PAEDS IN A PINCH

A PRACTICAL GUIDE FOR STUDENTS, BY STUDENTS, WITH SPECIALIST REVIEW

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Paeds in a Pinch

A Practical Guide to Paediatrics for Students by Students with Specialist Review

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DEDICATION

To the children we serve, you are our future. Be more than we imagined.

To the students and doctors who serve, we salute you. Remember why you were called.

FOREWORD

I have had the great privilege of both teaching and working on various projects with health sciences students over the years. In a world in which we have become accustomed to ‘leaders’ avoiding responsibility, I have watched these young people buck the trend. They have, instead, sought out problems, owned them and immersed themselves in the task to find solutions thereto. It is, thus, a great honour for me to be asked to provide a foreword to this student-led manual of paediatrics, a project that exemplifies these traits that I have just described and have come to admire in our students. The completion of this project also pays homage to what is possible when senior clinicians freely give of their time to guide junior colleagues to ensure the quality of the outcome, in a spirit of collaboration.

Children remain marginalised in our society. At times, the care they receive seems an afterthought once adults have had their fill. This also shows in the investment made in the training of medical students. Many a general practitioner speak of a feeling of having been inadequately trained to look after children as medical students. They often confess of being frankly terrified when faced with a sick child. As a paediatrician and a teacher, I am, therefore, suitably excited to see the students identify what they see as a potential gap in training tools for those who want to look after children suffering from common ailments competently, and endeavouring to close it.

This manual was put together by students in a format that reflects the way they found works best in learning and assimilating knowledge on how to look after ill children. The selected material prioritises what is essential core knowledge in paediatrics and child health while at the same time forming the foundation on which more knowledge can be built. The involvement of senior experienced colleagues has ensured that the content is reliable and up to date with current practice in paediatrics.

This project was led by students who have already graduated, but had the insight to hand the baton to the ones that came after them, who then saw it to completion. It is my hope that coming generations of health sciences students will use this manual, but will also take the responsibility of updating it to keep up with new ways of learning and the development of new knowledge in the field of paediatrics and child health.

Those who have had the opportunity of being properly trained to look after children will know the great joy of looking after these little ones and the satisfaction of making a real investment in the future of our society. May this effort give to all future generations of health sciences students access to such joy and satisfaction.

Rudzani Muloiwa

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Abstract

The Paeds in a Pinch study guide is a novel approach to teaching and learning. To the editors' knowledge, on the African continent (and even globally) there is no other published, open access learning resource for medical students written by medical students. This is aside from the fact that the information shared in the guide has been vetted by experts in several paediatric fields. It covers 17 core paediatric topics and is written in a concise and engaging manner, keeping the prospective reader (the busy medical student) in mind. It also includes numerous openly licensed and public domain images to further illustrate the authors' points and hold the reader's attention.

ABOUT THE BOOK

The idea for Paeds in a Pinch was developed by a group of students and doctors in 2017/2018. Their aim was to have students write a guide on paediatric topics for students that is easy to understand and engaging. This resource is to be used by final-year medical students when learning about the ever exciting but oft neglected discipline of paediatrics. In short, they wanted to write a guide which students will find useful, succinct and relevant.

The project was co-ordinated by Dr Lehlohonolo Ntlatlapo. When he graduated in 2018, he approached UCT PaedSoc to help complete the project. In 2019, Christine Ile took over the role of co-ordinator and, with the help of Prof. Carol Hlela, Prof. Rannakoe Lehloenya and Prof. Muloiwa, was able to complete the guide in 2021.

32 students and 16 paediatricians (or specialists with a special interest in paediatrics) came together to make this project a reality. The guide has 17 chapters which cover the basics of common paediatric conditions and should whet the appetite of medical students so that they go on to further explore the topics discussed. The guide covers the following topics:

- Genetics and Congenital Abnormalities
- Disorders of Development
- Endocrine Disorders
- Feeding and Fluid Management
- Nutritional Disorders
- Gastrointestinal disorders
- Cardiology
- Respiratory disorders
- Infectious Diseases
- Child Psychiatry
- Neurology
- Musculoskeletal System
- Dermatology
- Allergology
- Haematology
- Poisoning
- Nephrology

It is our hope that this free, open access resource will be used by students in South Africa and across the continent.

ACKNOWLEDGMENTS

There have been so many other people who helped make this study guide possible.

To the student authors and artists, thank you for sacrificing the little free time you have and freely offering your talents to make this guide a reality. You have once again shown that this generation of young people are willing and able to give more than anyone thought possible.

Thank you to Prof. Rudzani Muloiwa who was instrumental in the completion of the guide. Thank you for offering yourself as liaison between the students and the doctors, for encouraging your colleagues to work with us and endorsing our project. Thank you also to Dr Shamiel Salie for your counsel and guidance. We truly appreciate all of the help and support that you both gave.

Thank you to each consultant advisor for giving us your expert opinions and your willingness to take on this project despite your busy schedules and the tight deadlines.

Many thanks to the staff at UCT Libraries for all of your hard work in making this book appear as professional as it does and for guiding us through the publication process. A special thank you to Ms Jill Claassen (scholarly communications and communications manager at UCT Libraries) for your advice and support through the journey of publication.

Lastly, we would like to express our deepest gratitude to our families who have encouraged, counselled, consoled, strategised and rejoiced with and for us. It is not sufficient, but we say a heartfelt thank you.

Table of Contents

Chapter 1:

GENETICS AND CONGENITAL ANOMALIES

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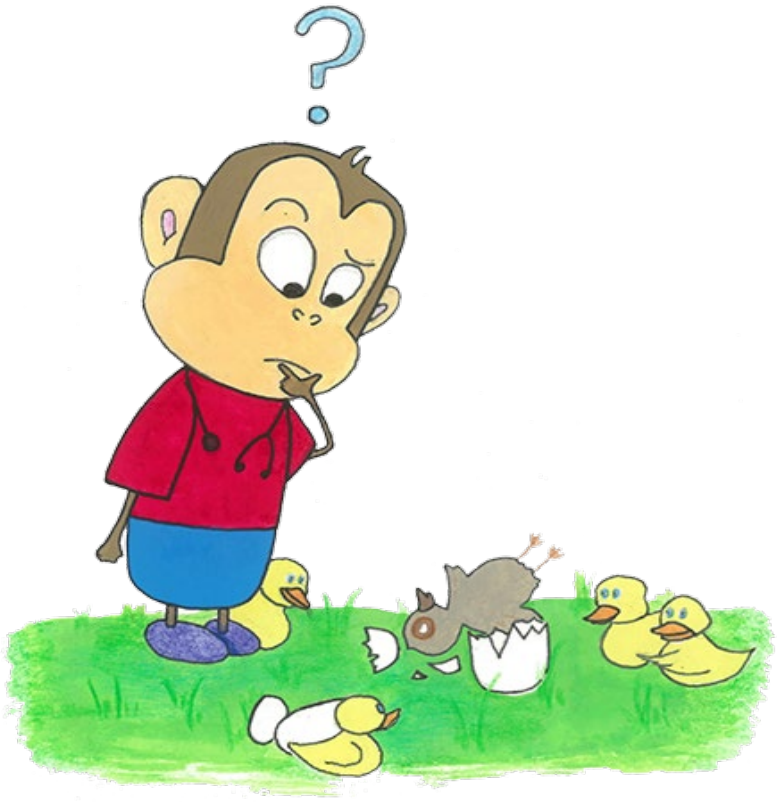

This chapter covers the following topics:

- Approach to dysmorphism and structural congenital anomalies
- Down syndrome
- Other trisomies
- Sex chromosome disorders
- Foetal alcohol spectrum disorder
- Short, dysmorphic children
- Other genetic syndromes and disorders
- Genetic testing

APPROACH TO DYSMORPHISM AND STRUCTURAL CONGENITAL ANOMALIES

Occasionally, one will encounter a neonate or child who looks “different”. These children may have a single dysmorphic feature, or a group of features, suggestive of a syndrome, many of which are caused by genetic abnormalities and others by teratogens. Many of these children will also have one or more structural abnormalities and developmental delay, while others may have structural abnormalities without unusual characteristics.

It is important to know how to approach these children and what should be done at a primary care level, as well as when to refer to a secondary or tertiary unit. As in all clinical practice, a good history and thorough clinical examination should always be the first step. Particular attention should be paid to the family history and perinatal history. The child’s growth measurements should be charted and a full systematic examination conducted.

Unique Features in the Child with a Genetic Disorder

Multi-system involvement is common. A variant (genetic difference which is present at conception) will usually be present in every cell of the body. This is especially true if the variance is due to teratogenicity (teratogens can act on various systems). Specialist care and treatment may be needed and the child is often best managed by a multidisciplinary team. For example, the child may need to be referred to a medical geneticist or other specialist to assist in diagnosis and management.

Additionally, the patient and his/her family may need specialised health care and psychosocial support for the rest of their lives, especially with conditions where there is a risk of recurrence of the disease in the affected child, future sibling and extended family members.

Aetiology of Dysmorphic Syndromes and Congenital Anomalies

There are different causes for dysmorphic syndromes and congenital anomalies, not all of which are hereditary. However, all causes affect cellular function in some way.

- Genetic causes:
    - Chromosomal anomalies:

        - They may be abnormalities of number (monosomy, trisomy) or structure (translocation or deletion) and include gains or losses of long segments of DNA.
        - These anomalies may be inherited or, more frequently, “de novo” (occur for the first time in the affected child).
    - Single gene mutations:
        - They include changes in the nucleotide sequence of one particular gene (e.g. deletions, insertions or substitutions) and are inherited in different ways.
        - Autosomal dominant disorders only require one copy of the abnormal gene to cause the disorder (commonly de novo in a severe, early-onset condition).
        - Autosomal recessive disorders require both copies of a gene to be abnormal to cause the disorder.
        - Sex-linked disease occurs when the gene is on the X chromosome. If the disorder is recessive, one normal copy of the two X chromosomes is largely protective (i.e. in females) and males are affected (as they have only one X chromosome).
        - Mitochondrial genome disorders are only maternally passed on.
    - Multifactorial causes imply multiple, smaller genetic and environmental contributors.
- Teratogenic causes:
    - Teratogens are external factors which disturb in-utero development, usually in early pregnancy). They may include:
        - Maternal medication e.g. sodium valproate
        - Maternal recreational drug exposure (especially alcohol)
        - Maternal illness e.g. diabetes
        - Congenital infections e.g. rubella
- Unknown aetiology (at least 30% of cases)

When to Suspect an Underlying Genetic or Syndromic Disorder

The features listed below should prompt you to look closely for additional features and, if appropriate, to refer for further evaluation. The clinician's suspicion should increase if any of the below occur together:

- Major structural abnormality (found in 2-3% of live births) i.e. major organ system defect
- Developmental delay/intellectual disability
- Family history of genetic or syndromic disorders
- ≥3 minor anomalies:
    - 1 minor anomaly is found in ~15% of neonates e.g. clinodactyly, hypertelorism, epicanthic folds, syndactyly
    - These "differences" have no medical implications but may be indicative of other abnormalities

DOWN SYNDROME

Down syndrome (also known as Trisomy 21) is the most common genetic syndrome, occurring in approximately 1 in 600 live births. Although an individual woman's risk of having a child with Down syndrome increases with age (particularly after 35), anyone at any age can have a child with Down syndrome. There are several screening tests, including blood tests and ultrasound scans, that are available to determine the risk of aneuploidy (an abnormal chromosome number) in a pregnancy. How these are applied depends partly on local resources. Women with a child with Down syndrome are at greater risk of having another child with aneuploidy and should be offered referral for appropriate counselling before they become pregnant again.

Aetiology

Down syndrome is caused by the presence of three copies of chromosome 21, usually due to an additional chromosome 21 not joined to any other chromosome (non-disjunction).

3–4% of cases are caused by a translocation (14/21 or 21/21). Parents of these children may carry a balanced translocation, which is why their family members are at higher risk for having more children with Down syndrome. The risk in these

families is independent of maternal age and is the reason why chromosome analysis is important.

About 2% of people with Down syndrome have mosaicism (there are two cell lines in the same zygote – some somatic cells contain the extra chromosome, with visual examples accessible on this link, and some do not).

Clinical Features

There are no distinct diagnostic dysmorphic features, but the overall pattern of recognisable features in the setting of hypotonia and developmental delay assists with diagnosis. On physical examination, one should look for:

- Brachycephaly
- Upslanted palpebral fissures
- Brushfield spots (in the iris)
- Epicanthic folds
- Flat nasal bridge
- Low set ears
- Protruding tongue
- Loose neck skin
- Short, broad hands and fingers
- Short stature
- Clinodactyly
- Single palmar crease
- Sandal gap

See related image here.

Systemic involvement is common, and the child may have:

- Cardiorespiratory manifestations:
    - ~50% of patients have congenital heart disease, especially atrioventricular septal defects (AVSDs). They may also have patent ductus arteriosus (PDA), ventricular septal defects (VSD) or tetralogy of Fallot (TOF).
    - Recurrent wheeze and frequent chest infections (increased morbidity) are also common.
- Hearing and vision problems:

    - The child may have a congenital cataract (thus, one must always check the red reflexes) or strabismus.
    - 80% of patients have ophthalmologic disorders by 12 years old (myopia is most common).
    - Hearing loss is present in 40–70% of patients (may be sensorineural, conductive or mixed).
- Neurological manifestations:
    - Developmental delay and some impaired cognitive function is universal in children with Down syndrome (moderate intellectual disability is most common – the reported IQ range is 25–70).
    - These children have better receptive language than expressive language.
    - Seizures and epilepsy are present in 8% of patients. One must look for infantile spasms.
    - Autism spectrum disorder (ASD) is present in 8–12% of patients.
    - Cervical spine instability can cause cord compression.
    - Alzheimer-type dementia develops in 20–25% of people with Down syndrome who are >40 years old. A late decline in cognition is also common.
- Endocrine manifestations:
    - Thyroid dysfunction is present in 15% of people. Thus, thyroid function should be checked throughout the patient's lifespan as thyroid dysfunction can contribute to many co-morbidities.
    - Diabetes (type 1 or 2) and obesity are also common. The patient and family should be given lifestyle advice early on.
- Gastrointestinal manifestations:
    - Structural defects (e.g. duodenal atresia, Hirschsprung disease) are present in 12% of patients.
    - Umbilical hernia and coeliac disease may also be present.
- Haematological manifestations:
    - Myelodysplasia is present in 10% of neonates with Down syndrome.
    - The risk of leukaemia is 15–20-fold higher in the individual with Down syndrome (2% risk of acute lymphoblastic leukaemia).
- Autoimmune disorders:

    - As mentioned above, these children are more likely to develop type 1 diabetes and coeliac disease (4–15%).
    - Other common autoimmune disorders in these patients include idiopathic thrombocytopaenic purpura (ITP) and thyroiditis.
- Musculoskeletal and cutaneous manifestations:
    - Hypotonia and joint laxity are common
    - Eczema is also common

Initial Evaluation and Management

The initial evaluation of the child clinically diagnosed with Down syndrome often includes karyotyping, so that the diagnosis is certain and causes other than nondisjunction can be excluded for family counselling reasons. Surveillance for the commonly associated health complications and early developmental stimulation can substantially improve the long-term outcome for children with Down syndrome. Early assessment for congenital cardiac abnormalities clinically by chest X-ray and by ECG should be done in all children with Down syndrome, bearing in mind that a large AVSD will not always cause a heart murmur. An echocardiogram is recommended where available. If there is a serious cardiac abnormality, the baby will not thrive and will generally have other clinical signs of concern. Long-term monitoring of growth, vision, hearing and speech are important, as are periodic checks of thyroid function. Other care can be directed by clinical need.

OTHER TRISOMIES

Down syndrome (T21), Edward syndrome (T18) and Patau syndrome (T13) are the only trisomies compatible with life. T18 and T13 frequently result in death shortly after birth or in utero, but a small group of children (<5%) will survive to childhood. This is important to know when counselling expectant parents. These trisomies are also commonly due to nondisjunction, but can be caused by mosaicism or balanced translocation in a parent. Therefore, karyotyping is important to determine recurrence risk and implications for other family members.

Edward Syndrome (Trisomy 18)

Edward Syndrome occurs in ~1 in 6 000–8 000 births. Clinical features of T18 include:

- Small for gestational age infant
- Congenital heart disease (>80%)
- Neural tube defects.
- Diaphragmatic hernia/omphalocele
- Overlapping fingers
- Rocker bottom feet/clubfoot
- Micrognathia
- Small mouth (microstomia)
- Low set ears
- Prominent occiput

Some visuals associated with T18 features are accessible online via this link.

Patau Syndrome (Trisomy 13)

It occurs in ~1 in 8 000–12 000 live births. Clinical features of T13 include:

- Holoprosencephaly sequence (60–70% of cases) – hypertelorism, cutis aplasia, low set ears, sloped forehead (however, holoprosencephaly can also be caused by other chromosomal abnormalities, single gene disorders or teratogenic disorders)
- Microphthalmia/anophthalmia (60-70% of cases)
- Congenital cardiac disease (80% of cases, especially ASD or VSD)
- Enlarged kidneys and/or kidney malformations
- Cleft lip/palate (especially when central; can be associated with other midline defects – check for hypoglycaemia, electrolyte abnormalities, pituitary dysfunction)
- Absent eyebrows
- Dysplastic ears
- Clenched hands/ulnar deviation of overriding fingers
- Postaxial polydactyly (60-70% of cases)
- Omphalocele

Visuals related to some facial features in T13 are available here.

SEX CHROMOSOME DISORDERS

Klinefelter Syndrome

Klinefelter syndrome (47XXY) occurs in phenotypic males and has an incidence of ~1 in 600 (see examples of 47XXY features here). Affected individuals are tall and have hypogonadism (are usually infertile). They may also have learning difficulties, gynaecomastia, hypotonia and low muscle mass. It is difficult to detect in childhood although 1/3 of patients may have undescended testes. There are other health associations of which one should be aware.

Turner Syndrome

Turner syndrome is most often associated with a 45X0 karyotype and these children often have high rates of mosaicism. These children are phenotypically female but should have a PCR test done to look for Y chromosomal material, as its presence can indicate a higher risk of gonadoblastoma. See an example of preoperative webbed neck in Turner syndrome available here.

Prenatally, hydrops fetalis is common. Children may present early with puffy feet and webbing of the neck or at preschool age with short stature. Ovarian dysgenesis can present as delayed puberty or infertility.

There are some associated health complications, including congenital cardiac diseases (e.g. coarctation of the aorta, ASD, VSD, bicuspid aortic valve), renal abnormalities, mild learning difficulties (especially spatial/perceptual skills), hearing loss and hypothyroidism. However, intellect is usually normal.

FOETAL ALCOHOL SPECTRUM DISORDER (FASD)

FASD is a spectrum of disorders, including alcohol-related birth defects (ARBDs), alcohol-related neurodevelopmental disorders (ARNDs), foetal alcohol syndrome (FAS) and partial foetal alcohol syndrome (PFAS). No amount of alcohol at any stage of pregnancy is safe.

Between 1 in 5 and 1 in 100 children in some parts of South Africa are affected, depending on the social setting. It is more common in communities where there is

poverty, low maternal education, high unemployment rates and heavy or binge drinking.

Mechanism

Alcohol is a teratogen that crosses the placenta and interferes with the normal growth and development of the foetus. As with all teratogens, the outcome is related to the timing of exposure in gestation, the quantity of exposure and the duration of exposure. The outcome will be influenced by additional environmental factors. The most damage occurs in the embryogenic period, during the first 10 weeks after conception. However, alcohol can cause adverse neurological effects throughout pregnancy.

Clinical Features

Clinical manifestations depend, in part, on the stage of pregnancy in which the embryo or foetus was exposed to alcohol. For example, the characteristic facial appearance is due to drinking between weeks 4 and 10 of gestation. A visual of a baby with alcohol syndrome is available here.

One should suspect FASD in children with combinations of the following:

- History of significant history maternal drinking during pregnancy
- Characteristic facies with 2 or more of the following features:
    - Short palpebral fissures
    - Smooth philtrum
    - Thin vermillion border
- Pre- and postnatal growth deficiency
- Neurobehavioural abnormalities:
    - Microcephaly
    - Developmental delay
    - Attention deficit hyperactivity disorder (ADHD)
- Structural congenital malformations (not in all):
    - Congenital heart defects (especially VSD and ASD)
    - Structural renal abnormalities
    - Radioulnar synostosis and vertebral abnormalities

SHORT, DYSMORPHIC CHILDREN

For children with short stature (remember to calculate a mid-parental height), one should determine whether they have normal body proportions. Those that are disproportionately short in the trunk or limbs have a high likelihood of skeletal dysplasia and skeletal radiography can be helpful. A short trunk usually implies spinal involvement and is seen in conditions like spondyloepiphyseal dysplasia and mucopolysaccharidoses. The most common skeletal dysplasia is achondroplasia, in which children present with disproportionately short limbs. Height abnormalities will be more extensively covered in the endocrine section.

Achondroplasia

Achondroplasia occurs in ~1 in 15 000–40 000 neonates. It is an autosomal dominant condition, although most cases are the result of a new mutation. Individuals who inherit two copies of the mutation have such severe achondroplasia that they are stillborn or die soon after birth. Phenotypically, individuals with achondroplasia are short (average male = 131 cm and female = 124 cm) with rhizomelic shortening of arms and legs (the proximal limb segments are most affected – humerus and femur – see also image here), relative macrocephaly with prominent foreheads and short fingers with a gap between the 2nd and 3rd digits (trident hands).

Children with achondroplasia have low tone and joint laxity. They are prone to:

- Upper airway obstruction (both central and obstructive apnoea)
- Obesity
- Ear infections
- Skeletal problems e.g. infantile kyphosis (usually resolves), lumbar lordosis, tibial bowing, spinal stenosis (later in life)

Macrocephaly is inevitable but true hydrocephalus is rare. There is always a narrow craniocervical junction and infants in particular should be closely monitored for any neurological abnormalities and referral for imaging should be considered. Growth should be plotted on an achondroplasia growth chart. Careful attention should be given to supporting the relatively heavy head in infancy and avoiding overextension or flexion of the neck.

OTHER GENETIC SYNDROMES AND DISORDERS

Neurocutaneous Disorders

They include:

- Neurofibromatosis:
    - It is an autosomal dominant condition.
    - Clinical features include Lisch nodules, axillary and inguinal freckling, café au lait spots, scoliosis and neurofibromas.
    - These children have an increased risk of learning difficulties and tumour risk.
- Tuberous sclerosis:
    - It is an autosomal dominant condition associated with CNS astrocytomas, renal angiomyolipomas and cardiac rhabdomyomas.
    - Clinical features include intellectual disability, autism, epilepsy (particularly infantile spasms), hypopigmented macules, facial angiofibromas, periungual fibromas and shagreen patches.
- Sturge-Weber syndrome:
    - It is a sporadic condition that is caused by mosaicism.
    - Clinical features include port wine stains/haemangiomas in the V1 distribution, hemiplegia and epilepsy (especially focal epilepsy).

Neuromuscular Disorders

They include:

- Spinal muscular atrophy:
    - The clinical severity of this autosomal recessive disease varies.
    - Patients will have lower motor neuron signs (fasciculations, areflexia, muscle wasting and muscle weakness that eventually involves the respiratory muscles).
- Duchenne's muscular dystrophy:
    - It is an X-linked recessive condition, so males are mostly affected.
    - The child will have proximal muscle weakness (Gowers's sign) with calf pseudohypertrophy. The weakness is progressive with eventual cardiac and respiratory involvement. Duchenne's muscular dystrophy is also associated with cardiomyopathy.

Additional Autosomal Recessive Disorders

These disorders may not be apparent in family history because they are recessive (both copies of the gene must be abnormal for disease to manifest). Most metabolic conditions and many causes of hearing and vision loss are autosomal recessive.

Sickle Cell Disease/Anaemia
In this condition, red blood cells have a sickle shape and haemoglobin has abnormal oxygen-carrying capacity of haemoglobin. Patients may present with pain crises, stroke or severe anaemia. Sickle cell anaemia is common in sub-Saharan Africa and other areas where malaria is prevalent.

Cystic Fibrosis
It is the result of a defect in the cystic fibrosis transmembrane conductance regulator (CFTR), resulting in thick secretions. This multisystemic disorder causes:

- Salty skin
- Pancreatic insufficiency and malabsorption (with resultant poor growth)
- Recurrent chest infections (can lead to chronic lung disease)
- Bowel obstruction (meconium ileus)

It is more common in those of European ancestry but occurs in all ethnicities.
Examples of red blood cells and sickle cells are accessible here.

Conditions Presenting with Developmental Delay and Intellectual Disability

Fragile X Syndrome
It is an X-linked condition, thus males are more severely affected. Females are protected by skewed inactivation and usually have milder symptoms. Children present with delayed milestones (particularly delayed speech at 2 years), hyperactive behaviour, mild-to-moderate intellectual disability and ASD. Physical features may include a long and narrow face, prominent forehead, large jaw, large ears and joint laxity.

Velocardiofacial Syndrome/DiGeorge Syndrome (22q11.2 Deletion Syndrome)
It is caused by a microdeletion of chromosome 22. Clinical features include:

- Cleft palate
- Thymic and parathyroid gland hypoplasia (present with hypocalcaemia)
- Congenital cardiac disease e.g. truncus arteriosus (usually caused by 22qdel), VSD and tetralogy of Fallot (75%)
- GORD
- Learning disabilities
- Tapered fingers
- Midface hypoplasia
- Deficient alae nasae
- Poorly developed upper helices of the ears

Psychiatric comorbidities (schizophrenia, bipolar mood disorder) may develop later on in some.

Prader-Willi Syndrome

It is an imprinting disorder that usually occurs in the absence of a family history. Patients often present in infancy with hypotonia and low birth weight or later on with insatiable hunger and obesity. Thus, food control is essential.

Prader-Willi syndrome is associated with delayed milestones, hypotonia, narrow forehead, small hands and feet. These children are prone to endocrine abnormalities including hypogonadism, hypocortisolism and hypothyroidism.

Pierre-Robin Sequence

A sequence is a series of sequential developmental effects. In this case, the primary abnormality is underdevelopment of the jaw which leads to displacement of the tongue posteriorly and can cause a cleft palate. This results in problems in early life including upper airway obstruction, feeding difficulties and failure to thrive (FTT). It may be isolated or part of a genetic syndrome.

Other Syndromes to Recognise

Alagille Syndrome

It is an autosomal syndrome condition in which there is intrahepatic bile duct paucity. The child will present with prolonged neonatal jaundice, cholestasis and pale stools. Other features include cardiac disease (VSD, pulmonary valve stenosis), skeletal

abnormalities (butterfly vertebrae), ocular abnormalities and typical facies (deep set eyes, pointed chin).

Peutz-Jeghers Syndrome

It is an autosomal dominant syndrome in which children have gastrointestinal polyps (may present with intussusception), hyper-pigmented mucosae and freckles on the face, hands, feet and digits. It is associated with early-onset cancers in adulthood especially GI, breast and pancreatic cancers.

Beckwith-Wiedemann Syndrome

It is an overgrowth syndrome with clinical features of macrosomia at birth, neonatal hypoglycaemia, macroglossia, midline abdominal defects and ear creases/pits. It is associated with an increased risk of embryonal tumours, including Wilms tumour and hepatoblastoma.

GENETIC TESTING

Genetic testing can be done for different reasons and the technique chosen will depend on the question being asked and the disorder in question. It is important to liaise with a geneticist and the laboratory to ensure you choose the best test for the situation and that you are aware of the limitations of that test.

Types of Genetic Tests

The genetic test may be:

- Diagnostic (to confirm a clinical diagnosis).
- Predictive (to provide information about future risk or disease; generally not advised in childhood unless a preventive intervention is available).
- Carrier (to check whether an individual carries a genetic variant that will have reproductive implications).

See related image here.

Genetic Test Results

As there is so much interindividual variability, it can be difficult to know if a genetic variant found on a test is the cause of a problem or not. This means there are three possible results from a genetic test:

- Positive – a pathogenic or likely pathogenic variant has been found.
- Negative – no variant or a benign variant has been found.
- Variant of uncertain significance (VUS) – at this stage, there is insufficient evidence to decide if the variant detected causes a problem or not (effectively also a negative result as one cannot use this result to make clinical decisions).

As more genes are tested (what with testing of the whole exome or whole genome), VUS is becoming a more frequent result (particularly in African populations, which are not well represented in datasets). Thus it is important to understand the concept of VUS. One must remember that information is rapidly being produced and variants may be reclassified in time. A genetic counsellor can help with the interpretation of test results and with communicating genetic information to patients.

Chapter 2:
DISORDERS OF DEVELOPMENT

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Specialist Advisor: Dr Mark Richards

This chapter covers the following topics:

- Developmental delay (delayed milestones)
- Intellectual developmental disorder (IDD)
- Autism spectrum disorder (ASD)
- Cerebral palsy (CP)

DEVELOPMENTAL DELAY (DELAYED MILESTONES)

Definition

It is a delay in developing cognitive, language and/or motor skills. This delay is an indicator of an underlying condition(s), meaning that it is a symptom rather than a diagnosis.

Each child reaches developmental milestones at his/her own pace, therefore temporary delays may occur in some children, but should not be alarming. Multiple or ongoing developmental delays are a cause for concern, as they may lead to problems later in life. Early detection of developmental delays may reduce or prevent long-term disability, through early intervention.

Pathogenesis

The pathogenesis of developmental delays is not always clear, but associations include (not in order of frequency):

- Genetic disorders e.g. Down syndrome, Fragile X syndrome
- Failure to thrive (any cause)
- Foetal alcohol syndrome
- Cerebral palsy
- Autism
- Landau-Kleffner syndrome
- Myopathies
- Intellectual disability
- Hydrocephalus
- Cystic fibrosis

Clinical Features

Developmental milestones are assessed using a Developmental Milestone Chart.

Table 2.1: Developmental Milestones by Age

AGE	FINE MOTOR	LANGUAGE	GROSS MOTOR	PSYCHOSOCIAL	WARNING SIGNS
6 weeks	Fixes and follows object through 90º.	Gurgles. Startles to loud sounds.	Head-lag is still present.	Smiles responsively.	
14 weeks / 3 months	Fixes and follows through 180º. Pulls at clothes. Hands loosely open.	Coos and chuckles. Quiets to familiar sounds. Turns head to sound.	Little/no head lag on pull-to-sit. Lifts head when prone (neck holding). Moro reflex is disappearing.	Smiles at primary caregiver (social smile at 2 months). Upset when caregiver leaves.	No visual fixation. No response to sound. Absent vocalisation. Floppy (++ head lag). Asymmetry of tone or movement. No social smile at 2 months.
6 months	Voluntarily reaches and grasps. Transfers objects between hands. Mouths objects.	Laughs. Vowel-type babbling (monosyllables). Turns to mother's voice across room.	Braces on pull-to-sit. Sits in tripod fashion. Lifts chest and shoulders when prone. Rolls over in both directions.	Takes everything to mouth. Recognises strangers.	Fails to track people or objects. No response/turn to sound or voice. No vocalising. No steady head control. Does not roll over. No affection for caregiver.
9 months	Points. Immature pincer grasp. Holds a small	Deliberate vocalisation. Babbles. Imitates sounds. Says	Sits without Support. Crawls. Pulls to stand.	Waves "bye bye". Has stranger anxiety.	Squints. Persistent primitive reflexes. No hand preference.

	object in each hand.	disyllabic words. Understands “bye” and “no”.	Stands with support.		Monotonous vocalisation. Unable to sit. Does not respond to own name and doesn’t play any games involving back-and-forth.
12 months	Pincer grasp matures.	Says 1-2 words with meaning. Responds to simple requests.	Creeps well. Walks but falls. Stands without support.	Comes when called. Plays simple ball games. Claps. Co-operates with dressing.	Immature pincer grasp. Does not search for things that are hidden or points. Does not say single words. Cannot stand when supported and does not crawl. Does not wave.
15 months	Imitates scribbling. Builds two-block towers.		Walks alone. Creeps upstairs.	Has jargon.	
18 months	Holds pen (palmar grasp) and scribbles. Builds 3-block towers.	Has 8-10-word vocabulary. Understands simple commands without hand gestures).	Walks and runs well (arms down). Throws a ball. Climbs onto an adult chair.	Copies parents in tasks. Handles spoon and cup. Indicates wet nappy.	No pincer grasp. Mouthing. Not walking. Does not notice or mind when a caregiver leaves or returns.
24 months	Spoon-feeds well. Imitates vertical line. Hand	Speaks in short phrases (2-3-word sentences). Identifies 5 body parts	Jumps. Walks up and down stairs, placing both feet on each	Asks for food, drink, and toilet. Spoon-feeds without spilling.	No single words. Cannot walk steadily.

	preferenc e is usually present. Builds 6-block towers.	(points). Obeys e.g. “Put the pen on the table.”	step. Kicks ball.		
36 months	Copies a circle. Builds 6-block towers. Builds bridge from blocks. Matches colours.	Able to talk in full sentences (3-4 words). Asks questions. Knows full name, age, and gender. Points to 5 colours. Rote counts to 3.	Can pedal a tricycle. Uses alternate feet when going upstairs. Walks on tiptoe. Throws and kicks ball.	Shares toys. Is toilet trained. Dresses with supervision. Uses knife and fork.	Only uses single words. Exhibits echolalia. Unable to understand and follow simple commands. No eye contact.
48 months	Copies a cross and square. Draws man with 3 parts.	Knows full name, address, age and colours. Can sing a song or say a poem. Tells stories. Counts to 10. Understands the past tense.	Climbs steps 1 foot per step (no handrail). Hops on preferred foot.	Washes and dries hands. Involved in make-believe play. Plays cooperatively. Goes to the toilet alone. Brushes teeth.	Speech is difficult to understand (to non-family). Difficulty with scribbling; Cannot jump in place. Does not play well with other children.
5-6 years	Copies a triangle and square. Draws a man with six parts. Can fasten and unfasten buttons.	Understands concepts – cold, tired, hungry (Ask “What should a person do if s/he is cold?”). Asks for the meaning of words.	Walks easily in a narrow line (heel to-toe). Hops on each foot. Bounces a ball.	Chooses his/her own friends. Uses a knife and fork with confidence. Helps with household tasks, dressing and undressing.	Has poor pencil grip. Is clumsy. Has poor posture. Fails to meet milestones.

				Acts out role play.	

INTELLECTUAL DEVELOPMENTAL DISORDER (IDD)

Definition

IDD is, according to the DSM-V, “a disorder with onset during the developmental period that includes both intellectual and adaptive functioning deficits in conceptual, social, and practical domains”.

Table 2.2: DSM-V Criteria for Diagnosing IDD

DSM-V Diagnostic Criteria (Intellectual Developmental Disorder)
A. Deficits in intellectual functions (e.g. reasoning, planning, problem-solving, abstract thinking, academic learning and learning from experience, judgment, and practical understanding) confirmed by clinical assessment and intelligence testing.
B. Deficits in adaptive functioning that lead to failure to meet developmental and sociocultural standards for independence and social responsibility. Without support, the adaptive deficits limit functioning in the activities of daily life (e.g. communication, independent living, social participation) across multiple contexts (e.g. home, school, work, recreation).
C. Onset of A & B is during the developmental period.

Intellectual disability can be classified as mild, moderate or severe on the basis of adaptive functioning scores. IQ measures are not used to classify severity as they are less valid in the lower end of the IQ range and it is the adaptive functioning that determines the level of support required, rather than the IQ score.

Pathogenesis

Often the cause is unknown. However, foetal alcohol syndrome (FAS) is the most common preventable cause of IDD. Other causes include:

- Genetic disorders e.g. Down’s syndrome
- CNS malformations of unknown aetiology
- External prenatal factors e.g. exposure to medication, alcohol, drugs or toxins, maternal illness (diabetes, hypothyroidism, hypertension, malnutrition), gestational disorders

- Perinatal factors e.g. neonatal septicaemia, pneumonia, meningitis, encephalitis, congenital infections, problems at delivery (asphyxia, intracranial haemorrhage or birth injury) or other neonatal complications (respiratory distress, hyperbilirubinaemia or hypoglycaemia)
- Postnatal factors (occurring in the first year of life) e.g. CNS infections, vascular accidents, tumours, head injury, hypoxic brain injury, exposure to toxic agents or psychosocial deprivation
- Other disorders of unknown aetiology e.g. cerebral palsy, epilepsy, autism spectrum disorders

Management

One should offer genetic counselling to families with a history of IDD and certain genetic disorders that increase the risk for IDD. The patient and the family should be provided with psychosocial support, in the form of emotional support and counselling, and social worker assistance with application for social grants. The parents should also be provided with information on the need to enrol the child in a special school.

The multidisciplinary team (doctors, occupational therapist, physiotherapist, speech and language pathologist, audiologist, social worker and counsellor) should be involved in the management of these children. The medical team must manage any medical problems that might be present or which are associated with the underlying condition. The patient receives routine paediatric health care.

AUTISM SPECTRUM DISORDER (ASD)

Definition

ASD is a group of lifelong neurodevelopmental disorders characterised by their effect on social and communication skills, as well as by a restricted, stereotyped, repetitive repertoire of interests, behaviours and activities.

Assessment

A comprehensive evaluation of the child must be done, preferably by a multidisciplinary team. Ancillary testing may be required to exclude mimicking conditions.

History and Examination

One must take a thorough history from caregivers and collaterals e.g. teachers. The child should be carefully observed, focusing on the developmental and behavioural features specified in the DSM-5, medical history and family history. The assessment should include the child's strengths, needs, skills and impairments. Gather collateral information from teachers.

A thorough physical examination should be conducted. Findings from the physical examination may help diagnose comorbid conditions or identify symptoms of disorders that are associated with ASD e.g. tuberous sclerosis complex (see related image here).

Investigations

Screening tools, such as the Childhood Autism Spectrum Test (CAST), may be used to screen for ASD. The child should then be referred to specialised services (e.g. paediatric neurodevelopmental clinic if <7 years or child psychiatry) for multidisciplinary assessments, and standardised ASD assessment with instruments such as the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview – Revised (ADI-R).

Diagnosis

This condition is diagnosed at an early age due to speech and language delays, and social communication developmental delays, and stereotyped behaviours. There are still some people who are only diagnosed as adolescents because these signs were not obvious in childhood.

Table 2.3: DSM-V Criteria for Diagnosing ASD

DSM-V Diagnostic Criteria for Autism Spectrum Disorder
A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive): B. Deficits in social-emotional reciprocity e.g. abnormal social approach, failure of normal back-and-forth conversation, reduced sharing of interests, emotions, or affect, failure to initiate or respond to social interactions. C. Deficits in non-verbal communicative behaviours used for social interaction e.g. poorly integrated verbal and non-verbal communication, abnormalities in eye

contact and body language, deficits in understanding and use of gestures, total lack of facial expressions and non-verbal communication. D. Deficits in developing, maintaining and understanding relationships e.g. difficulty adjusting behaviour to suit various social contexts, difficulty sharing imaginative play or making friends, disinterest in peers.
E. Restricted, repetitive patterns of behaviour, interests, or activities, as manifested by at least two of the following, currently or on history (examples are illustrative, not exhaustive): F. Stereotyped or repetitive motor movements, use of objects, or speech e.g. simple motor stereotypies, lining up toys, flipping objects, rocking, spinning, echolalia, idiosyncratic phrases. G. Insistence on sameness, inflexible adherence to routines, or ritualised patterns or verbal nonverbal behaviour e.g. extreme distress at small changes, difficulty with transitions, rigid thinking patterns, greeting rituals, need to take the same route or eat the same food every day. H. Highly restricted, fixated interests that are abnormal in intensity or focus e.g. strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interest. I. Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment e.g. apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement.
J. Symptoms must be present in the early developmental period, but may not become fully manifested until social demands exceed limited capacities or may be masked by learned strategies in later life.
K. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
L. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur. To make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below what is expected for that child's general developmental level.

Table 2.4: Levels of Severity of ASD

Severity level	Social communication	Restricted, repetitive behaviours
Level 1 "Requiring support"	Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful response to	Inflexibility of behaviour causes significant interference with functioning in one or more contexts. Difficulty

	social overtures of others. May appear to have decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose to- and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful.	switching between activities. Problems of organisation and planning hamper independence.
Level 2 "Requiring substantial support"	Marked deficits in verbal and non-verbal social communication skills. Social impairments are apparent even with supports in place. Limited initiation of social interactions and reduced or abnormal responses to social overtures from others. For example, a person who uses simple sentences, whose interaction is limited to narrow special interests and has markedly odd non-verbal communication.	Inflexibility of behaviour, difficulty coping with change, or other restricted/repetitive behaviours appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action.
Level 3 "Requiring very substantial support"	Severe deficits in verbal and non-verbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and only responds to very direct social approaches	Inflexibility of behaviour, extreme difficulty coping with change, or other restricted/repetitive behaviours markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.

Comorbidity

Common comorbid psychiatric conditions include:

- ADHD
- Developmental coordination disorder
- Anxiety
- Obsessive-compulsive disorder (OCD)
- Depression

See related image here.

Management

The goals of management for the child with ASD are to:

- Improve social functioning and play skills
- Improve functional and spontaneous communication
- Improve adaptive skills
- Decrease non-functional or negative behaviours
- Promote academic functioning
- Improve cognition

The parents and medical team must adapt the child's environment, activities and routines to suit him/her. The parents and multidisciplinary team must also liaise with educational services regarding appropriate support and school placement. If the child is at a mainstream school, s/he may need a facilitator.

The multidisciplinary team should consist of:

- Medical doctors (to provide the patient with routine paediatric health care):
  - Pharmacological management can be helpful, especially if there are comorbid conditions.
  - Risperidone can be given as short-term treatment of significant aggression and melatonin can be given to help with sleep disturbance.
- Social worker and counsellor
- School psychologist
- Occupational therapist (to improve functioning)
- Speech and language pathologist (to assist with communication difficulties)
- Social worker (to assist with the social grant application)

The patient and family should be provided with psychosocial and emotional support, and counselling. HelpGuide.org has information and action plans for parents including a guide to Helping your Child With Autism Thrive. See related image here.

CEREBRAL PALSY (CP)

Definition

CP is a group of disorders characterized by permanent, non-progressive injury to the developing brain, which manifest as impairments of movement and posture and limit activity. A graphic definition of CP is available here.

Pathophysiology

CP is attributed to non-progressive disturbances or a static injury to the developing brain that occurs in the developing foetus (i.e. in utero), infant or toddler (up to 2 years of age). Brain asphyxia was originally implicated as the main cause of CP but multiple ante-, peri-, and postnatal factors are now implicated in the pathogenesis. Environmental factors, which might interact with genetic vulnerability, have also been implicated.

Multiple biochemical factors resulting in a hypoxic-ischemic state, cell death and inflammation are thought to play a role. These factors include:

- Excessive production of proinflammatory cytokines
- Oxidative stress
- Maternal growth factor deprivation
- Extracellular matrix modifications
- Excessive release of glutamate, triggering the excitotoxic cascade

Table 2.5: Classification of the Causes of CP According to the Time of Insult

Prenatal	Perinatal	Postnatal
• Maternal/ foetoplacental disease e.g. pre-eclampsia • Foetal malformations e.g. cerebral malformations, hydrocephalus • Genetic syndromes • Chromosomal abnormalities • Intrauterine infections e.g. CMV, HIV, rubella • Intrauterine vascular events • Teratogens	• Hypoxic-ischaemic encephalopathy • Labour/delivery complications • Intraventricular haemorrhages • Infection/sepsis • Biochemical derangements e.g. bilirubin encephalopathy	• Trauma to the developing brain e.g. traumatic brain injury • Meningitis/ encephalitis (incl. TB meningitis) • Vascular disorders e.g. stroke • Toxins • Idiopathic

Clinical Features

The core feature of CP is motor impairment. It is important to remember that the clinical motor manifestations of CP are dynamic and the clinical picture will change depending on:

- Stage of development of the brain at which the insult occurred
- Extent and severity of the insult to the developing brain
- Stage of development of the brain at the time of insult

Therefore, over time, different types of CP may emerge, only to be replaced when other areas of the brain reach a stage of maturation and exert their influence on a damaged, but developing, brain.

However, generally, the clinical features of CP include:

- Inspection:
    - Scissoring of legs
    - Equinus deformity of the feet (leading toe walking)
    - Muscle wasting
- Tone:
    - Hypertonic fisting of the hand with the thumb adducted across palm
    - Truncal hypotonia with head lag, neck retraction and opisthotonus (due to increased tone)
- Reflexes:
    - Brisk deep tendon reflexes
    - Ankle clonus
    - Inappropriately positive Babinski
- Power (reduced)

Table 2.6 serves as a guide on how to classify motor involvement in the child with CP. Generally, the higher the level, the more severe the CP. However, all children are different.

Table 2.6: Gross Motor Functional Classification System of CP

AGE (years)	**LEVEL**				
	1	**2**	**3**	**4**	**5**
0-2	Learns to sit, uses	Can sit but with adult	Can roll and creep	Can roll. Can only sit	Voluntary control of

	both hands to play with objects. Can crawl and pull-to-sit on his/her own. Walks by 18 months.	assistance or when using his/her hands for support. May begin to crawl or “creep” on his/her belly.	forward while on his/her stomach. Needs lower back support when trying to sit.	with trunk assistance.	movements is impaired. No head and trunk control without support. Needs help with rolling.
2-4	Sits without assistance. May start to stand on his/her own. Walking starts being preferred over crawling.	Can sit with assistance. Reciprocal patterns are used when crawling. Walks with assistive devices or holding onto other objects.	Can sit unsupported but typically in a “rotated hips and knees” position. Can crawl (crawling is the preferred mode of moving around).	Can sit but uses hands & arms for support. May need adaptive equipment for sitting and standing. Crawling, creeping and/or rolling preferred.	All motor function areas are still limited, therefore, still needs assistance.
4-6	Can sit in chairs and get up from chairs without help. Walks freely and begins to run and jump.	Can sit on chairs without help. Assistance is needed to move from standing to the floor. Can walk short distances without support but cannot	Can sit upright on a chair but needs trunk support when using his/her hands. Can get off of chairs with assistance. Uses assistive devices to walk.	Can sit on chairs with trunk support and can move from chairs with support. Can walk short distances but may have problems turning and keeping	Can sit on chairs but needs adaptive equipment to hold him/herself in place. Needs to be transported even for daily activities.

		skip, run, or jump.		his/her balance.	
6-12	Can run, walk, jump and climb stairs on his/her own. *Note*: Balance and coordination may still be lacking.	Can walk with little to no assistance but needs help when walking in crowds or on inclined surfaces. Needs rails for climbing stairs, and shows minimal abilities for running, jumping and skipping.	Can walk with assistive devices. Uses handrails for stairs. Needs to be carried or use wheelchairs when travelling long distances or over uneven/ inclined surfaces.	Can maintain same mobility from age 6. May rely on wheelchairs and walking aids.	May be able to mobilise on his/her own with an electronic wheelchair, but still has limited mobility. Still cannot support the trunk and body. Expansive adaptation equipment used in some instances.

Types of CP

CP may be classified according to the part of the brain that is damaged.

Spastic CP

This is the most common type of cerebral palsy as the injury affects the cerebral motor cortex. The muscles feel stiff and their movements may look jerky. Spasticity is a form of hypertonia, which can make movement difficult or even impossible. Subtypes include:

- Monoplegia
- Hemiplegia
- Diplegia (legs are affected more than arms)
- Quadriplegia

Note: Paraplegia is not a form of CP because it is the result of a spinal injury and CP is the result of damage to the developing brain. A definition of CP is also provided here.

Extrapyramidal CP

These patients have variable movements that are involuntary and which are especially noticeable when attempting to move. Subtypes include:

- Dystonic (commonly caused by bilirubin encephalopathy)
- Athetoid
- Ataxic*
- Hypotonic*

The first two subtypes (also called dyskinetic CP, see visual here) are caused by damage to the basal ganglia and the latter are caused by damage to the cerebellum.

Note: Hypotonic and ataxic CP: these two rarely occur alone. When hypotonia does occur without ataxia (but with intellectual disability), this is NOT classified/ defined as CP.

Mixed CP

These patients present with a combination of the symptoms of spastic CP and extrapyramidal CP (dyskinetic and ataxic-hypotonic CP).

Associated Disorders and Complications

The motor disorders of CP are often accompanied by:

- Disturbances of sensation, perception, cognition, communication, and behaviour
- Epilepsy
- Secondary musculoskeletal problems
- Feeding difficulties e.g. GORD.

See related image here.

Investigations

They are guided by history and examination and may include:

- Neuroimaging (CT scan)
- Specific genetic or diagnostic tests
- Metabolic tests (amino acids, organic acids, thyroid function tests)
- X-rays (hips, spine)
- Electrophysiological studies (EEG, VER, ERG, BAER)

Management

The treating team must educate the family and child about the prognosis for people with CP and establish treatment priorities. Management may include:

- Identifying special needs – almost all individuals with CP have at least one other developmental disability
- Routine paediatric health care:
    - Regular nutritional assessment
    - Anthropometric assessment (on growth charts for CP children)
    - Regular follow-up
    - Adequate management of other health problems (the child must be sent to an audiologist for hearing screening)
- Supportive physical therapy:
    - Physiotherapy and occupational therapy:
        - The aim is to reduce muscle tone and improve positioning, posture and functionality through targeted exercises and with the help of assistive devices
        - These devices include walkers, splints, standing frames and wheelchairs (see image here)
    - Speech and language therapy:
        - The child and parents will be taught about oral coordination, how to manage drooling, using alternative/augmented communication and how to feed the child who has had a gastrostomy
- Medical interventions and orthopaedic surgery:
    - Muscle relaxants e.g. benzodiazepines (diazepam), baclofen

    - Botulinum A toxin injections (Botox® is an effective adjuvant to other therapies as it increases stretch in relaxed muscles and reduces dynamic spastic deformity)
    - Contracture release (improves mobility)
    - Hip subluxation/dislocation reduction or prevention
    - Reconstructive surgery
    - Neurosurgery – rhizotomy (for selected cases)
- Psychosocial support:
    - Social grant assistance (in South Africa, the care dependency grant)
    - Schooling intervention (especially for less severe forms)
    - Counselling for the parents and family

Prevention

CP may be prevented with good antenatal care, avoidance of prematurity, avoidance of IUGR, prevention of birth asphyxia with good perinatal care, good obstetrics and post-natal care. One may also decrease the incidence of CP in 2-year-old children if:

- Full-term neonates with moderate neonatal encephalopathy are treated with therapeutic hypothermia
- Magnesium sulphate administration to mothers in preterm labour

The complications of CP may be prevented with early diagnosis and intervention.

