Clinical improvement (fever resolution, reduced pain)
- Trend CRP every 48–72 hours
- Repeat ultrasound if effusion persists

40.9 Complications

Delayed or inadequate treatment may lead to:

- Joint destruction
- Growth plate damage → limb length discrepancy
- Pathological dislocations (especially hip)
- Chronic osteomyelitis
- Persistent functional disability

Early detection significantly improves outcomes.

40.10 Prognosis

With prompt diagnosis and appropriate therapy, most children recover fully. However, hip involvement, neonates, and delayed presentation (>4 days) are associated with worse outcomes.

40.11 Summary

Septic arthritis is a paediatric emergency requiring high clinical suspicion and prompt treatment. Haematogenous spread is the primary route, with *Staphylococcus aureus* the most common pathogen across all age groups. Early joint drainage and timely antibiotic therapy are essential to prevent long-term morbidity. Children in Ghana and West Africa may face unique challenges due to late presentation and limited imaging resources, making clinical acumen especially important.

40.12 Further Reading

- Nelson Textbook of Pediatrics – Chapter on Septic Arthritis
- WHO Guidelines on Management of Childhood Infections
- British Society for Paediatric and Adolescent Rheumatology (BSPAR) Guidelines
- Paediatric Infectious Diseases Society (PIDS) recommendations

Part VI

Oncology

41 General Principles

41.1 Introduction

Paediatric oncology is the branch of medicine that deals with the diagnosis, treatment, and long-term follow-up of cancers in children and adolescents. Although cancer is less common in children compared to adults, it remains a significant cause of morbidity and mortality worldwide. In many low- and middle-income countries, including those in sub-Saharan Africa, paediatric cancers are increasingly recognised due to improved awareness and diagnostic facilities.

Understanding the general principles of paediatric oncology is essential for medical students, as it forms the foundation for appreciating the biology, clinical behaviour, and management of childhood cancers.

41.2 Epidemiology of Childhood Cancers

- Childhood cancers account for about **1–4% of all cancers worldwide**.
- The incidence is approximately **100–150 cases per million children per year**.
- In high-income countries, survival rates exceed **80%**, but in low- and middle-income regions, survival may be **20–40%** due to late presentation, limited resources, and treatment abandonment.
- The most common paediatric cancers include:
  - **Leukaemias** (especially acute lymphoblastic leukaemia).
  - **Brain tumours** (medulloblastoma, astrocytoma).
  - **Lymphomas** (Burkitt's lymphoma, Hodgkin lymphoma).
  - **Solid tumours** (Wilms' tumour, neuroblastoma, retinoblastoma).

41.3 Biology of Childhood Cancers

Unlike adult cancers, childhood malignancies:
- Often arise from **embryonal tissues** or primitive cells rather than epithelial tissues.
- Show **fewer environmental associations** (e.g., smoking, alcohol, carcinogens).
- Are more commonly associated with **genetic predispositions** (e.g., RB1 mutations in retinoblastoma, TP53 in Li-Fraumeni syndrome).
- Tend to have **rapid growth rates**, making them highly responsive to chemotherapy and radiotherapy.

41.4 Clinical Presentation

Children with cancer may present with vague, non-specific symptoms that mimic common infections. High suspicion is necessary.

41.4.1 General warning signs of cancer in children (commonly remembered by the acronym CHILD CANCER):

- **C**ontinued, unexplained weight loss.
- **H**eadaches with early morning vomiting.
- **I**ncreased swelling or pain in bones/joints.
- **L**ump or mass in abdomen, chest, or neck.
- **D**evelopment of excessive bruising, bleeding, or rash.
- **C**onstant infections.
- **A** whitish glow in the eye (leukocoria).
- **N**eurological symptoms (seizures, persistent dizziness).
- **C**hanges in vision.
- **E**nlarged lymph nodes or persistent fever.
- **R**ecurrent unexplained fevers.

41.5 Diagnosis and Staging

Diagnosis of childhood cancer requires a **multidisciplinary approach**.

1. **Clinical evaluation** – thorough history and examination, with attention to family history of cancers or syndromes.

2. **Laboratory tests** – complete blood count, peripheral smear, biochemical markers (e.g., LDH, uric acid).

3. **Imaging** – X-rays, ultrasound, CT, MRI, and PET scans depending on tumour location.

4. **Histopathology** – biopsy for tissue diagnosis (except for retinoblastoma where clinical diagnosis is usually made).

5. **Molecular and cytogenetic studies** – identification of chromosomal translocations (e.g., t(8;14) in Burkitt's lymphoma, t(12;21) in ALL).

6. **Staging** – determines the extent of disease, using systems like:
   - Ann Arbor staging for lymphomas.
   - INSS (International Neuroblastoma Staging System).
   - TNM classification for some solid tumours.

41.6 Principles of Treatment

Treatment is multidisciplinary, involving oncologists, surgeons, radiation oncologists, pathologists, radiologists, nurses, and psychosocial support teams.

41.6.1 1. Surgery

- Plays a key role in diagnosis (biopsy) and treatment (resection of tumour).
- Examples: nephrectomy in Wilms' tumour, enucleation in advanced retinoblastoma.

41.6.2 2. Chemotherapy

- Mainstay of treatment for most paediatric cancers.
- Uses cytotoxic drugs targeting rapidly dividing cells.
- Often given in **cycles** to allow normal tissues to recover.
- Commonly used agents: vincristine, doxorubicin, cyclophosphamide, methotrexate, cytarabine.
- Side effects: bone marrow suppression, alopecia, nausea, infections.

41.6.3 3. Radiotherapy

- Used in selected cancers (e.g., brain tumours, Hodgkin lymphoma).
- Careful dosing required to avoid long-term growth and developmental complications.
- Increasingly replaced by more precise modalities such as proton therapy where available.

41.6.4 4. Stem Cell Transplantation

- Indicated in high-risk or relapsed cases (e.g., relapsed leukaemia).
- May involve autologous or allogeneic transplantation.

41.6.5 5. Targeted Therapy and Immunotherapy

- Monoclonal antibodies (e.g., rituximab in B-cell lymphomas).
- Tyrosine kinase inhibitors (e.g., imatinib in Philadelphia chromosome-positive ALL).
- CAR-T cell therapy emerging in refractory cases.

41.7 Supportive Care

Equally important as definitive treatment, supportive care ensures the child tolerates therapy.

- **Infection prevention and treatment**: use of antibiotics, antifungals, and sometimes prophylaxis.
- **Blood product support**: transfusions for anaemia and thrombocytopenia.
- **Nutritional support**: maintaining adequate nutrition to aid recovery.
- **Pain management**: opioids and adjuvants as required.
- **Psychological support**: counselling for child and family.
- **Management of treatment complications**: tumour lysis syndrome, neutropenic sepsis.

41.8 Emergency Presentations in Paediatric Oncology

Certain cancer-related emergencies require immediate recognition and intervention:
- **Febrile neutropenia** – life-threatening infection during chemotherapy-induced immunosuppression.
- **Tumour lysis syndrome** – rapid cell breakdown causing hyperkalaemia, hyperuricaemia, renal failure.
- **Mediastinal mass** – airway compression in lymphomas or leukaemia.
- **Spinal cord compression** – neuroblastoma or vertebral metastases.
- **Severe anaemia or bleeding** – marrow infiltration by leukaemia.

41.9 Long-Term Follow-Up and Survivorship

With improved survival, focus has shifted to long-term outcomes:
- **Late effects of therapy**:
- Growth retardation from cranial irradiation.
- Cardiomyopathy from anthracyclines.
- Infertility from alkylating agents.
- Secondary malignancies.
- **Rehabilitation and reintegration**: ensuring schooling and social development.
- **Psychological support**: addressing anxiety, depression, and stigma.

41.10 Prevention and Early Detection

- Unlike adult cancers, **primary prevention is limited** in childhood cancers.
- However, measures include:
  - Avoiding unnecessary exposure to ionising radiation in pregnancy and childhood.
  - Vaccination against viruses that can indirectly influence cancer risk (e.g., HBV to reduce hepatocellular carcinoma).
  - Screening in high-risk families with known cancer syndromes (e.g., RB1 mutation carriers).
- Public health education on early signs of cancer is vital in improving outcomes in low-resource settings.

41.11 Prognosis

- Prognosis depends on:
  - Type of cancer.
  - Stage at diagnosis.
  - Response to therapy.
  - Availability of supportive care.
- Survival is excellent in conditions like Hodgkin lymphoma (>90%) but poorer in advanced neuroblastoma or late-presenting retinoblastoma.

41.12 Conclusion

Paediatric oncology integrates principles of cell biology, clinical medicine, and multidisciplinary care. While outcomes have improved remarkably in high-resource settings, challenges remain in low- and middle-income countries, where late presentation and limited infrastructure hinder survival. For medical students, an appreciation of the **unique biology, presentation, and management** of childhood cancers is essential in recognising cases early, guiding families, and contributing to improved outcomes in resource-constrained environments.

42 Oncological Emergencies

42.1 Introduction

Oncological emergencies are acute, potentially life-threatening conditions that affect patients with cancer, either due to the malignancy itself or as complications arising from its treatment. Early recognition and prompt intervention are crucial in preventing morbidity and mortality. Understanding these emergencies is essential for all healthcare professionals, particularly in resource-limited settings like Ghana, where delays in cancer diagnosis and treatment are prevalent. Oncological emergencies are generally classified into three categories:

1. **Metabolic Emergencies**
2. **Hematological Emergencies**
3. **Structural/Mechanical Emergencies**

42.2 Metabolic Emergencies

42.2.1 Tumor Lysis Syndrome (TLS)

Definition: A life-threatening condition that occurs when massive tumor cell lysis releases intracellular contents (potassium, phosphate, uric acid) into the bloodstream, leading to acute kidney injury and cardiac arrhythmias.

Common Causes:

- High-grade lymphomas (especially Burkitt lymphoma)
- Acute leukemias (e.g., ALL)
- Solid tumors with high tumor burden after chemotherapy

Clinical Features:

- Nausea and vomiting
- Lethargy
- Muscle cramps
- Seizures
- Oliguria or anuria

- Arrhythmias

Diagnostic Criteria (Cairo-Bishop):

Laboratory TLS involves 2 of the following:

- Uric acid > 476 mol/L
- Potassium > 6.0 mmol/L
- Phosphate > 1.45 mmol/L
- Calcium < 1.75 mmol/L

Management:

- Aggressive IV hydratio
- Allopurinol or rasburicase (rasburicase preferred)
- Correction of electrolyte imbalances
- Dialysis for refractory cases

42.2.2 Hypercalcemia of Malignancy

Definition: Elevated serum calcium level (usually >2.6 mmol/L) due to malignancy.

Common Causes:

- Breast cancer
- Multiple myeloma
- Lung cancer
- Renal cell carcinoma
- Parathyroid hormone-related protein (PTHrP) production

Clinical Features:

- Nausea, vomiting
- Polyuria, polydipsia
- Constipation
- Confusion, coma
- Shortened QT interval

Management:

- IV hydration with normal saline
- Bisphosphonates (e.g., zoledronic acid)
- Calcitonin for rapid reduction
- Dialysis in severe cases

42.2.3 Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Definition: Excessive release of antidiuretic hormone leads to water retention and hyponatremia.

Common Causes:

- Small cell lung carcinoma
- CNS tumors

Clinical Features:

- Headache
- Confusion
- Seizures
- Coma

Management:

- Fluid restriction
- Hypertonic saline (3%) in severe hyponatremia
- Demeclocycline or vasopressin receptor antagonists in chronic cases

42.3 Hematological Emergencies

42.3.1 Febrile Neutropenia

Definition: Fever (>38°C) with absolute neutrophil count (ANC) $< 0.5 \times 10$ /L in a cancer patient.

Causes:

- Chemotherapy-induced bone marrow suppression

Clinical Features:

- Fever (often the only sign)
- Signs of infection may be subtle

Management:

- Broad-spectrum antibiotics within 1 hour (e.g., cefepime, piperacillin-tazobactam)
- Risk stratification (MASCC score)
- G-CSF in selected cases
- Isolate and monitor closely

42.3.2 Disseminated Intravascular Coagulation (DIC)

Definition: Widespread activation of the coagulation system leads to the consumption of clotting factors and platelets, resulting in bleeding and thrombosis.

Common Causes:

- Acute promyelocytic leukemia (APL)
- Metastatic cancers

Clinical Features:

- Bleeding (petechiae, ecchymosis, mucosal bleeding)
- Thrombosis
- Organ dysfunction

Laboratory Findings:

- Prolonged PT, aPTT
- Low fibrinogen
- Elevated D-dimer
- Thrombocytopenia

Management:

- Treat underlying cause (e.g., ATRA for APL)
- Transfusions (platelets, FFP)
- Heparin in cases with thrombosis

42.3.3 Hyperviscosity Syndrome

Definition: Increased blood viscosity due to elevated cellular or protein components.

Common Causes:

- Waldenström's macroglobulinemia (IgM)
- Multiple myeloma
- Leukemia with very high WBC

Clinical Features:

- Visual disturbances
- Headache
- Mucosal bleeding
- Confusion
- Heart failure

Management:

- Plasmapheresis
- Hydration
- Treat underlying cancer

42.4 Structural/Mechanical Emergencies

42.4.1 Superior Vena Cava (SVC) Syndrome

Definition:

Obstruction of blood flow through the superior vena cava, commonly due to external compression by tumors.

Common Causes:

- Small cell lung cancer
- Non-Hodgkin lymphoma
- Metastatic mediastinal tumors

Clinical Features:

- Facial and upper limb swelling
- Dyspnea
- Distended neck veins
- Cyanosis
- Cough and hoarseness

Diagnosis:

- Chest X-ray: mediastinal widening
- CT scan: to confirm compression
- Biopsy of mass (if unknown etiology)

Management:

- Elevate the head
- Steroids to reduce edema
- Radiotherapy or chemotherapy, depending on etiology
- Stenting in severe cases

42.4.2 Spinal Cord Compression

Definition:

Compression of the spinal cord due to a tumor, leading to neurological deficits.

Common Causes:

- Breast, prostate, and lung cancers
- Lymphomas
- Myeloma

Clinical Features:

- Back pain (worsened by lying down)
- Weakness in limbs
- Sensory loss
- Bladder/bowel incontinence

Diagnosis:

- MRI spine (preferred)
- Neurological exam

Management:

- High-dose corticosteroids (e.g., dexamethasone)
- Emergency radiotherapy or surgery
- Rehabilitation

42.4.3 Pericardial Tamponade

Definition:

Accumulation of fluid in the pericardial sac impairs cardiac output.

Common Causes:

- Lung and breast cancers
- Lymphomas
- Metastatic cancers

Clinical Features:

- Dyspnea
- Chest discomfort
- Hypotension

- Elevated JVP
- Muffled heart sounds (Beck's triad)

Diagnosis:

- Echocardiography: diagnostic
- ECG: low-voltage QRS or electrical alternans

Management:

- Urgent pericardiocentesis
- Fluid resuscitation
- Treat underlying malignancy

42.4.4 Intestinal Obstruction

Definition: Partial or complete blockage of the bowel lumen.

Common Causes:

- Colorectal cancer
- Ovarian cancer
- Gastric cance
- Peritoneal metastases

Clinical Features:

- Abdominal distension
- Vomiting
- Constipation
- Colicky abdominal pain

Diagnosis:

- Abdominal X-ray or CT scan

Management:

- Nasogastric decompression
- IV fluids and electrolytes
- Surgery if obstruction is complete or complications arise
- Stenting in selected cases

42.5 Increased Intracranial Pressure (ICP)

Causes:

- Brain metastases (lung, breast, melanoma)
- Primary CNS tumors
- Leptomeningeal disease

Clinical Features:

- Headache
- Vomiting (projectile)
- Seizures
- Altered mental status
- Papilledema

Diagnosis:

- Brain imaging (CT or MRI)

Management:

- Corticosteroids (dexamethasone)
- Mannitol for acute relief
- Neurosurgical consultation
- Radiotherapy/chemotherapy, depending on the cause

42.6 Approach to the Patient with an Oncological Emergency

1. ABCDE Approach

- **Airway:** Ensure patency, especially in patients with superior vena cava syndrome or airway tumors.
- **Breathing:** Provide oxygen if hypoxic.
- **Circulation:** Monitor for signs of shock (e.g., tamponade, disseminated intravascular coagulation).
- **Disability:** Assess for neurological compromise (e.g., spinal cord compression, raised ICP).
- **Exposure:** Full examination to identify other signs (e.g., petechiae, masses).

2. Laboratory and Imaging

- CBC, U&E, calcium, phosphate, uric acid
- Coagulation profile

- ECG and echocardiography
- CT/MRI depending on clinical suspicion

3. Specialist Referral

- Oncology, surgery, radiotherapy, hematology, or palliative care, depending on diagnosis.

Challenges in the Ghanaian Setting

- Limited access to imaging (CT/MRI)
- Delays in diagnosis and referral
- Shortage of oncologists and hematologists
- Limited availability of drugs (e.g., rasburicase, bisphosphonates)
- Inadequate supportive care facilities (ICU, dialysis)

Summary Table: Common Oncological Emergencies

Emergency	**Main Feature**	**Key Management**
Tumor Lysis Syndrome	Electrolyte disturbances, renal failure	Hydration, rasburicase
Hypercalcemia	Confusion, constipation	Hydration, bisphosphonate
SIAD	Hyponatremia, confusion	Fluid restriction, hypertonic saline
Febrile Neutropenia	Fever in neutropenia	Broad-spectrum antibiotics
DIC	Bleeding, low platelets	Treat the cause, transfusion
SVC Syndrome	Facial swelling, JVP	Steroids, radiotherapy
Spinal Cord Compression	Back pain, limb weakness	Steroids, MRI, radiotherapy
Tamponade	Hypotension, JVP	Pericardiocentesis
Bowel Obstruction	Abdominal pain, vomiting	NG tube, fluids, and surgery
Increased ICP	Headache, vomiting	Steroids, mannitol, imaging

Conclusion

Oncological emergencies require prompt identification and urgent management to prevent irreversible complications or death. In Ghana, with rising cancer incidence and limited resources, medical students and junior doctors must be adept at recognizing early signs and initiating life-saving interventions. Close collaboration with oncology, radiology, and surgical teams is essential for optimal outcomes.

43 Leukaemia

Leukaemia is the most common childhood malignancy, representing about one-third of all cancers diagnosed in children. It is a malignant disorder of the blood and bone marrow characterised by uncontrolled proliferation of abnormal white blood cells. These immature cells crowd the marrow, impairing the production of normal blood cells and leading to anaemia, thrombocytopenia, and neutropenia. For medical students, understanding leukaemia requires an integrated view of its epidemiology, aetiology, pathophysiology, clinical presentation, diagnosis, treatment, and outcomes.

43.1 Introduction

Leukaemia in children is a heterogeneous group of disorders arising from the malignant transformation of haematopoietic precursor cells. It is broadly divided into **acute lymphoblastic leukaemia (ALL)**, the most common type, and **acute myeloid leukaemia (AML)**. Chronic leukaemias are rare in childhood. The disease disrupts normal bone marrow function and causes systemic manifestations due to infiltration of organs by leukaemic cells.

43.2 Incidence and Prevalence

- Childhood leukaemia accounts for approximately **25–35% of all paediatric cancers**.
- The global incidence is about **3–4 per 100,000 children per year**.
- ALL is more common than AML, with a peak incidence between ages **2 and 5 years**.
- There is a slight male predominance and variation across ethnicities, with higher rates in high-income countries.
- Improvements in treatment have markedly increased survival, with 5-year survival rates for ALL exceeding **80%** in developed settings.

43.3 Aetiology

The exact cause of leukaemia remains unclear, but multiple interacting factors have been implicated:

- **Genetic predisposition**:
  - Children with syndromes such as Down syndrome, Li-Fraumeni syndrome, and Fanconi anaemia are at higher risk.
- **Chromosomal abnormalities**: Translocations such as *t(12;21)* in ALL or *t(8;21)* in AML are common.
- **Environmental factors**: Ionising radiation, certain chemotherapeutic agents, and exposure to benzene.
- **Infections and immune dysregulation**: Delayed immune development and abnormal immune responses to infections have been proposed.
- **Familial risk**: Having a sibling with leukaemia increases the risk modestly.

43.4 Pathophysiology

Leukaemia results from genetic mutations in haematopoietic stem or progenitor cells leading to:

1. **Uncontrolled proliferation** of abnormal blasts.
2. **Failure of differentiation**, with accumulation of immature cells.
3. **Bone marrow failure**, causing:
   - Anaemia → fatigue, pallor.
   - Neutropenia → infections.
   - Thrombocytopenia → bleeding.
4. **Tissue infiltration** by leukaemic cells:
   - Hepatosplenomegaly.
   - Lymphadenopathy.
   - CNS involvement (headache, vomiting, cranial nerve palsies).
   - Bone pain from marrow expansion.

43.5 Signs and Symptoms

Children typically present with non-specific symptoms, making early recognition challenging.

- **General symptoms**: Fatigue, fever, anorexia, weight loss.
- **Bone marrow failure manifestations**:
  - Pallor, tachycardia, and lethargy from anaemia.
  - Easy bruising, petechiae, and mucosal bleeding from thrombocytopenia.
  - Recurrent infections due to neutropenia.

- **Organ infiltration**:
  - Lymphadenopathy, hepatomegaly, splenomegaly.
  - Bone or joint pain, limp.
  - CNS signs: vomiting, seizures, headaches.
  - Testicular enlargement (especially in ALL).

43.6 Differential Diagnosis

Conditions that mimic leukaemia include:

- **Aplastic anaemia**.
- **Infectious causes**: EBV, HIV, tuberculosis.
- **Other malignancies**: Lymphomas, neuroblastoma.
- **Rheumatological disorders**: Juvenile idiopathic arthritis.
- **Storage disorders** with hepatosplenomegaly.

43.7 Investigations

Workup includes both laboratory and imaging studies:

- **Initial tests**:
  - Full blood count (FBC) often shows anaemia, thrombocytopenia, leukocytosis or leukopenia.
  - Blood film reveals circulating blasts.
- **Confirmatory tests**:
  - Bone marrow aspiration and biopsy showing >25% blasts.
  - Flow cytometry for immunophenotyping (B-cell vs T-cell ALL, AML subtypes).
- **Cytogenetics and molecular studies**: Prognostic significance (e.g., *t(9;22)* Philadelphia chromosome).
- **Additional workup**:
  - Lumbar puncture for CNS involvement.
  - Chest X-ray to check for mediastinal mass.
  - Biochemistry: uric acid, LDH, renal and liver function.

43.8 Treatment

Management of leukaemia is complex and requires a multidisciplinary team. It can be categorised into stages:

43.8.1 Emergency Management (at presentation)

- Stabilisation: Manage anaemia, thrombocytopenia, and infections.
- Blood product support: Packed RBCs, platelets.
- Treatment of tumour lysis syndrome: Hydration, allopurinol or rasburicase.
- Empirical antibiotics for febrile neutropenia.

43.8.2 Ongoing Management (definitive therapy)

- **Chemotherapy** is the backbone of treatment:
  - Induction → achieve remission.
  - Consolidation/intensification → eradicate residual disease.
  - Maintenance → prevent relapse.
- **CNS prophylaxis** with intrathecal methotrexate.
- AML requires more intensive regimens.
- Targeted therapies (e.g., tyrosine kinase inhibitors for BCR-ABL positive ALL).

43.8.3 3. Preparation for Discharge

- Education of caregivers about infection prevention, medication adherence, and follow-up.
- Arrangements for outpatient chemotherapy and monitoring.
- Psychosocial support for the child and family.

43.8.4 4. Long-Term Management

- Monitoring for relapse with clinical exam and minimal residual disease testing.
- Managing late effects of chemotherapy: growth retardation, infertility, cardiotoxicity.
- Vaccinations and infection prophylaxis.
- Consideration of stem cell transplant in high-risk or relapsed cases.

43.9 Complications

- **Early**: Tumour lysis syndrome, febrile neutropenia, bleeding, sepsis.
- **During therapy**: Chemotherapy toxicity (mucositis, hepatotoxicity, cardiotoxicity).
- **Late**: Relapse, secondary malignancies, growth and endocrine abnormalities, learning difficulties.

43.10 Prevention

- Currently, there are no definitive preventive strategies for most cases.
- Avoidance of unnecessary radiation and known chemical carcinogens is recommended.
- Genetic counselling for families with hereditary cancer syndromes.

43.11 Prognosis

- Prognosis depends on age, initial white cell count, cytogenetic abnormalities, and response to therapy.
- **ALL**: 5-year survival >80% in developed countries, lower in resource-limited settings.
- **AML**: Lower survival (~60%), requires more intensive therapy.
- Relapse remains a major challenge, with outcomes poorer after recurrence.

43.12 Conclusion

Childhood leukaemia, though the most common paediatric cancer, is a highly treatable condition with modern chemotherapy protocols. A good understanding of its presentation, investigations, and treatment approach is essential for practitioners, particularly in Ghana, where delayed diagnosis and limited resources pose challenges. With early recognition, appropriate supportive care, and treatment adherence, survival rates continue to improve globally.

44 Lymphoma

Lymphomas are malignant neoplasms arising from the lymphoid tissues and are the **third most common childhood cancer** after leukaemia and brain tumours. They account for approximately 10–15% of childhood malignancies. Lymphomas are broadly classified into **Hodgkin lymphoma (HL)** and **non-Hodgkin lymphoma (NHL)**, with the latter being more frequent in children. Among NHL subtypes, **Burkitt's lymphoma** is particularly common in tropical Africa, including Ghana, where it is one of the leading childhood cancers.

Understanding the epidemiology, aetiology, pathophysiology, clinical features, and treatment of childhood lymphoma is vital for medical students, as early diagnosis and timely intervention significantly improve outcomes.

44.1 Introduction

Lymphoma is a malignancy of the lymphoid system, originating from either **B lymphocytes** or **T lymphocytes** at various stages of differentiation. In children, the disease behaves more aggressively compared to adult lymphomas, but it is also more curable with modern treatment protocols.

- **Hodgkin lymphoma (HL)**: Characterised by the presence of Reed-Sternberg cells. Typically presents in older children and adolescents.
- **Non-Hodgkin lymphoma (NHL)**: Includes Burkitt's lymphoma, lymphoblastic lymphoma, and large cell lymphoma. These are high-grade tumours with rapid proliferation.

44.2 Incidence and Prevalence

- Lymphomas account for 10–15% of childhood cancers worldwide.
- NHL is more common in children than HL, particularly in those under 10 years of age.
- In sub-Saharan Africa, **Burkitt's lymphoma is endemic** and accounts for up to **50% of childhood cancers in some regions**.
- Peak age for Burkitt's lymphoma: **5–10 years**.
- Hodgkin lymphoma is less common in African children but occurs worldwide, often peaking in adolescence.
- There is a slight male predominance, particularly in the case of NHL.

44.3 Aetiology

The development of lymphoma is multifactorial and involves both genetic and environmental influences.

- **Genetic predisposition**: Mutations affecting oncogenes and tumour suppressor genes (e.g., *MYC* translocation in Burkitt's lymphoma).
- **Infectious agents**:
  - Epstein–Barr virus (EBV) is strongly associated with Burkitt's lymphoma and some cases of HL.
  - Human immunodeficiency virus (HIV) predisposes to NHL.
- **Immunodeficiency states**: Congenital (e.g., Wiskott–Aldrich syndrome) or acquired (HIV/AIDS, post-transplant immunosuppression).
- **Environmental factors**: Chronic malaria infection in endemic regions contributes to immune dysregulation, facilitating EBV-driven oncogenesis in Burkitt's lymphoma.

44.4 Pathophysiology

Lymphomas arise from **clonal proliferation of lymphoid cells**.

- **Hodgkin lymphoma**:
  - Originates from germinal centre B-cells that become transformed into Reed-Sternberg cells.
  - These cells secrete cytokines that recruit inflammatory cells, explaining the prominent systemic symptoms.
- **Non-Hodgkin lymphoma**:
  - High-grade and rapidly proliferating.
  - Burkitt's lymphoma is characterised by a translocation involving the *MYC* gene on chromosome 8 (t(8;14) most common).
  - Malaria-induced chronic immune stimulation reduces T-cell control over EBV-infected B-cells, facilitating malignant transformation.
- **Organ infiltration**: Lymphomas can spread to extranodal sites such as the bone marrow, CNS, and abdominal viscera.
- The hallmark of Burkitt's lymphoma in Africa is **jaw involvement**, though abdominal presentations are also common.

44.5 Signs and Symptoms

The presentation of lymphoma varies depending on the subtype and site of involvement.

- **General features**:
  - Fever, weight loss, night sweats ("B symptoms").
  - Fatigue, anorexia.
- **Hodgkin lymphoma**:
  - Painless lymphadenopathy (often cervical or supraclavicular).
  - Mediastinal mass causing cough, dyspnoea, or SVC obstruction.
  - Hepatosplenomegaly.
- **Non-Hodgkin lymphoma**:
  - Rapidly enlarging lymph nodes, often extranodal.
  - Abdominal involvement: distension, pain, palpable mass, intussusception, or bowel obstruction.
  - CNS infiltration: seizures, cranial nerve palsies, spinal cord compression.
  - **Burkitt's lymphoma**:
    - Endemic type: jaw/facial bone swelling, often bilateral.
    - Sporadic type: abdominal masses, ileocecal involvement.

44.6 Differential Diagnosis

Conditions that mimic childhood lymphoma include:

- **Infectious diseases**: Tuberculosis, HIV lymphadenopathy, EBV infection.
- **Other malignancies**: Leukaemia, neuroblastoma, Wilms' tumour.
- **Rheumatological disorders**: Juvenile idiopathic arthritis, systemic lupus erythematosus.
- **Benign causes of lymphadenopathy**: Reactive hyperplasia, cat-scratch disease.

44.7 Investigations

Evaluation of suspected lymphoma requires a combination of laboratory, imaging, and histological studies.

- **Laboratory tests**:

  - Full blood count: may reveal anaemia, cytopenias if marrow involvement.
  - ESR and LDH: often elevated.
  - Uric acid and renal function: to assess for tumour lysis risk.

- **Imaging**:
  - Chest X-ray: mediastinal mass.
  - Ultrasound/CT/MRI: delineate abdominal or nodal masses.

- **Histology**:
  - Excisional lymph node biopsy is the gold standard.
  - Reed-Sternberg cells → Hodgkin lymphoma.
  - "Starry sky" appearance → Burkitt's lymphoma.

- **Bone marrow aspiration and biopsy**: To check for infiltration.

- **Lumbar puncture**: Especially for Burkitt's lymphoma and lymphoblastic lymphoma to detect CNS disease.

44.8 Treatment

Management depends on subtype, stage, and extent of disease. Multidisciplinary care is essential.

44.8.1 Emergency Management

- Stabilise airway, breathing, circulation.
- Manage tumour lysis syndrome: hydration, allopurinol or rasburicase.
- Empirical antibiotics for febrile neutropenia.
- Blood products as required.

44.8.2 Definitive (Ongoing) Therapy

- **Chemotherapy** is the mainstay:
  - HL: ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) or equivalent protocols.
  - NHL: intensive multiagent regimens (e.g., cyclophosphamide, vincristine, doxorubicin, methotrexate, cytarabine).
  - Burkitt's lymphoma responds dramatically to short, intensive chemotherapy cycles.

- **Radiotherapy**: Occasionally used in HL but less so in children due to long-term side effects.
- **CNS prophylaxis**: Intrathecal chemotherapy for NHL.
- **Stem cell transplantation**: Considered in refractory or relapsed cases.

44.8.3 Preparation for Discharge

- Educate caregivers on infection prevention, adherence to chemotherapy, and recognition of complications.
- Ensure follow-up schedules are clear.
- Provide psychosocial and nutritional support.

44.8.4 Long-Term Management

- Monitor for relapse with clinical examination and imaging as indicated.
- Surveillance for late effects: growth disturbances, infertility, cardiotoxicity, secondary malignancies.
- Ongoing psychosocial support and school reintegration.

44.9 Complications

- **Early**: Tumour lysis syndrome, airway obstruction from mediastinal masses, sepsis.
- **During therapy**: Chemotherapy toxicities (mucositis, myelosuppression, cardiotoxicity).
- **Late**: Relapse, secondary cancers, endocrine dysfunction, infertility, psychosocial issues.

44.10 Prevention

- No definitive primary prevention strategies exist.
- Reducing malaria transmission may indirectly lower Burkitt's lymphoma incidence.
- HIV prevention and treatment help reduce NHL burden.
- Early recognition and referral are key to improving survival.

44.11 Prognosis

- Prognosis depends on subtype, stage, and response to therapy.
- **Hodgkin lymphoma**: Excellent prognosis with >90% 5-year survival in early-stage disease.
- **Non-Hodgkin lymphoma**: Cure rates of 70–90% with appropriate therapy.
- **Burkitt's lymphoma**: Rapidly fatal if untreated, but highly curable with intensive short-course chemotherapy. Survival is significantly improved when diagnosed early and managed promptly.

44.12 Conclusion

Childhood lymphoma is a significant health problem, particularly in sub-Saharan Africa, where **Burkitt's lymphoma is endemic**. It is an aggressive but highly treatable malignancy. For medical students, key learning points include recognition of clinical presentations, understanding the role of EBV and malaria in endemic Burkitt's lymphoma, and appreciating the importance of early diagnosis and intensive chemotherapy. With improved healthcare infrastructure, supportive care, and public health measures, outcomes for children with lymphoma can continue to improve.

45 Retinoblastoma

45.1 Introduction

Retinoblastoma is the most common **primary intraocular malignancy of childhood**, arising from the retina. It typically presents before the age of 5 years and carries major implications for vision, survival, and quality of life. The disease has become a paradigm for cancer genetics, as the RB1 tumour suppressor gene was the first tumour gene identified in humans.

Early diagnosis and treatment are critical: retinoblastoma is highly curable if detected early, but advanced disease can be fatal. In high-income countries, survival exceeds 95%, while in many low- and middle-income countries—including Ghana—delayed diagnosis often results in poorer outcomes.

45.2 Incidence and Prevalence

- Global incidence: about **1 in 15,000–20,000 live births**.
- Accounts for **3–4% of all childhood cancers**.
- Peak age:
  - Unilateral disease: 2–3 years.
  - Bilateral disease: diagnosed earlier, often before 1 year.
- No sex predilection.
- In Ghana and other sub-Saharan countries, children frequently present late, often with extraocular spread, which worsens survival rates.

45.3 Aetiology

The development of retinoblastoma is intimately linked to the **RB1 gene** on chromosome 13q14.

- **Heritable form** (40% of cases):
  - Germline mutation in one allele of RB1 gene is inherited.
  - Second hit occurs somatically in retinal cells.

  - Usually bilateral and multifocal.
  - Associated with increased risk of secondary malignancies (e.g., osteosarcoma).

- **Non-heritable form** (60% of cases):
  - Both RB1 mutations occur somatically.
  - Usually unilateral and unifocal.

Rarely, retinoblastoma may arise from **MYCN amplification** even without RB1 mutation.

45.4 Pathophysiology

The RB1 gene product regulates the **G1–S checkpoint** of the cell cycle. Loss of both functional RB1 alleles leads to uncontrolled retinal cell proliferation.

- Tumours originate from **retinal progenitor cells**.
- Can grow in various patterns:
  - **Endophytic**: growing into the vitreous.
  - **Exophytic**: growing beneath the retina, leading to retinal detachment.
  - **Diffuse infiltrating**: rare, spreading through the retina without forming a discrete mass.
- Spread:
  - Local invasion (into optic nerve, choroid, sclera).
  - Extraocular spread (orbit, brain via optic nerve, systemic metastasis to bone marrow, liver).

45.5 Clinical Features

Presentation varies depending on stage and extent of disease.

- **Most common presenting sign**:
  - **Leukocoria** (white pupillary reflex), often noticed in photographs with flash.
- Other features:
  - Strabismus (misalignment of eyes).
  - Red, painful eye (from secondary glaucoma, uveitis, or tumour necrosis).
  - Poor vision or blindness.
  - Hyphema (blood in anterior chamber).
  - Orbital swelling or proptosis (extraocular disease).
  - Rare systemic symptoms in metastatic disease (bone pain, weight loss, fever).

45.6 Differential Diagnosis

- Coats' disease (retinal telangiectasia with exudation).
- Persistent hyperplastic primary vitreous.
- Congenital cataract.
- Toxocariasis.
- Retinal detachment.
- Medulloepithelioma of the ciliary body.

45.7 Investigations

- **Ocular examination**:
  - Indirect ophthalmoscopy under anaesthesia (definitive for diagnosis).
- **Imaging**:
  - **Ultrasound B-scan**: reveals intraocular mass with calcification.
  - **CT scan**: useful for calcifications but limited due to radiation risk.
  - **MRI of orbits and brain**: preferred for local extension (optic nerve, CNS).
- **Laboratory tests**: not diagnostic, but baseline bloods useful before chemotherapy.
- **Genetic testing**:
  - Detects RB1 mutation.
  - Guides family counselling and screening of siblings.

Biopsy of the eye is avoided due to risk of tumour spread.

45.8 Staging

Two main systems:

1. **International Intraocular Retinoblastoma Classification (IIRC)** – based on disease extent within the eye (Groups A–E).
2. **International Retinoblastoma Staging System (IRSS)** – for post-enucleation staging, including extraocular spread and metastasis.

45.9 Treatment

Treatment depends on whether the disease is unilateral or bilateral, intraocular or extraocular, and the aim (life preservation, eye salvage, vision preservation).

45.9.1 Emergency Care

- Treat secondary glaucoma for pain relief.
- Manage raised intracranial pressure in cases of optic nerve invasion.

45.9.2 Definitive and Ongoing Management

- **Enucleation**: removal of the affected eye. Standard for unilateral advanced disease.
- **Focal therapies** (for small tumours):
  - Laser photocoagulation.
  - Cryotherapy.
  - Thermotherapy.
- **Chemotherapy**:
  - Systemic chemotherapy (vincristine, carboplatin, etoposide) for chemoreduction.
  - Intra-arterial chemotherapy (direct to ophthalmic artery).
  - Intravitreal chemotherapy (for vitreous seeds).
- **Radiotherapy**:
  - External beam (rare now, due to risk of secondary tumours in heritable cases).
  - Plaque brachytherapy for selected cases.
- **Bilateral disease**: efforts made to preserve at least one eye with useful vision.

45.9.3 Preparation for Discharge

- Educate parents on prosthesis care after enucleation.
- Importance of follow-up for recurrence detection.
- Genetic counselling for families with heritable disease.

45.9.4 Long-Term Management

- Regular ophthalmologic examinations under anaesthesia.
- Screening for second malignancies in heritable cases.
- Monitoring growth, vision development, and psychosocial adjustment.

45.10 Complications

- Local recurrence within the eye or orbit.
- Extraocular spread with poor prognosis.
- Metastases to CNS, bone marrow, or distant organs.
- Vision loss, especially in bilateral disease.
- Cosmetic issues after enucleation.
- Secondary malignancies in heritable retinoblastoma, particularly osteosarcoma and soft tissue sarcomas (especially after radiotherapy).

45.11 Prognosis

- In high-income countries: >95% survival.
- In sub-Saharan Africa: survival often <40%, mainly due to late presentation, extraocular disease, and limited treatment resources.
- Prognosis is best with early detection, small intraocular tumours, and access to multimodal therapy.

45.12 Prevention

- No known prevention for sporadic cases.
- **Genetic counselling and testing**: vital in families with heritable retinoblastoma.
- Screening of at-risk infants (regular eye exams from birth to 5 years).
- Avoid unnecessary exposure to ionising radiation in heritable cases.

45.13 Conclusion

Retinoblastoma is a highly curable childhood malignancy when detected early. The disease highlights the importance of integrating **clinical suspicion, imaging, genetic counselling, and multimodal therapy** in management. In Ghana and similar settings, community education to recognise leukocoria early, improved access to ophthalmic oncology, and support for families can dramatically improve survival and quality of life.

46 Nephroblastoma (Wilms' Tumour)

46.1 Introduction

Nephroblastoma, commonly known as **Wilms' tumour**, is the most common malignant renal tumour in childhood. It arises from embryonic renal tissue and typically presents between ages 2 and 5 years. The tumour has contributed greatly to the success story of paediatric oncology, with survival rates improving significantly due to advances in surgery, chemotherapy, and radiotherapy.
Although relatively rare compared to infections or malnutrition, nephroblastoma remains an important cause of morbidity and mortality in paediatrics, particularly in low- and middle-income countries where late presentation is common.

46.2 Incidence and Prevalence

Wilms' tumour accounts for about **6–8% of all childhood cancers**.
- The annual incidence is approximately **8 cases per million children** under 15 years.
- Peak age of presentation: **3–4 years**.
- Slight female predominance.
- Bilateral disease occurs in about **5–7%** of cases.

In sub-Saharan Africa, including Ghana, the incidence is comparable to global figures, but outcomes are poorer due to late presentation, limited access to multimodal therapy, and higher rates of advanced disease at diagnosis.

46.3 Aetiology

Most cases are sporadic, but both **genetic** and **environmental** factors play roles.

- **Genetic factors**:
  - Mutations in WT1 (chromosome 11p13) and WT2 (11p15) are implicated.
  - Other genes: WTX (X chromosome), CTNNB1 (beta-catenin pathway).
- **Syndromic associations**:

  - WAGR syndrome (Wilms tumour, Aniridia, Genitourinary anomalies, mental Retardation).
  - Denys–Drash syndrome (gonadal dysgenesis, nephropathy, Wilms tumour).
  - Beckwith–Wiedemann syndrome (organomegaly, hemihypertrophy, increased tumour risk).

- **Familial predisposition**: Rare but recognised, with siblings sometimes affected.
- **Environmental factors**: No strong evidence, though intrauterine exposures have been explored.

46.4 Pathophysiology

Wilms' tumour develops from **persistent metanephric blastema**, the embryonic renal precursor tissue that fails to differentiate normally.
- The tumour is typically a **triphasic neoplasm**, consisting of:
- **Blastemal cells** (small round blue cells).
- **Stromal elements** (spindle cells, connective tissue).
- **Epithelial components** (tubules, glomeruloid structures).
- Some tumours may be monophasic, dominated by one component.
- Tumour growth can distort the kidney, invade renal vessels, extend into the inferior vena cava, and metastasize, commonly to lungs, liver, and lymph nodes.

