Chapter

37 Anaesthesia for Oncology and Other Medical Procedures in Children

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Introduction

There are an increasing number of diagnostic and therapeutic interventions performed outside the theatre environment, and anaesthesia in remote locations is now a routine part of paediatric practice. Anaesthesia is required for painless procedures such as radiological scans where the child must remain immobile, or minor procedures that are uncomfortable or painful, such as lumbar puncture (LP), bone marrow aspirate (BMA) and endoscopy.

Anaesthetists have a key role to play in ensuring that these procedures are undertaken safely and efficiently, whilst minimising pain or distress for the child. The quality of the experience may influence the child's future attitude towards medical care. This chapter will consider the general principles for provision of remote anaesthesia, and specific requirements for oncology patients, muscle biopsy and joint injections. The development of safe sedation services and endoscopy for children is described in Chapter 16, and anaesthesia for radiology is covered in Chapter 36.

General Principles: Anaesthesia in Remote Locations

Children undergoing minor medical procedures are frequently admitted as day cases. Procedures may be undertaken in the main operating theatre on an ad hoc basis, but it is probably more efficient, and more pleasant for the child and family, to base their care in a dedicated day unit or day-case list. A stand-alone medical procedure unit is ideal for high-volume, rapid turnover services such as oncology or gastroenterology. It is important that in all these situations, the same standards of care are provided as in the main operating suite:

- There should be a clinical lead for anaesthesia in the non-theatre environment, responsible for developing the service, training and revalidation of staff and ensuring safety standards and audit are appropriate.
- The service should ideally be consultant delivered with appropriate supervision of trainees.
- There should be clear policies covering patient selection and preparation, and a forum to discuss high-risk patients at a multidisciplinary team meeting. Children with an abnormal airway, pulmonary hypertension, cardiomyopathy, congenital heart disease or mucopolysaccharidosis or children with unstable disease, ASA III or above, should be discussed as to their suitability for treatment in a remote location. Additional support and planning will be required for high-risk patients.
- There should be appropriately trained theatre and recovery staff, including a trained anaesthetic assistant, and a fully equipped recovery room. Emergency drills should be practised regularly.
- Procedure rooms should be large enough to accommodate equipment and personnel and include full resuscitation facilities, piped medical gases, suction, air exchange and a means of providing ventilation.
- Full anaesthesia monitoring should be available, according to national guidelines.
- There should be full access to appropriate anaesthetic equipment, disposables and anaesthetic drugs. Service contracts for equipment and pharmacy support should be the same as for the main operating theatre.
- There should be regular audit of patient outcomes, training of staff and feedback from parents about the quality of the service.

Paediatric Oncology

Cancer affects around 1:500 children under the age of 14 years in the United Kingdom, with around

1,900 new cases diagnosed each year (2015–2017). It is the most common cause of death in children aged 1–14 years in the United Kingdom. Since the early 1990s, incidence rates have increased by around a seventh (15%) in the United Kingdom, most likely related to improved cancer diagnosis and registration. Outcomes have improved markedly over the same period of time, owing to more intense treatment regimens with improved support and rescue therapies. The corollary of this is that there are more children surviving with long-term side effects from cancer treatments.

Cancer is more common in boys than girls (54% vs 46 %, respectively, 2015–2017), with most tumours presenting in children less than five years of age. The most common diagnoses are leukaemia, central nervous system (CNS) tumours and lymphomas; the overall five-year survival rate is 82%, but survival varies greatly according to diagnosis (see Table 37.1). Brain and CNS tumours account for most deaths, and retinoblastoma has the best survival rate (99% cure).