Chapter 3:

ENDOCRINE DISORDERS

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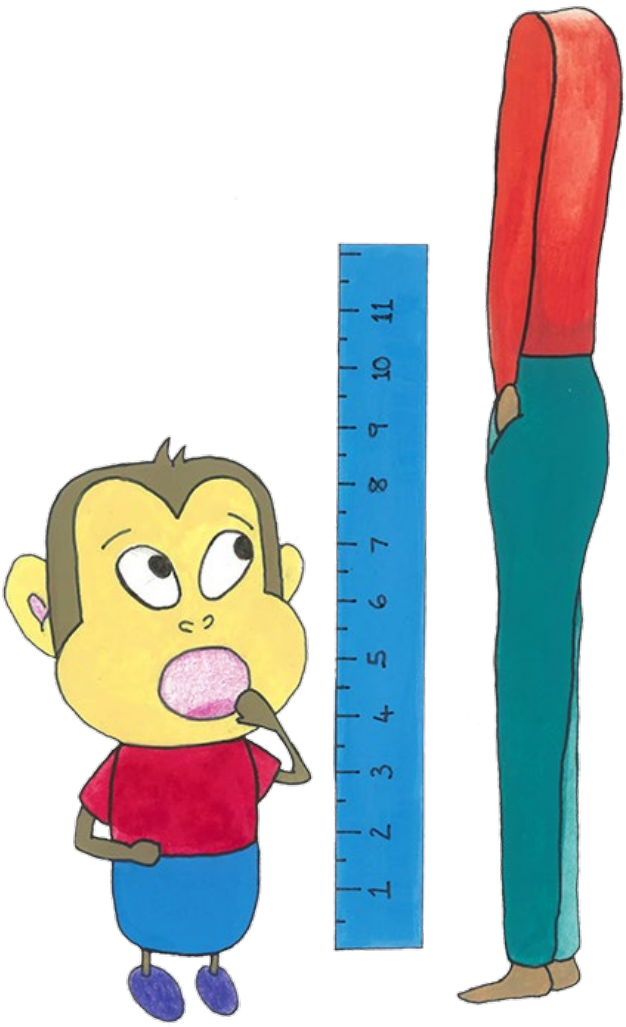


This chapter covers the following topics:

- Normal puberty
- Disorders of puberty
- Approach to growth disorders
- Thyroid disorders
- Diabetes mellitus
- Hypoglycemia

NORMAL PUBERTY

Definition

Puberty is a well-defined sequence of physical and physiological changes which occur during adolescence and culminate in the attainment of full physical and sexual maturity. In addition to physical changes, puberty is accompanied by cognitive and psychological maturation.

Physiology

Puberty is under the control of the hypothalamic-pituitary-gonadal axis. It begins when the hypothalamus starts releasing gonadotropin-releasing hormone (GnRH) into the hypophyseal portal system.

GnRH stimulates the pituitary gland to release the two gonadotropin hormones, luteinising hormone (LH) and follicle-stimulating hormone (FSH). LH and FSH signal the ovaries and testes to release sex hormones (oestrogen in females and testosterone in males), which trigger the maturation of the sex organs and the development of secondary sexual characteristics (SSCs). Another resource related to physiology is available here.

Tanner Staging

Sex-specific physical characteristics can be evaluated with Tanner staging, which represents a predictable set of steps that males and females go through during puberty. It divides the development of secondary sexual characteristics into five stages. For females, breast (B1–B5) and pubic hair (Ph1–Ph5) development are staged (Table 3.1). For males, the genitals (G1–G5) and pubic hair (Ph1–Ph5) are staged (Table 3.2).

Table 3.1: Stages of Pubertal Development in Females (Female Tanner Staging); also available here.

Females (usually begins around 10–14 years old)		
STAGE	BREAST	PUBIC HAIR
1	Prepubertal	Prepubertal

2	Slight enlargement of the papilla diameter (breast bud)	Sparse, long, slightly pigmented and curly hair along the labia
3	Further enlargement of the breast and areola with loss of contour separation between the breast and areola	Darker, coarser and curlier hair which progressively spreads over the mons
4	Areola and papilla form a secondary mound above the breast	Hair has increased in amount but is still limited to the mons
5	Mature areola and projection of only the papilla	Hair is distributed as an inverse triangle and spreads to the medial surface of the thighs
Note: Breast development may be unilateral for several months.		

Table 3.2: Stages of Pubertal Development in Males (Male Tanner Staging)

Males (usually begins around 12-16 years old)		
STAGE	GENITALS	PUBIC HAIR
1	Prepubertal	Prepubertal
2	Testes and scrotum enlarge and there is reddening and a change in texture of the scrotal skin	Sparse growth of slightly curly and pigmented hair at the base of the penis
3	Continued growth of scrotum and testis. Penis grows (mainly in length)	Hair is darker, coarser and curlier and spreads of junction of the pubes
4	Further growth of penis, testes and scrotum with the development of the glans and darkening of the scrotum	Hair covers the pubes
5	Adult stage	Hair spreads over the medial surface of the thighs

Age of Onset of Puberty

The normal age of onset of puberty and the development of SSCs depends on:

- Genetics

- Overall health
- Body fat and/or body composition.
- Social environment

Table 3.3: Age at SSC Development

Age at Development of SSCs in Boys	Age at Development of SSCs in Girls
● Genitalia: 10.5–12.5 years ● Pubic hair: 12.5–14.5 years ● Peak height velocity: 13.5–15 years	● Breast: 10.5–12.5 years ● Pubic hair: 10.5–12.5 years ● Menarche: 12.5–14.5 years

DISORDERS OF PUBERTY

Delayed Puberty

Definition

It is the absence or incomplete development of SSCs by an age 2–3 standard deviations above the mean age of onset of puberty (14 years for boys and 13 years for girls/no menarche by 15 years for girls).

Aetiology and Classification

Delayed puberty may be due to hyper- or hypogonadotropic hypogonadism.

Table 3.4: Comparison of Hypo- and Hypergonadotropic Hypogonadism

HYPERGONADOTROPIC (PRIMARY) HYPOGONADISM	HYPOGONADOTROPIC (SECONDARY) HYPOGONADISM
There is failure of sex hormone (oestrogen and testosterone) production by the gonads i.e. there is -- FSH and LH, $^{-}$ oestrogen/testosterone	There is hypothalamic or pituitary dysfunction, resulting in FSH and LH levels and, thus, low sex hormones levels i.e. there is $^{-}$ FSH and LH, $^{-}$ oestrogen/ testosterone

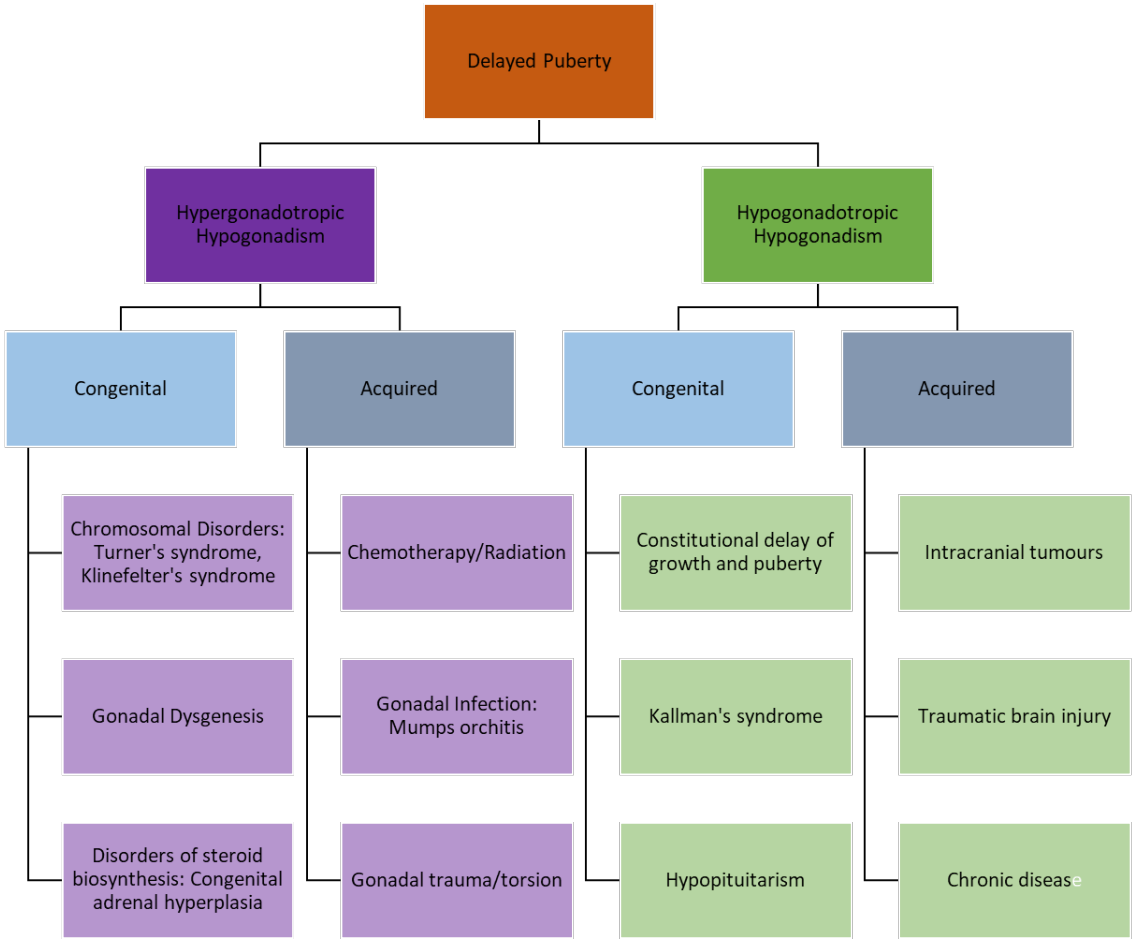


Figure 3.1: Classification of Causes of Delayed Puberty

Diagnosis

It is made based on:

- History – a detailed history should be taken (screen for the many possible physical and functional causes of delayed puberty)
- Observation and examination – measure height, weight and head circumference, thoroughly examine all systems, perform Tanner staging and review previous growth records
- Investigations – perform blood tests (LH, FSH, oestrogen/testosterone, TSH, prolactin routine bloods, karyotyping), get imaging (bone age X-ray, pelvic US, abdominal US, brain MRI) and other special investigations (GnRH test, hCG stimulation test)

Management

One must identify and treat the underlying pathological cause of precocious puberty. A GnRH analogue may need to be given. Psychological support is essential.

Precocious (Early) Puberty

Definition
It is the onset of SSCs at an age 2–3 standard deviations below the mean age of onset of puberty (9 years for boys and 8 years for girls/menarche before 9 years for girls).

Aetiology and Classification
Precocious puberty can either have a central or peripheral origin.

Table 3.5: Comparison of Central and Peripheral Precocious Puberty

CENTRAL (GONADOTROPIN-DEPENDENT) PRECOCIOUS PUBERTY	PERIPHERAL (GONADOTROPIN-INDEPENDENT) PRECOCIOUS PUBERTY
Puberty occurs as a consequence of early physiological (true) activation of the hypothalamic-pituitary-gonadal (HPG) axis i.e. ↑FSH and LH, ↑oestrogen/testosterone	Puberty is due to a mechanism that does not involve the physiological HPG axis. The resultant elevated sex hormones levels trigger the development of SSCs. The sex hormones may be endogenous (gonadal or extragonadal) or exogenous. The endogenous sex hormones are made independently of the HPG – there is no secretion of FSH/LH to trigger the testes or ovaries to produce sex hormones i.e. ⁻ FSH and LH, -oestrogen/testosterone

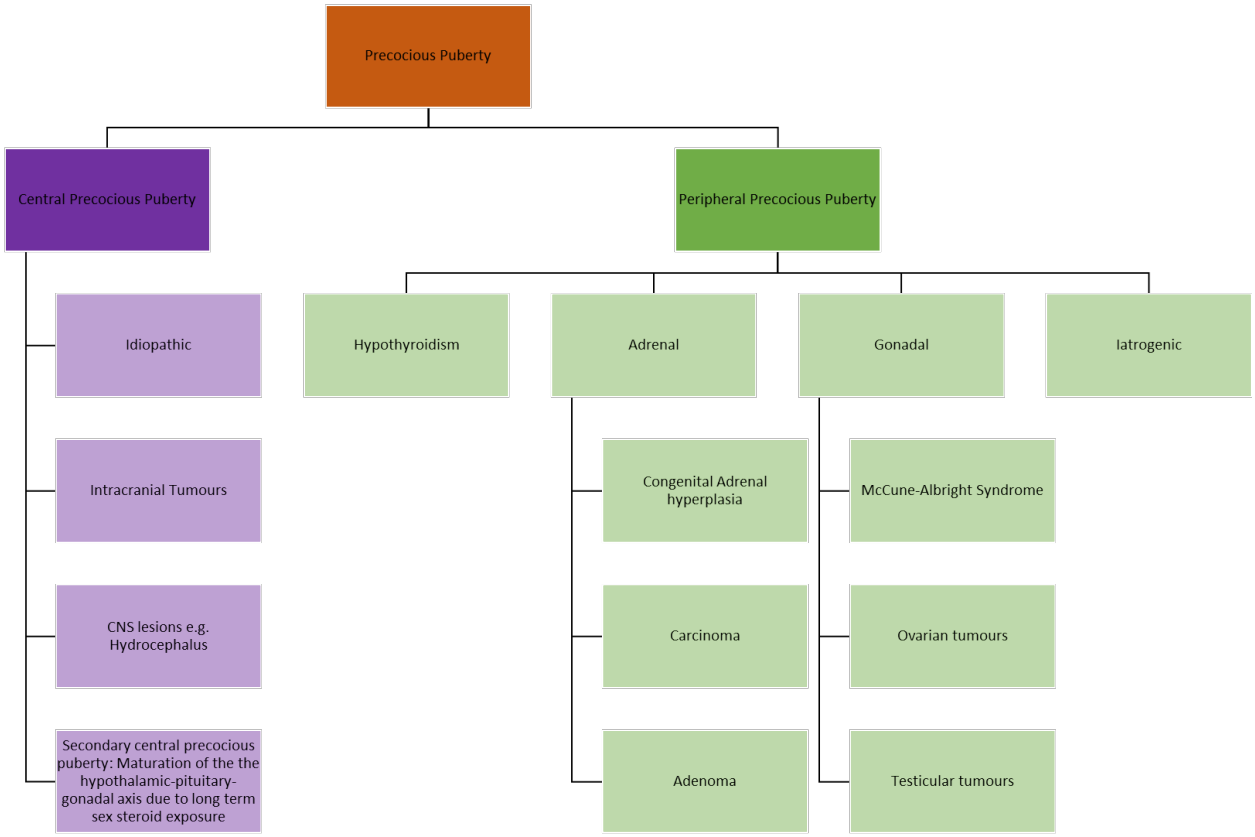


Figure 3.2: Classification of Causes of Precocious Puberty

Diagnosis

A diagnosis is made based on the demonstration of progressive pubertal development and increased growth rate, and laboratory evidence of increased sex hormone production.

A detailed history should be taken, with a focus on:

- Age when first signs of pubertal developmental observed
- Which features of puberty are present and in what order did they appear
- Evidence of growth acceleration
- Family history
- Systemic enquiry

The physical examination should include measurement of the height, weight, head circumference, a thorough systemic examination and assessment of SSCs for Tanner staging. One must also review the child's previous growth records.

Investigations should include:

- Blood tests – LH, FSH, oestrogen/testosterone, TSH, serum androgen levels (17 OH-progesterone, DHEAS, androstenedione)
- Radiological tests – bone age X-ray, pelvic US, abdominal US, brain MRI

- Other special investigations – GnRH test

Management
It includes treating the underlying cause, sex hormone therapy and the provision of psychological support.

APPROACH TO GROWTH DISORDERS

Growth is a dynamic process (involves changes over time) that is a sensitive barometer of health. Growth monitoring is important for assessing the general health of the child (normal growth is an indicator of good health). When poor growth is detected, one should look for a treatable cause. Malnutrition and systemic illness are associated with growth abnormalities. When evaluating abnormal growth, one needs to exclude nutritional deficiencies and systemic illness.

Phases and Parameters of Growth

The following parameters are measured when assessing the growth of children – length/height, weight, head circumference and mid-upper arm circumference (MUAC). When assessing growth over time, one must determine:

- If the growth is steady, slowing or accelerating
- What sort of growth should be happening in this child at this time

Children experience growth in three phases:

- Infantile growth – from conception and into the first year of life; this growth phase is almost entirely dependent on nutrition
- Childhood growth – is influenced by genetics, nutrition and growth hormone (GH) levels
- Pubertal growth – is influenced by both GH and sex hormone levels

Endocrine Causes of Abnormal Growth

They may be grouped according to the child's presentation or the pattern of growth:

- Short and fat – hypothyroidism, Cushing's syndrome
- Slow growth in length/height – GH deficiency, sex hormone deficiency, hypothyroidism
- Fast growth in length/height – excess GH, excess sex hormone, hyperthyroidism

THYROID DISORDERS

Normal Physiology

The hypothalamus produces thyrotropin-releasing hormone (TRH) which stimulates thyroid stimulating hormone (TSH) production and secretion in the pituitary gland. TSH, in turn, stimulates the production and secretion of thyroxine (T4) and triiodothyronine (T3) by the thyroid gland (see related image here). T4 can be converted to the active form, T3. T4 is predominantly bound to T4-binding globulin. Serum T4 regulates the secretion of both TRH and TSH by means of negative feedback loops. The synthesis of thyroid hormone requires the presence of iodine. Thyroid hormones affect every cell in the body, as they:

- Regulate the rate at which calories are burned (affecting weight loss or weight gain)
- Can slow down or speed up the heartbeat
- Can raise or lower body temperature
- Influence the rate at which food moves through the GIT
- Control the way muscles contract
- Control the rate at which dying cells are replaced

Hypothyroidism

Definition
It is a condition in which there is a thyroid hormone deficiency.

Aetiology and Classification
Hypothyroidism may be congenital or acquired (fig.3.3)

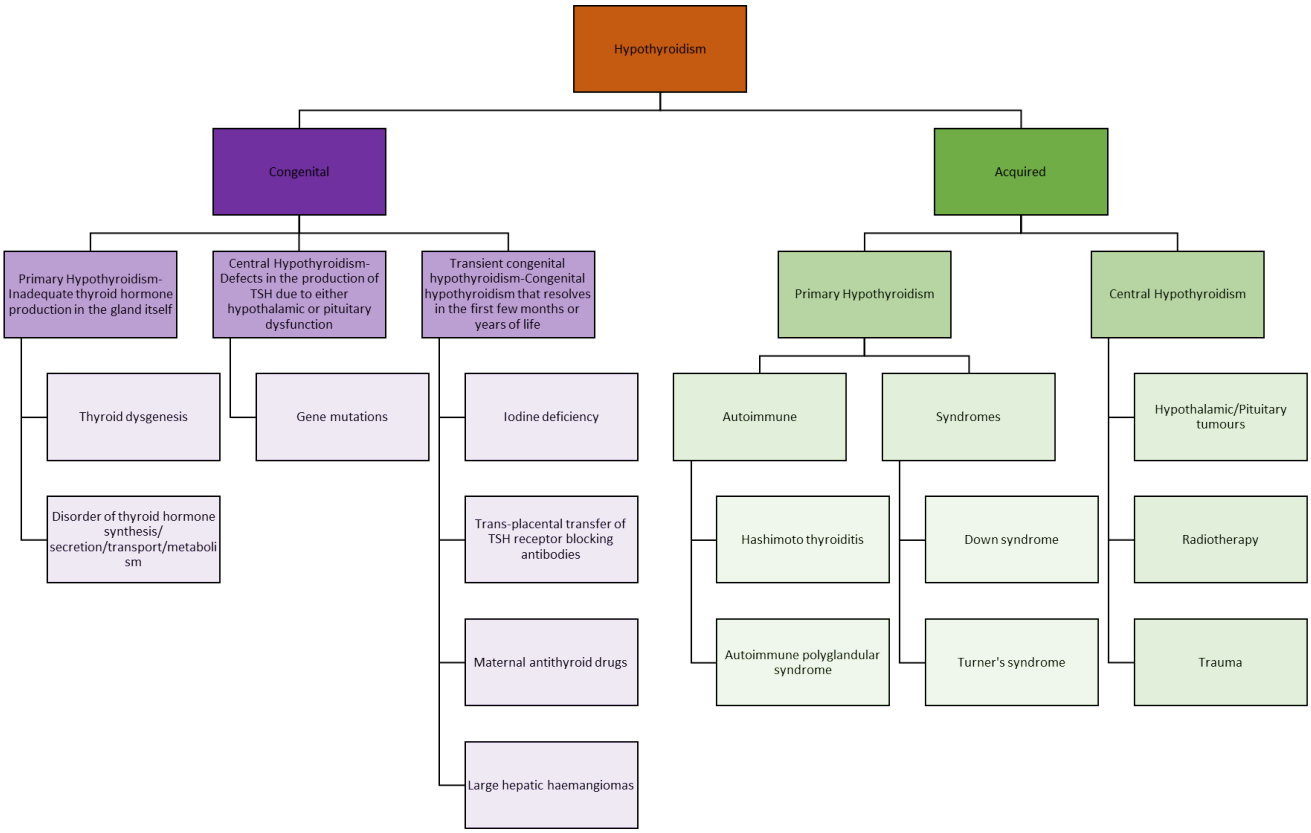


Figure 3.3: Classification of Causes of Hypothyroidism

Clinical Features

Table 3.6: Clinical Features of Congenital and Acquired Hypothyroidism

CONGENITAL HYPOTHYRDOISM	ACQUIRED HYPOTHYRDOISM
Clinical features are non-specific and difficult to detect in the first month of life. They include: ● Umbilical hernia ● Hypotonia ● Excessive sleepiness ● Delayed neurodevelopment ● Prolonged jaundice ● Hoarse cry ● Dry skin ● Constipation ● Poor feeding ● Coarse faces ● Excessive sleepiness	They include: ● Goitre ● Increased weight gain ● Decreased growth velocity ● Delayed skeletal maturation ● Fatigue ● Constipation ● Dry skin ● Precocious puberty

● Delayed neurodevelopment	

Complications
If left untreated, the following complications may occur:

- Neurodevelopmental delay
- Poor motor coordination
- Hypotonia
- Ataxia
- Poor growth and short stature

Investigations
They should include:

- Serum TSH concentration (primary [normal/high] vs secondary hypothyroidism [low])
- T4 (free and total) and T3 (free or total)
- Serum antithyroid antibody test
- Thyroid ultrasound
- Radionucleotide scanning

Management
One must find the underlying cause and appropriately manage. Oral thyroid hormone replacement (levothyroxine) may be required. The patient should be followed up and thyroid hormone levels monitored.

Hyperthyroidism

Definitions
It is characterised by hyperfunction of the thyroid gland, leading to a state of thyrotoxicosis (clinical, physiological and biochemical findings that are the result of tissue exposure to excess thyroid hormone).

Aetiology
The most common cause of hyperthyroidism is Graves disease.

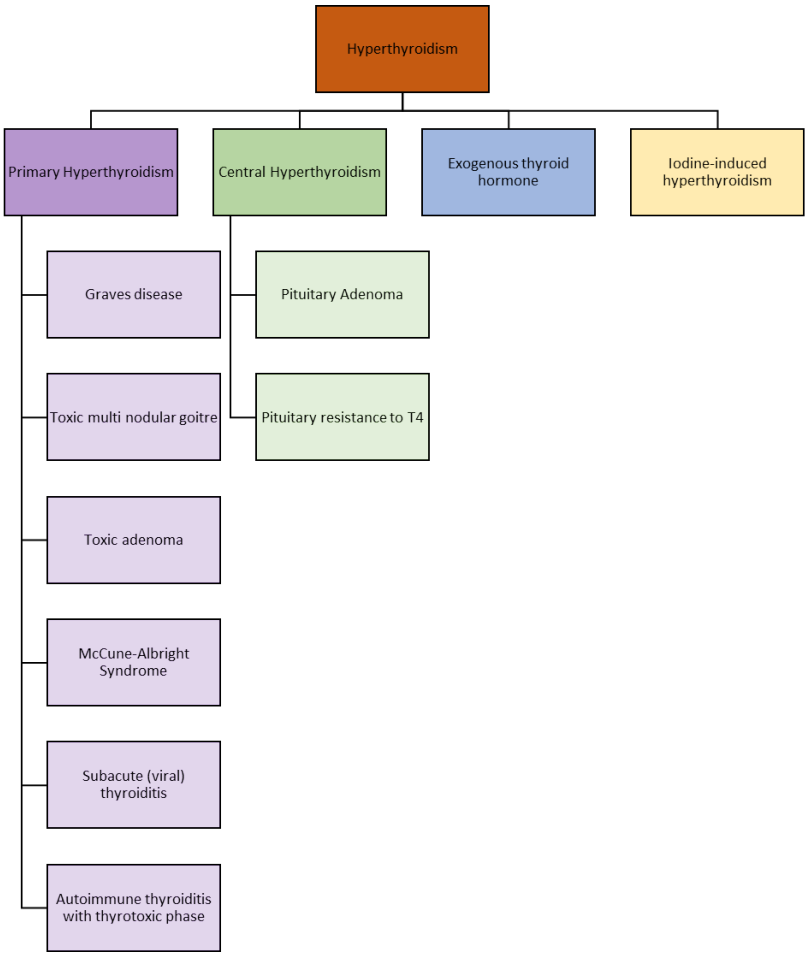


Figure 3.4: Classification of Causes of Hyperthyroidism

Clinical Features

The patient with hyperthyroidism may present with:

- Hyperactivity
- Irritability
- Poor concentration
- Insomnia
- Heath intolerance
- Fatigue
- Muscle weakness
- Altered bowel habits
- Menstrual irregularity
- Tachycardia
- Hyperreflexia
- Fine tremor
- Weight loss despite increased appetite

Investigations
They should include:

- Serum TSH concentration
- T4 (free and total) and T3 (free or total)
- Serum antithyroid antibody test
- Thyroid ultrasound
- Radionucleotide scanning

Management
One must find and treat the underlying cause. One should give antithyroid drugs (e.g. carbimazole, propylthiouracil) and manage thyrotoxic symptoms (a β-bocker may be given to manage the anxiety, tremor and tachycardia). The patient should be followed up to monitor thyroid levels.

DIABETES MELLITUS (DM)

Definition

DM is a condition in which the body is unable to process glucose due to an insulin insufficiency. There are various types of DM, including:

- Type 1 DM (most common type in children)
- Type 2 DM
- Gestational diabetes

Pathophysiology

Type 1 DM is the result of autoimmune destruction of the insulin-producing β-cells in the islets of Langerhans in the pancreas (see related image here). This process occurs in genetically susceptible people and is triggered by one or more environmental agents. It usually progresses over many months or years, during which the individual is asymptomatic and euglycaemic.

Clinical Features

The child may present with:

- Polyuria
- Polydipsia

- Nocturia/nocturnal enuresis
- Weight loss
- Fatigue
- Ketoacidosis (vomiting, deep sighing respiration, decreased level of consciousness and abdominal pain)

Investigations

The following investigations should be performed:

- Arterial blood gas
- Random blood glucose (will be >11.1 mmol/L in the diabetic patient)
- Fasting plasma glucose (will be >7 mmol/L on more than one occasion in the diabetic patient)
- Glycated haemoglobin (HbA1c)
- RFTs and electrolytes
- Diabetes-related autoantibodies e.g. islet cell antibody (ICA), anti-insulin antibody (IAA), anti-glutamic acid decarboxylase (anti-GAD) antibody
- Screening tests for other autoimmune diseases e.g. thyroid function tests/thyroid antibodies, coeliac antibody screen

Complications

They include:

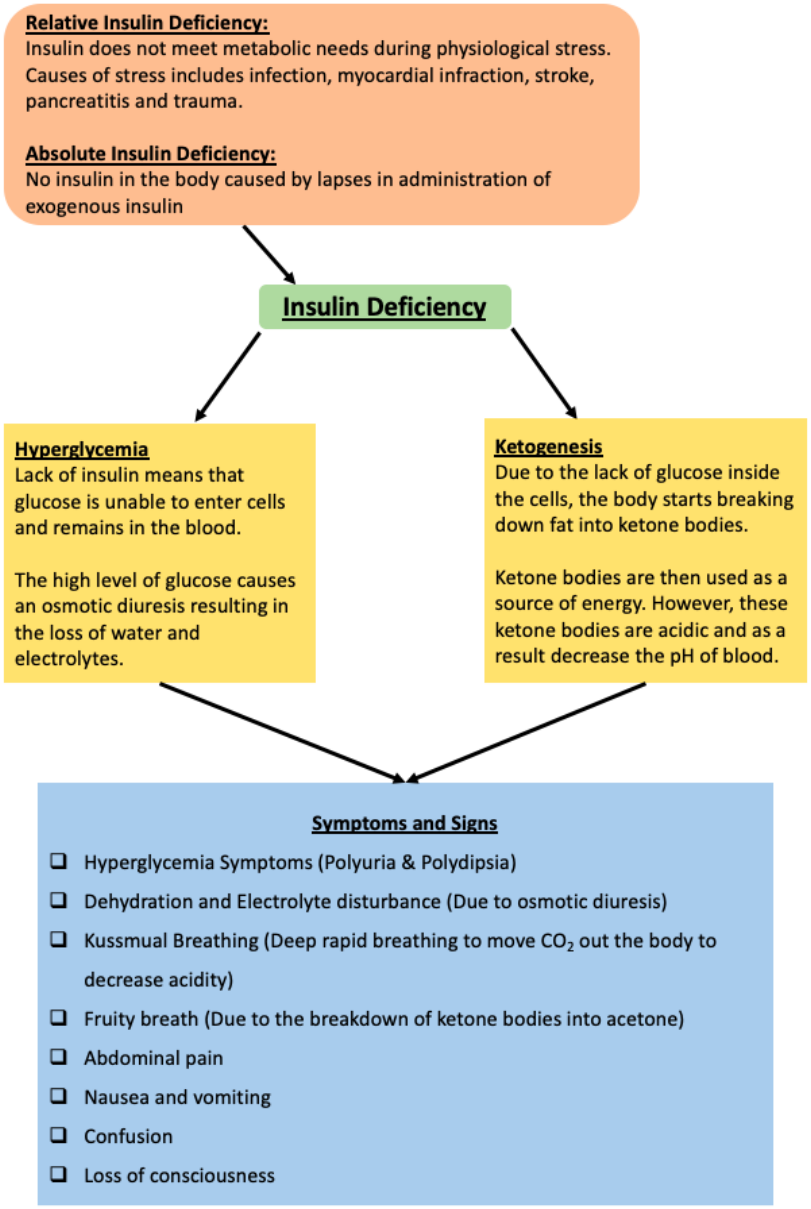
- Diabetic ketoacidosis
- Microvascular complications – diabetic retinopathy, peripheral neuropathy, diabetic nephropathy
- Macrovascular complications – cerebrovascular accident, coronary artery disease, peripheral vascular disease

Management

It will include:

- Insulin therapy
- Education of the child and family about DM
- Nutritional management
- Monitoring of glycaemic control

- Avoidance and management of hypoglycaemia
- Management of acute illness and avoidance of DKA
- Screening, prevention and treatment of the micro- and macrovascular complications of DM



HYPOGLYCAEMIA

Definition

Hypoglycaemia is defined as a plasma glucose level that is low enough to cause signs and symptoms of brain dysfunction (neuroglycopenic symptoms). Glucose below 2.8 mmol/L is considered to be low.

Aetiology

Hypoglycaemia may be caused by:

- Acute or critical illness e.g. sepsis, liver failure, diarrhoea in the setting of malnutrition
- Drugs e.g. oral hypoglycaemic agents, salicylates, β-blockers
- Insulin mediated disorders e.g. hyperinsulinism, insulinoma
- Disorders of glycogen metabolism
- Disorders of gluconeogenesis e.g. glycogen storage disease type 1, fructose-1,6-bisphosphatase deficiency, galactosemia
- Hormone deficiencies e.g. cortisol deficiencies, growth hormone deficiencies, pituitary hormone deficiencies
- Fatty acid oxidation disorders

Clinical Features

The child may present with:

- Autonomic symptoms:
    - These are early symptoms and include sweating, tachycardia, weakness, tremor, and anxiety or feeling of nervousness, and/or severe hunger
- Neuroglycopenic symptoms:
    - These symptoms develop with prolonged or severe hypoglycaemia
    - They include lethargy, irritability, confusion, uncharacteristic behaviour, and hypothermia
    - In extreme cases, there may be loss of consciousness, seizure, or coma

Infants may present with non-specific symptoms of irritability, feeding problems, lethargy, cyanosis, tachypnoea, and hypothermia.

Investigations

One should perform:

- Fingerpick and serum glucose
- LFTs

- Electrolytes
- Serum insulin, lactate, ketones, growth hormone, cortisol, C-peptide, amino acids and carnitine profile
- Urinalysis (look for ketones and glucose-reducing substances)
- Toxin screen

Management

Immediate management includes the administration of glucose/dextrose (orally in a conscious patient and IV in a patient with an altered level of consciousness or who is too young to drink it) and regular glucose monitoring. The dextrose infusion should be accordingly adjusted. One must then find and treat the underlying cause.

Chapter 4:

FEEDING AND FLUID MANAGEMENT

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Specialist Advisor: Dr Farhaad Khan

This chapter covers the following topics:

- Neonatal and infant feeding
- General fluid management

NEONATAL AND INFANT FEEDING

Breastfeeding

Breast milk should be the exclusive food for infants in the first six months of life. The World Health Organisation's (WHO's) Baby-Friendly Hospital Initiative encourages breastfeeding (see related image here) at all baby-friendly hospitals and has published a ten-step guideline to promote and support breastfeeding at these facilities.

Advantages

- Breast milk is free
- It reduces infant morbidity and mortality
- The constituents meet the neonate's nutritional needs and include fatty acids important for neurodevelopment and development of the retina
- Breast milk is safer than formula for the prevention of infection and does not require knowledge about sterilisation of cups or clean water
- It contains important immune-protective factors, like IgA and IgM
- The skin-to-skin contact is good for establishing a bond and passing on skin commensals to enhance immunity
- Breast milk reduces the risk of necrotising enterocolitis and sepsis, when compared to formula feeds
- Breastfeeding encourages the release of metabolic regulatory hormones and stimulates the growth of gastrointestinal bacteria like *Lactobacilli* and *Bifidobacteriae*

Practical advice

One must educate the mother antenatally about the advantages of breastfeeding and the technique, so that she knows how she will feed after delivery. The baby should latch over the whole areola, not just the nipple. The nurse on duty may help the mother with the latching technique.

The initial feed, colostrum, is very nutritious and, if possible, should be given within half an hour of birth. Early breastfeeding also stimulates prolactin and oxytocin and helps to promote uterine tone.

Breastfeeding should be done on demand and the infant allowed to drink from one breast until it is empty before moving on to the other breast. Breasts should be alternated at the start of each feed. Initially the baby will have small but frequent feeds, but over time this pattern will change. Neonates need to be fed at least three-hourly.

Mothers can also express the breast milk and this may be done using their hands. The infant should be fed this expressed milk with a cup rather than a teat. Pretoria pasteurisation/flash heating is the process of heat-treating breast milk so that it is safer for babies to drink in the case of maternal HIV. Expressed milk can be stored in a clean container with a tight lid:

- At room temperature – for up to four hours
- In the refrigerator – for up to four days
- In the freezer – for 6–12 months

If the mother is worried about the amount of food that the infant is receiving, one can educate her on the signs of correct feeding:

  - Approximately six wet nappies daily
  - Gaining weight
  - Good technique (high BFAS score)

Common Problems

Common problems during breastfeeding include:

- Concerns about inadequate milk supply:
  - Reassure, counsel, and ensure the mother has adequate nutrition and rest
- Full or engorged breasts:
  - Hot, lumpy, heavy breasts without fever are “full” and should resolve with demand feeds
  - Painful, shiny, erythematous breasts with poor expression are “engorged”. Demand feeds can continue. The application of warm compresses or warm water are often helpful for milk flow
  - Expressing before feeds can help soften the areola
- Blocked ducts:

    - Encourage frequent feeds, the use of warm/cold compresses and first breastfeeding with the affected breast
- Mastitis and breast abscesses:
    - The mother will present with severe breast pain and fever and/or pus.
    - These mothers require antibiotic treatment (e.g. flucloxacillin), analgesia and, sometimes, surgical management (incision and drainage; often in theatre)
    - The infant should be fed from the unaffected breast and the mother advised to express and discard the milk from the affected side
- Painful nipples:
    - Feeding should be observed to assess for correct positioning and attachment
    - She should be encouraged to express milk before the feed to soften the areola
- Breast candida infection:
    - The mother will present with an itchy/sore, red, shiny and flaky nipple
    - The baby's mouth will have the characteristic creamy white infection
    - One should treat the baby with an oral antifungal (nystatin) and the mother with an antifungal nipple cream
- Flat or inverted nipples:
    - The mother should be advised that continued feeds will help correct the shape. If it does not correct, cup feeds may be considered

Feeding Principles for the Preterm or Sick Neonate

The aim when feeding any neonate should be to maintain a growth rate similar to the intrauterine rate for the same gestational age, and to reach developmental goals for corrected gestational age. Premature and sick neonates struggle to meet their nutritional requirements through demand breastfeeding for the following reasons:

- They often have higher energy needs per kilogram because of their relative stress state and increased growth requirements
- They have reduced hepatic glycogen stores and are reliant on frequent external sources of glucose to avoid hypoglycaemia

- To breastfeed, the neonate needs to be able to root, latch and suck. Neonates below 35 weeks gestation may struggle to breastfeed because of immature feeding reflexes
- These infants often require higher amounts of sleep and get tired sooner when feeding, which can lead the mother to think the infant is full too early into a feed
- The breast milk supply of a sick or preterm mother (whose condition might pre-empt the birth of a sick or premature neonate) is likely to be lower and come in later

For these reasons, high-risk infants may need supplemental feeds, which can be given as enteral feeds or intravenously (parenteral feeds). There is a push by some to give as much volume enterally as is possible, if the baby tolerates oral cup or naso/oro-gastric feeds i.e. does not vomit and has a soft abdomen etc. This is an area of debate as the benefits of enteral feeds also come with the disadvantage of higher rates of necrotising enterocolitis in formula-fed infants. Expressed breast milk, if available, is used preferentially.

The mother should be encouraged to express after every feed or 8–10 times daily. The first bit of breast milk, the colostrum, is especially beneficial. However, waiting for colostrum should not delay feeding, as hypoglycaemia should be avoided in neonates. Very sick babies might require IV 10% dextrose solution within 30 minutes of birth. Donor breast milk can also be used.

Calculating Feeds in Sick and Premature Neonates

In general, the total daily fluid intake (TFI) is calculated in units of mL per kg per day and then split over routes of administration depending on how sick the infant is – IV (parenteral) and oral feeds. The neonate's highest weight achieved is used for the TFI. See Table 4.1 below for daily requirements. One is encouraged to memorise the first column for infants over 2 kg.

The TFI amount should be increased daily by 10–20 mL/kg/day, taking into consideration the new weight and age of the baby but making sure not to increase too fast as the neonate may not tolerate large volumes. The child can be switched to full enteral feeds when they comprise > 80% of the split. In premature neonates, TFI is often increased up to 160–180 mL/kg/day.

Table 4.1: TFI by Weight

	> 2000 g	1500–1999 g	1000–1499 g	< 1000 g
Day 1	60 mL/kg/day	70	80	90
Day 2	75	80	90	100
Day 3	100	110	120	130
Day 4	125	130	140	150
Day 5+	**150 mL/kg/day** Titrate mL/kg/day to growth from this point onwards – not an exact science Observe how infant feeds and tolerates increments If growing well (average 15 g/day over 3 days), maintain TFI NEVER increase TFI above 200 mL/kg/day without consultant input			

For enteral feeds, try to substitute some of the formula volume for expressed breast milk if the infant is too young to suck effectively. Blood glucose should be regularly checked (three hourly) and maintained within 2.6–7.0 mmol/L. Urgently treat hypoglycaemia with additional feeds and manage hyperglycaemia by switching to 5% glucose-containing fluids.

Table 4.2: Notes on and Examples of TFI Calculations

Notes:

- Term infants may feed three hourly or on demand
- Pre-terms should, at first, feed orally, two hourly (as far as they can tolerate)
- In general, give full parenteral feeds for infants < 1500 g (except for colostrum) with gradual introduction of enteral feeds starting at 24 mL/kg/day and increasing by 36 mL/kg daily via orogastric tube (this is a good route for all infants < 34 weeks)
- Give IV maintenance of 10% dextrose solution (also known as neonatalyte) at approx. 1 mL/kg/hour. However, neonates < 1000 g need 5% dextrose water for the first 36-48 hours
- Feeds should be increased (by 10–15 mL/kg/day) for infants receiving conventional phototherapy

- One can substitute a “feed” for a breastfeeding session. 100 mL of breast milk has 67 kcal, while 100 mL pre-term formula has 85–87 kcal
- Premature infants lose up to 15% of their weight from water loss in the first week (term infants lose about 10%)

Example: Write up feeds for a 2000 g 34-week prem with presumed neonatal sepsis on day 1 of life. What are her feeds on day 5, when she weighs 1800 g, and her sepsis has resolved?
Day 1: TFI = 60 m/kg/day, therefore baby requires 120 mL per day (60 x 2 = 120) in 2 hourly feeds. Thus, she should be given 10 mL per feed (120/12 = 10). Give colostrum if available. Give EBM if available, otherwise use formula. She will likely need cup feeds. If cup feeds are not tolerated, she should be given orogastric tube feeds. If she is very sick or has severe respiratory distress, she will need parenteral feeds.
Day 5: TFI = 150 mL/kg/day, therefore baby requires 300 mL per day (150 x 2 = 300; use her highest-ever weight, i.e. birth weight, rather than her current weight). This should be given in 2 hourly feeds of 25 mL per feed (300/12 =25). Give EBM if available, otherwise continue PreNAN®, Similac® or equivalent. Assess the mother’s breastfeeding technique and the baby’s suck to determine when to transition to breastfeeding.

Supplementation

One should work with a dietician, especially regarding formula and availability. Breast milk fortifier should be given to infants < 2000 g, once s/he is on full feeds i.e. 150 mL/kg/day. This supplement is usually called FM85 and 0.5–1g is added depending on feed volume. It should NOT be added to formula, only expressed breastmilk. Medium chain triglycerides may be given if there has been inadequate weight gain.
When the neonate has been switched to only enteral feeds, s/he should also be started on multivitamin drops until mixed feeding is well established (including breast milk).

Iron (ferrous gluconate/Ferrodrops®) should be given from one month old until the neonate is weaned as there is a high risk of anaemia in pre-term babies (have low iron stores).
One should also check phosphate and ALP levels in infants < 32 weeks and VLBW infants. Abnormal serum sodium can be an indicator of poor intake / inadequate fluid management.

Solid Food

It should be introduced when the child is six months old. Small amounts of solid food should be given, starting with cereals (see image here), puréed fruits and vegetables. There should be a gradual progression to a mixed diet and breastfeeding continued for as long as possible (WHO recommends two years).

If there is a family history of food allergy:

- Cow's milk should be avoided for six months
- No citrus/egg/cheese should be given before 9–12 months
- The child should only be given wheat-free cereals

GENERAL FLUID MANAGEMENT

Fluid requirements in paediatrics fall under four main categories – resuscitation, rehydration, maintenance and replacement of ongoing losses.

Resuscitation

Resuscitation fluids are indicated for the child in shock (an emergency). The following signs may be used to recognise the shocked child:

- Early:
    - Cold peripheries
    - Increased capillary refill time (3–4 seconds) – check this on the sternum in a young child)
    - Decreased urine output
- Late:
    - Decreased level of consciousness
    - Poor pulses

- Low systolic blood pressure – indicates decompensation (>20% loss); responds to gravity i.e., lifting legs in hypovolaemia
- Acidotic breathing (Kussmaul's) – fast, hungry for air

It may be difficult to identify these signs in a malnourished child.

Table 4.3: Types of Shock

Recall that there are four types of shock:

- Hypovolaemic:
  - Large volume e.g. acute gastroenteritis (AGE), burns, sepsis, abdominal pathology
  - Low volume e.g. myocarditis, severe acute malnutrition (SAM), drowning, diabetic ketoacidosis (DKA), traumatic brain injury (TBI), status epilepticus, toxins
- Cardiogenic
- Distributive:
  - Septic
  - Anaphylactic
  - Neurogenic
- Obstructive

Management

The correction efforts for hypovolaemia should have the same focus as any resuscitation situation:

- **A** – airway:
  - Maintain the airway and suction any secretions
- **B** – breathing:
  - Give supplemental oxygen via a facemask
  - One may need to give ventilatory support (PEEP, CPAP, etc.) depending on the scenario
- **C** – circulation:
  - Insert an IV or interosseous (IO) line (if no success after two attempts at a venous drip) and cautiously give fluid boluses

    - Rapidly give a 10 mL/kg bolus of isotonic crystalloids e.g. Ringer's lactate, modified Ringer's lactate (Plasma-Lyte A or B, normal saline) using a three-way tap and syringe. Check for improvement and check for signs of fluid overload e.g. enlarged liver, respiratory crackles, S3 gallop rhythm
    - If the patient is still shocked, give repeat boluses, but take care not to fluid overload the child, especially if s/he is malnourished (if overloaded, s/he will develop cardiac failure, hepatomegaly, cardiac gallop rhythm and/or basal lung crepitations). Also monitor urinary output
    - Oral feeding and fluid intake should be encouraged once perfusion is re-established
- **DEFG** – do not ever forgot glucose:
    - Administer dextrose if the fingerprick glucose level is <3 mmol/L

The patient's response to treatment should then be reassessed. If s/he is still shocked, give more fluid boluses and administer ceftriaxone (80 mg/kg stat to cover for possible sepsis). If after 15–20 minutes, the patient has still not improved, contact one's regional hospital to discuss further management and, if necessary, contact the flying squad to discuss transfer.

If the child is transferred to a provincial hospital, s/he may be started on inotropes (dopamine 10 μg/kg/min) and admitted to PICU.

Table 4.4: Management of the Malnourished Child with Shock

MANAGEMENT OF THE MALNOURISHED CHILD WITH HYPOVOLAEMIC SHOCK
Severely malnourished children have a high risk of mortality if they are given too much IV fluid because they are more likely to become fluid overloaded. Thus, IV fluid must be carefully titrated because it may not reverse the shock if too little is given, may be life-saving if the correct amount is given or may be life-threatening if given in excess. The approach to shock is initially the same as in the non-malnourished. Once perfusion is restored, the child should be switched to enteral fluids and rehydrated over 24 hours (see treatment section below).

If fluid overload develops then all fluids must be stopped and the child urgently discussed with a senior clinician; see related image here.

Rehydration

Evaluate the child's hydration status by assessing the characteristics laid out in the table below.

Table 4.5: Features of Mild-to-Moderate and Severe Dehydration

	5% Dehydrated (Mild-to-Moderate) **50 mL/kg loss**	**10% Dehydrated (Severe)** **100 mL/kg loss** *(>2 of the signs below)*
Body weight loss	5–10%	> 10%
Eyes	Sunken	Sunken
Thirst	Increased and drinking regularly	Drinking poorly
Activity	Restless/irritable	Lethargic
Skin turgor (pinch)	Normal (raised for < 2 seconds)	Decreased (stays raised for >2 seconds)
Mucous membranes	Dry	Dry
Tears	Normal/slightly reduced	Absent
Urine output	Oliguric	Oliguric or anuric
Anterior fontanelle	Normal	Sunken
Shock	No signs	May have signs if very severe – use resuscitation algorithm

One should also evaluate nutritional status – assess the patient for SAM as it is commonly associated with AGE.

Management

Admission criteria for the dehydrated child are:

- Shock
- Severe dehydration
- Neurological abnormalities (including coma/severe lethargy)
- Intractable vomiting
- Failure of oral rehydration solution (ORS) out of hospital
- Concerns about care or conditions needed for recovery at home

- Underlying condition exacerbating presentation e.g. bowel obstruction/prior surgery

Rapid Rehydration

Otherwise healthy children should be rapidly rehydrated via the gut. Enteral rehydration should be performed whenever possible. IV and IO lines are only for patients who are shocked or have failed oral therapy, since there is greater danger of fluid overload, among other concerns. A nasogastric tube can be used, especially in patients whose airways are at risk e.g. very lethargic children, severely dehydrated children who refuse to or are unable to drink. The estimated hydration status assessment shown above is important as one does not want to give too much fluid (such that the child cannot tolerate it and becomes fluid overloaded) nor too little fluid (such that the rehydration is ineffective). One may adjust the amount of rehydration fluid given if need be e.g. if the child is not responding after a few hours or does not tolerate the volume of feeds/fluids.