A subset of tumours shows **anaplasia**, which carries a poorer prognosis and resistance to therapy.

46.5 Clinical Features

Presentation depends on tumour size, stage, and presence of metastases.

- **Most common feature**:
  - Painless **abdominal mass**, often noticed by parents during bathing or dressing.
- Other features:
  - Abdominal pain or discomfort.
  - Hematuria (gross or microscopic).
  - Hypertension (due to increased renin secretion).
  - Anemia (from haemorrhage or bone marrow suppression).
  - Weight loss, anorexia, malaise (less common).

- Advanced disease:

  - Cough, dyspnea (lung metastases).
  - Hepatomegaly (liver metastases).

Unlike neuroblastoma, Wilms' tumour rarely crosses the midline in the abdomen.

46.6 Differential Diagnosis

Important conditions to consider when a child presents with an abdominal mass:
- **Neuroblastoma** (usually crosses midline, calcification common).
- Multicystic dysplastic kidney.
- Hydronephrosis.
- Mesoblastic nephroma (in neonates).
- Renal cell carcinoma (rare in children).
- Hepatoblastoma or hepatomegaly from other causes.

46.7 Investigations

Workup aims at confirming diagnosis, assessing extent, and staging.

- **Laboratory tests**:
  - CBC (anemia, baseline counts).
  - Renal function tests (creatinine, electrolytes).
  - Liver function tests.
  - Urinalysis (hematuria).

- **Imaging**:
  - **Abdominal ultrasound**: First-line; identifies renal origin of mass.
  - **CT or MRI of abdomen**: Defines tumour extent, contralateral kidney involvement, vascular invasion.
  - **Chest X-ray/CT**: Evaluate for lung metastases.
- **Histology**: Usually obtained after nephrectomy or biopsy in bilateral/advanced disease.

46.8 Staging

The **National Wilms' Tumor Study (NWTS)** staging system is widely used:
- Stage I: Limited to kidney, completely resected.
- Stage II: Extends beyond kidney but completely resected.

- Stage III: Residual tumour confined to abdomen (lymph nodes, peritoneal spillage).
- Stage IV: Hematogenous metastases (lung, liver, bone, brain).
- Stage V: Bilateral renal involvement.

46.9 Treatment

Successful management requires a **multimodal approach**: surgery, chemotherapy, and sometimes radiotherapy.

46.9.1 Emergency Management

- Stabilise child if anaemic, hypertensive, or in respiratory distress.
- Treat severe hypertension with antihypertensives.
- Blood transfusion for anaemia.
- Manage tumour rupture (can present with acute abdomen).

46.9.2 Definitive and Ongoing Treatment

- **Surgery**: Radical nephrectomy is standard for unilateral disease.
- **Chemotherapy**: Regimens typically include vincristine, actinomycin D, and doxorubicin (depending on stage and histology).
- **Radiotherapy**: Reserved for higher-stage disease or anaplastic histology.
- **Bilateral disease (Stage V)**: Initial chemotherapy to shrink tumour, followed by nephron-sparing surgery.

46.9.3 Preparation for Discharge

- Educate caregivers on:
  - Medication adherence.
  - Infection prevention during chemotherapy.
  - Monitoring for hypertension and renal function.
  - Nutrition and follow-up visits.

46.9.4 Long-Term Management

- Regular follow-up for recurrence surveillance.
- Monitor growth and development.
- Monitor renal function (risk of chronic kidney disease, especially in bilateral disease).
- Monitor for late effects of chemotherapy/radiotherapy (cardiotoxicity, infertility, secondary malignancies).

46.10 Complications

- Tumour rupture leading to haemorrhage and peritonitis.
- Hypertension due to renin production.
- Metastasis (lungs, liver).
- Chemotherapy-related: myelosuppression, mucositis, cardiotoxicity.
- Chronic renal impairment in bilateral disease.
- Psychological and social impact on family.

46.11 Prognosis

Wilms' tumour is one of the **paediatric oncology success stories**:
- Overall survival exceeds **85%** in high-income countries.
- Prognosis depends on:
- Stage at diagnosis.
- Histology (anaplastic variants worse).
- Age of child.
- In sub-Saharan Africa, survival is significantly lower (20–50%) due to late presentation, limited resources, and treatment abandonment.

46.12 Prevention

There are no established preventive measures for sporadic cases. However:
- **Genetic counselling** for families with syndromic or familial cases.
- **Surveillance imaging** (ultrasound every 3 months until age 7) for high-risk children (e.g., WAGR, Denys–Drash, Beckwith–Wiedemann, bilateral disease).
- Early detection and treatment significantly improve outcomes.

46.13 Conclusion

Nephroblastoma is the most common childhood renal malignancy and a leading cause of paediatric abdominal masses. It exemplifies how combined surgery, chemotherapy, and radiotherapy can yield excellent outcomes when implemented effectively. For Ghana and similar settings, the major challenge remains late presentation and limited access to oncology services. Strengthening health systems, raising community awareness, and improving access to multimodal therapy are essential to bridge the survival gap.

47 Other Pediatric Tumours

47.1 Introduction

Childhood cancers represent a diverse group of diseases distinct from adult malignancies in their biology, clinical behaviour, and response to treatment. While leukaemias, lymphomas, nephroblastoma, and retinoblastoma are among the most common, several other solid tumours also contribute significantly to paediatric cancer morbidity and mortality worldwide.

Understanding these conditions is crucial for early recognition, appropriate referral, and timely management. This chapter will cover neuroblastoma, hepatic tumours, sarcomas, bone tumours, brain tumours, and germ cell tumours, as well as selected rare entities.

47.2 Neuroblastoma

47.2.1 Introduction and Epidemiology

Neuroblastoma is the most common **extracranial solid tumour of childhood**, arising from neural crest cells of the sympathetic nervous system.
- Accounts for about **8–10% of childhood cancers**.
- Median age at diagnosis: **2 years**.
- Rare after 10 years.
- Common sites: adrenal medulla (40%), paraspinal sympathetic chain, posterior mediastinum.

47.2.2 Pathophysiology

- Originates from neural crest cells that fail to differentiate.
- Tumour behaviour is highly variable: can spontaneously regress (especially in infants) or progress aggressively with widespread metastases.
- Genetic features: amplification of **MYCN oncogene** is associated with poor prognosis.

47.2.3 Clinical Features

- Abdominal mass (often firm, irregular, crossing midline).
- Symptoms due to local invasion: constipation, urinary obstruction.
- Metastases: bone pain, periorbital ecchymoses ("raccoon eyes"), hepatomegaly.
- Paraneoplastic features: hypertension, diarrhoea (due to vasoactive intestinal peptide).

47.2.4 Investigations

- Imaging: ultrasound, CT/MRI of abdomen.
- MIBG scan: identifies tumour sites.
- Biopsy for histology.
- Elevated urinary catecholamines (VMA, HVA) in >90%.

47.2.5 Management

- Depends on risk stratification.
- Low-risk: Surgery alone may cure.
- Intermediate-risk: surgery + chemotherapy.
- High-risk: intensive chemotherapy, surgery, radiotherapy, stem cell transplant, immunotherapy.

47.2.6 Prognosis

- Variable. Infants with localised disease may do very well.
- High-risk disease has poorer survival despite aggressive therapy.

47.3 Hepatic Tumours

47.3.1 Hepatoblastoma

- Most common **primary liver tumour in children**.
- Usually diagnosed in children under **3 years**.
- Associated with prematurity and some genetic syndromes (e.g., Beckwith–Wiedemann).

Clinical Features:
- Painless abdominal mass.
- Abdominal distension.
- Elevated **alpha-fetoprotein (AFP)** in most cases.

Diagnosis:
- Ultrasound/CT scan showing liver mass.
- Biopsy for confirmation.

Treatment:
- Surgical resection (hepatectomy).
- Neoadjuvant/adjuvant chemotherapy (cisplatin-based).
- Liver transplant if unresectable.

Prognosis:
- Good if complete surgical removal is possible.

47.3.2 Hepatocellular Carcinoma (HCC)

- Less common in children but important in sub-Saharan Africa due to **hepatitis B infection**.
- Presents in older children and adolescents.
- AFP is elevated but less consistently than hepatoblastoma.
- Prognosis is generally poor, as tumours are often unresectable.

47.4 Rhabdomyosarcoma and Other Soft Tissue Sarcomas

47.4.1 Rhabdomyosarcoma (RMS)

- Most common **soft tissue sarcoma in children**.
- Arises from primitive mesenchymal cells committed to skeletal muscle lineage.
- Common sites: head and neck (orbit, nasopharynx), genitourinary tract, extremities.

Clinical Features:
- Mass on the affected site.
- Proptosis (orbital).
- Nasal obstruction, epistaxis (nasopharyngeal).
- Haematuria or vaginal bleeding (genitourinary).

Diagnosis:
- Imaging (MRI).
- Biopsy with histology (embryonal, alveolar, pleomorphic subtypes).
- Immunohistochemistry (desmin, myogenin positive).

Treatment:
- Multimodal: surgery, chemotherapy, radiotherapy.

Prognosis:
- Better in embryonal type.
- Depends on site, size, and extent.

47.4.2 Other Soft Tissue Sarcomas

- Include fibrosarcoma, synovial sarcoma, and malignant peripheral nerve sheath tumour.
- Less common but managed similarly with surgery, chemotherapy, and radiotherapy.

47.5 Bone Tumours

47.5.1 Osteosarcoma

- Most common **primary malignant bone tumour** in children and adolescents.
- Peak in adolescence during rapid bone growth.

- Common sites: metaphyses of long bones (femur, tibia, humerus).

Clinical Features:
- Localised bone pain (worse at night).
- Swelling, mass, limitation of movement.
- Pathological fractures may occur.

Investigations:
- X-ray: mixed lytic-sclerotic lesion, periosteal reaction ("sunburst" appearance, Codman triangle).
- MRI: local extent.
- Biopsy confirms diagnosis.

Treatment:
- Neoadjuvant chemotherapy, limb-sparing surgery (or amputation), adjuvant chemotherapy.

Prognosis:
- Improved with multimodal therapy.
- Presence of metastases (lung) worsens outlook.

47.5.2 Ewing Sarcoma

- Second most common bone tumour in children.
- Arises from primitive neuroectodermal cells.
- Typically affects diaphysis of long bones and pelvis.
- Associated with **t(11;22) translocation**.

Clinical Features:
- Pain, swelling, systemic symptoms (fever, weight loss).
- Can mimic infection (osteomyelitis).

Investigations:
- X-ray: "onion-skin" periosteal reaction.
- MRI: extent of disease.
- Biopsy for histology and cytogenetics.

Treatment:
- Chemotherapy, surgery, and/or radiotherapy.

Prognosis:
- Fair with localised disease.
- Poor with metastases.

47.6 Brain Tumours

Brain tumours are the most common **solid tumours of childhood**.

47.6.1 Medulloblastoma

- Most common malignant brain tumour in children.
- Originates in cerebellum.
- Highly radiosensitive.

Features: headache, vomiting, ataxia, papilloedema.
Treatment: surgery + craniospinal irradiation + chemotherapy.

47.6.2 Astrocytomas

- Low-grade astrocytomas (e.g., pilocytic astrocytoma) have excellent prognosis after surgical removal.
- High-grade astrocytomas are aggressive and carry poorer outcomes.

47.6.3 Ependymomas

- Arise from ependymal cells lining ventricles.
- Commonly present with hydrocephalus due to obstruction.
- Treatment: surgery and radiotherapy.

47.7 Germ Cell Tumours

47.7.1 Overview

- Can occur in gonads (testis, ovary) or extragonadal sites (sacrococcygeal, mediastinum, retroperitoneum).
- Derived from primordial germ cells.

47.7.2 Clinical Features

- Testicular: painless testicular mass.
- Ovarian: abdominal mass, pain, precocious puberty.
- Sacrococcygeal: mass at base of spine, sometimes visible externally.

47.7.3 Diagnosis

- Imaging (ultrasound, CT/MRI).
- Serum tumour markers: AFP, -HCG.
- Biopsy (except in some gonadal cases where orchiectomy/oophorectomy is primary treatment).

47.7.4 Treatment

- Surgery + chemotherapy (cisplatin-based).
- Prognosis generally good, especially for localised disease.

47.8 Other Rare Paediatric Tumours

- **Adrenocortical tumours**: may present with virilisation or Cushing's syndrome.
- **Thyroid carcinoma**: uncommon, but papillary carcinoma can occur, sometimes associated with prior radiation exposure.
- **Malignant rhabdoid tumour of the kidney or brain**: rare and aggressive.

47.9 Conclusion

Beyond leukaemia, lymphoma, nephroblastoma, and retinoblastoma, several other paediatric malignancies play a significant role in the spectrum of childhood cancer. These include neuroblastoma, hepatic tumours, sarcomas, bone tumours, brain tumours, and germ cell tumours. Although they differ in biology and clinical behaviour, successful management relies on **early diagnosis, multidisciplinary care, and supportive management**.

In resource-limited settings such as Ghana, improving survival will require increased awareness of early signs, timely referral, access to diagnostic facilities, and strengthening of paediatric oncology units.

Part VII

Nephrology

48 Spectrum of Kidney Diseases in Children

48.1 Introduction

The kidneys play a vital role in maintaining internal homeostasis through the regulation of water, electrolytes, acid-base balance, and the excretion of metabolic waste. In children, renal function is essential not only for maintaining physiologic stability but also for supporting growth and development. Kidney diseases in children encompass a wide spectrum ranging from congenital and inherited disorders to acquired glomerular, tubular, and systemic conditions.

In Ghana and other low- and middle-income countries, kidney diseases in children are increasingly recognized as important causes of morbidity and mortality. Limited diagnostic facilities, late presentation, and inadequate access to nephrology services remain major challenges. Understanding the diverse presentation and underlying mechanisms of renal disease is, therefore, critical for early diagnosis and effective management.

48.2 Epidemiology and Burden

Globally, the prevalence of paediatric kidney disease varies widely depending on the specific condition. Acute kidney injury (AKI) is estimated to occur in up to 25% of hospitalized children, while chronic kidney disease (CKD) affects 1–3 per 1,000 children. In sub-Saharan Africa, data are scarce, but renal disease often presents late and is associated with preventable causes such as infections, dehydration, and toxins.

In Ghana, children frequently present with conditions such as nephrotic syndrome, acute glomerulonephritis, urinary tract infections, and congenital anomalies of the kidney and urinary tract (CAKUT). Early childhood illnesses, poor sanitation, and limited access to pediatric nephrology care contribute to adverse outcomes.

48.3 Classification of Kidney Diseases in Children

Kidney diseases in children can be broadly classified into the following categories:

1. **Congenital and Structural Anomalies**

- Congenital anomalies of the kidney and urinary tract (CAKUT)
- Obstructive uropathy (posterior urethral valves, ureteropelvic junction obstruction)
- Renal dysplasia or hypoplasia
- Polycystic kidney disease

2. **Glomerular Diseases**

   - Nephrotic syndrome (minimal change, focal segmental glomerulosclerosis, membranoproliferative)
   - Glomerulonephritis (post-streptococcal, IgA nephropathy, lupus nephritis)
   - Rapidly progressive glomerulonephritis

3. **Tubulointerstitial and Tubular Disorders**

   - Acute interstitial nephritis
   - Renal tubular acidosis
   - Fanconi syndrome
   - Cystinosis and other metabolic tubular disorders

4. **Infective and Postinfectious Conditions**

   - Urinary tract infection (UTI)
   - Pyelonephritis
   - Reflux nephropathy
   - Schistosomiasis-related kidney disease

5. **Systemic and Secondary Causes**

   - Hypertension
   - Diabetes mellitus (rare in children but increasing)
   - Sickle cell nephropathy
   - HIV-associated nephropathy
   - Hemolytic uremic syndrome (HUS)

6. **Acute and Chronic Renal Failure**

   - Acute kidney injury (AKI)
   - Chronic kidney disease (CKD) and end-stage renal disease (ESRD)

48.4 Pathophysiological Overview

The kidney's response to injury varies depending on the site and nature of the insult.

48.4.1 Glomerular Diseases

These involve inflammation or damage to the glomeruli, leading to abnormal filtration.
- **Nephrotic syndrome** results from increased glomerular permeability to proteins, producing heavy proteinuria, hypoalbuminaemia, and oedema.
- **Glomerulonephritis**, on the other hand, causes hematuria, hypertension, and varying degrees of renal impairment. Immune-mediated mechanisms — such as deposition of immune complexes following infections — play a central role.

48.4.2 Tubulointerstitial and Tubular Disorders

Tubular diseases interfere with urine concentration, electrolyte handling, and acid-base balance.
- **Renal tubular acidosis** leads to metabolic acidosis due to defective hydrogen ion excretion or bicarbonate reabsorption.
- **Fanconi syndrome** affects multiple tubular transport mechanisms, leading to glycosuria, aminoaciduria, and phosphate wasting.

48.4.3 Vascular and Systemic Disorders

Conditions such as hemolytic uremic syndrome cause endothelial injury leading to microangiopathic hemolysis and acute renal failure. Hypertension, both a cause and consequence of renal disease, damages glomeruli and accelerates progression to chronic kidney disease.

48.4.4 Congenital and Structural Anomalies

CAKUT accounts for a significant proportion of pediatric renal failure. These abnormalities arise during embryogenesis and include renal agenesis, dysplasia, and obstructive lesions. Impaired nephron development or chronic obstruction eventually results in renal scarring and progressive dysfunction.

48.5 Clinical Presentation

Renal diseases in children present with diverse features depending on the site and extent of involvement.

Common presentations include: - **Oedema**, especially periorbital and pedal, typical of nephrotic syndrome.
- **Haematuria** (macroscopic or microscopic), often seen in glomerulonephritis.
- **Hypertension**, either as a primary finding or secondary to renal pathology.

- **Oliguria or anuria**, indicating renal failure.
- **Polyuria and polydipsia**, suggestive of tubular dysfunction.
- **Recurrent urinary tract infections**, possibly pointing to vesicoureteral reflux or obstruction.
- **Growth retardation and failure to thrive**, common in chronic kidney disease.

Infants may present with nonspecific signs such as poor feeding, vomiting, or failure to gain weight, necessitating a high index of suspicion.

48.6 Investigations

Diagnosis requires a combination of clinical assessment, laboratory tests, and imaging.

48.6.1 Laboratory Tests

- **Urinalysis:** detects proteinuria, hematuria, or pyuria.
- **Urine microscopy and culture:** identifies infection or casts.
- **Serum urea and creatinine:** assess renal function.
- **Electrolytes and bicarbonate:** for acid-base and electrolyte imbalances.
- **Complement levels (C3, C4):** decreased in post-streptococcal glomerulonephritis.
- **Autoantibody testing:** ANA, anti-dsDNA for lupus nephritis.
- **24-hour urine protein or spot protein-to-creatinine ratio** to quantify proteinuria.

48.6.2 Imaging

- **Renal ultrasound** for kidney size, structure, and obstruction.
- **Voiding cystourethrogram (VCUG)** for reflux diagnosis.
- **DMSA scan** for renal scarring.
- **CT/MRI** in complex anomalies or masses.

48.6.3 Renal Biopsy

Indicated in cases of nephrotic syndrome unresponsive to steroids, unexplained renal failure, or to confirm a specific glomerular disease.

48.7 Management Principles

The management of pediatric kidney disease depends on the underlying cause but follows certain common principles.

48.7.1 1. General Supportive Care

- Control of **blood pressure** using ACE inhibitors or calcium channel blockers.
- Maintenance of **fluid and electrolyte balance**.
- Correction of metabolic acidosis and anemia.
- Adequate nutrition to support growth and prevent catabolism.

48.7.2 2. Disease-Specific Therapy

- **Nephrotic syndrome:** corticosteroids are first-line; resistant cases may need cyclophosphamide or calcineurin inhibitors.
- **Acute glomerulonephritis:** mainly supportive; antibiotics for streptococcal infection; control of hypertension and edema.
- **UTIs:** treated with appropriate antibiotics and preventive measures such as hydration and bladder hygiene.
- **Obstructive uropathy:** surgical intervention to relieve obstruction.
- **AKI:** manage underlying cause, ensure adequate perfusion, and initiate dialysis when necessary.
- **CKD:** slow progression through blood pressure control, treat anemia, and prepare for renal replacement therapy.

48.7.3 3. Dialysis and Renal Replacement

Indicated in severe AKI or end-stage renal disease.
- **Peritoneal dialysis** is often preferred in children due to simplicity and better hemodynamic tolerance.
- **Haemodialysis** is used in older children when facilities permit.
- **Kidney transplantation** offers the best long-term outcome, though access is limited in Ghana.

48.7.4 4. Psychosocial and Family Support

Chronic kidney disease imposes psychological and financial burdens. Family counselling, nutritional education, and social support are integral to management.

48.8 Complications

Untreated or poorly managed kidney disease can result in severe complications: - Hypertensive crisis
- Chronic kidney disease and end-stage renal failure
- Electrolyte disturbances (hyperkalaemia, hyponatraemia)
- Growth failure and bone disease
- Cardiovascular complications
- Infections from immunosuppression or dialysis
- Anaemia and fatigue

48.9 Prevention

Many causes of renal disease in children are preventable.

Key preventive measures include: - **Antenatal care** to detect congenital anomalies early.
- **Prompt treatment of infections**, particularly streptococcal throat and skin infections.
- **Avoidance of nephrotoxic drugs** (e.g., aminoglycosides, NSAIDs).
- **Adequate hydration** during diarrhoeal or febrile illnesses.
- **Health education** on hygiene and sanitation to prevent UTIs.
- **Early referral** for persistent oedema, hematuria, or hypertension.

48.10 Prognosis

The outcome varies with the cause and stage at diagnosis.
- **Acute glomerulonephritis** generally resolves completely with supportive care.
- **Steroid-sensitive nephrotic syndrome** has an excellent prognosis though relapses are common.
- **Chronic kidney disease** progresses slowly but inevitably to renal failure without intervention.
Early detection and multidisciplinary care significantly improve survival and quality of life.

48.11 Conclusion

The spectrum of kidney diseases in children is wide and complex, encompassing congenital, infectious, immune, and systemic disorders. In Ghana and similar settings, late presentation and limited diagnostic resources often worsen outcomes.

Medical students and young clinicians must develop a strong foundation in recognizing early signs, performing appropriate investigations, and instituting timely management. With better public health measures, increased awareness, and improved access to paediatric nephrology services, the burden of childhood renal disease can be significantly reduced.

49 Hypertension

49.1 Introduction

Blood pressure is the force exerted by the blood against any unit area of the vessel wall. Physiologically,

$$BP = CO \times TPR = SV \times HR \times TPR$$

Where:

- HR is the Heart Rate
- BP is the Blood Pressure
- TPR is the Total Peripheral Resistance
- CO is the Cardiac Output
- SV is the stroke volume

49.2 Ways of measuring blood pressure

1. **Direct intra-arterial** measurements by placing a catheter into the vessel and measuring the pressure "in line" with the vessel (end-on-pressure). This method is used by physiologists and Intensivists. The principle is employed in the measurements of central venous pressure and intracranial pressure in clinical practice.
2. **The auscultatory method** is done with the use of a sphygmomanometer (either mercury or aneroid) and a stethoscope. This is the gold standard in clinical practice. Korotkoff sounds 1 and 5 sounds are measured for systolic and diastolic bleed pressures respectively. Values obtained are generally lower than direct & oscillometric measurements.
3. **The palpation method** (flush technique) is performed with the use of a sphygmomanometer and palpating finger. Largely unreliable. Only systolic blood pressure can be measured with this technique. The palpated pulse is generally lower than Korotkoff sound 1 by 10mmHg.
4. **The oscillometric method** uses a sphygmomanometer and a monitor e.g. digital blood pressure devices and Dynamap. Here, pulsatile blood flow through arterial wall oscillations is transmitted to the cuff encircling the extremity. Korotkoff sound 1 is recorded at the point of rapid increase in oscillation amplitude. Korotkoff sound 5 is recorded as

the point of a sudden decrease in oscillation amplitude. Values obtained by oscillometric measurements are generally higher than auscultatory.

5. **Doppler ultrasound technique**: Here a Doppler ultrasound is held over the pulse to magnify the sound so that it is audible without a stethoscope. The sound detected may be 5mmHg higher than Korotkoff sound 1.
6. **Ambulatory blood pressure measurements**. Here, multiple measurements are recorded over time (e.g. 24 hours) with digital devices attached to the limb whilst the patient engages in normal activities outside the hospital. Results are analysed on a computer or paper tracer built into the device using the mean of the readings. It provides a truer picture of blood pressure trends useful in diagnosing "white coat hypertension" and nocturnal hypertension (absence of a normal physiological drop in blood pressure during sleep).

49.3 Definition of Hypertension in children

In adults, the epidemiological definition is based on the risk of adverse events (e.g. Stroke) being>140/90mmHg. **In children**, hypertension is defined statistically based on normative data: 95th centile for age, height, and gender (Refer to height centile chart and blood pressure levels). By this statistical definition, 5% of children will be classified as hypertensives. Other definitions include:

- **Normal blood pressure**: < 90th centile for age, height, and sex.
- **Pre-Hypertension**: 90th – <95th centile for age, height, and sex
- **Stage 1 Hypertension**: 95th - 99th + 5 mmHg
- **Stage 2 Hypertension**: *> 99th centile + 5mmHg*

A sample of the blood pressure chart is shown below.

Blood Pressure Levels for Boys by Age and Height Percentile (Continued)

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91

Figure 49.1: Blood Pressure Centile Chart

49.4 Plotting the blood pressure centile

1. Measure the child's height.
2. Determine the height centile. If the height centile falls between 2 centiles, use the closest centile. Otherwise, use the lower height centile.
3. Determine the blood pressure centile.
4. Classify blood pressure using the definitions above.

49.5 Hypertensive emergency

This is an acutely elevated blood pressure with evidence of threatening end-organ damage involving the following organs:

- Brain (severe headache, visual changes, cranial nerve palsy, papilloedema)
- Heart (acute chest pain and tightness, shortness of breath)
- Kidney (decreased urine output acutely, proteinuria and haematuria on dipstick)

It is thus a symptomatic, severe Hypertension.

49.6 Hypertensive Urgency

This is severe hypertension without evidence of end-organ damage or symptoms. The blood pressure should nevertheless be treated urgently but not aggressively like in a hypertensive emergency to prevent progression into a hypertensive emergency. If possible, the patient should be managed as in-patient.

49.7 Rules of blood pressure measurement

1. Select the right cuff size.
    - The length of the inflation bladder should be at least 80% of the mid-arm circumference.
    - The width of the inflation bladder is at least 40th of the mid-arm circumference.
2. The child should rest for at least 5 minutes in a comfortable environment and position.
3. Arm resting and supported at heart level (The reference level. Values outside this reference level are higher). The lower edge of the cuff is 2cm above the cubital fossa.
4. Bladder tubings should lie over the brachial artery.
5. The Bell of the stethoscope is used.
6. Korotkoff sounds 1 and 5 are used for systolic and diastolic respectively.

7. Multiple measurements are made (preferably at different settings) and the lowest reading is taken. For research purposes, 3 measurements are taken and an average of the last 2 used.

Blood pressure readings obtained in the legs are 10-20mmHg higher than the arm pressure in any individual. Arm blood pressure higher than leg blood pressure occurs in aortic coarctation distal to ductus arteriosus.

49.8 When to suspect hypertension

Suspect hypertension in any child with any of the following conditions:

- Alteration in consciousness including aggressive behavior and convulsion
- Oedematous
- Known kidney disease or evidence of abnormal urinalysis
- Heart failure
- Obesity
- Failure to thrive
- Stroke or other palsies including cranial nerve palsy
- History of Low Birth Weight (small number of nephrons)
- Unexplained anaemia, or blurred vision
- Neurofibromatosis
- Other syndromes like Turner & Williams

49.9 Aetiology of hypertension

Generally, childhood Hypertension is considered to be of secondary cause until proven otherwise. This is particularly so among the very young and the severely hypertensive. The majority (~80%) are of renal origin. However, the number of children with essential Hypertension is on the rise, particularly among obese adolescents and those with a positive family history.

Broadly, aetiology can be categorized into:

- Renal disease
- Vascular disorders
- Endocrine causes
- Neurologic causes
- Renal tumours
- Catecholamine-secreting tumours
- Drug-induced
- Miscellaneous causes

However, since these are often age-specific categorizations are done by age as below:

49.9.1 Neonate to one-year

Congenital

- Congenital lesions of the vasculature
  - Renal Artery Stenosis
  - Aortic coarctation
- Congenital lesions of renal parenchyma
  - Polycystic Kidney disease
  - Dysplastic kidneys
  - Obstructive uropathy
- Congenital Adrenal Hyperplasia
  - 11- hydroxylase deficiency
  - 17- hydroxylase def

Acquired

- Renal artery or vein thrombosis secondary to umbilical artery or vein catheterisation
- Bronchopulmonary dysplasia
- Medications
  - Theophylline/caffeine
  - Phenylephrine and Ephedrine Nasal Drops in cold medications
  - Steroids
  - Vitamin D intoxication
- Total Parental Nutrition (high Ca2+)
- Maternal drug use: Cocaine, heroin

49.9.2 One- to five years

- Renal Artery Stenosis
- Glomerulonephritis
- Renal vein thrombosis
- Wilms tumour
- Neuroblastoma
- Phaeochromocytoma
- Cystic kidney disease
- Monogenic Hypertension (e.g. Liddle's syndrome)

49.9.3 Five- to ten-years

- Glomerulonephritis
- Renal scars from reflux nephropathies or Urinary Tract Infections
- Renal Artery Stenosis
- Cystic renal disease
- Endocrine tumours
- Essential Hypertension
- Obesity

49.9.4 Ten- to twenty-years

- Obesity
- Essential hypertension
- Reflux nephropathies with repeated Urinary Tract Infections
- Glomerulonephritis
- Renal Artery Stenosis
- Endocrine tumours
- Hyperthyroidism
- Drugs (Oral Contraceptive Pill, illicit drugs)

49.10 Evaluation of the Hypertensive Child

- Patient's history
- Symptoms of renal disease (haematuria, oliguria, evidence of bodily swelling, polyuria, enuresis)
- Symptoms of vasculitis or rheumatology (Joint swelling & rash)
- Past medical history (umbilical artery/vein catheterisation, previous renal disease e.g. Previous swelling)
- Drug History (steroids, Oral Contraceptive Pill, amphetamines, other illicit drugs)
- Birth History: Low Birth Weight
- Family History of Hypertension

Clues on physical examination include:

- Coarctation of the Aorta & Takayasu:
  - Femoral artery delay or imperceptible
  - Blood pressure discrepancy between arm & leg →COA, Takayasu arteritis
- Neurofibromatosis
  - Caf au lait spots

- RAS, Takayasu arteritis
  - Abdominal bruit
- Congenital adrenal hyperplasia
  - Ambiguous genitalia
- Dysmorphism suggestive of Turner or William syndromes
- Signs of Chronic Renal Failure: Growth failure (stunted), renal rickets, anaemia, oedema
- Bedside urine dipstick positive for protein and blood (± oedema)

49.11 Investigations

The rationale is 2-fold:

1. To define aetiology
2. To assess the presence of end-organ damage

Some of the investigations include:

- Full blood count
- Urine dipstick, microscopy and culture
- BUE, Serum Creatinine, Ca, Mg, PO4, blood gases
- Uric acid
- KUB ultrasound and Doppler studies to rule out Renal Artery Stenosis
- Chest X-ray for cardiomegaly
- Echocardiogram for Left Ventricular Hypertrophy (end organ damage)
- Fundoscopy
- Plasma Renin Activity (PRA) for RAS & renin secreting tumours
- Pre/post captopril nuclear scan
- MRA or CT Angiogram
- DMSA scan for renal scars
- Urine HVA & VMA for catechol amine secreting tumours/MIBG scintigraphy

49.12 Uric Acid and hypertension

Uric acid is increasingly being implicated in the pathogenesis of Hypertension in both adults and children. It is believed to cause endothelial dysfunction leading to microvascular and inflammatory injury to the kidneys. There are also reduced levels of endothelial-derived nitric oxide and associated elevation of the Renin-Aldosterone-Angiotensin System. Elevated uric acid levels in hypertensive individuals are associated with adverse outcomes like stroke. Allopurinol treatment is advocated for such individuals.

49.13 Complication of Hypertension

Some complications of Hypertension are listed below:

- Hypertensive encephalopathy
- Left Ventricular Failure
- Stroke
- Subarachnoid haemorrhage
- Secondary renal damage
- Retinopathy

49.14 Treatment of hypertension

49.14.1 Non-drug treatment

- Reducing salt intake
- Weight reduction for obesity-related hypertension
- Intake of more vegetables on account of potassium richness

49.14.2 Drug Treatment

Principles of anti-hypertensive therapy:

- Long-acting (once-daily medication)
- Maximise treatment dosage before adding on
- Agents used will come from the "ABCD" group:
  - **A**CE inhibitor and ARBs (Avoid if RAS suspected or in hypovolaemia)
  - **B**eta-blocker
  - **C**alcium channel blocker
  - **D**iuretic
  - **E**very other drug (methyl dopa, alpha-blockers, vasodilators like hydralazine

Generally, **A & B** drugs are not combined for Blood pressure control. Rather: **A + C + D** or **B + C + D**

49.15 Hypertensive encephalopathy

Hypertension with changes in mental status and/or seizures. Other manifestations are:

- Facial palsy
- Visual changes→blindness
- Coma

Pathophysiology: Disruption of the normal autoregulatory mechanisms of cerebral blood flow. The inability of cerebral vasculature to constrict appropriately in response to the abrupt increase in cerebral blood flow leads to cerebral hyperperfusion. Generally, short-acting antihypertensives are preferred in the initial instance of treatment so that any potentially harmful drop in blood pressure (which could lead to Posterior Reversible Encephalopathy Syndrome {PRES}) could be reversed. Subsequently, long-acting agents could be used Sublingual nifedipine could cause a precipitous drop in blood pressure so it is best avoided or should be used with extreme caution.

Treatment outline:

- Use anti-hypertensive drugs
- Blood pressure should be brought down slowly to a desirable level (?stage I) by 48hrs (though not to normal levels) as follows:
  - 1/3 of total blood pressure reduction in 1st 12-hrs
  - Next one-third of the subsequent 12-hrs
  - Final one-third over 24-hrs
- Alternatively, by a quarter within 6 hours, and the rest in the next 24-36hrs

Commonly preferred drugs include Labetalol infusion, Na nitroprusside infusion, and IV hydralazine infusion. After achieving the desired blood pressure target, oral antihypertensives are then started.

50 Urinary Tract Infection

50.1 Introduction

Urinary tract infection (UTI) is one of the most frequent bacterial infections in childhood, second only to respiratory infections. It represents an invasion of the urinary tract by pathogenic microorganisms, most commonly *Escherichia coli*.
In children, UTI can occur at any age and often presents with non-specific symptoms, especially in neonates and infants. Because the infection may indicate underlying structural or functional abnormalities of the urinary tract, careful diagnosis and follow-up are essential.

Globally, and in Ghana, UTI contributes significantly to paediatric morbidity and can lead to long-term complications such as renal scarring, hypertension, and chronic kidney disease if not promptly treated.

50.2 Epidemiology

The incidence of UTI in children varies with age and sex: - In the **neonatal period**, UTIs are more common in boys, particularly those who are uncircumcised. - After infancy, the **female-to-male ratio** increases sharply because of the shorter urethra and its proximity to the anus. - Approximately **8% of girls and 2% of boys** experience at least one symptomatic UTI before 7 years of age. - Recurrence rates may reach **30–40%**, especially among those with vesicoureteral reflux (VUR) or bladder dysfunction.

In low- and middle-income countries such as Ghana, poor hygiene, delayed treatment of fever, and limited access to imaging services may contribute to underdiagnosis and recurrent infections.

50.3 Aetiology and Risk Factors

50.3.1 Microbiology

- **Gram-negative bacilli** are predominant:
  - *Escherichia coli* (responsible for 70–90% of cases)

  - *Klebsiella*, *Proteus*, *Enterobacter*, *Pseudomonas*

- **Gram-positive organisms** such as *Enterococcus faecalis* and *Staphylococcus saprophyticus* are less common.
- In neonates, *Group B Streptococcus* and *Staphylococcus aureus* may be isolated.

50.3.2 Predisposing Factors

1. **Anatomical abnormalities** — posterior urethral valves, vesicoureteral reflux, hydronephrosis.
2. **Functional abnormalities** — neurogenic bladder, constipation, dysfunctional voiding.
3. **Incomplete bladder emptying** or **obstruction**.
4. **Poor perineal hygiene** and **urinary stasis**.
5. **Uncircumcised males** — foreskin colonization increases bacterial adherence.
6. **Instrumentation** — catheterization or cystoscopy.
7. **Systemic conditions** — diabetes mellitus, immunodeficiency, malnutrition.
8. **Dehydration** and inadequate fluid intake.

50.4 Pathophysiology

UTI occurs when microorganisms colonize the periurethral area and ascend through the urethra into the bladder (cystitis) and, in some cases, further to the kidneys (pyelonephritis).

50.4.1 Mechanisms

- **Ascending infection:** the most common pathway; bacteria migrate from the perineum, facilitated by poor hygiene or reflux.
- **Hematogenous spread:** less common; seen in neonates or immunocompromised children with bacteremia.
- **Lymphatic spread:** rare and of uncertain significance.

Virulence factors of uropathogens include: - **Fimbriae (pili):** enhance adherence to uroepithelial cells. - **Capsular polysaccharides:** resist phagocytosis. - **Hemolysins and toxins:** cause epithelial injury. - **Biofilm formation:** enables persistence and recurrence.

Host defenses such as urine flow, mucosal IgA, and epithelial turnover normally prevent infection. When these defenses are impaired, infection takes hold.

50.5 Classification

UTIs are classified based on location, severity, and recurrence.

50.5.1 Based on Location

- **Lower UTI (Cystitis):** infection confined to bladder and urethra.
- **Upper UTI (Pyelonephritis):** infection involves renal parenchyma, usually with systemic features.

50.5.2 Based on Severity

- **Uncomplicated:** infection in an otherwise healthy urinary tract.
- **Complicated:** associated with structural/functional abnormalities or systemic illness.

50.5.3 Based on Recurrence

- **Recurrent UTI:** 2 episodes in six months or 3 within a year.
- **Relapse:** infection by same organism within two weeks of treatment.
- **Reinfection:** infection by a new organism after successful therapy.

50.6 Clinical Features

The presentation varies with age, making clinical suspicion critical.

50.6.1 Neonates and Infants

- Fever (may be absent in neonates)
- Poor feeding, vomiting, lethargy
- Jaundice
- Failure to thrive
- Hypothermia or irritability

50.6.2 Older Children

- Dysuria, frequency, urgency
- Suprapubic pain
- Foul-smelling or cloudy urine
- Hematuria
- Fever and flank pain (if pyelonephritis)

50.6.3 School-Age and Adolescents

- Classic lower tract symptoms (frequency, dysuria)
- Abdominal or flank pain
- Occasionally incontinence or enuresis

Because symptoms are often non-specific, any child with unexplained fever, particularly under 2 years of age, should be evaluated for UTI.

50.7 Differential Diagnosis

- Viral cystitis
- Vulvovaginitis or balanitis
- Appendicitis
- Gastroenteritis
- Renal stones
- Glomerulonephritis (if hematuria and proteinuria present)
- Fever of unknown origin

50.8 Investigations

50.8.1 Urine Collection Methods

Accurate diagnosis depends on obtaining a clean sample. - **Clean-catch midstream urine** (toilet-trained children). - **Catheterization** or **suprapubic aspiration** (infants). - **Urine bag collection** — often contaminated; used only for screening.

50.8.2 Laboratory Evaluation

1. **Urinalysis**
   - **Leukocyte esterase and nitrite tests:** simple bedside screening.
   - **Microscopy:** 5–10 WBCs per high-power field suggests infection; presence of bacteria reinforces diagnosis.
2. **Urine Culture**
   - Gold standard for diagnosis.
   - Significant growth:
     - 10 CFU/mL (clean catch)
     - 10 CFU/mL (catheter specimen)
   - Identifies organism and antibiotic sensitivity.
3. **Blood Tests**
   - Full blood count (raised WBC count).
   - ESR or CRP (elevated in pyelonephritis).
   - Renal function tests (urea, creatinine, electrolytes).
4. **Imaging Studies**
   - **Renal and bladder ultrasound:** after first febrile UTI to detect structural anomalies.
   - **Micturating cystourethrogram (MCUG):** for recurrent or atypical cases to identify vesicoureteral reflux.
   - **DMSA scan:** assesses renal scarring and differential renal function.

50.8.3 Diagnostic Criteria

Diagnosis requires both **clinical features** and **microbiological evidence**.
In infants, UTI should be suspected in any febrile illness without an obvious focus, and confirmed through culture before or soon after antibiotic initiation.

50.9 Management

Prompt diagnosis and appropriate therapy are crucial to prevent renal damage.

50.9.1 1. Acute (Emergency) Management

Children presenting with fever, dehydration, vomiting, or systemic toxicity should be hospitalized and started on parenteral antibiotics after urine collection. - **Initial antibiotics (parenteral):** - Cefotaxime, ceftriaxone, or gentamicin (adjust to local resistance patterns). - **Supportive care:** - Adequate hydration (IV or oral). - Antipyretics and pain relief. - Monitor urine output and renal function.

50.9.2 2. Oral Therapy for Stable Patients

For older or less ill children with uncomplicated cystitis: - **Oral agents:** amoxicillin-clavulanate, cefixime, or cotrimoxazole (guided by culture). - Duration:
- Cystitis — 5–7 days
- Pyelonephritis — 10–14 days
Adjust antibiotics based on sensitivity results.

50.9.3 3. Follow-Up and Ongoing Management

- Reassess clinical response within 48–72 hours.
- Repeat urinalysis and culture after completion of therapy.
- Persistent fever or bacteriuria warrants imaging for obstruction or reflux.
- Evaluate for underlying abnormalities after first febrile UTI, especially in children <2 years.