Diagnosis in children is often delayed, as childhood cancer is rare and slow to be considered. The child may have non-specific symptoms such as weight loss and listlessness, and then develop signs such as:

- Bruising and petechial haemorrhage, lymphadenopathy or bone pain (haematological malignancy)
- Abdominal distension or pain (Wilms' tumour, (nephroblastoma or neuroblastoma)
- Headache with ataxia (posterior fossa tumour)

Spread to distant sites and bone marrow is common at presentation. The parents are often devastated when the diagnosis is made, and the child frightened, upset and unwell. One of the major achievements of paediatric cancer treatment, and one of the factors that has led to improvements in outcome, has been the centralisation of care and the development of international research registries. The UK Children's Cancer and Leukaemia Group (CCLG) is the national association for the treatment of cancer in children and young people. More than 70% of children with cancer in the United Kingdom are registered as part of a national or international clinical trial. The CCLG is also a registered charity and provides support and information for children and their families. There are currently 19 specialist centres with multidisciplinary teams undertaking the treatment of cancer in children in the United Kingdom, with 'shared care' with non-specialist centres. Treatment is continued over several months or years, and shared care allows children to stay as close to home as possible.

Anaesthesia may be required at many stages in the care of children with malignancy, for instance BMA, LP or biopsy for diagnosis or staging, routine scans, line insertion or definitive surgery. The

Table 37.1 UK children's cancer incidence and five-year survival rates

	Incidence children <14 years (% all cases)	Five-year survival (%)
Leukaemia	30	
Acute lymphoblastic leukaemia		90
Acute myeloid leukaemia		65
CNS tumours	26	
Astrocytoma		95
Ependymoma and choroid plexus tumours		60
Embryonal CNS tumours		60
Other gliomas		44
Lymphoma	11	
Hodgkin's lymphoma		95
Non-Hodgkin's lymphoma		90
Soft tissue tumours	6	70
Rhabdomyosarcoma		
Neuroblastoma	6	67
Nephroblastoma	5	92
Retinoblastoma	3	99
Bone tumours	4	
Ewing sarcoma of bone		66
Osteosarcoma		65
Germ cell tumours	4	93
Melanoma/ epithelioma	4	
Hepatic tumours	1	

Source: Cancer Research UK Childhood Cancer – Great Britain and UK and Children with Cancer UK

anaesthetist must be aware of how the condition affects the child, the effects of treatment and whether the child has undergone surgery, radiotherapy, chemotherapy or a combination of these. Children with cancer require repeated anaesthetics – some children may be relatively well, receiving long-term maintenance chemotherapy, but others may be acutely unwell as a result of their treatment or a complication of treatment.

Treatment of Specific Conditions

Current approaches to cancer treatment depend on clinical features and biological characteristics of the tumour, response to treatment and extent of residual disease (see Table 37.2).

Chemotherapy is given in cycles to increase efficacy and allow time for recovery. It is given either orally (PO) or IV, with intrathecal chemotherapy given to treat overt or potential CNS disease.

Standard-Risk Acute Lymphoblastic Leukaemia (ALL)

Treatment of standard-risk childhood acute lymphoblastic leukaemia has a relatively good prognosis, so the aim is to limit exposure to drugs associated with late toxic effects. Children receive induction therapy over four to six weeks to induce remission in blood and bone marrow (steroids, vincristine and daunorubicin), with treatment of CNS disease (intrathecal methotrexate), possible intensification blocks to remove residual cells (methotrexate or asparaginase), a maintenance phase of daily 6-mercaptopurine (6-MP) PO with weekly methotrexate PO and six-weekly intrathecal methotrexate to prevent CNS recurrence. This treatment continues for two to three years.

High-Risk ALL

High-risk ALL includes presentation <1 year of age, those presenting with high white cell count or CNS disease at diagnosis, those with chromosomal abnormalities such as the Philadelphia chromosome or those with poor response to induction treatment with increased minimal residual disease (MRD) in bone marrow. These children are treated with more intensive chemotherapy regimens associated with increased short- and long-term side effects, as for acute myeloid leukaemia (see the next section). Target drug therapy such as tyrosine kinase inhibitors is used to reduce cell proliferation, and immunotherapy including monoclonal antibodies and CAR T-cell therapy is employed in high-risk patients. Stem cell transplantation may be offered when the child is in first remission or presents with recurrent disease. Radiotherapy may be used for children presenting with CNS or testicular disease.