Table 4.6: Rehydration of Mild-to-Moderate and Severe Dehydration

Mild-to-moderate Dehydration	Severe Dehydration
● Give ORS at a rate of 10–12,5 mL/kg/hour for 4–6 hours (one is aiming to replace the 50 mL/kg loss i.e. 10 mL/kg/hour for 5 hours) ● Breastfeed if tolerated, but initially continue ORS feeds if the child is usually formula-fed ● Replace ongoing losses with ORS ● Resume age-appropriate diet once rehydrating	● Give ORS at a rate of 20–25 mL/kg/hour for 4–6 hours (one is aiming to replace the 100 mL/kg loss i.e. 20 mL/kg/hour for 5 hours) ● Breastfeed if tolerated, but initially continue ORS feeds if the child is usually formula-fed ● Replace ongoing losses with ORS ● Resume age-appropriate diet once rehydrating

If the child is not tolerating oral fluids, ½ Darrows dextrose (DD) may be given IV. However, in the child who is vomiting, one should give rehydration fluid (0,45% normal saline and 5% dextrose) with added potassium (20 mmol/L), as this is most appropriate.

Slow Rehydration

Rapid rehydration should be avoided in certain sick children. These children include those with:

- Shock
- SAM
- Age < 2 months or > 5 years
- Encephalopathy
- Cardiac disorders
- Severe pneumonia

Instead one should rehydrate these children over 24–48 hours, using the same amounts as above over the longer period i.e. 100 mL/kg/day for severe and 50 mL/kg/day for mild-moderate cases (see hydration formula recommended by UNICEF here).

Maintenance

Maintenance fluid requirements are calculated as follows for children less than 60 kg, and **added to the above** rehydration prescription if necessary:

Table 4.7: Maintenance Fluids

All ages	Can get fluids by breastfeeding on demand, replacing the below
< 3 months old	150 mL/kg/day
3 months – 1 year	120 mL/kg/day
> 1 year	1–10 kg: 100 mL/kg/day for 1st 10 kgs
	10–20 kg: 50 mL/kg/day for 2nd 10 kgs
	For every kg > 20 kg: 25 mL/kg/day

Maintenance fluids for children >1 year old can be remembered using the 4:2:1 rule: 4 x every kg in the first 10 kg, 2 x every kg in the next 10 kg, and 1 x every kg thereafter (i.e. >20 kg). The sum of these amounts gives you the hourly maintenance fluid requirement. If this sum is multiplied by 25, one will get the daily total.

Example: A 24 kg child needs 64 mL/hour (10x4 + 10x2 + 4x1) and 1600 mL/day (24x25). That can be distributed as nasogastric feeds at a rate of 67 mL per hour.
If maintenance is to be given intravenously only, one must choose an age-appropriate dextrose-containing solution e.g. neonatalyte (10% dextrose) in neonates and small infants; maintelyte (5% dextrose) in older children. These solutions are usually mildly hypotonic and often equivalents can be made up by adding the desired dextrose concentration to a crystalloid.
For small children and infants, total daily fluid intake should be carefully tallied, considering all supplemental fluids, including any dilutants for medications. These additional fluids should be considered part of fluid provision and, therefore, subtracted from the maintenance amount (see hospitalized child with Intravenous Fluids here).
The child should be weighed six-hourly to objectively assess gains or losses.

Ongoing losses
Ongoing losses should be calculated for continuous losses (usually stools but sometimes vomits). These can be counted precisely, using an estimate of 5–10 mL/kg/stool. These feeds can be given immediately after stools if stool passage is measured e.g. in a high-care setting where monitoring, care and staff is plentiful. Often such precision is impossible, and ongoing losses are assumed to be 20–30 mL/kg/day if the bout of acute gastroenteritis is known to be ongoing. This amount can be added to the daily fluid requirements for rehydration and maintenance.

Chapter 5:

NUTRITIONAL DISORDERS

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This chapter covers the following topics:

- Severe acute malnutrition (SAM)
- Failure-to-thrive (FTT)
- Rickets
- Vitamin and mineral deficiencies

SEVERE ACUTE MALNUTRITION (SAM)

Definition

SAM is diagnosed based on the presence of any one of the following:

- Weight-for-height below the -3 Z score on WHO standard growth charts
- Mid-upper arm circumference <11.5 cm
- Clinical signs of nutritional oedema

Pathophysiology

SAM affects many organs and organ systems. These include:

- Cardiovascular – decreased cardiac output, decreased stroke volume, decreased contractility, bradycardia, hypotension
- Urinary – decreased GFR, increased risk of UTIs
- Gastrointestinal – decreased gastric acid, decreased pancreatic digestive enzymes, decreased absorption of nutrients, loss of intestinal barrier function, atrophy of intestinal mucosa, diarrhoea (common)
- Liver – decreased albumin synthesis, decreased gluconeogenesis, decreased lipoprotein synthesis
- Immune – decreased cell-mediated immunity, decreased acute phase immune response, increased risk of sepsis
- Endocrine – decreased insulin, decreased cortisol and growth hormone levels
- Metabolism – impaired heat generation and heat loss, decreased basal metabolic rate (by 30%)
- Cells – decreased cell membrane permeability and sodium pump activity (result in increased intracellular sodium and decreased intracellular potassium levels)
- Haematological – increased risk of anaemia
- Neurological and psychological – increased irritability and apathy, decreased social responsiveness, attention disorders
- Dermatological and musculoskeletal – decreased skeletal muscle mass, decreased subcutaneous fat, atrophy of salivary glands

Clinical Features

The clinical features of a child with SAM can be divided into SAM with oedema or SAM without oedema or a combination of both (see also two types of malnutrition stated here).

Table 5.1: Comparison of the Clinical Features of SAM with Oedema to SAM without Oedema

SAM with Oedema (previously Kwashiorkor)	**SAM without Oedema (previously Marasmus)**

• Weight-for-age is variable
• Oedema:
  ○ May have facial oedema
  ○ Will have pitting oedema of the extremities
  ○ Ascites rarely occurs but the abdomen may be distended (due to hepatomegaly)
• Child is apathetic and listless
• Skin is hyperpigmented, dry and splits when stretched (crazy paving dermatosis)
• Hair is dry, dull and hypopigmented
See related image here.
	• Low weight-for-height
	• Head is large relative to body
	• Face has a "wizened" appearance and staring eyes
	• No oedema
	• Arms, thighs and buttocks appear emaciated due to loss of subcutaneous fat
	• Child is irritable and fretful
	• Skin is thin and dry
	• Hair is thin and sparse
	See related image here.

Children with SAM may also have features of vitamin and mineral deficiencies, dehydration, shock and/or infection. Clinical assessment of dehydration in children with SAM is difficult as the loss of subcutaneous fat makes the signs of dehydration (e.g. as skin turgor, sunken eyes) unreliable. Infection is also more difficult to diagnose as the features of infection (e.g. fever, leucocytosis) may also be absent in children with SAM due to the effect of the malnutrition on the body's immune system.

Investigations

Investigation choice should be guided by history and clinical examination.

Recommended tests include:

- Investigations for infections: blood culture, malaria blood film (in endemic areas), urine dipstick and Urine MCS, stool microscopy, especially if diarrhoea, chest X-ray if respiratory distress (for respiratory infections), HIV test and TB screening
- Blood glucose
- FBC and blood smear
- Electrolytes (Na, K, Ca, Pi, Mg)
- Serum albumin, LFTs
- Renal function tests

Complications

For the purposes of management, SAM may also be classified as complicated or uncomplicated.

Table 5.2: Features of Complicated and Uncomplicated SAM

Complicated SAM	Uncomplicated SAM
● Child < 6 months or less 4kg ● Pitting oedema (SAM with oedema) ● Dehydration ● Vomiting ● Refusing feeds or not eating well ● Hypoglycaemia ● Hypothermia ● Respiratory distress ● Convulsions ● Shock ● Lethargy ● Jaundice ● Weeping skin lesions ● Bleeding	● Child >6 months and >4 kg ● No pitting oedema ● Good appetite and feeding well ● Alert ● No danger signs

Management

SAM is managed according to the WHO Ten Steps. Management is divided into the stabilisation and rehabilitation phase. The stabilisation phase is the first few days of management, when one's focus is the restoration of metabolic and physical stability. The rehabilitation phase usually begins between day 3 and 7 of admission.

Complicated SAM should be managed from WHO step 1 while uncomplicated SAM may be managed from the rehabilitation phase.

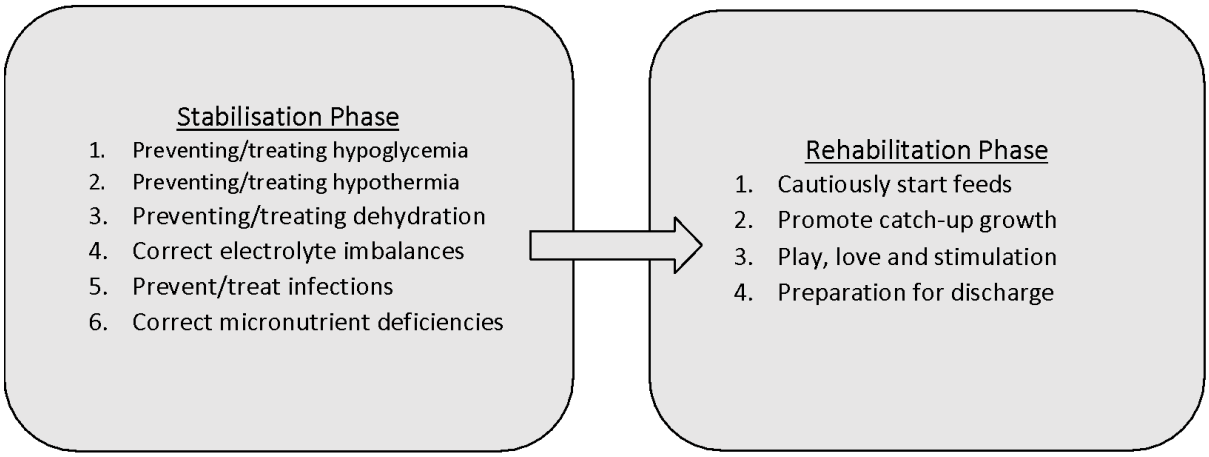

Figure 5.4: WHO Ten Steps

Table 5.3: WHO Ten Steps and Management Plans

WHO Ten Steps		
Step		**Management**
1	Treat/prevent hypoglycaemia (glucose <3mmol/l)	Treatment – give 50 mL 10% dextrose solution orally or by nasogastric tube (NGT if not tolerating oral feeds) every 30 mins for 2 hours; if unconscious or lethargic, give a 5mL/kg bolus of IV dextrose 10% Prevention – feed two hourly (including throughout the night)
2	Treat/prevent hypothermia (axillary temp <35°C)	Treatment – feed immediately; rewarm with clothes, blankets, a heater lamp or skin-to-skin contact (do not use a hot water bottle on direct skin); during rewarming, monitor temperature two hourly until >36.5°C

		Prevention – feed 2 hourly (day and night); keep the child covered and dry; change wet nappies, clothes and bedding; avoid exposure to cold environments; let the child sleep with his/her caregiver
3	Treat/prevent dehydration	Treatment – give 5 mL/kg ORS or rehydration solution for malnutrition (ReSoMal) every 30 mins for two hours and then give 5-10 mL/kg/hr; also replace the fluid lost from diarrhoea and vomiting; if the child is shocked, IV fluid is required (see *Shock* in *Feeding and Fluid Management* chapter) Prevention – give 10 mL/kg ORS after each watery stool and give maintenance fluids (e.g. continue with breastfeeds)
4	Correct electrolyte imbalances	All children with SAM have excess body sodium, even if plasma sodium is low. Deficiencies of potassium, magnesium and phosphate are common and require correction.
5	Treat/prevent infection	Broad-spectrum antibiotics are routinely given as the signs of infection are often absent in these children. Oral amoxicillin may be used in uncomplicated cases but IV gentamycin and ampicillin are used in complicated/severe SAM.
6	Correct micronutrient deficiencies	Children with SAM have multiple micronutrient deficiencies. Supplementation recommendations include multivitamins (especially vitamin A), folic acid (1 mg/day) and zinc (2 mg/kg/day). Copper (0.3 mg/kg/day) and iron (3 mg/kg/day) supplementation should be given for two weeks once the child has been stabilised.
7	Cautiously start feeds	Feeding should be started as soon as possible, but caution is needed due to the child's fragile state. Feeds should be small and frequent and should be given orally

		or via NGT. The WHO recommends use of the F75 formula.
8	Promote catch-up growth	Feeding is increased to achieve weight gain of 10 g/kg/day. The WHO recommends the use of the F100 formula.
9	Provide sensory stimulation and emotional support	Children with SAM may have delayed mental and behavioural development. They require care, a stimulating environment, play and physical activity.
10	Prepare for follow-up after discharge	Children can be discharged if they are not oedematous, have good appetites, show good weight gain, do not have infections, are playful and are alert. Parents/guardians need to be counselled on good feeding practices and the provision of structured playtime. A follow-up plan should be arranged to ensure that the child is growing well.

FAILURE-TO-THRIVE (FTT)

Definition

There is no formal definition for FTT. However, the term is generally used to describe children who have unsatisfactory weight gain (growth curve flattening or weight loss) or a low weight for age but a z-score of > -2 on WHO standard growth charts or the Road-to-Health charts (used in South Africa) when corrected for age, gender, genetic potential and medical condition.

Aetiology

There are many causes of FTT. A thorough history and examination is essential as one must find the underlying aetiology. The causes can be divided into four categories:

- Inadequate intake:
    - Feeding/social issues e.g. poverty, incorrect feeding techniques
    - Mechanical issues e.g. cleft palate, nasal obstruction
    - Inability or difficulty swallowing e.g. HIE, cerebral palsy
    - Gastroeosophageal reflux disease

- Inadequate nutrient absorption:
    - Malabsorption e.g. infection, cystic fibrosis, lactose intolerance, coeliac disease
    - Intestinal obstruction e.g. hernia, pyloric stenosis
    - Short bowel syndrome
- Increased nutrient utilisation:
    - Chronic diseases and infections e.g. TB, HIV, chronic cardiac and respiratory diseases
    - Genetic diseases
    - Metabolic conditions e.g. storage diseases
    - Endocrine disorders e.g. diabetes mellitus, hyperthyroidism
- Excess nutrient loss
    - Chronic gastroenteritis

Clinical Features

The child will have:

- Weight <3rd percentile for gestational age when plotted on the appropriate chart e.g. growth chart for the child with Down syndrome
- Weight for height <10th percentile when plotted on the appropriate chart
- Weight loss of ≥2 percentiles
- Daily weight gain less than expected for age

The child may also have features of underlying diseases causing FTT and/or features of vitamin and nutrient deficiencies.

Investigations and Management

Investigations should be guided by history and examination.

Management depends on the underlying aetiology. Outpatient treatment can be considered if the cause is impaired intake and enteral nutrition can meet patient requirements. Inpatient management is generally required for patients with other medical conditions, with severe malnutrition, who have suffered child abuse/neglect and/or significant psychosocial issues. Management should involve a

multidisciplinary team that may include a dietician, social worker and psychiatrist, depending on the needs of the child.

RICKETS

Definition

Rickets refers to the failure of mineralisation of bones in growing children.

Table 5.4: Pathophysiology of Vitamin D Metabolism

Vitamin D Metabolism

Vitamin D has two forms – Vitamin D2 (ergocalciferol) and Vitamin D3 (cholecalciferol). Vitamin D is either acquired directly from diet or through the conversion of 7-dehydrocholesterol to vitamin D3 when dehydrocholesterol in the skin is exposed to UV light. The vitamin D is then stored (in muscle or fat) or transported to the liver where it is hydroxylated to 25-hydroxyvitamin D (calcidiol – an inactive compound is inactive).

Calcidiol is hydroxylated in the kidney to its active form, 1,25 hydroxyvitamin D (calcitriol). Calcitriol promotes calcium and phosphate absorption in the gut and increases renal absorption of both calcium and phosphate. Parathyroid hormone (PTH) is responsible for the regulation of calcitriol. In response to low calcium levels, PTH increases the activity of 1-α-hydroxylase, an enzyme that is responsible for this conversion of calcidiol to calcitriol. High calcitriol levels act in a negative feedback mechanism and decrease PTH secretion.

Calcium and Phosphate Homeostasis

Calcium and phosphate are absorbed in the GIT (under the influence of calcitriol) and are mostly stored in the bone as hydroxyapatite. Ionised (free, non-protein-bound) calcium and phosphate are filtered by the kidney. Over 95% of filtered calcium is reabsorbed. (See a diagram showing the mechanisms of maintenance of calcium homeostasis here.)

PTH and calcitonin play an important role in calcium regulation. PTH is secreted in response to low serum calcium levels. It increases the calcium concentration by

increasing intestinal absorption and promoting renal reabsorption of calcium. It is worth noting that PTH has the opposite effect on phosphate as it decreases phosphate absorption by the kidney. PTH also causes bone resorption by increasing osteoclast activity resulting in the release of calcium from the bone.

Calcitonin is released when serum calcium levels are high. It is released from C cells in the thyroid gland and works to suppress calcium release from bone and decrease calcium absorption from the intestines and kidneys.

Aetiology

Calcium and phosphate play an important role in bone mineralisation. Deficiencies in either of these may, therefore, cause rickets. Dietary deficiency is the most common cause.

Table 5.5: Causes of Rickets in Children

Causes of Rickets in Children	
Calcium-deficiency rickets	● Vitamin D deficiency (more common in infants): ○ Dietary deficiency of Vitamin D ○ Inadequate exposure to sunlight ○ Impaired absorption of Vitamin D: Fat malabsorption, coeliac disease ○ Impaired hydroxylation of Vitamin D to 25-hydroxyvitamin D: liver immaturity, prematurity ○ Decreased renal synthesis of 1,25 dihydroxy vitamin D: renal failure ● Calcium deficiency (more common in older children): ○ Decreased dietary intake
Phosphate-deficiency rickets	● Decreased intake of phosphate ● Decreased intestinal absorption of phosphate: aluminium hydroxide ingestion ● Increased renal loss of phosphate: genetic disorders (X-linked), Fanconi syndrome, mesenchymal tumours.

Clinical Features

The child with rickets (see also an image of a child with rickets here) may have:

- Delayed closure of fontanelles:
    - The posterior fontanelle closes by 3 months, while the anterior fontanelle should be closed by 24 months
- Frontal and parietal bossing (protuberance of the skull):
    - Children with frontal bossing will have an unusually prominent forehead
- Craniotabes (softening of the skull bones)
- Rachitic rosary:
    - This is the widening of the ends of the anterior ribs at the costochondral junctions
    - It may be visible as beading or palpable as nodules at the costochondral junction
- Harrison's sulcus (groove in the lower margin of the thorax due to the pull of the diaphragm on the lower ribs)
- Widening of the wrist and bowing of the distal radius and ulna
- Lateral bowing of the femur and tibia (see figure 3.2)

The child may also have features of hypocalcaemia.

Diagnosis and Investigations

X-rays can be used to diagnose rickets (see X-ray here and here). Rachitic changes are best seen at the metaphysis of the knee (distal femur and proximal tibia), wrist (especially the distal ulna) and the anterior ribs (rachitic rosary). Features on X-ray include:

- Cupping and fraying of metaphysis (see figure 5.8)
- Widened epiphyseal plates.
- Poorly mineralised epiphyseal plates
- Cortical spurs
- Coarse trabeculation
- Deformities: bowing of long bone, fractures, frontal bossing

Calcium, phosphate, PTH and alkaline phosphatase (ALP) levels should also be measured. In calcium-deficiency rickets, calcium and phosphate levels are low while

ALP and PTH levels are high. In phosphate-deficiency rickets, phosphate levels are low while calcium, ALP and PTH levels may be raised or normal.

Management

Calcium-deficiency rickets is generally treated with Vitamin D supplementation of 1000 to 5000 IU/day for 4-6 weeks, as the most common cause of this rickets is dietary deficiency. If hypocalcaemia is present, this should be corrected. An X-ray should be done after 8-12 weeks of treatment to ensure adequate bone healing. Failure to respond to treatment requires further investigation and management will depend on the underlying cause.

Phosphate-deficiency rickets will generally require further investigations and management will, therefore, depend on the cause.

VITAMIN AND MINERAL DEFICIENCIES

Classification of Nutrients

Nutrients in food can be classified based on how much of the nutrient is needed by the body or based on the body's response to deficiency of the nutrient.

Classification Based on Quantity Required

Nutrients may be classified as:

- Macronutrients – carbohydrates, protein and fat
- Micronutrients – vitamins, macrominerals and microminerals

Classification Based on Response to Deficiency (Golden Classification)

Table 5.6: Golden Classification of Nutrients

TYPE I NUTRIENT DEFICIENCIES	TYPE II NUTRIENT DEFICIENCIES
● Deficiencies of these nutrients manifest with early clinical signs without abnormal anthropometry ● Examples include vitamins, iron, copper and iodine	● Deficiencies of these vitamins do not present with obvious, early clinical features and may therefore go unrecognised ● However, they lead to growth failure (stunting and wasting) ● Examples include protein, zinc, magnesium and potassium

Vitamins

Vitamins can be divided into two groups – fat-soluble vitamins (vitamins A, D, E and K) and water-soluble vitamins (vitamin B complex and vitamin C). Deficiencies of water-soluble vitamins tend to develop after weeks to months of malnutrition. However, deficiencies of fat-soluble vitamins take longer than a year to develop because the body is able to store larger amounts of these vitamins.

Minerals

Minerals can be divided into macrominerals and microminerals (also known as trace minerals). Macrominerals are needed in milligram amounts on a daily basis and include sodium, potassium, chloride and calcium. Microminerals are needed in smaller quantities and include copper and zinc. Chromium, fluoride, iodide, selenium and cobalt are also important minerals but are needed in even smaller amounts and are therefore known as ultra-trace minerals.

Chapter 6:

GASTROINTESTINAL DISORDERS

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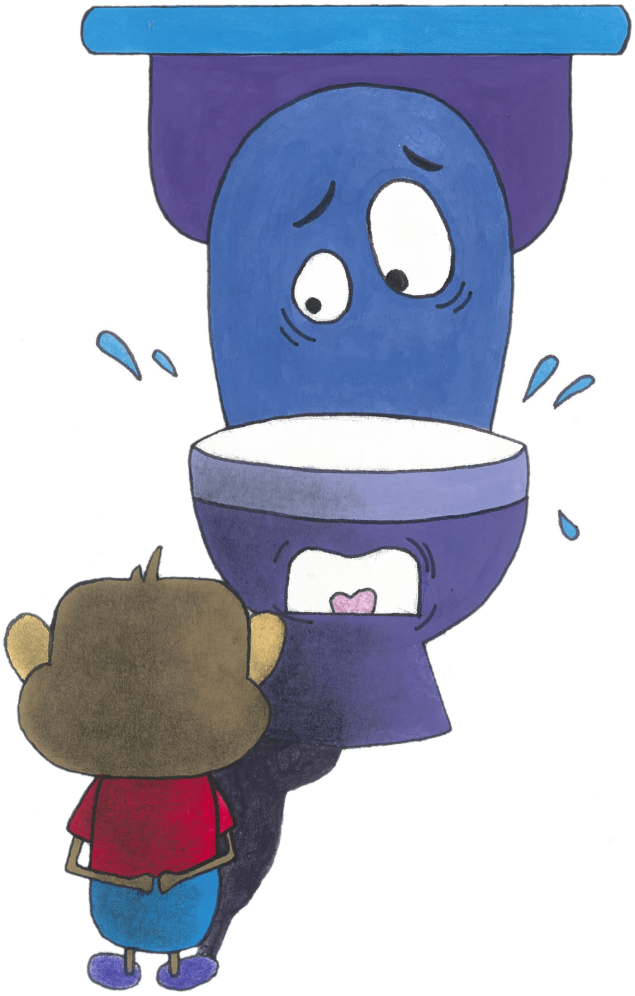

This chapter covers the following topics:

- Diarrhoea
- Hepatitis
- Portal hypertension
- Gastroesophageal reflux
- Constipation
- Jaundice
- Hepatosplenomegaly
- Gastrointestinal bleeding
- Functional abdominal pain (FAP)

DIARRHOEA

Diarrhoea is defined by the WHO as ≥3 watery stools in 24 hours. Almost every child will have diarrhoea at least once and approximately 1 in 3 hospital admissions in South Africa are due to diarrhoea. It remains a major cause of morbidity and mortality worldwide in children <5 years old. It is the second most common cause of death (after HIV) in South African children of that age group.

Classification, Pathophysiology and Aetiology

In diarrhoea, the excretion of water and electrolytes exceed net absorption. Diarrhoea may be classified according to pathophysiology or duration.

Pathophysiological Classification

Diarrhoea may be classified as:

- Osmotic diarrhoea:
    - It occurs when a large number of osmotically active particles are present in the lumen, leading to the passive flow of fluid into the bowel lumen.
    - Causes include laxatives, lactulose, lactose, and other food intolerances/allergies.
- Secretory diarrhoea:
    - An activated pathway (due to the release of a toxin by a pathogen that invaded the intestinal mucosa) or inherent abnormalities of enterocytes cause excessive amounts of fluid to be secreted.
    - Diarrhoea results when absorptive mechanisms become overwhelmed i.e. secretion exceeds absorption.
    - Infective causes of secretory diarrhoea include:
        - Viruses e.g. rotavirus, norovirus, calicivirus, Norwalk virus
        - Bacteria e.g. *Campylobacter jejuni*, *Salmonella* sp, *E. coli*, *C. difficile*, Shigella sp, *Yersinia enterocolitica*
        - Parasites e.g. *Cryptosporidium* sp*, Giardia lamblia*

Classification According to Duration

Diarrhoea may be considered:

- Acute:
    - There is a sudden onset of increased frequency of stools which lasts no longer than 14 days.
    - It is most commonly caused by a virus and laboratory investigation is not necessary to diagnose acute diarrhoea.
- Persistent diarrhoea:
    - It is an episode of diarrhoea of presumed infectious aetiology that begins acutely and lasts ≥14 days.
- Chronic diarrhoea:
    - It is a diarrhoeal episode that lasts ≥14 days and which most commonly has a non-infectious cause e.g. lactose intolerance, food allergies.

Clinical Features

The clinical presentation and course of diarrhoea depends on the aetiology of the diarrhoea and the host (see an image of a child threatened by severe diarrhoea here). The patient may present with:

- Features of dehydration:
    - Lethargy
    - Depressed level of consciousness
    - Sunken anterior fontanelle
    - Dry mucous membranes and no tears
    - Sunken eyes
    - Reduced skin turgor
    - Delayed capillary refill (>2 s)
- Complications of dehydration:
    - Electrolyte disturbances (hyponatraemia, hypokalaemia and metabolic acidosis)
    - Acute renal failure
    - Paralytic ileus
    - Convulsions
    - Cerebral damage
- FTT and malnutrition (diagnosed based on anthropometry measurements, reduced muscle/fat mass, peripheral oedema)

- Perianal erythema

Table 6.1: Recognising and Classifying Dehydration

Hydration	No dehydration	Some dehydration (5% dry)	Severe dehydration (≥10% dry)	Shock (an important danger sign)
Level of consciousness	Normal	Normal	Lethargic	Not responding
Eyes	Normal	Sunken	Very sunken	Dull
Mucous membranes	Moist	Dry	Very dry	Varies
Thirst	Drinks normally	Thirsty	Extremely thirsty	Does not want to drink
Skin	Normal skin turgor	Decreased skin turgor	Very decreased skin turgor	Mottled and cold
Anterior fontanelle	Normal	Sunken	Very sunken	-
Weight loss	None	<5%	5-10%	Varies
Pulse rate	Normal	Normal	Fast	Fast/slow
Pulse volume	Normal	Normal	Thready	Thready/impalpable
Respiration	Normal	Deep	Fast and deep	Irregular and difficult

Note: The most accurate measure of dehydration is loss of weight. One must remember that shock may occur even in the absence of other signs/symptoms of dehydration.

Complications

Diarrhoea may be complicated by:

- Electrolyte abnormalities:
    - Hypernatremia and hyponatraemia (common in secretory diarrhoea and the malnourished) – causes irritability and seizures
    - Hypokalaemia – causes hypotonia, paralytic ileus, bradycardia and respiratory failure in prolonged or recurrent episodes
    - Hypocalcaemia (may occur in secretory diarrhoea)
    - Hypomagnesaemia (may occur in secretory diarrhoea)

- Hypoglycaemia (due to catecholamine release and may develop in the malnourished, septic or hypothermic patient)
- Metabolic acidosis (caused by loss of bases in stool, poor tissue perfusion and decreased renal hydrogen clearance)
- Renal failure (in severe dehydration)
- Haemolytic uraemic syndrome – characterised by haemolytic anaemia, acute kidney injury (uraemia) and thrombocytopaenia
- Rhabdomyolysis
- Shock
- Death

Investigations

No routine investigations are required, as most children will recover spontaneously within a few days, regardless of the underlying causative organism. However, a urine dipstick and finger-prick glucose should be done on all children admitted to hospital. Investigations may include:

- Stool culture (always done for):
    - Children with bloody diarrhoea (send cultures for *C. difficile, Campylobacter* sp, *Shigella* sp and *E.coli*)
- Electrolytes, RFTs and ABG (always done for):
    - Severely dehydrated children
    - Moderately dehydrated children with an unusual clinical picture
    - Malnourished children
    - Children requiring IV fluids for rehydration
    - Children with complications
- ABG

Management

Primary Prevention

Diarrhoea may be prevented by:

- Ensuring a clean water supply
- Encouraging good sanitation and hygiene
- Giving vitamin A prophylaxis

- Encouraging breastfeeding
- Giving supplemental zinc
- Vaccinating against rotavirus

Secondary Prevention

This involves the prevention of dehydration and its complications. Acute diarrhoea is usually self-limiting. However, one must always assess the patient for danger signs (not drinking, lethargy, intractable vomiting, convulsions and bloody stools) and give supportive management.

Supportive management includes:

- Oral rehydration therapy (ORT; give as soon as possible)
- Zinc supplementation (10-20 mg daily for 10-14 days). See also the rehydration formula recommended by UNICEF here.

Tertiary Prevention

One's aim here is to prevent death from dehydration and complications. Thus, tertiary prevention involves appropriately managing the complications that the child has and appropriately managing dehydration and shock (refer to general fluid management in the *Feeds and Fluid Management* chapter).

HEPATITIS

Hepatitis is inflammation of the liver which can result in the damage and destruction of hepatocytes.

Aetiology

Common causes of hepatitis include viruses, autoimmune liver disease, and drugs and toxins.

Viral Hepatitis

In viral hepatitis, the damage to the liver is not due to the viral invasion but the immune response to the virus. In neonates the virus is usually vertically transmitted from the mother in the perinatal period. Viral causes of hepatitis include:

- Hepatitis viruses:

    - A (HAV) – transmitted via the faecal-oral transmission; the degree of hepatic injury depends on the host's immune response
    - B (HBV) – transmitted via bodily fluids e.g. blood, semen
    - C (HCV) – transmitted through contact with infected blood
    - D (HDV) – not common in children as it requires HBV co-infectivity for replication
    - E (HEV) – transmitted via the faecal-oral route
- CMV
- VZV
- HSV (especially in infants)
- Enterovirus
- Rubella
- Adenovirus
- Parvovirus

Autoimmune Liver Disease

They include:

- Autoimmune hepatitis
- Sclerosing cholangitis
- Kawasaki disease
- Graft-versus-host disease
- Immunodeficiencies

Drugs and Toxins

- Medication-induced hepatitis
- Paracetamol toxicity
- *Amanita phalloides* (a poisonous wild mushroom)

Clinical Features

They vary as they depend on the aetiology and the child's age of the child (infant vs child vs adolescent). Some children may be asymptomatic, while others may present with:

- Flu-like symptoms

- Malaise
- Jaundice
- Fever
- Nausea and vomiting
- Anorexia or poor feeding
- Abdominal discomfort
- Diarrhoea
- Dark urine and clay-coloured stools
- Tender hepatomegaly

Acute HBV infection is usually symptomatic, while chronic infection is often asymptomatic (children with the latter infection will grow and develop normally). Chronic infection may be associated with polyarteritis nodosa and glomerulonephritis, and can progress to cirrhosis and hepatocellular carcinoma. Most children with chronic HCV infection are asymptomatic, but can develop cirrhosis and hepatocellular carcinoma (especially if there is a hepatitis B co-infection).
Some children may present in acute liver failure i.e. fulminant liver failure without pre-existing liver disease (an uncommon medical emergency). Causes include infection with HAV, HBV, Reye's syndrome, drugs (e.g. paracetamol, anti-TB drugs) and toxins (e.g. traditional medication).

Investigations

One may order:

- Blood tests
    - Liver enzyme levels (ALT, AST, ALP, GGT)
    - LFTs (INR, albumin, etc.)
    - Antibody and PCR studies for suspected viral hepatitis: these results must be interpreted to differentiate between acute and chronic infection
    - FBC
    - Serum glucose
- Imaging (USS of the liver)

Pathophysiology, Diagnosis and Management

Table 6.2: Pathophysiology, Diagnosis and Management of Hepatitis A and B

	HAV	HBV
Pathophysiology	It is transmitted by the faecal-oral route and has an incubation period of 15-50 days. The child is most infectious 1-2 weeks before symptom onset. The child may be asymptomatic (young children) or may have a prodrome of nausea, anorexia and malaise. S/he may go on to develop jaundice, dark urine and tender hepatomegaly. Chronic infection does not develop and fulminant infection is very rare.	Children may be infected by horizontal, vertical or parenteral transmission. HBV has an incubation period of 2-6 months and a similar prodrome and clinical features to HAV (but the disease is more insidious and there is a longer prodrome). 90% of neonates and 30-40% of infected children become chronic carriers – asymptomatic in the beginning and then develop chronic hepatitis, cirrhosis and HCC.
Diagnosis	Current/recent HAV infection is diagnosed if the child is HAV IgM positive (can remain positive for 4-6 months). Previous infection can be diagnosed if the child is HAV IgG positive.	Acute HBV infection is diagnosed if the child is HBV IgM, HBsAg and HBeAg positive. Chronic HBV is also diagnosed using the above tests and may be: ● High-risk (HBeAg-positive. HBeAb-positive, HBV IgG-positive) ● Low-risk (HBeAg-negative. HBeAb-positive, HBV IgG-positive).
Management	The local authorities should be notified (HAV is a notifiable disease). Management includes: ● Giving supportive care (avoid liver toxic drugs and ensure adequate hydration)	Treatment of chronic HBV infection includes α-interferon, pegylated interferon and nucleotide/-sides (entecavir, tenofovir or lamivudine). Acute infection

	● Following an appropriate diet (high in calories and low in protein) ● Encouraging good hand hygiene and in-hospital isolation for 1 week after the onset of jaundice (to prevent transmission) ● Managing household contacts The child should be admitted if s/he has any danger signs (prolonged vomiting, dehydration, persistent fever, hypoglycaemia, confusion, intercurrent infection or raised INR).	is usually self-limiting and the patient should just isolate.
Prevention	Two doses of the HAV vaccine (0.5 mL IMI) should be administered. The HAV vaccine can also be used as post- or pre-exposure prophylaxis. Otherwise one can give a single dose of pooled human Ig (0.04 mL/kg IM).	HBV Ig may be given to: ● Non-immune children (2 mL IMI given 1-7 days after exposure) ● Children who have had a high-risk exposure (same as above plus a second dose 1 month later) ● Infants born to HBsAg-positive mothers (0.5 mL IMI within 12 hours of birth) The HBV vaccine is part of the routine vaccination programme in SA.

Prevention of other causes of hepatitis:

- HCV:
    - HCV is acquired during infancy and is most likely to clear spontaneously.
    - Interferon-α or ribavirin should be considered in children with chronic infection.
- Autoimmune hepatitis (give prednisone).

Note: See the *Infectious Diseases* chapter for management of other viral causes.

PORTAL HYPERTENSION

It is defined if the child has a portal pressure >10 mmHg or hepatic venous pressure gradient >4 mmHg. Chronic liver disease results in increased vascular resistance or blood volume within the portal venous system and may be complicated by portal hypertension.

Aetiology

Portal hypertension may be due to a pre-, intra- or post-hepatic cause.

- Pre-hepatic causes:
    - Portal or splenic vein obstruction
    - Congenital portal vein stenosis
    - Extrinsic compression of the portal vein
- Intrahepatic causes:
    - Biliary atresia
    - Cystic fibrosis
    - Autoimmune hepatitis
    - Choledochal cyst
    - Cirrhosis
    - Schistosomiasis
    - Congenital hepatic fibrosis
    - Veno-occlusive disease
    - Granulomatous diseases e.g. sarcoidosis, TB
- Post-hepatic causes:
    - Budd-Chiari syndrome
    - Inferior vena cava thrombosis
    - Congenital malformation of inferior vena cava
    - Constrictive pericarditis or right heart failure

Clinical Features

Portal hypertension should be suspected in any child with significant GI bleeding (acute variceal haemorrhage is the most serious complication) or unexplained

splenomegaly. The child may also present with signs of chronic liver disease such as:

- Ascites (see also image here)
- Periumbilical vascular collaterals
- Manifestations of hypersplenism e.g. bruising from vitamin K deficiency (leading to a prolonged INR)
- FTT

Patients with cirrhosis may present with hepatic decompensation and encephalopathy. Pre-hepatic causes may not cause jaundice.

Investigations

One must look for the underlying aetiology by performing:

1. Blood tests:
    - FBC
    - Liver enzyme levels
2. Imaging:
    - Doppler USS e.g. portal vein and splenic vein thrombosis
    - CT angiography (not routinely done but may be ordered depending on the clinical picture)
    - Liver biopsy (not routinely done but may be ordered depending on the clinical picture)
    - Endoscopy (to look for oesophageal varices)

Management

The aim is to treat the underlying aetiology and complications (especially if the child is bleeding). An early referral should be made to a hepatologist or gastroenterologist after the patient has been stabilised.

One must avoid morbidity and mortality after a bleeding episode. Management of the patient with an acute variceal haemorrhage may include:

- Resuscitation (ABCs):
    - The patient may need to be given fluids, FFP or a RBC transfusion (restrict fluids to 70% of maintenance). Vitamin K should also be administered.

    - Actively bleeding veins should be tamponaded with a Sengstaken-Blakemore tube.
- Monitoring vitals, urine output, haemoglobin and level of consciousness.
- Keeping the patient nil per os and inserting an NGT (avoid if ongoing variceal bleeding is suspected).
- Administering empiric, broad-spectrum antibiotics, octreotide and omeprazole as needed.
- Performing surgery:
    - One may perform endoscopic variceal ligation or injection sclerotherapy (the former is the preferred method).

GASTROESOPHAGEAL REFLUX (GOR)

It is the involuntary passage of gastric contents into the oesophagus and is a normal physiological process. Episodes occur in the distal oesophagus, last <3 mins and are asymptomatic. Secretions contain food, drink, saliva, and gastric, pancreatic and biliary secretions. See also an image related to Reflux Gastro-Oesophagien here.

Pathophysiology

GOR is usually due to transient relaxation of the lower oesophageal sphincter (LOS). Less commonly it may be due to low LOS tone (chalasia). When the refluxed material passes into the mouth, this is termed regurgitation. Regurgitation is common in infancy (present in 60% of infants at 3 months old; resolved in 90% of infants by 1 year old). GOR and regurgitation are often not pathological, but complications may arise in a few children.

Clinical Features and Complications

GOR disease (GORD) is diagnosed when there are complications of GOR. There are no clinical features that are diagnostic of GORD but the following clinical features suggest the diagnosis:

- Oesophagitis:
    - Peptic (reflux) oesophagitis causes pain, food refusal, irritability, posturing and, less frequently, haematemesis and iron-deficiency anaemia

- Dental erosions
- Respiratory disease/complications:
    - Stridor/laryngitis
    - Recurrent wheezing
    - Hoarseness
    - Chronic cough
    - Aspiration pneumonia
    - Bronchiectasis
    - Asthma exacerbations
- FTT and poor weight gain
- Oesophageal strictures (in children with long-standing GORD)
- Athetoid movements and posturing:
    - They are associated with GORD (Sandifer syndrome) and may be confused with seizures, especially in children with brain damage.
    - Children with cerebral palsy may have severe GORD that is resistant to treatment and are more prone to oesophageal strictures following erosive oesophagitis.
- Sinusitis and otitis media (this association has not been well-established)

Investigations

One may order the following investigations:

- Barium swallow:
    - It is performed if oesophageal, stomach or proximal bowel structural abnormalities are suspected (e.g. malrotation, hiatal hernia, oesophageal stricture) as these disorders may present similarly to GORD.
- 24-hour oesophageal pH-metry:
    - It is performed when the diagnosis of GOR is uncertain or to assess the effect of therapy, as it provides a quantitative measure of acid reflux.
- Upper GI endoscopy:
    - It is performed to look for features of reflux oesophagitis and to exclude eosinophilic oesophagitis, infectious causes and structural causes.

- Nuclear medicine “milk scan”/nuclear scintigraphy:
    - It allows one to quantify the volume, frequency and height of the reflux.
- Endoscopy and biopsy:
    - They are performed to identify and grade oesophagitis, and exclude eosinophilic oesophagitis.

One must, therefore, exclude other causes of chronic respiratory disease that may mimic GORD and assess the patient for signs of raised intracranial pressure, GI obstruction (e.g. projectile vomiting, abdominal distension) and urinary tract infection.

Management

GOR does not require treatment, however GORD does.

Management of Functional Regurgitation

It will include:

- Parental reassurance
- Advice regarding feeding technique (e.g. avoiding overfeeding, practising burping technique) and thickening feeds (reduces frequency of vomiting, not reflux)
- Changing feeds if milk protein sensitivity is suspected (a trial of extensively hydrolysed feed may be done)
- Positioning the infant in a prone position (regurgitate less often):
    - This should only be done in infants >1 year old who are no longer at risk of sudden infant death syndrome (SIDS).
    - Otherwise, placing the child on his/her side may provide some relief.
- Prescription of proton pump inhibitors (PPIs) e.g. omeprazole (0.7-1.4 mg/kg in the morning 20 mins before breakfast)

The child with GORD or severe reflux may need to have a Nissen fundoplication (if s/he does not respond to optimal medical treatment).

Management of GORD

Young infants with severe malnutrition or respiratory complications should be given = transpyloric (NGT) feeds and PPIs for acid-related complications. H_2-receptor antagonists may also help acutely (if the patient presents with gastritis), however

they should not be chronically used. Surgery may be performed if there is no response to optimal medical treatment

CONSTIPATION

Definitions

Constipation is the infrequent or irregular passage of unduly hard stools.
Faecal loading is the build-up of faeces due to ineffective or incomplete evacuation of stool. **Encopresis** is an apparently wilful passage of normal consistency stool into underclothes or other places. (Refer to child psychiatry.)
Soiling is involuntary leakage of small amounts of soft or watery stool secondary to faecal loading and rectal dysfunction.
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Aetiology

Causes may be grouped according to the age of the child.

- Neonate:
    - Intestinal obstruction e.g. atresias
    - Cystic fibrosis (meconium ileus, meconium plug)
    - Hirschsprung's disease
- Child in early infancy:
    - Misdiagnosis of normal, infrequent, breastfeeding stools
    - Hypothyroidism
    - Hirschsprung's disease
    - Dehydration
- Toddler:
    - "Toilet training" constipation
    - Transient constipation
    - Acute constipation
    - Cerebral palsy (unco-ordinated peristalsis and evacuation lead to constipation)
- School-going child:
    - Change in environment or lack of privacy
    - Side effects of medication

    - Abovementioned causes which have been inadequately or ineffectively managed
    - Lack of exercise or inactivity

Other causes of constipation include coeliac disease and drugs. See related image here.

Clinical Features

The child may have

- <3 bowel movements/week
- Hard, dry and difficult to pass stools
- Large stools which may obstruct the toilet
- Painful defecation (check for anal fissures, especially if there is blood in stool)
- Soiling of underwear or clothes (faecal incontinence)
- Abdominal pain
- Abdominal distension (mild)
- Weight loss
- Fever and/or vomiting

Investigations

They may include:

- Growth assessment
- Abdominal examination (a faecal mass may be palpated)
- Digital rectal examination (including inspection of the peri-anal area and rectum)
- Full neurological examination

Other tests that are not routinely done (but may be performed depending on the suspected aetiology) include:

- Barium enema X-ray
- Thyroid function tests and serum calcium levels (only done in resistant cases)
- Rectal biopsy (if Hirschprung's disease is suspected)
- Abdominal X-ray (not necessary to make the diagnosis)

Management

Immediate Management

The parents and child should be counselled on constipation and the importance of behavioural and dietary changes. The colon can then be cleared with repeated phosphate-containing enemas (for disimpaction) or a balanced electrolyte polyethylene glycol (PEG) solution.

Klean Prep® (15-25 mL/kg/hour) may also be given and an enema done (within the first hour of starting Klean Prep®. The solution should be continued until the rectum is clear and the abdomen is soft (~6-8 hours). However, the patient should be observed for aspiration.

Maintenance Therapy

It may need to be continued for months or years and may include

- Macrogol e.g. Movicol®
- Osmotic laxatives e.g. lactulose, sorbitol
- Stool lubricants e.g. liquid paraffin
- Glycerine suppositories and prune juice (for children <1yrs)
- Anaesthetic cream (for anal fissures)

Prevention

Constipation may be prevented with:

- Regular physical activity
- High-fibre diet (supplement with bulk laxatives)
- Good hydration (water or fruit juice)
- Regular toilet and daily bowel routine
- Star charts or a stool diary

JAUNDICE

Jaundice is the yellow discolouration of the skin and mucous membranes and is a sign of hyperbilirubinaemia.

Pathophysiology, Classification and Aetiology

Unconjugated Hyperbilirubinaemia

It may be further subclassified as:

- Neonatal jaundice (jaundice which usually develops on the second or third day of life and which persists for <14 days from birth):
  - Physiological jaundice:
    - It usually develops on the second or third day of life.
    - The short lifespan of foetal RBCs leads to increased haemolysis in the neonate and, therefore, increased bilirubin production.
    - However, the immature liver is unable to process these large amounts of bilirubin (decreased bilirubin conjugation) resulting in unconjugated hyperbilirubinemia.
  - Breastfeeding jaundice:
    - It occurs in the first week of life in some infants and is the result of decreased milk intake.
    - The resulting dehydration leads to increased enterohepatic circulation of bilirubin.
  - Haemolytic disease of the neonate
  - Haemorrhage
  - Polycythaemia
- Prolonged neonatal jaundice (jaundice persisting >14 days from birth):
  - Breast milk jaundice:
    - It occurs in some neonates, in the second week of life or later and is thought to be due to a substance in breast milk that affects the infant liver's metabolism of bilirubin.
  - Isoimmunisation
  - Cephalohaematoma
  - Hypothyroidism
  - Sepsis
  - ABO incompatibility

Conjugated Hyperbilirubinaemia

It is diagnosed if the conjugated bilirubin level is >34mmol/L or >15% of the total bilirubin level. Causes include:

- Infection:
    - Viruses – HAV, HBV, CMV, rubella, HIV, HSV (TORCH infections)
    - Bacteria – syphilis, sepsis, UTI
    - Protozoa – toxoplasmosis
- Biliary pathology:
    - Biliary atresia
    - Choledochal cyst
    - Alagille's syndrome
- Metabolic/genetic disease:
    - α_1-antitrypsin deficiency
    - Galactosaemia
    - Wilson's disease
    - Cystic fibrosis
- Drugs/toxins e.g. total parenteral nutrition (TPN)
- Autoimmune:
    - Autoimmune hepatitis
    - Sclerosing cholangitis

Clinical Features

The child may present with:

- Yellow sclera, mucous membranes and/or skin
- Poor feeding
- Weight loss >10% in a neonate
- Lethargy

Jaundice which develops within the first 24 hours of life is likely to be pathological and requires further investigation. Jaundice which develops after day 3 of life also needs close monitoring and investigation.

Investigations

They should include:

- Transcutaneous bilirubin (TCB) level (in neonates)
- Conjugated and total serum bilirubin (TSB) levels (in older children and/or infants with mild jaundice)
- Other LFTs
- Maternal and neonatal blood type and rhesus (Rh) factor screen, and Coombs test
- Haemoglobin level and reticulocyte count
- CRP
- Cholesterol level
- Thyroid function test
- Tests for viral and/or parasitic infection, as needed e.g. urine dipstick, blood culture

Management

It is important to diagnose and manage jaundice appropriately as it can result in kernicterus if left untreated. Generally, management includes:

- Continuing breastfeeding
- Starting phototherapy and/or exchange transfusion in neonates (use phototherapy chart for guidance in neonates)
- Treating the cause (if pathological and reversible)

Management of Early-Onset Jaundice

Jaundice which develops within the first 24 hours of life is most likely due to haemolytic disease of the neonate (ABO or Rh incompatibility). Management, therefore, includes:

- Checking the mother's blood group:
    - If the mother is type O then ABO incompatibility is most likely.
    - Isoimmune-haemolytic disease may be treated with IV gamma globulin (0.5 g/kg over 2 hrs) if the TSB is increasing at a fast rate despite phototherapy or if it is <50 mmol/L below the exchange value.
    - Haemolytic disease of the neonate may be prevented by administering anti-D globulin to Rh-negative mothers within 72 hours of giving birth to a Rh-positive child.