50.9.4 4. Management of Recurrent UTI

- Identify and treat predisposing factors such as constipation, dysfunctional voiding, or vesicoureteral reflux.
- Prophylactic low-dose antibiotics (e.g., nightly nitrofurantoin or trimethoprim) may be considered for high-risk patients.
- Encourage regular voiding and adequate hydration.
- Periodic urine monitoring.

50.9.5 5. Management of Complicated UTI

Complicated cases (e.g., with obstruction, abscess, or sepsis) require: - Hospitalization - IV antibiotics (broader spectrum) - Possible urologic intervention - Multidisciplinary care with paediatric nephrology/urology teams.

50.10 Complications

Untreated or recurrent UTI can lead to: - **Renal scarring** and cortical atrophy. - **Hypertension** (secondary to scarring). - **Proteinuria and CKD.** - **Perinephric abscess.** - **Urosepsis**, especially in neonates. - **Growth retardation** in chronic cases.

50.11 Prevention

Preventive measures are essential, especially in endemic and resource-limited settings.

50.11.1 Behavioural and Hygiene Measures

- Encourage frequent voiding and complete bladder emptying.
- Ensure adequate hydration.
- Teach proper perineal hygiene (front-to-back wiping for girls).
- Avoid prolonged use of tight or synthetic clothing.
- Manage constipation promptly.

50.11.2 Medical Measures

- Early treatment of bladder dysfunction or obstruction.
- Circumcision may reduce risk in recurrent UTI among boys.
- Prophylactic antibiotics in selected high-risk children.
- Immunization and prompt care of febrile illness.

50.11.3 Community and Public Health Measures

- Improve sanitation and access to clean water.
- Educate parents and caregivers on recognizing early signs of UTI.
- Integrate UTI screening into child health programs.

50.12 Prognosis

With early diagnosis and appropriate management, most children recover fully without long-term sequelae.
However, risk of renal damage increases with: - Delayed treatment (>48 hours of fever) - Recurrent infections - Presence of vesicoureteral reflux or obstruction - Poor adherence to therapy

Regular follow-up and imaging, where feasible, are key to preserving renal function.

50.13 Summary

UTI in children is a common but potentially serious infection. The clinical picture varies with age, making early recognition essential.
Diagnosis requires proper urine collection and culture confirmation.
Treatment should be prompt, guided by local bacterial sensitivity patterns, and followed by evaluation for underlying structural abnormalities.

In Ghana and other similar settings, emphasis must be placed on hygiene, caregiver education, and accessible diagnostic services. Preventing renal damage through timely treatment remains the ultimate goal of managing childhood UTI.

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51 Hematuria

51.1 Introduction

Hematuria refers to the presence of red blood cells (RBCs) in the urine. It is one of the most common and sometimes alarming urinary findings in children. While it may be transient and benign in some cases, in others it may signal significant renal or urinary tract pathology requiring urgent evaluation.

In paediatrics, distinguishing between glomerular and non-glomerular causes is crucial, as it guides both investigation and management. In Ghana and other low- and middle-income countries, infections, post-streptococcal glomerulonephritis, and schistosomiasis remain prominent causes, although hereditary and structural causes are also seen.

51.2 Definitions and Classification

Hematuria can be:

- **Macroscopic (gross):** Urine is visibly red or cola-coloured.
- **Microscopic:** RBCs are seen only under the microscope (>5 RBCs per high-power field in a centrifuged sample).

It may also be **transient** (short-lived, e.g., after fever, exercise, or minor trauma) or **persistent** (detected on 3 separate occasions over weeks).

51.3 Pathophysiology

The appearance of RBCs in urine reflects disruption along any part of the urinary tract.

- **Glomerular hematuria** occurs when the glomerular basement membrane (GBM) is damaged, allowing RBCs to pass into Bowman's space. These cells are often dysmorphic due to osmotic and mechanical stress as they traverse the nephron.

- **Non-glomerular hematuria** arises from bleeding beyond the glomerulus — the renal pelvis, ureter, bladder, or urethra where RBCs maintain their normal morphology.

Mechanisms include:

1. **Inflammation:** As seen in glomerulonephritis or cystitis.
2. **Mechanical injury:** From stones or trauma.
3. **Vascular abnormalities:** Such as renal vein thrombosis.
4. **Neoplastic infiltration:** Tumours like Wilms' tumour or rhabdomyosarcoma.
5. **Coagulopathies:** Affecting hemostatic mechanisms.

51.4 Common Aetiological Categories

51.4.1 Glomerular Causes

Usually accompanied by proteinuria, hypertension, or oedema:

1. **Post-streptococcal glomerulonephritis (PSGN):** Common in school-age children following throat or skin infection.
2. **IgA nephropathy:** Episodic hematuria following infections.
3. **Alport syndrome:** Familial nephritis with sensorineural hearing loss.
4. **Lupus nephritis:** Especially in adolescents.
5. **Henoch–Schönlein purpura (HSP):** Vasculitic process involving the kidneys.

51.4.2 Non-glomerular Causes

Typically associated with pain, dysuria, or clots in urine:

1. **Urinary tract infection (UTI):** Very common in young children.
2. **Urolithiasis:** Can occur with dehydration or metabolic disorders.
3. **Trauma:** From catheterization, accidents, or abuse.
4. **Structural lesions:** Such as posterior urethral valves or hydronephrosis.
5. **Tumours:** Wilms' tumour, rhabdomyosarcoma.
6. **Schistosomiasis:** Common in endemic areas such as parts of northern Ghana.

51.4.3 Systemic Causes

- **Bleeding diatheses:** e.g., platelet disorders, hemophilia.
- **Sickle cell disease:** Due to papillary necrosis or microinfarction.
- **Drugs:** e.g., cyclophosphamide, anticoagulants.

51.5 Clinical Evaluation

A meticulous history and examination are the cornerstone of assessment.

51.5.1 History

Key aspects include:

1. **Duration and pattern:** Is it single episode or recurrent?
2. **Associated symptoms:** Dysuria, fever, flank pain, oedema, or rash.
3. **Colour of urine:** Bright red (lower tract), cola-coloured (glomerular).
4. **Timing during micturition:** Initial (urethral), terminal (bladder neck), or total (upper tract).
5. **Recent infections:** Especially sore throat, skin lesions, or diarrhoea.
6. **Family history:** Kidney disease, hearing loss, or stones.
7. **Exposure:** To schistosomiasis, drugs, or toxins.

51.5.2 Examination

Focus on:

1. **General appearance:** Pallor (anemia), oedema (nephritis/nephrotic syndrome), or rash (vasculitis).
2. **Vital signs:** Hypertension suggests glomerular disease.
3. **Abdominal exam:** Palpable kidneys, masses, tenderness.
4. **ENT and hearing assessment:** For Alport syndrome.
5. **Skin and joint findings:** Indicate systemic disease (HSP, lupus).

51.6 Laboratory and Imaging Investigations

Investigations are guided by clinical suspicion.

1. **Urinalysis:**
    - Confirm presence of RBCs.
    - Assess for proteinuria, casts, or infection.
    - Dysmorphic RBCs or red cell casts → glomerular origin.
2. **Urine culture:**
    - Especially when infection suspected.

3. **Urine microscopy:**
    - Crystals (stones), schistosome ova, or RBC morphology.
4. **Blood tests:**
    - Full blood count (infection, anaemia).
    - Serum creatinine and urea (renal function).
    - Complement levels (low in PSGN).
    - ASO titre (evidence of streptococcal infection).
    - Autoimmune screen (ANA, anti-dsDNA).
5. **Imaging:**
    - **Renal ultrasound:** Detects structural abnormalities, masses, or hydronephrosis.
    - **CT scan:** For stones or tumours if indicated.
    - **Cystoscopy:** Rarely needed in children.
6. **Special tests:**
    - **Hearing test:** In suspected Alport syndrome.
    - **Renal biopsy:** For persistent hematuria, nephritic/nephrotic syndrome, or unexplained renal impairment.

51.7 Differential Diagnosis

Differentiate between glomerular and non-glomerular hematuria and other causes of red urine such as: - Hemoglobinuria or myoglobinuria (clear on centrifugation, dipstick positive but no RBCs). - Beetroot ingestion or drug-induced discoloration (rifampicin, phenazopyridine). - Porphyria (rare).

51.8 Management

The approach depends on the cause and severity.

51.8.1 General Principles

- **Reassurance and follow-up:** For isolated microscopic hematuria without other abnormalities.
- **Treat underlying cause:** Infection, stones, glomerulonephritis, etc.
- **Monitor renal function:** Especially in recurrent or persistent cases.

51.8.2 Specific Management

- **UTI:** Appropriate antibiotics based on culture.
- **PSGN:** Rest, salt restriction, antihypertensives, diuretics if needed.
- **HSP nephritis:** Supportive, steroids if severe.
- **Alport syndrome:** ACE inhibitors to reduce proteinuria, monitor progression.
- **Stones:** Hydration, pain relief, urologic intervention.
- **Schistosomiasis:** Praziquantel, and public health measures.
- **Bleeding disorders:** Correction with factor replacement or platelet transfusion.

51.9 Complications

If left untreated or unrecognized:

1. **Chronic kidney disease (CKD).**
2. **Hypertension.**
3. **Anemia from recurrent bleeding.**
4. **Renal scarring** (after recurrent infection).
5. **End-stage renal disease** in hereditary nephropathies.

51.10 Prognosis

The prognosis varies:

1. Transient and benign causes (e.g., post-exercise, mild UTI) resolve completely.
2. Glomerulonephritis often resolves but may progress to CKD in severe cases.
3. Genetic or structural diseases require lifelong monitoring.
4. Early diagnosis and management significantly improve outcomes.

51.11 Prevention

Preventive strategies should address both infection-related and genetic causes:

1. Early treatment of streptococcal infections.
2. Improved sanitation and control of schistosomiasis.
3. Safe use of nephrotoxic drugs.
4. Genetic counselling for familial disorders.
5. Routine urine screening in school health programs.

51.12 Summary

Hematuria in children should never be dismissed without evaluation. The clinician must first confirm its presence, identify whether it is glomerular or non-glomerular, and systematically search for the underlying cause.

In Ghana, infection-related causes such as PSGN, UTI, and schistosomiasis remain predominant, but clinicians should maintain a broad differential including congenital and systemic conditions. A structured approach beginning with good history-taking, urinalysis, and targeted investigations—guides effective management and follow-up, ensuring children retain optimal renal function into adulthood.

52 Nephrotic Syndrome

52.1 Introduction

Nephrotic syndrome (NS) is a common renal disorder in childhood characterised by **massive proteinuria**, **hypoalbuminemia**, **generalised oedema**, and **hyperlipidemia**. It results from increased permeability of the glomerular basement membrane, allowing abnormal leakage of plasma proteins into urine.

It is a major cause of morbidity among Ghanaian children, particularly between the ages of **2 and 8 years**, and is a frequent reason for referral to paediatric renal clinics. Early recognition and appropriate management are critical to prevent complications such as infection, thrombosis, and renal failure.

52.2 Incidence and Epidemiology

Nephrotic syndrome is one of the most common glomerular diseases in children worldwide, but its pattern varies by geography and race.

- **Age:** Most cases occur between **2 and 8 years**, with a peak around **4 years**.
- **Sex:** There is a male predominance (M:F 2:1).
- **Geographical variation:**
  - In **Europe and North America**, **minimal change disease (MCD)** accounts for 70–90% of idiopathic cases.
  - In **West Africa**, including Ghana, **focal segmental glomerulosclerosis (FSGS)** is more common, and steroid resistance rates are higher.
- **Secondary nephrotic syndrome** may be seen with infections such as *hepatitis B*, *malaria*, *HIV*, or *systemic diseases such as lupus nephritis.*

52.3 Aetiology and Classification

Nephrotic syndrome can be classified into **primary (idiopathic)** and **secondary** forms.

52.3.1 Primary (Idiopathic) Nephrotic Syndrome

No identifiable systemic cause. Includes:

- **Minimal Change Disease (MCD)** – the most common cause in younger children; characterised by normal light microscopy but podocyte effacement on electron microscopy.
- **Focal Segmental Glomerulosclerosis (FSGS)** – affects older children; may follow MCD or occur de novo; associated with steroid resistance.
- **Membranoproliferative Glomerulonephritis (MPGN)** – uncommon but causes persistent proteinuria and reduced complement levels.

52.3.2 Secondary Nephrotic Syndrome

Occurs due to identifiable systemic or renal disorders:

- **Infections:** Hepatitis B, HIV, malaria, syphilis, tuberculosis.
- **Systemic diseases:** Systemic lupus erythematosus (SLE), Henoch-Schönlein purpura.
- **Drugs:** NSAIDs, gold salts, penicillamine.
- **Metabolic and inherited conditions:** Diabetes mellitus, amyloidosis, Alport syndrome.

53 Pathophysiology

The glomerular filtration barrier, comprising the endothelium, basement membrane, and podocyte layer, normally prevents large proteins, such as albumin, from passing into the urine.

In nephrotic syndrome:

- **Podocyte injury** or **loss of charge selectivity** leads to massive proteinuria (>40 mg/m^2/hr or >3.5 g/day).
- **Loss of plasma proteins**, especially albumin, reduces plasma oncotic pressure, resulting in fluid movement into interstitial spaces → **oedema**.
- **Hypovolemia** triggers activation of the renin–angiotensin–aldosterone system and antidiuretic hormone, worsening sodium and water retention.
- The liver's compensatory response increases lipoprotein synthesis → **hyperlipidemia** and **lipiduria**.

Thus, the four hallmark features are:

1. Proteinuria
2. Hypoalbuminemia
3. Oedema
4. Hyperlipidemia

53.1 Clinical Features

53.1.1 General Presentation

Onset is usually insidious over days to weeks.

Main features:

- **Oedema:** Initially periorbital (especially in the morning), then generalized (anasarca).
- **Ascites and pleural effusion:** From fluid transudation.
- **Weight gain:** Due to fluid retention.
- **Reduced urine output (oliguria):** Often dark and frothy.
- **Fatigue and anorexia.**

53.1.2 Examination Findings

- Puffy face, periorbital and pedal oedema
- Distended abdomen with ascites
- Pleural effusion causing respiratory distress.
- In advanced cases, scrotal or labial swelling
- Pulse may be small due to hypovolemia.
- Blood pressure is usually normal or slightly raised (if renal impairment develops)

53.2 Differential Diagnosis

Other causes of oedema in children must be considered:

Condition	Distinguishing Features
Acute glomerulonephritis	Haematuria, hypertension, mild proteinuria, elevated ASO titre
Congestive heart failure	Cardiomegaly, hepatomegaly, pulmonary congestion
Liver disease	Jaundice, hepatomegaly, abnormal LFTs
Protein-losing enteropathy	Diarrhoea, malabsorption features
Severe malnutrition (Kwashiorkor)	Wasting, dermatosis, low total protein and albumin

53.3 Investigations

53.3.1 Urine Studies

- **Dipstick:** Heavy proteinuria (3+).
- **24-hour urinary protein:** >40 mg/m^2/hr or spot protein/creatinine ratio >200 mg/mmol.
- **Microscopy:** Few red cells and casts (in MCD, urine is bland).
- **Lipiduria:** Fat droplets or "Maltese crosses" under polarised light.

53.3.2 Blood Tests

- **Serum albumin:** <25 g/L.
- **Serum cholesterol:** Often >6.5 mmol/L.
- **Electrolytes, urea, creatinine:** Assess renal function.
- **Complement levels (C3, C4):** Reduced in lupus and MPGN.
- **ASO titre, Hepatitis B, HIV screening** as indicated.

53.3.3 Imaging

- **Renal ultrasound:** Usually normal in MCD; may show increased echogenicity in chronic or secondary disease.
- **Chest X-ray:** May reveal pleural effusion.

53.3.4 Kidney Biopsy

Indicated when:

- Age <1 year or >10 years
- Gross haematuria
- Persistent hypertension or renal failure
- Low complement levels
- Steroid resistance or frequent relapses

53.4 Diagnosis

The diagnosis of nephrotic syndrome is made clinically and supported by laboratory findings:

Diagnostic criteria:

1. Proteinuria >3+ on dipstick
2. Serum albumin <25 g/L
3. Oedema
4. Hyperlipidemia

The child is classified based on steroid responsiveness as:

- **Steroid-sensitive nephrotic syndrome (SSNS)**
- **Steroid-resistant nephrotic syndrome (SRNS)**
- **Frequent relapser** or **steroid-dependent**

53.5 Management

The approach to treatment depends on the underlying cause and the child's response to steroids.

53.5.1 Emergency and Supportive Care

Hospital admission is warranted for the first presentation or severe relapse with anasarca.

Fluid and salt management

- Restrict sodium intake.
- Maintain appropriate fluid balance, usually restricted to insensible loss plus urine output.
- Daily weight and urine monitoring.

Management of hypovolemia

- Suspect if tachycardia, abdominal pain, or cold extremities occur.
- Give **10–20 mL/kg of 4.5% albumin** or normal saline cautiously, followed by furosemide.

Infection prevention

- High risk for peritonitis (commonly *Streptococcus pneumoniae*), cellulitis, and sepsis.
- Start **broad-spectrum antibiotics** if infection suspected.
- Pneumococcal and varicella vaccination recommended.

Nutritional support

- Adequate calories and protein (1–2 g/kg/day).
- Avoid high-fat diets to prevent exacerbation of hyperlipidemia.

53.5.2 Specific Treatment

53.5.2.1 Corticosteroid Therapy

Prednisolone remains the cornerstone of therapy for idiopathic nephrotic syndrome.

Initial episode (ISPN guidelines):

- **Prednisolone 60 mg/m²/day** (max 60 mg) for **4 weeks**, followed by
- **40 mg/m² on alternate days** for another **4 weeks**, then taper gradually.

Response monitoring:

- Daily urine dipstick for protein.
- **Complete remission:** 3 consecutive days of negative or trace proteinuria.

53.5.2.2 Relapse

Reappearance of proteinuria (3+) for 3 days after remission. Treat with **prednisolone 60 mg/m²/day** until remission, then taper.

53.5.2.3 Steroid-Resistant Nephrotic Syndrome (SRNS)

No remission after 4 weeks of adequate steroid therapy. - Evaluate for **secondary causes** or **FSGS** (via biopsy).

- Consider **calcineurin inhibitors** (cyclosporine or tacrolimus), **mycophenolate mofetil**, or **cyclophosphamide**.
- Manage under paediatric nephrology care.

53.5.3 Management of Complications

Complication	Management
Infection	Prompt antibiotic therapy; pneumococcal prophylaxis
Hypovolemia	Albumin infusion + diuretics
Thrombosis (DVT, renal vein)	Anticoagulation (heparin → warfarin)
Acute renal failure	Supportive care, treat underlying cause
Dyslipidemia	Dietary modification; statins if persistent
Hypertension	ACE inhibitors (enalapril) beneficial for proteinuria

53.5.4 Preparation for Discharge

Before discharge: - Ensure oedema resolution and stable renal function.

- Teach caregivers how to **check urine protein at home**.
- Educate on **signs of relapse** and infection prevention.
- Arrange follow-up schedule (weekly initially, then monthly).
- Encourage vaccination where indicated.

53.5.5 Long-Term Management and Follow-Up

- **Monitor relapses:** Up to 70% of idiopathic cases relapse within 6 months.
- **Minimise steroid toxicity**: Screen for growth retardation, obesity, cataracts, and hypertension.
- **Address psychosocial impact:** School attendance and family anxiety.
- **Nephrology referral:** For steroid dependence or resistance.

53.6 Complications

Acute

- Infection (spontaneous bacterial peritonitis, cellulitis)
- Hypovolemia and shock
- Thrombosis (renal vein, cerebral venous sinus)
- Acute renal failure

Chronic

- Persistent proteinuria leading to chronic kidney disease
- Growth retardation and delayed puberty
- Steroid toxicity (hypertension, osteoporosis, Cushingoid features)

53.7 Prevention

While idiopathic cases cannot be prevented, complications can be minimized by: - Early diagnosis and appropriate steroid therapy

- Routine immunization, especially **pneumococcal and varicella vaccines**
- Avoiding nephrotoxic drugs (e.g., NSAIDs)
- Educating families on prompt infection treatment
- Regular follow-up at renal clinics

53.8 Prognosis

- **Minimal Change Disease:** Excellent prognosis; over 90% achieve remission with steroids.
- **FSGS or secondary causes:** Higher risk of chronic renal failure.
- **Steroid-dependent or frequent relapsers:** Often require second-line therapy but may maintain long-term renal function.

Relapses often decrease with age, and most children achieve permanent remission by adolescence.

53.9 Conclusion

Nephrotic syndrome remains a significant paediatric renal disorder in Ghana, accounting for substantial hospital admissions and morbidity. The majority of cases respond well to corticosteroids, though steroid-resistant forms, particularly FSGS, are increasingly recognized. A sound understanding of its clinical features, complications, and management principles is essential for medical students and practitioners.

Timely diagnosis, infection control, family education, and close follow-up remain the pillars of good outcomes in paediatric nephrotic syndrome.

54 Nephritic Syndrome

54.1 Introduction

Nephritic syndrome is a clinical syndrome resulting from inflammation of the glomeruli, leading to impaired renal filtration. It is characterised by **haematuria, mild-to-moderate proteinuria, oedema, hypertension, and varying degrees of renal impairment**. Unlike nephrotic syndrome, in which protein loss predominates, nephritic syndrome reflects glomerular injury due to immune-mediated inflammation, leading to red cell leakage and reduced glomerular filtration.

In Ghana, as in many developing countries, **post-streptococcal glomerulonephritis (PSGN)** remains the most common cause in children. However, other glomerulonephritides such as lupus nephritis and IgA nephropathy are also encountered.

Understanding nephritic syndrome is important because timely diagnosis and appropriate management can prevent progression to chronic kidney disease.

54.2 Epidemiology

Nephritic syndrome can occur at any age but is most common in **school-aged children between 5 and 12 years**.

- **Sex:** Slight male predominance (M:F 2:1).
- **Geography:** Higher prevalence in areas with poor sanitation, overcrowding, and high incidence of streptococcal skin or throat infections.
- **Seasonal variation:** Cases often peak following outbreaks of streptococcal infections, especially during the dry or cold season.

In Ghanaian children, **acute post-streptococcal glomerulonephritis (APSGN)** accounts for the majority of nephritic presentations.

54.3 Aetiology and Classification

Nephritic syndrome can be classified according to **clinical course** (acute, rapidly progressive, or chronic) or **underlying aetiology** (primary renal vs secondary systemic causes).

54.3.1 Primary Glomerular Causes

- **Acute post-streptococcal glomerulonephritis (APSGN):**
  The classic cause in children, occurring 1–3 weeks after group A -haemolytic streptococcal pharyngitis or skin infection (impetigo).
- **IgA nephropathy (Berger's disease):**
  Characterised by recurrent haematuria, often following upper respiratory tract infection.
- **Membranoproliferative glomerulonephritis (MPGN):**
  Chronic immune complex–mediated inflammation causing persistent haematuria and proteinuria.
- **Rapidly progressive glomerulonephritis (RPGN):**
  Severe form with crescent formation in glomeruli and rapid loss of renal function.

54.3.2 2. Secondary Glomerular Causes

- **Systemic lupus erythematosus (SLE):** Immune complex deposition in glomeruli.
- **Henoch-Schönlein purpura (HSP):** IgA-mediated vasculitis involving the kidneys.
- **Infections:** Hepatitis B/C, malaria, HIV.
- **Endocarditis or shunt nephritis:** Chronic infection leading to immune complex glomerulonephritis.

54.4 Pathophysiology

Nephritic syndrome arises from **inflammation and proliferation within the glomeruli**, usually mediated by **immune-complex** deposition or **autoantibodies**.

The general sequence is as follows:

1. **Immune complex formation** (e.g., streptococcal antigens with antibodies).
2. **Deposition in glomerular capillaries** and activation of the **complement system**.
3. **Inflammatory response** → neutrophil and macrophage infiltration.
4. **Glomerular injury** → capillary wall thickening, cellular proliferation, and reduced surface area for filtration.
5. **Reduced glomerular filtration rate (GFR)** → salt and water retention → oedema and hypertension.

6. **Leakage of red cells and some protein** into urine → haematuria and mild proteinuria.

54.5 Clinical Features

54.5.1 History

The onset is usually acute, developing within days to weeks following a **streptococcal throat or skin infection**.

Key presenting symptoms:

- **Haematuria:** Brown, smoky, or cola-coloured urine.
- **Oliguria:** Decreased urine output due to reduced GFR.
- **Facial puffiness:** Particularly periorbital oedema, worse in the morning.
- **Mild generalized oedema.**
- **Headache or visual disturbances:** Due to hypertension.
- **History of sore throat or impetigo** 1–3 weeks prior to illness.

54.5.2 Physical Examination

- **Oedema:** Usually mild, periorbital, and pedal.
- **Blood pressure:** Elevated in most cases (may be severe).
- **Urine colour:** Dark, tea-coloured urine.
- **Signs of volume overload:** Raised jugular venous pressure, basal crepitations.
- **Other findings:** Pallor (anaemia), mild hepatomegaly.

54.6 Differential Diagnosis

Condition	Distinguishing Features
Nephrotic syndrome	Marked oedema, massive proteinuria, normal complement
Haemolytic uraemic syndrome	Triad of anaemia, thrombocytopenia, and renal failure following diarrhoea
IgA nephropathy	Recurrent macroscopic haematuria after respiratory infection
SLE nephritis	Photosensitive rash, arthritis, positive ANA
Acute interstitial nephritis	Drug exposure, eosinophiluria

54.7 Investigations

54.7.1 Urine Tests

- **Urinalysis:**
  - **Haematuria:** Dysmorphic RBCs and red cell casts are diagnostic.
  - **Proteinuria:** Usually mild to moderate (1–2+).
  - **Specific gravity:** Often raised due to oliguria.
- **Microscopy:** RBC casts, WBCs.

54.7.2 Blood Tests

- **Renal function:** Elevated urea and creatinine indicate impaired filtration.
- **Complement levels (C3):** Low in post-streptococcal GN, normal in IgA nephropathy.
- **ASO titre / anti-DNase B:** Elevated after streptococcal infection.
- **Serum electrolytes:** May show hyperkalaemia or hyponatraemia.
- **Full blood count:** Mild anaemia, leukocytosis possible.
- **Antinuclear antibody (ANA):** For suspected lupus nephritis.

54.7.3 Imaging

- **Renal ultrasound:** Normal or slightly enlarged kidneys with increased echogenicity.
- **Chest X-ray:** Pulmonary oedema or cardiomegaly from volume overload.

54.7.4 Kidney Biopsy

Indications include:

- Atypical course (no recovery after 2–3 weeks)
- Persistent renal dysfunction
- Gross proteinuria (>3 g/day)
- Absence of low complement
- Suspected lupus nephritis or RPGN

54.8 Diagnosis

Diagnosis is based on the presence of the following:

1. **Haematuria** (microscopic or macroscopic)
2. **Oliguria** with elevated urea and creatinine
3. **Mild-to-moderate proteinuria**
4. **Hypertension**
5. **History of preceding infection**

54.9 Management

Treatment of nephritic syndrome is mainly **supportive**, aimed at controlling hypertension, oedema, and preventing complications. The underlying cause guides specific therapy.

54.9.1 General Measures

- **Hospital admission** for monitoring of blood pressure, urine output, and renal function.
- **Bed rest** during the acute phase to reduce workload on kidneys.
- **Fluid restriction** to match output + insensible loss (usually 400–600 mL/m^2/day).
- **Sodium restriction** to prevent oedema and hypertension.

54.9.2 Control of Oedema

- **Loop diuretics (furosemide 1–2 mg/kg)** if the child is not oliguric.
- Avoid excessive diuresis in oliguric states to prevent hypovolemia.
- **Fluid overload** with pulmonary oedema may require **frusemide + antihypertensive therapy** or dialysis.

54.9.3 Hypertension Management

Hypertension in nephritic syndrome is mainly volume-dependent.

- **First-line:** Loop diuretics.
- **If persistent:** Add **nifedipine** or **hydralazine**.
- **Severe hypertension or hypertensive encephalopathy:** Use IV antihypertensives cautiously (e.g., labetalol infusion).

54.9.4 Infection Management

- If there is an ongoing streptococcal infection, give **benzathine penicillin** or **amoxicillin**.
- **Antibiotic prophylaxis** is not usually required once the infection has cleared.

54.9.5 Dietary Advice

- **Salt restriction** until oedema and hypertension resolve.
- **Protein intake:** Normal for age (avoid restriction unless renal failure develops).
- **Potassium restriction** if hyperkalaemia occurs.

54.9.6 Dialysis Indications

Dialysis may be required if there is: - Refractory fluid overload.

- Severe hyperkalaemia
- Rising urea/creatinine
- Uremic encephalopathy or seizures

54.10 Specific Therapy

54.10.1 Post-Streptococcal Glomerulonephritis

- Mainly supportive care.
- Prognosis excellent; most recover fully within 6–8 weeks.
- Persistent proteinuria or haematuria may last months.

54.10.2 IgA Nephropathy and MPGN

- Often chronic; may need **ACE inhibitors** or **immunosuppressants** (prednisolone, azathioprine).
- Regular follow-up of renal function is essential.

54.10.3 Lupus Nephritis

- Requires systemic corticosteroids and immunosuppressive therapy (mycophenolate mofetil or cyclophosphamide).
- Managed in collaboration with a paediatric nephrologist.

54.10.4 Rapidly Progressive Glomerulonephritis

- Aggressive management with high-dose corticosteroids, cyclophosphamide, and sometimes plasma exchange.
- Early treatment may prevent irreversible renal failure.

54.11 Complications

- **Hypertensive encephalopathy:** Seizures, vomiting, blurred vision.
- **Acute renal failure:** Due to severe glomerular inflammation.
- **Fluid overload:** Pulmonary oedema or heart failure.
- **Electrolyte imbalances:** Hyperkalaemia, hyponatraemia.
- **Chronic kidney disease:** From unresolved inflammation.

54.12 Prognosis

Most children with **post-streptococcal nephritic syndrome** recover completely.

- **Microscopic haematuria** may persist for up to 6–12 months.
- **Renal function** returns to normal in >95% of cases.
- **Poor prognostic factors:** Persistent hypertension, heavy proteinuria, reduced complement for >8 weeks, and histologic evidence of crescentic GN.

Chronic or secondary causes (e.g., lupus, MPGN) may progress to **end-stage kidney disease** if not adequately managed.

54.13 Prevention

- Early diagnosis and treatment of streptococcal infections (pharyngitis, impetigo).
- Improved sanitation and hygiene to reduce transmission.
- Community health education to promote prompt medical attention for children with swelling or dark urine.
- Regular follow-up for children with known glomerular diseases.

54.14 Conclusion

Nephritic syndrome in children, particularly post-streptococcal glomerulonephritis, remains a significant cause of acute kidney disease in Ghana. It typically follows streptococcal infection and manifests with haematuria, oedema, and hypertension. While most cases resolve spontaneously with supportive care, early recognition and careful monitoring are essential to prevent complications and chronic kidney damage. A solid grasp of its pathophysiology and management principles is crucial for medical students and paediatric practitioners, ensuring timely and appropriate care for affected children.

55 Kidney Failure

Kidney failure in children represents a significant cause of morbidity and mortality, especially in low- and middle-income countries such as Ghana. It may occur acutely, following a transient insult to the kidneys, or chronically, as the final stage of progressive renal disease. Understanding the causes, pathophysiology, clinical features, investigations, and management of kidney failure is critical for all medical students and healthcare providers involved in child health.

55.1 Introduction

Kidney failure refers to the inability of the kidneys to perform their normal regulatory, excretory, and endocrine functions. In children, it can present as **acute kidney injury (AKI)** or **chronic kidney disease (CKD)**. AKI involves a rapid decline in renal function over hours or days, while CKD involves irreversible deterioration over months or years. The distinction is important because their causes, management, and outcomes differ.

In sub-Saharan Africa, including Ghana, the prevalence of kidney failure is underestimated due to limited diagnostic resources. However, hospital-based data show that AKI is a common complication of severe infections, dehydration, and nephrotoxic exposure in children, while CKD often results from congenital anomalies or glomerular diseases.

55.2 Classification

Kidney failure in children can be classified as:

- **Acute Kidney Injury (AKI):**
  - Rapid onset (hours to days).
  - Often reversible if recognized and treated promptly.
  - Common causes: dehydration, sepsis, nephrotoxic drugs, malaria, and hemolytic uremic syndrome.
- **Chronic Kidney Disease (CKD):**
  - Gradual and irreversible loss of kidney function lasting over three months.

- Often associated with congenital anomalies, reflux nephropathy, or glomerular diseases.
- May progress to end-stage renal disease (ESRD), requiring dialysis or transplantation.

55.3 Epidemiology

Global data show that kidney failure accounts for approximately 1–3% of paediatric hospital admissions, though regional variations exist. In Ghana and similar settings, AKI is more frequent than CKD, with mortality rates reaching up to 30% due to late presentation and limited access to dialysis. CKD is less common but often underdiagnosed until advanced stages.

55.4 Aetiology

55.4.1 Acute Kidney Injury

1. **Pre-renal causes (impaired perfusion)**
   - Severe dehydration (e.g., diarrhoeal diseases)
   - Septic shock
   - Congestive heart failure
   - Hemorrhage
2. **Intrinsic renal causes**
   - Acute glomerulonephritis
   - Hemolytic uremic syndrome
   - Acute tubular necrosis
   - Nephrotoxins (e.g., aminoglycosides, NSAIDs, herbal medicines)
   - Malaria (especially falciparum infection)
3. **Post-renal causes (obstruction)**
   - Posterior urethral valves
   - Kidney stones
   - Tumours compressing urinary outflow

55.4.2 Chronic Kidney Disease

1. **Congenital anomalies of the kidney and urinary tract (CAKUT)**
    - Renal dysplasia
    - Obstructive uropathy
    - Vesicoureteral reflux
2. **Glomerular diseases**
    - Nephrotic and nephritic syndromes
    - Focal segmental glomerulosclerosis
    - Chronic glomerulonephritis
3. **Inherited and metabolic diseases**
    - Polycystic kidney disease
    - Cystinosis
    - Alport syndrome
4. **Systemic diseases**
    - Lupus nephritis
    - Sickle cell nephropathy

55.5 Pathophysiology

The kidneys maintain homeostasis through filtration, tubular reabsorption, secretion, and endocrine regulation. In kidney failure, these functions are impaired, leading to:

- **Accumulation of waste products:** Elevated blood urea nitrogen (BUN) and creatinine.
- **Fluid imbalance:** Volume overload, edema, and hypertension.
- **Electrolyte abnormalities:** Hyperkalemia, hyponatremia, and metabolic acidosis.
- **Endocrine dysfunction:** Reduced erythropoietin production causes anemia; decreased vitamin D activation leads to hypocalcemia and bone disease.

In CKD, progressive nephron loss leads to compensatory hyperfiltration in the remaining nephrons, which accelerates further damage, forming a vicious cycle that leads to end-stage disease.

55.6 Clinical Features

55.6.1 Acute Kidney Injury

- Oliguria or anuria
- Peripheral or generalised oedema
- Vomiting, lethargy, and poor feeding
- Hypertension
- Pallor (from anemia)
- Seizures due to uremic encephalopathy or electrolyte imbalance

55.6.2 Chronic Kidney Disease

- Growth retardation
- Persistent pallor and fatigue
- Polyuria and nocturia
- Bone deformities (renal osteodystrophy)
- Pruritus, anorexia, nausea, or vomiting
- Late-stage uremic symptoms: confusion, pericarditis, and bleeding tendency

55.7 Investigations

1. **Basic Laboratory Tests**
    - Serum creatinine, urea, electrolytes (Na , K , Cl , HCO)
    - Urinalysis (proteinuria, hematuria, specific gravity)
    - Urine output monitoring
    - Full blood count (for anemia and infection)
2. **Special Tests**
    - Renal ultrasound: kidney size, echogenicity, and obstruction
    - Renal biopsy (for glomerular diseases)
    - 24-hour urine protein estimation
    - Serum calcium, phosphate, alkaline phosphatase, and parathyroid hormone in CKD
3. **Imaging**
    - Voiding cystourethrogram (VCUG) for reflux nephropathy
    - DMSA or MAG3 scans for renal scarring or differential function

55.8 Management

55.8.1 Emergency Management (AKI)

- **Stabilization:**
  - Secure airway, breathing, and circulation.
  - Correct fluid deficits cautiously to avoid overload.
  - Treat underlying causes: antibiotics for sepsis, antimalarials, or stop nephrotoxic drugs.
- **Monitor urine output** with a catheter.
- **Manage complications:**
  - Hyperkalemia: calcium gluconate, insulin with glucose, and sodium bicarbonate.
  - Hypertension: diuretics, antihypertensives.
  - Dialysis if unresponsive or in severe uremia.

55.8.2 Ongoing Management (CKD and AKI Recovery)

- Maintain fluid and electrolyte balance.
- Nutritional support, adequate calories and protein.
- Control hypertension using ACE inhibitors or ARBs.
- Manage anaemia with erythropoietin and iron supplements.
- Prevent bone disease with phosphate binders and vitamin D analogues.

55.8.3 Renal Replacement Therapy

Indications include:

- Persistent hyperkalemia
- Severe metabolic acidosis
- Fluid overload unresponsive to diuretics
- Uremic complications (encephalopathy, pericarditis) Modalities:
- Peritoneal dialysis (preferred in infants and young children)
- Hemodialysis - Kidney transplantation (definitive for ESRD)

55.8.4 Preparation for Discharge

- Educate caregivers on dietary and medication adherence.
- Schedule follow-up with a paediatric nephrologist.
- Screen for underlying or recurrent causes.

55.8.5 Long-Term Management

- Regular monitoring of growth, blood pressure, and kidney function.
- Early management of infections.
- Psychosocial support for the child and family.
- Planning for eventual renal transplantation.

55.9 Complications

- Electrolyte disturbances (hyperkalemia, acidosis)
- Hypertension
- Chronic anemia
- Growth failure
- Bone deformities
- Cardiovascular disease (secondary to uremia)
- Infections due to immunosuppression
- Progression to ESRD

55.10 Prevention

- Prompt treatment of infections such as malaria and urinary tract infections.
- Avoidance of nephrotoxic drugs.
- Good hydration during illness.
- Early detection and referral of congenital renal anomalies.
- Regular follow-up for children with known renal disease.

55.11 Prognosis

The outcome depends on the underlying cause, promptness of treatment, and availability of renal replacement therapy.

- **AKI** has a good prognosis if managed early, though severe cases may progress to CKD.
- **CKD** often progresses to ESRD without timely intervention.
  Access to dialysis and transplantation markedly improves survival and quality of life.

55.12 Conclusion

Kidney failure in children is a major clinical problem requiring early recognition and multidisciplinary management. In resource-limited settings like Ghana, prevention through early diagnosis and community awareness remains the most effective strategy. Improving access to dialysis and transplant facilities is essential for long-term survival and better quality of life for affected children.

56 Obstructive Uropathy

56.1 Introduction

Obstructive uropathy refers to any structural or functional impediment to the normal flow of urine along the urinary tract, leading to an increase in intraluminal pressure and, ultimately, damage to the kidneys. The obstruction may occur at any point from the renal pelvis to the urethral meatus and may be **acute or chronic**, **partial or complete**, **unilateral or bilateral**.

In children, the condition is of particular concern because prolonged obstruction, even if partial, can lead to **irreversible renal parenchymal damage**, which has lifelong implications for growth, development, and renal function. Early recognition and prompt intervention are therefore essential.

In Ghana and other parts of sub-Saharan Africa, obstructive uropathy in children is not uncommon. The causes vary with age, ranging from **posterior urethral valves** in neonates and infants to **ureteropelvic junction obstruction** and acquired causes such as **stones** or **iatrogenic injury** in older children.

56.2 Basic Anatomy and Physiology

The urinary tract consists of:

- **Kidneys:** Filter blood to form urine.
- **Ureters:** Conduct urine from the kidneys to the bladder.
- **Bladder:** Stores urine temporarily.
- **Urethra:** Expels urine from the body.

Normal urine flow is maintained by a combination of:

1. The peristaltic activity of the ureters,
2. The presence of competent valves (such as the vesicoureteric junction),
3. Coordinated bladder contraction and sphincter relaxation.

Any lesion disrupting these mechanisms can cause obstruction and consequent back pressure on the kidneys, resulting in **hydronephrosis** and possible **renal impairment**.

56.3 Pathophysiology

When urine flow is obstructed, several changes occur in the urinary tract and renal parenchyma:

1. **Increased pressure proximal to the obstruction:** Leads to dilatation of the collecting system (hydronephrosis) and stretching of the renal capsule.
2. **Altered renal blood flow:** Initially, renal blood flow increases but eventually declines as interstitial pressure rises, leading to ischemic injury.
3. **Tubular dysfunction:** Impaired concentrating ability and reduced glomerular filtration rate (GFR).
4. **Inflammation and fibrosis:** Chronic obstruction leads to tubular atrophy, interstitial inflammation, and fibrosis, resulting in progressive loss of renal function.

The reversibility of renal damage depends on the **duration and severity** of the obstruction. Complete obstruction for more than a few weeks can cause **irreversible renal scarring**.

56.4 Classification

56.4.1 Based on Duration

- **Acute Obstructive Uropathy:** Sudden onset (e.g., calculus obstruction, trauma).
- **Chronic Obstructive Uropathy:** Long-standing (e.g., posterior urethral valves, congenital stenosis).

56.4.2 Based on Site

- **Upper tract obstruction:** Affecting renal pelvis or ureter.
- **Lower tract obstruction:** Involving the bladder or urethra.

56.4.3 Based on Laterality

- **Unilateral:** One kidney affected (may preserve overall renal function).
- **Bilateral:** Both kidneys affected (risk of renal failure).

56.4.4 Based on Nature of Lesion

- **Intrinsic:** Due to lesion within the urinary tract (e.g., valves, stricture, stone).
- **Extrinsic:** Due to external compression (e.g., tumour, retroperitoneal fibrosis).