Table 37.2 Treatment for children's cancers

Cancer	Treatment
Acute lymphoblastic leukaemia	Steroids, chemotherapy, radiotherapy, target cancer drug, immunotherapy, stem cell or bone marrow transplant
Acute myeloid leukaemia	Chemotherapy, radiotherapy, target cancer drugs, immunotherapy, stem cell or bone marrow transplant
Hodgkin's lymphoma	Surgery (stage 1 disease), chemotherapy, radiotherapy
Non-Hodgkin's lymphoma	Chemotherapy, radiotherapy, donor stem cell or bone marrow transplant if relapse
Brain and CNS tumours	Surgery, chemotherapy, radiotherapy for children >3 years and proton beam therapy
Neuroblastoma	Surgery, chemotherapy, stem cell transplant, immunotherapy
Retinoblastoma	Surgery, laser, cryotherapy, systemic chemotherapy, radiotherapy, selective ophthalmic artery chemosurgery (SOAC)
Nephroblastoma	Surgery, chemotherapy, radiotherapy
Osteosarcoma	Surgery, chemotherapy, radiotherapy
Rhabdomyosarcoma	Surgery, chemotherapy, radiotherapy

Acute Myeloid Leukaemia

Acute myeloid leukaemia (AML) has a lower cure rate; treatment involves high-dose induction and intensification chemotherapy that may induce prolonged marrow suppression requiring in-patient stay with associated episodes of febrile neutropenia or mucositis. Stem cell transplantation is often used for children with high-risk disease.

Solid Tumours

For solid tumours such as Wilms' or neuroblastoma, tumour staging is carried out at diagnosis with CT/MRI, bone marrow and tumour biopsy. Current UK practice is to reduce tumour size and vascularity with several courses of chemotherapy prior to definitive surgery, followed by further courses of chemotherapy or radiotherapy.

Tumours Associated with Anterior Mediastinal Mass

Children presenting with T-cell ALL, lymphomas, neuroblastoma or intrathoracic germ cell tumour may present with a mass in the anterior mediastinum. This may result in airway compression, superior vena cava (SVC) obstruction or cardiorespiratory collapse in severe cases.

Anaesthesia is required for tumour staging and line insertion. Induction of anaesthesia is particularly high risk for children with an anterior mediastinal mass (see Chapters 30 and 36).

Timing of procedures such as diagnostic BMA, LP and line insertion should be made after discussion with the oncology team. A possible option is to start chemotherapy and monitor symptoms. Biopsies need to be undertaken within five days of starting treatment if an accurate tissue diagnosis is to be obtained.

Bone Marrow Transplantation

Bone marrow transplantation is used to treat high-risk malignant disease such as relapsed ALL or AML, or non-malignant disease such as aplastic anaemia, severe combined immune deficiency, sickle cell anaemia or inborn errors of metabolism. Stem cells may be obtained from the patient (autologous transplant) or from a matched related or unrelated donor (allogeneic transplant). Autologous transplant is used as 'rescue' after high-dose chemotherapy, and allogeneic transplant is used for treatment of malignant or non-malignant disease.

Autologous stem cells may be obtained from bone marrow harvest or peripheral blood stem cell (PBSC). PBSCs are harvested by apheresis after granulocyte colony stimulating factor (G-CSF) is given to increase the stem cell count in peripheral blood. Allogeneic stem cells may be obtained from bone marrow, peripheral blood or cord blood. Children donating bone marrow to a sibling require general anaesthesia. The child is placed in the prone position and a volume of approximately 10 ml kg^{-1} marrow is collected under aseptic conditions. Intravenous fluids and multimodal analgesia are required. The relative risks and benefits of the procedure to the healthy donor should be considered.

The recipient receives 'conditioning' chemotherapy and/or total body irradiation before transplant, followed by reinfusion of harvested stem cells. Conditioning may result in complete ablation of the recipient bone marrow to remove residual cancer cells, but less aggressive regimens associated with fewer complications are currently being investigated, particularly for non-malignant conditions. The child will require intensive supportive therapy after conditioning and until engraftment occurs and will be extremely vulnerable to infection. Full barrier precautions should be used when treating these patients.