- Performing three-hourly TSBs
- Starting phototherapy

The following tests should also be done:

- Direct Coombs test
- Hb or packed cell volume (to diagnose anaemia)
- Peripheral blood smear

Rarely, one may need to test for glucose-6-phosphate-dehydrogenase (G6PD) deficiency and do Hb electrophoresis.

Management of Late-Onset Jaundice

If the jaundice develops >24 hours after birth and the unconjugated bilirubin is above the normal limit, one must:

- Check the blood groups of the mother and child (exclude blood group incompatibility)
- Exclude sepsis or cephalohaematoma in a neonate
- Check that the neonate is sucking well and weigh baby (breastfeeding jaundice)
- Measure packed cell volume (the child may be polycythaemic i.e. have haematocrit (Hct) >70%)

HEPATOSPLENOMEGALY

It is enlargement of both the spleen and the liver.

Aetiology

Causes of hepatosplenomegaly include:

- Inflammation:
    - Infection – malaria, toxoplasmosis, infectious mononucleosis, HIV, rubella, congenital syphilis, HSV, CMV, schistosomiasis, etc. (TORCH infections)
    - Autoimmune disease
    - Drugs
    - Obstruction
- Infiltration:

    - Disseminated TB
    - Malnutrition
    - Septicaemia
    - Malignancy
    - Sarcoidosis
    - Reye's syndrome
    - Amyloidosis
- Congestion:
    - Biliary atresia
    - Cardiac failure (congestive or right-sided failure)
    - Constrictive pericarditis
    - Budd-Chiari syndrome
    - Cirrhosis
- Storage disorders:
    - Galactosaemia
    - Glycogen storage disease
    - Lipidosis
    - Uncontrolled diabetes
- Space-occupying lesions:
    - Abscess
    - Neoplasm (benign or malignant)
- Metabolic disease:
    - Wilson's disease
    - Gaucher's disease
    - Niemann-Pick disease
- Haematological disorders
    - Leukaemia
    - Lymphoma
    - Sickle cell anaemia
    - Thalassaemia
- Miscellaneous
    - Juvenile rheumatoid arthritis
    - Systemic lupus erythematosus (SLE)

Clinical Features

The child may present with:

- Fever
- Jaundice
- FTT
- Dyspnoea
- Vomiting
- GIT bleeding
- Pallor
- Petechiae, purpura or ecchymosis
- Lymphadenopathy
- Tender hepatosplenomegaly
- Ascites
- Raised JVP (if there is a cardiac cause for the hepatosplenomegaly)

Investigations

Investigations should only be performed as indicated. They may include:

- LFTs
- FBC
- Blood culture
- Mantoux test
- Imaging – USS, chest X-ray, CT scan
- Other tests e.g. α-fetoprotein, HBV antigen, PTT, INR, sweat chloride test, ceruloplasmin

Management

One must treat the cause. Thus, the patient should be referred to the relevant paediatric specialist depending on the cause or a hepatologist if the cause is unknown.

GASTROINTESTINAL (GI) BLEEDING

Upper GI bleeding (UGIB) is GI bleeding which is proximal to the ligament of Treitz (the junction of the duodenum and jejunum) i.e. oesophagus, stomach or duodenum. These patients often present with haematemesis and/or melena.

Lower GIGI bleeding (LGIB) is bleeding which is distal to the ligament of Treitz i.e. small bowel or colon. These patients usually present with haematochezia.

Aetiology

The causes of GI bleeding vary depending on the child's age.

Table 6.3: Causes of UGIB and LGIB

Age Group	Cause of UGIB	Cause of LGIB
Neonates	● Swallowed maternal blood i.e. not true bleeding ● Vitamin K deficiency/ haemorrhagic disease of the neonate ● Vascular malformations ● Stress gastritis or ulcers associated with critical illness ● Coagulopathy ● Cow's milk protein intolerance ● Gastric or duodenal ulcers ● GI duplication cyst	● Swallowed maternal blood (not true bleeding) ● Anorectal fissures ● Necrotising enterocolitis ● Malrotation with midgut volvulus ● Hirschsprung's disease with enterocolitis ● Coagulopathy ● Brisk UGIB ● Vascular malformations
Infants and toddlers	● Mallory-Weiss syndrome ● Oesophageal or GI foreign body ● Oesophagitis ● Peptic ulcers and gastritis	● Meckel's diverticulum ● Intussusception ● Anal fissures (especially around the time of the introduction of solid food or cow's milk) ● Milk- or soy protein-induced colitis (allergic colitis) ● Infectious colitis

	● Bleeding oesophageal varices or gastric varices ● Arterial bleeding (rare)	● Lymphonodular hyperplasia ● GI duplication cyst ● Coagulopathy ● Eosinophilic GI disease ● Infantile and very early-onset inflammatory bowel disease (IBD)
Pre-school going age		● Anal fissures ● Intussusception ● Meckel's diverticulum ● Other causes e.g. infectious colitis, haemolytic uraemic syndrome, IgA vasculitis, Henoch-Schonlein purpura, juvenile polyps, very early-onset IBD, solitary ulcer syndrome
School going age		● Anal fissures ● Juvenile polyps ● Infectious colitis (*Salmonella sp, Shigella sp, Campylobacter sp, E.coli, Clostridium difficile* are the most common) ● Inflammatory bowel disease ● Meckel's diverticulum ● Solitary rectal ulcer syndrome ● IgA vasculitis (Henoch-Schonlein purpura ● Haemorrhoids

Clinical Features

The child may present with:

- Haematemesis (vomiting of bright red blood or coffee ground-like material)
- Melena (passage of black and tar-like stools with a strong odour):
    - The colour and smell are due to the haemoglobin in the blood being altered by the digestive enzymes and intestinal bacteria.
    - It is important to note that black stools may also be caused by certain medications and foods.

- Haematochezia (passage of bright red/maroon-coloured blood or fresh clots per rectum):
    - It is usually due to LGIB but can be due to UGIB in cases of short intestinal transit time or massive UGIB.
- Occult GI bleeding (bleeding is not visible to the naked eye of the patient or physician):
    - Patients usually present with iron-deficiency anaemia or occult GI bleeding may be identified by testing the stool for occult blood.

Approach

When a patient presents with GI bleeding, one must ask the following questions

1. Is the patient haemodynamically stable or is resuscitation indicated?
2. Is it blood?
3. Is the blood from the upper GIT (dark red/black) or lower GIT (bright red)?
4. What are the most likely causes of the bleed?

The patient should then be assessed based on:

- History and examination:
    - One should ask about:
        - This episode of bleeding – chronology of the bleeding episode, estimated blood loss, colour of blood and any associated symptoms e.g. abdominal pain, fever, weight loss and fatigue, recent use of NASIDs, etc.
        - Associated symptoms (paying attention to GI symptoms) – dyspepsia, heartburn, abdominal pain, dysphagia, and weight loss, poor feeding or irritability (in infants), history of jaundice, easy bruising, or change in stool colour (liver disease).
        - Possible causes: easy bruising/bleeding, personal or family history of liver, kidney, heart disease or coagulopathies, drug history, travel history, diet, etc.
    - On examination one should look for signs of shock and possible causes of bleeding. Thus, a full examination (including a rectal examination) must be done.
- Diagnostic studies; may include:

- Bloods – FBC, CRP, ESR, coagulation studies
- Stool MC&S – *C. difficile*, enteric pathogens, ova and parasites
- RFTs and/or LFTs (in cases where related causes are suspected)
- Plain radiographs (to identify for foreign bodies)
- Abdominal USS
- Endoscopy (if the patient has brisk or unexplained bleeding after a thorough examination, or if s/he is in shock)
- Angiography (if the source of the bleeding could not be found on endoscopy)
- Colonoscopy

Management

Emergency Management

A gastroenterologist and general surgeon should be immediately called for any patient with severe acute UGIB. The patient should then be resuscitated and stabilised:

- If the child is shocked or has orthostatic hypotension (i.e. had a severe GI bleed), s/he should be admitted to ICU for resuscitation and close observation.
- Two large-bore IV catheters should be inserted and fluid boluses given. A transfusion may be required (if Hb <8 g/dL).
- Surgical intervention may be required for uncontrollable bleeds.

Follow-up visits should be scheduled, especially for first-time bleeders.

Routine Management

Patients who have had a UGIB:

- The patient should be resuscitated (ABCs) and the cause treated.
- Pharmacological management includes:
  - Acid suppression in clinically significant UGIB (IV PPIs or H_2-receptor antagonists).
  - Temporising the difficult to control bleed (e.g. variceal bleeding) with somatostatin and octreotide.
- Surgical management:

- Sengstaken-Blakemore tube placement.
- Endoscopic treatment (within 24-48 hours of presentation) e.g. sclerotherapy, elastic ligature (also used for haemorrhoids), transjugular intrahepatic portosystemic shunt (TIPS) for variceal bleeds.
- Catheter tamponade (used if medical management fails, to stop a continuously bleeding vessel which has been identified using a catheter; only perform in theatre or the ICU setting).

The cause of the lower GI bleed should be identified and treated. See also a figure on Deployed Sengstaken-Blakemore Tube in the Patient with an UGIB here.

FUNCTIONAL ABDOMINAL PAIN (FAP)

These disorders are the most common causes of chronic (>2 months) abdominal pain in children and adolescents.

Pathophysiology

The pathophysiology is poorly understood but it is thought to involve an interplay between enteric and CNS regulatory factors. These disorders may be associated with:

- Visceral hyperalgesia:
  - Eating may be associated with onset of pain and the patient is, therefore, likely to skip meals in an attempt to avoid pain.
- Reduced pain threshold
- Referred pain following rectal distension
- Impaired gastric relaxation response to meals

Diagnosis, Classification and Clinical Features

The diagnosis is made in the child with chronic abdominal pain, no danger signs, normal examination and stool which is negative for occult blood. Certain recognisable patterns of symptoms may be used to classify the FAP:

- Functional dyspepsia
- Irritable bowel syndrome (a disorder of large intestine) – cramping, abdominal pain, bloating, gas, diarrhoea and/or constipation

- Abdominal migraine (most common in children) – abdominal pain, nausea, vomiting, family or personal history of migraines
- FAP not otherwise specified

Management

It should be managed in a primary care setting. The goal of treatment is a return to normal function rather than complete elimination of pain. However, a referral may be made if the pain cannot be managed at a primary care level.

Management is individualised and depends on the child's and family behaviours, triggers and symptoms. Regardless of the subtype of FAP, the management includes:

- Assuring the patient and family that a treatment will be initiated and the patient (and family, as they may also be affected by the condition) followed up on a regular basis.
- Patient education:
    - FAPDs are best treated using the biopsychosocial model of care. Before starting therapy, one must define the expectation of the patient and parents and be realistic about treatment aims.
    - One must reassure the patient and family by acknowledging that the pain is real and has affected important activities in the patient's life.
    - They must be informed that FAP is common and can be exacerbated or made to persist by environment and psychosocial factors e.g. stress, anxiety, social reinforcement. However, they are not life threatening.
    - They must also be told that management focuses on rehabilitation rather than treatment, and includes avoiding triggers and improving coping skills.
- Prescribing a return to structured activities of daily living (including school):
    - School absenteeism adds to family stress and can interfere with school performance), see also an image of active children in a classroom.
    - One must implement a plan ahead for pains at school, such as keeping the first back at school short, arranging for the child to go to the nurse's office until the pain stops and use the bathroom whenever necessary.

A letter should be written to make the school aware of the condition and plan.
    - The family must be given guidelines for when the pain is severe enough to warrant going home or missing school.
    - School-related stressors must be identified and dealt with.
- Behaviour modification (positive, well behaviours should be reinforced, and triggers and behaviours that cause pain should be stopped/avoided).
- Strategies to improve pain tolerance and coping:
    - Psychological treatments which improve coping should form part of the management of children and adolescents with FAP e.g. relaxation techniques, distraction, and cognitive behavioural therapy (CBT).
    - Psychological interventions appear to be more effective than pharmacological interventions.
- Symptomatic management.

Chapter 7:

CARDIOVASCULAR DISEASES

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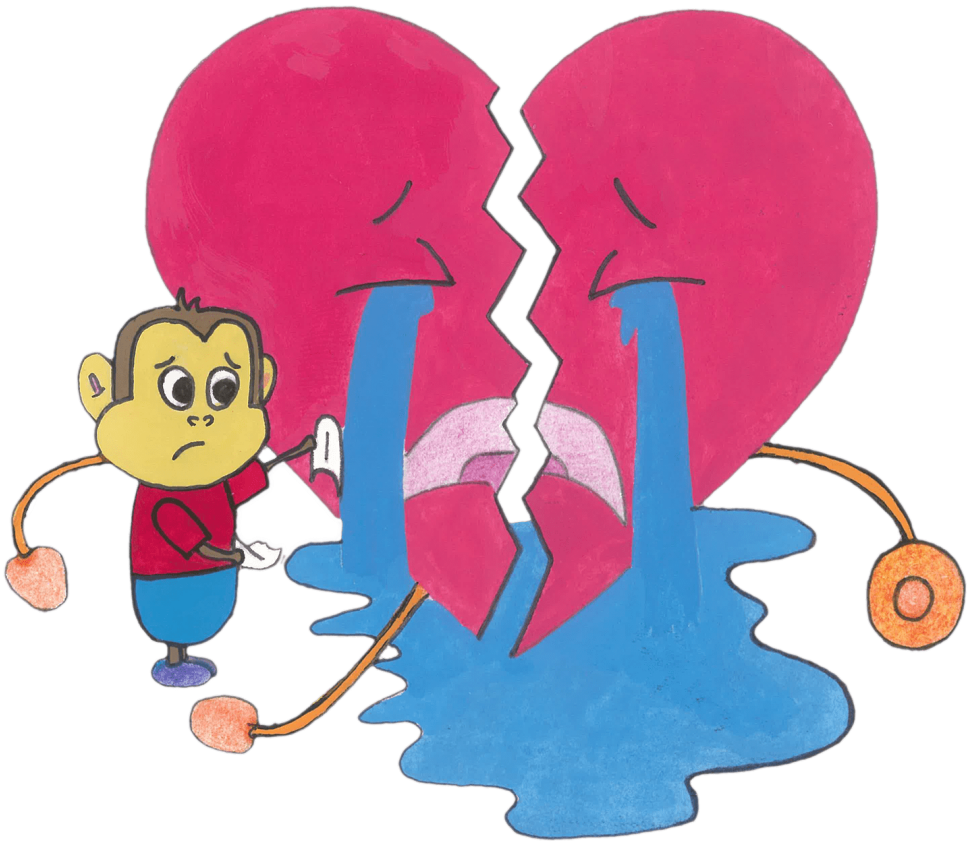

This chapter covers the following topics:

- Murmurs
- Acute rheumatic fever (ARF)
- Rheumatic heart disease (RHD)
- Cardiac failure
- Congenital heart disease
- Prevention of conditions which affect cardiovascular health

MURMURS

Murmurs are distinct sounds which arise when blood flows through narrowed or leaky cardiac valves, or through anatomical defects.

Pathophysiology

Systolic murmurs are heard in systole, between S1 and S2. These are further classified by their timing into early, mid or late systolic murmurs. Murmurs that last throughout systole are known as holo- or pansystolic murmurs. Systolic murmurs can be functional (benign). These are known as innocent murmurs and are common in infancy and childhood, but disappear in adulthood. Febrile or exertional states are commonly associated with these murmurs. The volume of a systolic murmur is graded on a six-point scale.

Diastolic murmurs can be classified into early diastolic (regurgitation through the aortic or pulmonary valves) or mid-to-late diastolic (in mitral or tricuspid stenosis). Diastolic murmurs are almost always pathological but are not as commonly heard as systolic murmurs in children with congenital cardiac defects. The volume of a systolic murmur is graded on a four-point scale. All murmurs (systolic and diastolic) louder than grade 3 are pathological.

Table 7.1: Six-point (Levine) Grading Scale for Systolic Murmurs

Grade	Volume	Thrill?
1/6	Barely audible	No
2/6	Soft	No
3/6	Easily audible	No
4/6	Easily audible	Yes
5/6	Can be heard with the stethoscope partially off the chest	Yes
6/6	Audible with stethoscope completely off the chest	Yes

Table 7.2: Four-point Grading Scale for Diastolic Murmurs

Grade	Volume	Thrill?
1/4	Soft	No
2/4	Easily audible	No
3/4	Can be heard with the stethoscope partially off the chest	Yes
4/4	Audible with stethoscope completely off the chest	Yes

See related figure available here.

Table 7.3: Listening Areas for Common Paediatric Heart Murmurs

Area	Murmur
Upper right sternal border	Aortic stenosis or regurgitation
Upper left sternal border	Pulmonary stenosis, pulmonary flow murmurs, right ventricular outflow tract obstructive murmurs, patent ductus arteriosus
Lower left sternal border	Still's murmur, ventricular septal defect, tricuspid valve regurgitation, hypertrophic cardiomyopathy, subaortic stenosis
Apex	Mitral regurgitation

Clinical Features

The clinical presentation of a child with heart disease depends on the cause and severity of the heart lesion and/or the presence of complications. Below is a list of important clinical features:

- Cyanosis
- Easy fatiguability (in paediatrics, it is often related to feeding)
- Poor exercise tolerance
- Failure-to-thrive (FTT; inability to meet and maintain appropriate growth standards)
- Diaphoresis (sweating)
- Wheezing in babies
- Chronic cough

Older children and teenagers may also present with:

- Dizziness
- Near-syncope or syncope
- Palpitations
- Chest pain

Investigations

The child with heart disease should have the following investigations:

- ECG
- Chest X-ray
- Echocardiogram

Management of Valvar Disease

The severity of the patient's symptoms and the severity of the lesion must be assessed (history, examination and investigations). In most valvar lesions, the patient's symptoms are treated medically until they worsen or a specific echocardiographic variable (e.g. chamber size, gradient across a valve) necessitates further surgical management i.e. reaches a recognisable threshold. Thereafter, surgery to repair or replace the valve is recommended.

ACUTE RHEUMATIC FEVER

Acute rheumatic fever (ARF) is an autoimmune, inflammatory process that develops as a sequela to a group A β-haemolytic streptococcal infection e.g. 'strep' throat or scarlet fever. Rheumatic fever mainly affects children aged 5-15 years with a history of group A β-haemolytic streptococcal infection. It develops several weeks after the pharyngitis has resolved in some children and adolescents (0.3-3% of pharyngitis cases); see also image with signs and symptoms of rheumatic fever here.

Pathophysiology

Molecular mimicry is responsible for the tissue injury observed in ARF. The humeral and cellular immune responses of an individual who is genetically predisposed are both implicated in the development of the disease. In this process, the patient's immune response (both B-cell- and T-cell-mediated immunity) is unable to differentiate between the invading microorganism and some host tissues, leading to inflammation. The resultant inflammation may persist well beyond the acute infection and produce the manifestations of ARF. Cardiac involvement is the most serious complication of ARF and causes significant morbidity and mortality.

Clinical Features and Diagnosis

The revised Jones criteria are used to diagnose ARF. ARF is diagnosed if the patient has 1 required criterion and one of the following:

- 2 major criteria
- 1 major and 2 minor criteria

The required criteria are evidence of recent streptococcal infection:

- Throat cultures growing group A β-haemolytic streptococcal infection
- Elevated antistreptolysin O titres

Table 7.4: 2015 (Revised) Jones Criteria

Low-Risk Population ARF incidence ≤2 per 100 000 school-aged children or all-age rheumatic heart disease (RHD) prevalence of ≤1 per 1000 population year	**Moderate/High-Risk Population** Children not clearly from a low-risk population
MAJOR CRITERIA	
Clinical and/or subclinical carditis	Clinical and/or subclinical carditis
Polyarthritis	Monoarthritis, polyarthritis and/or polyarthralgia
Sydenham's chorea	Sydenham's chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
MINOR CRITERIA	
Prolonged PR interval	Prolonged PR interval
Polyarthralgia	Monoarthralgia
Fever (temperature ≥38.5°C)	Fever (temperature ≥38.5°C)
Inflammatory markers (peak ESR ≥60 mm in 1 hour and/or CRP ≥3.0 mg/dL)	Inflammatory markers (peak ESR ≥30 mm in 1 hour and/or CRP ≥3.0 mg/dL)
Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4832790/	

Note: Subclinical carditis is valvar involvement diagnosed on echocardiography while clinical carditis is the presence of a murmur consistent with aortic or mitral regurgitation.

Investigations

Relevant investigations include:

- Throat culture (usually negative by the time symptoms develop)
- Anti-streptococcal antibodies:
    - Symptoms of ARF develop when the antibodies are at their peak, so this test is very useful for detecting previous streptococcal infection. They should be checked at fortnightly in order to detect a rising titre.
    - Example of an extracellular antistreptococcal antibody – antistreptolysin O titre (ASOT).

    - Examples of intracellular antistreptococcal antibodies – anti-streptococcal polysaccharide, anti-teichoic acid antibody, anti-M protein antibody.
- Acute phase reactants – CRP and ESR (have a high sensitivity but low specificity for ARF)

Treatment

Primary Prevention

Administering a penicillin or another appropriate antibiotic for ARF in the patient with a sore throat (strep infection) decreases the risk of ARF by ~80%. One can prevent ARF with a 10-day course of oral penicillin V to treat pharyngitis. One may also give IM benzathine penicillin G or a benzathine/procaine penicillin combination. A single dose of IM is likely better to avoid non-compliance.
Should there be a penicillin allergy, one of the following antibiotics may be prescribed:

- Erythromycin
- Azithromycin for 5 days
- Clarithromycin for 10 days
- Narrow-spectrum (first-generation) cephalosporin for 10 days

Secondary Prevention

The aim here is to prevent additional streptococcal infections as patients with a history of ARF are at a high risk of recurrence, which may cause further damage to the heart. The patient should be given a course of antibiotics (penicillin G benzathine; if penicillin-allergic, erythromycin or sulfadiazine). The duration of the antibiotic course depends on his/her clinical features:

- ARF with carditis and clinically significant residual heart disease – for ≥10 years following the most recent episode (at least until the age of 40-45 years; usually lifelong prophylaxis).
- ARF with carditis and no residual heart disease besides mild mitral regurgitation – for 10 years or until 25 years old (whichever is longer).
- ARF without carditis – for 5 years or until 18-21 years old (whichever is longer).

The patient should also be given:

- Anti-inflammatory drugs (salicylates and corticosteroids)
    - It is important to avoid anti-inflammatories until the diagnosis of ARF is confirmed, as they may mask signs and symptoms essential to making the diagnosis.
- Analgesia (paracetamol for joint pain)

Patients must be closely monitored until all acute symptoms have resolved and they have returned to baseline function. ARF is a notifiable condition and all cases must be reported to the relevant local authority.

RHEUMATIC HEART DISEASE (RHD)

Pathophysiology

It is a cardiac manifestation of ARF (cardiac inflammation and scarring triggered by autoimmune reaction to a group A β-haemolytic streptococcal infection. In acute disease, the patient will have pancarditis [endo-, myo-, and pericarditis]). In chronic disease (2-10 years following acute rheumatic fever), the patient will have:

- Valvar fibrosis (leading to stenosis and/or valve insufficiency/regurgitation)
- Atrial dilatation
- Arrhythmias (including atrial fibrillation)
- Ventricular dysfunction (most serious complication of RHD)

The mitral valve is the most commonly affected valve and the aortic valve is the second most commonly affected valve. The tricuspid valve is only affected in 10% of cases and this is often in association with mitral and aortic lesions. The pulmonary valve is rarely affected. Severe valve insufficiency in the acute state may result in heart failure and/or even death.

Clinical Features

The clinical manifestations of RHD are the same as in ARF, with/without the signs and symptoms of the associated complications.

Investigations

An ECG may be done in addition to those for ARF (listed above). Sinus tachycardia often accompanies RHD, but sinus bradycardia may also occur. Other arrhythmias

may develop in RHD. ECGS may also help determine which chambers are enlarged.

Treatment

It may be

- Medical:
    - The aim here is to prevent recurrent attacks of rheumatic fever.
    - One may prescribe oral penicillin V (250mg twice daily), an oral sulphonamide (0,5-1 g twice daily) or erythromycin (250 mg twice daily).
- Surgical:
    - The affected valves may be surgically corrected or replaced.

CARDIAC FAILURE

Pathophysiology

Congestive cardiac failure (CCF) occurs when the heart fails to meet the body's metabolic demands at normal, physiologic venous pressure. Typically, the heart can compensate for increased demands by:

- Increasing the heart rate through humoral and neural responses
- Increasing ventricular contractility of the ventricles (secondary to the release and circulation of catecholamines and autonomic input)
- Enhancing the preload through renal preservation of intravascular volume (sodium and fluid retention)

When these compensatory mechanisms fail, the signs and symptoms of CCF appear.

Systolic dysfunction is characterised by decreased ventricular contractility. It leads to an impaired ability to increase the stroke volume to meet systemic demands. Diastolic dysfunction is characterised by decreased ventricular compliance. It leads to an increase in venous pressure to maintain adequate ventricular filling.

During acute CCF, the sympathetic nervous system and renin-angiotensin aldosterone system (RAAS) maintain blood flow and blood pressure to the vital organs. Increased neurohormonal activity leads to increased myocardial

contractility, selective peripheral vasoconstriction, salt and fluid retention, and, ultimately, blood pressure maintenance. As a chronic state of failure continues, these same mechanisms cause adverse effects.

In chronic heart failure, myocardial cells die from lack of nutrients, cytotoxic mechanisms (cause necrosis) or the acceleration of apoptosis. Necrosis stimulates fibroblast proliferation, which leads to the replacement of myocardial cells with collagen and scarring. The loss of myocardial cells results in cardiac dilation, an increased afterload and wall tension, and further systolic dysfunction.

Aetiology

The most likely causes of cardiac failure depend on the age of the child.

Table 7.5: Causes of Cardiac Failure Categorised by Age Group

Foetus	**Neonates and Infants <2 Months Old**	**Older Children**
CHF/ hydrops can be detected with a foetal echocardiogram. At this stage, CHF may be due: ● Underlying anaemia (reduced oxygen-carrying capacity) e.g. Rh sensitization, foetomaternal transfusion ● Arrhythmias (usually supraventricular tachycardia) ● Myocardial dysfunction (myocarditis, cardiomyopathy) ● Structural heart disease (rare)	● Respiratory illness (very common cause of heart failure) ● Critical congenital heart disease (CHD) – can present with CCF due to structural disease; systemic and pulmonary circulation may depend on the PDA, especially in those presenting in the first few days of life ● Primary myopathic abnormalities or inborn errors of metabolism (especially if associated with muscle weakness or lactataemia)	● Left-sided obstructive disease (valvar or subvalvar aortic stenosis or coarctation) ● Myocardial dysfunction (myocarditis, cardiomyopathy) ● Renal failure (fluid overload and anaemia) ● Arrhythmias (rare) ● Hypertension (rare) ● Illicit drug use (esp. in unexplained CHF) e.g. cocaine, other stimulants

	● Anaemia ● Infection	

Clinical Features

They depend on the severity of the heart failure and whether it is compensated or not. Clinical features include:

- Venous congestion
    - Right-sided heart failure:
        - In infants – hepatosplenomegaly (oedema and ascites are less common and jugular veins are difficult to assess)
        - In older children – abdominal pain, hepatosplenomegaly, jugular venous distention, oedema, ascites and/or pleural effusions
    - Left-sided heart failure – tachypnoea from pulmonary oedema, respiratory distress (retractions, nasal flaring, grunting), crackles and wheeze (cardiac asthma)
- Low cardiac output manifesting as:
    - Fatigue
    - Pallor
    - Sweating (during feeding in infants)
    - Cool extremities
    - Nausea and vomiting
    - Poor growth
    - Dizziness
    - Altered level of consciousness
    - Syncope
- Respiratory failure

Uncompensated congestive heart failure in infants is mainly characterised by failure to thrive. This may be followed by renal and hepatic failure in severe cases.
Uncompensated CCF in older children is characterised by fatigue. The child may complain of cool extremities, abdominal pain, nausea/vomiting, exercise intolerance, dizziness, or syncope.
Marked failure of one ventricle may lead to failure of the other.

Investigations

One should perform:

- Blood tests – arterial blood gas, FBC, cardiac biomarkers, RFTs, LFTs, RFTs (findings of renal and liver dysfunction may be present)
- Imaging – CXR, echocardiogram (should be performed to assess cardiac function and identify potential cardiovascular causes in the child with unexplained CCF e.g. structural heart lesions)
- ECG

Treatment

The goals of medical therapy for CCF are to:

- Reduce the preload
- Enhance cardiac contractility
- Reduce the afterload
- Improve oxygen delivery
- Enhance nutrition

Thus, the following medications are given

- Oral/IV diuretics (e.g. furosemide, thiazides, metolazone) – to reduce preload
- IV agents (e.g. dopamine) or mixed agents (e.g. dobutamine) – to enhance contractility
- Oral ACE-inhibitors – for afterload reduction

IV hydralazine, nitroprusside and alprostadil are only used for afterload reduction in the ICU and are not easily sourced.

Other, appropriate treatment should be instituted.

CONGENITAL HEART DISEASE

The critical congenital heart diseases include:

- The five T's
    - Truncus arteriosus
    - Transposition of the great arteries
    - Tricuspid atresia/tricuspid regurgitation (Ebstein's anomaly)
    - Tetralogy of Fallot (TOF)

    - Total anomalous pulmonary venous drainage (TAPVD)
- The four left-sided lesions:
    - Interrupted aortic arch
    - Critical aortic stenosis
    - Univentricular heart
    - Hypoplastic left heart syndrome

Acyanotic Heart Diseases

Left-to-right shunting occurs because blood flows from areas of high pressure (left heart) to areas of low pressure (right heart) through a congenital structural defect in the heart.

Acyanotic heart defects include:

- Atrial septal defect (ASD)
- Ventricular septal defect (VSD)
- Patent ductus arteriosus (PDA)
- Atrioventricular septal defect (AVSD) / endocardial cushion defect (ECD)

Atrial Septal Defect (ASD)

In this condition, blood flows from the left atrium (LA) through ASD and into the right atrium (RA) i.e. is added to normal atrial flow. On auscultation, one will hear a fixed, split second sound and grade 2/6 pulmonary ejection systolic murmur (flow murmur across the pulmonary valve). A tricuspid diastolic murmur may be heard. The child may suffer from recurrent chest infections.

Investigations

One may request:

- Chest X-ray – will show a large main pulmonary artery and plethoric lung fields)
- ECG – will show right axis deviation in primum defects (inferior), left axis deviation in secundum (upper portion) and RsR pattern in V1; these changes are the result of RA enlargement and right ventricular (RV) hypertrophy

Management

The child should undergo surgical or device closure, preferably before s/he reaches school-going age (especially if the defect is large).

Ventricular Septal Defect (VSD)

It is the most common congenital heart disease (see also related image here). Children with large defects present when they are 2-6 weeks old (slightly later but later if live at higher altitudes) as the pulmonary vascular resistance decreases from the foetal level around this time.

Clinical Features

The child will present with FTT because s/he becomes breathless during feeds as a result of the large L-to-R shunt which causes overloading and failure of the left ventricle (LV).

With an early VSD:

- Blood flows from the LV blood through the VSD and into the RV, in addition to the blood from the RA. Thus, there is LA and LV enlargement in early VSD.
- A small VSD produces a pansystolic murmur (heard at the left lower sternal border).
- A medium-to-large VSD produces ejection systolic and mid-diastolic murmurs (heard at the apex). If there is pulmonary hypertension, there will also be a loud P2.
- If the child fails to respond to anti-failure therapy, a co-existing defect must be suspected (e.g. PDA or COA) and earlier intervention will be required sooner.
- Moderately sized defects may become smaller, and small defects may spontaneously close, whereas children with large defects present with CCF and require surgical closure.

With a late VSD:

- There is RV hypertrophy and increased pulmonary vascular resistance. This results in the reversal of the shunt from right to left – Eisenmenger syndrome.
- Signs then include a very loud P2 (and irreversible pulmonary HPT), RV heave and eventually a single P2.

- Eisenmenger syndrome occurs in any longstanding L-to-R shunt. Patients become cyanosed and are generally >10 years old e.g. the child with Down syndrome and an AVSD (at high risk of early irreversible change).

Although currently less common, the child with a VSD may also have a pulmonary artery band (PAB). In these patients, there is a higher RV outflow tract gradient, ejection systolic murmur and mild cyanosis.

Patent Ductus Arteriosus (PDA)

Preterm neonates often have a PDA and develop a significant L-to-R shunt in the first week of life, especially if they have been hypoxic.

Clinical Features

The infant will present with:

- Tachypnoea
- Systolic murmur on the left sternal border just below the clavicle
- Mid-systolic murmur at the apex if the PDA is large
- Bounding/collapsing peripheral pulses

Management

PDAs usually close by the time the children reach their expected term dates. However, non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol may be used to close the PDA in preterm neonates (not effective in term infants). Surgical ligation is performed if NSAIDs are not working. Ligation is required in all term infants even if they are asymptomatic because PDAs in these children do not spontaneously close (should be performed before 6-12 months). Percutaneous closure using PDA devices is the most common intervention in children beyond the neonatal period.

Atrioventricular Septal Defect (AVSD) / Endocardial Cushion Defect (ECD)

AVSDs may be complete (there is an ASD in the ostium primum and an inlet VSD with a common atrioventricular valve) or partial (there is only an ASD in the ostium primum).

It is common for a child to present with a primum ASD and a cleft in the mitral valve, which causes mitral regurgitation or allows a L-to-R shunting from the LV to the RA. The defect may be large enough to cause cardiac failure early in life. 50% of these children have Down syndrome. Thus, AVSD must be actively excluded in children with Down syndrome (must have an echo before 6 weeks of age).

Clinical Features

The child with a complete AVSD will have a pansystolic murmur at the apex (due to mitral regurgitation) and an ejection systolic murmur (due to increased pulmonary valve flow) at the left sternal border or apex. However, the absence of a murmur does not exclude a VSD.

An ECG will show left anterior hemiblock and an RSr' pattern in V1 if there is RV hypertrophy.

Cyanotic Heart Diseases

They are the result of R-to-L shunts and may have increased or decreased pulmonary blood flow.

They may be classified as:

- Disorders with right ventricular outflow obstruction
- Mixing disorders
- Mixing disorders with RV outflow obstruction
- Disorders with parallel circulation

Tetralogy of Fallot (TOF)

It is the most common cyanotic heart disorder. In this condition, there is decreased pulmonary flow as it is characterised by:

- Infundibular and valvar pulmonary stenosis
- RV hypertrophy
- Overriding aorta (the aorta is placed over the VSD)
- VSD

One must always suspect TOF in any infant 6 months to 5 years old presenting with central cyanosis, RV hypertrophy, a single second heart sound and an ejection

systolic murmur over the pulmonary area radiating to the left clavicle; see also diagram depicting features of Tetralogy of Fallot available here.

Pathophysiology and Clinical Features

The clinical picture depends on the degree of RV outflow obstruction. If the stenosis is severe, there will be a R-to-L shunt via the VSD. This leads to early persistent central cyanosis, clubbing, polycythaemia and acidosis (sends positive feedback to the stenosis). The lungs will be oligaemic and dark lung fields will be seen on CXR (due to the decreased pulmonary blood flow).

Clinical features include:

- Cyanosis
- Ejection systolic murmur
- Single S2

The child may also experience tetralogy/tet spells. During the spells, the child suddenly becomes cyanosed after crying or feeding, or when agitated due to the rapid drop in the levels of oxygen in blood.

Treatment

Emergency treatment for tet spells includes

- Soothing the child
- Administering oxygen and putting him/her in the knee-chest
- Sedating the child with chloral hydrate (if available and necessary)
- Administering morphine 0.1- 0.2mg/kg IV, SC or IM
- Siting a drip and giving fluids (10 mL/kg; feel the liver)
- Administering sodium bicarbonate (2 mL/kg of a 4.5% solution) to counteract the metabolic acidosis
- Administering esmolol (0.5 mg/kg) or propranolol (0.1 mg/kg IV or 1-5mg/kg/day orally in divided doses)

Definitive treatment of TOF is surgical repair, which is usually performed when the child weighs around 8-10 kg. It is important to note that there may be long-term issues post-repair, therefore the patient will need lifelong follow up.

Palliative procedures which may be performed include:

- Right modified Blalock-Taussig-Thomas shunt (between the aorta and R pulmonary artery) – post-surgery, the child will have mild cyanosis, a lateral thoracotomy scar and a shunt murmur
- Central shunt (between the aorta and main pulmonary artery; usually via a median sternotomy)

Transposition of the Great Arteries (TGA)

In TGA, the great arteries arise from the incorrect ventricles – the aorta from the RV and pulmonary trunk from LV. Therefore, deoxygenated, systemic venous blood travels through the RA, RV and aorta and back to the rest of the body, while oxygenated, pulmonary venous blood travels through the LA and LV and back to the pulmonary circulation. It is, therefore, a cyanotic congenital heart disease with increased pulmonary blood flow. The child has two separate parallel circuits, which is incompatible with life.

Clinical Features

The child will present with cyanosis in the 1st week of life (usually soon after birth) and is dependent on a PDA, VSD or ASD for survival. As RV outflow goes to the aorta and the LV empties into the pulmonary artery, there is severe cyanosis, CCF and LA and LV enlargement. Murmurs are not usually heard. The child develops extreme right ventricular outflow obstruction when the duct closes. Thus, mixers with unrestricted flow present when pulmonary vascular resistance drops between 4–6 weeks.

Investigations

All children with suspected TGA must be referred for specialist assessment and management. ECGs may point to the diagnosis but echocardiography is the main diagnostic tool (is essential). Catheterisation and CTA angiogram may be performed to assess pulmonary artery structure and size. Here is a visualisation of Transposition of Great Vessels.

The CXR will be plethoric (due to the increased pulmonary blood flow) and an egg-on-side cardiac silhouette with a narrow pedicle will be seen.

Treatment

While the child is at the peripheral hospital or awaiting surgery, one should give him/her oral or (if needed) IV prostaglandin to keep the duct open. Other interventions which may need to be employed include:

- Compression of the abdominal aorta with a BP cuff
- Sedating the child with IV ketamine (0.5-1 mg/kg; may need to repeat give repeat ketamine doses or sodium bicarbonate/esmolol)
- Intubating the child
- Transfusing the child if s/he is anaemic

Once at the referral hospital, the child will be intubated (if not already) and admitted to the PICU where she will be paralysed (or given more ketamine) and started on phenylephrine (via an arterial line). If there is no improvement, the child will have to be taken for surgery.

These children are palliated with a Rashkind atrial/balloon septostomy – allows the blood to flow from the L heart to the R heart through the septum i.e. raises peripheral SaO2 by increasing pulmonary to systemic shunting. It is then followed by an arterial switch operation.

PREVENTION OF CONDITIONS AFFECTING CARDIOVASCULAR HEALTH

Some of the causes of adult heart disease that start in childhood and which can be prevented include:

- Obesity
- Atherosclerosis (build-up of plaque/fat deposits in the arteries)
- Unhealthy changes in cholesterol levels
- High blood pressure
- Diabetes

Chapter 8:

RESPIRATORY DISORDERS

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This chapter covers the following topics:

PAEDIATRIC PNEUMONIA/LOWER RESPIRATORY TRACT INFECTIONS (LRTIS)

Pneumonia is an infection of one or both lungs by pathogens including bacteria/mycobacteria, viruses, or fungi. It forms part of a broad spectrum of acute lower respiratory tract illnesses (LRTIs) in children (see a related image here). This terminology recognises that LRTI is a spectrum of illness (ranging from airway to parenchymal disease) which is dependent on the pathogen(s) and the host response.

Pathophysiology

The pneumonia may have an extrinsic (due to exposure to the causative organism) or intrinsic cause (relating to the host e.g. loss of protective reflexes leading to aspiration). When infective, the causative organism finds its way into the lung parenchyma through inhalation or haematogenous spread. The virulence of the organism and the host's defence mechanisms/immune status determine whether the infected individual will develop pneumonia.

Whatever the cause, the affected patient will have inflammation of the alveoli, which may be filled with fluid or pus. This causes the signs and symptoms of pneumonia, which may include cough, tachypnoea, wheezing.

Aetiology

Causative organisms include:

- Bacteria; depends on the age of the patient:
    - In neonates, common organisms include group B streptococci, *Listeria monocytogenes* and Gram-negative bacilli (e.g. *Escherichia coli*, *Klebsiella pneumoniae*)
    - In infants, the most common bacterial cause is *Streptococcus pneumoniae*. Other causes include *Haemophilus influenzae* and *Staphylococcus aureus*. Atypical causative bacteria include *Mycoplasma pneumoniae, Chlamydia trachomatis and Chlamydia pneumoniae*

    - In older children and adolescents, the causes are the same as in infants but atypical organisms (especially *Mycoplasma* sp.) are more common
- Viruses:
    - Respiratory syncytial virus (RSV) is the most common viral cause
    - Other causes include human metapneumovirus, parainfluenza types 1 & 3, adenoviruses, influenza viruses A & B, rhinovirus, measles virus, cytomegalovirus, varicella zoster virus and bocavirus
- Fungi;
    - Common causes are *Pneumocystis jiroveci* and Candida sp.
- Mycobacteria:
    - TB can cause acute pneumonia or chronic infection (see Pulmonary TB in the *Infectious Diseases* chapter)

Clinical Features

The signs and symptoms of pneumonia are often non-specific and vary depending on the child's age. They include:

- Neonates:
    - Poor feeding
    - Irritability
    - Excessive work of breathing i.e. tachypnoea, intercostal retractions, alar flaring, grunting and hypoxaemia (saturation <90%)
- Infants:
    - Cough
    - Excessive work of breathing
    - Congestion
    - Fever
    - Irritability
    - Decreased feeding
- Adolescents generally have similar symptoms to younger children and infants, but symptoms may also include:
    - Headache
    - Pleuritic chest pain

- Vague abdominal pain
- Vomiting
- Diarrhoea
- Pharyngitis
- Otalgia/otitis

Cyanosis may be present in severe cases. Children tend to present with bronchopneumonia and diffuse signs, including hyperinflation, wheezing and crackles. Signs of localised disease include dullness on percussion and bronchial breathing, although this is less common in childhood.

It is most important to observe the child's respiratory rate. The WHO respiratory rate thresholds for identifying children with pneumonia are:

Table 8.1: WHO Thresholds for Tachypnoea

Age	Respiratory rate
Birth - 2 months	≥ 60 breaths/min
2-11 months	≥ 50 breaths/min
12-59 months	≥ 40 breaths/min

According to the WHO, severe/very severe pneumonia should be diagnosed if the child has:

- Chest retractions
- Stridor
- Any general danger signs e.g. intractable vomiting, inability to drink or breastfeed, convulsions, lethargy, loss of consciousness

Investigations

One may request the following investigations:

- Blood culture (but is a low-yield investigation)
- FBC
- C-reactive protein (CRP)
- Nasopharyngeal aspirate cultures (for viral aetiology)
- Sputum sample for:

    - Sputum cultures
    - TB GeneXpert® (on induced sputum)
    - Sputum viral serology
- Chest X-ray

General Management of Pneumonia

The child with signs of excessive work of breathing should immediately be given respiratory support. The type of respiratory support depends on the severity of the distress (watch the oxygen saturation to assess for adequate ventilation and oxygenation). Below are different options for respiratory, which can be used in a step-up or step-down fashion depending on the child's condition:

- Intubation and invasive ventilation – if there is severely increased work of breathing and the child is unable to maintain oxygenation or s/he has a decreased level of consciousness
- Positive pressure ventilation (PPV)
- Continuous positive airway pressure (CPAP; a non-invasive intervention) – used if there is severe respiratory distress
- High flow nasal cannula (HFNC) oxygen – delivers oxygen at high flow rates (see related image here)
- Low flow oxygen support

Other components of management include:

- Adequate fluids and feeds – via an NGT or IV if not tolerating oral fluids/feeds
- Micronutrients e.g. zinc supplementation, vitamin A (if malnourished)
- Antipyretics e.g. paracetamol
- Antibiotics:
    - Oral antibiotics should be given to outpatients:
        - High-dose oral amoxicillin is the first-line agent for children with uncomplicated community-acquired pneumonia. Alternatives to amoxicillin are second- or third-generation cephalosporins and macrolides e.g. azithromycin.
        - Combination therapy (ampicillin and gentamicin OR cefotaxime) is usually used as first-line therapy in neonates and young infants.

- Hospitalised patients can also usually be treated with a narrow-spectrum penicillin e.g. as IV ampicillin. Fluoroquinolones (e.g. ciprofloxacin, moxifloxacin) are reserved for cases where other antibiotics fail. An infectious disease specialist should be consulted before starting these as they have good cover for all childhood bacterial respiratory pathogens but have potential adverse effects e.g. short-term tendon damage, the development of resistance.

ASTHMA

See *Allergology* chapter.

BRONCHIOLITIS

Bronchiolitis is acute inflammation of the bronchioles, usually due to a viral infection (commonly RSV). RSV is highly contagious and spreads via direct contact with nasal secretions, airborne droplets and fomites. Children of any age can present with bronchiolitis but it primarily affects young infants and the most severe symptoms are seen in this age group. Although it is usually seasonal, different viruses cause bronchiolitis during different seasons.

Aetiology

Most cases are due to a viral pathogen with multiple viruses usually being involved. Causative organisms include:

- RSV A & B:
  - They are the most common causes of RSV in children <2 years old.
  - Type A causes more severe infections.
  - There is viral shedding for 6-21 days after symptoms develop
- Rhinovirus:
  - It causes the common cold but may also cause bronchiolitis.
  - Patients with bronchiolitis caused by rhinovirus have shorter hospitalisation compared to those with bronchiolitis caused by RSV.
- Human metapneumovirus
- Parainfluenza virus:
  - Type 3 is more likely to cause bronchiolitis than types 1, 2 and 4.

    - The latter three types have a greater association with croup.
- Adenovirus
- Coronavirus
- Influenza virus
- Human bocavirus:
    - It causes both upper respiratory tract infections (URTIs) and LRTIs.
    - Type 1 is implicated in both bronchiolitis and pertussis-like syndromes.

Pathophysiology

The effects of bronchiolar injury are similar to asthma. Viral invasion leads to alveolar cell death and increased mucous secretion and mucous debris. This leads to bronchial obstruction and constriction, air trapping and atelectasis (see related image here). A ventilation-perfusion (V/Q) mismatch is produced due to decreased ventilation and there is resultant increased work of breathing.

Type 1 (IgE-mediated) allergic reaction may account for some clinically significant bronchiolitis. Breastfed infants appear to be more protected against bronchiolitis likely due to the IgA present in breastmilk.

Clinical Features

The child may present with:

- Difficulty feeding
- Low-grade fever (although infants <1 month may have hypothermia)
- Coryza and nasal congestion
- Apnoea (in infants or young children)
- Tachycardia
- Fine wheezing
- Hypoxia
- Otitis media

If the bronchiolitis is severe, the child may have the following symptoms for >48 hours:

- Increased work of breathing (tachypnoea, nasal flaring and retractions, with or without cyanosis)
- Irritability

Investigations

Although bronchiolitis is a clinical diagnosis. Investigations may still be necessary to exclude other diagnoses or causes of cough in infants and determine the viral cause. One may perform:

- Arterial blood gas (if severe)
- Imaging (a chest x-ray is not always warranted as it is usually non-specific and may only show signs of hyperinflation)

Management

Non-Pharmacological Management

Conservative management includes:

- Providing supplemental oxygenation
- Maintaining hydration
- Suctioning the nose and mouth
- Performing respiratory checks
- Monitoring vital signs

Pharmacological Management

It is patient-specific and depends on the severity of disease. One may need to prescribe:

- Antibiotics (if there is a concern of bacterial co-infection) e.g. ampicillin, ceftriaxone, azithromycin
- Intranasal decongestants e.g. saline nasal drops, oxymetazoline
- Salbutamol:
    - However, there is limited evidence to support its routine use.
    - A bronchodilator response test can be done to check its effect.
- Oral corticosteroids (not routinely given)

ASPIRATION SYNDROMES

This term includes all conditions in which foreign contents are inhaled into the lungs.

Aetiology

The causes of aspiration syndromes may be anatomically grouped:

- Mouth:
    - Cleft palate
- Oesophagus:
    - Dysphagia (anatomical, neurological or physiological)
    - Gastroesophageal reflux (GORD); see related image here
    - Oesophageal atresia
    - Tracheoesophageal fistula
- Stomach and intestine:
    - GOR disease (GORD)
    - Duodenal obstruction
    - Malrotation
- Larynx:
    - Laryngeal cleft
    - Superior laryngeal nerve damage
    - Vocal cord paralysis
- Other causes:
    - Muscular dystrophy
    - Cerebral palsy

Clinical Features

In patients with GORD, the volume of reflux may be significant enough to cause acute symptoms associated with penetration of gastric contents into the airway. However, there may also be episodes where small amounts of saliva or gastric reflux enter the airway, leading to intermittent or persistent symptoms.

Acute aspiration may be associated with:

- Coughing
- Wheezing
- Fever
- Chest discomfort

If there has been massive aspiration then the child may also have cyanosis and/or pulmonary oedema, resulting in severe respiratory distress syndrome.