56.5 Aetiology

The causes of obstructive uropathy in children vary by age group:

56.5.1 Neonates and Infants

- **Posterior urethral valves (PUV):** The most common cause in male infants.
- **Ureteropelvic junction (UPJ) obstruction**
- **Ureterovesical junction (UVJ) obstruction**
- **Prune-belly syndrome**
- **Congenital megaureter**

56.5.2 Older Children and Adolescents

- **Urolithiasis**
- **Urethral stricture (post-infective or traumatic)**
- **Pelvi-ureteric junction obstruction (if not detected earlier)**
- **External compression (tumours, retroperitoneal fibrosis)**
- **Neurogenic bladder dysfunction**

56.5.3 Acquired Causes (relevant in Ghana and sub-Saharan Africa)

- **Schistosomiasis (S. haematobium):** Chronic infection can lead to ureteric fibrosis and obstruction.
- **Tuberculosis:** Genitourinary TB may cause ureteric strictures.
- **Trauma:** Pelvic trauma from road traffic accidents or traditional circumcision mishaps.
- **Iatrogenic injuries:** Following urethral catheterisation or pelvic surgery.

56.6 Epidemiology and Local Context

In Ghana, the exact incidence of obstructive uropathy in children is not well documented due to limited national registry data. However, tertiary centres such as **Komfo Anokye Teaching Hospital** and **Korle Bu Teaching Hospital** frequently report cases, often presenting late with significant renal compromise.

Key local factors contributing to delayed diagnosis include:

- Limited access to antenatal ultrasound screening,
- Late referral from peripheral hospitals,
- Reliance on traditional herbal treatments before hospital presentation,

- Scarcity of paediatric urologists and specialized imaging facilities.

Commonly observed patterns:

- **Posterior urethral valves** remain the most frequent congenital cause in male infants.
- **Schistosomiasis-related strictures** and **ureteric calculi** are notable acquired causes in endemic rural areas, especially along the Volta Basin and northern Ghana.

56.7 Clinical Features

The presentation of obstructive uropathy depends on:

1. The site and degree of obstruction,
2. The duration (acute vs. chronic),
3. The age of the child.

56.7.1 Neonates and Infants

- **Antenatal hydronephrosis:** Detected on prenatal ultrasound.
- **Poor urine stream** or **dribbling of urine** (especially in boys with PUV).
- **Palpable bladder** or **abdominal distension**.
- **Failure to thrive** or **recurrent urinary tract infections (UTIs)**.
- **Azotaemia** or features of renal failure (e.g., vomiting, lethargy).

56.7.2 Older Children

- **Flank or abdominal pain** (colicky if due to stones).
- **Urinary frequency, urgency, or incontinence**.
- **Haematuria**.
- **Recurrent UTIs**.
- **Palpable kidney or bladder** on examination.
- **Hypertension** in chronic cases.
- **Signs of chronic renal insufficiency** (pallor, growth retardation).

56.8 Investigations

Investigations aim to:

1. Confirm the presence and site of obstruction,
2. Identify the underlying cause,

3. Assess renal function and the degree of damage.

56.8.1 Laboratory Investigations

- **Urinalysis:** Proteinuria, haematuria, pyuria, or evidence of infection.
- **Urine culture and sensitivity:** To guide antibiotic therapy.
- **Serum urea, creatinine, and electrolytes:** Assess renal function.
- **Full blood count:** Anaemia or infection.
- **Urine specific gravity:** Low in chronic cases due to tubular dysfunction.

56.8.2 Imaging Studies

56.8.2.1 Ultrasound (USS)

- First-line investigation.
- Detects hydronephrosis, hydroureter, bladder wall thickening, and residual urine.
- Antenatal ultrasound can detect hydronephrosis as early as the second trimester.

56.8.2.2 Micturating Cystourethrogram (MCUG)

- Essential for diagnosing **posterior urethral valves** and **vesicoureteric reflux**.
- Should be performed after treating any active UTI.

56.8.2.3 Diuretic Renogram (using MAG3 or DTPA)

- Differentiates between obstructive and non-obstructive dilatation.
- Provides functional information on differential renal function.

56.8.2.4 Intravenous Urography (IVU)

- May show delayed excretion, dilated calyces, or level of obstruction.
- Limited use in children due to radiation exposure and replaced largely by renography.

56.8.2.5 Other Imaging

- **CT Urography or MRI Urography:** For complex cases or extrinsic causes.
- **Cystoscopy:** Direct visualization of posterior urethral valves or strictures.

56.9 Management

Management depends on the **site, cause, and severity** of the obstruction, as well as the **presence or absence of renal failure**.

56.9.1 General Principles

1. **Prompt relief of obstruction.**
2. **Preservation of renal function.**
3. **Treatment of infection and prevention of recurrence.**
4. **Correction of underlying cause.**
5. **Long-term follow-up** for renal growth and function.

56.9.2 Initial Stabilization

- **Assess hydration status** and **correct electrolyte imbalance**.
- **Treat infections** aggressively with appropriate antibiotics.
- **Bladder decompression** using catheterization if there is lower tract obstruction.
- **Nephrostomy** or **ureterostomy** for upper tract obstruction if necessary.

56.9.3 Specific Treatment Based on Cause

56.9.3.1 Posterior Urethral Valves

- **Initial management:** Catheterization for bladder drainage.
- **Definitive management:** Endoscopic valve ablation (fulguration).
- In cases with severe renal impairment, **temporary vesicostomy** may be indicated.

56.9.3.2 Ureteropelvic Junction (UPJ) Obstruction

- **Observation** if mild and renal function preserved.
- **Surgical correction (pyeloplasty)** if obstruction is significant or progressive.

56.9.3.3 Ureterovesical Junction (UVJ) Obstruction / Megaureter

- **Reimplantation surgery** or **tailoring** of the ureter as needed.

56.9.3.4 Urolithiasis

- **Hydration and analgesia.**
- **Medical expulsive therapy** for small distal stones.
- **Surgical removal** (ureteroscopy or open surgery) for larger or impacted stones.

56.9.3.5 Schistosomiasis

- **Praziquantel** (40 mg/kg single dose) for all infected individuals.
- Management of resultant strictures may require **endoscopic or surgical correction**.

56.9.3.6 Neurogenic Bladder

- **Clean intermittent catheterization (CIC)**.
- **Anticholinergic medications** to reduce detrusor overactivity.
- **Bladder augmentation** in refractory cases.

56.9.4 Chronic Management

- **Monitoring renal function** periodically.
- **Blood pressure control** with antihypertensives if needed.
- **Treatment of recurrent infections.**
- **Nutritional support** to promote growth.
- **Parental counseling** regarding long-term prognosis.

56.10 Complications

- **Hydronephrosis**
- **Recurrent UTIs**
- **Hypertension**
- **Chronic kidney disease (CKD)**
- **Bladder dysfunction**
- **Growth retardation**
- **Electrolyte disturbances**

In Ghana, late presentation often means that children may already have advanced CKD by the time of diagnosis. This underscores the importance of early detection through **antenatal screening** and **newborn examination**.

56.11 Prevention and Early Detection

1. **Antenatal ultrasound** for detection of hydronephrosis.
2. **Neonatal screening** for poor urinary stream in male infants.
3. **Public education** on early symptoms and the need for prompt medical evaluation.
4. **Training of peripheral health workers** to identify signs of obstructive uropathy.
5. **Mass treatment and prevention of schistosomiasis** in endemic regions.

56.12 Prognosis

Prognosis depends on:

- Age at diagnosis,
- Duration and completeness of obstruction,
- Residual renal function,
- Presence of infections.

With **early diagnosis** and **appropriate intervention**, many children can achieve good long-term outcomes. However, delayed cases may progress to **chronic renal failure**, requiring dialysis or renal transplantation — services that are still limited in many parts of Ghana.

56.13 Key Points

- Obstructive uropathy is a major cause of preventable renal failure in children.
- Posterior urethral valves are the most common congenital cause in male infants.
- Early detection through antenatal and postnatal screening is critical.
- Management requires a multidisciplinary approach involving paediatricians, urologists, and nephrologists.
- In endemic areas, schistosomiasis remains a significant preventable contributor.

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57 Acid-Base Disorders

57.1 Introduction

Acid-base balance is vital for normal cellular metabolism and physiological function. In children, acid-base disturbances can arise from a variety of causes and often signal serious underlying pathology. The developing physiology of infants and children also makes them particularly vulnerable to imbalances.

This guide aims to provide medical students, particularly in Ghana, with a comprehensive understanding of acid-base disorders, their causes, clinical manifestations, diagnosis, and management, with a focus on conditions commonly encountered in paediatric practice in resource-limited settings.

57.2 Physiology of Acid-Base Balance

57.2.1 Normal pH and Buffer

- Normal arterial blood pH: **7.35 – 7.45**
- Key buffer systems:
  - **Bicarbonate buffer** (HCO / H CO)
  - **Phosphate buffer**
  - **Protein buffer (e.g., haemoglobin)**

57.2.2 Regulation Mechanisms

1. **Lungs**: Excrete CO (volatile acid)
2. **Kidneys**: Reabsorb bicarbonate and excrete H (non-volatile acids)
3. **Buffers**: Immediate but temporary pH regulation

57.3 Classification of Acid-Base Disorders

Acid-base disorders are classified as:

1. **Metabolic Acidosis**
2. **Metabolic Alkalosis**
3. **Respiratory Acidosis**
4. **Respiratory Alkalosis**

Each has **compensatory mechanisms** that attempt to restore pH toward normal.

57.4 Metabolic Acidosis

57.4.1 Definition

Characterized by **decreased pH and bicarbonate** (< 22 mmol/L)

57.4.2 Causes

In Ghana and other resource-limited settings, common causes include:

High Anion Gap	**Normal Anion Gap (Hyperchloremic)**
Diabetic ketoacidosis (DKA)	Diarrhea (bicarbonate loss)
Lactic acidosis (sepsis, hypoxia, severe anaemia)	Renal tubular acidosis (RTA)
Inborn errors of metabolism	Early renal failure
Uraemia	Use of carbonic anhydrase inhibitors

Anion Gap (AG) = Na – (Cl + HCO)
Normal AG: 8 – 12 mmol/L

57.4.3 Clinical Features

- Kussmaul breathing (deep, rapid)
- Lethargy, confusion
- Hypotension
- Signs of dehydration

57.4.4 Diagnosis

- Arterial blood gas (ABG): ↓pH, ↓HCO
- Serum electrolytes
- Urine analysis (in RTA)
- Blood glucose and ketones (in DKA)

57.4.5 Management

- Treat the **underlying cause**
- Rehydration (e.g., with normal saline)
- **DKA**: Insulin therapy, fluids, potassium replacement
- **Severe acidosis (pH $<$ 7.1)**: Consider sodium bicarbonate cautiously
- Monitor electrolytes, especially **K**

57.5 Metabolic Alkalosis

57.5.1 Definition

Elevated pH and bicarbonate ($>$ 28 mmol/L)

57.5.2 Causes

Chloride-Responsive	**Chloride-Resistant**
Vomiting or nasogastric suction	Primary hyperaldosteronism
Diuretic therapy	Congenital adrenal hyperplasia
Volume depletion	Severe hypokalemia

57.5.3 Clinical Features

- Muscle cramps, weakness
- Tetany (due to hypocalcemia)
- Hypoventilation (compensatory)
- Confusion, seizures (severe)

57.5.4 Diagnosis

- ABG: ↑pH, ↑HCO
- Serum electrolytes: Look for **hypokalemia**, **hypochloremia**
- Urine chloride

57.5.5 Management

- Volume replacement with normal saline
- Potassium supplementation
- Correct underlying cause
- If resistant to saline: consider aldosterone antagonists (e.g., spironolactone)

57.6 Respiratory Acidosis

57.6.1 Definition

↓pH and ↑pCO (> 45 mmHg)

57.6.2 Causes

Due to hypoventilation:

- CNS depression (head injury, infections)
- Neuromuscular disorders (e.g., Guillain-Barré syndrome)
- Chest wall deformities
- Airway obstruction (e.g., asthma, foreign body)
- Respiratory muscle fatigue

57.6.3 Clinical Features

- Altered mental status
- Headache
- Tachycardia
- Cyanosis
- Papilledema (chronic)

57.6.4 Diagnosis

- ABG: ↓pH, ↑pCO
- Evaluate oxygenation (PaO)
- Chest X-ray, pulmonary function tests (if available)

57.6.5 Management

- Support ventilation (e.g., oxygen, non-invasive or mechanical ventilation)
- Treat the **underlying cause** (e.g., bronchodilators for asthma)
- Caution: Over-oxygenation can suppress respiratory drive in chronic cases

57.7 Respiratory Alkalosis

57.7.1 Definition

- ↑pH and ↓pCO (< 35 mmHg)

57.7.2 Causes

- Anxiety, pain (hyperventilation)
- Fever
- Sepsis
- Salicylate poisoning (early)
- Central causes (e.g., meningitis)
- High altitude (rare in Ghana)

57.7.3 Clinical Features

- Light-headedness, dizziness
- Perioral numbness
- Muscle cramps
- Tachypnoea

57.7.4 Diagnosis

- ABG: ↑pH, ↓pCO
- Serum calcium and phosphate (often decreased)

57.7.5 Management

- Address the underlying cause
- Calm the child (rebreathing bag if appropriate)
- Treat fever or infections
- Sedation may be necessary in extreme anxiety

57.8 Mixed Acid-Base Disorders

Children can present with **more than one disorder** simultaneously, especially in critical illness.

Examples:

- **DKA with vomiting** → Metabolic acidosis + metabolic alkalosis
- **Sepsis with respiratory failure** → Metabolic acidosis + respiratory acidosis

Clues to Mixed Disorders:

- pH is normal, but CO and HCO are abnormal
- Compensation appears inadequate or excessive

Use **Winter's formula** to assess expected respiratory compensation in metabolic acidosis:

Expected pCO $= (1.5 \times \text{HCO}) + 8 \pm 2$

57.9 Pediatric Considerations

- **Neonates** have immature kidneys → limited ability to excrete acid
- **Dehydration** is a common cause of acid-base disturbances
- **Malaria, severe diarrhoea, and pneumonia** are leading paediatric conditions in Ghana that may present with acid-base imbalance

57.10 Laboratory Evaluation

Key investigations:

1. **ABG Analysis**
2. **Serum electrolytes** (Na , K , Cl , HCO)
3. **Anion gap calculation**
4. **Urine pH and electrolytes** (in RTA)

5. **Lactate**, **ketones**, **glucose**

57.11 Approach to a Child with Suspected Acid-Base Disorder

1. **Assess airway, breathing, and circulation (ABC)**
2. **Clinical history**
   - Diarrhoea, vomiting, fever, polyuria
   - Diabetes, drug use
3. **Examination**
   - Level of consciousness
   - Respiratory pattern (Kussmaul, hypoventilation)
   - Signs of dehydration or oedema
4. **ABG + Electrolytes**
5. **Determine primary disorder and compensation**
6. **Treat the cause and monitor**

57.12 Resource-Limited Considerations (Ghana Context)

- ABGs may not be widely available — rely on **clinical signs**, **serum bicarbonate**, **venous blood gases**
- In emergencies, treat based on likely diagnosis (e.g., give fluids for suspected DKA even before lab confirmation)
- **Point-of-care testing** (glucometers, lactate meters) can aid rapid decision-making

57.13 Summary Table

Disorder	**pH**	**HCO**	**pCO**	**Compensation**
Metabolic Acidosis	↓	↓	↓ (respiratory)	Hyperventilation
Metabolic Alkalosis	↑	↑	↑	Hypoventilation
Respiratory Acidosis	↓	↑ (renal)	↑	Renal HCO retention
Respiratory Alkalosis	↑	↓ (renal)	↓	Renal HCO loss

57.14 Conclusion

Understanding acid-base disorders in children is crucial for early recognition and effective treatment, particularly in acute settings like emergency departments and paediatric wards. In Ghana, common contributors include dehydration from diarrhoea, infections, and diabetic ketoacidosis (DKA). A systematic clinical and laboratory approach allows timely diagnosis and management, even in resource-constrained environments.

Part VIII

Neurology

58 Basic Neuroscience

58.1 Introduction

Understanding paediatric neurology begins with grasping the fundamentals of the nervous system's anatomy and physiology. The nervous system in children is dynamic and continuously developing, exhibiting distinct features compared to that of adults.

a. **Structure and Development**

- The **nervous system** comprises the **central nervous system (CNS)**—brain and spinal cord—and the **peripheral nervous system (PNS)**—cranial and spinal nerves.
- **Neural tube development** begins in the third week of gestation, giving rise to the brain and spinal cord.
- **Myelination**, the process of forming the myelin sheath around neurons, continues from the prenatal stage into adolescence. In children, the degree of myelination affects neurological function and should be taken into consideration during assessments.

b. **Brain Regions and Functions**

- **Cerebrum**: Higher functions like cognition, voluntary movement, and perception.
- **Cerebellum**: Coordination, balance, and motor control.
- **Brainstem**: Regulates vital functions like respiration, heart rate, and consciousness.
- **Spinal cord**: Conveys messages between the brain and the rest of the body.

c. **Peripheral Nervous System**

- Consists of **motor, sensory**, and **autonomic** nerves.
- Motor neurons control muscle activity, while sensory neurons transmit information like pain, temperature, and proprioception.
- Autonomic nerves regulate involuntary functions (e.g., heart rate, digestion).

d. **Neurotransmitters**

- **Acetylcholine**, **dopamine**, **GABA**, and **glutamate** play crucial roles in neural signalling.
- Imbalances are implicated in various neurological disorders like epilepsy, movement disorders, and developmental conditions.

58.2 Pathological Processes in Neurology

Paediatric neurological diseases result from a variety of underlying mechanisms:

a. **Congenital Disorders**

- Neural tube defects (NTDs), e.g., spina bifida and anencephaly, due to folate deficiency in pregnancy. cy.
- **Cerebral palsy (CP)**: A group of permanent movement disorders from non-progressive disturbances in the developing foetal or infant brain.

b. **Genetic and Metabolic Disorders**

- **Neurocutaneous syndromes**: e.g., Tuberous Sclerosis and Neurofibromatosis.
- **Inborn errors of metabolism**: Can cause neurodegeneration or developmental delay (e.g., phenylketonuria, Tay-Sachs disease).

c. **Infectious Causes**

- **Meningitis**, **encephalitis**, and **brain abscesses** are common in low-resource settings.
- Causative agents include *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Herpes Simplex Virus*, and *Plasmodium falciparum* (cerebral malaria).

d. **Inflammatory and Autoimmune Conditions**

- **Acute disseminated encephalomyelitis (ADEM)**: Post-infectious or post-vaccination immune response.
- **Guillain-Barré Syndrome (GBS)**: Acute polyneuropathy causing weakness, often post-infection.

e. **Epilepsy and Seizure Disorders**

- **Febrile seizures** are common in Ghanaian children aged 6 months to 5 years.
- **Epilepsy** can be idiopathic, structural, metabolic, or secondary to infection or trauma.

f. **Trauma**

- Head injury from road traffic accidents or falls is a leading cause of morbidity.
- May result in skull fractures, intracranial haemorrhage, or brain oedema.

g. **Tumours**

- Paediatric CNS tumours include **medulloblastoma**, **astrocytoma**, and **ependymoma**.
- Present with increased intracranial pressure, focal deficits, or seizures.

58.3 Neurological Signs and Symptoms in Children

Children may not accurately describe their symptoms, so observation and parental history are crucial.

a. **Seizures**

- Generalized (tonic-clonic, absence) or focal.
- Observe the duration, type, postictal state, and presence of triggers (fever, sleep deprivation).

b. **Developmental Delay**

- Failure to achieve motor, cognitive, language, or social milestones.
- Global developmental delay affects multiple domains.

c. **Headache**

- Can result from infection (meningitis), intracranial pressure, or tension.
- Red flags: morning headache, vomiting, visual changes, altered consciousness.

d. **Ataxia and Gait Abnormalities**

- Unsteady gait or coordination problems can suggest cerebellar disease or vestibular dysfunction.
- Sudden onset may indicate infection, tumor, or intoxication.

e. **Altered Consciousness**

- Ranges from drowsiness to coma.
- Common causes: CNS infection, trauma, metabolic disturbances (e.g., hypoglycemia), or seizures.

f. **Motor Weakness and Paralysis**

- May be upper motor neuron (spasticity, brisk reflexes) or lower motor neuron (flaccidity, fasciculations).
- Acute flaccid paralysis is notifiable (e.g., poliomyelitis, GBS).

g. **Sensory Disturbances**

- Less commonly reported in young children.
- May include numbness, tingling, or loss of proprioception.

h. **Abnormal Movements**

- Includes tremors, chorea, dystonia, or tics.
- Seen in conditions like Sydenham chorea (post-streptococcal), dystonic CP, or genetic syndromes.

58.4 Localization Along the Neuro-axis

Understanding where a lesion is located helps narrow the differential diagnosis.

a. **Cerebral Cortex**

- Lesions cause **hemiparesis**, **seizures**, or **language deficits**.
- Can result from ischemia, trauma, infection, or malformations.

b. **Basal Ganglia**

- Involved in movement control.
- Disorders cause **involuntary movements** (e.g., chorea, dystonia).

c. **Brainstem**

- Cranial nerve deficits (e.g., facial palsy), eye movement abnormalities, and vital sign instability.
- Lesions are often life-threatening.

d. **Cerebellum**

- **Ataxia**, **dysmetria**, and **intention tremor**.
- Tumours or infections like cerebellitis are common culprits.

e. **Spinal Cord**

- **Motor and sensory level deficits**, reflex changes, and incontinence.
- Trauma or transverse myelitis is a common cause.

f. **Peripheral Nerves**

- Symmetrical weakness, absent reflexes, and distal sensory loss.
- Seen in GBS or hereditary neuropathies.

g. **Neuromuscular Junction**

- Fluctuating weakness, especially ocular and bulbar muscles.
- Example: Myasthenia Gravis.

h. **Muscle**

- Proximal weakness and hypotonia.
- Seen in **muscular dystrophies**, **myopathies**, and metabolic muscle diseases.

58.5 Basic Neurological Investigations

Timely and appropriate investigations help confirm clinical suspicion.

a. **Neuroimaging**

- **CT scan**: Good for acute trauma or haemorrhages. Widely available in Ghana, but it has been linked to radiation exposure.
- **MRI**: Better for soft tissue detail, congenital malformations, or tumours. Less accessible but ideal for subacute and chronic conditions.

b. **Electroencephalography (EEG)**

- Assesses the brain's electrical activity.
- Useful in seizure evaluation, epilepsy classification, and encephalopathy.

c. **Lumbar Puncture**

- Essential for evaluating CNS infections.
- CSF analysis helps differentiate bacterial, viral, or tuberculous meningitis.
- Ensure no signs of raised intracranial pressure before performing.

d. **Blood Tests**

- **CBC**, **electrolytes**, **blood glucose**, **renal/liver function**, **malaria test**.
- Metabolic screening for inborn errors if available.

e. **Nerve Conduction Studies (NCS)/Electromyography (EMG)**

- Evaluate peripheral nerve and muscle function.
- Useful in GBS, neuropathies, and myopathies.

f. **Genetic Testing**

- For suspected inherited or syndromic conditions.
- May be limited in availability and affordability.

58.6 Basic Neurological Procedures

These are diagnostic and sometimes therapeutic.

a. **Lumbar Puncture (Spinal Tap)**

- Performed in suspected meningitis, encephalitis, or to measure intracranial pressure.
- Atraumatic technique is important. Avoid in cases of suspected elevated ICP or spinal deformities.

b. **EEG Application**

- Involves placing electrodes on the scalp using the 10-20 system.
- Should be interpreted by trained personnel.

c. **Neuroimaging Requests**

- Clinicians should provide clear clinical information and suspected diagnosis when requesting CT/MRI.
- Sedation may be required in children for MRI.

d. **Muscle Biopsy**

- Used in diagnosing myopathies.
- Requires sterile technique and histopathological expertise.

e. **Botulinum Toxin Injections**

- Used for spasticity in conditions like CP.
- Requires experience and is often performed under sedation.

f. **CSF Shunt Insertion**

- Performed by neurosurgeons in hydrocephalus.
- Ventriculoperitoneal (VP) shunt is common. Risks include infection and obstruction.

58.7 Final Notes for Medical Students in Ghana

- Paediatric neurological disorders are common, and early recognition is crucial for better outcomes.
- Focus on **comprehensive history-taking** and **detailed neurological examination**.
- Understand the **developmental context**: some signs that are abnormal in adults are normal in infants (e.g., primitive reflexes).
- Pay attention to **public health issues** like malaria, meningitis, malnutrition, and trauma, which are common in Ghana and major contributors to paediatric neurological morbidity.
- Always consider **preventable causes**—promote antenatal care, immunizations (e.g., against polio, Hib, pneumococcus), good nutrition, and road safety.
- Collaborate with neurology, paediatrics, radiology, and rehabilitation teams when managing neurological cases.

59 Spectrum of Neurological Disorders

59.1 Introduction

Neurological disorders in children represent a diverse group of conditions that affect the brain, spinal cord, peripheral nerves, or neuromuscular junctions. These disorders can lead to developmental delays, motor dysfunction, seizures, and cognitive impairments. In Ghana, the burden of childhood neurological disorders is significant due to factors such as limited resources, perinatal complications, infections, malnutrition, and lack of early diagnosis and intervention.

Understanding the spectrum of pediatric neurological conditions is vital for early identification, diagnosis, treatment, and referral.

59.2 Classification of Pediatric Neurological Disorders

Neurological disorders in children can be classified into the following major categories:

1. Neurodevelopmental Disorders
2. Epileptic Disorders
3. Cerebrovascular Disorders
4. Neuromuscular Disorders
5. Infectious and Post-infectious Disorders
6. Metabolic and Genetic Disorders
7. Neurocutaneous Syndromes
8. Brain Tumors and Space-occupying Lesions
9. Head Trauma and Acquired Brain Injuries

59.3 Neurodevelopmental Disorders

These disorders typically manifest early in development and are characterized by impairments in personal, social, academic, or occupational functioning.

1. **Cerebral Palsy (CP)**

1. **Definition:** A group of permanent movement disorders due to non-progressive disturbances in the developing brain.
2. **Types:** Spastic (most common), dyskinetic, ataxic, and mixed.
3. **Causes:**
   - Perinatal asphyxia (common in Ghana)
   - Premature birth
   - Neonatal jaundice (kernicterus)
   - Infections (TORCH)

2. **Clinical Features:**

   - Delayed milestones
   - Abnormal tone (increased or decreased)
   - Reflex abnormalities

3. **Management:**

   - Multidisciplinary approach: physiotherapy, occupational therapy, antispastic medications (e.g., baclofen), orthopedic interventions.
   - Early intervention programs are critical.

B. Autism Spectrum Disorder (ASD)

- **Definition:** Neurodevelopmental disorder characterized by deficits in social interaction and communication, with restricted, repetitive behaviors.
- **Diagnosis:** Based on DSM-5 criteria.
- **Onset:** Before age 3.
- **Red Flags:**
  - Lack of eye contact
  - No single words by 16 months
  - No two-word phrases by 2 years
- **Management:**
  - Behavioral therapy
  - Speech therapy
  - Structured educational support

C. Attention-Deficit/Hyperactivity Disorder (ADHD)

- **Symptoms:** Inattention, hyperactivity, impulsiveness.
- **Diagnosis:** Based on clinical history and observation.
- **Management:**
  - Behavioral therapy
  - Medications (e.g., methylphenidate—rarely used in Ghana due to availability)

59.4 Epileptic Disorders

Epilepsy is a common neurological disorder in Ghanaian children due to high rates of perinatal insults, CNS infections, and trauma.

A. Seizure Classification

- Focal (Partial) Seizures
- Generalized Seizures
- Absence Seizures
- Febrile Seizures
- Infantile Spasms (West Syndrome)

B. Etiology

- Idiopathic (genetic)
- Structural (trauma, tumor)
- Metabolic (hypoglycemia, electrolyte imbalance)
- Infectious (meningitis, cerebral malaria)

C. Diagnosis

-
- Clinical history
-
- EEG
-
- Neuroimaging (CT or MRI if accessible)
-
- Blood tests for metabolic derangements
-

D. Management

-
- Acute seizure: Diazepam or lorazepam
-
- Long-term: Carbamazepine, sodium valproate, phenobarbital (commonly used in Ghana)
-

- Treat the underlying cause
-
- Educate caregivers
-

59.5 Cerebrovascular Disorders

Relatively rare but essential to consider.

A. Stroke in Children

-
- **Causes:**
  -
  - Sickle Cell Disease (SCD) is common in Ghana
  -
  - Congenital heart disease
  -
  - Infections (e.g., meningitis, endocarditis)
  -
-
- **Signs:**
  -
  - Hemiplegia
  -
  - Altered consciousness
  -
-
- **Diagnosis:**
  -

  - Neuroimaging
  -
  - Blood tests (e.g., sickling test)
  -

-
- **Management:**
  -
  - Supportive care
  -
  - Antiplatelets (aspirin)
  -
  - Transfusion in SCD
  -

-

59.6 Neuromuscular Disorders

These affect motor nerves, neuromuscular junctions, or muscles.

A. Duchenne Muscular Dystrophy (DMD)

-
- **Genetic disorder:** X-linked recessive
-
- **Onset:** 2–5 years
-
- **Signs:**
  -
  - Gower's sign
  -

  - Proximal muscle weakness
  -
  - Calf pseudohypertrophy
  -

-
- **Diagnosis:**
  -
  - Elevated CK
  -
  - Genetic testing (if available)
  -

-
- **Management:**
  -
  - Steroids
  -
  - Physiotherapy
  -
  - Monitor respiratory and cardiac function
  -

-

B. Guillain-Barré Syndrome (GBS)

-
- **Acute autoimmune polyneuropathy**
-
- **Trigger:** Often post-infectious (e.g., Campylobacter, CMV)
-
- **Symptoms:**

  -
  - Ascending paralysis
  -
  - Areflexia
  -
-
- **Management:**
  -
  - Supportive care
  -
  - IVIG (limited availability)
  -
  - Monitor respiratory function
  -
-

59.7 Infectious and Post-Infectious Disorders

A significant cause of neurological disease in children in Ghana.

A. Bacterial Meningitis

-
- **Causes:** *S. pneumoniae*, *N. meningitidis*, *H. influenzae*
-
- **Symptoms:**
  -
  - Fever, neck stiffness, bulging fontanelle (infants)
  -
  - Altered consciousness, seizures

  –
-
- **Diagnosis:**
  –
  – CSF analysis
  –
-
- **Complications:**
  –
  – Hydrocephalus
  –
  – Hearing loss
  –
  – Epilepsy
  –
-
- **Treatment:**
  –
  – IV antibiotics (ceftriaxone)
  –
  – Supportive care
  –
-

B. Cerebral Malaria

-
- **Caused by:** *Plasmodium falciparum*
-

- **Symptoms:**
  -
  - Seizures
  -
  - Coma
  -
-
- **Diagnosis:**
  -
  - Blood smear
  -
-
- **Treatment:**
  -
  - IV artesunate
  -
  - Anticonvulsants
  -
-
- **Prevention:**
  -
  - Insecticide-treated nets
  -
  - IPT in pregnancy
  -
-

C. Tuberculous Meningitis

-
- **Symptoms:**
  -
  - Gradual onset of fever, headache, vomiting, neck stiffness
  -
-
- **Diagnosis:**
  -
  - CSF (high protein, low glucose)
  -
  - GeneXpert (if available)
  -
-
- **Treatment:**
  -
  - Anti-TB drugs for 12 months
  -
  - Steroids (dexamethasone)
  -
-

59.8 Metabolic and Genetic Disorders

Rare, but often underdiagnosed in Ghana due to a lack of advanced diagnostics.

A. Phenylketonuria (PKU), Tay-Sachs, and Others

-
- **Symptoms:**
  -
  - Developmental delay
  -
  - Seizures
  -
  - Hypotonia
  -
-
- **Diagnosis:**
  -
  - Requires metabolic screening (Guthrie test—limited availability)
  -
-
- **Management:**
  -
  - Dietary modifications
  -
  - Genetic counseling
  -
-

B. Mitochondrial Disorders

-

- Often present with multisystem involvement.
-
- Poor feeding, lactic acidosis, seizures.
-

59.9 Neurocutaneous Syndromes

A. Tuberous Sclerosis Complex (TSC)

-
- **Signs:**
  -
  - Seizures (infantile spasms)
  -
  - Skin lesions (ash leaf spots, shagreen patches)
  -
  - Intellectual disability
  -
-
- **Diagnosis:**
  -
  - Clinical + imaging (MRI may show cortical tubers)
  -
-
- **Management:**
  -
  - Seizure control
  -
  - Multidisciplinary follow-up

  - –
-

B. Neurofibromatosis Type 1

-
- **Signs:**
  - –
  - Café-au-lait spots
  - –
  - Neurofibromas
  - –
  - Learning disabilities
  - –
-
- **Complications:**
  - –
  - Optic gliomas
  - –
-
- **Management:**
  - –
  - Surveillance for tumors
  - –
  - Genetic counseling
  - –
-

59.10 Brain Tumors and Space-Occupying Lesions

Though rare, brain tumors must be considered, especially in children with persistent headaches, vomiting, or seizures.

Common Types in Children:

-
- Medulloblastoma
-
- Astrocytoma
-

Symptoms:

-
- Headache
-
- Morning vomiting
-
- Papilledema
-
- Focal deficits
-

Diagnosis:

-
- CT/MRI
-
- Biopsy (if accessible)
-

Management:

-

- Surgical resection
-
- Radiotherapy
-
- Chemotherapy
-

59.11 Head Trauma and Acquired Brain Injury

Frequent in Ghana due to road traffic accidents and falls.

A. Types:

-
- Concussion
-
- Contusion
-
- Hematomas (epidural, subdural)
-

B. Signs:

-
- Loss of consciousness
-
- Vomiting
-
- Seizures
-
- Pupillary changes
-

C. Management:

-
- ABCs (Airway, Breathing, Circulation)
-
- Neuroimaging
-
- Neurosurgical referral
-

D. Prevention:

-
- Use of helmets, child restraints
-
- Public health education
-

59.12 Diagnostic Approach to a Child with Neurological Symptoms

1.
2. **History Taking**
    -
    - Antenatal, birth, and developmental history
    -
    - Family history
    -
    - Onset and progression of symptoms
    -
3.
4. **Physical Examination**

-
- Neurological exam: tone, reflexes, cranial nerves
-
- General exam: dysmorphic features, skin lesions
-

5.
6. **Investigations**
    -
    - Imaging (CT/MRI)
    -
    - EEG
    -
    - CSF analysis
    -
    - Laboratory (CBC, glucose, electrolytes, infection screening)
    -
    - Genetic/metabolic workup (if available)
    -
7.

59.13 Challenges in Ghana

-
- Limited access to pediatric neurologists
-
- Inadequate neuroimaging facilities in rural areas
-
- Delayed diagnosis and referral
-

- Financial constraints
-
- Stigmatization and lack of awareness
-

59.14 Recommendations for Medical Students and Health Workers

-
- Recognize early signs of neurological disorders
-
- Take a thorough developmental and birth history
-
- Use clinical judgment when diagnostic tools are limited
-
- Educate parents and caregivers
-
- Refer early to tertiary centers (e.g., Korle-Bu, Komfo Anokye Teaching Hospital)
-
- Advocate for public health interventions and awareness
-

59.15 Conclusion

Neurological disorders in children in Ghana are diverse, with significant morbidity. Early recognition, timely referral, and multidisciplinary care are crucial. Despite resource limitations, medical students and practitioners can make a significant impact through clinical acumen, advocacy, and community education.

60 CNS Infections

Central nervous system (CNS) infections are among the most serious medical conditions affecting children, often leading to high morbidity and mortality if not promptly diagnosed and treated. They include infections that involve the brain (encephalitis), meninges (meningitis), or both (meningoencephalitis). In sub-Saharan Africa, including Ghana, CNS infections are common due to the high burden of bacterial, viral, parasitic, and fungal diseases. Understanding the pathophysiology, presentation, and management of these infections is crucial for all medical students and clinicians caring for children.

60.1 Introduction

CNS infections encompass a spectrum of conditions caused by microorganisms that invade the central nervous system, leading to inflammation of the brain, spinal cord, or their protective coverings. The major forms are:

- **Meningitis:** Inflammation of the meninges, often bacterial or viral.
- **Encephalitis:** Inflammation of the brain parenchyma, usually viral.
- **Meningoencephalitis:** Combination of both meningitis and encephalitis.
- **Brain abscess:** Localized collection of pus within the brain.
- **Subdural or epidural empyema:** Collection of pus between meningeal layers or between dura and skull.

These infections are medical emergencies. Early diagnosis and aggressive management can prevent death and long-term neurological sequelae such as hearing loss, seizures, and cognitive impairment.

60.2 Epidemiology

CNS infections occur worldwide but are particularly common in low-resource settings.
In **Ghana and West Africa**, they remain leading causes of hospitalization and death in children under five years.

- **Bacterial meningitis** is endemic in the "meningitis belt," which includes northern Ghana, and outbreaks occur periodically.

- **Viral infections**, especially enteroviruses, herpes simplex virus (HSV), and arboviruses (e.g., West Nile virus), are also significant.
- **Parasitic infections** such as **cerebral malaria** remain a major cause of CNS involvement in endemic regions.
- **Fungal infections** (Cryptococcus neoformans, Candida species) occur primarily in immunocompromised children.

The burden of CNS infections in African countries is magnified by delayed presentation, limited access to diagnostic tools, and poor vaccination coverage.

60.3 Aetiology

60.3.1 Bacterial Causes

Common organisms vary by age:

- **Neonates:** Group B *Streptococcus*, *Escherichia coli*, *Listeria monocytogenes*.
- **Infants and young children:** *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae* type b (Hib).
- **Older children and adolescents:** *Neisseria meningitidis* and *Streptococcus pneumoniae*.

60.3.2 2. Viral Causes

- Enteroviruses (Coxsackie, Echovirus)
- Herpes simplex virus type 1 and 2
- Varicella-zoster virus
- Mumps and measles viruses
- Arboviruses (e.g., Japanese encephalitis, West Nile virus)

60.3.3 3. Parasitic Causes

- *Plasmodium falciparum* (cerebral malaria)
- *Toxoplasma gondii*
- *Trypanosoma brucei* (African sleeping sickness)

60.3.4 4. Fungal Causes

- *Cryptococcus neoformans*
- *Candida albicans*
- *Aspergillus* species (rare)

60.4 Pathophysiology

The CNS is normally protected by the **blood-brain barrier (BBB)** and the **meningeal layers**. Infection occurs when microorganisms breach these defenses via:

1. **Hematogenous spread**: The most common route, from systemic infection or nasopharyngeal colonization.
2. **Contiguous spread**: From otitis media, sinusitis, or mastoiditis.
3. **Direct inoculation**: From trauma, surgery, or congenital defects (e.g., spina bifida).
4. **Retrograde neuronal spread**: seen with HSV and rabies.

Once pathogens enter the CNS:

- They trigger an **inflammatory response** involving cytokines, prostaglandins, and leukocyte infiltration.
- This causes **cerebral edema**, **increased intracranial pressure (ICP)**, **reduced cerebral perfusion**, and **neuronal injury**.
- In meningitis, inflammation of the leptomeninges leads to **disruption of CSF flow** and **hydrocephalus**.
- In encephalitis, direct infection of neurons and glial cells causes **necrosis** and **demyelination**.

60.5 Clinical Features

The presentation depends on the child's age and the specific infection but can be broadly grouped.

60.5.1 In Neonates

- Fever or hypothermia
- Poor feeding and lethargy
- Irritability, high-pitched cry
- Bulging fontanelle
- Seizures

- Apnea or cyanosis

60.5.2 In Older Infants and Children

- Fever, headache, vomiting
- Neck stiffness (meningism)
- Photophobia
- Altered level of consciousness
- Seizures
- Signs of raised intracranial pressure (ICP): papilledema, bradycardia, hypertension, and irregular respiration (Cushing's triad)
- Focal neurological deficits (in encephalitis or abscess)

60.5.3 Specific Clues

- **Petechial rash** → *Neisseria meningitidis* infection.
- **Paralysis, ataxia, movement disorders** → viral encephalitis.
- **Severe anemia and coma** → cerebral malaria.

60.6 Differential Diagnosis

CNS infections must be differentiated from other causes of altered sensorium or seizures in children:

- Cerebral malaria
- Epilepsy or status epilepticus
- Febrile seizures
- Metabolic disorders (hypoglycemia, hyponatremia, uremia)
- Intracranial hemorrhage or tumor
- Toxic encephalopathy

60.7 Investigations

60.7.1 Laboratory Investigations

1. **Full blood count:** Leukocytosis in bacterial infections; lymphocytosis in viral causes.
2. **Blood cultures:** Identify causative bacteria in 30–50% of cases.
3. **Lumbar puncture (LP):**

- Gold standard for meningitis diagnosis unless contraindicated (e.g., raised ICP, focal neurological signs).
- **CSF findings:**
  - **Bacterial meningitis:** High protein, low glucose, turbid appearance, neutrophil predominance.
  - **Viral meningitis:** Normal or mildly elevated protein, normal glucose, lymphocyte predominance.
  - **Fungal/TB meningitis:** Elevated protein, low glucose, lymphocytes, positive India ink or acid-fast bacilli.

4. **CSF Gram stain and culture:** Identifies specific bacteria.
5. **Polymerase chain reaction (PCR):** Detects viral DNA/RNA (HSV, enteroviruses).
6. **Rapid antigen tests:** Useful for *Neisseria meningitidis*, *H. influenzae*, and *S. pneumoniae*.

60.7.2 Neuroimaging

- **CT or MRI brain** before LP if raised ICP or focal signs are suspected.
- May reveal cerebral edema, abscess, or hydrocephalus.

60.7.3 Other Tests

- Blood glucose and electrolytes.
- Malaria smear or rapid diagnostic test (to exclude cerebral malaria).
- HIV screening in chronic or atypical infections.

60.8 Management

CNS infections constitute a **medical emergency**. Prompt empirical therapy, supportive care, and control of complications are vital.

60.8.1 1. Initial Stabilization

- Airway, breathing, and circulation support.
- Control seizures with intravenous diazepam or phenobarbital.
- Manage raised ICP: elevate head, restrict fluids, give mannitol if needed.
- Correct dehydration, hypoglycemia, and electrolyte imbalance.

60.8.2 2. Empirical Antimicrobial Therapy

Start antibiotics **immediately after blood and CSF samples** are collected (or sooner if LP delayed).