Graft-versus-Host Disease

Graft-versus-host disease (GvHD) is the term given to the immunological reaction of donor cells introduced to an immunocompromised host. It is usual after allogeneic bone marrow transplantation, and is an indication that engraftment is taking place. It may be useful to clear residual cancer cells. GvHD may also be seen after transfusion of non-irradiated blood to an immunocompromised patient (transfusion-related GvHD).

Acute GvHD occurs within 100 days of transplant and is associated with generalised skin rash, hepatitis and diarrhoea. Severe GvHD has a high mortality. Chronic GvHD occurs later with a more indolent course with characteristics of a chronic autoimmune disease affecting multiple organ systems, including skin, liver and gastrointestinal tract. Severe GvHD should ideally be prevented, for instance by improved matching of donor and recipient, by less severe recipient

conditioning regimens and ensuring the use of irradiated blood in vulnerable patients. Treatment is supportive, including immunosuppression (e.g. steroids, tacrolimus, ciclosporin, mycophenolate [MMF]) or immunotherapy. Children with severe GvHD usually require admission to a paediatric intensive care unit (PICU).

Side Effects of Chemotherapy Treatment

Cytotoxic agents commonly induce bone marrow suppression, hair loss, nausea and vomiting. Other drug-specific side effects are described in Table 37.3. Children with bone marrow suppression require support with platelet and red cell transfusions, and they may require broad-spectrum antibiotics and removal of a central venous line during a period of febrile neutropenia. G-CSF may be given to aid recovery from neutropenia and allows more intensive chemotherapy to be given in high-risk disease. Some specific complications of treatment relevant to the anaesthetist are described in the next section.

Steroids and Tumour Lysis Syndrome

Steroids are a mainstay of treatment in ALL, but they are given in short courses, so adrenal suppression is rarely a problem.

Tumour lysis syndrome results from the massive release of intracellular metabolites. It is seen in the first 12–72 hours of the start of treatment in children with high tumour load or high proliferative rate, or those where tumours are very chemosensitive. Anaesthetists should be aware that tumour lysis syndrome may be triggered by dexamethasone given as an antiemetic to a child in an at-risk category; dexamethasone must be avoided in this situation.

Table 37.3 Commonly used agents and side effects of treatment

Drug	Conditions treated	Common side effects of drug
Vincristine	ALL	Myelosuppression, syndrome of inappropriate antidiuretic hormone (SIADH), peripheral neuropathy, mucositis
Anthracyclines (daunorubicin,doxorubicin, epirubicin)	Acute leukaemia, sarcoma, Wilms tumour, neuroblastoma, Hodgkin's disease	Myelosuppression, cardiomyopathy, arrhythmias
Cyclophosphamide	Non-Hodgkin's lymphoma, neuroblastoma, sarcoma, conditioning prior to bone marrow transplant	Myelosuppression, cardiomyopathy, arrhythmias, haemorrhagic cystitis
Ifosfamide	Non-Hodgkin's lymphoma, sarcoma, bone tumours	Myelosuppression, Fanconi's syndrome, renal failure
Cisplatin	Neuroblastoma, germ cell tumour	Seizures, hypomagnesaemia, renal failure
L-Asparaginase	ALL	Coagulopathy, allergic reaction, pancreatitis
Nitrosoureas		Pneumonitis, renal failure
Bleomycin	Hodgkin's disease, germ cell tumours	Allergic reactions, pulmonary fibrosis, Reynaud's
Methotrexate	ALL	Myelosuppression, mucositis, pneumonitis, renal failure
Actinomycin D	Wilms tumour, sarcoma	Coagulopathy, liver failure, acute respiratory distress syndrome
Busulfan	Conditioning prior to bone marrow transplant	Hepatic veno-occlusive disease, seizures

Children at risk of tumour lysis syndrome include those with:

- High count ALL
- AML
- Hodgkin's lymphoma, non-Hodgkin's lymphoma, Burkitt's lymphoma

Tumour lysis results in hyperuricaemia, hyperkalaemia, hyperphosphataemia, hypocalcaemia and uraemia and is associated with deposits of uric acid or calcium phosphate in the renal tubules. Children present with nausea and vomiting, muscle cramps, renal impairment, seizures or arrhythmias. Children who are at risk should be closely monitored and treated with hydration and rasburicase, which promotes the metabolism of uric acid to soluble metabolites, or allopurinol, which reduces the formation of uric acid.