Chronic aspiration may be associated with:

- Recurrent wheezing
- Chronic cough (≥3 weeks)
- Apnoea
- Recurrent pneumonia

Table 8.2: Clinical Features of Aspiration Syndromes

General Symptoms of Aspiration Syndromes	General Signs of Aspiration Syndromes
● Recurrent vomiting ● Wheezing ● Noisy breathing ● Choking, gagging, coughing, and/or spitting during feeds ● Cyanotic episodes ● Chest discomfort ● Recurrent noisy breathing ● Hoarseness ● Sore throat ● Purulent sputum ● Unexplained fever at night ● Chronic cough ● Excessive salivation	● General examination: ○ Dysmorphisms e.g. cleft palate, micrognathia, macroglossia ○ Fever ○ Clubbing ○ Hypoxaemia ○ Weak suck ○ Hoarse voice or cry and/or irritability ○ Dental erosions ○ Excessive drooling ● Respiratory examination: ○ Increased work of breathing ○ Added breath sounds (wheezing, crackles, stridor) ○ Noisy breathing ○ Apnoea ● Congestion ● Shock ● Bradycardia

However, the aspiration is sometimes silent and the child does not have any clinical features.

Note: It is important to evaluate for aspiration in asthmatics who have unexplainable nocturnal symptoms, have flares not associated with allergens, URTIs or exercise, or fail to respond to treatment.

Comorbidity

Other conditions which can lead to or are associated with paediatric aspiration syndromes include:

- FTT
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Pulmonary abscess
- Pulmonary fibrosis
- Bronchiectasis
- Chronic bronchitis
- Obliterative bronchiolitis
- Interstitial lung disease

Investigations

The work-up of the child with a suspected aspiration syndrome includes:

- Laboratory studies
- Imaging studies
- Procedures
- Histological evaluation

Lab studies	Imaging studies	Procedures	Histological
● FBC ● Pulse oximeter ● Sweat chloride ● Lung function test ● Skin-prick test (SPT) for allergen-	● Chest X-ray – may show hyperinflation, uni- or bilateral diffuse interstitial or perihilar infiltrates, peribronchial thickening, pleural effusion, lobar or	● Oesophageal pH (24-hour monitoring for acid reflux) ● Multi-channel intraluminal impedance and pH monitoring (for acid and non-acid reflux) ● Oesophagogastro-	Bronchoscopy (bronchoalveolar lavage fluid will show lipid-laden macrophages)

specific serum Ige (if eosinophilic esophagitis is being considered)	segmental consolidation, bronchiectasis or atelectasis ● Barium swallow/ contrast swallow (to assess for anatomical or physiological abnormalities of the upper GIT) ● Radio-isotope “milk” scan (to assess the severity of the reflux and risk of aspiration)	duodenoscopy with biopsies (to assess for eosinophilia, distal oesophageal erythema, erosions, ulcers, and mucosal friability) ● Immunocytochemical staining of alveolar microphages for milk proteins	

Management

A multidisciplinary approach is required. Management options may be divided into medical and surgical interventions.

Medical Interventions

They include:

- Conservative management:
  - Place the infant upright during feeds.
  - Avoid placing the infant in a lying position for ~1.5 hours after feeding.
  - Avoid feeding <90 min before bedtime.
  - Elevate the head by 30°.
- Dietary modifications (dietician):
  - Change the texture of the child’s food. One may consider thickening the infant formula.
  - Breastfeeding is encouraged.
  - Give smaller, more frequent feeds.
- Employing swallowing exercises (speech or occupational therapist)
- Feeding with an NGT or NJT
- Pharmacological management may include:

- Prokinetic agents (for gastrointestinal disorders) e.g. metoclopramide
- H_2-receptor blockers (to inhibit gastric acid production) e.g. ranitidine, cimetidine
- PPIs (to inhibit gastric acid production) e.g. omeprazole, lansoprazole, esomeprazole

Surgical Interventions

One may perform:

- Nissen fundoplication
- Gastrostomy

FOREIGN BODY ASPIRATION

It is most common in children <3 years old. Children are more prone to aspirating foreign bodies for several reasons:

- They are unable to chew large chunks of food because they do not have molars.
- They run, talk, laugh, etc. while eating.
- They experiment by putting non-food stuff in their mouths.

Clinical Features

The child may present with a history of sudden coughing or choking while eating or playing.

The choking episode is often not witnessed or recalled by the carer. Children with unwitnessed aspiration may present with:

- Wheezing
- Persistent or recurrent cough
- Persistent or recurrent pneumonia
- Lung abscess
- Focal bronchiectasis
- Haemoptysis

If the foreign body (see image here) is in the subglottic space, the child may have stridor, recurrent or persistent croup, or haemoptysis. Total or near-total occlusion of the airway may occur, leading to death or hypoxic brain damage.

Investigations

One should request:

- Chest X-ray
- Rigid or flexible bronchoscopy

Note: All children with suspected foreign body aspiration require bronchoscopy to exclude the diagnosis, even if they do not have any clinical signs.

Management

First aid for the patient with an obstructed airway should be performed (Heimlich manoeuvre). Endoscopy should be performed and the foreign body removed with a rigid bronchoscopy (if identified).

PNEUMOTHORAX

It is an abnormal collection of air in the pleural space (potential space between the mesothelial membranes covering the lungs and chest wall).

Pathophysiology

It occurs when air leaks into the pleural space, pushing the lung and causing it to collapse. This leak may happen suddenly or develop slowly. The severity of the pneumothorax depends on where the leak occurs, how quickly it develops, the amount of air leaking, the extent of lung collapse and the underlying clinical status of the patient. Paediatric pneumothoraces are uncommon but can be life threatening. Loss of intrapleural negative pressure following a spontaneous pneumothorax (rupture of visceral pleura) or traumatic pneumothorax (rupture of either pleura) causes the lung(s) to collapse. This decreases the patient's vital capacity and leads to a decrease in arterial oxygen partial pressure; see related image to pneumothorax here.

Classification and Aetiology

There are four types of paediatric pneumothoraces:

- Primary spontaneous pneumothoraces (in children with no known lung disease)

- Secondary spontaneous pneumothoraces (complication of chronic or acute lung disease e.g. asthma, cystic fibrosis, pneumonia)
- Traumatic pneumothoraces (secondary to blunt or penetrating trauma)
- Iatrogenic pneumothoraces (complication of certain diagnostic or therapeutic procedures e.g. central line insertion)

Pneumothoraces can be further classified as:

- Simple pneumothoraces:
    - In these cases, the air in the pleura does not build up significant pressure and there is no further expansion of the pneumothorax, but it still causes the lung to collapse by 10-30%.
    - If it is small enough, it can be tolerated with no symptoms.
- Complicated pneumothoraces:
    - They are progressive as there is continued leakage of air into the pleural space, but this air does not exit during exhalation.
    - This produces positive hemithorax pressure and causes mediastinal shift (tension pneumothorax).
- Tension pneumothoraces:
    - They are emergencies as they cause decreased venous return, decreased cardiac output and rapidly progressive shock.
    - The patient will die if this is not treated.

The prognosis is excellent in the patient with an isolated pneumothorax that is diagnosed and treated early.

There is a risk of recurrence. The risk is highest in those with secondary or spontaneous pneumothoraces and in patients who participate in activities such as deep-sea diving.

Clinical Features

A simple pneumothorax may be asymptomatic. The symptomatic patient may present with:

- Pleuritic chest pain (may be preceded by a popping sensation)
- Dyspnoea
- Dry or non-productive cough.
- Tachypnoea

- Cyanosis
- Scars if due to trauma
- Hyperresonance on the affected side
- Decreased breath sounds on the affected side
- Subcutaneous emphysema with crackles (occasionally present)

Babies may present with non-specific signs and symptoms, such as irritability, restlessness, tachypnoea, grunting, nasal flaring, retractions, anaemia and cyanosis. The patient with a tension pneumothorax may be shocked (tachycardic and hypotensive), display excessive work of breathing and/or have tracheal deviation towards the unaffected side.

Investigations

A pneumothorax (especially a tension pneumothorax) is a clinical diagnosis. A chest X-ray should only be performed if the patient is stable and can be used to confirm the diagnosis.

Management

If the patient has a simple, asymptomatic pneumothorax, s/he may be conservatively treated with 100% oxygen via a non-rebreather face mask (give for a short period to avoid oxygen toxicity). As the leak seals, the trapped air is absorbed.
A simple, traumatic pneumothorax should be managed with an intercostal drain (ICD) because there is a high risk of a tension pneumothorax developing (especially if the patient is given PPV.
A large or significantly symptomatic pneumothorax should be managed with an ICD, administration of 100% supplemental oxygen and appropriate pain management. In an emergency, the air may also be removed by needle decompression (with a syringe attached to suction out the air). This should be followed by the insertion of an ICD.

PLEURAL EFFUSION

A pleural effusion is an abnormal collection of fluid in the pleural space.

Pathophysiology

Pleural effusions develop because of excessive filtration of fluid into the pleural space or defective absorption of pleural fluid. They may be primary manifestations or secondary complications of many disorders.

Mechanisms by which pleural effusions occur include:

- Infection within the pleural space
- Abnormal permeability of the capillaries
- Increased hydrostatic or decreased oncotic pressure in the setting of normal capillaries
- Abnormal lymphatic absorption
- Accumulation of blood in the pleural space from any cause (including trauma)

Clinical Features

The child's presentation depends on the aetiology (underlying disease), size and location of the effusion. S/he may present with:

- Dyspnoea
- Cough
- Chest pain
- Decreased chest expansion on the affected side
- Tracheal deviation to the contralateral side
- Dullness to percussion
- Decreased tactile and vocal fremitus

Investigations

They should include:

- CRP
- FBC
- LDH
- ABG
- Blood culture
- Chest X-ray
- Pleural tap – send fluid for microscopy, culture and sensitivity testing (MC&S), pH, glucose, LDH, amylase, cell count and TB GeneXpert®

- Saturation monitoring

Light's Criteria is used to differentiate a transudative effusion from an exudative one.

Table 8.3: Light's Criteria

Light's Criteria		
CRITERIA	TRANSUDATE	EXUDATE
Pleural fluid:serum protein ratio	≤0.5	>0.5
Pleural fluid LDH:serum LDH	≤0.6	>0.6
Pleural fluid LDH	≤200	>200

Management

One must treat the underlying cause and provide respiratory support if the child has signs of increased work of breathing.

Indications for chest tube drainage include:

- An effusion that is large or enlarging and causing respiratory compromise
- Evidence of an infection (pus on thoracentesis, positive culture and gram stain, pleural fluid pH <7, glucose <40 mg/dL or LDH >1000 IU)

Children with parapneumonic effusions or empyema should be followed up within 4–6 weeks of discharge.

EMPYEMA

It is a type of pleural effusion which is characterised by a collection of pus in the pleural space. It is most commonly caused by a bacterial infection and often requires extensive therapy, is associated with longer hospital stays and has high morbidity rates. An empyema often develops in the context of pneumonia, a lung abscess, bronchiectasis, injury or post-thoracic surgery of/on the ipsilateral lung. It is the most common pleural effusion seen in paediatric patients.

Pathophysiology

An empyema develops because of:

- Increased pleural permeability (secondary to pneumonia, lung abscesses, trauma, or malignancy)

- Retropharyngeal, retroperitoneal, or paravertebral infective processes that extend to adjacent structures and involve the pleura

Infective Pleural Effusions

The pleural space normally contains small volumes of transudative fluid with protein (<1.5 g/dL), lymphocytes, microphages and mesothelial cells but no neutrophils. The gradual development of an empyema may be divided into three stages.

- Exudative stage or stage 1:
    - Pleural inflammation from the infection leads to increased permeability of the pleura and formation of a small fluid collection (which contains neutrophils).
    - The collection has a normal pH and normal glucose levels, and is often sterile as the culprit microorganism is attached to the pleura and not within the actual space.
- Fibrinopurulent stage or stage 2:
    - Microorganisms invade the pleural space leading to progressive inflammation and significant leukocyte invasion.
    - There is an increase in fibrin deposition which results in partitions or loculations within the pleural space.
    - Inflammation leads to a decrease in pleural fluid glucose and pH levels and, increased protein and LDH levels.
- Organizing stage or stage 3:
    - A pleural peel is created by the resorption of fluid and is associated with fibroblast proliferation.

After appropriate and adequate treatment, the inflammatory cellular and cytokine production declines and there is no longer a neutrophil predominance in the parapneumonic effusion (with resolution of the inflammation, the influx of macrophages helps to clear the neutrophils). Migration of mesothelial cells to areas of stripped pleura leads to re-epithelialisation and recovery of normal function. On the contrary, following severe pleural inflammation, there is an increased potential for fibrosis and restrictive lung disease.

Aetiology

In paediatrics, the most commonly implicated organisms are *S pneumoniae, S aureus,* and group A streptococci. There may also be anaerobic infections secondary to aspiration, or fungal or mycobacterial infections in immunosuppressed patients. NSAIDs are associated with an increased risk of empyema in children.

Clinical Features

Most patients present with clinical features suggestive of bacterial pneumonia:

- Pyrexia (may be absent in the immunocompromised)
- Pleuritic chest pain
- Cough
- Dyspnoea
- Dullness on percussion
- Crackles
- Decreased breath sounds
- Pleural rub

The child may be cyanosed, and may have abdominal pain and vomiting because of the inflammation of the pleural space (see related diagram here). The latter four signs may be difficult to elicit in a younger child because of discomfort they are experiencing and the fact that they are often less cooperative.

Investigations

They should include:

- FBC and differential count
- Blood culture
- Serum LDH
- Thoracentesis (a pleural tap both diagnostic and therapeutic and must be done before initiating antibiotics); fluid should be sent away for:
    - Total protein
    - Glucose concentration
    - Bacterial, mycobacterial and fungal cultures
    - Gram staining
    - Serological studies

    - pH level
    - FBC and differential count
- Chest X-ray

Management

It should include:

- Drainage of pleural fluid (thoracentesis and ICD insertion; remove the tube when the lung re-expands and drainage stops)
- Antibiotics:
    - Broad-spectrum antibiotics should initially be given and then narrow antibiotics given once the culture or Gram stain results are back.
    - The choice of antibiotic should be based on the common bacterial causes of pneumonia in one's setting.
    - A 10-14-day (or longer) course of IV and then oral antibiotics is given, until the patient is afebrile, off supplemental oxygen and appropriately responds to therapy.

Fibrinolytics may be instilled into the pleural space to break down loculations. Surgical intervention may be considered for complicated cases with adhesions.

Note: An empyema is an advanced type of parapneumonic effusion. Other types include uncomplicated parapneumonic effusion (neutrophil effusion) and complicated parapneumonic effusion. The latter requires thoracentesis, tube thoracostomy or surgery.

CROUP/LARYNGOTRACHEOBRONCHITIS

Croup is an infection and inflammation of the larynx, trachea and bronchial airways. It is contagious, especially during the first few days.

Aetiology

It is commonly due to viral infection:

- Parainfluenza virus
- Influenza virus
- Measles virus

- Adenovirus
- RSV

It is less commonly due to bacterial infection (*Corynebacterium diphtheriae, S. aureus, S. pneumoniae, H. influenzae and M. catarrhalis*). Bacterial infection can be primary or may be secondary to viral infection.

Clinical Features

They often begin as a typical cold (fever and runny nose) and are characterised by:

- Barking cough
- Stridor
- Hoarse voice

Symptoms often start or are worse at night and normally last for 1-2 days. Breathing difficulties are of major concern.

Investigations

Before croup can be diagnosed, epiglottitis and foreign body aspiration must have first been excluded. Further investigations are not usually needed. However, an X-ray may show the characteristic steeple sign (see a related image here).

Grading and Management

The management will depend on the severity of the croup.

Table 8.4: Severity and Management of Croup

Severity	Inspiratory Stridor	Expiratory Stridor	Pulsus Paradoxus	Management
Grade 1	+	-	-	• Provide supportive care • Give nebulised adrenaline • Avoid crying, • Give systemic steroids (oral prednisone 2 mg/kg)
Grade 2	+	Passive	-	

Grade 3	+	Active	+	● Give supplemental oxygen ● Give continuous nebulised adrenaline ● Give systemic steroids (oral prednisone 2 mg/kg or IV dexamethasone 0.6mg/kg) ● Sedate as needed
Grade 4	Same as grade 3 plus marked retraction, apathy and cyanosis			● Urgent intubation

Antimicrobials may also be given based on the suspected causative organism:

- Antibiotics (tracheitis)
- Acyclovir (herpes simplex)
- Ganciclovir (cytomegalovirus; CMV)
- Fluconazole (candida)

Many cases of croup may be prevented with influenza and diphtheria immunisations.

Note: Corticosteroids (e.g. dexamethasone, prednisone, budesonide) decrease swelling and the need for salvage nebulised epinephrine.

BRONCHIECTASIS

It is the dilatation of bronchi secondary to destruction of the elastic and muscular components of their walls.

Pathophysiology

Obstruction and/or inflammation of the airway (from a previous insult, most commonly an infection) causes airflow limitation, abnormal quality and quantity of mucous and ciliary dyskinesia. This leads to reduced mucous clearing and increased bacterial colonisation and infection. Thus, there is a vicious cycle of infection and dysregulated airway inflammation, resulting in the progressive destruction of bronchial walls, bronchial dilatation and airflow obstruction. Bronchiectasis is,

therefore, the result of interactions between the host, pathogens and the environment (see also related image here).

Aetiology

Bronchiectasis may be caused by:

- Infection or post-infectious complications:
    - This is seen in patients with severe, chronic or recurrent pneumonia, postinfectious bronchiolitis obliterans and Swyer-James syndrome.
    - Associated organisms include TB, *Mycobacterium avium*, other mycobacteria, pertussis, adenovirus, measles and *Aspergillus fumigatus*.
- Congenital or genetic disorders (primary impairment of mucociliary clearance):
    - Cystic fibrosis
    - Primary ciliary dyskinesia
    - Young syndrome
- Acquired disorders:
    - Foreign body aspiration (leading to airway obstruction)
    - Chronic aspiration
    - Severe tracheomalacia or bronchomalacia with impairment of mucociliary clearance
- Immunodeficiencies (predispose the host to recurrent infections and the development of bronchiectasis):
    - Congenital immunodeficiencies e.g. immunoglobulin deficiencies, leukocyte dysfunction, complement deficiencies, combined immunodeficiencies
    - Acquired immunodeficiencies e.g. HIV infection, malnutrition, malignancy

Clinical Features

Bronchiectasis is often localised and produces recurrent cough and infectious exacerbations. However, when it is diffuse the patient will often have additional signs

and symptoms of generalised airway obstruction and reduced lung function (which may lead to respiratory failure). These features include:

- Daily cough productive of a fetid sputum which persists for >4 weeks
- Recurrent lung infections (including pneumonia)
- Exertional dyspnoea
- Recurrent wheezing
- Clubbing

Complications of bronchiectasis include atelectasis and life-threatening haemoptysis.

Investigations

The following investigations may be done to look for the underlying cause:

- Speech therapist analysis (to assess for possible dysphagia with aspiration)
- Sweat chloride test (to diagnose cystic fibrosis)
- Serum immunoglobulin levels (to diagnose immunodeficiencies)
- HIV test
- Sputum culture, oropharyngeal swabs and GeneXpert® tests (to identify an infectious cause)
- Chest X-ray and CT scan (to identify airway obstructions and lung pathology)
- Barium swallow test (to assess for anatomical or physiological abnormalities of the upper GIT which may be causing chronic aspiration)
- Lung function testing

Management

It should include:

- Treating acute exacerbations with appropriate antibiotics (send sputum samples off for MC&S to identify the causative organism)
- Using airway clearance techniques e.g. nebulisation using hypertonic saline, administering recombinant DNASE (Pulmozyme®)
- Initiating immunomodulating therapies e.g. azithromycin
- Ensuring immunisations are up to date
- Giving the influenza vaccine annually
- Optimising nutrition

Chapter 9:

INFECTIOUS DISEASES

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This chapter covers the following topics:

- Tuberculosis
- HIV
- Measles
- Mumps
- Chicken pox
- Pertussis (whooping cough)
- Rubella (German measles)
- Influenza
- Poliomyelitis
- Meningitis
- Malaria
- Diphtheria
- Rabies
- Typhoid
- Cholera
- Bilharzia
- Antibiotic Stewardship

TUBERCULOSIS (TB)

Pulmonary TB

Pathophysiology

Mycobacterium tuberculosis is the organism that causes TB. Infection occurs through exposure of the lungs or mucous membranes to infected aerosols i.e. droplet spread/airborne transmission. The inhaled droplets are deposited in the alveoli, where they form Ghon foci that drain to regional lymph nodes. The organisms grow for 2-12 weeks until the colony is of a size significant enough to elicit a cellular immune response. It is at this stage that the patient will have a positive tuberculin skin test reaction.

The infection can be cleared by the host's immune system, suppressed (latent TB) or develop into active TB infection. Only patients with active TB can spread the disease. Latent TB can develop into active TB should the host's immunity be suppressed, therefore becoming less effective at containing the infection.

The risk of developing TB disease is highest in the first year following exposure. Young children (<5 years old), especially those under 1 year of age, are at a particularly high risk for developing severe forms of disease e.g. miliary TB, TB meningitis.

Clinical Features

Younger patients with primary TB often present with non-specific symptoms and signs:

- FTT
- Cough
- Weight loss
- Fever
- Lymphadenopathy
- Disinterest in play

Adolescents with primary or reactivated TB may present with:

- Cough
- Chest pain
- Weakness and fatigue
- Loss of appetite

- Night sweats
- Fever

Investigations

If TB is suspected, one should perform the following investigations:

- Tuberculin skin test (see related image here)
- Sputum microscopy and culture (with staining for acid-fast bacilli and TB culture)
- TB GeneXpert (a polymerase chain reaction/PCR test which may be done on induced sputum or gastric aspirate)
- HIV test

See related image here.

Other Clinical Manifestations of TB

Pleural Effusion

It is more common in those older than 5 years. Smear microscopy and culture is usually negative.

Disseminated (Miliary) TB

In these patients, the immune response was unable to control the infection leading to occult, haematogenous dissemination of TB bacilli to other sites. Patients are usually wasted with generalised lymphadenopathy and hepatosplenomegaly. They may also present with fever, poor feeding and lethargy. There may be cutaneous manifestations (inflammatory papules, verrucous plaques, suppurative nodules, ulcers and other lesions) which can be biopsied for further investigations.

Respiratory symptoms may be limited (e.g. only tachypnoeic). The patient may have the typical “snowstorm”, reticulonodular pattern throughout both lung fields. The radiograph may also be normal. In these cases, the diagnosis can be confirmed with liver or bone marrow biopsy.

TB meningitis (TBM)

TBM is often associated with disseminated TB and occurs because the TB bacilli usually embed themselves in the meninges during the primary infection. Other less common routes of infection include transmission from disease affecting the middle ear, mastoid or spine. The bacilli create tuberculous granulomata in the brain (Rich foci) which undergo caseation and discharge into the CSF. This elicits an inflammatory response which causes a thick exudate to cover the base of the brain. This may result in obstructive hydrocephalus.

Clinical Features and Diagnosis

Patients with TBM usually present with non-specific signs, such as irritability, lethargy, headache and vomiting. In South Africa, TBM is divided into three stages based on the clinical features with which the patient presents:

- Stage 1 – non-specific signs, conscious, no focal neurological signs, no hydrocephalus
- Stage 2 – signs of meningeal irritation, confusion, and/or focal neurological signs
- Stage 3 – stupor, delirium, coma and/or neurological signs e.g. hemiplegia

Early diagnosis and treatment at Stage I carries the best prognosis. Diagnosis may be made based on suggestive:

- History and examination
- Neuroimaging e.g. infarctions, hydrocephalus, tuberculoma, basal enhancement
- Cerebrospinal fluid (CSF) findings i.e. low glucose, lymphocyte predominance, high protein (but CSF findings can be variable)
- CXR (may show features of primary TB)

A positive TST supports the diagnosis but a negative TST does not rule out infection, even in severe disseminated disease. If in doubt, one should start anti-TB therapy until TB has been excluded.

Superficial Lymphadenitis

TB lymphadenitis is usually cervical but is occasionally inguinal or axillary.

Abdominal TB

It may develop because the patient swallowed sputum containing TB bacilli or because there was haematogenous spread. Abdominal TB may manifest as intestinal TB, abdominal lymphadenopathy, peritoneal disease or solid organ TB e.g. liver, spleen.

TB Pericarditis

The pericardium may become involved due to spread from adjacent lymph nodes or haematogenous dissemination. Pericarditis and pericardial effusion develop because of fibrous organisation or calcification of the pericardium. The patient with TB pericarditis may have a pericardial friction rub, increased cardiac dullness, impalpable apex and muffled heart sounds. If there is tamponade or constriction, the patient will have a raised JVP, hepatomegaly and oedema.

TB of the Upper Respiratory Tract

The mouth and tonsils may be infected via a contaminated pacifier or contaminated milk. Infection may spread to the middle ear (through the Eustachian tube), adenoids and larynx.

Ocular TB

TB can affect the conjunctiva, cornea, lacrimal gland, iris, uvea and retina. However, involvement of the eye is rare.

TB of the Ears and TB Mastoiditis

The most common ear manifestation is otorrhea but TB can also cause conductive hearing loss (due to perforation of the tympanum) or facial nerve palsy (due to local lymph node enlargement. From the ear, the infection can spread to CNS.

Cutaneous TB

The skin may be involved through:

- Direct contact with the skin and subsequent infection (can cause a warty lesion)

- Haematogenous spread (can produce multiple nodular lesions, a large plaque, ulcers, multiple abscesses or chronic, indurated, destructive lesions)
- Hypersensitivity reactions to TB resulting in cutaneous lesions (tuberculids) e.g. papules (ears, elbows) and erythema nodosum

Osteoarticular TB

It may involve the spine (most commonly), hips, knees, other joints and other bones. X-rays will show decreased bone density, cysts and periostitis.

Urogenital TB

It can affect any organ along the urinary tract or reproductive tracts. However, urogenital TB is rare in children.

Management

When one suspects that a child has TB, one must ask oneself:

- Why does the child have TB?
    - Is s/he malnourished?
    - Is s/he immunocompromised?
    - Is s/he a close contact of someone with TB?
- What implications does this diagnosis have for those around the child?
    - Does the child attend a creche?
    - Are there other children (and adults) at home who are at risk for developing TB?

General and Supportive Measures

They include:

- Regularly monitoring the child's neurological status (to detect hydrocephalus early)
- Ensuring adequate nutrition (nasogastric feeding may be required)
- Rehabilitation (most patients will need physiotherapy and/or occupational therapy)

- Counselling and educating the child's family and caregivers

Specific Treatment

Drug-Sensitive TB (DS-TB)

DS-TB is treated with isoniazid (INH or H), rifampicin (RIF), pyrazinamide (PZA or Z) and ethambutol (EMB or E) (see also diagram available here). Isoniazid competes with vitamin B6 (pyridoxine) and can result in peripheral neuropathy, ataxia and paresthesia. For this reason, Isoniazid should always be prescribed with a pyridoxine supplement.

For the child <8 years or <30 kg with:

- Uncomplicated TB (i.e. HIV negative) – treat for 6 months
    - Intensive phase (first 2 months) – PZA, INH and RIF
    - Continuation phase (subsequent 4 months) – RIF and INH
- Complicated (HIV positive) – treat for 6 months
    - Intensive phase (first 2 months) – RIF, INH, PZA and E
    - Continuation phase – RIF and INH
- TBM/miliary TB – treat with RIF, INH, PZA and E for 6-9 months (duration depending on response to treatment)

For the child >8 years and >30kg

- Treat all TB that is not MDR-TB for 6 months
- Give RIF, INH, PZA, and E for 2 months and then RIF and INH for 4 months

Drug-Resistant TB (DR-TB)

The treatment of DR-TB in children should always be done in consultation with a clinician experienced in managing DR-TB in children.

HIV & TB Co-Infection

If the HIV and TB are diagnosed at the same time, one must treat as follows (to prevent immune reconstitution inflammatory syndrome):

- If non-neurological TB, start ART as soon as the patient is tolerating TB treatment, i.e. within the first 2 weeks of starting anti-TB treatment
- If TBM, defer ART initiation for 4 to 8 weeks

Table 9.1: Note on Steroid Use in TB Patients

Co-Administration of Steroids
Steroids are used in TB meningitis or if there are large intrathoracic lymph nodes causing airway compression. In these cases, one will give oral prednisone (2mg/kg daily) for 4 weeks, then taper to stop.

HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

HIV is an enveloped RNA retrovirus which can be transmitted from mother to child in-utero, during labour or postnatally (through breastfeeding). It can also be transmitted through sexual contact or contact with contaminated blood e.g. needlestick injuries, infected blood splashing on an open wound. Fortunately, childhood HIV infection has been significantly reduced with the success of the Prevention of Mother to Child Transmission (PMTCT) programme. See related image here.

Pathogenesis

The virus (see structure here) primarily infects CD4 T lymphocytes, replicates within these T lymphocytes and subsequently kills these cells. This loss of T lymphocytes leads to impaired immunity.

Clinical Features

Children infected in early childhood may present with persistent generalised lymphadenopathy, recurrent infections, FTT or opportunistic infections e.g. TB. Many children of HIV-infected mothers receive prophylaxis or are diagnosed in the early asymptomatic stages due to the PMTCT program.

Diagnosis

In children under 18 months, a PCR test is done because maternal antibodies persist for up to 18 months i.e. antibody tests can give false positive results. From 18 months until 2 years of age, a rapid HIV antibody screening test can be done (see HIV rapid test kit available here). If this antibody test is positive it needs to be confirmed with a PCR.

From the age of 2 years, two positive rapid HIV antibody tests are needed in order to confirm the diagnosis of HIV.

Management

Early initiation of ART is important. The family (and the child, if appropriate) must be counselled as treatment, once commenced, must be continued lifelong. Baseline investigations should be done before initiating treatment e.g. full blood count (FBC), alanine transaminase (ALT), CD4 count. Thereafter, regular follow up is needed to assess adherence and treatment response.

General Measures

HIV-positive children on ART are encouraged to continue breastfeeding (even if mixed feeding) until 2 years of age. The healthcare worker must support ongoing treatment adherence in the child and mother.

Specific Treatment

The specific drugs and dosages used to treat the child with HIV are determined based on the child's age and weight. One should always refer to the most updated dosing chart provided by the Department of Health. At the time of publication, first line treatment for children:

- >4 weeks old and <20kg – abacavir (ABC) + lamivudine (3TC) + lopinavir/ritonavir (LPV/r)
- 20-35kg or <10 years old – ABC + 3TC + dolutegravir (DTG)
- ≥ 35kg and ≥10 years old – tenofovir (TDF) + 3TC + DTG

MEASLES

Measles is caused by the measles/rubeola virus, which is an RNA paramyxovirus. Measles is an acute and highly contagious disease. Its incidence has been greatly reduced by immunisation programs.

Transmission and Pathogenesis

Measles spread is through the inhalation of infected respiratory droplets. The virus replicates within respiratory epithelial cells before migrating to lymphatic tissue via the bloodstream, from where it spreads to other organs (see related image here).

Clinical Presentation

Once exposed, there is an incubation period of 10-11 days after which a prodrome of fever, cough, coryza and conjunctivitis occurs. Koplik spots (small red spots with white centres which appear on the buccal and labial mucous membranes) are pathognomonic for measles infection and appear on day 2 of the prodrome. A maculopapular rash, which affects the face, trunk and limbs, also appears.

Symptoms usually resolve after a few days provided that no complications arise.

Complications

Croup, diarrhoea and/or pneumonia may occur as a result of measles or may predispose the child to a secondary bacterial or viral infection. Otitis media and corneal ulceration may also occur. Rarely, encephalitis (acute and subacute sclerosing panencephalitis), nephritis, myocarditis and pericarditis can occur.

Management

The infection is usually self-limiting and supportive care is all that is required. This includes maintaining nutrition and hydration, early diagnosis and treatment of complications. Administration of vitamin A (100 000-200 000 IU) has been shown to reduce the risk of complications. Lifelong immunity develops following infection.

MUMPS

Mumps is caused by the mumps virus which is an RNA paramyxovirus. It is highly contagious but is less common due to the effect of the combined measles, mumps and rubella (MMR) vaccine (see related image here). Unfortunately, this vaccine is only available in the private sector in South Africa.

Transmission and Pathogenesis

Humans are the sole host of the mumps virus. The virus spreads via airborne droplets and direct contact with infected saliva. It has an affinity for the parotid glands and causes parotitis. Infected individuals are contagious for 3 days before and up to 9 days after disease onset (onset of parotitis).

Clinical Features

Once exposed, there is an incubation period of 14-21 days. Parotitis will then develop and may be unilateral or bilateral. The parotitis is characterized by tender swelling of the parotid, which may impair mouth opening and displace the ear lobe. This is accompanied by headache, malaise, low-grade fever and anorexia. Submandibular and sublingual lymphadenopathy may also occur.

Symptoms usually resolve after a week and the disease is self-limiting. There may be further dissemination of the virus to the lacrimal and mammary glands, pancreas, testes, ovaries and CNS.

Complications

Complications of mumps include:

- Epididymo-orchitis (can cause infertility)
- Oophoritis
- Meningoencephalitis
- Pancreatitis
- Thyroiditis
- Mastitis

Investigations

Viral serology can be done but the diagnosis of mumps is usually clinical. Positive serum IgM confirms the diagnosis. Alternatively, the pathogen can be detected through real-time reverse transcriptase PCR (rRT-PCR) or viral culture from infected body fluids.

Management

Treatment is supportive because mumps is usually self-limiting and has a good prognosis. The patient is, therefore, treated with:

- Paracetamol (for pain and fever)
- Bedrest
- Fluids
- Ice packs (to soothe parotitis)

Mumps can be prevented with the MMR vaccine (which is not part of the EPI). Lifelong immunity develops following mumps.

CHICKEN POX

Chicken pox is caused by primary infection with the varicella-zoster virus (VZV)/human herpesvirus type 3 (HHV-3). Infection usually occurs in childhood.

Transmission and Pathogenesis

VZV is highly contagious and the virus spreads through droplets or direct contact with vesicular fluid. It can also spread across the placenta. After infection of the mucosa and regional lymph nodes, there is viraemia with viral replication within the epidermis. This causes the characteristic vesicular rash.

Chicken pox only occurs once as the VZV antibodies persist for life (see related image available here). However, the virus can lie dormant in ganglion cells for many years and become reactivated if the immune system is compromised. This results in shingles (herpes zoster) which follows the affected dermatome.

Clinical Features

Following an incubation period of 13-17 days, a mild prodrome of fever, headache and malaise occurs. After 1-2 days, a crop of red papules appear and then turn into clear vesicles. The rash starts on the trunk and spreads over the face, scalp, conjunctivae and mucous membranes. The vesicles progress from clear to cloudy, develop a central

depression and eventually dry to scabs. Once scabs have formed, the patient is no longer contagious. The rash is severely pruritic (see *Dermatological Conditions* chapter for more information).

Investigations

The diagnosis is usually made clinically, based on the presence of the characteristic rash. However, a Tzanck smear, PCR, viral culture or viral serology can be performed if the diagnosis is unclear. These investigations may be performed in older, immunosuppressed or pregnant patients and are not commonly performed in children.

Complications

More common complications include:

- Secondary bacterial infection (with staphylococci and streptococci)
- Reactivation of latent VZV (causing shingles/herpes zoster)
- Scarring

Thrombocytopenia, pneumonia, hepatitis and encephalitis are rarer complications of VZV infection.

Management

Drying lotions and antipruritics can be prescribed for the rash. Calamine lotion or pramoxine gel may help to relieve the itch. If there is severe pruritus, oral antihistamines may be useful. Acyclovir can be prescribed for severe disease or in immunocompromised patients. Antibiotics may be prescribed if there is a secondary bacterial infection.

A live attenuated vaccine has been developed but is not part of the EPI.

PERTUSSIS (WHOOPING COUGH)

Pertussis is caused by infection with *Bordetella pertussis*.

Transmission and Pathogenesis

Bordetella pertussis is spread via droplets. The organism causes necrosis of ciliated respiratory epithelium, which leads to sloughing of cells and mucous production. This leads to micro-aspiration and coughing.

Clinical Features

There is an incubation period of 7 days followed by a catarrhal stage characterised by a low-grade fever, nasal secretions and a mild cough. The paroxysmal stage then follows. During this stage, patients have a paroxysmal cough (sudden and occurring at any time) followed by a forceful inspiration and ‘whoop’. This cough is often accompanied by vomiting of mucus or feeds. In young infants the cough is atypical. These children may present with apnoea or cyanosis. The paroxysmal stage lasts 2-4 weeks.
It is followed by the convalescent phase which lasts 2-4 weeks and is characterised by a decrease in severity and frequency of the cough. However, the cough can persist for 3 months or more.

Complications

They include:

- Pneumonia
- Atelectasis
- Encephalopathy
- FTT
- Subconjunctival haemorrhage (see related image here)
- Epistaxis

Investigations

Performing a PCR test on nasal swabs is the preferred investigation to detect the causative organism. One may perform an FBC as leucocytosis may be present.

Management

Hospital admission is warranted in severe cases where supplemental oxygen or mechanical ventilation is required, or if the child has apnoeic or cyanotic spells. The cough is best controlled by avoiding stimuli such as unnecessary suctioning, throat examinations and NGT insertion.

Antibiotics are administered with the aim of eradicating *Bordetella pertussis* and preventing secondary transmission. Macrolide antibiotics (e.g. clarithromycin, azithromycin and erythromycin) are highly effective at eradicating *Bordetella pertussis* from the nasopharynx.

The incidence of pertussis has largely been reduced due to immunisations (the vaccine is part of the EPI).

RUBELLA (GERMAN MEASLES)

It is caused by the rubella virus, which is an RNA virus.

Transmission and Pathogenesis

Rubella is transmitted via airborne droplets. It invades the respiratory epithelium and spreads via the blood (primary viraemia) to regional and distal lymphatics and replicates within the reticuloendothelial system. There is a second viraemia ~6 days after infection, causing the virus to spread to many different sites. The second viraemia peaks just before the rash develops.

Clinical Features

The incubation period lasts 14-21 days and is followed by a prodrome of malaise, coryza, conjunctivitis and tender lymphadenopathy (sub-occipital, post-auricular and cervical). There is then an exanthem phase in which a pink-red, maculopapular rash appears on the face. The rash typically starts behind the ears and then progresses distally to cause a generalized maculopapular rash that spares the palms and soles. The rash usually lasts 2-3 days (see *Dermatological Conditions* chapter for more information).

Complications

They include:

- Arthralgia
- Encephalitis
- Thrombocytopenic purpura

Investigations

The diagnosis is usually clinical. However, viral serology can be performed to confirm the diagnosis.

Management

Management is mostly supportive (symptom control). Generally, immunity develops after infection. Rubella can be prevented with the MMR vaccine (not on the EPI).

POLIOMYELITIS (POLIO)

It is caused by the poliovirus, which is an RNA virus.

Transmission and Pathogenesis

The poliovirus is spread via the faeco-oral route but may also be spread via oral-to-oral transmission. The virus multiplies in the gastrointestinal tract (GIT) and produces an immune response. If this response is adequate, the virus is neutralised. However, if the response is inadequate the virus continues to proliferate and gains access to the central nervous system (CNS) via the bloodstream or along nerve pathways from the GIT. It then attacks anterior horn cells, resulting in acute flaccid paralysis.

Clinical Features

The clinical presentation is variable and may include:

- Subclinical disease

- Mild, non-paralytic disease – fever, sore throat, abdominal pain, nausea and vomiting
- Meningism
- Various patterns of paralytic disease – weakness of the neck, trunk, abdomen, diaphragm and limbs (spinal) or muscles innervated by cranial nerves (bulbar) or a combination (bulbospinal)
- Encephalopathy – irritability, drowsiness, a tremor and disorientation

During the recovery period, those with paralytic disease may recover some muscle strength but there is often residual weakness and resultant deformities.

Investigations

All cases of suspected polio must be investigated as per the acute flaccid paralysis protocol. This involves sending two stool samples to the National Institute of Communicable Diseases (NICD) for viral isolation within fourteen days of onset of paralysis.

Management

Management in the acute phase is mainly supportive, with a major aim being the prevention of secondary respiratory tract infections. The patient may also require assisted ventilation if s/he has respiratory muscle paralysis. In the recovery phase, physiotherapy is key to facilitating muscle strengthening and preventing contractures and deformities. If the residual weakness results in deformities, orthopaedic surgery may be required.

Polio (see related image here) has been eradicated in most parts of the world due to vaccination programmes. It is part of the EPI.

INFLUENZA

Influenza is caused by the influenza virus, which is an RNA virus with three types – A, B and C.

Transmission and Pathogenesis

The influenza virus is spread via airborne droplets and has hemagglutinin and neuraminidase surface proteins. The hemagglutinin binds to respiratory epithelial cells which allow it to infect the host and replicate. The neuraminidase allows newly replicated virions to break free from the cell membrane and spread.

Clinical Presentation

The child may present with a sudden onset of fever, headache, myalgia, malaise, sore throat, rhinitis, vomiting and respiratory symptoms (e.g. coughing). Recovery usually occurs over a few days. However, the malaise may persist for a few weeks.

Complications

They include:

- Febrile seizures, encephalitis
- Reye's syndrome
- Pericarditis
- Myocarditis
- Secondary bacterial infection (causing pneumonia or otitis media)

Management

Management is mainly supportive but antiviral agents can be used e.g. oseltamivir, zanamivir (zanamivir is rarely used in South Africa and is only licensed for use in people >7 years). Some children may require hospitalisation and oxygen therapy if they are hypoxic or have secondary pneumonia.
Influenza may be prevented by annual vaccination (as there is new strain every year).

MENINGITIS

Aetiology

Meningitis may be caused by:

- Bacteria e.g. Group B streptococci (GBS), *Neisseria meningitidis* (infants and older children), *Haemophilus influenzae* type b (Hib; now uncommon because of vaccination), *E. coli*, *Listeria monocytogenes*, Klebsiella (neonates)
- Mycobacteria e.g. TB
- Viruses e.g. herpes simplex virus (1+2), Epstein-Barr virus (EBV), adenovirus, mumps, coxsackie, echovirus, poliovirus
- Fungi e.g. *Cryptococcus neoformans* (also causes a chronic basal meningitis; characterised by high CSF pressures)

Transmission and Pathogenesis

The route of transmission depends on the causative organism but is usually via haematogenous spread.

Inflammation and damage are largely due to the inflammatory response and release of inflammatory cytokines, as opposed to direct damage caused by the organism. This is particularly true for bacterial meningitis. Viral meningitis has a more benign self-limiting course and full recovery usually occurs. TBM and cryptococcal meningitis have a more chronic course.

Clinical Presentation

In neonates and infants, the presentation is non-specific.

Table 9.2: Clinical Features of Meningitis Categorised by Age Group

Neonates and Infants	Older Children
● Irritability ● Lethargy ● Poor feeding ● Bulging fontanelle ● Hyper/hypothermia	● Fever ● Nausea and vomiting ● Features of meningism (headache, neck stiffness, photophobia, and positive Kernig and Brudzinski signs)

In severe cases there may be signs of encephalopathy or coma. Meningococcal meningitis is usually more rapid in onset and has a characteristic petechial, purpuric rash.

Complications

Venous thrombosis is the main complication. It can lead to:

- Infarctions
- Subdural effusions
- Epileptic fits
- Cerebral oedema
- Hydrocephalus
- SIADH
- Cranial nerve palsies
- Brain abscesses

Investigations

One should perform a lumbar puncture (LP). One may find results similar to those outlined in the table below.

Table 9.3: CSF Findings in Infectious Meningitis

	Bacteria	Viruses	TB	Cryptococcus
Cells	100-50000 cells with neutrophil-predominance	25-500 cells with lymphocyte-predominance	25-100 cells of lymphocyte predominance (may have an early neutrophil-predominance)	Similar to TBM
Glucose	Low	Normal	Very low	

Protein	Mild-to-moderately increased	Mildly increased	Moderately increased	
Other tests	Gram stain and culture will reveal the causative organism			India Ink staining, culture and cryptococcal latex agglutination test (CLAT) will be positive for cryptococcus

Management

If there is high clinical suspicion of bacterial meningitis, antibiotics should be started immediately after the LP and blood culture samples have been taken. Other investigations which may be performed include CXR, FBC and urea and electrolyte levels.

Management of Bacterial Meningitis

For Infants <2 Months Old

Initial therapy is with cefotaxime 50mg/kg 8 hourly (12 hourly if <7 days old) AND ampicillin 50mg/kg 6 hourly (8 hourly if <7 days old).

If the child has GBS, treat with cefotaxime or ampicillin for 14 days. An aminoglycoside may be added to either drug. If the meningitis is caused by Gram-negative. enteric bacilli, treat with cefotaxime and an aminoglycoside for 31 days. If the meningitis is caused by *L. meningitis*, treat with ampicillin or penicillin for 14 days.

For Children > 2 Months Old

Initial therapy is with ceftriaxone 100mg/kg stat then 80-100mg/kg daily or 40-50mg/kg twice daily. If the meningitis is due to:

- Hib infection, treat for 7-10 days
- *S. pneumoniae*, treat for 10-14 days
- *N. meningitidis*, treat for 7 days

If the causative organism is a penicillin-resistant pneumococcus, add vancomycin.

Management of TBM

Treat with RIF, INH, PZA and E for 6-9 months (duration of treatment depending on the child's response to treatment).

Management of Cryptococcal Meningitis

Treat with amphotericin B 1mg/kg/day and 5-fluorocytosine 150mg/kg/day divided into 6-hourly doses for 1 week, followed by high dose fluconazole.

MALARIA

Aetiology

Malaria is caused by protozoa species of the *Plasmodium* genus, namely *P. falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi. P. falciparum* is the most prevalent species and causes the most severe disease.

Transmission and Pathogenesis

Malaria is spread via a vector, namely the female *Anopheles* mosquito (see related image here). When bitten by the mosquito, sporozoites (immature protozoa produced during the sexual phase that occurs within the mosquito) of the protozoa are injected into the bloodstream. These sporozoites develop in the liver before invading circulating red blood cells (RBCs). They mature and multiply in the RBCs until these cells rupture. The sporozoites go on to infect other RBCs. Gametocytes form in the RBCs and are sucked up by a feeding mosquito. Once in the mosquito, the sexual phase is completed and the life cycle starts again. See also the life cycle of the malaria parasite here.

Clinical Features

The patient may have a history of recent travel to an endemic area. After an incubation period of 7-12 days in *P. falciparum* malaria and 10-30 in the other species, a fever develops. The fever is classically intermittent (occurs in 48-72-hour cycles depending on the species). This fever may be associated with rigor, headache, myalgia, arthralgia, nausea, vomiting, malaise and sweating. Splenomegaly is usually present and there may also be anaemia, leucopaenia and thrombocytopenia.

Complications

Complicated malaria may have any one of the following features and should be treated as an emergency:

- Severe anaemia (Hb <7 g/dl)
- Parasitaemia (>10000/μ or >5% infected RBCs)
- Renal failure
- Pulmonary oedema
- Circulatory collapse
- Hypoglycaemia
- Disseminated intravascular coagulation (DIC)
- Repeated generalised convulsions
- Severe metabolic acidosis
- Hepatic necrosis (will present jaundiced)
- Haemoglobinuria
- Features of cerebral malaria e.g. apathy, disorientation, psychotic behaviour, focal neurological signs, extrapyramidal signs, convulsions, coma

Investigations

They may include:

- Peripheral blood smear – will show infected erythrocytes.
- Rapid dipstick antigen test (to detect *P. falciparum*)
- FBC
- Renal function tests (RFTs; urea, electrolytes and creatinine)

- Liver function tests (LFTs)
- Blood glucose
- Urine dipsticks

Management

Treatment of Uncomplicated Malaria

It is treated with artemether/lumefantrine (20 mg/120 mg e.g. CoArtem®). The child should be given a stat dose and then a second dose 8 hours later. This should be followed by 12-hourly doses for the next two days. Therefore, the child should be given 6 doses in total.

The number of tablets that the child is given is dependent on her/his weight. If s/he weighs:

- 5-14.9 kg – 1 tablet/dose
- 15-24-9 kg – 2 tablets/dose
- 25-34.9 kg – 3 tablets/dose
- ≥35 kg – 4 tablets/dose

The CoArtem® must be administered with fat-containing food or full-cream milk to ensure adequate absorption.

Children <5 kg should be given oral quinine 10 mg/kg 8 hourly for 7-10 days and clindamycin 10 mg/kg 12 hourly for 7 days.

Complicated Malaria

Those with complicated malaria (have the features listed above, are vomiting or are unable to tolerate oral medication) should ideally be treated with IV artesunate. If the child weighs <20 kg, s/he should be given 3 mg/kg IV artesunate at 0, 12 and 24 hours and then once daily until s/he can tolerate oral CoArtem®. The full Coartem® course should be completed thereafter. If the child weighs >20 kg, s/he should be given 2.4 mg/kg IV artesunate and the same schedule followed as above.

However, IV artesunate may be difficult to acquire and IV quinine may need to be used as an alternative. The child should be given a loading dose of IV quinine (20 mg/kg; 20 mg salt/kg mixed with 5-10 mL/kg of 5% dextrose or dextrose saline) over 4 hours. The

maintenance dose should be given 8 hourly (10 mg/kg slow IV quinine over 4 hours). Once the patient can tolerate oral therapy, CoArtem® OR oral quinine and clindamycin (10 mg/kg/dose 12 hourly orally for 7 days) may be given.
Note: Patients on IV quinine should have regular blood glucose and ECG monitoring.

Prevention

If possible, children <5 years of age should not be taken to high-risk areas. Measures should be taken to prevent mosquito bite, such as:

- Only visiting malaria areas in the dry season
- Staying indoors after dark
- Using mosquito nets and mosquito repellants
- Sleeping under bed nets where available
- Dressing the child in long-sleeved shirts and trousers

Antimalarial prophylaxis is also effective in limiting the risk of malaria.