60.8.2.1 Empirical Antibiotic Regimens:

- **Neonates:** Ampicillin + Gentamicin or Cefotaxime (covering GBS, *E. coli*, *Listeria*).
- **Infants and children:** Ceftriaxone or Cefotaxime ± Vancomycin (for *S. pneumoniae* resistance).
- **Suspected meningococcal infection:** Add high-dose Penicillin G or continue ceftriaxone.
- **TB meningitis:** Standard anti-TB therapy (HRZE) with adjunctive corticosteroids.
- **Fungal infections:** Amphotericin B or Fluconazole.
- **Cerebral malaria:** Intravenous artesunate.

60.8.2.2 Antiviral Therapy:

- For suspected HSV encephalitis → IV **Acyclovir** 10 mg/kg every 8 hours for 14–21 days.

60.9 Supportive Care

- **Antipyretics** for fever.
- **Fluid management:** Maintain euvolemia; avoid fluid overload.
- **Nutritional support:** Enteral feeding as soon as tolerated.
- **Seizure control:** Maintain anticonvulsant therapy.
- **Corticosteroids:** Dexamethasone 0.15 mg/kg every 6 hours for 4 days in bacterial meningitis due to *H. influenzae* or *S. pneumoniae* (reduces hearing loss risk).
- **Monitoring:** Vital signs, neurological status, urine output, and electrolyte balance.

60.10 Complications

CNS infections can lead to devastating outcomes if not promptly managed.

Early complications: - Seizures and status epilepticus

- Cerebral edema and herniation
- Hydrocephalus
- Subdural effusion or empyema

- Shock and multi-organ failure

Late complications:

- Hearing impairment
- Developmental delay and learning difficulties
- Epilepsy
- Vision loss
- Motor deficits (paresis, ataxia)
- Behavioral and cognitive problems

60.11 Prevention

60.11.1 Immunization

Vaccination remains the most effective preventive measure:

- **Haemophilus influenzae type b (Hib) vaccine**, introduced into Ghana's EPI, has drastically reduced cases.
- **Pneumococcal conjugate vaccine (PCV13)** protects against *Streptococcus pneumoniae*.
- **Meningococcal vaccine** useful during outbreaks in northern Ghana.
- **Measles and mumps vaccines** prevent postinfectious encephalitis.

60.11.2 Chemoprophylaxis

Close contacts of meningococcal meningitis cases should receive **Rifampicin**, **Ciprofloxacin**, or **Ceftriaxone** as prophylaxis.

60.11.3 Public Health Measures

- Early detection and treatment of ear and respiratory infections.
- Improved sanitation and reduced overcrowding.
- Health education and prompt healthcare-seeking behavior.

60.12 Prognosis

The prognosis of CNS infections depends on:

- The causative organism
- The age of the child
- Speed of diagnosis and initiation of treatment
- Availability of intensive care and rehabilitation

Mortality from bacterial meningitis in Africa remains between 15–30%. Survivors frequently suffer long-term sequelae, including hearing loss, epilepsy, and neurodevelopmental delays.

Viral meningitis usually has a good prognosis, while HSV encephalitis can cause permanent neurological impairment despite treatment. Cerebral malaria remains a leading cause of childhood neurological disability in endemic regions.

60.13 Conclusion

Central nervous system infections in children represent a critical emergency that demands prompt recognition and treatment. In Ghana and other tropical settings, bacterial meningitis, cerebral malaria, and viral encephalitis are the significant causes. Improved immunization coverage, early diagnosis, and effective antimicrobial therapy are essential to reduce mortality and prevent neurological sequelae. Strengthening laboratory capacity and surveillance systems will further enhance early detection and appropriate management.

61 Cerebral Palsy

61.1 Introduction

61.1.1 Definition

Cerebral palsy describes a group of permanent disorders of movement and/or posture resulting from non-progressive (static) disturbances (insult/injury) to the developing foetal or infant brain.

Although the injury is non-progressive (static), the neurological manifestations evolve.

Disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems, often accompany the motor disorders of cerebral palsy. Cerebral palsy was first described by Dr William Little in 1860. It is also known as Little's disease, cerebral paralysis, or static encephalopathy. It is usually evident by the time a child is 2 years old. The incidence is approximately 2.2 per 1,000 live births in well-resourced countries. The incidence is higher in lower- and middle-income countries (LMIC). Cerebral palsy is the most common cause of physical disability in children. It is associated with multiple comorbidities.

61.1.2 Classification of cerebral palsy

Cerebral palsy is traditionally classified based on the nature of the motor disorder (tone abnormality) and its topographical distribution. Using the motor disorder classification, cerebral palsy is categorized as spastic (pyramidal), dyskinetic (extrapyramidal or athetoid), ataxic, hypotonic, or mixed. Using the topographic distribution, cerebral palsy is classified as quadriplegia, diplegia, hemiplegia, triplegia, and monoplegia.

Recent classifications of cerebral palsy describe the functional assessment of motor abilities using an objective scale. Examples include:

- Gross Motor Functional Classification Scale (GMFCS) for gross motor function
- Manual Ability Classification System (MACS) for upper limb function
- Communication Functional Classification System (CFCS) for communication
- Eating and Drinking Ability Classification System (EDACS) for eating and Drinking

61.1.3 Aetiology and Risk Factors

The risk factors and aetiologies of CP can be grouped based on the timing of the insult as genetic, preconceptional, prenatal, perinatal, or postnatal.

Genetic causes/risk factors include

- Chromosomal syndromes
- Single gene or microdeletion syndromes

Preconceptional risk factors include:

- Maternal illness—seizures, intellectual disability, thyroid disease, iodine deficiency
- Maternal history of stillbirth or neonatal death
- Maternal age over 40
- Low socio-economic status

Prenatal risk factors

- Intrauterine infections (TORCHES)
- Placental abnormalities
- Bleeding in the second or third trimesters
- Eclampsia/pre-eclampsia

Chorioamnionitis

- Maternal drug use, e.g., alcohol, cocaine, cigarette
- Oligo/polyhydramnios
- Intrauterine growth restriction
- Multiple pregnancy

Perinatal risk factors

- Foetal distress
- Difficult deliveries
- Breech delivery
- Prolonged labour
- Instrumental deliveries incl. emergency caesarean section
- Meconium aspiration
- Birth asphyxia à Hypoxic ischaemic encephalopathy
- Birth injuries affecting the brain

Postnatal risk factors

- Prematurity
- Low birth weight

- Respiratory distress syndrome
- Hypoglycaemia
- Kernicterus à bilirubin-induced neurological dysfunction
- Neonatal seizures
- Infections, e.g., meningitis, encephalitis
- Trauma à head injuries
- Child abuse, e.g., shaken baby syndrome
- Strokes
- Submersion injuries

61.2 Types of cerebral palsy

61.2.1 Spastic Cerebral Palsy

This is the most common form of CP, accounting for about 70% of cases. It results from injury to the corticospinal (pyramidal) tract or the motor cortex. The features are usually not present at birth, but develop within the first 2 years of life, and include:

- Delayed motor milestones
- Hypertonia (spasticity)
- Hyperreflexia
- Seizures
- Intellectual/learning disability

Spastic CP is further classified based on the anatomical distribution as:

- Monoplegia
- Diplegia
- Hemiplegia
- Triplegia
- Quadriplegia

61.2.1.1 Spastic hemiplegia

This is when the weakness is on one side of the body. On the affected side, the upper limb is usually more severely affected than the lower limb. It results from focal pathology in the cerebral cortex, often due to cerebral malformations or vascular causes such as intrauterine haemorrhage.

Early manifestations of spastic hemiplegia include:

- Fisting on the affected side

- Early handedness (lateralization before 1 year of age)
- Delayed sitting (falls over as affected leg hyper-extends)
- The child does not bear weight on the affected side when held upright
- May not be recognized until 5-6 months of age or later

Late manifestations of spastic hemiplegia include:

- Spastic hemiplegic CP is the most ambulatory form of CP. They typically walk independently by the age of 3.
- Tiptoe walking in the affected foot
- Hemiplegic gait/hemiparesis
- Seizures may occur in 50-60% of patients, usually in the first 2 years of life.
- Intelligence may not be affected

61.2.1.2 Spastic diplegia

This affects all four limbs, but the lower limbs are severely affected, leaving the upper limbs relatively spared. Common etiologic or risk factors are prematurity and hypoxic-ischemic encephalopathy in the preterm infant. The pathological finding in the brain is periventricular leukomalacia.

Early manifestations in infants with spastic diplegia:

- They are usually alert and have good socialization
- Their hands open (no fisting)
- They have a normal tone (or even hypotonia) during the first 4 months
- Delayed motor milestones (They delay in sitting and often extend their legs when pulled to sit).

Late manifestations of spastic diplegia:

- They later develop increased tone in the lower limbs (especially in the hip adductors, hamstrings, and gastrocnemius)
- Also, increased deep tendon reflexes, clonus, and Babinski sign in the lower limbs.
- Commando crawling, bottom shuffling, or rolling movement
- Scissoring gait and tiptoeing when pulled to stand
- Delayed walking
- Hip subluxation in children with severe lower limb spasticity
- Usually normal intelligence
- Usually no seizures

61.2.1.3 Spastic quadriplegia

In this type of cerebral palsy, all four limbs are affected. It also affects the face, neck, and trunk. It is caused by diffuse brain injury, such as:

- Hypoxic-ischemic damage in a term infant
- Intrauterine disease
- Cerebral malformations

The typical pathological findings are watershed infarcts.

Early manifestations of spastic quadriplegic cerebral palsy are

- Poor socialization
- Poor neck control
- Infantile reflexes (Moro and tonic-neck) are obligatory, stereotyped, and persist after age 6 months
- The patient may be hypotonic in infancy and later evolve into spasticity.
- Cortical fisting in both hands

Late manifestations of spastic quadriplegia include:

- Severe to profound global developmental
- Microcephaly
- Seizures are common
- Severe intellectual disability
- Diffused increased tone
- Increased deep tendon reflexes, clonus, Babinski sign
- Supranuclear bulbar palsy (dysphagia, dysarthria) presenting as drooling and recurrent aspirations.
- They may never walk or sit alone
- They tend to have cortical visual impairment, disturbances in ocular motility, and hearing impairment.

Less common forms of spastic cerebral palsy are spastic triplegia and spastic monoplegia.

Figure **??** summarises the types of spastic cerebral palsy.

61.2.2 Dyskinetic cerebral palsy

This is also called extrapyramidal/choreoathetoid cerebral palsy. Common aetiologies for this form of cerebral palsy include kernicterus and sudden hypoxic-ischaemic episodes, as in uterine rupture or placenta abruptio. The brain pathology shows damage in the extrapyramidal system and the basal ganglia.

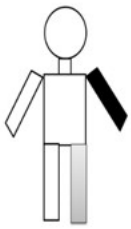
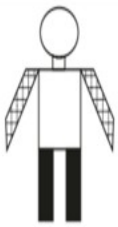
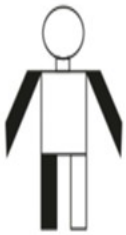
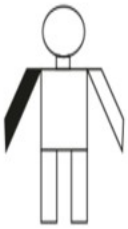
Topographical distribution					
Description	**Hemiplegia** One side of the body is affected. The arm is usually more involved than the leg	**Diplegia** All four limbs are involved. Both limbs are more severely affected than the arms	**Quadriplegia** All four limbs are involved	**Triplegia** Three limbs are involved, usually both arms and a leg	**Monoplegia** Only one limb is affected, usually an arm
Pathology	Focal lesion in one cerebral cortex	Periventricular leukomalacia	Watershed infarcts		

Figure 61.1: Types of spastic cerebral palsy

Early manifestations of dyskinetic cerebral palsy include:

- No choreoathetosis in the first 2 years of life
- Often hypotonic, but sometimes presents with fluctuating muscle tone
- Delayed motor milestones
- Poor neck control
- Sensorineural deafness
- Normal socialization

Late manifestations include:

- Movement disorders: Choreoathetosis, dystonia
- Symmetrical distribution
- Dental enamel dysplasia
- Difficulty with speech (dysarthria)
- Swallowing difficulty leading to drooling
- Affected children may or may not walk independently
- Intelligence can be normal
- Seizures are not common

61.2.3 Ataxic cerebral palsy

This results from damage to the cerebellum. Patients experience problems with balance and deep perception, presenting with an unsteady gait and difficulty with movement that requires a lot of control, such as writing. Their muscle tone may be increased or decreased.

61.2.4 Mixed cerebral palsy

Patients with mixed cerebral palsy have more than one type of cerebral palsy, usually a mixture of spasticity and athetoid movements, with tight muscle tone and involuntary reflexes. In mixed CP, different parts of the brain are affected. Figure **??** shows the topographical and physiologic classification of cerebral palsy.

61.3 Comorbidities of cerebral palsy

These are conditions that occur with greater frequency in children with cerebral palsy than in the general population. They include:

- Developmental delays
- Seizures

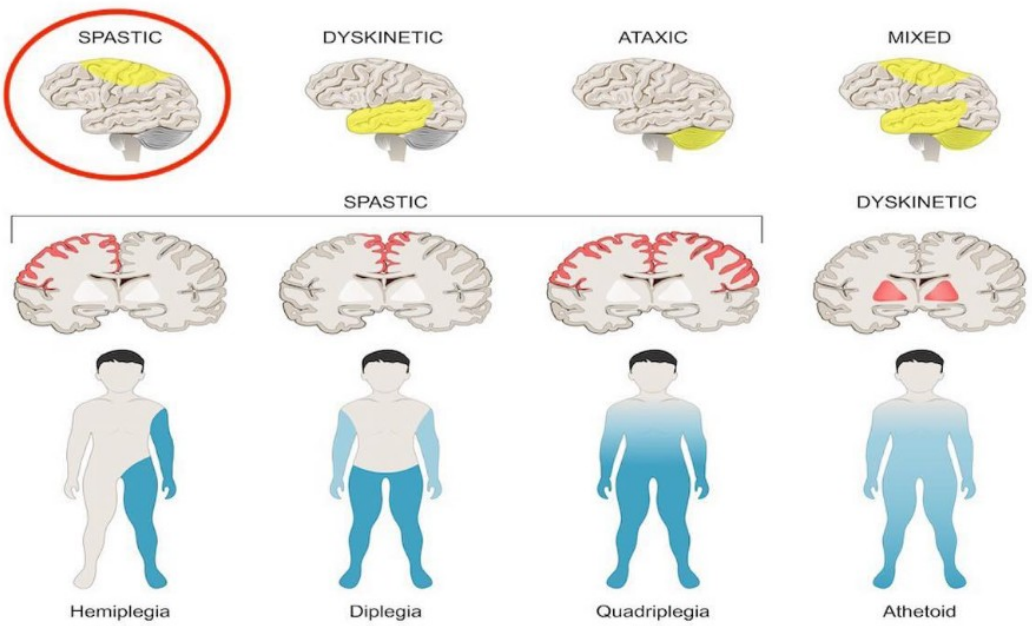


Figure 61.2: Topographical and physiologic classification of cerebral palsy

- Ophthalmologic/visual abnormalities including Cortical visual impairment, Disorders of ocular motility, Refractive errors, and Optic atrophy
- Hearing impairment
- Speech defects, including delayed speech, poor articulation, loss of voice modulation
- Learning/intellectual disability
- Feeding problems/swallowing difficulties
- Aspiration pneumonia
- Gastroesophageal reflux
- Gait abnormalities
- Contractures
- Hip subluxation
- Failure to thrive/neglect/abuse
- Behavioural and emotional problems such as ADHD, depression, and ASD

61.4 Diagnosis

The diagnosis of CP is clinical. It is based on the constellation of symptoms and signs in the affected child. Special investigations have a limited role in confirming the diagnosis but may contribute to determining the aetiology and the timing of the insult. Investigations may also help to exclude differential diagnoses and to identify comorbidities.

Investigations that may be employed include various modalities of neuroimaging, such as transcranial USG, brain CT scan, and brain MRI

Transcranial ultrasound: This is useful in the neonate up to 6 months, for the detection of large structural abnormalities

Brain CT Scan/MRI: These give a better definition of structures. The CT is used in children >1 year old due to the risk associated with radiation in younger children, while the MRI is helpful at any age. However, the MRI is more challenging to perform due to its limited availability, high cost, and the prolonged sedation required.

61.5 Features that suggest a progressive CNS disorder rather than CP

- Abnormally increasing head circumference: think hydrocephalus, tumour, leukodystrophies
- Eye abnormalities such as cataract, retinal pigmentary degeneration, optic atrophy: think neurodegenerative disease
- Skin abnormalities such as hypopigmentation, café-au-lait spots, nevus flammeus, etc: think neurocutaneous disorders, e.g., Sturge-Weber syndrome, neurofibromatosis, etc.
- Hepatomegaly with or without splenomegaly: think storage disease
- Sensory abnormalities: think peripheral nerve disorders.

Figure **??** lists a few examples of disorders that are sometimes misdiagnosed as cerebral palsy

Polyneuropathy	Ataxia	Spasticity-Chorea	Floppy
GM1 gangliosidosis	Abetalipoprteinaemia	Familial spastic paraplegia	Down syndrome
Hereditory motor and sensory neuropathies	Ataxia-telangiataxia	Lesch-Nyhan syndrome	Krabbe disease
Infantile neuroaxonal dystrophy	Friedreich ataxia	Niemann-pick disease	SMA
Leukodystrophy	Spinocerebellar ataxias	Rett syndrome	Hypothyroidism
			Myasthenia gravis

Figure 61.3: Disorders that are sometimes misdiagnosed as cerebral palsy

61.6 Management of the child with cerebral palsy

In the management of the child with cerebral palsy, the main goals of treatment should be to help the child reach their full potential by:

1. Maximizing mobility through physical therapy
2. Providing physical support using aids such as splints, walkers, and wheelchairs
3. Speech and occupational therapy
4. Surgery to correct abnormalities, improve mobility, and reduce spasticity
5. Special educational services

It is essential to adopt a multidisciplinary approach in the management of .the child with cerebral palsy. In contrast, the child remains under the care of one paediatrician, usually a developmental paediatrician.

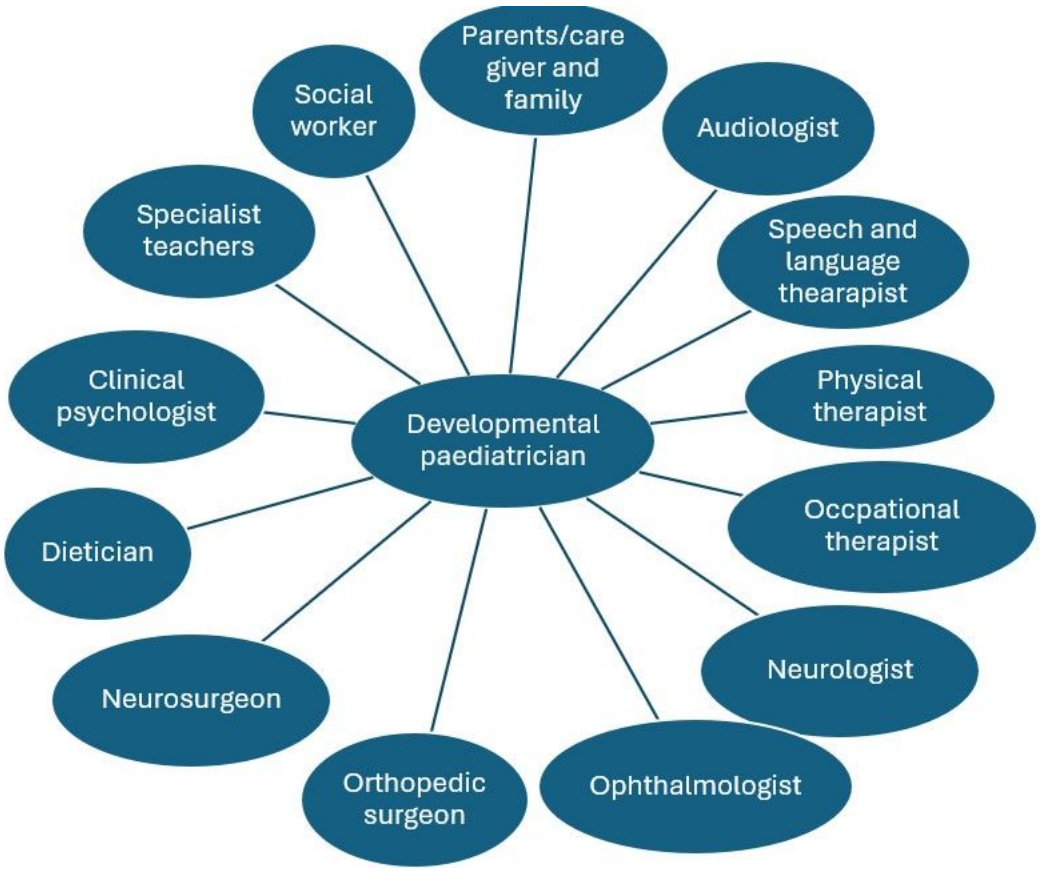


Figure 61.4: MDT management of cerebral palsy

The role of the multidisciplinary team (MDT) members in the management of cerebral palsy includes:

1. Developmental paediatrician – monitors a child's development and coordinates multidisciplinary care for the patient.
2. Neurologist – management of neurological disorders, including seizures and movement disorders.
3. Audiologist – hearing assessment
4. Speech therapist –assessment of speech and swallowing
5. Ophthalmologist – visual defects
6. Nutritionist/Dietician – growth failure, nutritional deficiencies
7. Specialist teachers
8. Physiotherapist – addressing spasticity, posture, and gait abnormalities, among others.
9. Orthopaedic surgeon – structural deformities, contractures, scoliosis.
10. Neurosurgeon – surgical management of spasticity and scoliosis.
11. Occupational therapist – difficulties with fine movements and activities of daily living (ADLs)
12. Clinical psychologist
13. Social/community worker

61.6.1 Management of spasticity

Spasticity may be focal or generalised, and treatment modalities are either reversible or permanent. For generalised spasticity, some reversible modalities used are oral therapy (baclofen, diazepam, etc.) and intrathecal baclofen pumps. Permanent modalities for generalised spasticity include deep brain stimulation and selective dorsal rhizotomy.

For focal spasticity, botulinum toxin A injection provides reversible relief, whereas focal surgeries, such as tendon release, provide permanent relief.

These are summarised in Figure **??** below.

61.7 Preventive strategies for cerebral palsy

1. Antenatal measures
    - Use of magnesium sulphate for neuroprotection
    - Use of antenatal corticosteroids in anticipated preterm deliveries
    - Tocolysis
    - Measures to prevent preterm births
    - Appropriate antibiotic use in PROM
    - Vaccination against rubella and congenital infections
    - Regular ANC check-ups
    - Avoid alcohol, tobacco, and drugs
    - Maintaining a healthy lifestyle for the mother

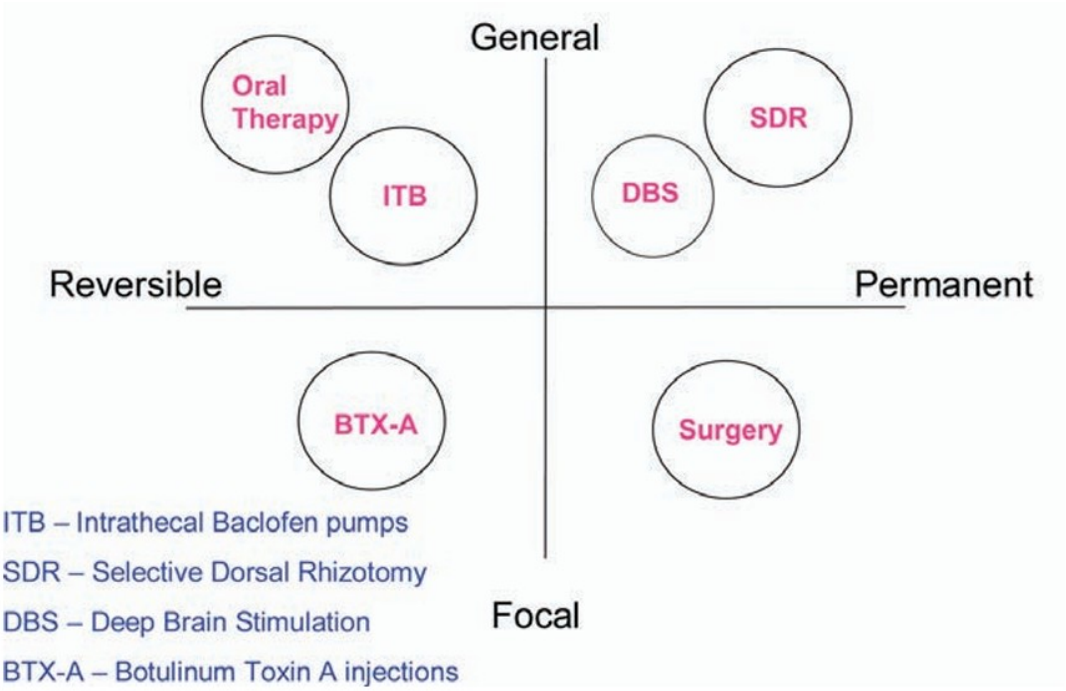


Figure 61.5: Management of spasticity in cerebral palsy

2. Perinatal/neonatal care
    - Early detection and management of neonatal care
    - Neuroprotection with moderate hypothermia for newborns with HIE
    - Avoidance of unnecessary oxygen supplementation
    - Early detection and treatment of neonatal hypoglycaemia
3. Postnatal and childhood care
    - Measures to prevent head injury, including the use of baby care seats, the prevention of falls, and shaking.
    - Genetic screening and counselling for families with cerebral palsy

61.8 Current innovations in the management of cerebral palsy

Systemic hypothermia: Controlled medical cooling of the body's core temperature may protect the brain and decrease the rate of death and disability from brain injuries. Hypothermia is effective in treating neurologic symptoms in babies with hypoxic-ischemic encephalopathy (HIE)

Stem cell therapy is being investigated as a potential treatment for cerebral palsy. Stem cells are capable of differentiating into various cell types within the body. Scientists are hopeful that stem cells may be able to repair damaged nerves and brain tissues. Clinical studies are examining the safety and tolerability of umbilical cord blood stem cell infusion in children with cerebral palsy.

61.9 Prognosis

Cerebral palsy is not a progressive condition, and so living into old age is possible. Regression or worsening of long-term symptoms is not characteristic. Prognosis varies according to the severity of the disorder. The lifespan of patients with cerebral palsy is usually reduced by complications such as reduced mobility, feeding difficulties, respiratory infections, and epilepsy. In the US, the average life span of patients with cerebral palsy was reported as 35 years in 2008.

62 Seizure Disorders

62.1 Introduction

The term seizure vaguely refers to anything that "seizes" or "takes hold" of a person. These may be epileptic or non-epileptic events. In this chapter, unless otherwise specified, the term seizure is used to refer to epileptic events.

62.2 Definitions

62.2.1 Seizures

The International League Against Epilepsy (ILAE) defines epileptic seizure as a *transient occurrence of signs and/or symptoms due to abnormal, excessive, or synchronous neuronal activity in the brain.* These may manifest as paroxysmal motor, sensory, autonomic, and/or behavioral or cognitive function abnormalities or impaired consciousness.

62.2.2 Convulsions

These are the motor manifestations of a seizure. These include tonic (stiffening), clonic (jerking), myoclonic (massive jerking), vibratory (trembling), or hypermotor (thrashing about). Seizures with no motor manifestations are termed non-convulsive and include motor arrest, e.g., unresponsive stare or drop attacks. Sensory disturbances during a seizure may include visual, auditory, or tactile disturbances. Some patients may describe changes in smell or taste.

Non-epileptic seizures in children include many events such as cardiac syncope, vasovagal syncope, breath-holding spells, infantile gratification, shuddering spells, etc. These are sometimes referred to as seizure mimics.

62.3 Classification of Seizures

The ILAE published its most recent classification of seizures in 2017. In this classification, seizures are broadly classified based on their onset within the brain as focal, generalized, or unknown onset.

- Focal-onset seizures originate from a focus within one hemisphere.
- Generalized-onset seizures originate from both hemispheres.
- Unknown onset – where the onset is not known at the time of the evaluation.

Focal-onset seizures (previously known as partial seizures) are further subclassified based on whether awareness is preserved or lost during the seizure and secondary generalization.

- Focal seizures with intact awareness (or focal aware seizures): These are focal seizures in which awareness is preserved. This was previously known as simple partial seizures.
- Focal seizures with loss of awareness (or focal unaware seizures): These are focal seizures in which awareness is lost during the event. They were previously referred to as complex partial seizures.
- Focal seizures evolving into bilateral tonic-clonic seizures: These are focal seizures that go on to become generalized. They were previously referred to as focal seizures with secondary generalization.

Generalised-onset seizures are further subclassified based on their manifestations as:

- Clonic seizures: having repetitive jerky movements.
- Tonic seizures: characterised by increased tone.
- Tonic-clonic seizures: They have two phases: a tonic phase and a clonic phase.
- Tonic-clonic-tonic, or other combinations
- Atonic seizures: These are characterized by loss of muscle tone, leading to drop attacks.
- Myoclonic seizures: These are characterized by sudden jerks of a group of muscles.
- Absence seizures: These are characterized by blank stares during which the patient loses awareness. They may be associated with lip-smacking or eyelid fluttering. A typical absence seizure starts abruptly, lasts about 5-15 seconds, and ends abruptly with no postictal events. An atypical absence may last >15 seconds or may have a slow recovery.
- Epileptic spasms: These are characterized by repetitive flexor (or extensor) jerks of the limbs and trunk, occurring in clusters.

62.4 Febrile seizures

62.4.1 Definition

A febrile seizure is accompanied by fever in a child aged 6 months to 6 years without intracranial infection/inflammation [ref]. It affects about 3% of all children between 6 months and 6 years

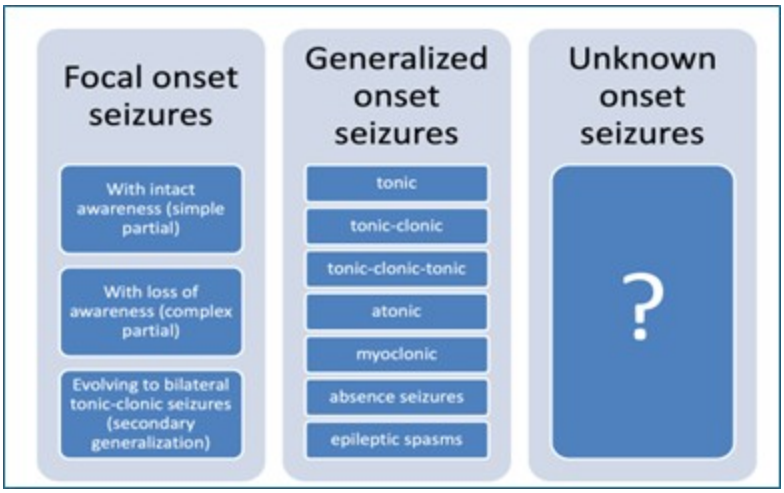


Figure 62.1: ILAE classification of seizures

old.

Biological Basis

The exact mechanism leading to febrile seizures is not clearly understood; biology is related to the immature brain in young children, fever, and genetic predisposition. The fever activates the cytokine networks (IL-1 alpha, IL-1 beta), increasing neuronal excitability. There is a complex inheritance involving multiple genes and environmental factors for children with genetic predisposition. Monozygotic twins have a higher concordance rate than dizygotic twins.

The risk for a first febrile seizure in a child is increased in those with

- Delayed neonatal hospital discharge
- Slow neurological development as judged by the parent
- Family history of febrile seizures (especially in a first-degree relative)
- Attendance at day care

62.4.2 Etiology

Common causes of febrile seizures include malaria, URTI, otitis media, pharyngitis, transient viral infections, and gastroenteritis. Some children develop a fever following vaccination with whole-cell DPT or measles vaccine.

62.4.3 Classification

Febrile seizures are classified as simple or complex. Table **??** below shows the differences between simple and complex febrile seizures.

Table 62.1: Simple versus Complex Febrile Seizures

Feature	Simple febrile seizure	Complex febrile seizure
Seizure type	Generalized	Maybe focal
Duration	Brief (<15 min)	Prolonged
Number of episodes	Single episode during the febrile illness	Repeated episodes in the same illness
Outcomes	Do not cause brain damage	Increased risk of brain damage

62.4.4 Risk of recurrence

In children with febrile seizures, the risk factors for recurrence are

- Young age at the time of the first febrile seizure (< 15 months)
- Family history of febrile seizures (first-degree relative)
- Low temperature at the time of the seizure (< 40 degrees)
- Short duration of illness before the seizure [Berg et al, 1997]

Having a complex febrile seizure and neurologic dysfunction are not consistent predictors of recurrence.

62.4.5 Risk of subsequent epilepsy

The risk of epilepsy in children with febrile seizures is slightly higher than the incidence in the general population. The risk is increased with:

- Complex febrile seizures (focal, prolonged, repeated within a single illness)
- Developmental delay or neurologic dysfunction
- Family history of epilepsy

The number of febrile seizures is not a predictor of subsequent epilepsy.

62.4.6 Long-term cognitive and behavioural outcomes

Febrile seizures are "benign". Studies have shown that children with febrile seizures have the same academic progress, intellect, and behaviour as other children.

62.5 Acute scenarios: prolonged seizures versus status epilepticus

62.5.1 Definitions:

Prolonged seizures: Most convulsive seizures in children are brief (lasting < 3 minutes). However, some may go on beyond 5 minutes. These are termed prolonged seizures.

Status epilepticus, on the other hand, is a prolonged seizure lasting more than 30 minutes or multiple seizures without recovery of consciousness. This definition applies to convulsive seizures. The duration of non-convulsive seizures differs based on the seizure type.

62.5.2 Pathophysiology of status epilepticus

In the initial seizure phase, the body undergoes autoregulation, leading to increased heart rate, cardiac output, and cerebral perfusion. This ensures that there is increased oxygen and glucose delivery to the brain. Also, increased cerebral perfusion helps remove carbon dioxide and metabolic waste, which build up in the brain during seizures. Beyond 30 minutes, this autoregulation breaks down, reducing cardiac output, decreasing systemic blood pressure, and decreasing cerebral perfusion. In the end, there is decreased oxygenation (hypoxia) and buildup of metabolic waste, which trigger a cascade of events with resultant neuronal deaths. This is why it is essential to stop any seizure from progressing into a status epilepticus.

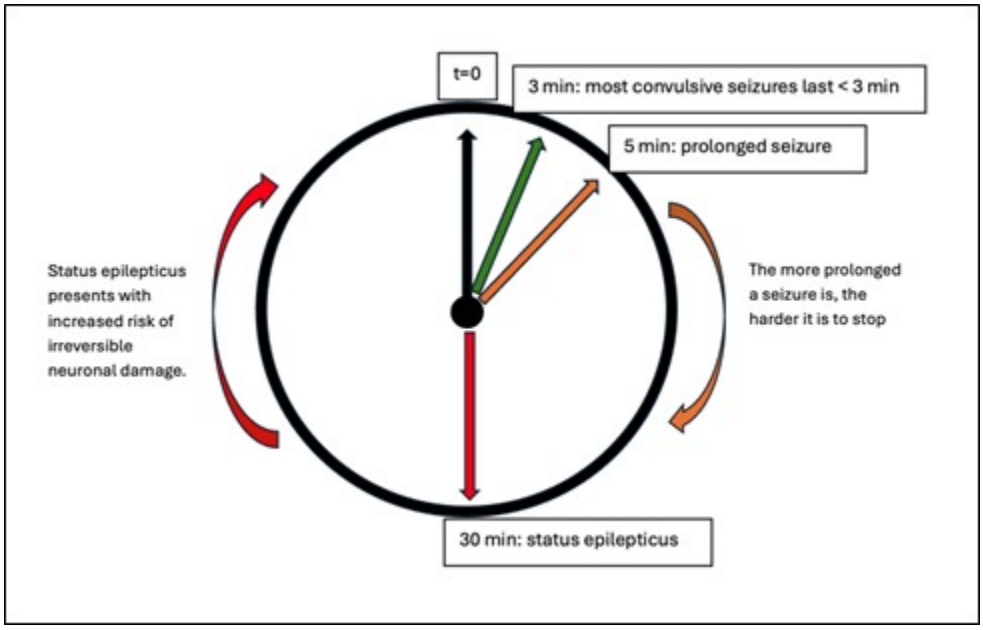


Figure 62.2: Timing of seizures in the acute scenario and the clinical implications

62.5.3 The Do's and Don'ts in acute scenarios

In the first few minutes of a seizure, it is essential to undertake basic first aid measures to protect the patient. These are termed the **Do's** and include:

- Protect the person from injury (eg, remove harmful objects from nearby, cushion their heads, etc.)
- When the seizure is over, gently place the patient in recovery. This positioning aids breathing by ensuring the patient does not choke on their secretions.
- Stay with the patient until the seizure is over.
- Stay calm and reassuring.

Some traditional practices can be harmful and should be discouraged. These are referred to as the **Don'ts** and include:

- Do not restrain the person's movements. Forcefully restraining their movement does not stop the seizures and may instead result in needless injuries like fractures and dislocations.
- Do not put anything in their mouth. This could lead to the patient biting on the spoon or spatula and causing damage to their teeth, gums, or palate. Also, please do not put your finger in their mouth. A forceful bite on your figure can lead to severe injuries, including amputation.
- Do not try to move them unless they are in danger.
- Do not give them anything to eat or drink until they fully recover.
- Do not attempt to bring them around. Practices such as pouring cold water on the patient, smearing them with garlic or other noxious substances are harmful and do not stop the seizures.

Indications for bringing the patient to the emergency room include:

1. If this is the person's first seizure.
2. If the seizure continues for more than five minutes.
3. If one seizure follows another without the person regaining consciousness between seizures.
4. If the person is injured.
5. If you believe the person needs urgent medical attention.

62.5.4 General principles of management of Prolonged Seizures and Status Epilepticus

In the first 5 minutes, critical interventions should include:

- General emergency measures including

  - A = airway
  - B = breathing
  - C = circulation
  - D = disability (such as hypoglycemia)
  - E = exposure

- Check blood glucose and correct hypoglycemia, if present.
- Remember the Do's and Don'ts.

If the seizure persists after 5 minutes, initiate drug management.

- 1st line drugs are benzodiazepines: these commonly include diazepam (rectal/IV, midazolam (buccal/nasal), and lorazepam (IV/rectal). These may be repeated after 10 minutes if the seizure persists.
- 2nd line drugs include phenobarbital (IV), phenytoin (IV), valproate (IV), or levetiracetam (IV).
- 3rd line drugs include anesthetic agents and should be given in the intensive care unit or in a center where the patient's breathing can be supported. They include thiopentone, propofol, and ketamine. Alternatively, continuous infusions of midazolam or repeated intravenous boluses of phenobarbitone may be used.

This stepwise approach to the management of ongoing seizures is illustrated in Table **??** below:

Table 62.2: Stepwise approach to status epilepticus

Time	**Action required**	**Notes**
t = 0 (seizure onset)	Ensure patient's safety (remember the Do's and Don'ts) Check the ABCDs. • Ensure airway patency. • Monitor vitals (HR, RR, BP, SpO2) • If SpO2 <90%, give supplemental O2 • Secure venous access • Check RBS. If there is hypoglycemia, correct with dextrose.	Most seizures will stop on their own within 3 minutes of onset.

Time	Action required	Notes
t = 5 min	Start 1st line pharmacologic treatment with a benzodiazepine.	Commonly used benzodiazepines include: 1. Diazepam (rectal or IV) 2. Midazolam (buccal or nasal) 3. Lorazepam (rectal or IV)
t = 15 min	If seizure persists to time t = 15 min (10 minutes after the first benzodiazepine), repeat the dose of benzodiazepine.	Benzodiazepines may be repeated once only. Avoid >2 doses of benzodiazepines.
t = 25 min	Start the 2nd line pharmacologic treatment.	Commonly used 2nd line drugs are: • Phenobarbitone (IV) • Phenytoin (IV) • Sodium valproate (IV) • Levetiracetam (IV)
t = 40-60 min	Start the 3rd line pharmacologic treatment.	This stage employs anesthetic agents. It should be done in a center where the patient's breathing can be supported.

62.5.5 Prognosis of Status Epilepticus in Children

In patients who present with convulsive status epilepticus (CSE), there is a mortality rate of 3-9% within 30 days of the CSE. The mortality rate is worse in low- and middle-income countries.

In those who survive, the neurological sequelae depend on the type and duration of the seizure, the patient's age, and the underlying etiology.

- Duration of the SE – the single most important determinant of prognosis. Worse outcome for prolonged SE.
- Age – worse neurological sequelae in infants (30% vs. 6% in older children)
- Seizure type – worse outcome for convulsive SE
- Underlying etiology

62.6 Epilepsy

62.6.1 Definition:

Epilepsy is a disease of the brain defined by any of the following conditions:

a. At least two unprovoked seizures occurring >24 hours apart.
b. One unprovoked seizure and an increased probability of further seizures
c. Diagnosis of an epileptic syndrome

It affects over 50 million people worldwide, and 1 in 200 children worldwide.