Mucositis

Mucositis is painful inflammation and ulceration of all mucous membranes, seen in all children receiving high-dose chemotherapy, 50% of children receiving head and neck radiotherapy, and 5–10% of children receiving standard chemotherapy. Severe mucositis may limit therapy. Treatment is symptomatic with intravenous fluids and total parenteral nutrition (TPN) if required. Abdominal pain should be treated with IV morphine patient- or nurse-controlled analgesia (PCA/NCA), with added ketamine if required.

Vincristine

Vincristine is neurotoxic; children are monitored for possible sensory or motor neuropathy, and doses adjusted accordingly.

Vincristine and other vinca alkaloids such as vinblastine and vindesine are universally fatal if given intrathecally. There have been more than 50 deaths reported internationally involving accidental intrathecal administration of vinca alkaloids, often due to systems errors and human factors identified as the root cause. Administration of chemotherapy in the United Kingdom is now tightly regulated and can only be given by registered individuals with appropriate training, in designated areas, and following specified checks. Intrathecal and intravenous agents are given on different days, and vincristine is often prepared in intravenous mini-bags to prevent accidental intrathecal administration. Non-Luer spinal needles that are incompatible with intravenous Luer connections have been introduced to prevent such accidents in future.

Anthracyclines and Other Agents Associated with Cardiac Toxicity

Anthracyclines (doxorubicin, daunorubicin, epirubicin) are commonly used in children with the following conditions:

- AML
- Non-Hodgkin's lymphoma (NHL)
- Wilms tumour
- Neuroblastoma
- Bone tumours

Anthracyclines are cardiotoxic, particularly when given in high doses. Risk factors for anthracycline cardiotoxicity include treatment for relapsed disease, high cumulative dose (>300 mg m^{-2}), associated radiotherapy and if there have been signs of early cardiac toxicity. All children are monitored with regular echocardiograms during treatment and long-term follow-up. Mortality associated with overt cardiomyopathy is high (50%), so many of these children will be candidates for cardiac transplantation. Subclinical cardiomyopathy is common (a degree of cardiac impairment has been reported in up to 65% of such children) and may be un-masked at times of increased demand, such as puberty, pregnancy or intercurrent illness, and possibly during anaesthesia and surgery. A high index of suspicion should be maintained when anaesthetising these children, and a recent echo should be available.

Cyclophosphamide is associated with cardiomyopathy or cardiac arrhythmias when used in high doses to induce bone marrow ablation (conditioning) before bone marrow transplant. Fluorouracil is occasionally associated with cardiac toxicity.

Bleomycin

Bleomycin is used in the treatment of children with Hodgkin's lymphoma and germ cell tumours. It is associated with an inflammatory pneumonitis and progressive pulmonary fibrosis, particularly when given in high doses. Risk factors for bleomycin toxicity include increasing age (toxicity rarely

seen in children), increasing dose, radiotherapy and renal impairment.

Bleomycin is used to induce fibrosis in animal models of pulmonary fibrosis and is deactivated in the lungs by pulmonary hydroxylases. The role of oxygen in promoting bleomycin toxicity is controversial, with evidence mainly from case reviews. Hyperoxia should be avoided after recent exposure to bleomycin and if there is evidence of pre-existing pulmonary disease. It is sensible to use the lowest possible inspired oxygen during anaesthesia.

Anaesthesia for LP and BMA

In our institution, oncology procedures are undertaken on dedicated lists, usually in the dedicated procedure unit, with a senior nurse acting as a list coordinator to book patients, coordinate review by the oncologists and prepare children with up-to-date blood counts. It is our preference to provide general anaesthesia for these short, painful procedures rather than deep sedation or local anaesthesia alone.

From an anaesthesia perspective, the child requires careful assessment, particularly if newly diagnosed, receiving high-dose chemotherapy or suffering from acute GvHD. Active sepsis should be excluded. Children receiving long-term maintenance chemotherapy are generally well and often develop their own 'routine', which is helpful for the anaesthetist to follow.