TETANUS

It is caused by the bacterium *Clostridium tetani*, an obligate anaerobe that exists in spore-form and is found in soil and animal faeces. It is also called ‘lockjaw’ as this characteristic clinical feature is sometimes present.

Transmission and Pathogenesis

The spores enter the body via wounds exposed to contaminated dirt, faeces or saliva. As *C. tetani* is an anaerobe, it generally requires wounds with compromised blood supplies in order for it to germinate and multiply. Thus, deep, penetrating wounds, open fractures, surgical procedures and burns are ideal replicating environments because of the associated ischaemia and necrosis. However, any wound can be tetanus prone. The spores multiply and produce neurotoxins called tetanospasmin and tetanolysin. Tetanospasmin reaches the central nervous system (CNS) via retrograde axonal transport, where the toxin binds to the peripheral nerve receptors and is transported to interneurons in the CNS via vesicles. It prevents the action of inhibitory

neurotransmitters (GABA and glycine), leading to uninhibited activation of α-motor neurons, muscle spasms, rigidity and autonomic instability. Tetanolysin causes haemolysis and also has cardiotoxic effects.

Clinical Features

There is an incubation period of 3-21 days. Early signs include trismus (lockjaw) progressing to generalised muscle rigidity and intermittent spasms. Risus sardonicus is a term used to describe the sustained facial muscle spasms that produce a characteristic sardonic (mocking) grin and raised eyebrows. Dysphagia and odynophagia can also occur. A generalised tetanic posture is classically that of opisthotonus (abduction and flexion of the shoulders, flexion of the elbows and wrists, clenched fists and extension of the legs). Autonomic disturbance also commonly occurs, with the patient developing labile hypertension, episodes of hypotension, tachycardia, arrhythmias, peripheral vasoconstriction and sweating.

Complications

They include:

- Upper airway obstruction or diaphragmatic spasm leading to respiratory failure
- Autonomic instability with sudden cardiac death
- Venous thrombo-embolism
- Stress ulcers
- Contractures
- Joint dislocations

Diagnosis

The diagnosis is clinical and is made based on history and examination i.e. muscle spasms with rigidity in the context of a susceptible wound and inadequate immunisation.

Management

Treatment

Management is supportive and aims to control infection, eliminate toxin production and neutralise the toxins already present. Therefore, the wound should be cleaned and debrided. Patients should be allowed to recover in quiet environments with minimal external stimuli, as these can trigger spasms. Intubation and ventilation may be required in some.

Pharmacological management includes the administration of:

- Tetanus immunoglobulin 500–2 000 IU IM as a single dose
- Metronidazole 7.5 mg/kg/dose IV 8 hourly for 10 days (alternatively use penicillin G)
- Diazepam 0.1–0.2 mg/kg/dose IV 4–6 hourly (to control spasms)

After recovery, patients should be fully immunised.

Prevention

Most cases are prevented through immunisation. As tetanus immunisation is included in the EPI, the incidence of tetanus is low. In children with major wounds, tetanus toxoid (0,5 mL IM) can be administered. If the wound is seriously contaminated or older than 6 hours, tetanus immunoglobulin (250 U IM into the limb opposite to the one exposed to the toxoid) can also be given. Additionally, 5 days of antibiotics (penicillin/metronidazole/erythromycin/cephalosporin) may be given. Tetanus toxoid can be given every 5 years to prevent tetanus infection.

DIPHTHERIA

Diphtheria is caused by *Corynebacterium diphtheriae* (see related image here).

Transmission and Pathogenesis

Corynebacterium diphtheriae is transmitted through droplet spread. The virulent diphtheria bacilli lodge in the nasopharynx where they multiply and produce a toxin. This toxin causes local tissue necrosis and an anti-inflammatory and exudative process,

which results in the formation of a pseudomembrane. Once the toxin enters the blood, it can affect other organs. However, it has an affinity for myocardial and neural tissue. This organism can occasionally infect skin and the patient may present with leg ulcers.

Clinical Features

Patients initially present with a sore throat, fever, malaise and non-specific symptoms of an upper respiratory tract Infection (URTI). There is subsequent development of a white-grey pseudomembrane in the nose, pharynx, tonsils, palate and/or glottis. Cervical lymphadenopathy can give a ‘bull neck’ appearance.
If myocarditis develops the child may present 1-2 weeks later with signs and symptoms of cardiac failure. 3-6 weeks after the initial onset of symptoms, neuritis may manifest as dysphagia, nasal speech, regurgitation, strabismus, diplopia and, in extreme cases, respiratory muscle paralysis. Weakness of the limbs can also occur if peripheral nerves are involved.

Complications

They may include:

- Myocarditis
- Congestive cardiac failure
- Neuritis and its manifestations
- Pneumonia
- Renal failure
- Disseminated intravascular coagulopathy
- Thrombocytopenia

Investigations

Nose and throat cultures can be done to confirm the diagnosis. However, one must not wait for confirmation before initiating treatment if diphtheria is suspected.

Management

The dose of anti-diphtheria serum (ADS; antitoxin) depends on the extent of infection (20 000-100 000 U IM or IV). One must be wary of anaphylaxis when administering this medication. Procaine penicillin (50 000 IU/kg/day IM in 2 doses for 10 days) or erythromycin (50 mg/kg/day oral in 4 doses for 10 days) should also be given.
Bed rest is warranted if the patient has myocarditis. One should restrict fluids, diurese and use digoxin as necessary, if the patient has congestive cardiac failure (CCF). Nasogastric feeds and supportive therapy with physiotherapy may be required. The patient should be isolated and airborne precautions should be implemented.

Prevention

Isolation and airborne precautions should be enforced. Contacts need nose and throat cultures followed by antibiotic treatment for those with a positive result.
An infected person will also require immunisation after recovery. Immunisation in childhood has largely reduced the incidence of diphtheria.

RABIES

It is caused by the rabies virus, which is a single-stranded RNA virus that is bullet shaped.

Transmission and Pathogenesis

Rabies is transmitted when a wound is contaminated with saliva from a rabid animal, such as a stray dog, bat or meerkat. The principle vector may vary in different countries but it is widespread in warm-blooded animals. Once the virus gains entry through the skin, it multiplies in the striated muscles. It then enters peripheral nerves, and travels along axons until it reaches the CNS where it multiplies and causes severe damage within the brainstem, pyramidal cells, cranial nerves, posterior horns of the spinal cord and other CNS structures. The virus then migrates to the salivary glands.

Clinical Features

There is an initial incubation period ranging from a few weeks to 2-3 months where the patient is asymptomatic. This is followed by the prodromal phase when the patient may present with fever, malaise, anorexia, vomiting, headaches and paraesthesia at the site of the wound (pathognomonic but may not always occur).

An acute neurologic phase (furious rabies) occurs after a few days of the prodrome. It is characterised by hydrophobia, aerophobia and alternating periods of hyperactivity, hallucinating, biting and bizarre behaviours. There are then periods of calm, co-operation and normal behaviour. Eventually, there is ascending symmetrical paralysis, areflexia, coma and death (due to respiratory muscle paralysis or arrhythmias). In some cases, there is ascending symmetrical paralysis without the furious phase.

Complications

Death is almost inevitable as only a handful of people have survived rabies.

Investigations

One should perform serum antibody tests, nuchal skin biopsies and tests on the saliva for the rabies virus (see rabies vaccine related image here).

Management

Treatment – Post-Exposure Prophylaxis

In patients with a suspected bite by a rabid animal, clean the wound with soap and water and apply a virucidal solution e.g. 10% povidone iodine.

Administer rabies immunoglobulin (RIG) at the wound and the rest at a distant site (20 IU total dose). Administer human diploid cell vaccine on days 0, 3, 7, 14, 30 and 90 at a separate site from where the RIG was given.

Give supportive management if the patient presents with symptoms.

Prevention

Rabies may be prevented by vaccinating all domestic animals and eliminating stray animals. High-risk individuals (e.g. vets, health inspectors, cave explorers, those who work with wildlife) should receive regular vaccinations.

TYPHOID

It is caused by infection with *Salmonella typhi* (bacteria).

Transmission and Pathogenesis

Salmonella is spread via the faeco-oral route – contaminated food/water and poor hand hygiene. During the incubation period (usually 7-14 days but up to 30 days), organisms multiply in the reticuloendothelial system of the small bowel before invading the bloodstream. The disease can disseminate to various organs and cause focal liver necrosis, inflammation within the biliary tract and reinvasion of the small bowel with ulceration, perforation or haemorrhage. The organism also releases an endotoxin which causes multisystem reactions.

Clinical Features

Typhoid classically has three clinical stages. After the incubation period, there is an onset of fever, with anorexia, headaches, malaise, diarrhoea and vomiting. This usually lasts about one week (see related diagram here).

In the second week, there is persistent fever, abdominal pain with diarrhoea and rose-coloured spots on the abdomen. Complications may develop in the third week, namely hepatosplenomegaly, perforation and intestinal bleeding, secondary bacteraemia and peritonitis. Multiple organ systems can be involved, thus patients can have a wide range of clinical presentations (cough, delirium, meningeal irritation, myalgia, arthralgia, abdominal pain).

Complications

They include but are not limited to:

- GI haemorrhage/perforation (most common)
- Myocarditis
- Meningitis
- Delirium
- Psychosis

Investigations

One may order:

- Blood tests, which will show:
    - Anaemia
    - Leucopaenia/leucocytosis
    - Abnormal liver functions
    - *S. typhi* grown on blood culture
- Urine and stool cultures

Management

Treatment

Antibiotics are given in addition to supportive management and early diagnosis and treatment of complications. Uncomplicated disease may be treated with fluoroquinolones e.g. ciprofloxacin 30 mg/kg/day orally in two divided doses for 7-10 days. Severe infection may be treated with third-generation cephalosporins e.g. ceftriaxone 80 mg/kg IM/IV once daily for 10-14 days (maximum 4 g/day).

Prevention

Typhoid may be prevented with good hygiene and sanitation, and a vaccination before travelling to endemic areas.

CHOLERA

It is caused by *Vibrio cholerae*.

Transmission and Pathogenesis

It is transmitted through the faeco-oral route – contaminated food/water and poor hand hygiene. The bacteria grow well in an alkaline medium, thus a high infective dose is required to cause disease in the acidic gastric environment. Once in the small bowel, the organism produces an enterotoxin that causes the secretion of large amounts of fluid and electrolytes (mainly chloride) into the gut lumen i.e. it causes a severe secretory diarrhoea.

Clinical Presentation

There is an incubation period of 1-5 days. Symptoms include fever, vomiting and diarrhoea. The diarrhoea in cholera (see image cholera patient here) quickly becomes colourless and mucoid, producing the characteristic 'rice water' appearance.
The diarrhoea is often complicated by severe dehydration, shock and electrolyte abnormalities. It usually lasts a few days and is self-limiting, but, if no interventions are instituted to mitigate the dehydration, death can occur.

Complications

They may include:

- Severe dehydration
- Shock
- Death

Pneumonia is also possible.

Management

Treatment

Rapid fluid and electrolyte replacement and rehydration are the mainstays of treatment. Antibiotics are not routine but ciprofloxacin (if <8 years old) or tetracycline (if >8 years old) can be given to shorten the duration.

Enteric precautions, regular weight, hydration and blood pressure (BP) checks, and input and output monitoring are essential. Regular electrolyte monitoring is also important.

Prevention

Good hygiene and sanitation and the availability of clean water are key components of prevention.

BILHARZIA

It is caused by schistosomes which are parasitic trematodes or flukes of the genus *Schistosoma*: *Schistosoma haematobium* affects the genitourinary tract, while *Schistosoma mansoni* and *Schistosoma japonicum* affect the intestine and liver. In SA, *S. haematobium* is more common than the others.

Transmission and Pathogenesis

The organism's life cycle involves freshwater snails (intermediate hosts) and humans (definitive host) (see related image here). Infected humans excrete schistosome eggs in urine and faeces. Eggs present in infected water hatch and infect freshwater snails. Once in a more mature form, they pass from the snail and penetrate the skin of humans who are in the water.

The schistosomes migrate to the portal vessels where they mature into adults. They mate and migrate either to the bladder's venous plexus (*S. haematobium*) or inferior mesenteric vessels (*S. mansoni* and *S. japonicum*). Eventually they migrate into the bladder and large intestine from where they can be excreted and the cycle begins again.

Eggs may deposit in other tissues, such as the lungs and CNS. They tend to stimulate an eosinophilic reaction which varies among individuals and also depends on the parasite load. Pathology is mainly linked to the degree of the host's hypersensitivity reaction and involves the formation of granulomas.

Clinical Features

Initially there is a pruritic, erythematous maculopapular rash at the site of entry with a local reaction, often called ‘swimmer’s itch’ or cercarial dermatitis. After 4-6 weeks patients may present with fever, rash, lymphadenopathy, oedema and hepatosplenomegaly (Katayama fever). Patients may also encounter bronchospasm, severe headache and features of encephalopathy and cardiac disease. In urogenital disease they may be asymptomatic or have terminal haematuria (pathognomonic). In some cases there may be dysuria or suprapubic pain. GIT disease often presents with abdominal pain and dysentery. If chronic there may be anaemia and ascites. If infection affects the liver it may lead to periportal fibrosis leading to Portal HPT and its sequelae. Deposition of eggs can lead to chronic inflammation with granuloma formation.

Complications

They usually develop in patients with chronic infection and may include:

- GI ulcers
- GI obstruction
- Pyelonephritis
- Chronic renal failure
- Chronic lung disease
- Pulmonary HPT
- Portal HPT
- Encephalitis
- Spinal cord lesions
- Urinary tract obstruction
- Bladder calcification

Investigations

Serology is the most sensitive diagnostic investigation for travellers but cannot distinguish between a current or past infection (not useful in patients from an endemic area). Direct visualisation of schistosome eggs via stool or urine microscopy is, thus, the gold standard and can also determine the schistosome subtype.

Management

Treatment

Corticosteroids are used to treat the acute syndrome as they dampen the immune system's inflammatory response. Prednisone (1-2 mg/kg) must be promptly administered if there is neuroschistosomiasis, to prevent irreversible tissue damage secondary to the inflammatory response.

After acute symptoms have resolved the patient should be given a single dose of praziquantel (30-45 mg/kg orally). This may be repeated after 1 month. One should also implement specific management of the complications if present.

Prevention

Good sanitation, avoidance of swimming or urinating in water, especially in endemic areas. Wear protective clothing if swimming in freshwater in endemic areas. Boil drinking water.

ANTIBIOTIC STEWARDSHIP

Antibiotic stewardship refers to a set of coordinated strategies that are employed to improve the use of antimicrobial medications. The goal is to enhance patient health outcomes, reduce antibiotic resistance and decrease unnecessary costs. It is important because resistance to antibiotics is on the rise and the rate at which new drugs are being produced is not sufficient.

Principles of Rational Antibiotic Prescribing

One must:

- Consider the indication for the antibiotic i.e. does the patient have a bacterial infection?
- Perform cultures before administering antibiotics (if appropriate) in hospitalised patients or outpatients with recurrent infections
- Choose an appropriate empiric antibiotic

- Ensure the correct dose and route are prescribed
- Quickly start antibiotics in patients with severe infections
- Ensure early and effective source control
- Evaluate appropriateness of continued antimicrobial therapy on a daily basis and use a narrow-spectrum drug if possible

It is also important to prevent the spread of resistant organisms with good infection control (hand hygiene is key).

See related image here.

IMMUNISATIONS

Table 9.4: Immunisations

According to the South African expanded programme on immunisation (EPI) schedule (which can be sourced from www.westerncape.gov.za), children are vaccinated against:

- Polio
- Measles
- Hepatitis B
- Haemophilus influenza B
- Pertussis
- Diphtheria
- Pertussis
- TB

The catch-up schedule can be sourced on the NICD website at www.nicd.ac.za

Chapter 10:

CHILD AND ADOLESCENT PSYCHIATRY

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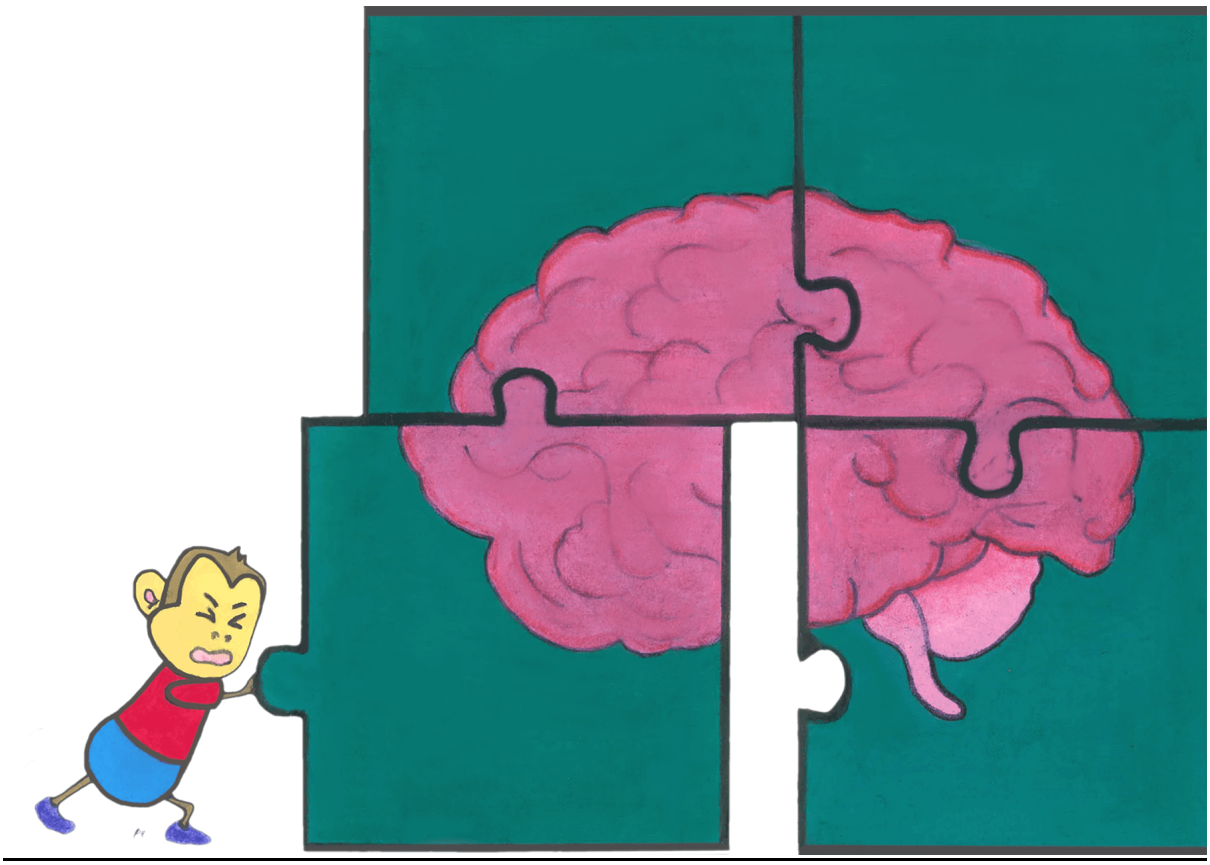

This chapter covers the following topics:

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)/HYPERKINETIC DISORDER

Definition

It is defined as persistent inattentiveness, hyperactivity, impulsivity, disinhibition, and/or distractibility. These symptoms may all be transitory and part of normative developmental patterns (see ADHD related word cloud here). However, ADHD can be diagnosed if the symptoms impair daily living.

It is important to be able to recognise and manage ADHD because it is common, can be serious, can be persistent, is often stigmatised and is treatable.

Diagnosis

The diagnosis is exclusively made on clinical grounds. The child must have:

- 6 of 9 inattentive symptoms and/or 6 of 9 hyperactive-impulsive symptoms
- Symptoms for at least 6 months
- Symptoms starting before age 12
- Symptoms in ≥2 or more situations e.g. home, school, extracurricular activities
- Significant difficulty with school, social or activities of daily living as a result of the symptoms

The symptoms must also not be attributable to another cause e.g. medical condition, intoxication, emotional distress.

Table 10.1: Differential Diagnoses for ADHD

Differential Diagnoses
These psychiatric conditions can mimic ADHD: ● Anxiety ● Post-traumatic stress disorder (PTSD) ● Bipolar mood disorder (BMD) ● Depression ● Psychosis ● Autism spectrum disorder (ASD) ● Oppositional defiant disorder (ODD) ● Intellectual disability disorder (IDD)

Classification and Clinical Features

ADHD is classified as one of the following subtypes:

- Predominantly hyperactive/impulsive symptoms
- Predominantly inattentive symptoms
- Combined inattentive and hyperactive/impulsive symptoms

Table 10.2: Clinical Features of Inattentive- and Hyperactive-Type ADHD

INATTENTIVE SYMPTOMS	HYPERACTIVITY-IMPULSIVE SYMPTOMS
● Carelessness ● Easily distractible ● Difficulty listening when spoken to ● Easily loses focus ● Fails to complete tasks ● Avoids tasks that require focus ● Forgetful ● Easily loses items	● Fidgets ● Squirms ● Talks excessively ● Has difficulty waiting his/her turn ● Often runs and jumps around ● Is unable to sit still or remain quiet for a reasonable amount of time ● Often intrudes or interrupts others ● Is over-familiar with strangers ● Prone to accidents

These symptoms may manifest differently depending on the child's age:

- Preschool age – plays for <3 mins, does not listen, has no sense of danger
- Primary school age – performs activities for <10 mins, is forgetful, distracted, restless, intrusive and/or disruptive
- Adolescence – can attend for <30 mins, has difficulty focusing and/or planning, is fidgety and reckless

Associated features include:

- Defiance, aggression and antisocial behaviour
- Problems with social relationships
- IQ lower than the general population
- Specific learning problems
- Coordination problems
- Specific developmental delay
- Poor emotional self-regulation

The consequences of all this are that the child may have poor performance in school or sport, may become withdrawn, anxious or socially isolated and may be prone to accidents.

Clinical Assessment

It should consist of the following:

- Interviews with the child, caregivers and teachers
    - One must get information about the child in at least two contexts/settings.
    - One must also get a family history (ask parents if they had similar difficulties themselves or with their other children).
- Medical and psychiatric assessment (also assess for psychiatric comorbidities)

No additional tests are necessary to make the diagnosis, as it is made on clinical grounds according to the DSM-5 and ICD-10. However, rating scales are used as screening tools and are useful for monitoring symptoms at baseline and once treatment has been initiated. An example of this is the Swanson, Nolan and Pelham Rating Scale (SNAP IV), which is completed by both teachers and parents.

Psychiatric Assessment (Mental State Examination)

One must observe the relationship between the child and parent(s) in the consulting room. Often, due to difficulties related to ADHD, the parent-child relationship may be very strained.

During the consultation, the child may have difficulty sitting still and may make inappropriate interruptions. S/he may climb over furniture or leave the consultation early. One must observe how the parent performs limit-setting and enforces boundaries during the consultation.

For children on methylphenidate or other medication, it is important to ask whether the child has taken his/her medication that day and at what time it was taken. This may influence the clinical picture and whether ‘top-up’ doses of medication are needed.

Medical Assessment

One must exclude any comorbidities or other medical conditions that could better explain the patient's symptoms.

One must measure and plot growth parameters e.g. height-for-age, weight-for-age. Blood pressure measurement, pulse monitoring and cardiac examination are also important, especially if the child is on stimulants.

If there is a family history of sudden cardiac death, one must do an ECG and consult with a paediatrician.

Assessment Algorithm

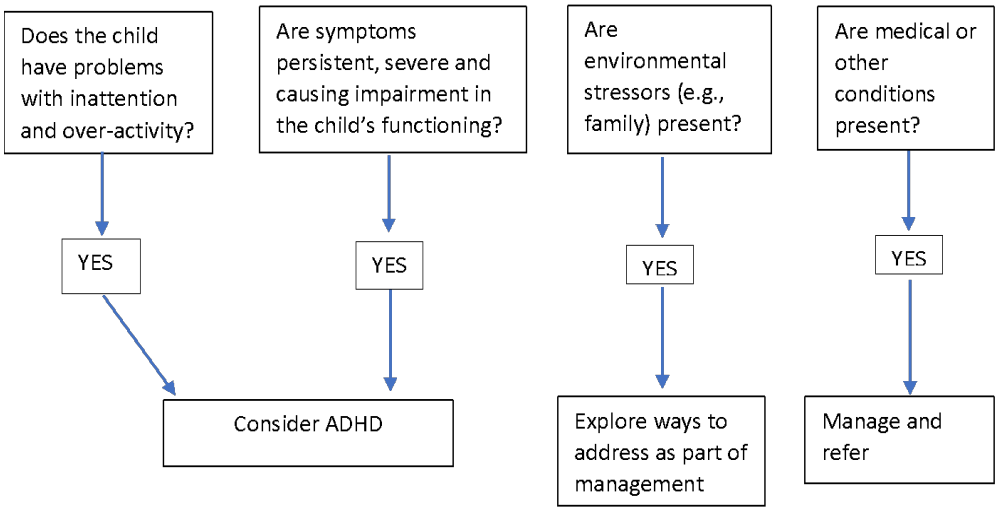

Figure 10.2: Assessment Algorithm for ADHD

Management

The aims of treatment in the child with ADHD are to reduce symptoms, improve educational outcomes and reduce family and school-based problems.

Non-Pharmacological Management

It includes school and home-based behavioural interventions. The parents and teachers should, therefore, receive psychoeducation and the child should be referred to a mental health service, as behavioural interventions are effective in mild-to-moderate cases.

Parents should receive management training and support. They must be taught to constructively deal with their child's behaviour, by teaching them how to positively

reinforce desirable behaviours and extinguish misbehavior. This is a first-line intervention for younger children and mild cases of ADHD.
One must also liaise with the school and, if appropriate, ask for extra help for the student e.g. sit the child in the front of class, give short tasks, give extra time to complete assessments.

Pharmacological
One may prescribe:

- Stimulant medications:
    - They have the best evidence of effectiveness in the management of the child with ADHD.
    - Short-acting oral methylphenidate may be prescribed by a general practitioner at a maximum dose of 1 mg/kg/day. Its effects last 3-4 hours.
    - Long-acting oral methylphenidate-long may be prescribed alone or with short-acting methylphenidate (if giving combined treatment, make sure that both doses do not exceed 1 mg/kg/day). Its effects last 6-8 hours.
    - Extended-release methylphenidate (e.g. Concerta® lasts ~12 hours and must be prescribed by a psychiatrist or paediatrician.
    - Common side effects of these drugs are nausea, weight loss, insomnia, and agitation. More serious side effects are tics, psychosis, elevated blood pressure and growth retardation.
- Non-stimulant medications:
    - They are less effective and may have adverse effects. Thus, they should only be prescribed when stimulants are not appropriate or not tolerated.
    - Atomoxetine is a selective norepinephrine reuptake inhibitor (SNRI) which is used as a second-line agent when there are serious side effects to methylphenidate (see related image here), comorbidities, risk of drug diversion and to treat comorbid anxiety. It must be prescribed by a psychiatrist.
    - Clonidine is an α_1- agonist and is a third-line agent which is specialist-initiated.

Referral
One should refer the child who:

- Is <7 years old and in whom one suspects ADHD
- Has shown no response to treatment after 8 weeks
- Has intolerable side effects to medication
- Has an uncertain diagnosis
- Has comorbid psychiatric conditions, including substance use
- Has uncontrollable seizures
- Is post TBI
- Is RVD positive

Prognosis
Up to 60% of ADHD cases will continue into adulthood, however the symptoms may vary with time.

ANXIETY DISORDERS

Children may suffer from anxiety disorders, such as separation anxiety disorder, specific phobia, generalised anxiety disorder, social anxiety disorder and panic disorder. Post-traumatic stress disorder and obsessive-compulsive disorder may also be diagnosed during childhood and adolescence. However, the DSM-5 no longer classifies these under anxiety disorders.

Definition

Fear is a reaction to a real threat, whereas anxiety is the cognitive, emotional and physiological reaction to a real or imagined threat. Both anxiety and fear can be adaptive. Many childhood anxieties are developmentally appropriate, thus it is important to keep the age and developmental stage of the child in mind.
An anxiety disorder may be diagnosed when the anxious reaction results in psychic distress and/or interferes with daily functioning. The fears and anxiety are usually out of keeping with the child's developmental stage.
Anxiety disorders are the most common psychiatric disorders in childhood and are associated with a poor quality of life, depression and social limitations. Often, children with panic disorders are labelled with treatment-resistant asthma.

Anxiety disorders are often comorbid with other anxiety disorders, depression or behavioural disorders, see related image here.

Classification and Clinical Features:

The child with anxiety will develop maladaptations, which are:

- Behavioural e.g. avoidance of situations that may result in the feared event
- Cognitive e.g. distress over a feared event that may occur
- Physiological e.g. autonomic symptoms of sympathetic nervous system

Clinical features specific to the anxiety disorder are shown in the table.

Table 10.3: Clinical Features of Various Anxiety Disorders

Anxiety Disorder	Clinical Features
Separation anxiety disorder	• Developmentally inappropriate and excessive worry of being separated from caregiver/attachment figure which occurs outside the developmental phase of separation anxiety and is present for >4 weeks • May lead to school refusal
Selective mutism	• Refusal/inability to speak in select situations (e.g. at school) which interferes with social relationships and educational achievement and is present for >4 weeks
Specific phobia	• Disproportionate fear of a specific situation or object for >6 months
Social anxiety disorder	• Excessive fear of social situations or being observed in public which is present for >6 months
Panic disorder	• Unprovoked panic attacks and/or fear of having a panic attack (after excluding a medical cause) which is present for >4 weeks
Agoraphobia	• Avoidance of public spaces, crowds or enclosed spaces for >6 months
Generalised anxiety disorder	• Severe worry about everyday tasks or situations which is present for >6 months

Aetiology

Anxiety disorders may develop because of:

- Witnessing abuse or violence
- Neglect

- Frequent relocation
- Serious illness in the child or caregiver
- School-related issues e.g. bullying, poor academic performance
- Death of a close relative
- Learnt fears
- Difficulties with primary attachment

One must get a detailed history from the child and parents as the anxiety may be warranted for the child's context e.g. abuse.

Management

Non-Pharmacological Management
This may include:

- Psychotherapy – it is important to psychoeducate the child and parents about anxiety and the appropriate management thereof; may be individual or group therapy
- Cognitive behavioural therapy (CBT)
- Skills-based programs – usually consist of psychoeducation, relaxation techniques, exposure, contingency management, cognitive restructuring, social skills, assertiveness training and parent training

Pharmacological Management
Medication is used in severe cases. One may prescribe:

- Benzodiazepines – short term; use with extreme caution in children and for no longer than 2 weeks as it can lead to paradoxical disinhibition and can potentially lead to dependence and avoidance of anxiety
- Antidepressants – long term; selective serotonin reuptake inhibitors (SSRIs) are generally used for anxiety (fluoxetine is the only SSRI licenced for use in children)

Referral
The child should be referred to a child and adolescent psychiatry service if s/he has a poor response to treatment, s/he has psychiatric co-morbidities, there is a need for diagnostic clarification or there is no access to psychotherapeutic services at primary or secondary healthcare levels.

Prognosis
These children are at higher risk for anxiety disorders, mood disorders, suicidality and substance use disorders in adulthood.

SUICIDE RISK ASSESSMENT

Suicidality in children may be underestimated as it may be misinterpreted as the child or adolescent is ‘seeking attention’ or ‘acting out’. Unless otherwise specified, suicidality is a broad term that refers to the cognitions, activities or behaviour of persons seeking their own death, including thoughts/ideations, utterances, threats, plans, intent, actions or omissions.
Whereas, suicidal behaviour refers to any behaviour that is often intentional, potentially harmful or lethal to the child. It is the result of psychological pathology or a reaction to adverse life events. Suicidal behaviour may also be a reaction to abuse (physical, emotional or sexual), neglect or poor home circumstances. This needs to be explored in detail in a child or adolescent who presents with suicidality.

Criteria and Clinical Features

The criteria for suicidality include:

- Suicide attempt within last 24 months
- Not attempted suicide in a state of cognitive impairment e.g. delirium, confusional state
- Does not meet non-suicidal self-injury criteria
- Not applied to suicidal ideation

The child may present with a history of:

- Well planned, lethal attempt
- Failed suicide attempt
- Unplanned, impulsive acts
- Threats of suicide

Associated Comorbidity

The child may have a psychiatric disorder at the time of the suicide attempt.
Common comorbid conditions include:

- Conduct disorders
- Major depressive disorder
- Eating disorder
- ADHD
- Personality disorders:
    - Although one cannot diagnose a personality disorder in someone <18 years, an adolescent can present with emerging traits of certain personality disorders e.g. borderline personality disorder.
- Traumatic stress disorders e.g. PTSD

The child may also have:

- Poor relationship with caregiver or parent
- Poor emotional support
- Experienced neglect
- Parent-child relational difficulties
- Experienced harsh, punitive or inconsistent discipline and boundary-setting by parents/caregivers

Management

Management should be individually tailored and should consider risk factors specific to individual patients. One must:

- Conduct a risk assessment – assess current severity and intensity of ideations and behaviour, lethality of plans and access to lethal means
- Take a detailed history of predisposing, precipitating, perpetuating and protective factors
- Identify comorbid depression, psychosis, substance abuse and conduct disorder
- Manage co-morbid conditions

The treatment plan should include psychotherapeutic, psychopharmacological and/ or social interventions to achieve relief from acute psychosocial stressors. However, the interventions employed will largely depend on the clinical services available.

Principles of Management

They include:

- Actively involving the patient and parent(s) in the planning and implementation of interventions
- Referral to child psychiatry
- Supporting the family through other issues e.g. divorce, parental mental illness substance misuse
- Organising support from social services and child welfare agencies, if indicated
- Organising relief from excessive demands e.g. school demands exceeding patients' current capacity
- Treating underlying psychiatric disorders
- Regularly monitoring for recurrence of suicidal behaviour
- Developing a post-discharge emergency and safety plan for an acute suicidal crisis
- Offering flexible treatment sessions (adapt time and frequency to the patient's needs)
- Developing strategies to improve adherence to treatment (short, accessible interventions)
- Effectively communicating with all the professionals involved (social worker, psychotherapist, child and adolescent psychiatrist, paediatrician or general practitioner)

See related image here.

Admission

Hospitalisation is generally indicated if:

- There is a high suicide risk, especially if there are no alternative ways of ensuring the patient's safety
- The patient has had a recent suicide attempt requiring intensive medical care
- It is not possible to reliably estimate suicide risk

Ideally, inpatient treatment of a child should be in a secure child psychiatry ward or paediatric ward and ensure close supervision, monitoring and support of the patient.

Non-Pharmacological Management
The child should be offered psychotherapy – CBT and dialectical behavioural therapy (DBT). DBT adapted for use in adolescents with suicidal behaviour involves training in mindfulness, interpersonal skills, emotion regulation, and stress tolerance. The parents should be involved in the psychosocial interventions and strategies to improve the parent-child relationships implemented e.g. improving problem solving within the family, parenting techniques and communication skills.
See related image here.

Pharmacological Management
There are no specific medications for suicidality. However, psychoactive medication may be needed to treat underlying psychiatric disorders. SSRIs may be prescribed to treat comorbid depression or anxiety. The caregiver and child must be educated on the potential side effects of SSRIs (e.g. increase in suicidal thoughts in the initial weeks of treatment) and the importance of close follow up.

AUTISM SPECTRUM DISORDER (ASD)

See the *Disorders of Development* chapter.

ENURESIS

It is the voiding of urine into clothing or in bed after the age of 4-5 years i.e. intermittent urinary incontinence.

Classification

It may be clinically classified as:

- Monosymptomatic:
    - The child has enuresis (diurnal or nocturnal) without daytime lower urinary tract symptoms.
    - This type of enuresis is more common in children >5 years old.
- Non-monosymptomatic:
    - The child has enuresis (diurnal or nocturnal) with daytime lower urinary tract symptoms e.g. urgency, incontinence, increased voiding frequency.

    - In these children, one must exclude serious pathologies, such as ectopic ureteric insertion and tethered cord syndrome.

Nocturnal enuresis may be primary (the child has never gained bladder control; more common) or secondary (the child had gained bladder control for >6 months but now has recurrent bedwetting). Nocturnal enuresis should not be over-investigated.

Aetiology

Causes or precipitating events include:

- Medical conditions:
    - UTI
    - Diabetes
    - Epilepsy
    - Bladder instability
    - Low bladder capacity
    - Nocturnal polyuria (decreased vasopressin levels at night)
    - Lack of arousal from sleep
    - Other neurological disorders
- Traumatic events in the child's life
- Birth of a new sibling
- Family relocation
- Parental separation
- Disturbed behaviour
- Depressed mood

Assessment

Evaluation should include:

- Detailed history (noting any social or psychological problems)
- Thorough physical examination
- Morning urine dipsticks (paying special attention to specific gravity)

Management

It includes:

- Non-pharmacological interventions:

- Increasing daytime fluid intake
- Treating constipation
- Restricting fluid intake near bedtime and avoiding caffeinated beverages
- Voiding the bladder before bed
- Increasing bladder capacity
- Dry bed training
- Following a quiet bedtime routine
- Using a night light and bedding protection
- Waking the child to urinate during the night (night-time lifting)
- Employing alarm therapy and a pad system (very effective but takes a few weeks to work)
- Positive reinforcement – reward the child for dry nights and self-arousal e.g. a star chart and rewards (an activity that child and parent enjoys doing together) for maintaining dryness; not a monetary reward or screen time
- Refer the child for psychological evaluation

See related image here.

- Pharmacological interventions (may be tried in the child <7 years old):
  - Imipramine (10-25 mg at bedtime; titrate up in older children) – there is a risk of cardiotoxicity
  - Desmopressin:
    - It may increase control when added to other drug therapies.
    - It can be kept for special occasions when bedwetting is particularly undesirable e.g. sleepovers.
    - It should not be taken with excessive amounts of water later in the day or in the early evening.
  - Oxybutynin hydrochloride (give early in the evening/with supper)
  - Tolterodine tartare (give early in the evening/with supper)

ENCOPRESIS

It is the (usually involuntary) voiding of faeces in inappropriate spaces (according to social or cultural norms) after the age of 4 years in a child who has obtained bowel control.

Aetiology

Causes include:

- Anxiety-related diarrhoea
- Psychological factors e.g. expressing anger, response to traumatic event

Assessment

A detailed history must be taken and medical/organic causes excluded e.g. Hirschsprung's disease, spina bifida, cord lesions, overflow incontinence in the chronically constipated patient.

Diagnostic Criteria

They include:

- Repeated passage of faeces in inappropriate places (involuntary or intentional)
- At least one such event a month for at least 3 months
- Chronological age ≥4 years (or an equivalent developmental age)
- Physiological causes or medical conditions have been excluded

Management

If a medical cause for the incontinence is found, it should be managed e.g. disimpaction and routine laxative therapy (polyethylene glycol, enemas) for the child with constipation. Behavioural therapy is effective (such as star charts). Parents must be educated on how to appropriately manage difficulties. The home circumstances must be assessed and prior history of traumatic events (including sexual abuse) elicited if present. The child should be referred to a child psychiatry and adolescent service if the encopresis is persistent.

OTHER PSYCHIATRIC DISORDERS TO RECOGNISE

Psychotic Disorders

Psychosis in children is very rare. It is most often due to a general medical condition that produces psychotic features e.g. epilepsy, head trauma, inborn errors of metabolism, delirium. Medical causes of psychosis and the effect of illicit substances and substance withdrawal need to be ruled out before psychosis is diagnosed.

Childhood-Onset Schizophrenia (COS)

It is the onset of schizophrenia before the age 13 years, whereas early-onset schizophrenia (EOS) refers to the onset of schizophrenia before 18 years of age. It tends to develop in children aged 5-12 years.

Diagnostic Criteria

The diagnostic criteria for COS are the same as for schizophrenia in adults:

- ≥2 characteristic symptoms:
    - These characteristic symptoms are hallucinations, delusions, disorganised speech, disorganised or catatonic behaviour and/or negative symptoms.
    - During the active phase, hallucinations, delusions, or disorganised speech must be present.
- Duration of at least 1 month (or shorter if successfully treated)
- Persistence of symptoms for at least 6 months
- Associated significant decline in functioning:
    - In children and adolescents, a decline in function may include the failure to achieve age-appropriate levels of interpersonal or academic development.

Perceptual disturbances are common. Auditory hallucinations are most common, however visual hallucinations are more common in children than in adults. Negative symptoms (amotivation, flat or blunted affect, poverty of speech and paucity of thoughts) and cognitive symptoms (impaired attention, memory and executive functioning) are very common and are usually the first to manifest (before hallucinations). Changes in mood, anxiety and agitation are also common.

Premorbid dysfunction, which may coexist, includes social withdrawal and isolation, disruptive behaviour problems, academic difficulties, speech and language problems, and cognitive delays.

Management
Antipsychotic medication is the primary treatment for schizophrenia spectrum disorders in children and adolescents. Maintenance medication is required to improve functioning and prevent relapse. In young people with treatment-resistant schizophrenia spectrum disorders, a trial of clozapine should be considered. Psychotherapeutic interventions should be implemented in combination with pharmacological interventions.
On follow-up, one must:

- Ask about medication-related adverse effects
- Ask about family history of cardiac disease or diabetes
- Repeat the physical examination, including height, weight, body mass index and waist circumference
- Perform laboratory investigations – FBC, urea, electrolytes, LFTs, fasting glucose and lipids (if on risperidone or olanzapine), and prolactin levels (if on risperidone)

Conduct Disorder

Definition
Conduct disorder is the persistent violation or defiance of age-appropriate norms, rules of society or expectations by a child over a 12-month period.

Diagnosis
The child with conduct disorder will:

- Show aggression towards people or animals e.g. violent behaviour, cruelty to animals (see related image here)
- Destroy property e.g. fire-setting, vandalism (see related image here)
- Be deceitful or steal (see related image here)
- Seriously violate rules e.g. stay out at night despite parental prohibitions, be truant

The child, caregivers and collaterals must be interviewed to obtain medical and social information. The above behaviours are displayed in the absence of a mood or psychotic disorder. It is particularly important to exclude abuse, maltreatment and neglect.

Comorbidity
Children with conduct disorder may also have:

- Learning problems
- ADHD
- Substance abuse disorder
- Antisocial behaviour

Management
The mainstays of management are family and behaviour therapy as well as parenting skills training. The child should undergo educational assessment and be offered school and emotional support. Placement in a child and youth care centre should be considered a last resort

Tic Disorders

Definition
A tic is a sudden rapid, recurrent, non-rhythmic vocalisation or purposeless motor movement. The tics are absent during sleep and are exacerbated by stress.

Classification
The child may have:

- Motor tics (facial, upper limb or torso tics are common) e.g. abnormal blinking, facial twitching, rude gestures
- Vocal tics e.g. shouts, repetition of specific words or phrases, swearing

Tic disorders may be classified as:

- Provisional tic disorder – single or multiple motor or vocal tics for <1 year
- Persistent (chronic) motor or vocal Tic Disorder – single or multiple motor or vocal tics for > 1 year
- Tourette's disorder – multiple motor tics AND one or more vocal tics for > 1 year; often associated with OCD or ADHD

Management
The child, family and teachers should receive psychoeducation and the former two provided with emotional support. The child should be referred to child and adolescent psychiatry services for habit reversal therapy and pharmacological intervention. The child may be started on a low-dose of a first-generation antipsychotic (e.g. haloperidol) or second-generation antipsychotic (e.g. risperidone).

Mood Disorders

Depression
Children with depression present slightly differently to adults with depression. The depression may be precipitated by bereavement or environmental stress (such as family break-up) and is often associated with anxiety disorders.

Clinical Features
The child may have:

- Depressed mood
- Irritability (may have angry outbursts)
- Sadness and misery
- Tearfulness
- Loss of energy
- Changes in feeding and sleep pattern (can manifest as FTT despite adequate food intake)
- Changes or deterioration in academic performance
- Anxiety and social withdrawal
- Self-blame and inappropriate feelings of guilt

Comorbidity
Common comorbid conditions include:

- Anxiety disorders
- OCD
- PTSD
- Conduct problems
- ADHD

- Learning difficulties

Management

One must perform a detailed assessment to exclude medical causes for this presentation e.g. vitamin B12 deficiency, hypothyroidism, sexually transmitted infections. Psychosocial stressors must be explored in detail with the child, caregivers and teachers and these stressors managed. A social worker referral should be performed, if necessary.

Family counselling should be performed, particularly psychoeducation surrounding the diagnosis. The child should be assessed for suicide risk and referred for psychotherapy, particularly CBT. Antidepressants may be started after excluding BMD and the child has been deemed a low suicidal risk

Mania and Bipolar Mood Disorder (BMD)

BMD can start in childhood but has higher prevalence rates in adolescence. They present with persistent and rapidly changing moods (depression and mania).

Clinical Features

The child may have:

- Elevated or irritable mood
- Grandiosity inconsistent with the child's development stage
- Hypersexuality unrelated to sexual abuse
- Decreased need for sleep
- Increased loquacity
- Flight of ideas or racing thoughts
- Distractibility
- Increased goal-directed activity or psychomotor agitation

Psychiatric Comorbidity

Comorbid conditions include:

- ADHD
- Disruptive behavior disorders
- Anxiety disorders
- Substance use disorders (in adolescents)

BMD is associated with fractured family and peer relationships, poor academic performance, chronic mood symptoms or mixed presentations, psychosis, suicide attempts and hospitalisations.

Assessment

One must assess if there is a family history of cardiac disease, diabetes or thyroid disease. Medical causes and the potential role of substances (both illicit and prescribed) must be excluded. A thorough physical examination should be performed, including height, weight, BMI and waist circumference. One should perform the following investigations:

- Pregnancy test (in adolescent females)
- Urine drug screen
- FBC
- RFTs
- TSH & free T4
- Calcium, magnesium and phosphate
- LFTs
- Lithium levels (if on lithium)
- Fasting glucose and lipids (if on risperidone or olanzapine)
- Prolactin levels (if prescribed risperidone)

Management

The child and caregivers must be provided with psychoeducation and advised on the importance of sleep hygiene and routine. They should be referred to a child and adolescent psychiatry service for further management. With acute episodes, one may treat the patient with a mood stabiliser e.g. second-generation antipsychotic, lithium or anticonvulsant.

Chapter 11:

NEUROLOGICAL DISORDERS

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This chapter covers the following topics:

- Non-accidental injury (NAI)
- Acute flaccid paralysis (ASD)
- Temper tantrums
- Night terrors
- Breath-holding attacks
- Microcephaly
- Hydrocephalus
- Movement disorders
- Seizure disorders
- Paediatric stroke
- Headache
- Myelomeningocoele/meningomyelocoele
- Spinal muscular atrophy (SMA)
- Neurocutaneous syndromes

NON-ACCIDENTAL INJURY (NAI)

It is a common problem and can be potentially life-threatening. Healthcare professionals have a duty to report any suspected or confirmed NAI to the relevant authorities e.g. senior clinical staff or child protection services.

Aetiology

NAI may be the result of maltreatment in the form of:

- Physical abuse
- Neglect
- Sexual assault
- Psychological abuse
- Medical abuse

Clinical Features

The child may present with:

- Pain
- Swelling
- Bruising
- Limping

Below (table 11.1) are some red flags which may indicate that the child has suffered an NAI:

Table 11.1: NAI Red Flags

Red Flags on History	Red Flags on Examination
● Variable/inconsistent history ● Injuries not consistent with history ● Delay in seeking treatment ● Multiple injuries ● Repeated admissions or presentations to the emergency unit ● Unexplained symptoms e.g. factitious	● Findings not in keeping with developmental age of child e.g. non-mobile child with bruising/fracture ● Bruises that resemble the shape of instruments or a hand ● Many bruises and bruises of different ages ● Bruises over soft tissue

	● Burns e.g. cigarette burns (common) ● Forced hot water immersion (will have glove and stocking distribution) ● Recurrent fractures (must exclude metabolic bone disease) ● Overbearing parent/guardian ● Fractures (especially metaphysical, posterior rib, skull, scapula or sternum) ● Retinal haemorrhage ● Signs of neglect

Investigations

They should include

- Skeletal survey (X-rays)
- CT scan
- Ophthalmologic assessment

Management

One must carefully record the child's injuries and contact the relevant authorities e.g. child protection services, senior staff, police.

ACUTE FLACCID PARALYSIS (AFP)

It is a clinical syndrome characterised by the rapid onset of weakness and reduced muscle tone without an obvious cause. Early diagnosis improves both morbidity and mortality.

Pathophysiology

The syndrome is the result of anterior horn cell injury which is usually secondary to viral infection (e.g. polio; however polio has nearly been completely eradicated) or immune-mediated peripheral pathologies.

Aetiology, Clinical Features and Investigations

Guillain Barré syndrome (GBS) is the most common cause of AFP in SA. It is classically preceded by a URTI and is characterised by symmetrical motor weakness of the lower limbs which ascends to involve the trunk and upper limbs to varying degrees. Fortunately, 80% of patients make a full recovery. Pertinent clinical signs include:

- Weakness of the limbs, face, bulbar muscles and respiratory muscles
- Reduced or absent reflexes
- Sensory loss in a glove and stocking pattern of distribution
- Autonomic instability (unstable BP, irregular HR, urinary incontinence)

An LP should be done as it will show isolated raised CSF protein in GBS and can be used to exclude other causes.