62.6.2 Classification

The ILAE classifies Epilepsy into four main types based on the seizure type (or types) [3]. These are:

- Focal epilepsy
- Generalised epilepsy
- Combined generalised and focal epilepsy
- Epilepsy with unknown seizure type(s)

62.6.3 Causes

All causes of epilepsy can be grouped into six main categories as follows:

a. Structural: e.g., lissencephaly, tumours, calcifications, post-stroke, tuberous sclerosis complex, etc.
b. Genetic: e.g., familial neonatal seizures, Dravet syndrome, etc.
c. Infections: e.g., neurocysticercosis, HIV, post-meningitis, etc.
d. Metabolic: e.g., hypoglycemia, electrolyte imbalance, inborn errors of metabolism, vitamin deficiency, etc.
e. Immune-mediated: autoimmune encephalitis
f. Unknown

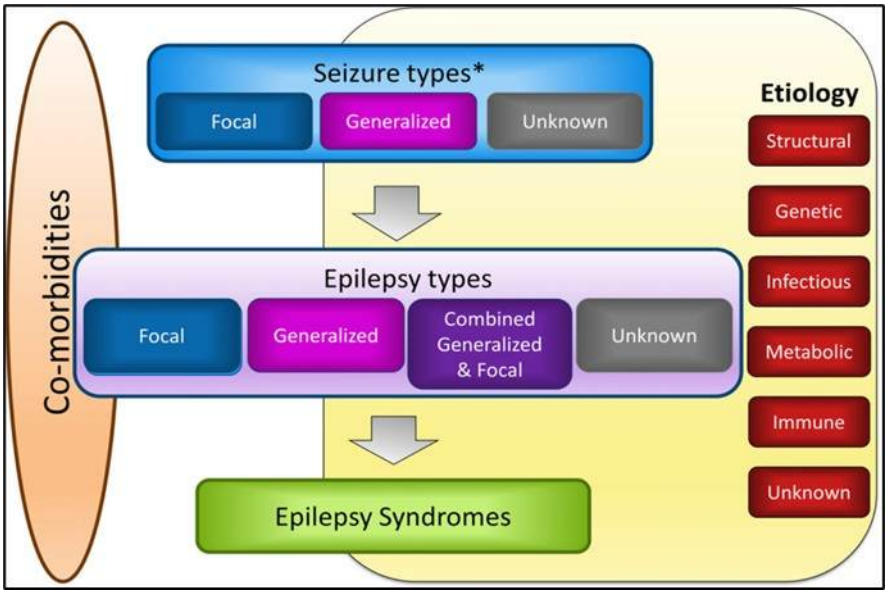


Figure 62.3: ILAE classification of epilepsies

62.6.4 Clinical evaluation of the child with epilepsy

In evaluating a child with epilepsy, it is important to obtain a good history, perform a thorough physical examination, and then form a clinical diagnosis (or impression). Investigations are then employed to define the seizure type(s), confirm the clinical diagnosis, identify the underlying etiology, assess the effect of treatment, rule out differential diagnoses, and evaluate comorbidities.

History: An eyewitness account is useful when taking the history of a child with epilepsy. Ask the older child for an account of the episodes. Home videos of the seizure episodes, if available, will complement the history. Key aspects of the seizure history should include:

- Age at onset: This is important in making an epilepsy syndrome diagnosis, as specific epilepsy syndromes have different ages at onset.
- Patient's baseline neurological status: This may differ from patient to patient and becomes essential in clinical decision-making. For example, the approach to a 3-year-old previously healthy child presenting with seizures will be different from that of a 3-year-old known with cerebral palsy, which will also be different from another 3-year-old known with HIV infection.
- Seizure semiology: This is a detailed description of what happened during the seizure. It is useful to describe the seizure semiology in terms of the different stages, namely the aura (if any), the ictal event, and the postictal event.
- The aura is often a sensory feeling that the patient experiences at the start of the seizure. It is seen in focal-onset seizures. Please note that younger children may not be able to

describe an aura.

- Description of the ictal event should include the seizure type (or types), non-motor manifestations (such as behavioral arrest, autonomic dysfunctions, etc.), seizure progression and duration, as well as timing of the events (e.g. shortly after going to sleep, during sleep, on awakening, whilst watching television, etc.).
- Post-ictal events: This is a description of what the patient does after the seizures have stopped. They include events such as falling into deep sleep, changes in behaviour or mood, transient focal weakness (Todd paralysis), etc. Please note that some seizure types (e.g., absence seizures) have abrupt recovery with no post-ictal phase. If there are post-ictal events, the duration should also be noted.
- Developmental/cognitive outcome and co-morbidities: The seizure history should describe the patient's development and any cognitive fallouts or neurobehavioral comorbidities noted since the onset of the seizures.
- Drug history: This should include a detailed list of all anti-seizure medications used in the past, their contribution to seizure control, and the reason for stopping the drug. Other long-term medications (including herbs) and known allergies should also be described.
- Family history: If other family members have seizures, they should be described in detail, including their relation to the index patient, the seizure type(s), response to treatment, prognosis, etc.

Physical examination

The purpose of the physical examination is to identify risk factors and comorbidities associated with epilepsy and evaluate treatment effectiveness. The initial examination should be comprehensive and include anthropometry, a skin examination for neurocutaneous manifestations, a detailed neurological assessment, a developmental evaluation, and an examination of other systems.

62.6.5 Investigations

It is important to remember that the diagnosis of epilepsy is mostly clinical and that the clinician should not overrely on investigations. However, investigations may be useful in diagnosing epilepsy syndrome, identifying the underlying etiology, assessing the effect of treatment, ruling out differential diagnoses, and evaluating comorbidities.

Basic investigations in the evaluation of the child with epilepsy include:

- Blood counts
- Serum electrolytes
- Liver function and renal function tests

Advanced investigations include:

- Electroencephalogram (EEG)

- Neuroimaging (CT, MRI, SPECT, PET)
- Metabolic screening
- Autoimmune antibody assays
- Molecular genetic testing

62.6.6 Treatment of Epilepsy

The various modalities for treating epilepsy include:

1. Medical treatment – traditional and newer Anti-seizure medications (ASMs)
2. Hormonal treatment – ACTH or Steroids (Prednisolone) for epileptic spasms
3. Vitamins – pyridoxine, folinic acid, and biotin for vitamin-responsive seizures
4. Surgical treatment
5. Dietary treatment (ketogenic diet)

Medical treatment: This uses traditional or newer Anti-Seizure Medications (ASMs). Not all children with epilepsy require ASM therapy. When needed, ASM selection should be based on seizure type, epilepsy syndrome, and potential side effects. In a low-resource country, availability and affordability should be considered in ASM selection.

Monotherapy is always preferred. However, a few patients will require rational polypharmacy. It is essential to select ASM at the minimum dosage that provides reasonable seizure control with minimal adverse effects. ASM therapy may be discontinued after the patient has had 2 years of seizure freedom.

ASMs have a variety of side effects. Some are dose-related and others are idiosyncratic (non-dose related)

Table **??** below shows the traditional anti-seizure medications and their specific indications.

Table 62.3: Traditional Anti-seizure medications (ASMs)

Drug	**Indications**	**Side Effects**
Phenobarbitone	Status epilepticus Neonatal seizures Epilepsy (both focal and generalized seizures)	**Dose-related:** Drowsiness, respiratory depression **Idiosyncratic:** Rash, Stevens-Johnson syndrome

Drug	Indications	Side Effects
Phenytoin	Status epilepticus Neonatal seizures Peri-operative seizures	**Dose-related:** Drowsiness **Chronic toxicity:** Gingival hyperplasia, coarse facial features, hirsutism, neuropathy, megaloblastic anemia **Idiosyncratic:** Rash, Stevens-Johnson syndrome, serum sickness
Sodium valproate	Broad spectrum Generalized seizures Absence seizures	**Dose-related:** Intention tremor, weight gain, polycystic ovaries, teratogenicity (risk of neural tube defects) **Idiosyncratic:** Hepatic failure, pancreatitis
Carbamazepine	Focal seizures Avoid in the absence and myoclonic seizures	**Dose-related:** Dizziness, drowsiness, diplopia, ataxia **Idiosyncratic:** Aplastic anemia, rash, Stevens-Johnson syndrome
Ethosuximide	Absence seizures	**Dose-related:** Dizziness, nausea, weight loss

Some newer ASMs include Lamotrigine, Topiramate, Levetiracetam, Clonazepam, Clobazam, Vigabatrin (for the treatment of epileptic spasms), Gabapentin, Pregabalin, Felbamate, Oxcarbazepine, Fosphenytoin, Lacosamide, Stiripentol, Tiagabine, and Zonisamide.

Hormonal therapy in the treatment of epilepsy includes:

- Adrenocorticotropic hormone (ACTH) – for treatment of epileptic spasms
- Prednisone or prednisolone – for treatment of epileptic spasms, Landau-Kleffner syndrome, etc.

Vitamins may be employed in the treatment of some epilepsies (known as vitamin-responsive or vitamin-dependent seizures). These include:

- Pyridoxine
- Folinic acid
- Biotin

Surgical treatment of epilepsy includes:

- Focal resection
- Lobectomy

- Hemispherectomy
- Corpus callosotomy
- Vagus nerve stimulation

Ketogenic diet: This employs high-fat, low-carbohydrate, and low-protein diets in treating patients with epilepsy. When used, the patient assumes a fasting state, and the brain relies on fatty acids instead of glucose as the primary source of energy. The exact mechanism of action is not known, but it leads to a reduction in seizure frequency and duration. It is effective for all seizure types.

62.7 Epilepsy syndromes

An epilepsy syndrome is defined as a characteristic cluster of clinical and electroencephalographic (EEG) features, often supported by specific etiological findings (structural, genetic, metabolic, immune, and infectious) [ILAE, 2022]

This is to say that some epilepsies can be clustered together as a syndrome based on their features, such as etiology, age at onset, seizure type(s), EEG findings, response to treatment, comorbidities, and long-term prognosis.

Epilepsy syndromes often have age-dependent presentations, may have age-dependent remission, and are usually strongly correlated with other co-morbidities.

Common epilepsy syndromes in children include:

- Early infantile epileptic encephalopathy (Ohtahara syndrome)
- Infantile epileptic spasms syndrome (West syndrome)
- Severe myoclonic epilepsy of infancy (Dravet syndrome)
- Lennox-Gastaut syndrome
- Myoclonic astatic epilepsy (Doose syndrome)
- Epilepsy-aphasia (Landau-Kleffner syndrome)
- Childhood absence epilepsy
- Juvenile absence epilepsy
- Self-limiting epilepsy with centro-temporal spikes (previously Benign Rolandic epilepsy)
- Juvenile myoclonic epilepsy

62.8 Neonatal Seizures

62.8.1 Definition

These are seizures in newborns 0-28 days (up to 2 months in clinical practice). They are often poorly organized and difficult to distinguish from normal activity. Clinical patterns include:

- Tonic stiffening of the body
- Tonic deviation of the eyes
- Apnea
- Focal clonic movements of one limb or both limbs on one side
- Myoclonic jerks
- Paroxysmal laughing
- Cycling movement of the limbs

Generalized tonic-clonic movements do not occur in the neonatal period.

The term **subtle seizures** refers to all the different patterns without tonic or clonic movement of the limbs.

62.8.2 Causes of seizures in neonates by age

Within 24 hours:

- Hypoxic-ischaemic encephalopathy
- Intrauterine infections
- Intracranial haemorrhage (IVH or SAH)
- Metabolic disorders (commonly pyridoxine deficiency)

24 to 72 hours

- Neonatal sepsis (including meningitis)
- Drug withdrawal
- Metabolic disorders
- Congenital malformations (cerebral dysgenesis)

After 72 hours

- Familial neonatal seizures
- Kernicterus
- Cerebral malformations
- Metabolic disorders
- Congenital malformations (cerebral dysgenesis)

62.8.3 Management of neonatal seizures

- Remember ABCDs
- Phenobarbital is the first-line drug of choice
- Avoid benzodiazepine (unless in a specialist center with respiratory support)

- Repeated Phenobarbital, Phenytoin, or IV infusion of Midazolam may be used as 2nd line or 3rd line
- 3rd line: must be in the NICU where ventilators are available.
- Give vitamins for vitamin-responsive or vitamin-dependent seizures. These include pyridoxine, biotin, and folinic acid.
- Identify and treat the underlying cause.

62.9 Seizure mimics

These are "events" that resemble seizures and may be misdiagnosed as seizures if not carefully evaluated. Common seizure mimics in neonates include:

- Benign sleep myoclonus
- Jitteriness
- Opisthotonos
- Apnea (especially in preterm newborns)

In infants and older children, common seizure mimics include:

- Psychogenic non-epileptic seizures (PNES)
- Jitteriness
- Sandifer syndrome (GERD)
- Breath-holding spells
- Movement disorders (Tics, chorea, paroxysmal dyskinesias, etc.)
- Benign sleep myoclonus
- Opsoclonus myoclonus syndrome
- Migraine variants
- Parasomnias
- Syncope (vasovagal or cardiac)
- Self-gratification
- Hypnic jerks
- Hypertonicity in a patient with CP or anoxic brain injury
- Cataplexy

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63 Neuromuscular Disorders

Neuromuscular disorders (NMDs) encompass a wide range of conditions that affect the motor unit, the functional link between the nervous system and muscles responsible for movement. They are characterized primarily by muscle weakness, hypotonia, and impaired motor development. These disorders may be inherited or acquired, acute or chronic, and involve any level of the motor pathway from the anterior horn cell in the spinal cord to the muscle fiber itself.

In Ghana and other sub-Saharan African countries, neuromuscular disorders are often underdiagnosed or misdiagnosed due to limited access to electrophysiological, genetic, and imaging studies. Nonetheless, careful clinical assessment can identify most cases early and guide appropriate referral and management.

63.1 Common Terminologies

Understanding basic terms is crucial for describing and classifying neuromuscular disorders:

- **Motor unit:** The combination of a motor neuron, its axon, and all the muscle fibers it innervates.
- **Hypotonia:** Reduced muscle tone leading to floppiness and poor resistance to passive movement.
- **Weakness:** Reduction in the ability to generate voluntary muscle force.
- **Fatigability:** Diminished ability to sustain muscle contraction during repeated or prolonged activity.
- **Atrophy:** Loss of muscle bulk, usually due to disuse or denervation.
- **Fasciculations:** Fine, involuntary muscle twitches visible under the skin, often seen in anterior horn cell disease.
- **Pseudohypertrophy:** Apparent muscle enlargement due to fatty or fibrous replacement, as in Duchenne muscular dystrophy.
- **Myopathy:** Primary disorder of the muscle fiber.
- **Neuropathy:** Disease of peripheral nerves.

63.2 Common Presentations

Children with neuromuscular disorders may present in various ways depending on the site and nature of pathology. Typical features include:

- **Delayed motor milestones** – not sitting, standing, or walking at expected ages.
- **Hypotonia** – often noted at birth or during infancy ("floppy baby").
- **Muscle weakness** – proximal (difficulty rising from sitting) or distal (foot drop).
- **Reduced or absent deep tendon reflexes.**
- **Gait abnormalities** – waddling or high-stepping gait.
- **Cranial nerve involvement** – facial weakness, ptosis, difficulty swallowing.
- **Respiratory distress** – due to diaphragmatic or intercostal weakness.
- **Skeletal deformities** – scoliosis, contractures.

A key clinical clue is that cognition and sensation are usually **preserved** in primary muscle diseases but may be affected in neuropathies or central lesions.

63.3 The Floppy Infant Syndrome

Definition:
The term "floppy infant" describes a neonate or young infant with decreased resistance to passive movement of limbs and trunk due to hypotonia.

63.3.1 Causes

Floppiness may be due to central or peripheral causes:

- **Central (CNS):** Hypoxic-ischemic encephalopathy, intracranial hemorrhage, metabolic encephalopathy, chromosomal syndromes (e.g., Down syndrome, Prader–Willi).
- **Peripheral:** Disorders of the motor unit — anterior horn cell (SMA), peripheral nerves, neuromuscular junction (congenital myasthenic syndrome), or muscle (congenital myopathy, muscular dystrophy).

63.3.2 Clinical Features

- Frog-leg posture.
- Head lag on traction.
- Poor spontaneous movement but preserved alertness (suggesting peripheral cause).
- Weak cry and suck.
- Respiratory difficulty in severe cases.

63.3.3 Evaluation

- Assess tone, reflexes, and antigravity movement.
- Presence of brisk reflexes suggests central cause; diminished reflexes indicate peripheral lesion.
- Look for dysmorphic features or systemic illness.

63.4 Site of Lesion

Neuromuscular disorders are localized anatomically by identifying where in the motor unit the pathology lies:

Level of Lesion	Examples	Characteristic Features
Anterior horn cell	Spinal muscular atrophy, poliomyelitis	Flaccid weakness, fasciculations, atrophy, absent reflexes
Peripheral nerve	Guillain–Barré syndrome, Charcot–Marie–Tooth disease	Distal weakness, areflexia, sensory loss
Neuromuscular junction	Myasthenia gravis, botulism	Fatigable weakness, normal reflexes, cranial involvement
Muscle	Muscular dystrophies, congenital myopathies, dermatomyositis	Proximal weakness, preserved sensation, normal or reduced reflexes

Accurate localization is the first step in diagnosis and guides further investigations such as electromyography (EMG) and genetic testing.

63.5 Specific Neuromuscular Disorders

63.5.1 Spinal Muscular Atrophy (SMA)

A **genetic disorder** caused by homozygous deletion or mutation of the *SMN1* gene, leading to degeneration of anterior horn cells.

Clinical Types:

- **Type I (Werdnig–Hoffmann):** Onset before 6 months, severe hypotonia ("floppy infant"), poor feeding, respiratory distress, early death.

- **Type II:** Onset 6–18 months; able to sit but not walk unaided. - **Type III (Kugelberg–Welander):** Late onset; mild weakness, able to walk initially.

Investigations: EMG (denervation), genetic testing.
Management: Supportive care, respiratory support, physiotherapy, new therapies (nusinersen, gene therapy) where available.

63.5.2 Poliomyelitis

A viral infection caused by *poliovirus* that selectively destroys anterior horn cells. Though now rare due to immunization, sporadic cases or vaccine-derived poliovirus can still occur.

Clinical features: - Fever and malaise followed by asymmetric, flaccid paralysis. - No sensory loss. - Reflexes absent in affected limbs.

Diagnosis: Isolation of poliovirus from stool or throat swabs.
Prevention: Oral and inactivated polio vaccines (OPV and IPV).
Public health relevance: Surveillance is vital as Ghana remains part of the global polio eradication initiative.

63.5.3 Guillain–Barré Syndrome (GBS)

An acute, immune-mediated demyelinating polyneuropathy, often post-infectious.

Presentation:

- Rapidly progressive, symmetrical ascending weakness.
- Areflexia.
- May involve respiratory and autonomic dysfunction.

Investigations:

- CSF: High protein, normal cells (albuminocytologic dissociation).
- Nerve conduction studies: Demyelination.

Management:

- Supportive care and monitoring for respiratory failure.
- IV immunoglobulin (IVIG) or plasmapheresis.

Prognosis: Good in children; most recover fully.

63.5.4 Charcot–Marie–Tooth Disease (CMT)

A **hereditary motor and sensory neuropathy** caused by demyelination or axonal degeneration.

Features:

- Distal weakness (especially peroneal muscles).
- Foot drop and high-arched feet (pes cavus).
- Reduced reflexes and distal sensory loss.
- Slowly progressive.

Diagnosis: Nerve conduction studies, genetic testing.
Management: Supportive — physiotherapy, orthotics, and counseling.

63.5.5 Myasthenia Gravis

An autoimmune disorder affecting the **neuromuscular junction**, where antibodies attack acetylcholine receptors.

Features: - Fluctuating weakness, worsening with exertion. - Ptosis, diplopia, facial weakness. - Bulbar symptoms (dysphagia, dysarthria). - Normal sensation and reflexes.

Diagnosis: Edrophonium test, AChR antibodies, EMG.
Treatment: Pyridostigmine, corticosteroids, thymectomy in selected cases.

63.5.6 Duchenne Muscular Dystrophy (DMD)

An **X-linked recessive** myopathy due to absence of **dystrophin** protein.

Features:

- Onset at 2–5 years.
- Progressive proximal weakness, calf pseudohypertrophy.
- Gowers' sign (using hands to "walk up" thighs).
- Wheelchair-bound by early teens.
- Cardiomyopathy and respiratory failure later.

Investigations: Markedly elevated CK, genetic confirmation.
Management: Corticosteroids, physiotherapy, cardiac and respiratory care.

63.5.7 Congenital Myopathies

A group of inherited disorders characterized by structural defects in muscle fibers (e.g., nemaline, central core, myotubular myopathy).

Features:

- Neonatal hypotonia ("floppy infant").
- Delayed motor milestones.
- Facial and ocular weakness.

Usually non-progressive or slowly progressive. Diagnosis is confirmed by muscle biopsy and genetic analysis.

63.5.8 Metabolic Myopathies

Caused by enzyme defects in muscle metabolism (e.g., glycogen storage diseases, fatty acid oxidation defects).

Features:

- Exercise intolerance.
- Recurrent rhabdomyolysis or myoglobinuria.
- Hypoglycemia in systemic types.

Management focuses on dietary modification and avoiding fasting or strenuous exercise.

63.5.9 Dermatomyositis

An **autoimmune inflammatory myopathy** affecting both skin and muscle.

Features:

- Symmetrical proximal weakness.
- Heliotrope rash (purple discolouration of eyelids).
- Gottron's papules (over knuckles).
- May involve myocardium and lungs.

Investigations: Elevated CK, EMG, muscle biopsy, autoantibody screen.
Treatment: Corticosteroids, immunosuppressants, physiotherapy.

63.6 Acute Flaccid Paralysis (AFP)

63.6.1 Case Definition

Acute flaccid paralysis is defined as **sudden onset of weakness or paralysis in a child under 15 years**, with reduced or absent muscle tone and reflexes. It includes **poliomyelitis** and **non-polio causes** such as Guillain–Barré syndrome and transverse myelitis.

63.6.2 Differential Diagnosis

- Poliomyelitis
- Guillain–Barré syndrome
- Transverse myelitis
- Traumatic neuritis
- Myasthenia gravis
- Botulism

63.6.3 Public Health Importance

AFP surveillance is central to **polio eradication** efforts.

- Every case of AFP must be reported within 24 hours to health authorities.
- Stool specimens (two within 14 days of onset) are collected for viral isolation.
- Early detection enables rapid outbreak response and immunization campaigns.

In Ghana, AFP surveillance has been instrumental in maintaining polio-free certification and detecting vaccine-derived strains.

63.7 Summary and Key Points

- Neuromuscular disorders affect any part of the motor unit, causing weakness and hypotonia.
- Careful clinical localisation is essential since advanced diagnostics are often unavailable.
- Common disorders in children include SMA, DMD, GBS, and myasthenia gravis.
- The floppy infant syndrome is a key early presentation of several NMDs.
- Acute flaccid paralysis remains a **notifiable condition** due to its link with polio surveillance.
- Multidisciplinary care, physiotherapy, respiratory and nutritional support—is crucial to improving outcomes.

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64 Neurocutaneous Syndromes

64.1 Introduction

Neurocutaneous syndromes, also known as *phakomatoses*, are a diverse group of congenital disorders characterised by abnormalities of the skin and nervous system, often involving other organs such as the eyes, bones, and endocrine glands. They result primarily from genetic mutations that affect the development and differentiation of tissues derived from the ectoderm. Because both the skin and the nervous system originate from the ectodermal layer during embryogenesis, a developmental insult to this germ layer can explain the frequent coexistence of neurological and cutaneous manifestations.

Recognition of these disorders is crucial in paediatrics, as cutaneous findings may serve as visible markers of significant underlying neurological disease. Early diagnosis allows for timely surveillance, prevention of complications, and genetic counselling for families. The most common and well-studied neurocutaneous syndromes include **Neurofibromatosis type 1 and 2**, **Tuberous sclerosis complex**, **Sturge–Weber syndrome**, and **Von Hippel–Lindau disease**. Other less frequent syndromes include **Ataxia telangiectasia**, **Incontinentia pigmenti**, and **Hypomelanosis of Ito**.

64.2 Embryological and Pathophysiological Basis

During the third to fourth week of embryonic development, the ectoderm differentiates into two main tissues: the **neural ectoderm**, which forms the nervous system, and the **surface ectoderm**, which gives rise to the skin and its appendages. Genetic defects that disrupt the proliferation or migration of neural crest cells, progenitors for melanocytes, Schwann cells, meninges, and components of the peripheral nervous system, underlie most neurocutaneous disorders.

These mutations often affect genes involved in **tumour suppression**, **cell growth regulation**, and **signal transduction pathways**, such as the **RAS/MAPK** and **mTOR** pathways. The result is dysregulated cell proliferation, hamartoma formation, and predisposition to both benign and malignant tumours.

The underlying pathophysiological mechanisms therefore include:

- Hamartomatous growths in skin, brain, and other organs

- Vascular malformations
- Abnormal neuronal migration
- Predisposition to neoplasia

64.3 General Clinical Features

Neurocutaneous syndromes present variably, but some general features include:

- **Cutaneous findings:** café-au-lait macules, hypopigmented macules, angiofibromas, shagreen patches, or port-wine stains.
- **Neurological manifestations:** seizures, developmental delay, learning disability, and focal neurological deficits.
- **Ocular features:** retinal hamartomas, optic gliomas, and choroidal angiomas.
- **Skeletal anomalies:** scoliosis, pseudoarthrosis, and bone cysts.
- **Endocrine abnormalities:** precocious puberty or adrenal lesions in certain syndromes.

Diagnosis relies on recognizing these characteristic associations, supported by neuroimaging and genetic testing.

64.4 Major Neurocutaneous Syndromes

64.4.1 Neurofibromatosis Type 1 (NF1)

NF1, also known as *von Recklinghausen disease*, is the most common neurocutaneous disorder, occurring in about 1 in 3,000 live births. It is caused by mutations in the **NF1 gene** on chromosome 17, which encodes **neurofibromin**, a tumour suppressor that regulates the RAS pathway.

Key clinical features:

- 6 café-au-lait macules (>5 mm prepubertal, >15 mm postpubertal)
- Axillary or inguinal freckling
- 2 neurofibromas or one plexiform neurofibroma
- Lisch nodules (iris hamartomas)
- Optic pathway glioma
- Bony lesions (e.g., sphenoid dysplasia, pseudoarthrosis)
- A first-degree relative with NF1

Neurological features: learning difficulties, attention deficit, seizures, and risk of intracranial tumours.
Complications: hypertension due to renal artery stenosis or pheochromocytoma, malignant peripheral nerve sheath tumours, and scoliosis.

Management: multidisciplinary, dermatologic surveillance, annual ophthalmology, developmental assessment, and blood pressure monitoring.

64.4.2 Neurofibromatosis Type 2 (NF2)

NF2 results from mutations in the **NF2 gene** on chromosome 22, which encodes **merlin (schwannomin)**, another tumour suppressor. It is rarer (1 in 25,000 births) and typically presents in adolescence or early adulthood.

Hallmark features:

- Bilateral vestibular schwannomas causing hearing loss and imbalance
- Meningiomas, spinal schwannomas, and ependymomas
- Posterior subcapsular cataracts in children

Cutaneous findings are less prominent than in NF1.
Management: MRI surveillance, hearing monitoring, and neurosurgical intervention when necessary.

64.4.3 Tuberous Sclerosis Complex (TSC)

TSC is an autosomal dominant disorder due to mutations in **TSC1 (hamartin)** or **TSC2 (tuberin)** genes, which regulate the **mTOR** signalling pathway. It affects about 1 in 6,000 births.

Cutaneous features:

- Hypomelanotic macules ("ash leaf" spots)
- Facial angiofibromas (adenoma sebaceum)
- Shagreen patch (connective tissue nevus)
- Periungual fibromas

Neurological manifestations:

- Cortical tubers, subependymal nodules, and subependymal giant cell astrocytomas (SEGAs)
- Epilepsy (infantile spasms common)
- Cognitive impairment and autism spectrum disorder

Other organ involvement:

- Cardiac rhabdomyomas (often regress spontaneously)
- Renal angiomyolipomas and cysts
- Pulmonary lymphangioleiomyomatosis (especially in females)

Management:

- mTOR inhibitors (everolimus, sirolimus) for SEGA or renal angiomyolipomas
- Antiepileptic therapy
- Developmental and genetic counselling

64.4.4 Sturge–Weber Syndrome (SWS)

SWS is a sporadic neurocutaneous disorder caused by somatic mutations in the **GNAQ gene**. It is characterized by vascular malformations involving the leptomeninges and facial skin.

Clinical features:

- Facial port-wine stain (nevus flammeus) along the ophthalmic branch of the trigeminal nerve
- Leptomeningeal angioma causing seizures, stroke-like episodes, and hemiparesis
- Glaucoma and visual impairment

Neuroimaging: CT shows "tram-track" calcifications; MRI reveals leptomeningeal enhancement.
Management: seizure control, ophthalmologic follow-up, and laser therapy for port-wine stains.

64.4.5 Von Hippel–Lindau Disease (VHL)

An autosomal dominant disorder caused by mutations in the **VHL tumour suppressor gene** on chromosome 3.

Major features:

- Retinal and cerebellar hemangioblastomas
- Renal cell carcinoma and pancreatic cysts
- Pheochromocytoma

Pediatric significance: retinal angiomas may present in adolescence.
Management: regular MRI screening and surgical or laser intervention for tumours.

64.4.6 Ataxia Telangiectasia (AT)

AT is an autosomal recessive disorder due to mutations in the **ATM gene**, which regulates DNA repair.

Key features:

- Progressive cerebellar ataxia beginning in early childhood
- Oculocutaneous telangiectasias (especially conjunctivae)
- Immunodeficiency (low IgA and IgE)
- High risk of malignancy, particularly lymphoma and leukemia

Management: supportive care, physiotherapy, infection prophylaxis, and avoidance of ionizing radiation.

64.4.7 Incontinentia Pigmenti (IP)

An X-linked dominant disorder lethal in males, caused by **IKBKG gene** mutations affecting NF- B signalling.

Stages of skin lesions:

1. Vesicular stage (blistering rash in neonates)
2. Verrucous stage (wart-like lesions)
3. Hyperpigmented streaks along Blaschko's lines
4. Hypopigmented atrophic patches in adolescence/adulthood

Associated findings: seizures, intellectual disability, dental anomalies, and ocular defects.

64.4.8 Hypomelanosis of Ito

Characterized by **whorled or streaked hypopigmented lesions** along Blaschko's lines. It represents chromosomal mosaicism rather than a single gene defect.

Associated features: developmental delay, seizures, scoliosis, and ocular anomalies. Diagnosis is clinical; management is supportive.

64.5 Investigations

Diagnostic evaluation depends on the suspected syndrome but generally includes:

- **Neuroimaging (MRI brain/spine):** for intracranial lesions, calcifications, or tumours
- **Dermatological examination:** Wood's lamp for hypopigmented lesions
- **Ophthalmological assessment:** slit-lamp and retinal evaluation
- **Genetic testing:** confirmation of specific mutations
- **Renal ultrasound:** in NF1 and TSC for cysts or angiomyolipomas
- **EEG:** in children with seizures
- **Audiometry:** in NF2 for vestibular schwannoma detection

64.6 Management Principles

Management is multidisciplinary, involving paediatric neurologists, dermatologists, ophthalmologists, geneticists, and surgeons. The principles include:

- **Early recognition** through skin examination
- **Regular surveillance** for neurological, renal, and ocular complications
- **Seizure management** using appropriate antiepileptics
- **Surgical intervention** for accessible tumours or disfiguring lesions
- **Use of targeted therapies** (e.g., mTOR inhibitors in TSC)
- **Genetic counselling** and screening of at-risk family members

64.7 Prognosis

Prognosis varies widely depending on the syndrome and severity of organ involvement. For example:

- NF1 and TSC are compatible with long survival but carry risks of malignancy.
- Sturge–Weber and AT have more guarded outcomes due to neurological decline.
- Early diagnosis and targeted interventions have improved life expectancy and quality of life.

64.8 Public Health Importance

In Ghana and other low-resource settings, recognition of neurocutaneous syndromes is often delayed due to limited access to dermatology and genetic services. Raising awareness among healthcare providers is essential for early identification and referral. Establishing registries

and integrating genetic counselling into paediatric services will improve outcomes and guide family planning.

65 Cerebrovascular Disease

Cerebrovascular diseases in children encompass a group of disorders that affect the blood vessels supplying the brain, leading to transient or permanent neurological deficits. Although stroke is far less common in children than in adults, it remains an important cause of morbidity and mortality in paediatrics, often resulting in lifelong neurological impairment if not promptly recognized and managed. Understanding the anatomy of cerebral circulation, mechanisms of injury, and approach to management is essential for clinicians caring for children.

65.1 CNS Circulation

The brain's blood supply is derived from two major arterial systems—the **anterior circulation** from the **internal carotid arteries** and the **posterior circulation** from the **vertebral arteries**.

- The **internal carotid arteries** divide into the **anterior cerebral** and **middle cerebral arteries**, supplying the frontal, parietal, and parts of the temporal lobes.
- The **vertebral arteries**, arising from the subclavian arteries, unite to form the **basilar artery**, which then gives rise to the **posterior cerebral arteries** supplying the brainstem, cerebellum, and occipital lobes.
- These arteries interconnect at the **Circle of Willis**, providing collateral circulation that can partly compensate for occlusion or stenosis in one vascular territory.

Venous drainage occurs through the **dural venous sinuses** (such as the superior sagittal, straight, and transverse sinuses), which ultimately drain into the **internal jugular veins**. The integrity of this circulation is critical to maintaining cerebral perfusion and oxygenation.

In neonates and infants, cerebral blood flow is more vulnerable to fluctuations in systemic perfusion due to immature autoregulatory mechanisms, predisposing them to ischemic or hemorrhagic events under stress conditions like hypoxia, dehydration, or infection.

65.2 Definitions

65.2.1 Stroke

Stroke is defined as a sudden onset of neurological deficit resulting from a disturbance in cerebral blood flow, either due to **ischemia** (interruption of blood supply) or **hemorrhage** (bleeding into or around the brain), lasting more than 24 hours or leading to death.

65.2.2 Transient Ischaemic Attack (TIA)

A **Transient Ischaemic Attack (TIA)** is a brief episode of neurological dysfunction caused by temporary cerebral ischemia, typically lasting less than 24 hours and without permanent radiological evidence of infarction. TIAs in children may herald an impending stroke and warrant urgent evaluation.

65.3 Classification of Stroke

Stroke in children is classified based on the underlying pathophysiology and anatomic distribution:

1. **Ischemic Stroke**
    - **Arterial Ischemic Stroke (AIS)**: Due to obstruction of an artery by thrombus or embolus.
    - **Cerebral Sinovenous Thrombosis (CSVT)**: Caused by thrombosis of cerebral veins or dural sinuses, leading to venous congestion and infarction.
2. **Hemorrhagic Stroke**
    - **Intracerebral Hemorrhage (ICH)**: Bleeding within brain parenchyma.
    - **Subarachnoid Hemorrhage (SAH)**: Bleeding into the subarachnoid space.
3. **Perinatal or Neonatal Stroke**
    - Occurs between 20 weeks of gestation and 28 days of life, often associated with perinatal asphyxia, maternal infections, or coagulation disorders.

The distinction between these subtypes is essential for appropriate investigation and management.

65.4 Common Causes of Stroke in Children

Unlike adults, where atherosclerosis dominates, pediatric strokes have diverse causes. These can be grouped as follows:

- **Cardiac causes**: Congenital heart disease (cyanotic heart lesions, endocarditis), cardiomyopathy, arrhythmias, and post-cardiac surgery emboli.
- **Hematologic disorders**: Sickle cell disease (most common in sub-Saharan Africa), iron deficiency anemia, polycythemia, and coagulation disorders.
- **Vascular abnormalities**: Moyamoya disease, arteriovenous malformations, aneurysms, fibromuscular dysplasia, and vasculitis.
- **Infections**: Bacterial meningitis, varicella, HIV, tuberculosis, and malaria.
- **Metabolic and systemic causes**: Homocystinuria, mitochondrial diseases, and diabetic ketoacidosis.
- **Trauma**: Head injury causing arterial dissection or hemorrhage.
- **Perinatal factors**: Birth asphyxia, maternal hypertension, and placental embolism.

In Ghana and similar regions, **sickle cell disease and severe malaria** are particularly important causes of childhood stroke.

65.5 Approach to the Child with Stroke

The approach involves early recognition, stabilization, identification of the cause, and institution of appropriate therapy.

65.5.1 History and Physical Examination

A detailed **history** and **neurological examination** are crucial.

Key historical points include:

- Onset and evolution of neurological symptoms (sudden or gradual)
- Perinatal history in neonates
- Past medical history — notably sickle cell disease, cardiac disease, trauma, or infection
- Family history of thrombophilia or stroke

Symptoms and signs may include: - Focal weakness or paralysis (hemiparesis) - Seizures (common in neonates) - Speech difficulties (aphasia) - Altered consciousness - Headache, vomiting - Gait disturbances or ataxia (posterior circulation involvement) - Papilledema in venous thrombosis

In neonates, manifestations are often subtle—poor feeding, irritability, or asymmetric limb movements.

65.6 Investigations

A structured approach to investigations helps confirm the diagnosis, identify etiology, and guide treatment.

65.6.1 Neuroimaging

- **CT scan**: Quick and useful for detecting hemorrhage; less sensitive for early ischemia.
- **MRI/MRA**: The gold standard for identifying ischemic lesions and vascular abnormalities.
- **MR venography (MRV)**: For cerebral venous sinus thrombosis.
- **Transcranial Doppler ultrasound**: Used for screening sickle cell disease patients at risk of stroke.

65.6.2 Laboratory Investigations

- Full blood count: To detect anemia, polycythemia, or leukocytosis.
- Sickle cell screening: Mandatory in all African children with stroke.
- Coagulation profile: PT, aPTT, fibrinogen, D-dimers.
- Inflammatory markers: ESR, CRP.
- Blood cultures: If infection is suspected.
- Serum electrolytes and glucose: To rule out metabolic causes.
- Lumbar puncture: If infection is suspected and there is no raised intracranial pressure.

65.6.3 Cardiac Evaluation

- **Echocardiography**: To identify congenital heart defects or mural thrombi.
- **ECG**: For arrhythmias.

66 Management and Rehabilitation

The goals of management are to **stabilize**, **prevent progression**, **treat underlying causes**, and **rehabilitate**.

66.1 Acute Phase Management

66.1.1 Stabilization

- Ensure airway, breathing, and circulation.
- Control seizures with anticonvulsants (e.g., phenobarbital, diazepam).
- Correct hypoxia, hypoglycemia, and dehydration.
- Manage raised intracranial pressure (elevate head, restrict fluids, osmotic agents if needed).

66.1.2 Specific Treatment

- **Ischemic stroke**:
  - Antithrombotic therapy (aspirin 3–5 mg/kg/day) once hemorrhage is excluded.
  - Anticoagulation (heparin or LMWH) in venous sinus thrombosis or cardioembolic stroke.
  - Exchange transfusion in sickle cell-related stroke to reduce HbS <30%.
- **Hemorrhagic stroke**:
  - Control hypertension, correct coagulopathies.
  - Neurosurgical intervention for hematoma evacuation or shunt insertion in hydrocephalus.

66.1.3 Infection Control

- Empirical antibiotics if meningitis or sepsis is suspected.
- Malaria treatment if smear-positive.

66.2 Secondary Prevention

- Chronic transfusion programs in sickle cell disease to prevent recurrence.
- Hydroxyurea therapy to maintain HbF and reduce stroke risk.
- Long-term aspirin therapy for certain vasculopathies.
- Management of cardiac or metabolic causes.

66.3 Rehabilitation

Early initiation of **multidisciplinary rehabilitation** is vital:

- **Physiotherapy** for muscle strength and mobility.
- **Occupational therapy** for daily activity independence.
- **Speech therapy** for language recovery.
- **Psychological support** for emotional and cognitive adaptation.
- **Educational interventions** for learning difficulties.

67 Prognosis

Prognosis depends on the cause, timeliness of intervention, and extent of brain injury.

- **Mortality** in pediatric stroke is about 10–20%.
- **Neurological sequelae**, including hemiparesis, epilepsy, and cognitive deficits, occur in up to 60% of survivors.
- Recurrence is particularly high in sickle cell disease and untreated vascular anomalies.

68 Public Health Importance

Although less frequent than adult stroke, cerebrovascular disease in children carries a **high burden of disability** and **economic cost** due to long-term care needs. In sub-Saharan Africa: - Late diagnosis and limited access to imaging delay treatment.
- Sickle cell disease–related strokes are a major preventable cause.
- Strengthening **neonatal screening**, **malaria control**, and **access to transfusion programs** could significantly reduce incidence.

Public health strategies should therefore include: - Early detection and management of high-risk conditions (e.g., sickle cell disease).
- Training healthcare workers to recognize early symptoms.
- Improving neuroimaging availability and multidisciplinary care.

69 Conclusion

Cerebrovascular diseases in children, though uncommon, represent a significant cause of acute neurological morbidity and long-term disability. The underlying causes differ markedly from those in adults, with hematologic, infectious, and congenital heart diseases predominating in the tropics. Prompt recognition, neuroimaging, and targeted management are key to improving outcomes. Strengthening preventive strategies, particularly for sickle cell disease and infectious causes, remains essential in reducing the burden of childhood stroke in Ghana and across Africa.

Part IX

Endocrinology

70 Basics

70.1 Introduction

Endocrinology is the study of hormones and the glands that produce them. In children, the endocrine system governs critical processes such as growth, puberty, metabolism, and stress response. **Pediatric endocrinology** focuses on disorders affecting hormone production, secretion, and action during the developmental years.

Unlike adults, endocrine disorders in children often present with **growth disturbances**, **delayed or precocious puberty**, or **developmental abnormalities**, rather than classical systemic symptoms. A strong understanding of endocrine physiology, growth assessment, and hormonal feedback mechanisms is essential for early recognition and management.

This essay outlines the anatomy and physiology of the endocrine system, key hormones, principles of endocrine function testing, and an overview of common endocrine disorders in children.

70.2 Anatomy and Physiology of the Endocrine System

The endocrine system consists of specialized glands that secrete hormones directly into the bloodstream to act on distant target organs. These hormones regulate metabolism, electrolyte balance, growth, and reproduction.

70.2.1 Major Endocrine Glands in Children

Gland	Major Hormones	Primary Functions
Hypothalamus	CRH, TRH, GHRH, GnRH	Regulates pituitary secretion
Pituitary	GH, ACTH, TSH, LH, FSH, Prolactin	Growth, metabolism, reproduction
Thyroid	T3, T4, Calcitonin	Metabolism, growth, brain development
Parathyroid	PTH	Calcium and phosphate balance
Adrenal	Cortisol, Aldosterone, Androgens	Stress response, electrolyte control

Gland	Major Hormones	Primary Functions
Pancreas	Insulin, Glucagon	Blood glucose regulation
Gonads	Oestrogen, Testosterone	Pubertal development
Pineal	Melatonin	Circadian rhythm

These glands communicate through a hierarchy known as the **hypothalamic–pituitary–target gland axis**.

70.3 The Hypothalamic–Pituitary Axis

The **hypothalamus** integrates neural and hormonal signals to regulate endocrine function. It secretes releasing or inhibiting hormones into the hypophyseal portal system that act on the **pituitary gland**.