Commonly accepted minimum platelet counts for procedures are shown in Table 37.4.

BMA and LP are quick procedures and ideally suited to total intravenous anaesthesia (TIVA) with propofol, with assisted/spontaneous ventilation with a face mask. This technique facilitates early discharge home (see Table 37.5 for the suggested protocol). Supplementary local anaesthesia and IV paracetamol are indicated if bone marrow trephine is performed.

Table 37.4 Minimum platelet count for oncology procedures

Procedure	Platelet count ($\times 10^{9\ -1}$)
Line insertion	100
LP	50
Trephine	20
BMA	No minimum count Specified

Children usually have an in-dwelling central line, which may be used for anaesthesia provided full aseptic precautions are taken when accessing the line. *It is the responsibility of the anaesthetist to ensure that the line is flushed after use to remove residual anaesthesia drugs.*

Anaesthesia for Radiotherapy

Targeted radiotherapy is used as a primary therapy or to clear microscopic disease in children with CNS tumours, Hodgkin's lymphoma, Wilms tumour, neuroblastoma and sarcoma of bone and soft tissue. Radiotherapy is delivered in fractionated daily doses over six weeks; side effects are localised to the area of treatment and may include redness and blistering of the skin, mucositis, neurocognitive impairment and pituitary damage. Damage to normal tissue is minimised by use of three-dimensional targeted beams (3D conformational radiotherapy, or 3D CRT), and modulating the intensity of the beams (intensity-modulated radiotherapy, or IMRT). Proton beam radiotherapy enables treatment to be targeted at a precise depth, ideal for cranial irradiation in children Radiotherapy units are usually based in adult hospitals, and special arrangements may need to be made for paediatric patients.

Each treatment typically takes 10–45 minutes. The child must remain by themselves in the treatment room and is required to wear an immobilisation device. With careful preparation and play therapy, treatment can often be performed without sedation in children >8 years (and some younger children). When required, a propofol-based anaesthetic is ideal with a SAD for airway control. As for any anaesthesia service for children, trained staff and full monitoring are required. The anaesthetist cannot stay with the child during treatment, and output from the monitors must be relayed to the control room.

Table 37.5 Alternative anaesthesia protocols for short oncology procedures such as BMA, LP or trephine

Propofol 3–5 mg kg^{-1} IV + remifentanil 1 mcg kg^{-1} IV bolus Repeat propofol 1–2 mg kg^{-1} IV if required
Propofol 3–5 mg kg^{-1} IV + alfentanil 5 mcg kg^{-1} IV bolus Repeat propofol 1–2 mg kg^{-1} IV if required

Anaesthesia for Selective Ophthalmic Artery Chemosurgery (SOAC)

Advanced retinoblastoma that does not respond to conventional treatment or those who develop recurrent disease may require selective ophthalmic artery chemosurgery (SOAC). A microcatheter is inserted into the ophthalmic artery for chemotherapy to be delivered selectively to the affected eye. Typically, three treatment cycles are required with post-treatment examination under anaesthesia (EUA) being performed after each cycle. During catheter placement, profound but transient cardiorespiratory collapse of unknown aetiology has been observed, typically (but not always) during the second cycle. A reduction in tidal volume, a slow rising non-plateauing $ETCO_2$ with difficulty maintaining adequate ventilation is seen, which is followed by a rapid progressive fall in $ETCO_2$ and arterial desaturation. This is accompanied with marked haemodynamic instability with hypotension and bradycardia. Patients should receive prophylactic atropine at induction, and the anaesthetist should have appropriate resuscitation drugs such as adrenaline and fluid boluses prepared to treat such a response.

Rare 'Non-malignant' Medical Conditions

Haemophagocytic Lymphocytic Histiocytosis

Haemophagocytic lymphocytic histiocytosis (HLH) is a rare disease presenting in infancy associated with high mortality. It is caused by activation of normal macrophages and T-lymphocytes, which results in an overwhelming inflammatory response with release of cytokines and phagocytosis of normal cells by activated macrophages. It is inherited as an autosomal recessive condition, but secondary HLH may occur in older children after systemic infection, immune deficiency or associated with underlying malignancy. Typical presentation is with fever, skin rash, hepatosplenomegaly and pancytopenia. CNS involvement including seizures is common. Skin, lymph node, liver and bone marrow biopsy confirm diagnosis. Treatment is with supportive therapy followed by bone marrow transplantation.

Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH) is a rare condition, previously known as histiocytosis X. It is a proliferative disorder of epidermal Langerhans cells, typically associated with lytic lesions in bone, with skin involvement in many cases. Controversy exists as to whether LCH is an inflammatory or malignant condition, but recent evidence suggests that it is a distinct myeloid neoplasm. There is a spectrum of disease, with three typical presentations:

- Eosinophilic granuloma. One or more bone lesions, classically in the skull but may affect other sites, including vertebra or femur. Recurrent mastoiditis and otitis media may occur because of destruction of the mastoid bone. Diabetes insipidus may occur because of destruction of the sella turcica.
- Hand–Schüller–Christian disease. Multifocal disease with classical triad of bony defects of the skull, exophthalmos and diabetes insipidus. Mucocutaneous and systemic involvement may occur.
- Letterer–Siwe disease. Fulminant disorder associated with generalised skin rash, fever, hepatosplenomegaly, lymphadenopathy, bone lesions and marrow infiltration.

Diagnosis is by imaging, skin or bone marrow biopsy. Isolated LCH of bone may be treated by surgical curettage and local injection of steroid. Mild systemic LCH is treated by chemotherapy, particularly where LCH involves vulnerable sites such as the skull or there is a risk of fracture; multi-system disease is treated by chemotherapy but may be associated with up to 20% mortality. Children with diabetes insipidus should continue desmopressin (DDAVP) in the perioperative period.

Severe Combined Immune Deficiency

Severe combined immune deficiency (SCID) is associated with life-threatening infection, dermatitis, diarrhoea and failure to thrive. SCID results from one of a range of gene defects causing impairment of T-cell, B-cell and NK-cell function. It is inherited as an autosomal recessive condition, X-linked or may be sporadic. A subgroup of children with immune deficiency and DiGeorge syndrome have a hypoplasia of the thymus with absent T-cells (associated with chromosome 22q11 deletion).

Children with SCID present with severe opportunistic infection in the first three months of life, which may be bacterial, viral or fungal, for example *Candida* or *Aspergillus*. Without treatment, SCID is usually fatal by two years of age. Allogeneic bone marrow transplantation is ideally performed before the age of six months to avoid the effects of repeated infections. Children with SCID or other conditions associated with immune deficiency must not receive live vaccines. They must only receive irradiated blood products to prevent GvHD from immunocompetent lymphocytes in donor blood or blood products.

Neuromuscular Disorders and Myopathy

Muscle biopsy may be required as a diagnostic procedure in children with suspected neuromuscular disorders or in children with mitochondrial myopathy. Muscle is taken from the anterolateral aspect of the thigh, either as a needle biopsy or excised as a small strip. It is a short, painful procedure, usually requiring general anaesthesia, although it can be performed under regional block in older children.

The choice of anaesthesia for muscle biopsy may be difficult. Volatile agents may cause anaesthesia-induced rhabdomyolysis (AIR) in patients with one of the muscular dystrophies or may trigger malignant hyperthermia (MH) in susceptible patients. Conversely, TIVA using propofol may cause propofol-related infusion syndrome (PRIS), particularly if the child has a mitochondrial disorder. PRIS is associated with metabolic acidosis, lipidaemia, bradycardia, rhabdomyolysis and heart failure.

Suxamethonium must not be used in any patient with abnormal muscle, as fasciculations may cause hyperkalaemic cardiac arrest. Non-depolarising muscle relaxants should be avoided or used in reduced dose in a child who has a myopathy.