Management

One's immediate management priorities are to diagnose the child with AFP and provide:

    - Supportive management
    - Monitoring of respiratory status
    - Physiotherapy and occupational therapy (indicated in immobile children; help improve functioning)

IV gamma globulin is also used.

AUTISM SPECTRUM DISORDER (ASD)

See the *Disorders of Development* chapter.

TEMPER TANTRUMS

They are unpleasant and disruptive behaviours and emotional outbursts. They may be common in some communities and usually manifest between the ages of 15 months and 3 years.

Temper tantrums are associated with unmet needs or desires i.e. the child is not allowed to ‘have his/her own way’. They form part of the ‘negative stage of child development’ and are worsened by the child’s lack of vocabulary to fully express their feelings.

Clinical Features

Generally, the parent will give a history of the child lying down, kicking and screaming. The physical exam will be normal and is only done to reassure the parent.

Red flags include:

- Tantrums which worsen after 4 years of age (see related image here)
- Self-injury or damaging of property during the tantrum
- Breath-holding (especially if the child faints)
- Developmental regression
- Refusal to eat or sleep
- Headaches
- Development of anxiety

Management

Temper tantrums are usually a passing phase and these children generally respond well to counselling. Parents must be reassured and given encouragement. They should not reinforce the negative behaviour by acquiescing to the child, but need to be taught coping strategies. Principles of management include:

- Offering alternatives to the desired object or activity to avoid frustrating situations
- Ignoring or walking away from the child
- Not punishing the child (do not hit or argue with the child)
- Showing approval and giving attention when the child displays positive or acceptable behaviour
- Maintaining consistency

Problems occur when parental control is lacking or the family has a chaotic lifestyle. Important factors to consider when managing these patients are:

    - Child’s temperament

- Parent's temperament
- Inconsistency of the parent's behaviour towards the child

NIGHT TERRORS

This term refers to episodes when the child suddenly wakes up at night and is very upset.

Clinical Features

Night terrors generally occur during phase 3 non-REM (deep) sleep and usually occur early in the night. The episode tends to last 10-20 minutes and the child usually has 2-3 episodes weekly. Clinical features include:

- Screaming and jumping out of bed as if running away from something scary
- Hitting in all directions
- Having eyes wide open
- Disorientation on waking
- Failure to recognise someone who is trying to help him/her
- Failure to remember the episode the next day

Management

There is no specific treatment for night terrors. The child cannot be soothed during the episode but s/he will fall asleep after an episode. One must not try to wake the child.

If the night terrors take place at the same time every night, the child can be woken up 15 minutes before the time to try and prevent the episode. The child is then allowed to stay awake for a few minutes before falling asleep again.

BREATH-HOLDING ATTACKS

They are closely related to temper tantrums and are usually present between the ages of 6 and 18 months (rare in children >4 years).

Classification and Clinical Features

Breath-holding attacks may be of the cyanotic- or pale-type. Anoxia precipitates both types of attack and both types are associated with iron-deficiency anaemia.

- Cyanotic-type:
    - It is more common and is associated with temper tantrums. Episodes typically last 10-30 seconds.
    - The child's crying turns into hyperventilating and the child may become apnoeic and cyanosed. The child may even develop increased limb tone or clonic movements.
    - These clinical features cease when the child starts breathing normally. S/he will be apathetic but fully conscious afterwards.
- Pale-type:
    - It is associated with minor injury or fear.
    - The child develops severe pallor, bradycardia and may, in some instances, become asystolic (due to increased vagal tone).

Management

The parents must be reassured that the condition is benign and is unrelated to epilepsy. However, a full history must be done and thorough physical examination done. Iron-deficiency should also be corrected, if present.

ENURESIS

See the *Child and Adolescent Psychiatry* chapter.

ENCOPRESIS

See the *Child and Adolescent Psychiatry* chapter.

MICROCEPHALY

It is defined as an abnormally small head (head circumference >2 standard deviations below normal. Microcephaly (see related image here) may be isolated or

may be associated with congenital anomalies. It is a disorder of cell proliferation and brain growth as a whole is defective. The frontal lobes are usually more affected following perinatal insults. The cerebellum is usually relatively spared.

Aetiology

Causes of microcephaly include:

- Normal variant
- Hypoxic ischaemic encephalopathy (most common cause)
- Foetal alcohol syndrome (FAS) – see related features here
- Infections:
    - Toxoplasmosis
    - CMV
    - Zika virus
- Intrauterine growth restriction
- Inborn errors of metabolism
- Other genetic conditions

Clinical Features

The child may present with:

- Neurodevelopmental delay
- Hearing or vision problems
- Epilepsy
- Cerebral palsy

Management

No treatment is available to reverse microcephaly. Parents should be counselled and individual problems treated by the multidisciplinary team, such as audiology referral to manage for hearing impairment, and occupational therapist referral to teach the child skills which help him/her better integrate into society. Anticonvulsants may be prescribed for the child with seizures.

HYDROCEPHALUS

It is an abnormally large head with an increased CSF volume and/or pressure.

Pathophysiology

Hydrocephalus is the result of:

- Obstruction of CSF flow
- Overproduction of CSF
- Decreased absorption of CSF

Aetiology

Hydrocephalus may be caused by:

- Infection e.g. TB, other causes of meningitis
- Genetic factors
- Malignancy (rare)
- Trauma
- Congenital disease e.g. aqueduct stenosis, Arnold-Chiari Malformations

See related image here.

Clinical Features

The child may present with:

- Macrocephaly (diagnosed at birth or antenatally)
- Setting-sun eyes
- Bulging fontanelles
- Anorexia
- Vomiting
- Irritability
- Lethargy

Management

Serial head circumference measurements should be taken and plotted to track progression. The child should be referred early for the insertion of a shunt

(ventriculoperitoneal shunt or third ventriculostomy). Once a shunt has been placed, the child must be regularly followed up to ensure that it has been correctly inserted.

MOVEMENT DISORDERS

They include:

- Ataxia
- Chorea
- Dystonia
- Athetosis:
    - This term refers to slow, writing movements of limbs.
    - It may occur in patients with chorea or hypoxic ischaemic encephalopathy resulting in cerebral palsy.
- Tics (see *Child and Adolescent Psychiatry* chapter)
- Tremor:
    - A tremor is an involuntary, oscillatory movement with a fixed frequency.
    - One must exclude hypothyroidism.
- Myoclonus:
    - These rapid muscle jerks have decreased frequency and severity when the patient is asleep.
    - However, unlike tics, they do not disappear in sleep.

Ataxia

It is unco-ordination of postural control and gait, as well as unco-ordination of skilled movements involved in fine hand movements and speech.

Aetiology

Disturbances in cerebellar function generally lead to ataxia. One must be able to differentiate acute causes from chronic conditions.

- Acute causes:
    - Infection:
        - Viruses (which cause meningitis) e.g. VZV, coxsackie virus, Epstein-Barr virus, influenza, mumps, measles

        - Bacteria (which cause meningitis or cerebral abscesses) e.g. diphtheria, pertussis, typhoid, scarlet fever
    - Alcohol
    - Toxins or metabolic disease e.g. hypoglycaemia, lead, glue, mercury
    - Drugs e.g. phenytoin, carbamazepine, phenobarbitone
    - Posterior fossa tumours
    - Trauma (cerebellar haemorrhage)
    - Basilar migraine
    - Pseudo-ataxia (non-convulsive status epilepticus)
- Chronic causes may be perinatal or postnatal

Table 11.2: Perinatal and Postnatal Causes of Ataxia

Perinatal Causes	Postnatal Causes
• Birth asphyxia • Congenital malformations • Primary cerebellar hypoplasia • FAS • Friedrich's ataxia • Hydrocephalus • Meningitis • Metabolic disease (hypoglycaemia, hyperbilirubinaemia)	• Hypoxic insults • Hypoglycaemia • Thyroid deficiency • Chronic phenytoin use • Thiamine deficiency • Trauma • Genetic causes e.g. ataxia telangiectasia, Friedrich's ataxia

Clinical Features

The cerebellum matures with age, therefore signs which are considered pathological in the adult may be physiological in the child. Clinical features may include:

- Truncal ataxia – poor posture, exaggerated joint angles, head lag, truncal hypotonia
- Volitional ataxia – dysmetria, dysdiadochokinesia, nystagmus, dysarthria, staccato speech
- Hypotonia

Chorea

Choreas are rapid, brief, jerky movements that are irregular and unpredictable. They are often associated with hypotonia. It is thought that the caudate nucleus and subthalamic nuclei are involved in the pathophysiology of chorea.

One must always consider rheumatic fever as a cause of the chorea (Sydenham's chorea).

Sydenham's Chorea

It is characterised by abrupt, irregular and purposeless movements. ARF is the most common cause of acquired chorea in the young (see *Cardiovascular Diseases* chapter). Sydenham's chorea is common in the developing world.

Clinical Presentation

This major manifestation of ARF is characterised by:

- Insidious onset (4 months post initial infection)
- Migratory chorea
- Hypotonia
- Emotional lability
- Fidgeting

Management

One must investigate to exclude cardiac pathology. All affected children should be given penicillin V followed by prophylaxis, if ASOT titres and anti-DNAse levels are raised. The chorea is treated with the lowest-tolerated dose of haloperidol (see related image here) or with sodium valproate. The child should be referred to a paediatrician if his/her activities of daily living have been affected.

Dystonia

It is simultaneous, sustained contraction of agonist and antagonist muscles, leading to posture disturbances and involuntary movements of the trunk, limbs and face. These movements are slow, laboured and repetitive in nature (alternate between flexion and extension).

It may be caused by:

- Drugs e.g. haloperidol, metoclopramide
- Bilirubin encephalopathy:
    - Severe neonatal jaundice leads to the deposition of bilirubin in the basal ganglia (will see kernicterus on pathological examination).

- These children often present with dyskinetic movements.

SEIZURE DISORDERS

Seizures are caused by abnormal and excessive neuronal activity in the brain, and lead to transient signs and symptoms

Aetiology

Seizures may be caused by:

- Infection
- Hypoxia during gestation and/or after birth
- Intracranial haemorrhage
- Hypoglycaemia
- Drug withdrawal
- Developmental abnormalities

Diagnosis and Investigations

A seizure disorder may be diagnosed if the child has had >2 unprovoked seizures. However, a thorough and reliable history is very important, especially eyewitness reports (video footage can be very helpful). Other investigations which may be helpful include:

- Brain MRI (to look for lesions in the brain which may be causing the seizures)
- Electroencephalogram (EEG; can be used to rule-in seizures but cannot be used to rule them out)

See related image here.

Classification and Clinical Features

Seizure disorders may be classified into syndromes based on clinical features:

- Generalized seizures e.g. tonic-clonic, myoclonic, absence, atonic
- Focal seizures
- Other e.g. neonatal seizures
  - Neonatal seizures are subtle – due to relatively underdeveloped cortex

- Facial grimacing, nystagmus, sudden loss of time, eye blinking and chewing

Febrile Seizures

They are generalised seizures which occur because of an extracranial cause of fever. They affect children aged 6 months to 5 years and do not usually last longer than 15 minutes. There is often a family history of febrile seizures.

Classification

There are two categories of febrile seizures:

- Simple febrile seizures:
  - They are generalised seizures which last <15 mins and do not recur within a 24-hour period.
  - They are most commonly generalised tonic-clonic seizures.
- Complex febrile seizures:
  - They have a focal onset, last >15 mins and recur within 24 hours

Infantile Spasms

They mainly occur in children within the first year of life and are characterised by

- Epileptic spasms (flexor, extensor or mixed flexor-extensor spasms)
- Hypsarrhythmia on EEG

Aetiology

Causes of infantile spasms include:

- Neurocutaneous syndromes e.g. tuberous sclerosis
- Hypoxia
- Infections
- Trauma
- Hypoglycaemia
- Inborn errors of metabolism

When the diagnosis of infantile spasms is made, one must assess the child for West syndrome. West syndrome is diagnosed based on the presence of the following triad:

- Flexor or extensor spasms
- Hypsarrhythmia on EEG
- Mental retardation

Management

Infantile spasms are a neurological emergency, therefore an EEG must be urgently done. However, they are strongly resistant to conventional anti-epileptic treatment. The treatment of choice is with a combination of steroids and vigabatrin. Vigabatrin alone may be given to patients with tuberous sclerosis.

Table 11.3: Status Epilepticus

Status Epilepticus
It is an epileptic seizure which is sufficiently long or regularly repeated to produce a varying and enduring epileptic condition, in terms of convulsions or mental state i.e. the child has seizures lasting 30 mins or longer with no recovery of consciousness between seizures. Status epilepticus is common in the first two years of life.

General Management of Seizures

The aim of management is to maintain vital functions. Thus, one must identify the cause and treat it according to the relevant protocol.

General management principles include:

- Attempting to control symptoms with monotherapy (although resistant forms may need 2 or 3 anticonvulsants before control is gained)
- Gradually titrating up doses of new anticonvulsants (weekly)
- Monitoring the child for side effects

If one is unable to control seizures with the correct agent that is being given at the appropriate dose, the child should be referred to a paediatrician or paediatric neurologist.

Non-specialist management options may be grouped according to seizure type:

- Generalised or focal seizures – phenobarbitone, phenytoin (only use for status epilepticus in children), carbamazepine, sodium valproate
- Absence seizures – sodium valproate, ethosuximide
- Complex partial or focal seizures – carbamazepine, phenytoin

- Febrile seizures – diazepam (phenobarbitone and sodium valproate are seldom used for febrile seizures)
- Myoclonic seizures – sodium valproate, clonazepam

PAEDIATRIC STROKE

It may occur in a child with any of the following risk factors:

- Inflammation or infection e.g. meningitis (bacterial or mycobacterial), HIV
- Cardiac disease
- Haematological or thrombotic syndromes

Classification

Paediatric strokes may be classified according to

- Lesion type (haemorrhagic or ischaemic)
- Vessel type (arterial vs venous)

If the stroke is arterial, it may be further classified as embolic or thrombotic.

Aetiology

An ischaemic stroke may be the result of:

- Vascular disease:
    - Vasculopathies e.g. focal cerebral arteriopathy (may occur post-VZV infection)
    - Vasculitides e.g. meningitis, Takayasu's arteritis
- Intravascular disease:
    - Haematological conditions e.g. sickle cell, leukaemia, polycythaemia
    - Prothrombotic state, which may be due to:
        - Congenital conditions e.g. protein C or S deficiency, factor V Leiden mutations
        - Metabolic disease e.g. hyperlipidaemia, homocysteinaemia
- Embolic cause:
    - Congenital heart disease
    - Acquired heart disease e.g. rheumatic heart disease, infective endocarditis, prosthetic heart valve

A haemorrhagic stroke may be the result of:

- Vascular disease:
    - Congenital vascular anomalies e.g. arteriovenous malformation, venous angioma, cavernous malformation, intracranial aneurysm
    - Vasculopathies e.g. moyamoya disease, connective tissue disorders, sickle cell disease
- Intravascular disease (haematological disorders):
    - Idiopathic thrombocytopenic purpura (ITP)
    - Thrombotic thrombocytopenic purpura
    - Haemophilic states
    - Clotting factor deficiencies
    - Liver dysfunction
    - Vitamin K deficiency

Clinical Features

The child will present with a specific stroke syndrome based on the artery involved:

- Internal carotid artery:
    - Hemiplegia
    - Hemianopia
    - Aphasia (if the dominant hemisphere is affected)
- Middle cerebral artery (MCA):
    - Hemiplegia (arm and face are more affected than leg)
    - Hemianopia
    - Aphasia (if the dominant hemisphere is affected)
- Anterior cerebral artery (ACA):
    - Hemiplegia (leg is more affected than arm or face)
- Posterior cerebral artery (PCA):
    - Hemiparesis
    - Homonymous hemianopia
    - Ataxia
    - Vertigo
- Penetrating branches:
    - Pure motor involvement

    - Pure sensory involvement
    - Sensorimotor involvement
    - Speech involvement (occasional)

Approach

History

The child may present with:

- Sudden onset of neurological deficit (suggestive of an embolic event)
- Gradual onset of neurological deficit (suggestive of an arteriopathy or thrombotic event)
- History of recent illness (e.g. chicken pox) or trauma to the head
- Family history of young strokes

Examination

One must pay look for attention to:

- Changes in GCS
- Evidence of raised intracranial pressure
- Evidence of meningitis
- Neurological deficits (including aphasia/dysphasia)
- Evidence of bleeding abnormality or vasculitis
- Cardiovascular disease

Investigations

They should include:

- Blood tests:
    - FBC and differential count
    - ESR
    - Infection screen (HIV, TB, VZV, toxoplasma)
    - Hb electrophoresis (dependent on ethnic group)
    - Fasting lipogram
    - Lupus screen
- LP (to assess CSF for infection)
- Imaging:

- CT (to exclude haemorrhage and define the territory involved)
- MRI and magnetic resonance angiography (MRA)
- Conventional angiography

Differential Diagnoses

Paediatric stroke mimics include:

- Seizures and epilepsy (Todd's paresis)
- Migraine
- Psychogenic disease
- Inflammatory disease
- Intracranial infections
- Metabolic causes

Management

The aim of acute management is to preserve the penumbra. This is done by:

- Maintaining a low-to-normal body temperature
- Ensuring euglycaemia
- Maintaining good oxygen saturation
- Ensuring adequate cerebral perfusion

Secondary prevention should be started in patients with underlying cardiovascular disease. Start the child on anticoagulation with low molecular weight heparin. It is recommended that these children are managed in consultation with the relevant specialist (paediatric neurologist, haematologist or cardiologist).

Rehabilitation is multidisciplinary and should involve a physiotherapist, occupational therapist, audiologist and speech therapist. One must address issues with feeding, nutrition, pain, communication, mobility and positioning.

HEADACHES

Headaches are common in children and their frequency increases with age. Most headaches are benign. However, one must take a detailed history of the pain (SOCRATES) and ask about social and psychological factors.

Aetiology

Headaches may be caused by:

- Primary headache syndromes:
    - Migraine
    - Tension headache
- Secondary headache syndromes:
    - Sinusitis
    - Meningitis
    - Encephalitis
    - Hydrocephalus
    - Sleep apnoea or hypoventilation
    - Benign intracranial hypertension
    - Haematoma
    - Brain abscess
    - Brain tumour

Approach

One must rule out pathological causes of headaches by asking about the following danger signs:

- Headache which interrupts sleep
- Headache present on waking
- Visual disturbances
- Altered level of consciousness
- Focal neurological deficits
- Hypertension

If any of the above features are present, one must investigate further with:

- Lumbar puncture (to exclude meningitis)
- CT scan

Patients with danger signs and who cannot be managed at the primary care level should be referred to a paediatrician or paediatric neurologist.

MYELOMENINGOCOELE/MYELOMENINGOCOELE

A myelomeningocoele (see related image here) is a midline defect of the skin and vertebral arch which contains both meninges and neural tissue. The lumbosacral region of the spinal cord is the most commonly affected area. One must look for sensorimotor impairment as well as bladder and bowel incontinence.

Aetiology

The aetiology of myelomeningocoeles is poorly understood. However, evidence suggests that there is an association with inadequate levels of folate before conception and during the first trimester. There is an increased risk of recurrence in subsequent pregnancies.

Arnold-Chiari malformations are the most commonly associated congenital anomalies (lead to hydrocephalus).

Diagnosis and Investigations

Myelomeningocoeles may be diagnosed:

- In-utero via ultrasound (termination may be offered at this point)
- At birth

Once diagnosed, one should perform a CT scan and cranial USS (to assess initial ventricular size so that subsequent monitoring can be done).

Management

Prenatal counselling should

- Prenatal counselling

One should attempt to diagnose the condition early – in-utero or at birth. If diagnosed in-utero, prenatal counselling should be performed. If diagnosed at birth, one should initiate emergency management:

- Keep the defect and tissues sterile and moist (place saline-soaked gauze over the defect)
- Refer the child for urgent surgical correction (within 48 hours of delivery)

Associated abnormalities must then be excluded. A multidisciplinary team must be involved in the care of this child (neurologist, orthopaedic surgeon/neurosurgeon, physiotherapist, urologist).

MENINGITIS

See *Infectious Diseases* chapter.

SPINAL MUSCULAR ATROPHY (SMA)

It is an autosomal recessive disorder which is characterised by progressive hypotonia and muscular weakness. It is a common genetic cause of mortality in children, with males being affected more commonly than females (2:1). There is a high prevalence in Central and Eastern Europe.

Pathophysiology

The primary pathology involves progressive degeneration of α-motor neurons on anterior horn cells in the spinal cord. This is caused by a mutation in the gene responsible for the survival of motor neurons.

Clinical Presentation

The child will present with:

- Abnormal posture (pronated arms)
- Proximal weakness with atrophy
- Cranial nerve involvement, especially bulbar signs (in some patients) e.g. tongue fasciculations
- Reduced tone
- Areflexia
- Bell-shaped chest
- Normal sensation
- Normal intelligence
- Sparing of involuntary muscles (heart, sphincters, GIT)

Classification

SMA is classified into four types according to the age of onset of clinical features and most advanced physical milestone achieved:

- Type 1 – the children typically present within the first six months of life; they are unable to sit unsupported
- Type 2 – the children typically present at 3-15 months old; they are able to sit without support but are never able to stand or walk
- Type 3 – the children typically present between 18 months old and adulthood; they achieve independent ambulation
- Type 4 – the patient presents after 30 years of age (latest onset disease); all motor milestones have been achieved and independent ambulation is usually maintained through life

The prognosis is worse the younger the age of onset is. The median age of death is 10 years old and is normally due to respiratory compromise.

Management

Children with SMA are all affected differently, therefore treatment should be catered to the individual. Management is mainly supportive and involves a multidisciplinary team (pulmonologist, orthopaedic surgeon, nutritionist, genetic counsellor, social worker, occupational therapist, physiotherapist and orthotist). Surgical interventions are considered to treat scoliosis, contractures and fractures.

Thus far, no cure has been found but research is ongoing. Currently, scientists are looking at inhibitors of GABA synthesis and genetic therapy which attempts to fix/replace the affected gene.

NEUROCUTANEOUS SYNDROMES

They are congenital disorders that are due to genetic changes. Tissues and organs derived from the ectoderm are generally affected (i.e. skin, nervous tissue, eyeballs and retina), however bones and visceral organs may also be affected. The conditions evolve slowly throughout childhood and the lesions have malignant potential.

Diagnosis

Neurocutaneous syndromes may be diagnosed based on the results of:

- Genetic tests
- MRI scan
- CT scan
- EEG
- Eye exam
- Lesion biopsy

Classification

Neurocutaneous syndromes include:

- Tuberous sclerosis
- Sturge-Weber syndrome
- Neurofibromatosis

Tuberous Sclerosis

It is an autosomal dominant with variable expression. Features evolve as the child grows. It is diagnosed based on the presence of two major features, or one major feature and two minor features. TSC1 gene mutations are familial and TSC2 gene mutations are associated with adult polycystic kidney disease.

Sturge-Weber Syndrome

In this syndrome angiomas cross the leptomeninges and involve the skin of the face, producing a characteristic skin lesion (typically in the ophthalmic or maxillary region of the trigeminal nerve). The associated mutation is sporadic and there are three subtypes of the syndrome.

Affected children may present with:

- Facial naevus (port wine stain)
- Seizures
- Hemiparesis
- Hemianopia
- Headaches
- Glaucoma

- Learning difficulties
- Developmental delay

Neurofibromatosis (NF)

There are two types – NF 1 and 2. Males and females are equally affected (1:1) in both types (see related image here).

Neurofibromatosis Type 1 (Nf1)/Von Recklinghausen's Disease

This is an autosomal dominant condition which is more common than NF2. The child may present with:

- Cafe-au-lait spots
- Benign tumours – neurofibromas (see image linked above)
- Lisch nodules
- Seizures
- Scoliosis
- Facial pain
- Numbness
- Variable degree of intellectual disability
- Attention deficit disorder

NF1 is diagnosed based on the presence of specific diagnostic criteria:

- First-degree relative with confirmed NF1
- ≥6 café-au-lait spots
- Neurofibromas
- Optic glioma
- Axillary freckling
- Lisch nodules
- Bone lesions e.g. sphenoid dysplasia

Neurofibromatosis Type 2 (Nf2)

The child may present with:

- Hearing loss (due to vestibular schwannomas)
- Meningiomas
- Spinal tumours

- Neuropathies
- Headaches
- Facial pain
- Problems with balance and walking
- Neurofibromas
- Café-au-lait spots

Management

There is no cure for neurocutaneous syndromes. Management depends on the individual child's needs and requires input from a multidisciplinary team:

- Paediatric neurologist
- Plastic surgeons
- Genetic counsellor
- Neurosurgeon
- Ophthalmologist
- Dermatologist
- Oncologist
- Occupational therapist
- Speech therapist
- Physiotherapist

CEREBRAL PALSY

See *Disorders of Development* chapter.

Chapter 12:

MUSCULOSKELETAL DISORDERS

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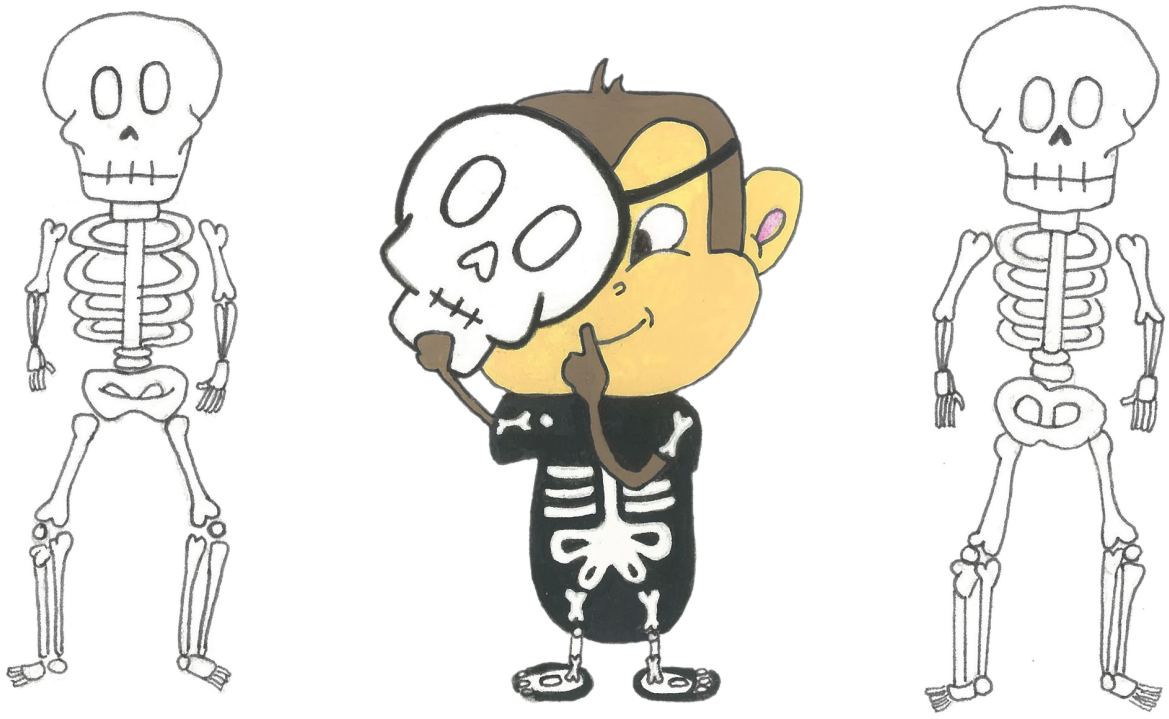

This chapter covers the following topics:

- Juvenile idiopathic arthritis (JIA)
- In-toeing/pigeon-toeing
- Genu valgum (knock knees)
- Genu varum (bow legs)
- Septic arthritis
- Osteomyelitis
- Systemic lupus erythematosus (SLE)
- Congenital myopathies
- Duchenne muscular dystrophy (DMD)
- Perthes disease
- Slipped upper femoral epiphysis (SUFE)
- Juvenile dermatomyositis (JDM)

JUVENILE IDIOPATHIC ARTHRITIS (JIA)

It is a chronic (>6 weeks duration) inflammatory condition which develops in children <16 years old. It develops in the absence of infection and has no known cause.

Pathogenesis

The pathogenesis of JIA is unclear, however there are multiple factors that interact and contribute to its development:

- Genetic factors – certain genetic sequences predispose families to JIA
- Immune mechanisms – many human leukocyte antigen (HLA) classes contribute to JIA e.g. HLA-DR8, HLA-DR11
- Environmental factors – it has been theorised that certain infections (e.g. rubella, EBV, *C. trachomatis*, influenza A) contribute to the development of seasonal JIA

Clinical Features

Generally, the child with JIA may present with:

- Joint symptoms and signs:
    - Pain
    - Early morning stiffness
    - Gelling (stiffness especially after periods of immobility e.g. after sleeping or long drives)
    - Swelling and inflammation of the joint with thickening of the synovium
    - Swelling of the soft tissues surrounding the joint
- A change in walking style (development of a limp)
- Mood and behavioural changes
- Decreased enjoyment of usual activities and avoidance of certain physical activities

Investigations

One should order:

- Blood tests:
    - FBC
    - ESR and CRP

    - Rheumatoid factor (RF), ANA and anti-cyclic citrullinated peptide antibodies (anti-CCP)
    - Hb
    - HIV
    - Liver enzymes (to check liver function before therapy is initiated)
- Mantoux test
- Imaging:
    - Chest X-ray
    - X-ray of the affected joint(s)
    - Ultrasound
    - MRI

Classification of JIA

There are at least six different subtypes of JIA:

- Oligoarticular JIA (involves of ≤4 joints; has a good prognosis)
- Polyarticular JIA (involves >4 joints)
- Systemic JIA (arthritis is associated with fever and rash)
- Psoriatic arthritis
- Enthesitis-related arthritis (ERA)
- Unclassified arthritis (does not fit into any of the abovementioned subtypes)

Table 12.1: Classification and Features of JIA

JIA Subtype	Age of Onset	Sex ratio (F:M)	Articular pattern	Extra-articular features	Laboratory Findings
Oligoarticular JIA	1-4years	4:1	Involves ≤4 joints (usually knee, ankle or wrist). >4 joints may be involved after 6 months (extended oligoarticular arthritis).	Chronic anterior uveitis (in 20% of cases) and leg length discrepancy.	70% of patients are ANA-positive. Acute phase reactants (APRs) and platelets may be raised.
RF-positive polyarthritis	1-3 years	3:1	Involves the small joints of the hand (including the distal	Iridocyclitis.	APRs and platelets are elevated

			interphalangeal (DIP) joints.		RF-negative but ANA-positive in 40% of cases.
RF-negative polyarthritis	Late adolescence	6:1	Widespread joint involvement. Symmetrical small joint involvement but with sparing the metacarpophalangeal (MCP) joints.	Iridocyclitis is not a feature.	Elevated APRs, anaemia, RF-positive (on two occasions) and anti-CCP-positive.
Systemic JIA	1-10 years	1:1	Initially no arthritis (just arthralgia or myalgia), but then oligo- or polyarthritis.	Fever with evanescent rash, lymphadenopathy, serositis and hepatosplenomegaly.	Raised APRs, neutrophilia, thrombocytosis and anaemia. RF-negative.
ERA	6-16 years old	1:7	Arthritis or enthesitis of the sacroiliac joint, inferior pole of patella, Achilles tendon or plantar fascia insertion into the calcaneus.	Sacroiliitis or lumbosacral pain, first-degree relative with ERA or ankylosing spondylitis and anterior iridocyclitis.	HLA-827-positive, elevated ESR and anaemia.
Psoriatic arthritis	1- 16 years old	2:1	Similar to oligoarthritis	1. Dactylitis 2. Nail abnormalities 3. Family history of psoriasis 4. Iridocyclitis	RF-negative. Half of patients are ANA-positive.

Management

Non-Pharmacological Management

The patient, his/her parents and teachers must be counselled and educated on the condition.

Referrals to a physiotherapist and occupational therapist should be made.

Pharmacological Management

The patient should be prescribed:

- Non-steroidal anti-inflammatories e.g. ibuprofen, diclofenac
- Intra-articular steroid injections
- Oral steroids (start at 1 mg/kg and increase until effective then attempt to taper to the lowest possible dose)

If symptoms and signs are not controlled on the above treatment, one should prescribe disease-modifying anti-rheumatic drugs (DMARDs) e.g. methotrexate 0.4 mg/kg orally or subcutaneously. If control is still not gained, refer for specialist opinion (will likely start biological agents e.g. anti-tumour necrosis factor/TNF).

Complications

They may include:

- Chronic anterior uveitis:
    - Children with JIA should have regular ophthalmology appointments, especially if they have oligoarticular JIA and are antinuclear antibody (ANA)-positive.
- Flexion contractures of the joints:
    - They develop because the joints are chronically held in the most comfortable position to minimise pain.
- Growth failure:
    - It occurs because of anorexia, chronic disease and systemic corticosteroid use.
- Leg length discrepancy (due to overgrowth of a localised area)
- Osteoporosis:
    - It is caused by systemic corticosteroid use, poor diet and decreased weight-bearing.

IN-TOEING/PIGEON-TOEING

Pathophysiology and Aetiology

The abnormal positioning of the leg may be due to:

- Femoral anteversion:

    - Normal children are born with ~40º femoral anteversion but this gradually corrects as the child grows.
- Internal/medial tibial torsion:
    - It is a variation of normal anatomy and is partially caused by the child's position in-utero.
- Metatarsus adductus (inward curving of the foot):
    - Its exact cause is unknown, however it is believed to be due to in-utero positioning.

Thus, the cause of the in-toeing may be at the hips, legs or feet, respectively.

Clinical Features

The child will have his/her:

- Feet turned inwards when walking
- Patella face inwards when standing with the feet facing forward

'W' sitting position is more comfortable for the child.

Management

It is rarely treated. However, one may offer:

- Conservative management:
    - Reassure and observe.
    - Encourage the parents to gently stretch the foot of the child with metatarsus adductus to neutral a few times a day.
    - Suggest that the parents buy the child straight-last/reverse-last shoes
- Surgical management:
    - Refer the child to an orthopaedic surgeon for femoral anteversion (derotational femoral osteotomy; not to be done before 8 years of age).

GENU VALGUM (KNOCK KNEES)

Aetiology

Genu valgum may be part of normal growth and development or it could be a sign of an underlying bone disease e.g. osteomalacia, rickets (due to a lack of calcium, phosphorus or vitamin D). Occasionally, it may be the result of injury to the tibial growth plate. It is important to differentiate the above mentioned causes from

obesity-related genu valgum. However, obesity can worsen genu valgum in patients with any of the abovementioned causes.

Clinical Features

When standing, the child's knees will touch (symmetrically lean inward) but the ankles will not touch (in a child with an average weight). This is best seen with the child's toes pointed forward.

Management

Management may be:

- Conservative:
    - Reassure the parents and observe the child who is 2-5 years old.
    - Suggest splints or braces if the genu valgum (see related image here) does not spontaneously correct by the age of 7 years or if there is an underlying systemic or metabolic cause.
- Surgical:
    - Refer the child to an orthopaedic surgeon who will perform a guided-growth procedure (done if significant deformity persists to the age of 10-11 years) (see related images here).

GENU VARUM (BOW LEGS)

Pathophysiology

It is mostly physiological in children under 2 years. However, it may be the result of an underlying condition e.g. Blount's disease (caused by an abnormality of the tibial growth plate), rickets.

Clinical Features

Either or both legs may be affected. The child will have a distinct space between the lower legs and knees when standing with his/her feet together. This bowing is exaggerated by walking (see related image here). Adolescents with Blount's disease will have pain associated with the bowing.

Investigations

One may perform:

- Blood tests:
    - Calcium, phosphorus, parathyroid hormone and, when indicated, vitamin D studies
    - Urinary pH and renal function tests (to assess for rickets)
- X-ray

Management

It may be:

- Conservative:
    - Reassure and observe
    - Give braces for Blount's disease (if caught early)
- Medical:
    - Vitamin D supplementation for the patient rickets
- Surgical:
    - Refer to an orthopaedic surgeon if:
        - Rickets persist despite treatment.
        - The child has physiological genu varum which is severe and is not correcting with time.
        - The child has Blount's disease which is worsening despite the use of braces or if the diagnosis is only made in adolescence.

SEPTIC ARTHRITIS

It is a serious infection as it can lead to bone destruction. Infection of the joint can be caused by bacteria, fungi, viruses or mycobacteria.

Pathophysiology and Aetiology

It is most common in children <2 years old and usually spreads to the joint:

- Haematogenously
- Through a wound or infected skin (VZV infection)
- From adjacent osteomyelitis

S aureus is the most common cause of septic arthritis. Organisms implicated in neonatal septic arthritis are group B streptococci, *N. gonorrhoea* and Gram-negative bacilli.

Clinical Features

The child may present with a history of trauma or underlying osteomyelitis. On examination, one may find:

- Signs of inflammation of the involved joint (swelling, tenderness and limited mobility of the joint) (see related image here)
- Maintenance of the joint in a specific position, decreased mobilisation of that joint and refusal to weight bear
- Neonates and young infants:
    - Subtle signs and symptoms
    - Involvement of >1 joint
- Older children and adolescents:
    - Pain on active and passive movement (key feature)
    - Constitutional symptoms e.g. fever, irritability, poor appetite, tachycardia, malaise

*Note***:** If more than one joint is involved, then the diagnosis of septic arthritis needs to be reviewed.

Investigations

They should include:

- Bloods tests:
    - FBC with differential count
    - CRP and ESR
    - Blood culture
- Joint aspiration and analysis of synovial fluid:
    - FBC and differential count
    - Microscopy, culture and sensitivity
- Imaging:

- X-ray of the joint (to exclude any fractures and identify capsular swelling)
- Ultrasound or MRI (to detect joint effusions)

Management

Diagnosis and management should be carried out quickly and efficiently to prevent long- term damage to bones and joints. The child should be managed in conjunction with an orthopaedic surgeon. Management includes:

- Arthrocentesis:
  - It is the cornerstone of management.
  - The joint should be drained and a lavage done via arthrotomy, arthroscopy or needle aspiration.
- Antibiotic therapy:
  - Empiric antibiotic therapy should be given as soon as possible, if the child has any of the classical signs of infection and positive blood results.
  - The antibiotic should cover for *S. aureus* in all age groups and any other relevant organisms depending on the child's age.
  - If the child is <3 months old, the antibiotic should cover for *S. aureus*, group B streptococci and Gram-negative bacilli.
  - If the child is ≥3 months, the antibiotic should cover for *S. aureus* and Gram-positive organisms.

OSTEOMYELITIS

It is inflammation of the bone and is usually caused by bacterial infection (see related image here).

Pathophysiology

In children, the infection is spread haematogenously but can be spread from other sources as well. This is because there is a rich vascular supply to the bones as they are still growing. Circulation within the metaphyseal capillary loops is sluggish, which is why infection tends to start there. Commonly affected bones include the femur, tibia, and humerus.

Aetiology

Common causative organisms include *S. aureus*, *S. pneumoniae and S. pyogenes.* Other causes include *Pseudomonas aeruginosa*, fungi (in the immunocompromised patient), *Salmonella* sp (in sickle cell anaemia and other haemoglobinopathies).

Clinical Features

The child may have:

- Cardinal signs of inflammation (fever, bone pain, swelling and erythema)
- Guarding
- Inability to weight-bear
- Asymmetrical movement of the limbs (pseudoparalysis; an early sign in neonates and young infants)

Investigations

One must exclude cellulitis, subcutaneous abscess, fractures and bone tumours. Thus, the following investigations are done:

- Bloods:
    - FBC
    - CRP and ESR
    - Blood culture or bone/joint aspirate culture
- Imaging (MRI or X-ray)

Management

The patient should be started on antibiotics (after taking samples for the lab). Cloxacillin is usually given or vancomycin may be given if the child has a penicillin allergy.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

SLE is an autoimmune, inflammatory condition that leads to the damage of essential organs. Its natural history is unpredictable as patients may present with chronic symptoms or acute life-threatening disease. Its cause remains poorly understood.

Clinical Features and Complications

The child may present with:

- Haemolytic anaemia, thrombocytopaenia, leukopaenia, or lymphopaenia
- Nephrotic or nephritic syndrome
- Psychosis, seizures, cognitive disorders or peripheral neuropathies
- Pulmonary haemorrhage, fibrosis or infarct
- GIT manifestations
- Serositis
- Arthritis
- Endocrinopathies
- Cardiac abnormalities
- Rash (malar, annular, discoid, psoriasiform, etc.)

See related image here.

Diagnosis

The Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria are used to diagnose SLE. For the diagnosis to be made, the patient must have:

- ≥4 criteria (of which there is at least 1 clinical criterion and 1 laboratory criterion) OR
- Biopsy-proven lupus nephritis with a positive ANA or anti-doubled stranded DNA antibody (anti-dsDNA) result

Table 12.2: SLICC Classification Criteria

Clinical Criteria	Laboratory Criteria
• Acute cutaneous lupus • Chronic cutaneous lupus • Oral or nasal ulcers • Nonscarring alopecia • Arthritis • Serositis • Renal dysfunction • Neurological symptoms • Haemolytic anaemia • Leukopenia • Thrombocytopenia (<1 000 000/mm^3)	• Positive ANA • Positive anti-dsDNA • Positive anti-Smith antibodies (anti-Sm) • Positive antiphospholipid antibodies • Low complement (C3, C4 or CH50) • Positive direct Coombs test (unreliable in the presence of haemolytic anaemia)

Investigations

See table 12.2 above for guidance on which investigations to order.

Management

The patient should be referred to a tertiary care facility. Management depends on the organ involved and the severity of its involvement. Non-pharmacological management includes dietary restrictions driven by the patient's medical therapy and pharmacological management ranges from NSAIDs and steroid therapy to cyclophosphamide.

CONGENITAL MYOPATHIES

Congenital myopathies are a heterogenous group of primary muscle disorders. Although they are present from birth, their expression may be delayed.

Pathophysiology

In these children, the muscle fibres do not function properly, leading to muscle weakness and/or hypotonia. The weakness is either stable or slowly progresses.

Clinical Features

The child may present with:

- Decreased facial animation (myopathic facies)
- External ophthalmoplegia (in some cases)
- Bulbar dysfunction e.g. poor cough, soft voice
- Hypotonia with head lag
- Proximal muscle weakness
- Decreased tendon reflexes
- Delayed motor milestones
- Normal intelligence

In some cases, distal muscles are affected, however myopathy usually affects proximal muscle more than distal muscles. Respiratory muscle is almost always affected. This usually occurs later in the disease.

Investigations

One should perform:

- Muscle biopsy
- Genetic testing
- Creatine kinase (CK) levels (usually distinguish myopathy from dystrophy)

Management

Although there is no known cure for congenital myopathies, symptomatic management is offered and patients should have regular consultations with specialists (such as orthopaedics and pulmonologists) to assess the progression of the disease. Rehabilitation with physiotherapists, speech and language pathologists and occupational therapists can help manage symptoms. Low-impact exercises can help maintain muscle bulk and strength e.g. swimming, walking.

DUCHENNE MUSCULAR DYSTROPHY (DMD)

It is an X- linked recessive disorder that results in progressive degeneration of muscle (see related image here).

Pathophysiology

Dystrophin connects the cytoskeleton of a muscle fibre to the extracellular matrix through the cell membrane. In DMD, there is a deletion in the dystrophin gene. It results in myofiber necrosis with an elevated creatine kinase (CK).

Clinical Features

The history may allude to the fact that there is a familial pattern of DMD. The child may present with:

- Proximal muscle atrophy with pseudohypertrophy of the calves
- Contractures
- Scoliosis (common complication)
- Decreased tone
- Proximal muscle weakness
- Decreased or absent reflexes

- Gait abnormalities (waddling)
- Positive Gowers's sign (the child must turn prone to rise after lying supine)
- Bulbar dysfunction (later in disease)
- Respiratory muscle weakness
- Cardiomyopathy with displaced apex (may also have a loud P2)
- Language delay (may or may not be present)
- Inability to perform certain physical activities e.g. climbing stairs, running (usually much slower and clumsier than other children in their age group)

These children have decreased life expectancies because of respiratory failure or associated cardiomyopathy. Due to the progressive nature of the disease, the average age of diagnosis is 5 years old and most children are no longer ambulant by 10-14 years old.

Investigations

They should include

- CK levels (usually elevated)
- Genetic analysis (for depletions, duplications or point mutations)

Management

The child should be managed by a multidisciplinary team:

- Physiotherapists (can help prevent the development of contractures)
- Cardiologists (initiate the patient on enalapril and regularly monitor his/her ejection fraction)
- Surgeons (may perform Achilles tendon lengthening and scoliosis surgery)

Due to the respiratory muscle weakness, children with DMD may develop nocturnal hypoxia and may require overnight CPAP to improve breathing.
Glucocorticoids may be prescribed as they also help preserve mobility and prevent scoliosis. However, their exact mechanism of action is not known. Glucocorticoids have also been shown to benefit cardiac muscle function.

PERTHES DISEASE

It is more common in males (M:F = 5:1) and mainly affects children 5-10 years old.

Pathophysiology

There is avascular necrosis of the epiphysis of the femoral head due to loss of the blood supply. This is followed by revascularisation and re-ossification.

Clinical Features

They are usually insidious. The child will usually present with hip or knee pain and/or limp of acute onset. The disease is bilateral in 10-20% of cases.

Investigations

One should request a frog-leg lateral X-ray of both hips. The X-ray will show increased density, flattening, sclerosis and fragmentation of the femoral head.

Management

It includes rest, physiotherapy (to increase hip movement) and, in some cases, traction, casts or surgery.

SLIPPED UPPER FEMORAL EPIPHYSIS (SUFE)

It is defined as displacement of the femoral epiphysis from the femoral neck along the physeal plate.

Aetiology

The displacement is caused by a force exerted on the femoral head which exceeds the strength of the femoral physis. Factors which contribute to the weakening of a weak femoral physis include:

- Normal periosteal thinning and widening of the physis
- Trauma
- Obesity
- Inflammatory changes
- Genetic predisposition
- Irradiation (as in cancer patients)
- Endocrine abnormalities (hypothyroidism and hypogonadism)

Clinical Features

The child may present with limb or hip pain which may be referred to the knee. On examination, one will find restricted abduction and internal rotation of the hip.

Investigations

A frog-leg lateral X-ray of the hips will show the slipped upper femoral epiphysis.

Management

These patients are managed surgically with pin fixation.

JUVENILE DERMATOMYOSITIS (JDM)

It is an autoimmune myopathy which is primarily caused by a capillary vasculopathy. It is 2-5 times more common in females than males,

Pathophysiology and Causes

JDM is associated with systemic vasculopathy and is sometimes associated with occlusive arteriopathy and capillary necrosis, which eventually lead to capillary loss and tissue ischemia. As with adult dermatomyositis (see images of dermatomyositis here and here), it is likely an antibody-dependent, complement-mediated disease in which capillary injury results in muscle fibre atrophy.

Although the aetiology remains unclear, it has been proposed that JDM is caused by an autoimmune reaction in genetically susceptible individuals, possibly in response to infection or environmental triggers e.g. prenatal exposure to tobacco smoke and particulate inhalants. Thus, it may be the result of:

- Genetic susceptibility
- Immunological mechanisms
- Infection

Clinical Presentation

The child will present with:

- Muscle weakness (symmetrical muscle weakness that is more apparent proximally than distally)

- Heliotrope discoloration of the eyelids and malar or facial erythema
- Scaly, red rash on the knuckles with Gottron papules (erythematous, papulosquamous eruption over the dorsal surfaces of the knuckles)
- Constitutional symptoms (fever, weight loss, fatigue and headache):
    - They may be the initial finding prior to the onset of muscle weakness and rash.
- Nonerosive arthralgia and arthritis
- Lipodystrophy

Investigations

One should perform:

- Biopsy of affected skin:
    - The hallmark biopsy finding in JDM is perifascicular atrophy.
- Elevated serum muscle enzyme levels (CK, LDH, aldolase, ALT, AST):
    - This is indicative of muscle damage and is common in JDM.

Management

Mild-to-moderate disease may be managed with oral prednisone or steroid sparing drugs e.g. methotrexate. Severe or life-threatening disease may be managed with IV methylprednisolone or IV cyclophosphamide.

Chapter 13:

DERMATOLOGICAL CONDITIONS

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This chapter covers the following topics:

DESCRIBING SKIN LESIONS

Skin lesions may be primary or secondary. They may be further categorised according to the arrangement or distribution e.g. sun-exposed areas.

Primary Skin Lesions

They may be:

- Flat or raised
- Solid or fluid-filled (if raised)

Flat Lesions

Macules are well-circumscribed, flat, non-palpable lesions that are <1 cm in diameter. Patches are well-circumscribed, flat, non-palpable lesions that are >1 cm in diameter, see related image here.