The **pituitary**, often termed the "master gland," releases trophic hormones that stimulate target organs such as the thyroid, adrenal glands, and gonads.

70.3.0.1 Example of Hormonal Axes

Axis	Hypothalamic Hormone	Pituitary Hormone	Target Organ	Target Hormone
Thyroid	TRH	TSH	Thyroid gland	T3, T4
Adrenal	CRH	ACTH	Adrenal cortex	Cortisol
Gonadal	GnRH	LH, FSH	Ovaries/Testes	Oestrogen, Testosterone
Growth	GHRH	GH	Liver	IGF-1

Feedback loops maintain hormone balance: elevated target hormones inhibit hypothalamic and pituitary secretion, preventing overproduction.

70.4 Principles of Hormone Action

Hormones exert their effects through **specific receptors** located either on the cell membrane (peptide hormones) or within the cell (steroid and thyroid hormones).

70.4.1 Types of Hormones

Type	Examples	Mechanism of Action
Peptide hormones	GH, insulin, ACTH	Bind to cell-surface receptors → activate second messengers
Steroid hormones	Cortisol, oestrogen, testosterone	Enter cells → bind nuclear receptors → modulate gene transcription
Amine hormones	T3, T4, catecholamines	Derived from tyrosine → act on nuclear or membrane receptors

Because of these mechanisms, hormone effects may be **rapid** (e.g., insulin, catecholamines) or **delayed but sustained** (e.g., thyroid or steroid hormones).

70.5 Growth and Development: A Central Theme

Growth is the most visible reflection of endocrine health in children. It results from the interplay between genetics, nutrition, and hormones—particularly **growth hormone (GH)**, **thyroid hormones**, **cortisol**, **sex steroids**, and **insulin**.

70.5.1 Growth Hormone Axis

- GH is secreted by the anterior pituitary in a pulsatile fashion.
- Stimulated by GHRH and inhibited by somatostatin.
- Acts on the liver to produce **Insulin-like Growth Factor-1 (IGF-1)**, which mediates bone and tissue growth.

Deficiency of GH leads to short stature with normal body proportions, while **excess GH** (rare in children) causes gigantism.

70.6 Assessment of Endocrine Function in Children

Because hormone levels fluctuate with time of day, age, and physiological state, interpretation of results must be age-appropriate.

70.6.1 Clinical Assessment

1. **Detailed history**
    - Growth pattern, family history of endocrine disorders.
    - Pubertal changes, appetite, and energy levels.
2. **Physical examination**
    - Height and weight plotted on growth charts.
    - Pubertal staging (Tanner).
    - Dysmorphic features, goitre, pigmentation, or obesity.

70.6.2 Laboratory Evaluation

- **Basal hormone levels:** measured at specific times (e.g., morning cortisol).
- **Dynamic tests:**
    - *Stimulation tests* (for suspected deficiency): e.g., GH stimulation, ACTH stimulation.
    - *Suppression tests* (for suspected excess): e.g., dexamethasone suppression test.
- **Imaging:** MRI of hypothalamic-pituitary region, thyroid ultrasound, or adrenal CT where indicated.
- **Genetic testing:** for congenital or syndromic causes.

70.7 Common Endocrine Disorders in Children

70.7.1 Disorders of Growth and Pituitary Function

70.7.2 Growth Hormone Deficiency (GHD)

- Causes: congenital pituitary hypoplasia, tumours, trauma, or idiopathic.
- Features: short stature, delayed bone age, infantile face, hypoglycaemia.
- Diagnosis: low IGF-1, failed GH stimulation.
- Treatment: recombinant GH therapy.

70.7.3 Growth Hormone Excess

- Usually from a pituitary adenoma.
- Causes excessive linear growth (gigantism) or acromegalic features.
- Managed surgically or with somatostatin analogues.

70.8 Thyroid Disorders

70.8.1 Congenital Hypothyroidism

- Caused by thyroid dysgenesis or dyshormonogenesis.
- Features: prolonged neonatal jaundice, macroglossia, hypotonia, umbilical hernia.
- Early detection via newborn screening.
- Treatment: lifelong levothyroxine replacement.

70.8.2 Juvenile Hypothyroidism

- Often autoimmune (Hashimoto's thyroiditis).
- Features: growth retardation, fatigue, dry skin, constipation.
- Managed with thyroid hormone replacement.

70.8.3 Hyperthyroidism

- Most commonly Graves' disease (autoimmune).
- Presents with weight loss, tachycardia, goitre, tremor.
- Treatment includes antithyroid drugs (carbimazole), beta-blockers, or surgery.

70.9 Adrenal Disorders

70.9.1 Congenital Adrenal Hyperplasia (CAH)

- Autosomal recessive enzyme defect (most often 21-hydroxylase deficiency).
- Features: ambiguous genitalia in females, dehydration, salt wasting.
- Diagnosis: elevated 17-hydroxyprogesterone.
- Treatment: hydrocortisone and fludrocortisone replacement.

70.9.2 Adrenal Insufficiency (Addison's Disease)

- Causes: autoimmune, infections (TB), or congenital defects.
- Features: fatigue, hyperpigmentation, hypotension, salt craving.
- Treatment: hydrocortisone and mineralocorticoid replacement.

70.9.3 Cushing Syndrome

- From prolonged steroid therapy or adrenal tumour.
- Features: obesity, moon facies, striae, growth retardation.
- Managed by reducing steroid dose or surgical excision of the tumour.

70.10 Disorders of Puberty

70.10.1 Precocious Puberty

- Onset of secondary sexual characteristics before 8 years in girls, 9 years in boys.
- May be central (early activation of HPG axis) or peripheral (excess sex steroids).
- Requires MRI brain and hormonal evaluation.
- Managed with GnRH analogues for central forms.

70.10.2 Delayed Puberty

- Absence of pubertal changes beyond 13 years (girls) or 14 years (boys).
- May result from constitutional delay, hypogonadism, or chronic illness.
- Treatment involves reassurance or sex steroid replacement when indicated.

70.11 Disorders of Glucose Metabolism

70.11.1 Type 1 Diabetes Mellitus (T1DM)

- Autoimmune destruction of pancreatic beta cells.
- Commonest endocrine disorder in children.
- Symptoms: polyuria, polydipsia, weight loss, fatigue.
- Complication: diabetic ketoacidosis (DKA).
- Management: insulin therapy, dietary regulation, self-monitoring.

70.11.2 Type 2 Diabetes Mellitus (T2DM)

- Increasingly seen in obese adolescents.
- Features: obesity, acanthosis nigricans, mild hyperglycaemia.
- Managed by lifestyle changes, metformin, and sometimes insulin.

70.11.3 Parathyroid and Calcium Disorders

- **Hypocalcaemia** due to hypoparathyroidism, vitamin D deficiency, or pseudohypoparathyroidism → tetany, seizures, Chvostek and Trousseau signs.
- **Hypercalcaemia** due to hyperparathyroidism or malignancy → polyuria, vomiting, bone pain.
- Management focuses on correcting calcium and vitamin D levels.

70.12 Diagnostic Principles in Pediatric Endocrinology

Because hormone secretion in children changes with age and puberty, interpretation requires **age-specific reference ranges**. For example: - Neonates have higher cortisol and thyroid hormone levels. - GH secretion is pulsatile; random measurements are unreliable. - Pubertal staging is crucial for evaluating gonadal hormones.

Dynamic testing remains a cornerstone of diagnosis:

- *Stimulation tests* (GH, ACTH, GnRH) evaluate deficiency.
- *Suppression tests* (dexamethasone, glucose tolerance) assess hormone excess.

In addition, **imaging** helps detect structural lesions, and **genetic testing** confirms syndromic causes such as Prader–Willi, Turner, or Kallmann syndromes.

70.13 Principles of Management

70.13.1 Hormone Replacement

- Use physiological doses to mimic normal secretion (e.g., hydrocortisone 3 times daily rather than dexamethasone).
- Regular adjustment according to growth and puberty.

70.13.2 Suppression of Hormone Excess

- Antithyroid drugs, glucocorticoid therapy for CAH, or GnRH analogues for precocious puberty.

70.13.3 Treatment of Underlying Causes

- Surgery for tumours, antibiotics for infections, or withdrawal of exogenous steroids.

70.13.4 Long-Term Follow-Up

- Regular growth and pubertal assessment.
- Monitoring for treatment side effects (e.g., growth suppression from steroids).
- Transition planning for adult endocrinology care.

70.14 Growth Monitoring and Interpretation

Growth assessment is central to paediatric endocrinology.
Essential tools include:

- **Growth charts:** plot height, weight, BMI, and head circumference.
- **Mid-parental height:** predicts target range.
- **Growth velocity:** <4 cm/year after age 4 suggests pathology.
- **Bone age:** X-ray of left hand/wrist compared with standards (Greulich–Pyle).

Discrepancy between bone age and chronological age helps differentiate **constitutional delay** from **endocrine causes** of short stature.

70.15 Psychosocial Aspects

Endocrine disorders can profoundly affect self-esteem, body image, and school performance. Children with delayed puberty or short stature may face bullying or anxiety, while those with obesity or hirsutism may experience social withdrawal.

Management should include:

- Psychological counselling.
- Support groups and family education.
- Encouragement of normal participation in school and sports.

70.16 Summary Table

Domain	Common Disorders	Key Hormones	Typical Features
Growth	GH deficiency/excess	GH, IGF-1	Short/tall stature
Thyroid	Hypo-/hyperthyroidism	T4, TSH	Growth delay, goitre
Adrenal	CAH, Addison's, Cushing's	Cortisol, Aldosterone	Virilisation, fatigue, obesity
Puberty	Precocious, delayed	LH, FSH, sex steroids	Early/late sexual changes
Glucose	T1DM, T2DM	Insulin, glucagon	Polyuria, weight change
Calcium	Hypo-/hyperparathyroidism	PTH, Vit D	Tetany, bone pain

70.17 Key Takeaways

- **Pediatric endocrinology** deals with hormonal disorders affecting growth, metabolism, and development.
- Early recognition is crucial to prevent irreversible effects on growth and neurodevelopment.
- **Growth failure**, **pubertal delay**, or **unexplained obesity** should prompt endocrine evaluation.
- Lifelong follow-up, family education, and psychosocial support are integral to successful management.

70.18 Suggested Reading

1. Nelson Textbook of Pediatrics, 22nd Edition.
2. Sperling M. A., *Pediatric Endocrinology*, 5th Edition.
3. Brook CGD, Clayton PE. *Clinical Pediatric Endocrinology*, 7th Edition.
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5. ESPE Clinical Practice Guidelines, 2023.

71 Diabetes Mellitus

71.1 Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.
In children, diabetes is one of the most common endocrine and metabolic disorders encountered in clinical practice. The two main types seen are **Type 1 diabetes mellitus (T1DM)** and **Type 2 diabetes mellitus (T2DM)**, though other rare forms such as **monogenic diabetes** and **secondary diabetes** also occur.

In Ghana and many parts of sub-Saharan Africa, the incidence of Type 1 diabetes is increasing, with children presenting frequently in diabetic ketoacidosis (DKA). In recent years, Type 2 diabetes has emerged among adolescents due to rising rates of obesity and sedentary lifestyles.

This chapter provides a detailed overview of diabetes mellitus in children — covering definitions, classification, pathophysiology, clinical features, diagnosis, management, and complications — with special emphasis on practical approaches for medical students and paediatric residents.

71.2 Classification of Diabetes Mellitus

The **American Diabetes Association (ADA)** and **World Health Organization (WHO)** classify diabetes as follows:

Category	Description	Pathophysiology
Type 1 Diabetes Mellitus (T1DM)	Autoimmune destruction of pancreatic -cells leading to absolute insulin deficiency	Immune-mediated; often associated with islet autoantibodies
Type 2 Diabetes Mellitus (T2DM)	Combination of insulin resistance and relative insulin deficiency	Associated with obesity, puberty, and family history
Monogenic Diabetes (MODY/Neonatal DM)	Single-gene defects affecting -cell function	Often autosomal dominant inheritance

Category	Description	Pathophysiology
Secondary Diabetes	Secondary to other conditions	Pancreatitis, cystic fibrosis, steroid therapy, endocrine disorders

71.3 Epidemiology

- **Global trends:** T1DM accounts for over 90% of diabetes in children globally. The incidence varies widely, from <1/100,000 in sub-Saharan Africa to >30/100,000 in Europe.
- **In Ghana:** Studies in Kumasi, Accra, and Cape Coast indicate increasing T1DM cases among children aged 5–15 years, often presenting with DKA at diagnosis.
- **Type 2 diabetes:** Previously rare, it is now reported among Ghanaian adolescents, especially those with obesity and a strong family history.

The rise in diabetes prevalence among children is attributed to improved awareness, urbanization, lifestyle changes, and possibly environmental triggers.

71.4 Physiology of Insulin and Glucose Homeostasis

The **pancreas** plays a central role in glucose metabolism.
The **-cells of the islets of Langerhans** secrete insulin, a peptide hormone that facilitates glucose uptake by muscle and adipose tissue and suppresses hepatic glucose production.

71.4.1 Key Actions of Insulin

- Increases glucose uptake via GLUT-4 transporters.
- Promotes glycogen synthesis in liver and muscle.
- Inhibits gluconeogenesis and glycogenolysis.
- Enhances lipid and protein synthesis.

Deficiency or resistance to insulin leads to **hyperglycaemia**, **lipolysis**, **ketogenesis**, and **protein catabolism**, which underlie the metabolic disturbances seen in diabetes.

71.5 Pathophysiology

71.5.1 Type 1 Diabetes Mellitus (T1DM)

An **autoimmune process** targets pancreatic -cells, resulting in progressive loss of insulin production.

71.5.1.1 Mechanism

- Genetic predisposition (HLA-DR3, DR4, DQ2, DQ8).
- Environmental triggers (viral infections—Coxsackie B, enterovirus, or toxins).
- Presence of autoantibodies: GAD65, ICA, IA-2, or ZnT8.

Destruction of >80% of -cells leads to insulin deficiency, hyperglycaemia, and ketone formation.

71.5.1.2 Natural History

1. **Genetic predisposition**
2. **Autoimmunity initiation**
3. **Progressive -cell destruction**
4. **Clinical diabetes** (symptomatic hyperglycaemia or DKA)

71.5.2 Type 2 Diabetes Mellitus (T2DM)

Characterized by **insulin resistance** and **relative insulin deficiency**.

- Strongly linked to obesity, acanthosis nigricans, and family history.
- Insulin resistance is worsened by puberty hormones, sedentary lifestyle, and high-calorie diets.

71.5.3 Other Forms

- **Monogenic diabetes:** Often presents in infancy or early childhood; may respond to sulfonylureas rather than insulin.
- **Secondary diabetes:** Can follow steroid therapy, Cushing syndrome, or pancreatitis.

71.6 Clinical Features

The presentation of diabetes in children depends on its type and stage at diagnosis.

71.6.1 Classical Symptoms of Type 1 Diabetes

1. **Polyuria** – due to osmotic diuresis.
2. **Polydipsia** – compensatory thirst.
3. **Polyphagia** – despite weight loss.
4. **Weight loss and fatigue** – from catabolism.
5. **Enuresis or nocturia** – previously toilet-trained child.
6. **Recurrent infections** – especially skin and vulvovaginal candidiasis.

In many Ghanaian children, the disease is recognized **late**, often presenting as **diabetic ketoacidosis (DKA)** with vomiting, abdominal pain, and dehydration.

71.6.2 Features of Type 2 Diabetes

- Often asymptomatic or mildly symptomatic.
- Associated with **obesity**, **acanthosis nigricans**, **hypertension**, or **dyslipidaemia**.
- May also present with ketosis (ketosis-prone T2DM).

71.7 Diabetic Ketoacidosis (DKA)

DKA is the most serious acute complication of diabetes in children and remains a major cause of morbidity and mortality in Ghana.

71.7.1 Pathophysiology

Absolute or relative insulin deficiency → increased lipolysis → free fatty acids converted to ketone bodies (acetoacetate, -hydroxybutyrate) → metabolic acidosis.

71.7.2 Diagnostic Criteria (WHO/ISPAD)

- Blood glucose >11 mmol/L
- Venous pH <7.3 or bicarbonate <15 mmol/L
- Presence of ketonaemia or ketonuria

71.7.3 Clinical Features

- Dehydration
- Kussmaul breathing (deep, laboured)
- Fruity (acetone) breath
- Abdominal pain, vomiting
- Drowsiness or altered consciousness

71.7.4 Complications

- **Cerebral oedema** (most feared, especially in children)
- **Shock and electrolyte imbalance**

71.7.5 Management Principles

1. **Fluid resuscitation:** 0.9% saline initially, then adjusted.
2. **Insulin therapy:** IV infusion 0.05–0.1 U/kg/hr after initial fluid resuscitation.
3. **Electrolyte correction:** especially potassium.
4. **Treatment of precipitating cause:** infection, missed insulin dose, etc.
5. **Close monitoring:** vital signs, glucose, electrolytes, and neurological status.

71.8 Diagnostic Evaluation

71.8.1 Diagnostic Criteria for Diabetes (WHO)

Test	Diagnostic Value
Fasting plasma glucose	7.0 mmol/L (after 8 hours fasting)
Random plasma glucose	11.1 mmol/L with symptoms
2-hour OGTT plasma glucose	11.1 mmol/L
HbA1c	6.5% (in standardized lab)

In children, diagnosis is typically based on **random glucose** and **clinical presentation**, especially when symptomatic.

71.8.2 Additional Laboratory Tests

- Urine dipstick for glucose and ketones
- Serum electrolytes, urea, creatinine
- Blood gas for acidosis (if DKA suspected)
- HbA1c for baseline control
- Autoantibody screening (GAD, ICA) when available
- Lipid profile (for T2DM)

71.9 Differential Diagnosis of Polyuria and Polydipsia

Condition	Key Features
Diabetes mellitus	Hyperglycaemia, glucosuria, ketonuria
Diabetes insipidus	Dilute urine, normal glucose
Psychogenic polydipsia	Normal glucose, no ketones
Chronic renal disease	Proteinuria, elevated creatinine

71.10 Management of Type 1 Diabetes Mellitus

The cornerstone of management is **lifelong insulin therapy** with education, diet regulation, and psychosocial support.

71.10.1 Insulin Therapy

71.10.1.1 Types of Insulin

Type	Onset	Peak	Duration
Rapid-acting (Lispro, Aspart)	10–15 min	1–2 hr	3–5 hr
Short-acting (Regular)	30–60 min	2–4 hr	6–8 hr
Intermediate (NPH)	2–4 hr	6–10 hr	12–18 hr
Long-acting (Glargine, Detemir)	1–2 hr	Minimal	24 hr

71.10.1.2 Insulin Regimens

- **Conventional:** Two daily injections (mixed short- and intermediate-acting).
- **Basal–bolus:** Long-acting basal + rapid-acting at meals.
- **Insulin pump therapy:** Rarely available in Ghana but ideal for motivated families.

71.10.1.3 Dose

- Starting total daily dose: 0.5–1.0 units/kg/day.
- Adjust according to blood glucose trends.

71.10.1.4 Monitoring

- **Self-monitoring of blood glucose (SMBG):** before meals and at bedtime.
- **HbA1c:** every 3–6 months; target <7.5%.
- **Growth and pubertal assessment** at each visit.

71.10.2 Nutritional Management

Dietary management aims at maintaining normoglycaemia while ensuring adequate growth.

71.10.2.1 Principles

- Balanced diet with appropriate carbohydrate distribution (50–55% of calories).
- Encourage high-fibre complex carbohydrates; limit refined sugars.
- Consistent meal timing, coordinated with insulin action.
- Carbohydrate counting for insulin adjustment.
- Avoid fasting or skipping meals.

In Ghana, diets can incorporate **local foods** — e.g., whole grain banku, kontomire stew, beans, plantain — with attention to portion control and reduced oil.

71.10.3 Exercise

Regular physical activity improves insulin sensitivity and cardiovascular health.

Precautions: - Monitor glucose before and after exercise.
- Take extra carbohydrates if prolonged activity (>60 min).
- Avoid vigorous exercise if glucose >14 mmol/L with ketones.

71.10.4 Education and Psychosocial Support

Education is central to successful management. Children and caregivers must be taught:

- Insulin injection technique and site rotation.
- Glucose monitoring and record keeping.
- Recognition and management of **hypoglycaemia** and **DKA**.
- Importance of adherence, diet, and exercise.

Psychosocial counselling is essential to address school integration, stigma, and family stress. Peer support groups (e.g., Diabetes Youth Care Ghana) are beneficial.

71.11 Management of Type 2 Diabetes Mellitus

Management begins with **lifestyle modification**, followed by **pharmacotherapy** if control is inadequate.

71.11.1 Lifestyle Modification

- Weight reduction through diet and exercise.
- Reduction of sugary beverages and fried foods.
- Screen family members for diabetes and obesity.

71.11.2 Pharmacological Treatment

- **Metformin** is the first-line agent (500 mg once or twice daily, titrated as tolerated).
- **Insulin** may be required temporarily if hyperglycaemia is severe or during intercurrent illness.
- Blood pressure and lipid control are also essential.

71.12 Acute and Chronic Complications

71.12.1 Acute Complications

Complication	Description	Prevention
Hypoglycaemia	Glucose <3.9 mmol/L due to excess insulin or missed meals	Regular meals, dose adjustment, carry glucose snacks
Diabetic Ketoacidosis (DKA)	Life-threatening metabolic acidosis	Early recognition and adherence
Infections	Urinary tract, skin, respiratory	Good hygiene, immunizations

71.12.2 Chronic Complications

These are rare in well-controlled paediatric patients but may develop after years of poor control.

System	Complication	Screening
Eyes	Retinopathy	Fundoscopy from 11 years or 2 years post-diagnosis
Kidneys	Microalbuminuria → nephropathy	Annual urine albumin/creatinine ratio
Nerves	Peripheral neuropathy	Clinical exam annually
Cardiovascular	Hypertension, dyslipidaemia	BP check, lipid profile

Prevention lies in **good glycaemic control (HbA1c <7.5%)**, healthy lifestyle, and regular follow-up.

71.13 Follow-Up and Long-Term Care

71.13.1 Key Components

- Growth and pubertal monitoring.
- Annual screening for complications.

- Psychosocial evaluation.
- Immunizations: influenza, pneumococcal, hepatitis B.
- Transition planning from paediatric to adult diabetes care.

71.13.2 School Support

- Teachers and school nurses should understand the child's condition.
- Allow glucose monitoring and snacks when needed.
- Create an emergency plan for hypoglycaemia.

71.14 Special Considerations in Ghana

- **Late presentation** due to limited awareness and poor access to diagnostic tools.
- **Insulin affordability** remains a challenge; reliance on hospital pharmacies or NHIS coverage is common.
- **Refrigeration** issues in rural areas affect insulin storage; traditional clay pot coolers may help.
- **Cultural beliefs** sometimes lead to trial of herbal remedies, delaying therapy.
- **Education of healthcare workers** at peripheral centres is vital to improve early diagnosis and management.

71.15 Emerging Trends

- Use of **continuous glucose monitoring (CGM)** and **insulin pens** is increasing in urban Ghana.
- **Tele-diabetes follow-up** and community-based screening programmes are expanding.
- Research into **autoantibody prevalence** and **genetic profiles** in African children with diabetes is ongoing.

71.16 Summary Table

Type	Mechanism	Key Features	Management
Type 1	Autoimmune -cell destruction → insulin deficiency	Polyuria, weight loss, DKA	Insulin + diet + education
Type 2	Insulin resistance + relative deficiency	Obesity, acanthosis nigricans	Lifestyle + metformin ± insulin
Monogenic	Single gene mutation	Neonatal/childhood onset, family history	May respond to sulfonylureas
Secondary	Due to other diseases/drugs	Variable	Treat underlying cause

71.17 Key Takeaways

- Diabetes mellitus is an **increasingly common chronic condition** in Ghanaian children.
- **Type 1 diabetes** remains predominant, with DKA as the main presenting feature.
- **Insulin therapy**, **dietary regulation**, and **education** are the cornerstones of management.
- Early recognition, regular follow-up, and psychosocial support significantly reduce morbidity.
- Improving awareness and healthcare access remain critical to improving outcomes.

71.18 Suggested Reading

1. International Society for Pediatric and Adolescent Diabetes (ISPAD) Clinical Practice Guidelines, 2022.
2. Nelson Textbook of Pediatrics, 22nd Edition.
3. WHO Pocket Book of Hospital Care for Children, 3rd Edition.

4. Ghana Health Service (GHS) Clinical Guidelines, 2024 Edition.

5. Amissah-Arthur MB, et al. “Profile of childhood diabetes mellitus at Komfo Anokye Teaching Hospital, Kumasi.” *Ghana Medical Journal* 2020.

72 Thyroid Disorders

72.1 Introduction

The thyroid gland plays a critical role in regulating growth, metabolism, and neurodevelopment in children. Thyroid disorders are among the most common endocrine problems in paediatrics and may present with growth retardation, developmental delay, or changes in metabolic rate. Because thyroid hormones influence almost every organ system, the clinical manifestations of their dysfunction are diverse and often subtle, especially in infants and children.

This note provides an overview of thyroid physiology, outlines common thyroid disorders in children, and discusses their clinical presentation, investigation, and management.

72.2 Anatomy and Physiology

The thyroid gland is a butterfly-shaped organ located in the anterior neck. It secretes the hormones **thyroxine (T4)** and **triiodothyronine (T3)** under the control of **thyroid-stimulating hormone (TSH)** from the anterior pituitary, which is regulated by **thyrotropin-releasing hormone (TRH)** from the hypothalamus.

Functions of thyroid hormones:

- Regulation of **metabolic rate** and energy expenditure.
- Promotion of **growth and skeletal maturation**.
- Essential for **brain development**, especially in the first 2–3 years of life.
- Maintenance of **cardiovascular, gastrointestinal, and neuromuscular functions**.

72.3 Classification of Thyroid Disorders

Thyroid diseases in children may be classified as:

Category	Examples
Functional abnormalities	Hypothyroidism, Hyperthyroidism
Structural abnormalities	Goitre, Thyroid nodules, Thyroid carcinoma

Category	Examples
Inflammatory/autoimmune disorders	Hashimoto's thyroiditis, Graves' disease
Congenital abnormalities	Thyroid dysgenesis, Dyshormonogenesis, Thyroid hormone resistance

72.4 Congenital Hypothyroidism

72.4.1 Definition

A condition present at birth due to a deficiency of thyroid hormone production, leading to impaired neurodevelopment and growth if untreated.

72.4.2 Aetiology

1. **Thyroid dysgenesis (85%)** — agenesis, ectopia, or hypoplasia.
2. **Dyshormonogenesis (10%)** — enzyme defects in hormone synthesis.
3. **Central hypothyroidism (rare)** — pituitary or hypothalamic dysfunction.
4. **Transient causes** — maternal antithyroid drugs, iodine deficiency or excess.

72.4.3 Pathophysiology

Lack of thyroid hormone during early infancy leads to irreversible brain damage and developmental delay. Early detection and treatment are therefore crucial.

72.4.4 Clinical Features

Symptoms are often subtle at birth due to transplacental maternal T4.
Typical features include:

- Prolonged neonatal jaundice
- Feeding difficulties and lethargy
- Large fontanelle, macroglossia, umbilical hernia
- Hypotonia and dry skin
- Later: growth retardation, developmental delay, coarse facial features, hoarse cry.

72.4.5 Diagnosis

- **Newborn screening:** Elevated TSH, low T4.
- **Confirmatory tests:** Serum TSH and free T4.
- **Imaging:** Thyroid ultrasound or radionuclide scan to assess gland structure.

72.4.6 Management

- **Levothyroxine:** 10–15 µg/kg/day orally, initiated as soon as diagnosis is made (ideally within 2 weeks of birth).
- **Monitoring:** TSH and free T4 every 2–4 weeks initially, then every 3 months after 6 months of age.
- **Long-term care:** Normal growth and neurodevelopment if therapy is started early and adherence is maintained.

72.5 Acquired Hypothyroidism

72.5.1 Aetiology

1. **Autoimmune thyroiditis (Hashimoto's disease)** — the most common cause in older children and adolescents.
2. Iodine deficiency or excess.
3. Drugs (lithium, amiodarone, antithyroid medications).
4. Post-irradiation or post-surgical.
5. Pituitary or hypothalamic dysfunction (secondary hypothyroidism).

72.5.2 Clinical Features

- Growth failure and delayed bone age.
- Lethargy, cold intolerance, and constipation.
- Weight gain, dry skin, brittle hair.
- Bradycardia and delayed puberty.
- Diffuse or nodular goitre (in autoimmune thyroiditis).

72.5.3 Investigations

- Serum TSH (usually elevated) and free T4 (low).
- Antithyroid antibodies (anti-TPO, anti-thyroglobulin) are positive in Hashimoto's disease.
- Thyroid ultrasound — may show heterogeneous echotexture in cases of autoimmune disease.

72.5.4 Management

- **Levothyroxine replacement:** 2–4 µg/kg/day in children; adjust based on growth and lab monitoring.
- Regular monitoring of growth velocity, TSH, and T4 levels.
- Lifelong therapy in autoimmune cases; temporary therapy in transient hypothyroidism.

72.6 Hyperthyroidism in Children

72.6.1 Overview

Hyperthyroidism results from excessive circulating thyroid hormones, leading to increased metabolic rate and sympathetic overactivity.
It is much less common in children than hypothyroidism, but is most often due to **Graves' disease**.

72.6.2 Aetiology

1. **Graves' disease (autoimmune)** — antibodies stimulate TSH receptors → excess hormone synthesis.
2. Toxic multinodular goitre or adenoma.
3. Thyroiditis (transient thyrotoxicosis due to gland inflammation).
4. Iatrogenic (excessive thyroxine intake).

72.6.3 Clinical Features

- Weight loss despite a good appetite.
- Heat intolerance, sweating, palpitations.
- Tremor, irritability, hyperactivity, poor school performance.
- Tachycardia, goitre, and exophthalmos (Graves' disease).
- Accelerated bone maturation and growth.

72.6.4 Diagnosis

- **Low TSH**, **elevated T3 and T4**.
- **Thyroid antibodies:** positive TSH receptor antibodies in Graves' disease.
- **Radioiodine uptake:** diffuse in Graves', focal in toxic adenoma, low in thyroiditis.

72.6.5 Management

72.6.5.1 Antithyroid Drugs

- **Carbimazole (0.5–1 mg/kg/day)** or **Methimazole** are first-line.
- Treatment is usually continued for 12–24 months, with gradual tapering.
- Monitor for side effects: agranulocytosis, rash, hepatotoxicity.

72.6.5.2 Beta-blockers

- **Propranolol (1–2 mg/kg/day)** for control of tachycardia, tremor, and anxiety.

72.6.5.3 Definitive Therapy

- Radioiodine ablation (rarely used in children under 10).
- Subtotal thyroidectomy for drug-resistant or relapsed cases.

72.6.5.4 Long-Term Follow-Up

- Regular assessment of growth, heart rate, and thyroid function.
- Watch for iatrogenic hypothyroidism after definitive treatment.

72.7 Autoimmune Thyroiditis (Hashimoto's Disease)

72.7.1 Pathophysiology

Autoimmune destruction of the thyroid gland mediated by T-lymphocytes and antibodies against thyroid peroxidase (TPO) and thyroglobulin.
It may coexist with other autoimmune disorders (e.g., type 1 diabetes, Addison's disease).

72.7.2 Clinical Features

- Painless, firm, diffuse goitre.
- Features of hypothyroidism may develop gradually.
- Occasionally presents with transient hyperthyroidism ("Hashitoxicosis").

72.7.3 Investigations

- Elevated TSH, low or normal T4.
- Positive anti-TPO or anti-thyroglobulin antibodies.
- Ultrasound: heterogeneous echotexture.

72.7.4 Management

- Levothyroxine replacement for hypothyroid patients.
- Observation for euthyroid patients with small goitres.
- Screening for other autoimmune diseases (diabetes, celiac disease).

72.8 Goitre in Children

72.8.1 Definition

An enlarged thyroid gland is visible or palpable in the neck.

72.8.2 Causes

Category	Examples
Physiological	Pubertal growth spurt
Iodine deficiency	Endemic goitre
Autoimmune	Hashimoto's, Graves'
Dyshormonogenesis	Genetic enzyme defects
Neoplasms	Benign nodules, carcinoma

72.8.3 Clinical Evaluation

- Size, symmetry, tenderness, and presence of nodules.
- Symptoms of pressure or dysfunction (dysphagia, hoarseness, hypo-/hyperthyroid signs).

72.8.4 Investigations

- Serum TSH and free T4.
- Thyroid antibodies.
- Ultrasound: to distinguish diffuse vs nodular enlargement.
- Fine-needle aspiration cytology (FNAC) for suspicious nodules.

72.8.5 Management

- Treat the underlying cause.
- Iodine supplementation in deficiency areas.
- Levothyroxine suppressive therapy for benign goitres.
- Surgical excision for compressive or suspicious nodules.

72.9 Thyroid Nodules and Cancer

72.9.1 Overview

Thyroid nodules are uncommon in children but carry a higher risk of malignancy (20–25%) than in adults.

72.9.2 Risk Factors

- Prior head and neck irradiation.
- Family history of thyroid cancer (MEN2, familial medullary carcinoma).
- Chronic lymphocytic thyroiditis.

72.9.3 Types

1. **Papillary carcinoma** – most common (70–80%).
2. **Follicular carcinoma** – second most common.
3. **Medullary carcinoma** – associated with MEN2 syndromes.
4. **Anaplastic carcinoma** – extremely rare in children.

72.9.4 Clinical Features

- Solitary firm nodule, sometimes fixed to surrounding tissue.
- Cervical lymphadenopathy.
- Hoarseness or dysphagia (advanced disease).

72.9.5 Investigations

- **Ultrasound:** solid hypoechoic nodule with microcalcifications.
- **FNAC:** gold standard for cytological diagnosis.
- **Thyroid function tests:** usually normal.
- **Thyroglobulin:** tumour marker in differentiated cancers.

72.9.6 Management

- **Surgery:** near-total or total thyroidectomy.
- **Radioiodine ablation** for residual tissue or metastases.
- **Thyroxine suppression therapy** to prevent TSH stimulation.
- **Long-term follow-up** with thyroglobulin levels and imaging.

72.10 Investigations in Suspected Thyroid Disorders

Investigation	Purpose
Serum TSH and free T4	Assess functional status
Thyroid antibodies	Autoimmune thyroid disease
Ultrasound scan	Structure, nodules, cysts
Radioiodine uptake scan	Evaluate the function and nodules
FNAC	Cytological diagnosis
Newborn screening	Early detection of congenital hypothyroidism

72.11 Key Points in Paediatric Thyroid Disorders

- Early detection and treatment of **congenital hypothyroidism** are crucial for preventing irreversible brain damage.
- **Autoimmune thyroiditis** is the most common cause of acquired hypothyroidism in children.
- **Graves' disease** is the leading cause of paediatric hyperthyroidism.
- **Thyroid nodules in children** should be thoroughly evaluated due to a higher risk of malignancy.
- Long-term follow-up with growth and developmental monitoring is essential in all thyroid disorders.

72.12 Summary Table

Disorder	Key Features	Diagnostic Findings	Main Treatment
Congenital Hypothyroidism	Prolonged jaundice, macroglossia, poor growth	↑TSH, ↓T4	Levothyroxine 10–15 µg/kg/day
Hashimoto's Thyroiditis	Goitre, growth failure, and autoimmune markers	↑TSH, anti-TPO +	Levothyroxine
Graves' Disease	Weight loss, tachycardia, exophthalmos	↓TSH, ↑T3/T4, TRAb +	Carbimazole ± -blockers
Goitre (Iodine Deficiency)	Diffuse neck swelling	Normal or ↑TSH	Iodine or thyroxine
Thyroid Cancer	Solitary firm nodule	FNAC positive	Surgery ± radioiodine

72.13 Suggested Reading

1. Nelson Textbook of Paediatrics, 22nd Edition.
2. Sperling MA. *Pediatric Endocrinology*, 5th Edition.
3. WHO. *Guidelines for the Management of Thyroid Disorders in Children.*
4. ESPE (European Society for Paediatric Endocrinology) Clinical Practice Recommendations, 2023.

73 Adrenal Gland Disorders

73.1 Introduction

The adrenal glands are essential endocrine organs responsible for the production of glucocorticoids, mineralocorticoids, and androgens. They play a central role in maintaining metabolism, electrolyte balance, and the stress response.
In children, adrenal gland disorders are particularly important because they can interfere with growth, puberty, and survival during physiological stress.

This lecture provides an overview of the anatomy and physiology of the adrenal glands, followed by a discussion of common paediatric adrenal disorders including **adrenal insufficiency**, **congenital adrenal hyperplasia**, **Cushing syndrome**, **adrenal tumours**, and **disorders of adrenal medulla**.

73.2 Anatomy and Physiology

Each adrenal gland is composed of two distinct regions:

1. **Adrenal cortex** — makes up about 90% of the gland.
   It has three zones:
   - **Zona glomerulosa** → secretes **aldosterone** (mineralocorticoid)
   - **Zona fasciculata** → secretes **cortisol** (glucocorticoid)
   - **Zona reticularis** → secretes **androgens** (DHEA and androstenedione)
2. **Adrenal medulla** — produces catecholamines (epinephrine and norepinephrine) under sympathetic nervous control.

Regulation:

- **ACTH (adrenocorticotropic hormone)** from the anterior pituitary regulates cortisol and androgen synthesis.
- **Renin-angiotensin-aldosterone system (RAAS)** primarily controls aldosterone secretion.

73.3 Major Adrenal Hormones and Their Actions

Hormone	Site of secretion	Major effects
Cortisol	Zona fasciculata	Gluconeogenesis, anti-inflammatory effect, stress response
Aldosterone	Zona glomerulosa	Sodium retention, potassium excretion, water balance
Androgens (DHEA)	Zona reticularis	Pubic/axillary hair development
Catecholamines	Medulla	"Fight or flight" response

73.4 Classification of Adrenal Disorders in Children

Adrenal disorders can be broadly classified into:

Category	Examples
Hypofunction (Adrenal insufficiency)	Primary (Addison's disease), Secondary (ACTH deficiency), Congenital adrenal hyperplasia
Hyperfunction	Cushing syndrome, Hyperaldosteronism, Adrenogenital syndromes
Adrenal masses/tumours	Neuroblastoma, Adrenocortical carcinoma, Adenoma
Disorders of medulla	Pheochromocytoma

73.5 Adrenal Insufficiency

73.5.1 Definition

A condition in which the adrenal glands do not produce sufficient quantities of corticosteroids (cortisol ± aldosterone).

73.5.2 Classification

1. **Primary adrenal insufficiency (Addison's disease):**
    - Destruction or dysfunction of the adrenal cortex.

- Cortisol and aldosterone deficiency.

2. **Secondary adrenal insufficiency:**
   - Due to decreased ACTH secretion from the pituitary.
   - Cortisol deficiency only.
3. **Tertiary adrenal insufficiency:**
   - Resulting from hypothalamic dysfunction or prolonged exogenous steroid therapy.

73.5.3 Aetiology in Children

- **Autoimmune adrenalitis** (most common in developed settings).
- **Congenital adrenal hyperplasia (CAH)**.
- **Adrenal haemorrhage or infarction** (e.g., Waterhouse–Friderichsen syndrome).
- **Infections:** Tuberculosis, CMV, fungal infections.
- **Infiltrative diseases:** Adrenoleukodystrophy, metastatic neuroblastoma.
- **Surgical or drug-induced** (ketoconazole, etomidate).

73.5.4 Clinical Features

- Failure to thrive and weight loss
- Fatigue, weakness, lethargy
- Hyperpigmentation (in primary cases)
- Hypotension, dehydration, salt craving
- Hypoglycaemia and hyponatremia
- Nausea, vomiting, abdominal pain

In neonates: prolonged jaundice, shock, or ambiguous genitalia (in CAH).

73.5.5 Investigations

- **Serum cortisol:** low morning level (< 100 nmol/L is suggestive).
- **Plasma ACTH:** elevated in primary, low in secondary.
- **Electrolytes:** hyponatremia, hyperkalemia, hypoglycemia.
- **ACTH stimulation test (Synacthen test):**
  - Failure of cortisol to rise confirms adrenal insufficiency.
- **Adrenal autoantibodies** for autoimmune cause.
- **Imaging:** CT or MRI of the adrenal glands when a structural cause issuspected.

73.5.6 Management

73.5.6.1 Acute Adrenal Crisis (Emergency)

Presentation: Shock, vomiting, dehydration, hypoglycaemia.

Management steps:

1. Immediate IV access.
2. **Hydrocortisone:** 50 mg/m² IV stat, then 50–100 mg/m²/day divided q6h.
3. **IV fluids:** 0.9% saline with 5% dextrose for rehydration and glucose correction.
4. Correct electrolytes.
5. Identify and treat precipitating cause (infection, steroid withdrawal, stress).

73.5.6.2 Chronic Replacement Therapy

- **Glucocorticoid:** Hydrocortisone 8–10 mg/m²/day orally (divided 3 doses).
- **Mineralocorticoid:** Fludrocortisone 0.05–0.2 mg daily.
- **Education:** "Sick day" rule—double or triple steroid dose during illness or surgery.

- **Monitoring:** Growth, weight, blood pressure, electrolytes.

73.6 Congenital Adrenal Hyperplasia (CAH)

73.6.1 Definition

A group of **autosomal recessive** enzyme defects in cortisol biosynthesis, leading to cortisol deficiency, variable aldosterone deficiency, and androgen excess.

73.6.2 Most Common Type

- **21-hydroxylase deficiency (90–95%)**

73.6.3 Pathophysiology

- Block in cortisol synthesis → increased ACTH → adrenal hyperplasia.
- Excess precursors diverted to androgen pathway → virilisation.
- In salt-wasting forms → aldosterone deficiency causes hyponatremia and hyperkalemia.

73.6.4 Classification

Type	Features
Classical (Severe)	Salt-wasting or simple virilising
Non-classical (Mild)	Partial enzyme deficiency, late onset virilisation

73.6.5 Clinical Features

73.6.5.1 Salt-wasting type

- Neonatal onset (first 2 weeks).
- Vomiting, dehydration, weight loss, shock.
- Hyponatremia, hyperkalemia, hypoglycemia.