Children presenting for muscle biopsy usually fall into four main categories:

- *The child presents for investigation as a 'floppy baby'.* It is best to use a volatile anaesthetic rather than use TIVA, which may not be a familiar technique in this age group and may induce significant hypotension.
- *An older child is being investigated for MH or suspected central core disease.* A trigger-free anaesthetic must be given. Central core disease is associated with a mutation of the RyR1 gene and an abnormality of the intracellular ryanodine receptor. It is inherited as an autosomal-dominant disease, but sporadic cases occur. Children present with hypotonia from birth, with truncal weakness, delayed motor milestones, muscle cramps, mild facial weakness, contractures and scoliosis. The disease is slowly progressive, but children generally walk. There is a characteristic appearance on biopsy, and a genetic test from a blood sample is also available.
- *A boy with raised creatine kinase (CK) is being investigated for failure to walk, aged three to four years.* The likely diagnosis is Duchenne muscular dystrophy (DMD). TIVA with propofol should probably be given, as volatile agents may trigger AIR and hyperkalaemic cardiac arrest, usually in recovery when the child starts to move again. There is usually a family history in a boy with DMD, with characteristic hypertrophic calves and global hypotonia. A raised CK should act as a 'red flag' for the anaesthetist. Volatile agents have been used uneventfully in this group but are best avoided, particularly in young DMD patients when they still have significant muscle mass. If it is not possible to obtain venous access in these patients, it is acceptable to use a volatile agent for induction, then switch to TIVA.
- *The child is suspected to have a mitochondrial myopathy.* Prolonged high-dose propofol infusion should be avoided. Mitochondrial myopathies are associated with abnormalities of the electron transfer chain or oxidative phosphorylation. Mitochondrial disorders may be associated with myopathy, encephalopathy, epilepsy, lactic acidosis or gastrointestinal disorders. Mitochondrial myopathies are not associated with MH, and volatile agents are safe. The child should also be given dextrose-containing intravenous fluids to avoid lactic acidosis.

A careful history should be taken and the case discussed with the referring team with respect to the most likely differential diagnosis, so that the risks and benefits of each technique can be

assessed. It may be logical to use TIVA as the default technique for all patients (except babies); it avoids the risk of MH or rhabdomyolysis, and since muscle biopsy takes less than 15 minutes, the exposure to propofol will not be long enough to develop PRIS in children with mitochondrial myopathies.

Anaesthesia may be given by intermittent bolus injection, and the airway maintained with a SAD – mix propofol 200 mg with alfentanil 1 mg in a 20 ml syringe and give propofol 3–5 mg kg^{-1} for induction, with increments as required.

Juvenile Arthritis

Juvenile idiopathic arthritis (JIA) is an autoimmune condition associated with painful swollen joints that may affect children from around six months of age. There are several types of JIA, including:

- Systemic JIA. Associated with fevers, rash, lymphadenopathy and splenomegaly. Inflammation and stiffness may affect any joint.
- Oligoarthritis. Pain, stiffness and swelling affecting the wrist and knees.
- Polyarticular arthritis. Affects small joints of the hands, weight-bearing joints and the neck; more common in girls than boys. Fifteen per cent of children are rheumatoid factor positive and may develop joint damage and erosions.
- Psoriatic arthritis. Associated with psoriatic rash and/or family history of psoriasis.

The treatment of JIA is analgesia (NSAIDs), physiotherapy and exercise. Children who do not respond may be treated with oral methotrexate. Injections of steroids help to reduce pain and disability associated with an acute exacerbation. These procedures are usually undertaken as day cases. Joints to be injected should be clearly marked, and an image intensifier should be available. For large joints, the steroid may be combined with local anaesthetic to reduce post-procedural pain. Injections into multiple small joints are more painful, and morphine may be required.

Key Points

- The demand for anaesthesia services outside the main theatre is rising; the same standard of care should be available in all areas.
- Children receiving chemotherapy may be unwell if newly diagnosed, receiving high-dose chemotherapy or suffering from sepsis, or they may be in good health if receiving long-term maintenance treatment. High-dose anthracyclines may cause cardiomyopathy.
- The choice of anaesthetic for undiagnosed muscle biopsy is difficult. TIVA is preferred in older children to prevent anaesthesia-induced rhabdomyolysis and reduce the risk of MH. PRIS is unlikely after a short procedure.
- Children undergoing joint injections are managed as day cases; adequate analgesia is required.

Further Reading

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