- Female: ambiguous genitalia (virilisation).
- Male: normal genitalia but presents with adrenal crisis.

73.6.5.2 Simple virilising type

- Ambiguous genitalia in females at birth.
- Precocious puberty, accelerated bone age.
- No salt wasting.

73.6.5.3 Non-classical type

- Later onset (childhood/adolescence).
- Hirsutism, acne, irregular menses in girls.
- Early pubarche in boys.

73.6.6 Diagnosis

- **17-hydroxyprogesterone (17-OHP):** elevated (>30 nmol/L basal or post-ACTH).
- **Electrolytes:** hyponatremia, hyperkalemia.
- **Genetic testing:** CYP21A2 mutations.
- **Ultrasound:** assess internal genitalia in virilised females.

73.6.7 Management

73.6.7.1 Hormone Replacement

- **Hydrocortisone:** 10–15 mg/m²/day (3 divided doses).
- **Fludrocortisone:** 0.05–0.2 mg/day in salt-wasting forms.
- **Sodium supplementation:** especially in neonates.

73.6.7.2 Surgical Correction

- **Genitoplasty** for virilised females (timing individualized).

73.6.7.3 Long-Term Care

- Growth monitoring (avoid overtreatment leading to growth suppression).
- Periodic bone age assessment.
- Psychological and genetic counselling.
- Lifelong follow-up in endocrinology clinic.

73.7 Cushing Syndrome

73.7.1 Definition

A state of **chronic glucocorticoid excess**, either due to endogenous overproduction or exogenous steroid use.

73.7.2 Aetiology

Type	Cause
Exogenous	Prolonged corticosteroid therapy (most common in children)
Endogenous	ACTH-secreting pituitary adenoma (Cushing disease), adrenal adenoma or carcinoma, ectopic ACTH secretion (rare)

73.7.3 Clinical Features

- Growth failure and weight gain
- Moon facies, truncal obesity, buffalo hump
- Striae (purple), acne, hirsutism

- Hypertension, glucose intolerance
- Mood changes (depression, irritability)
- Osteopenia or fractures
- Delayed puberty or amenorrhea

73.7.4 Investigations

1. **Screening tests**
   - 24-hour urinary free cortisol: elevated.
   - Late-night salivary cortisol: loss of diurnal variation.
   - Low-dose dexamethasone suppression test: failure to suppress cortisol.
2. **Differentiation tests**
   - Plasma ACTH:
     - Low → adrenal cause
     - Normal/high → ACTH-dependent cause.
3. **Imaging**
   - MRI pituitary (Cushing disease).
   - CT or MRI adrenals for adenoma/carcinoma.

73.7.5 Management

- **Exogenous:** Gradual tapering of steroid dose.
- **Pituitary adenoma:** Trans-sphenoidal surgery.
- **Adrenal tumour:** Surgical excision ± radiotherapy.
- **Medical therapy:** Ketoconazole, metyrapone, or mitotane when surgery is contraindicated.

73.7.6 Prognosis

- Normal growth may resume post-treatment, but final height may be compromised if prolonged disease.
- Requires careful perioperative steroid coverage to prevent adrenal insufficiency.

73.8 Adrenal Tumours

73.8.1 Overview

Adrenal tumours in children may be **benign (adenoma)** or **malignant (carcinoma)**, and may secrete hormones or be non-functioning.

73.8.1.1 Adrenocortical Tumours

- **Adenomas:** often hormonally active (Cushing, virilisation).
- **Carcinomas:** aggressive, may secrete multiple hormones.

Clinical features:

- Rapid virilisation in girls.
- Cushingoid features.
- Precocious puberty in boys.
- Abdominal mass or pain.

Diagnosis:

- Elevated serum and urinary steroid precursors.
- Imaging (CT/MRI): large irregular mass.
- Histopathology confirms diagnosis.

Treatment:

- Surgical excision is mainstay.

- Chemotherapy for carcinoma (mitotane, cisplatin-based regimens).
- Lifelong hormonal follow-up.

73.8.1.2 Neuroblastoma

A malignant tumour arising from **neural crest cells** of the adrenal medulla.

Clinical features:

- Abdominal mass, weight loss, hypertension.
- Opsoclonus–myoclonus syndrome (rare paraneoplastic sign).

Investigations:

- Elevated urinary catecholamine metabolites (VMA, HVA).
- Imaging: calcified adrenal mass.
- Bone marrow or MIBG scan for metastases.

Treatment:

- Surgery, chemotherapy, and radiotherapy as appropriate.
- Prognosis depends on stage and age (better in <1 year).

73.9 Disorders of the Adrenal Medulla

73.9.1 Pheochromocytoma

A rare catecholamine-secreting tumour of chromaffin cells.

73.9.1.1 Clinical Features

- Paroxysmal or sustained hypertension.
- Headache, palpitations, sweating.
- Pallor, tremor, anxiety.

- May be part of **MEN2A/2B syndromes**.

73.9.1.2 Investigations

- 24-hour urinary **metanephrines and catecholamines** (diagnostic).
- Plasma free metanephrines.
- MRI or MIBG scan to localize tumour.

73.9.1.3 Management

1. **Preoperative preparation:**
   - Alpha-blockade (phenoxybenzamine) for 1–2 weeks.
   - Then beta-blocker (propranolol) if tachycardia.
2. **Definitive surgery:** Adrenalectomy.
3. **Postoperative monitoring** for hypotension or recurrence.

73.10 Investigation Summary Table

Disorder	Key Test	Diagnostic Findings
Adrenal insufficiency	ACTH stimulation	Low cortisol response
CAH	17-hydroxyprogesterone	Elevated
Cushing syndrome	Dexamethasone suppression	Failure to suppress cortisol
Adrenocortical tumour	Urinary steroids, imaging	Elevated androgens/cortisol
Pheochromocytoma	Urinary metanephrines	Elevated catecholamines

73.11 Long-Term Management Considerations

- **Hormone replacement therapy** requires frequent adjustment as the child grows.
- **Stress dosing** of steroids during illness or surgery is lifesaving.

- **Growth monitoring** is crucial to avoid overtreatment or under-replacement.
- **Psychological support** is vital for children with virilisation or chronic illness.
- **Family education** on emergency management (e.g., injectable hydrocortisone) is essential.

73.12 Summary Points

- Adrenal gland disorders in children range from life-threatening adrenal insufficiency to hormone-secreting tumours.
- **Congenital adrenal hyperplasia** is the most frequent inherited adrenal disorder.
- **Adrenal crisis** is a paediatric emergency; treat promptly with IV fluids and hydrocortisone.
- **Cushing syndrome** in children commonly results from exogenous steroids.
- **Pheochromocytoma**, though rare, should be suspected in children with unexplained hypertension.
- Lifelong follow-up and interdisciplinary care (paediatric endocrinology, surgery, psychology) improve outcomes.

73.13 Suggested Reading

1. Nelson Textbook of Pediatrics, 22nd Edition.
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74 Pituitary Gland Disorders

74.1 Introduction

The pituitary gland, often called the **"master gland"**, plays a central role in the regulation of growth, metabolism, reproduction, and stress response. Its hormones influence nearly every endocrine organ, including the thyroid, adrenal glands, and gonads. Disorders of the pituitary gland, therefore, have wide-ranging systemic effects and are of great importance in paediatric practice.

In Ghana, pituitary disorders in children are likely underdiagnosed due to limited access to hormonal assays and imaging facilities. Many children with growth failure or delayed puberty are labelled as "constitutional" cases without proper evaluation. Moreover, paediatric endocrinology services are still emerging, and awareness among frontline health workers remains low. Recognising pituitary disorders early can prevent serious complications, including permanent growth failure, adrenal crisis, or infertility.

This chapter provides an overview of pituitary anatomy and physiology, discusses common and important pituitary disorders in childhood, and outlines their diagnosis and management, with emphasis on **practical approaches in resource-limited settings**.

74.2 Anatomy and Physiology of the Pituitary Gland

The pituitary gland is a small, oval-shaped endocrine organ located at the base of the brain in the **sella turcica**, just below the hypothalamus. It is connected to the hypothalamus by the **pituitary stalk (infundibulum)** and is divided into two main parts:

- **Anterior pituitary (adenohypophysis)** — produces six key hormones:
  - Growth hormone (GH)
  - Adrenocorticotropic hormone (ACTH)
  - Thyroid-stimulating hormone (TSH)
  - Luteinizing hormone (LH)
  - Follicle-stimulating hormone (FSH)
  - Prolactin (PRL)

- **Posterior pituitary (neurohypophysis)** — stores and releases two hypothalamic hormones:
  - Antidiuretic hormone (ADH, also called vasopressin)
  - Oxytocin

The hypothalamus regulates pituitary function through releasing and inhibiting hormones. These hormones are secreted into the **hypophyseal portal circulation**, linking the hypothalamus and pituitary into an integrated **hypothalamic–pituitary axis**.

74.3 Classification of Pituitary Disorders

Pituitary gland disorders in children can be broadly classified as follows:

1. **Hypopituitarism** — deficiency of one or more pituitary hormones
2. **Hyperpituitarism** — excess secretion of one or more hormones
3. **Posterior pituitary disorders** — abnormalities of ADH secretion (diabetes insipidus or SIADH)
4. **Structural lesions** — pituitary adenomas, cysts, craniopharyngiomas, or infiltrative diseases

Each disorder manifests differently, depending on which hormones are affected and at what stage of development the dysfunction occurs.

74.4 Hypopituitarism

74.4.1 Definition

Hypopituitarism refers to partial or complete deficiency of anterior and/or posterior pituitary hormones. It may be **congenital** (present at birth) or **acquired** (occurring later due to injury, tumour, or infection).

74.4.2 Causes

Congenital causes include: - Midline developmental defects (septo-optic dysplasia, holoprosencephaly)

- Genetic mutations affecting pituitary transcription factors (PROP1, POU1F1)
- Perinatal asphyxia or trauma
- Structural anomalies of the pituitary or hypothalamus on MRI

Acquired causes include: - Central nervous system tumours (especially craniopharyngioma)

- Head trauma or irradiation
- Infections such as meningitis or tuberculosis
- Infiltrative diseases (e.g., Langerhans cell histiocytosis)

In Ghana, birth asphyxia, CNS infections, and head trauma are likely the commonest causes of acquired hypopituitarism.

74.4.3 Clinical Features

The clinical presentation depends on the number and severity of hormone deficiencies:

- **Growth hormone deficiency (GHD):** short stature, increased fat mass, immature face, delayed dentition
- **TSH deficiency:** secondary hypothyroidism (fatigue, poor growth, cold intolerance)
- **ACTH deficiency:** adrenal insufficiency (hypoglycaemia, hypotension, fatigue)
- **Gonadotropin deficiency:** delayed or absent puberty
- **Prolactin deficiency:** failure of lactation in post-partum females (less relevant in children)

Infants with panhypopituitarism may present with **hypoglycaemia, prolonged jaundice, micropenis, and poor feeding**. Without recognition, mortality may occur due to adrenal crisis.

74.4.4 Diagnosis

Diagnosis requires both **biochemical assessment** and **neuroimaging**.

- Basal hormone levels: TSH, free T , cortisol, GH, IGF-1, LH/FSH, prolactin
- Dynamic testing (e.g., insulin tolerance test, ACTH stimulation test) — when available
- MRI of the brain to identify structural anomalies or tumours

In Ghana, access to dynamic testing may be limited to teaching hospitals such as KATH or KBTH. Clinicians in regional hospitals may rely on **clinical findings**, basic thyroid function tests, and growth parameters to guide management.

74.4.5 Management

Treatment focuses on **hormone replacement** and **management of underlying causes**.

- **Hydrocortisone** for ACTH deficiency (8–10 mg/m^2/day in divided doses)
- **Levothyroxine** for TSH deficiency
- **Recombinant GH** for GHD (0.025–0.035 mg/kg/day subcutaneously)
- **Sex steroids** for pubertal induction when older

In resource-limited settings, the high cost of GH therapy limits access, and prioritization is often necessary. Multidisciplinary care involving paediatric endocrinologists, dietitians, and psychologists yields the best outcomes.

74.5 Growth Hormone Deficiency (GHD)

GHD is the most common isolated pituitary hormone deficiency in children. It may be **idiopathic**, **genetic**, or **secondary** to structural lesions.

74.5.1 Clinical Features

Children typically present with:

- Short stature with normal body proportions
- Delayed skeletal maturation
- Chubby face and truncal obesity
- Delayed dentition and puberty

In Ghana, such children are often brought late for evaluation, sometimes after unsuccessful use of herbal remedies or growth tonics.

74.5.2 Diagnosis

- Low serum IGF-1 and IGFBP-3 levels
- GH stimulation tests (e.g., clonidine, insulin) to confirm deficiency
- MRI to assess pituitary morphology

74.5.3 Treatment

Daily subcutaneous **recombinant GH** therapy leads to excellent catch-up growth if started early. Monitoring of growth velocity, pubertal development, and thyroid function is essential.

Where GH therapy is unavailable, **nutritional optimisation**, **thyroid screening**, and **regular monitoring** are still beneficial. Psychosocial support for affected children is also essential.

74.6 Hyperpituitarism

74.6.1 Definition and Causes

Hyperpituitarism refers to excessive secretion of one or more pituitary hormones, often due to **pituitary adenomas**. In children, these are usually **benign** but can cause significant morbidity by compressing adjacent structures or overproducing hormones.

Common examples include:

1. **GH-secreting adenoma:** gigantism
2. **Prolactin-secreting adenoma (prolactinoma):** galactorrhoea, delayed puberty
3. **ACTH-secreting adenoma:** Cushing's disease

74.6.2 Growth Hormone Excess (Gigantism)

74.6.2.1 Clinical Features

- Rapid linear growth with tall stature
- Coarse facial features, broad hands and feet
- Headaches and visual disturbances due to tumour mass
- Glucose intolerance or diabetes mellitus

74.6.3 Diagnosis

- Elevated IGF-1 levels
- Failure of GH suppression after oral glucose load
- Pituitary MRI showing macroadenoma

74.6.3.1 Management

- **Trans-sphenoidal surgery** (definitive)
- **Somatostatin analogues (octreotide)** if surgery fails or is not available
- **Radiation therapy** for residual tumour

In Ghana, collaboration between neurosurgery and endocrinologyis essential but often limited to tertiary centres.

74.6.4 Prolactinoma

Prolactinomas cause hyperprolactinaemia, leading to **delayed puberty**, **amenorrhoea**, or **galactorrhoea**.

- Diagnosis: elevated serum prolactin, pituitary MRI
- Treatment: **dopamine agonists** (cabergoline or bromocriptine)
- Surgery if medical therapy fails

74.7 Posterior Pituitary Disorders

The posterior pituitary releases **antidiuretic hormone (ADH)**, which regulates water balance. Two major disorders may occur:

74.7.1 Diabetes Insipidus (DI)

74.7.1.1 Pathophysiology

Caused by deficiency (central DI) or resistance (nephrogenic DI) to ADH. Central DI may result from:

- Head trauma
- Craniopharyngioma or other tumours
- Post-surgical damage
- CNS infections such as meningitis or tuberculosis

74.7.1.2 Clinical Features

- Polyuria and polydipsia
- Nocturia or enuresis
- Dehydration and hypernatraemia
- Low urine osmolality despite high plasma osmolality

74.7.1.3 Diagnosis

- Water deprivation test (if facilities allow)
- Low urine specific gravity (<1.005)
- Response to **desmopressin** confirms central DI

74.7.1.4 Management

- **Desmopressin (DDAVP)** intranasal or oral
- Adequate hydration
- Treatment of the underlying cause

Access to desmopressin can be a challenge in Ghana, requiring coordination with major teaching hospitals or pharmacies that stock specialised endocrinology drugs.

74.7.2 Syndrome of Inappropriate ADH Secretion (SIADH)

SIADH results from **excess ADH secretion**, leading to **hyponatraemia** with low serum osmolality and concentrated urine.

Common causes include CNS infections, pulmonary disease, or drugs (e.g., carbamazepine). Management involves **fluid restriction**, **salt supplementation**, and addressing the underlying cause.

74.8 Craniopharyngioma and Other Structural Lesions

Craniopharyngioma is a benign but locally aggressive tumour arising from remnants of Rathke's pouch. It is the **most common suprasellar tumour** in children and a leading cause of acquired hypopituitarism.

74.8.1 Clinical Features

- Growth failure and delayed puberty
- Visual impairment (bitemporal hemianopia)
- Headache, vomiting due to raised intracranial pressure
- Diabetes insipidus or other pituitary deficiencies

74.8.2 Diagnosis

- MRI of the brain: cystic, calcified suprasellar mass
- Endocrine evaluation for pituitary dysfunction

74.8.3 Management

- **Surgical resection** (ideally, subtotal to preserve function)
- **Postoperative hormone replacement** (hydrocortisone, thyroxine, GH, DDAVP)
- **Radiation therapy** for residual tumour

Children require **lifelong follow-up** due to the risk of recurrence and permanent panhypopituitarism.

In Ghana, neurosurgical expertise exists in teaching hospitals, but postoperative endocrine support is sometimes inadequate, underscoring the need for closer multidisciplinary collaboration.

74.9 Approach to a Child with Suspected Pituitary Disorder

A structured evaluation includes:

1. **History:** growth pattern, perinatal events, head trauma, CNS infections, puberty timing, polyuria/polydipsia
2. **Examination:** height/weight, visual fields, facial features, pubertal staging, hydration status
3. **Baseline Investigations:**
    - Serum electrolytes, glucose
    - Thyroid function tests
    - Morning cortisol
    - IGF-1 levels
    - LH, FSH, prolactin
4. **Imaging:** Pituitary MRI if available

5. **Referral:** to a paediatric endocrinologist for specialized testing and management

74.10 Challenges in the Ghanaian Context

- Limited access to hormone assays (especially GH, IGF-1, cortisol)
- Lack of standardised growth monitoring in many clinics
- Cost and availability of hormone replacement (GH, desmopressin)
- Few centres with multidisciplinary paediatric endocrine teams

Improving training in **growth assessment**, expanding **laboratory capacity**, and integrating **endocrine screening** into routine child health services are key to improving diagnosis and management outcomes.

74.11 Conclusion

Pituitary gland disorders in children, though relatively uncommon, have far-reaching effects on growth, development, and overall health. Early recognition and prompt hormone replacement can transform outcomes.

In Ghana and similar settings, raising clinicians' awareness, ensuring theavailability of key diagnostic tests, and strengthening referral pathways are vital steps forward. Every child with unexplained growth failure, delayed puberty, or abnormal thirst and urination deserves a careful evaluation of pituitary function.

74.12 Further Reading

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75 Calcium and Bone Metabolism

75.1 Introduction

Calcium and bone metabolism form a vital part of paediatric growth and development. Bones are not static structures; they are dynamic organs that undergo continuous remodeling, with bone formation and resorption occurring simultaneously. This dynamic process depends heavily on an intricate balance between calcium homeostasis, hormonal regulation, and adequate nutrition.

Calcium is not only essential for skeletal integrity but also for neuromuscular function, blood coagulation, and intracellular signaling. Disturbances in calcium or bone metabolism can lead to conditions such as **rickets**, **osteopenia**, **hypocalcaemia**, or **hypercalcaemia** — all of which are relatively common in paediatric practice in Ghana and sub-Saharan Africa.

Understanding calcium and bone metabolism is fundamental for diagnosing and managing paediatric metabolic bone disorders, especially given the high burden of **nutritional rickets** and **vitamin D deficiency** observed in resource-limited settings.

75.2 Overview of Bone Structure and Function

Bone serves multiple physiological roles:

- **Structural support and protection** for internal organs.
- **Reservoir for minerals**, mainly calcium and phosphate.
- **Site of haematopoiesis** within the bone marrow.
- **Endocrine organ**, influencing energy metabolism through osteocalcin secretion.

Bone tissue consists of:

- **Organic matrix (osteoid):** Composed mainly of type I collagen, providing tensile strength.
- **Inorganic mineral component:** Primarily calcium hydroxyapatite [Ca (PO) (OH)], which gives hardness and rigidity.
- **Cells:** Including osteoblasts (bone-forming), osteoclasts (bone-resorbing), and osteocytes (mature cells embedded in bone).

The balance between bone formation and resorption maintains bone mass and structural integrity. This balance is regulated by both systemic hormones and local cytokines.

75.3 Calcium Homeostasis

75.3.1 Distribution of Calcium

Approximately **99%** of total body calcium is stored in the skeleton and teeth. The remaining **1%** is distributed in extracellular and intracellular compartments.

Compartment	Approximate percentage	Form
Bone and teeth	99%	Hydroxyapatite crystals
Extracellular fluid	1%	Ionized (50%), protein-bound (40%), complexed (10%)

Ionized calcium is the physiologically active form that participates in neuromuscular and enzymatic processes.

75.3.2 Normal Serum Calcium Levels

- **Total calcium:** 2.1–2.6 mmol/L
- **Ionized calcium:** 1.1–1.3 mmol/L

These levels vary slightly with **age**, **protein status**, and **acid-base balance**.

75.3.3 Sources and Absorption of Calcium

75.3.3.1 Dietary Sources

- **Breast milk:** Primary source in infancy, though low in calcium, it is highly bioavailable.
- **Cow's milk, fish with bones (e.g., sardines), green leafy vegetables (kontomire),** and **fortified foods** are important dietary sources in Ghana.

75.3.3.2 Absorption

- Occurs mainly in the **duodenum and proximal jejunum**.
- Facilitated by **active transport** (vitamin D-dependent) and **passive diffusion**.
- Factors enhancing absorption:
  - Adequate vitamin D.
  - Acidic gastric pH.
  - Presence of lactose in infants.
- Factors reducing absorption:
  - Phytates (in cereals), oxalates (in spinach), and high phosphate intake (soft drinks).
  - Chronic diarrhoeal diseases or fat malabsorption.

75.4 Hormonal Regulation of Calcium and Phosphate Metabolism

Calcium balance is maintained by a **homeostatic triad** involving:

1. **Parathyroid hormone (PTH)**
2. **Vitamin D (calcitriol)**
3. **Calcitonin**

These hormones act on the **bone**, **kidney**, and **gastrointestinal tract** to regulate calcium and phosphate concentrations.

75.4.1 Parathyroid Hormone (PTH)

75.4.1.1 Source

Secreted by the **chief cells** of the parathyroid glands.

75.4.1.2 Stimulus

Released in response to **low serum ionized calcium**.

75.4.1.3 Actions

- **Bone:** Stimulates osteoclast-mediated bone resorption, releasing calcium and phosphate.
- **Kidney:**
  - Increases calcium reabsorption in distal tubules.
  - Decreases phosphate reabsorption (phosphaturia).
  - Enhances 1 -hydroxylase activity → increases active vitamin D production.
- **Intestine:** Indirectly increases calcium absorption via vitamin D activation.

75.4.1.4 Net Effect

Raises serum calcium and lowers serum phosphate.

75.4.2 Vitamin D (Calcitriol)

75.4.2.1 Sources

- **Endogenous synthesis:** From 7-dehydrocholesterol in the skin upon exposure to sunlight (UVB rays).
- **Dietary intake:** From fish oil, fortified milk, eggs, and supplements.

75.4.2.2 Metabolism

1. **Liver:** Converts cholecalciferol to **25-hydroxyvitamin D [25(OH)D]**.
2. **Kidney:** Converts 25(OH)D to **1,25-dihydroxyvitamin D [1,25(OH) D]**, the active form.

75.4.2.3 Actions

- **Intestine:** Increases absorption of calcium and phosphate.
- **Bone:** Promotes mineralization and bone formation.
- **Kidney:** Facilitates calcium reabsorption.

75.4.2.4 Net Effect

Increases both serum calcium and phosphate.

75.4.2.5 Ghanaian Context

Children in Ghana should theoretically have adequate vitamin D due to abundant sunlight. However, **urbanization**, **use of sunscreen**, **indoor lifestyles**, **dark skin pigmentation**, and **maternal deficiency during pregnancy** contribute to suboptimal vitamin D levels in both mothers and infants. Consequently, **nutritional rickets** remains prevalent in some communities, particularly among exclusively breastfed infants without supplementation.

75.4.3 Calcitonin

75.4.3.1 Source

Secreted by **parafollicular (C) cells** of the thyroid gland.

75.4.3.2 Actions

- Inhibits osteoclastic bone resorption.
- Promotes renal calcium excretion.

75.4.3.3 Net Effect

Lowers serum calcium levels — physiologically less significant in children compared to adults.

75.5 Bone Remodeling

Bone is constantly renewed through **remodeling cycles**, which consist of:

1. **Activation:** Recruitment of osteoclasts to resorption sites.
2. **Resorption:** Breakdown of mineral and matrix by osteoclasts.
3. **Reversal:** Transition phase.
4. **Formation:** Osteoblasts lay down new osteoid, which becomes mineralized.

During **childhood and adolescence**, bone formation exceeds resorption, resulting in net bone gain. **Peak bone mass** is achieved around the third decade of life, after which bone loss begins gradually.

Factors influencing bone remodeling include:

- **Mechanical stress:** Weight-bearing stimulates bone formation.
- **Hormones:** Growth hormone, PTH, sex steroids.
- **Nutrients:** Calcium, phosphate, magnesium, and vitamin D.

- **Cytokines:** IL-1, TNF- , and RANKL/OPG pathway.

75.6 Disorders of Calcium and Bone Metabolism in Children

75.6.1 Hypocalcaemia

75.6.1.1 Causes

- **Neonatal:**
  - Prematurity.
  - Maternal diabetes.
  - Birth asphyxia or sepsis.
  - Hypoparathyroidism or pseudohypoparathyroidism.
- **Childhood:**
  - Vitamin D deficiency (nutritional rickets).
  - Chronic renal disease.
  - Hypomagnesaemia.
  - Malabsorption syndromes.

75.6.1.2 Clinical Features

- Tetany (carpopedal spasm, laryngospasm).
- Seizures.
- Paresthesiae.
- Chvostek's and Trousseau's signs.
- Irritability or poor feeding in infants.

75.6.1.3 Management

- Acute: IV calcium gluconate (0.5–1 mL/kg of 10% solution).
- Chronic: Oral calcium and vitamin D supplementation.
- Treat underlying cause (e.g., magnesium deficiency).

75.6.2 Hypercalcaemia

75.6.2.1 Causes

- Iatrogenic (excess vitamin D or calcium).
- Primary hyperparathyroidism (rare in children).
- Malignancy (leukaemia, lymphoma).
- Granulomatous diseases (sarcoidosis, tuberculosis).
- Prolonged immobilization.

75.6.2.2 Clinical Features

- Nausea, vomiting, constipation.
- Polyuria, polydipsia.
- Lethargy, confusion.
- Renal calculi or nephrocalcinosis.

75.6.2.3 Management

- Adequate hydration.
- Loop diuretics (furosemide).
- Corticosteroids for vitamin D-related causes.
- Bisphosphonates in refractory cases.

75.6.3 Rickets and Osteomalacia

75.6.3.1 Definition

Defective mineralization of bone matrix, leading to soft and deformed bones in children (rickets) and adults (osteomalacia).

75.6.3.2 Causes

- **Nutritional vitamin D deficiency:** Most common in Ghana.
- **Calcium deficiency:** Seen in diets low in dairy or with high phytate content.
- **Chronic kidney disease:** Renal rickets.
- **Genetic:** Vitamin D–dependent or resistant rickets.

75.6.3.3 Clinical Features

- Delayed closure of fontanelle.
- Frontal bossing, rachitic rosary.
- Bowed legs (genu varum) or knock knees (genu valgum).
- Widened wrists and ankles.
- Growth retardation.

75.6.3.4 Investigations

- Low calcium and phosphate.
- Elevated alkaline phosphatase.
- Low 25(OH) vitamin D.
- Radiographs: Cupping and fraying of metaphyses.

75.6.3.5 Management

- Vitamin D supplementation (2,000–6,000 IU daily for 3 months, then maintenance).
- Dietary calcium supplementation.
- Adequate sunlight exposure.
- Health education for caregivers.

75.6.3.6 Local Note

Studies from Ghana and Nigeria have shown a **mixed calcium and vitamin D deficiency** pattern in rickets. Exclusive reliance on sunlight exposure without dietary correction may therefore be inadequate.

75.6.4 Osteopenia and Osteoporosis of Prematurity

75.6.4.1 Definition

Reduced bone mineral content in preterm infants due to inadequate mineral accretion.

75.6.4.2 Causes

- Prematurity (most calcium accretion occurs in the third trimester).
- Prolonged parenteral nutrition.
- Chronic diuretic or steroid use.
- Limited physical activity.

75.6.4.3 Prevention and Management

- Adequate calcium and phosphate supplementation in preterm feeds.
- Use of fortified breast milk.
- Gentle physical therapy.

75.6.5 Renal Osteodystrophy

75.6.5.1 Pathophysiology

Chronic kidney disease leads to: - Impaired phosphate excretion (hyperphosphataemia), - Reduced calcitriol production, - Secondary hyperparathyroidism, - Bone demineralization and deformities.

75.6.5.2 Management

- Dietary phosphate restriction.
- Phosphate binders.
- Active vitamin D analogues (calcitriol).
- Correction of metabolic acidosis.

75.7 Laboratory Evaluation of Bone and Calcium Metabolism

Test	Interpretation	Clinical Utility
Serum calcium (total/ionized)	↓ in hypocalcaemia, ↑ in hypercalcaemia	Basic screen
Serum phosphate	↓ in rickets, ↑ in renal disease	Assess phosphate balance
Alkaline phosphatase (ALP)	Elevated in bone formation or rickets	Marker of bone turnover
Parathyroid hormone (PTH)	High in secondary hyperparathyroidism	Helps classify calcium disorders
25(OH) vitamin D	Reflects vitamin D stores	Deficiency common in rickets
1,25(OH) D	Active form; low in renal disease	Used selectively
Urinary calcium and phosphate	To assess renal losses	Useful in metabolic bone diseases

Radiologic investigations (wrist or knee X-rays) complement biochemical findings in rickets and other bone disorders.

75.8 Nutritional Considerations and Public Health Implications

In Ghana, dietary calcium intake among children is often **below recommended levels**, particularly in rural communities where milk consumption is limited. Staple diets based on maize, millet, and cassava have high phytate content, reducing calcium bioavailability.

Strategies to improve calcium and vitamin D status include: - Promoting exclusive breastfeeding with appropriate maternal nutrition. - Fortification of complementary foods with calcium and vitamin D. - Encouraging outdoor play for sunlight exposure. - Supplementation programs for at-risk groups (infants, adolescents, pregnant women).

Public health campaigns should also emphasize the dangers of excessive soda intake, as **phosphoric acid** in carbonated drinks can impair calcium absorption.

75.9 Summary

- Calcium and phosphate metabolism is tightly regulated by **PTH**, **vitamin D**, and **calcitonin**.
- The skeleton serves as the main calcium reservoir, undergoing constant remodeling.
- Disorders such as **rickets**, **hypocalcaemia**, and **renal osteodystrophy** are common in paediatric practice.
- **Nutritional deficiency**, **limited sunlight exposure**, and **chronic kidney disease** are leading causes in Ghana.
- Early diagnosis, supplementation, and community education are vital for prevention and management.

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76 Reproductive Disorders

76.1 Introduction

Reproductive endocrinology in children involves the study of the development, function, and disorders of the hypothalamic–pituitary–gonadal (HPG) axis. Unlike adults, in whom the system operates cyclically or continuously, the paediatric HPG axis undergoes distinct phases of activation and quiescence from fetal life through puberty.

Reproductive disorders in children manifest as abnormalities in sexual differentiation, pubertal timing, gonadal development, or fertility. These conditions often present with clinical signs such as ambiguous genitalia, delayed or precocious puberty, or menstrual irregularities in adolescents.

In Ghana and sub-Saharan Africa, limited access to endocrine diagnostic testing, late presentation, and sociocultural sensitivities surrounding reproductive development pose additional challenges. Hence, an understanding of normal reproductive physiology and early recognition of pathological patterns is crucial for paediatricians.

76.2 Physiology of the Hypothalamic–Pituitary–Gonadal Axis

The HPG axis controls reproductive development and function through the coordinated actions of:

1. **Hypothalamus:** Secretes gonadotropin-releasing hormone (GnRH) in a pulsatile fashion.

2. **Pituitary gland:** Responds to GnRH by releasing luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

3. **Gonads (testes and ovaries):** Produce sex steroids (testosterone, estrogen, progesterone) and gametes in response to LH and FSH.

76.2.1 Phases of Activity

- **Fetal life:** HPG axis active; sex differentiation occurs.
- **Mini-puberty (first 6 months postnatal):** Temporary activation, useful for early diagnosis of some disorders.
- **Childhood:** Relative quiescence of the axis.
- **Puberty:** Reactivation leading to secondary sexual characteristics and fertility.

76.3 Classification of Paediatric Reproductive Disorders

Reproductive disorders can be broadly grouped into:

1. **Disorders of Sexual Differentiation (DSD)**
2. **Pubertal Disorders**
3. **Gonadal Dysfunction**
4. **Menstrual and Fertility Disorders**

Each category encompasses multiple aetiologies, with some overlap.

76.4 Disorders of Sexual Differentiation (DSD)

These are congenital conditions in which chromosomal, gonadal, or anatomical sex is atypical.

76.4.1 Classification

- **46,XX DSD:** Often due to exposure to excess androgens (e.g., congenital adrenal hyperplasia).
- **46,XY DSD:** Results from under-virilization due to gonadal dysgenesis or androgen insensitivity.
- **Sex Chromosome DSD:** Such as Turner syndrome (45,X) and Klinefelter syndrome (47,XXY).

76.4.2 Clinical Presentation

- Ambiguous genitalia at birth
- Inguinal or labial masses (testes)
- Discordance between genetic and phenotypic sex
- Failure of virilization in adolescence

76.4.3 Diagnosis

- **Karyotyping:** Determines chromosomal sex.
- **Hormonal assays:** Measure 17-hydroxyprogesterone, testosterone, LH, FSH, and AMH.
- **Pelvic ultrasound:** Evaluates internal genital structures.
- **Genetic testing:** Useful where available.

76.4.4 Local Context

In Ghana, many cases of ambiguous genitalia present late due to cultural stigma and inadequate neonatal screening. Early multidisciplinary assessment (paediatrician, endocrinologist, surgeon, psychologist) is critical for optimal outcomes and family counselling.

76.4.5 Management

- Gender assignment based on diagnostic clarity and cultural sensitivity.
- Surgical correction where indicated.
- Hormone replacement (e.g., glucocorticoids in CAH).
- Psychosocial support for the patient and family.

76.5 Disorders of Puberty

76.5.1 Definition

Puberty is the process leading to sexual maturation and reproductive capability. It involves the activation of the HPG axis.

- **Precocious puberty:** Onset of secondary sexual characteristics before age 8 in girls or 9 in boys.
- **Delayed puberty:** Absence of such characteristics by age 13 in girls or 14 in boys.

76.5.2 Precocious Puberty

76.5.2.1 Types

- **Central (GnRH-dependent):** Premature activation of the HPG axis.
- **Peripheral (GnRH-independent):** Due to excess sex steroids from gonadal, adrenal, or ectopic sources.

76.5.2.2 Causes

- Central: Idiopathic (especially in girls), CNS lesions (e.g., hypothalamic hamartoma), CNS infections (common post-meningitic sequelae in sub-Saharan Africa).
- Peripheral: Congenital adrenal hyperplasia, ovarian cysts or tumours, McCune-Albright syndrome, exogenous hormones.

76.5.2.3 Clinical Features

- Early breast development (thelarche), pubic hair (pubarche), or menses in girls.
- Testicular enlargement, penile growth, or voice deepening in boys.
- Advanced bone age and accelerated growth.

76.5.2.4 Investigations

- LH and FSH (basal and GnRH-stimulated).
- Sex steroids (estradiol, testosterone).
- Bone age (left hand/wrist X-ray).
- MRI brain for CNS pathology.

76.5.2.5 Management

- **Central:** GnRH analogues to suppress premature axis activation.
- **Peripheral:** Treat underlying cause (e.g., tumour resection, corticosteroid replacement in CAH).
- **Psychological support:** Essential in early-developing children in conservative societies.

76.5.3 Delayed Puberty

76.5.3.1 Causes

- **Constitutional delay:** Most common; familial and benign.
- **Hypogonadotropic hypogonadism:** Due to pituitary/hypothalamic defects (e.g., Kallmann syndrome, chronic malnutrition).
- **Hypergonadotropic hypogonadism:** Primary gonadal failure (e.g., Turner, Klinefelter, mumps orchitis).

76.5.3.2 Clinical Features

- Absence of breast or testicular development.
- Short stature or growth failure.
- Psychosocial distress among peers.

76.5.3.3 Investigations

- LH, FSH, and sex steroid levels.
- Karyotype where indicated.
- MRI for central lesions.
- Bone age assessment.

76.5.3.4 Management

- Observation in constitutional delay.
- Hormone replacement therapy (estrogen or testosterone).
- Treat underlying systemic or nutritional disorders.

76.5.3.5 Ghanaian Context

Malnutrition, chronic infections, and delayed recognition of hypogonadism remain frequent contributors to delayed puberty. Clinical suspicion and affordable initial hormonal testing are essential in regional hospitals.

76.6 Gonadal Dysfunction

76.6.1 Primary Gonadal Failure

Results from intrinsic gonadal abnormalities leading to **hypergonadotropic hypogonadism**. Common causes include:

- Turner syndrome (45,X)
- Klinefelter syndrome (47,XXY)
- Chemotherapy or radiotherapy-induced damage
- Autoimmune oophoritis or orchitis

76.6.1.1 Clinical Features

- Absent or incomplete pubertal development
- Infertility
- Amenorrhea in females
- Small, firm testes in males

76.6.1.2 Management

- Hormone replacement therapy (HRT) for puberty induction and maintenance.
- Fertility counselling.
- Monitor for associated comorbidities (e.g., cardiovascular risk in Turner syndrome).

76.6.2 Secondary Gonadal Failure

Due to hypothalamic or pituitary defects causing **hypogonadotropic hypogonadism**.
Causes: CNS tumours, trauma, chronic systemic illness, or genetic syndromes like Prader-Willi.

76.7 Menstrual and Fertility Disorders

Although more relevant in late adolescence, early recognition of abnormal menstrual patterns is important.

#A# Common Disorders - **Primary amenorrhea:** No menses by age 15 or within 3 years of thelarche.
- **Secondary amenorrhea:** Absence of menses for >3 months in a previously menstruating girl.
- **Oligomenorrhea:** Infrequent menses (>35 days apart).

#A# Causes - Anatomic (imperforate hymen, Müllerian agenesis)
- Ovarian (PCOS, gonadal dysgenesis)
- Pituitary (hyperprolactinaemia)
- Hypothalamic (stress, undernutrition, excessive exercise)

76.7.1 Investigations

- Serum LH, FSH, prolactin, TSH, estradiol.
- Pelvic ultrasound.
- Progesterone challenge test.

76.7.2 Management

- Treat underlying cause (e.g., surgical correction, nutritional rehabilitation).
- Hormonal therapy for regulation.
- Psychological counselling.

76.8 Approach to a Child with a Reproductive Disorder

1. **Detailed history**
   - Onset and progression of puberty
   - Family history of delayed or precocious puberty
   - Neonatal genital appearance, chronic illnesses
   - Drug and toxin exposure
2. **Physical examination**
   - Tanner staging
   - Height, weight, and growth velocity
   - Dysmorphic features or signs of chronic disease
3. **Laboratory evaluation**
   - Hormonal profile (LH, FSH, estradiol/testosterone, prolactin, TSH)
   - Karyotyping where indicated
4. **Imaging**

- Pelvic/abdominal ultrasound
- MRI brain/pituitary for central causes

5. **Psychosocial assessment**
    - Critical in addressing stigma and self-image concerns, particularly in the Ghanaian context.

76.9 Challenges in the Ghanaian and Sub-Saharan Context

- **Limited endocrine testing:** Many hospitals lack the capacity for detailed hormonal assays.
- **Late presentation:** Families may delay seeking medical advice due to cultural stigma.
- **Cost barriers:** HRT and genetic testing may be unaffordable for many patients.
- **Need for multidisciplinary care:** Involving paediatric endocrinologists, surgeons, psychologists, and social workers.
- **Education and awareness:** Community sensitization and training of primary care workers are key.

76.10 Key Takeaways

- Reproductive disorders in children arise from dysfunction of the HPG axis or abnormalities in sexual differentiation.
- Early recognition and hormonal evaluation are crucial to prevent long-term physical and psychosocial complications.
- In Ghana, limited diagnostic resources demand pragmatic, symptom-based approaches supplemented by clinical acumen.
- Psychosocial support and culturally sensitive counselling are integral to care.

76.11 Further Reading

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77 Growth Disorders

77.1 Introduction

Growth is one of the most visible and sensitive indicators of a child's health and overall well-being. In paediatrics, monitoring growth is an essential part of clinical care, as deviations from normal patterns often signal underlying disease, malnutrition, or hormonal imbalance.

A **growth disorder** refers to any condition that results in abnormal stature or growth velocity compared with reference standards for age and sex. These disorders may present as **short stature**, **tall stature**, or **abnormal growth velocity**, and they can have **endocrine**, **genetic**, **systemic**, or **nutritional** causes.

In Ghana and much of sub-Saharan Africa, poor nutrition, chronic infections, and delayed recognition of endocrine disorders remain major contributors to abnormal growth. The limited availability of specialized diagnostic tests often necessitates a pragmatic, clinically guided approach.

77.2 Normal Growth Physiology

Normal growth is influenced by the complex interplay between genetic, nutritional, hormonal, and environmental factors. The main hormones involved are:

1. **Growth Hormone (GH):** Secreted by the anterior pituitary in a pulsatile manner, stimulating hepatic production of insulin-like growth factor 1 (IGF-1).
2. **IGF-1 and IGFBP-3:** Mediate the growth-promoting effects of GH at the tissue level.
3. **Thyroid hormones:** Essential for normal bone maturation and growth velocity.
4. **Sex steroids (estrogen and testosterone):** Promote pubertal growth spurt and epiphyseal closure.
5. **Cortisol:** In excess, inhibits growth.
6. **Insulin:** Promotes growth through anabolic effects.