Raised Lesions

They may be:

- Solid lesions (well-circumscribed, raised, palpable lesions which extend into the dermis or subcutaneous tissue):
    - Papules – solid lesions <1 cm in diameter
    - Plaques – flat-topped lesions >1cm diameter (see related image here)
    - Nodules – dome-shaped lesions >1cm diameter (see related image here)
- Fluid-filled:
    - Vesicles – well-circumscribed, raised lesions <1cm diameter which are filled with clear fluid (see related images here)
    - Bullae – well circumscribed, raised lesions >1cm diameter which are filled with clear fluid
    - Pustules – well-circumscribed, raised lesions <1cm diameter which are filled with pus

Secondary Lesions

They include:

- Scale – accumulated fragments of stratum corneum produced from shed skin
- Crust – dried serum, blood or pus

- Erosion – open area of the skin which is the result epidermal loss
- Fissure – linear, open area of the skin which is the result epidermal loss
- Ulcer – irregular, open area of the skin which is the result epidermal loss and at least partial dermal loss
- Excoriation – superficial skin abrasion that usually results from scratching.
- Lichenification – dry, thickened, dark (hyperpigmented) skin with accentuated skin markings

Arrangement of Lesions

Lesions may be:

- Annular (ring-shaped) e.g. tinea corporis (ringworm), pityriasis rosea, syphilis, urticaria, lichen planus, psoriasis, seborrheic eczema
- Grouped e.g. herpes simplex (see related image here), insect bites, warts, molluscum contagiosum
- Linear e.g. scratch marks, scar, keloid, scabies, psoriasis, lichen planus, warts

ECZEMA/DERMATITIS

Eczema is a chronic inflammatory skin disease which is common in children. It mainly affects the epidermis and may be complicated by secondary infection by bacteria (*Staphylococcus aureus, Streptococcus pyogenes*), viruses (HSV) or fungi (*Candida albicans)*. Children may present with:

- Atopic eczema (see related image here and here)
- Nummular eczema
- Seborrhoeic eczema
- Napkin eczema
- Perioral eczema

Atopic/Allergic Eczema

This is a chronic condition that has acute exacerbations and which is often associated with asthma, allergic rhinitis and allergic conjunctivitis (see related image here).

Pathophysiology

The pathophysiology is poorly defined, but there are two hypotheses:

- Primary immune dysfunction leads to IgE sensitisation, allergic inflammation and secondary epithelial barrier disturbance.
- A primary epithelial barrier defect leads to secondary immunologic dysregulation and inflammation as bacteria are able to enter through the skin.

It is associated with elevated serum IgE levels and there is usually a family history of atopy. Symptoms generally start at 3 months old, fluctuate and remit by school-going age in 50% of children. See images related to children with atopic eczema on this web page.

Clinical Features

The child will present with:

- Acute eczema – red and swollen skin, weeping/oozing vesicles (clear, serous fluid), crusting (when the fluid dries up)
- Subacute eczema – mild erythema with or without oozing, scaling, early thickening
- Chronic eczema – lichenification (leathery, thickened skin, hyper/hypopigmentation, prominent skin markings)

The child's presentation may vary depending on his/her age. Infants present with a red, wet and/or scaling eruption which involves the head, extensor areas and trunk. There is nasal sparing.

Older children usually have localized lesions in the flexures. They may have other signs which are pathognomonic of atopy (atopic diathesis):

- Eyes
    - Allergic shiners (dark circles under the eyes which are the result of nasal or sinus congestion)
    - Dennie-Morgan folds/infraorbital folds (lines on the skin below the lower eyelid)
    - Muddy sclera (brown discolouration of the sclera)
- Ears

    - Infra-auricular fissures (fissures beneath the earlobes, which may be weeping)
- Nose
    - Headlamp sign (nasal/central face-sparing when there is eczema of the face).
    - Nasal crease (produced because of chronic upward rubbing of the nose)
    - Salute sign (action of rubbing the nose)
- Lips
    - Lip hyperlinearity
    - Angular cheilitis (erythematous, swollen, and painful patches in the corners of the mouth
- Limbs
    - Hyperlinearity of the palms and soles
    - Keratosis pilaris (dry and rough patches on the skin of the upper arms, thighs, and cheeks)

Diagnosis

The UK Working Party Diagnostic Criteria is used to diagnose atopic eczema. For the diagnosis to be made, the child must have 1 major and 3 minor criteria.

- Major criterion – pruritis
- Minor criteria:
    - Family/personal history of atopy
    - Onset <2 years old
    - History of dry skin
    - History of flexural dermatitis
    - Visible flexural dermatitis

Investigations

Atopic eczema is a clinical diagnosis, therefore no investigations are necessary. However, it may be helpful to do skin prick testing (SPT) to identify triggers.

Management

The mnemonic ASSEBLIEF can be used to remember the approach to management for the child with atopic eczema (see related image here).

Table 13.1: ASSEBLIEF Mnemonic for the Management of Atopic Eczema

A - Antihistamines	Oral antihistamines may be given to sedate the child and avoid nocturnal scratching. The child <2 years old may be given chlorphenamine (0.1 mg/kg/dose at night) and the child >2 years old may be given cetirizine (5-10 mg at night).
S – Steroids	Use potent topical steroids daily (initially and for flares). Use hydrocortisone 1% on the face or skin folds and use beclomethasone 0.1% on the rest of the body.
S - Scratching	An important aspect of treating eczema is avoiding scratching by keeping the skin moist (liberally use moisturisers). Explain the itch-scratch-itch cycle to the parents and child.
E - Education	Inform the parent and child that eczema is a chronic condition caused by barrier dysfunction. Provide support and counselling.
B – Bacteria	Eczema is vulnerable to bacterial/viral infection, especially *S. aureus* (impetiginised eczema) and HSV (eczema herpeticum). Keep the infected skin clean and moist. Treat with antibiotics if necessary.
L – Look	Look for associated atopic conditions and avoid triggers e.g. soaps, bubble bath, wool and other irritating fibres in clothing. Children with atopic eczema are more likely to have atopic rhinitis, conjunctivitis or asthma.
I – If	If severe, use wet wraps unless there is a secondary infection of that area.
E - Emollients	Use emollients as a soap substitutes (help remove crusts but is gentle on the skin) and moisturisers e.g. emulsifying ointment, cetomacrogol.
F – Forever	This condition is lifelong.

Occlusive, wet dressings are to be used for severe or thick, lichenified skin. However, they must not be used if there is a sign of infection as it will promote spread of the infection.

Table 13.2: Impetiginised Eczema

Impetiginised Eczema
It is superficial infection of eczematous skin with *S. pyogenes* or *S. aureus*. The affected skin will have yellow-brown crusting. If severe, there may be systemic signs (fever, malaise, lymphadenopathy). Impetiginised eczema is managed by:

- Removing crusts with wet dressings soaked in saline
- Giving antibiotics – with antibiotic-steroid ointment/cream (for small areas) and systemic erythromycin or cloxacillin (for severe or widespread infection).

Table 13.3: Drugs Used in Dermatology

Drugs Commonly Used in Dermatology

Weak topical steroids (typically used on the face)	● Hydrocortisone 0.5% (Cutaderm®, Dilucort®) ● Hydrocortisone 1% (Mylocort ®, Procutan ®)
Moderate topical steroids	● Alclometasone (Aclosone®) ● Clobetasone (Eumovate®)
Potent topical steroids (typically used on the body)	● Beclomethasone (Propaderm®) ● Fluticasone (Cutivate®) ● Methylprednisolone (Advantan®) ● Mometasone (Elocon®)
Very potent topical steroids	● Clobetasol (Dovate®)

Nummular/Discoid Eczema

Aetiology Pathophysiology

The cause and pathophysiology of nummular eczema are not known, but it may be associated with atopic eczema. Stress and bacterial infection can aggravate the condition.

Clinical Features

The child will have well-rounded (discoid), discrete patches of eczema, usually with a crusted or weeping surface. They are most common on the limbs (especially on the legs) but may occur anywhere on the body.

Management

Patients are managed with potent topical steroids (clioquinol where possible) and antibiotics (e.g. flucloxacillin 250 mg 6 hourly), if infected.

Seborrhoeic Eczema (‘Greasy Eczema’)

It is most common in children.

Aetiology and Pathophysiology

The cause and pathophysiology are unknown but it is associated with large sebaceous glands and is common in immunocompromised individuals. The condition may be aggravated by stress and yeast infection of the hair follicles.

Clinical Features

The child will have erythematous, ill-defined lesions with greasy scale. Lesions are usually found in areas with many sebaceous glands e.g. flexural areas, scalp, face, scalp and nappy area.

Management

The condition is usually self-limiting in infants. Skin lesions should be treated with hydrocortisone 1% cream, and scalp lesions treated with detergent shampoo (tar, detergent, selenium sulphide, ketoconazole or zinc pyrithione) and hydrocortisone 1% (if the scalp is inflamed). Oral antibiotics should be prescribed if the skin is infected.

Napkin Eczema

This is a common form of irritant, contact eczema which may be due to soaps or prolonged exposure to urine and faeces in the diaper. Candidal infection may aggravate the condition.

Clinical Features

The eczema ranges in severity from mild to severe:

- Mild napkin eczema:
    - It is usually asymptomatic but the child may have some erythematous patches and papules. There is minimal maceration.
- Moderate napkin eczema:
    - The child may have pain or discomfort.
    - The skin will be shiny/glazed, red and macerated with superficial erosions.
- Severe napkin eczema:
    - The child will have pain.

- There will be significant erythema, and glossy erosions, papules and nodules).

Management

One must advise the parents to regularly change the child's diapers and leave the child nappy-free for a few hours daily. Nappy cream should be applied (acts as a barrier). One should also apply a weak topical steroid (hydrocortisone 1%) mixed with aqueous cream twice daily. If candida is suspected, the child should be prescribed steroid 10% and nystatin 20% in zinc cream.

Table 13.4: Contact Eczema

Contact Eczema
It is due to a skin irritation (irritant contact eczema) or an allergic reaction to substances in contact with the skin (allergic contact eczema). Common causes include cosmetics, creams, jewellery and detergents. The child will, therefore, present with a localised rash and compatible history. *Irritant Contact Eczema* There are two main types – napkin eczema (see above) and dry skin eczema. Dry skin dermatitis is usually due to excessive moisture exposure, such as soap or sweating. The child might experience burning, stinging and discomfort. On examination, the skin is dry and cracked with macular erythema. The mainstay of treatment is emollient therapy. *Allergic Contact Dermatitis* It is an inflammatory reaction of the skin secondary to exposure to an absorbed allergen or antigen. The child will present with itching and a rash. If acute, there will be oedema, erythema and vesicles that often rupture and form crusts. If subacute or chronic, there will be lichenification, erythema and scaling.

Perioral Eczema

Its pathophysiology is not well understood but it is associated with prolonged topical corticosteroid use.

It most commonly affects young females. They present with small, inflammatory papules around the mouth and nose.

Management includes:

- Discontinuing topical corticosteroids
- Avoiding skin irritants

- Using topical calcineurin inhibitors
- Using oral tetracyclines

Pityriasis Sicca Alba

This is regarded as a mild phenotype of eczema due to unknown cause. It is thought to be caused by a genetic predisposition to impaired skin barrier function.

Clinical Features

The child will have hypopigmented macules and patches with a fine scale (most common on the face). Central hyperpigmentation may also occur.

Management

This is self-limiting condition but management may include:

- Allergen identification and avoidance
- Topical treatment
    - Steroids (hydrocortisone 1%/LPC 5% in aqueous cream for the face, 10% steroid/ LPC 5% in emulsifying ointment for the body)
    - Calcineurin inhibitors e.g. tacrolimus, pimecrolimus).

Antihistamines and wet dressings may also be employed.

AUTOIMMUNE SKIN CONDITIONS

Albinism

This is a congenital skin condition.

Clinical Features

The child will have diffuse depigmentation of the skin, hair and eyes. Chronic sun exposure can lead to premature aging, solar keratoses and sun-associated skin cancers.

Management

Supportive measures include:

- Providing genetic counselling and emotional support
- Preventing the complications associated with sun exposure by encouraging sun avoidance, sunscreen use and wearing modest clothing

- Closely monitoring the child to detect skin cancers early

Vitiligo

Pathophysiology

It is an autoimmune disorder in which there is melanocyte destruction, leading to depigmentation. Re-pigmentation may spontaneously occur and is often triggered by sun exposure.

Clinical Features

The child will present with macular depigmentation that is often symmetrical but may be focal. Secondary sun damage (redness, thickening and scaling) and hair loss may also occur.

Re-pigmentation tends to start at the hair follicles. Acral areas (hands and feet), lips and genitalia seldom regain pigment.

Management

Non-pharmacological management includes

- Counselling the child and family (must be informed that vitiligo is an autoimmune, lifelong condition with no definitive cure), see related image here.
- Encouraging moderate sun exposure but discouraging burning
- Camouflage cosmetics

Pharmacological management:

- Vitamin C
- Oral antihistamines
- Potent topical steroids

Lichen Planus

Pathophysiology

This is a cell-mediated immune response of unknown origin. It is sometimes seen in sun-exposed areas and may be a response to drugs e.g. thiazide diuretics, hypoglycaemic agents, methyldopa and anti-TB treatment. Mucosal surfaces and skin are involved (wrists, forearms, palms, soles and nail folds).

Clinical Features

Lichen planus is described using the six Ps – pruritic, purple, planar (flat-topped), polygonal, papules/plaques which can be polymorphous. Lesions may also have Wickham's striae (white lacy network on the surface). The Koebner phenomenon may be present (appearance of new lesions at an area of injury).

Management

Non-pharmacological management includes sunscreen use (if the rash is photo-distributed) and adjusting medication (if there is suspicion that it is drug-induced). Pharmacological management is with steroids (topical or systemic). Oral lesions may be treated with a steroid spray or gel.

Psoriasis

This is an inflammatory immune-mediated condition which results in hyperkeratinisation.

Pathophysiology

Psoriasis usually starts in early adult life, see related image here. The patient has a genetic predisposition but the exact trigger is unknown.

An immune response is activated by the presence of antigenic stimuli in the skin and results in T cell differentiation. These T cells release cytokines which cause keratinocyte hyperproliferation.

Clinical Features

The child may present with:

- Skin involvement:
    - There will be pink-to-red, well-demarcated, pruritic plaques with a silver scale. Pustules are occasionally seen.
    - Scratching the lesions may be associated with the Koebner phenomenon.
    - Lesions are mostly seen on the scalp (crossing the hairline) and extensor surfaces (elbows and knees), but can occur anywhere on the body e.g. flexural areas, perineum.
- Nail signs e.g. pitting, onycholysis, opaque, deformed and crumbling nails

- Joint involvement (psoriatic arthritis)

Management

Non-pharmacological management includes:

- Counselling and educating the patient and family
- Exposure to sunlight
- Avoidance of triggers like stress and streptococcal infection

Pharmacological management includes:

- For the skin:
    - LPC 10% or salicylic acid (to remove scales)
    - Emollients
    - Weak steroids for the face and potent steroids for the body
- For the scalp:
    - LPC 10% or salicylic acid overnight
    - Shampoo in the morning with a detergent or tar preparation
    - Tar/dilute steroid lotion
- Systemic therapy (dermatologist-initiated)

INFECTIONS

Molluscum Contagiosum

It is caused by infection with a poxvirus.

Pathophysiology

The virus can be transmitted via direct skin contact or via contact with fomites e.g. bath towels, sponges, gymnasium equipment, shared bathwater. It may be inoculated into sites of minor skin trauma.

The lesions usually undergo spontaneous resolution in 6 months to a year, but may take longer.

Clinical Features

The child will have one or more round, dome-shaped, skin-coloured or pearly papule(s) which has an umbilicated centre and contains a caseous plug. Lesions can

be anywhere in the body, but typically occur on the trunk, arms, legs, face or genitalia. See related image here.

Management

There is no universally effective treatment. However, whatever the treatment, one must try to avoid scarring.

The lesions may just be observed if they do not bother the child. Otherwise they may be treated with:

- Benzoyl peroxide cream (applied daily)
- Wart paint (applied to individual lesions)
- Liquid nitrogen (applied to individual lesions every 2-3 weeks)
- Tretinoin (applied to individual lesions)
- Imiquimod cream
- Surgical removal under local anaesthetic

Tinea

Pathophysiology

Tinea is caused by fungal infection with dermatophytes. These fungi can be found on humans, animals or in the soil.

Tinea of the nails may lead to recurrence.

Classification and Clinical Features

The child may have:

- Tinea capitis (scalp) – pruritic lesions with central scaling and patchy alopecia
- Tinea corporis/faciei (body/face) – erythematous, pruritic, scaly lesions (papules/pustules) with central clearing and raised, active edges (from which extension occurs)
- Tinea cruris (groin) – pruritic, inflamed, scaly lesions with well-defined edges and central clearing
- Tinea pedis/manuum (foot/hand) – grouped, pruritic blisters or scaly patches along the plantar line, on the sole, on the instep of the foot and/or involving the web spaces

Investigations

The scale may be scraped and specimens sent for light microscopy or fungal culture.

Management

Topical antifungals may be given e.g. Whitfield's ointment, imidazole cream (such as clotrimazole 1%). However, these agents alone are not effective in tinea capitis. Oral antifungal agents (e.g. fluconazole) are given for tinea capitis or any other form of tinea which is extensive. A different diagnosis (e.g. psoriasis, eczema) must be considered if the rash is not resolving with adequate treatment.

Tinea Versicolor (Pityriasis Versicolor)

It is caused by infection with a yeast commensal (*Pityrosporum orbiculare)*. Predisposing factors include high humidity and excessive sweating.

Clinical Features

The child will have depigmented macules with or without fine scale, usually on the trunk. The presence of scale is indicative of active infection. The rash is sometimes hyperpigmented and may be pruritic.

Investigations

One may examine skin scrapings under the microscope (will show short, unbranched hyphae and spores).

Management

Topical treatment is with selenium sulphide shampoo (apply to the whole body once weekly for 3 weeks) or imidazole/terbinafine cream. The absence of scale means that there has been adequate treatment.

Pityriasis Rosea

Its pathophysiology is unknown, but it is thought to be a response to viral infections.

Clinical Features

The child will have a herald patch (single lesion with an active edge) that usually precedes other lesions by a few days. It is often mistaken for tinea until the generalised eruption occurs.

Lesions are oval, have a fringe of scale and are confined to the trunk. They can be pruritic.

Management

The condition is self-limiting and resolves in 4-8 weeks. The child and family should be counselled and informed that the condition is not infectious and will spontaneously resolve. However, antihistamines can be given to help control itch and sedate e.g. chlorphenamine, cetirizine.

Folliculitis

Pathophysiology and Aetiology

It is inflammation of the hair follicle and may be superficial or deep. The most common infective cause is *S. aureus* but may be due to other bacteria or fungi. The non-infective causes of folliculitis include follicular trauma and occlusion.

Clinical Features

The child will have papules or pustules with an erythematous halo. These may occur in clusters.

Management

Non-pharmacological management involves keeping the area dry and clean, removing predisposing factors and using antiseptic agents. Pharmacological management is with antibiotics (given if there is severe folliculitis e.g., flucloxacillin). The patient should be referred if there is no response to treatment.

Furunculosis (Boils)

Aetiology and Pathophysiology

It is caused by *S. aureus* infection of the hair follicle. The organism is carried in the nose or under the fingernails. Individuals are prone to recurrent attacks unless eradication therapy is given.

Clinical Features

The patient will have a painful, firm, red swelling which eventually develops a necrotic centre and releases a pustular discharge. It is particularly common on the thighs or buttocks.

Management

Treatment may include:

- Bathing with a povidone-iodine wash and shampoo
- Cutting the nails short and regularly scrubbing them
- Antibiotics:
    - Topical (apply antiseptic cream to the nostrils to eradicate *S. aureus*)
    - Systemic (flucloxacillin)
- Analgesia

Plane Warts

They are caused by human papilloma virus (HPV) infection (spread via direct contact or inoculation).

Clinical Features

The child will have flat, skin-coloured papules with smooth surfaces. The most common sites are the finger (especially around the nailfold), hands, arms and face.

Management

The warts usually spontaneously resolve. They should not be excised. Keratolytics should be used instead e.g. tretinoin, salicylic acid, instead. Cryotherapy (with liquid nitrogen) is another option.

Herpes Simplex

Pathophysiology

It is caused by infection with HSV 1 or HSV 2, which is transmitted by close physical contact with an infected individual. The virus remains latent in nearby nerve root ganglia and can reactivate and cause further active infections. See images related to herpes simplex here.

Clinical Features

The child will have grouped, painful vesicles on an erythematous base. There may also be systemic signs.

Management

The lesions resolve after 10 days. Thus, treatment is with analgesia. Oral acyclovir may be given for moderate or severe disease.

The child and family must be counselled on how to prevent the spread of cold sores.

Scabies

Pathophysiology

It is caused by mites, which are spread through close contact. The mites burrow into the upper layer of skin (see related images here).

Clinical Features

Many members of the household may be affected. The child will present with an intensely pruritic, non-specific rash (papules, pustules, eczematous changes). Burrows help make the diagnosis of scabies. They are small, scaly, linear lesions with a white/black dot at the end (mite). Burrows are usually found in web spaces, and on the wrist, feet, axillae, umbilicus and palms.

Management

All members of the household must be treated at the same time to prevent re-infection. All linen, towels and clothes should be washed in hot water and exposed to direct sunlight (to kill the mites). Children >2 years are treated with benzyl benzoate 25% lotion and those <2 years are treated with permethrin 5% lotion or diluted benzyl benzoate.

Erythematous Rash with Fever

Chicken Pox (Varicella Infection)

It is a highly infectious viral disease. The child will present with mild headache, fever, malaise and generalised, vesicular rash. There is permanent immunity once infected. It is treated with acyclovir, analgesia and calamine lotion.

Erythema Infectiosum

It is caused by parvovirus B19 infection. The child will have arthropathy, “slapped cheek” appearance, perioral pallor, fever, coryza, headache and a lacy rash on the trunk. It is a self-limiting condition and does not require treatment.

Erythema Nodosum

The most important causes of erythema nodosum are *S. pyogenes* and TB. The child will have tender, red nodules, commonly on the anterior lower leg.
The child should be investigated with tuberculin skin testing, ASOT and a CXR. The underlying cause must then be treated.

Hand, Foot and Mouth Disease

It is a viral illness caused by coxsackie virus. The child will present with:

- Fever
- Malaise
- Abdominal pain
- Painful oral vesicles and erosions
- Sparse, small, grey vesicles on the hands or feet (see related image here)

Symptomatic treatment is given.

Kawasaki Disease

It is characterised by:

- Fever for >4 days
- Bilateral conjunctival injection
- Lip or oral cavity changes (strawberry tongue)
- Rash (mostly affecting the trunk)
- Lymphadenopathy

Investigations should include:

- Blood tests – CRP, ESR and FBC
- Urinalysis
- Imaging – ECG, CXR and echocardiogram

Treatment is with aspirin and IVIG. Specialist referral is necessary.

Measles

It is a highly contagious virus which is characterised by:

- Koplik spots
- Conjunctivitis
- Cough
- Fever
- Coryza

Supportive treatment is given.

Roseola Infantum

It is most commonly caused by HHV6. The patient will have a high fever, facial oedema and blanching rash. It is a self-limiting condition and is managed with supportive treatment.

Rubella

It is a viral infection which causes skin disease that is less severe than measles. The child will have a discrete rash, palatal petechiae and occipital lymphadenopathy. Management is symptomatic, see related image here.

Streptococcal/Staphylococcal Infection

The child may have:

- Impetigo (characterised by crusting)
- Cellulitis (characterised by indistinct borders)
- Erysipelas (tender, warm, bright red, well-demarcated rash and swollen skin)

These infections are treated with penicillin.

CONGENITAL SKIN CONDITIONS

Port-Wine Stain

Aetiology

It is a congenital vascular malformation which may be part of a syndrome:

- Sturge-Weber syndrome – characterised by eye manifestations (glaucoma), skin manifestations (port-wine stain) and CNS manifestations (seizures)

- Klippel-Trenaunay syndrome – characterised by port-wine stain, varicose veins, and bony and soft tissue hypertrophy of the affected limb, see related image here.

Clinical Features

The segmental, blanchable, erythematous patches are present from birth and persist for the rest of the child's life.

Management

The patient may need to be referred to the relevant specialist, depending on the site(s) involved. If the lesion involves the eye or upper third of face, refer to a neurologist.

Haemangioma (Strawberry Naevus)

This is a benign vascular tumour that is present at birth or develops in the first few weeks of life.

Pathophysiology

The naevus undergoes marked proliferation in the first year of life. This is followed by spontaneous involution/regression of the vascular component with replacement by fibrofatty tissue. Its exact cause is unknown but evidence suggests that hypoxia may play a key role in its development.

Clinical Features

The child will have a red nodule or plaque which has been present from birth or developed in the first few weeks of life. Lesions may be multiple and can occur on internal organs.

Management

One must reassure the patient and parents that treatment is not necessary, unless:

- The tumour obstructs a vital organ
- The tumour has the potential to impair function
- The tumour is on a site where life may be threatened, e.g. epiglottis (may obstruct the airway)

- There are multiple lesions (>5) on the skin (as that may imply internal organ involvement)

In these cases, the patient should be referred to a dermatologist for possible topical corticosteroids, oral propranolol or laser treatment.

Congenital Syphilis

Pathophysiology

Treponema pallidum can cross the placenta in an infected and untreated mother, and can infect the foetus. Foetal infection can occur at any stage of pregnancy. *T. pallidum* can also be transmitted to exposed neonates. Clinical manifestations may appear within the first 2 years of life (early disease) or after 2 years of life (late disease – not infectious).

Untreated syphilis during pregnancy (especially early syphilis) can lead to miscarriage.

Congenital syphilis has no primary stage (see images related to secondary syphilis here.

Clinical Features

Early congenital syphilis can present with only a rash, which may delay diagnosis. The child may have vesicles and bullae or a maculopapular rash on the palms and soles. There may be associated desquamation.

Other signs and symptoms include:

- Fever
- Lymphadenopathy
- FTT
- Hepatosplenomegaly
- Jaundice
- Meningitis
- Osteochondritis
- Pneumonitis
- Rhinitis
- Prematurity/low birth weight
- Deafness
- Neurological impairment

- Bone deformities

Investigations

One should order:

- Maternal TPHA/RPR
- FBC (to identify anaemia and thrombocytopaenia)
- LFTs
- Chest X-ray
- Full body X-ray

Management

One must try and prevent vertical transmission. Therefore, all pregnant patients with syphilis should be treated with 2.4 MU benzathine penicillin IM weekly for three weeks.

The symptomatic child with a positive syphilis test should be treated with penicillin G (50 000 IU/kg IVI twice daily for 10 days). Treatment must not be interrupted. The asymptomatic child with a positive test should be treated with penicillin G (50 000 IU IMI stat).

Pigmented Naevus

Its cause is unknown but it is the result of benign proliferation of melanocytes. One should be suspicious of malignancy if:

- A – there is asymmetry
- B – borders are poorly defined
- C – the colour is not uniform
- D – the lesion has a diameter >6 mm
- E – the lesion is evolving (changes in shape, size or colour)

Clinical Features

The child will have a well-circumscribed, brown/black papule or macule.

Management

The benign acquired naevus does not require excision. The large congenital naevus (see related images here) should be regularly monitored. The child with an atypical naevus should be referred to a dermatologist.

Mongolian Spot

It is common in Asian and Black neonates and less common in Caucasian neonates.

Pathophysiology

This lesion is benign and often fades. It is the result of the delayed disappearance of dermal melanocytes.

Clinical Features

The child will have congenital, blue-grey patches with indefinite borders. These patches are most common in the sacral area.

Café-au-Lait Spot

It is a localised area of increased melanogenesis of unknown cause.

Clinical Features

The child will have pigmented macules or patches which are present from birth or appear during early childhood. The colour of these lesions ranges from tan to dark brown.

Management

Café-au-lait spots are associated with neurofibromatosis (the presence of six or more spots is a diagnostic criterion). Patients who meet this criterion should be referred to neurology.

HAIR CONDITIONS

Alopecia Areata

Pathophysiology

The hair loss is possibly due to an autoimmune process. However, the exact mechanism remains unknown. The hair loss is sudden and occurs at any age

without preceding inflammation. Spontaneous regrowth is expected in ~6-18 months in patients with mild disease. The more the hair loss, the worse the prognosis.

Clinical Features

The child will have well-defined, patchy hair loss with normal underlying scalp.

Management

The child and parents should be reassured if there is only a single patch. However, a potent topical steroid gel or lotion may still be applied.

Patients with extensive or recurrent hair loss should receive emotional support and can be encouraged to purchase a wig, as treatment might not work.

Traction Alopecia

Pathophysiology

This hair-loss (reflecting on images here) is as the result of bad hair-grooming practices which cause breaking of the hair e.g. trichotillomania (the patient pulls out his/her own hair. In children, this may signify family stress. There may be permanent hair loss in patients with traction alopecia if the damage is severe.

Clinical Features

The child will present with hair loss at traction sites, commonly the scalp borders or vertex. At the site of alopecia, there will be damaged, brittle and broken off hair.

Management

One must explain the likely cause to the patient and parents and give advice on hairdressing techniques.

Scarring Alopecia

Pathophysiology

This type of hair loss can follow a traumatic, inflammatory or neoplastic process. The loss of hair is usually permanent.

Clinical Features

Affected scalp is bound down by fibrosis (see related images here). There is also a change in pigmentation.

Management

One must explain that the hair loss is permanent. Chloroquine should be given if the child has discoid lupus. A dermatology referral should be made if the cause is unknown. Referral to a plastic surgeon may be considered.

Pediculosis (Lice Infestation)

It is common in children and is spread by close contacts. Therefore, there are often outbreaks at schools.

Clinical Features

The child will present with intense scalp pruritus and white nits attached to the hairs. The constant scratching can lead to impetigo and secondary eczema.

Management

Apply permethrin 5% topical lotion to kill the lice. The nits may be removed by going through the freshly-washed hair with a fine-toothed comb or shaving the head. Patients with lice-infested eyelashes should be referred as there might have been sexual abuse.

TRAUMA, DRUG REACTIONS AND BITE REACTIONS

Keloid

Pathophysiology

It is an abnormal growth of scar tissue in individuals who are genetically predisposed. It may grow in response to trauma or spontaneously appear (see related images here).

Clinical Features

The child will present with firm, rubbery nodules that vary in size. Keloid lesions tend to cross the scar borders and are less painful.

Management

A zinc oxide (pressure) plaster and intralesional steroids should be applied. The patient should be referred to a plastic surgeon if the lesion is unresponsive or severe.

Hypertrophic Scar

Pathophysiology

An excessive amount of collagen is deposited, producing a raised scar. It is similar to a keloid but the lesion is within the margins of the injury.

Clinical Features

These lesions stay within the scar border, are inflamed and are very painful.

Management

The patient should be treated with intralesional steroid injections or silicone gel compression.

Fixed Drug Eruption

Pathophysiology

This is a skin reaction that tends to appear following ingestion of certain medications or substances. Any drug has a potential to cause a fixed drug eruption, but it is most commonly seen with laxative, analgesic or sulphonamides use.

Clinical Features

The patient will have round, sharply-demarcated, hyperpigmented macules. They are initially erythematous but go on to blister and then resolve (purple-grey colour). These lesions recur at the same spot every time the patient takes the offending medication/substance (see related images here).

Management

Treat the patient with an alternative drug and order a MedicAlert bracelet.

Pyogenic Granuloma

It is a small, benign vascular tumour that develops in response to trauma (see related images here).

Clinical Features

Pyogenic granulomata are common on the fingers. The child will have a nodule with a glistening, smooth and eroded surface. It easily bleeds on contact.

Management

Treatment may be with one of the options below:

- Excision or curettage removal followed by electrocautery of the base
- Application of very potent steroids
- Chemical cauterisation with a silver nitrate stick

Papular Urticaria

It is a common, chronic pruritic condition which is caused by allergy to insect bites. It usually affects young children.

Clinical Features

The lesions/bites occur in a line (“breakfast, lunch, dinner” distribution) or a group.

Management

It includes:

- Informing the patient and parents of the cause of the allergy
- Educating the family about chronicity
- Treating pets for fleas
- Checking mattresses for bed bugs
- Fumigating the home
- Applying topical corticosteroids
- Treating infected lesions with antibiotics
- Prescribing antihistamines for itch control and sedation

DERMATOLOGY SUMMARY (CHEAT SHEET)

Table 13.5: Brief Summary of Dermatological Conditions in Children

Eczema	Acute	
	Chronic	
	Face or flexures	Atopic eczema
	Sun-exposed areas	Photosensitivity
	Area of contact	Contact eczema
	Perineum or thighs in infants	Napkin eczema
	Round lesions	Nummular eczema
	Scalp, face, chest or napkin area	Seborrhoeic eczema
Scaly papules and plaques	Pink or red plaques with scale	Psoriasis
	Pink or red plaques on the trunk	Pityriasis rosea
	Purple/brown/silver papules	Lichen planus
Erythematous and purple lesions	Single red area	Erysipelas
	Tender pustule	Boil
	Flat and congenital	Port-wine stain
	Raised and congenital	Haemangioma
	Several, raised and itchy	Urticaria
	Raised, red and non-itchy	Fixed drug eruption
	Tender nodules	Erythema nodosum
	Widespread, erythematous rash	Viral infection, streptococcal infection or drug reaction
Papules and nodules	Red or pink	Erythema nodosum, boil or acne
	Purple	Lichen planus
	Brown or black	Pigmented naevus or wart
	Skin-coloured	Wart, molluscum contagiosum or keloid
Blistering diseases	Vesicles on erythematous skin	Herpes simplex, chickenpox or acute eczema
	Vesicles on normal skin	Papular urticaria
	Round, large and transparent	Bullous impetigo
	Concentric circles with a bullous centre	Erythema multiforme, fixed drug eruption
	Pustular	Scabies, acne, boil or folliculitis
Altered pigmentation	Smooth, depigmented skin	Albinism or vitiligo
	Scaly, hypopigmented skin	Pityriasis sicca alba or tinea versicolor

	Smooth, hyperpigmented skin	Mongolian spot or café-au-lait spot (see related images here)
	Scaly, hyperpigmented skin	Tinea versicolor

Chapter 14:

ALLERGOLOGY

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This chapter covers the following topics:

- Allergic rhinitis
- Urticaria
- Asthma
- Anaphylaxis
- Food allergy
- Drug hypersensitivity
- Other conditions to recognise

ALLERGIC RHINITIS

Allergic rhinitis is characterized by intense sneezing, rhinorrhoea, nasal obstruction, and itching of the eyes (see related image here), nose and palate. It may be intermittent/seasonal (hay fever) or persistent/perennial (all year round).

Pathophysiology

Atopic individuals produce allergen-specific immunoglobulin E (IgE) when exposed to allergens. IgE antibodies then bind to the IgE receptors on mast cells in the respiratory mucosa. Upon subsequent exposure to the same allergen, the allergen binds and cross-links IgE on the mast cell surface, resulting in the activation and release of inflammatory mediators (histamine, prostaglandins, leukotrienes platelet-activating factor, bradykinin and others). The release of inflammatory mediators results in the signs and symptoms of allergic rhinitis.

Table 14.1: Summary Table of Intermittent and Persistent Allergic Rhinitis

	Intermittent or Seasonal	**Persistent or Perennial**
Timing	It is usually precipitated by exposure to certain seasonal pollens e.g. grass or tree pollen. Thus, it usually occurs in spring and at the change of seasons.	It is usually due to sensitivity to allergens present all year round e.g. grass pollen, house dust mites, pet allergens, fungal spores.
Clinical Features	The patient may have: ● Nasal symptoms – congestion, otorrhoea, itching, sneezing ● Ocular symptoms – itching, tearing ● Postnasal drip – sore throat, cough (see related image here) On examination, one may find allergic facies, characterised by: ● Allergic shiners ● Allergic salute and resultant nasal crease (from chronic performance of the salute) ● Swollen and pale nasal mucous membranes ● Wet turbinates with watery nasal discharge (turbinates may obstruct by >50% and there may be a post-nasal drip oral examination) ● Mouth-breathing ● Injected sclera	

	● Intense sneezing ● Rhinorrhoea ● Itching of the nasal, palate and auditory canals	● Nasal itching not common ● Obstruction and rhinorrhoea
Investigations	● Total IgE (Immuno-CAP) is non-specific. One may do nasal smears of nasal mucous stained with Hansel's stain to look for eosinophil clumping. ● Skin prick testing (SPT) is the gold standard for identifying allergens. ● Radioallergosorbent testing (RAST) is often performed as an inhalant mix, although it is more expensive than SPT and does not identify individual causative organisms.	
Management	Non-pharmacological management includes allergen avoidance (usually difficult) and desensitisation through immunotherapy (effective in monosensitive patients). Pharmacological management includes the use of: ● Short-acting non-sedating oral antihistamines for itching, rhinorrhea and sneezing e.g. second-generation antihistamines (cetirizine, loratadine). Newer agents (e.g. desloratadine) have the added benefit of not being sedating, which is important for school-going children. ● Intranasal corticosteroids for nasal congestion e.g. beclomethasone, budesonide,	Non-pharmacological management also includes allergen avoidance desensitisation through immunotherapy (effective if monosensitive to a single unavoidable allergen). Pharmacological management includes the use of: ● Intranasal corticosteroids for nasal congestion. They are given as "controller" medication for persistent allergic rhinitis and are very effective in this form of rhinitis e.g. beclomethasone, budesonide, fluticasone, mometasone, ciclesonide. Correct intranasal steroid technique is imperative to allow optimal delivery and minimise side effects, which include nasal irritation, sneezing and bleeding. ● Decongestants in the short-term (5-7 days).

	fluticasone, mometasone, ciclesonide. Adverse effects include nasal irritation, sneezing and bleeding.	Adverse effects include rebound rhinitis, tachycardia, anxiety, insomnia.

Note: Allergic rhinitis is a common comorbidity . It may be treated with antihistamine eye drops (olopatadine or ketotifen eye drops have mast cell-stabilising action) and non-sedating, oral antihistamines as above.

ECZEMA

See *Dermatological Conditions* chapter.

URTICARIA

It is characterised by the presence of itchy lesions varying from flat, erythematous papules to large plaques or wheals. These skin lesions appear within minutes and disappear within hours with no trace. It may be acute (lasting <6 weeks) or chronic (lasting >6 weeks).

Infection-associated urticaria is the most common cause of acute urticaria (see related image here). It is commonly misdiagnosed as antibiotic allergy if the child has been prescribed an antibiotic for the acute infection.

Pathophysiology and Clinical Presentation

Lesions are red due to vasodilation and the oedema is the result of increased permeability of blood vessels from the release of histamine and other immune mediators in the skin.

Angioedema results when deeper vessels are involved. Laryngeal oedema and respiratory compromise are life-threatening.

Aetiology

Causes include:

- Infection and infestation – tonsillitis, otitis, UTI, sinusitis, multiple viral triggers, worm infestation, schistosomiasis

- Drugs – aspirin, penicillin
- Food – hen's eggs, peanuts, cow's milk, fish, preservatives

Investigations

No routine investigations are indicated for acute urticaria. The clinician may tailor investigations to the child based on his/her clinical condition and presentation. It is imperative to exclude food allergy on history in any child presenting with acute urticaria.

Baseline investigations for chronic idiopathic urticaria are done to identify underlying infection or systemic disease. Investigations may include FBC, erythrocyte sedimentation rate (ESR), urine dipstick and blood pressure monitoring.

Management

The child must avoid identified triggers. Non-sedating oral antihistamine should be given to the child who has had a mild attack of unknown cause. Systemic antibiotics are given if an underlying infection is suspected.

Chronic urticaria requires discussion with a paediatric allergist or suitably trained clinician. Severe attacks may require systemic corticosteroids

ASTHMA

Pathophysiology

Asthma is a chronic inflammatory condition which leads to airway narrowing through various mechanisms, including:

- Spasm of the smooth muscle of the airways
- Mucous-plugging in airways
- Inflammation in airways – due to infiltration by inflammatory cells, membrane thickening secondary to collagen deposition epithelial damage of the airways or activation of mast cells

These processes can be triggered by exposure to allergens and irritants, and can lead to acute bronchoconstriction and chronic inflammation.

Precipitating factors

- Viral respiratory tract infections

- Exercise
- Weather/seasons
- Cigarette smoke
- Stress
- Allergens
    - House dust mite
    - Animal dander
    - Pollens
    - Moulds
    - Grasses
- Irritants
    - Paint
    - Chemicals – cleaning products
    - Perfumes
    - Fumes
    - Nitrogen dioxides
    - Room deodorizers

Clinical Features and Investigations

History

The child may present with a history of:

- Cough
- Wheeze
- Dyspnoea
- Chest tightness
- Chest pain
- Symptoms related to the seasons
- Symptoms worse at night
- Family history of asthma (see related image here) or atopy

Examination

It is usually normal unless there is an acute exacerbation. On general examination, one may find dry cough, atopic facies, and signs of rhinitis, conjunctivitis or eczema. Respiratory examination may show:

- Hyperinflation
- Long expiratory phase
- Wheeze on auscultation
- Signs of infection

In a severe acute attack, the child may present with:

- Anxiety
- Restlessness
- Tachycardia
- Wheezing
- Unable to speak
- Pulsus paradoxus

Investigations

One should get peak flow meter readings and perform lung function tests.

Assessment

Assessment of Control

Long-term asthma control is determined based on symptoms, activity limitation, frequency of reliever use and lung function tests.

Table 14.2: Assessment of Asthma Control

	Intermittent	**Mild**	**Moderate**	**Severe**
Symptoms	<2 days/week	>2 days/week but not daily	Daily	Throughout the day
Nocturnal symptoms	<2 times/month	3-4 times/month	>1/week but not every night	Often, 7 times/week
Daily activity	No limitation	Minor limitation	Some limitation	Extreme limitation

β_2-agonist use	≤2 days/week	>2 days a week but not daily	Daily	Several times a week
Lung function tests	Normal FEV_1 FEV_1 >80% FEV_1/FVC >85%	FEV_1 >80% FEV_1/FVC >80%	FEV_1 60-80% FEV_1/FVC 75-80%	FEV_1 <60% FEV_1/FVC <75%

Assessment of Attack Severity

The severity of an asthma attack is determined based on the patient's clinical features:

- Moderate:
    - Saturation < 92%
    - No signs of severe
    - PEF ≥50%
- Severe:
    - Saturation <92%
    - Tachycardia
    - Tachypnoea
    - Accessory muscle use
    - PEF 33-50%
- Life-threatening:
    - Saturation <92% and one of:
    - Silent chest
    - Poor respiratory effort
    - Altered consciousness
    - PEF <33%
    - Cyanosis

Management

Routine Management

Non-pharmacological management includes:

- Avoiding triggers
- Avoiding/reducing exposure to allergens or irritants

- Treating comorbid conditions e.g. allergic rhinitis

Pharmacological management includes the use of:

- Relievers (should be given to all patients) – β_2-agonists
- Controllers (given to persistent asthmatics) – inhaled corticosteroids, leukotriene receptor antagonists, and long acting be β_2-agonists

The choice of controller is dependent on the severity of the asthma.

Management of an Acute Attack

If the child is having:

- Moderate asthma attack:
    - Give a β_2-agonist (2-10 puffs via spacer; increase by 2 puffs every 2 minutes if not responding)
    - Give oral prednisone (2 mg/kg)
- Severe asthma attack:
    - Admit and give facemask oxygen
    - Give a β_2-agonist (10 puffs via spacer or 2.5-5 mg via nebuliser)
    - Give oral prednisone (2 mg/kg) or IV hydrocortisone (4 mg/kg)
    - If there is a poor response, add ipratropium bromide (0.25 mg via nebuliser)
    - Repeat β_2-agonist and ipratropium every 20-30 minutes as needed
- Life-threatening asthma attack:
    - Admit and give facemask oxygen
    - Give nebulised β_2-agonist (2.5-5 mg) and ipratropium bromide (0.25 mg)
    - Give IV hydrocortisone (4 mg/kg)
    - Repeat bronchodilators every 20-30 minutes as needed
    - Admit to PICU if there is a poor response

See diagram related to asthma here.

ANAPHYLAXIS

Definition

It is an acute, life-threatening, multi-systemic reaction to an allergen that may be mediated by IgE and causes a systemic release of mast cell mediators. Causes include food, drugs and insect bites/stings e.g. *Hymenoptra* allergy – wasps, bees, ants. The reaction may also be non-IgE-mediated (previously termed an anaphylactoid reaction).

Pathophysiology and Clinical Features

The IgE-mediated response leads to the release of mast cell mediators, such as histamine, tryptase and others. These mediators produce a rapid response in the skin, respiratory system, GIT and cardiovascular system (CVS), leading to the following clinical features:

- Skin – rash (e.g. urticaria), itching, flushing, tongue swelling, conjunctival swelling, angioedema, flushing, pruritus
- Respiratory system – shortness of breath, wheezing, stridor, rhinorrhoea or congestion, sensation of the closing of the throat, stridor
- GIT – nausea, vomiting, diarrhoea, abdominal pain (usually cramping), abdominal tenderness
- CVS – dizziness, collapse, palpitations, tachycardia, hypotension

Diagnostic

Anaphylaxis can be diagnosed if one of these criteria is met:

- Criterion 1 – acute onset of respiratory dysfunction, hypotension or symptoms associated with hypotension (e.g. syncope) AND skin and/or mucosal involvement in the patient with no known allergies
- Criterion 2 – two or more of the following occurring in the patient with a known allergy and a history of recent allergen exposure (but not necessarily to the allergen to which s/he is known to be allergic):
    - Skin and/or mucosal involvement
    - Respiratory dysfunction
    - Hypotension or symptoms associated with hypotension such as syncope

    - Persistent signs and symptoms of gastrointestinal dysfunction
- Criterion 3 – hypotension in the patient with a known allergy after exposure to that allergen
    - Low systolic BP (SBP) is age-specific in children – 1 month to 1 year = SBP <70 mmHg; 1-10 years = SBP <70 mmHg + (2 x age in years); 11-17 years = SBP <90 mmHg

Investigations

Mast cell tryptase levels should be measured at the time of reaction, 6 hours after the reaction and again at 12 hours. Other investigations related to the systemic effects of anaphylaxis and the resuscitation required may be performed.

Management

Non-pharmacological management includes:

- Calling for help
- Resuscitating the patient – assessing the airway, breathing and circulation and managing as required
- Removing the cause, if known

Pharmacological management includes

- Administering adrenaline IM (1:1000, 0.3-0.5 mL; can be repeated in 20 min-intervals if needed) (see related image here)
- Administering antihistamines e.g. promethazine (0.25-0.5 mg/kg IM)
- Giving IV fluids (crystalloids)
- Giving facemask or nasal prong oxygen
- Administering aminophylline (slow IV at 4 mg/kg; if there is bronchospasm)
- Administering hydrocortisone (100-200 mg IV 4-6 hourly for 24 hours and longer if needed)

FOOD ALLERGY

Pathophysiology

Food allergies are IgE-mediated or non-IgE mediated, abnormal responses to a particular food. This leads to the release of mast cell mediators and a systemic response.

Aetiology

Food allergy is commonly caused by:

- Egg
- Cow's milk
- Soya
- Peanuts
- Wheat
- Fish

See related image here.

Clinical Features

They include:

- Gastrointestinal manifestations – vomiting, diarrhoea
- Skin manifestations – urticaria, atopic dermatitis, angio-oedema
- Respiratory – nasal obstruction, wheezing

Investigations

- SPT
- ImmunoCAPRAST

See related image here.

Management

Non-pharmacological management includes avoidance of the offending food or ingredient in non-food items. Pharmacological management includes antihistamines for mild itching and rashes and anaphylaxis management (if required).

DRUG HYPERSENSITIVITY

This is an adverse reaction which occurs after exposure to a drug and it can be immunologic or non-immunologic. SPT may be done to identify the offending agent.

Clinical Features

The hypersensitivity reaction can be immediate (60 minutes), accelerated (1-72 hours) or late (>72 hours). Skin manifestations are most common e.g. serum sickness, dermatitis, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN). However, anaphylaxis can occur.

Management

It includes:

- Education
- Avoidance of the offending drug
- Wearing a MedicAlert bracelet
- Desensitisation
- Management of anaphylaxis

The patient should be referred if there are severe skin reactions.

OTHER CONDITIONS TO RECOGNISE

Hereditary Angioedema

It is characterised by recurrent episodes of angioedema without urticaria or pruritus. The swelling is usually self-limiting and resolves within a few days. It is thought to arise from a deficiency in or dysfunction of C1 inhibitor (C1INH; an acute-phase reactant).

Hereditary angioedema should be suspected in patients with:

- Recurrent episodes of angioedema without urticaria or pruritus and which last 2-5 days
- Positive family history of angioedema
- Unexplained laryngeal oedema
- Unexplained recurrent episodes of self-limited, colicky, abdominal pain
- Low complement component 4 level

See related image here.

Once the diagnosis has been made, family members should be encouraged to get tested. It is important to note that infants under <1 year normally have lower levels of C1INH, which makes diagnosis difficult. Thus, testing is usually done when the infant is older to avoid false-positives and false-negatives.

Most patients do not respond to antihistamines and glucocorticoids.

Inherited Complement Deficiency

Inherited complement deficiencies are very rare. Individuals lose function of the specific, deficient protein as well as the function of the proteins that follow in that specific cascade. Thus, those affected are predisposed to recurrent bacterial infections and/or SLE.

Screening is indicated in patients with:

- Recurrent unexplained pyogenic infections with no obvious aetiology
- Recurrent *Neisseria* infections
- Multiple family members with *Neisseria* infections

Management involves patient education (to look out for early signs of infection) and vaccinations against organisms to which the patient has a higher risk of infection.

Sinusitis or Rhinosinusitis

It is the infection of the paranasal sinuses and can be caused by various microorganisms, but is commonly caused by viruses. It is also known as the common cold.

One must differentiate uncomplicated viral sinusitis from acute bacterial sinusitis. Both present with similar symptoms but have different clinical courses. Common symptoms include cough, fever, nasal discharge or congestion, headache and facial pain.

Viral sinusitis is usually self-limiting and will resolve within 7-10 days, with symptoms peaking in days 3-6. Antibiotics do not help with the treatment of viral sinusitis

In bacterial sinusitis, the above symptoms persist for longer than 10 days and are often more severe (e.g. higher temperatures) or may worsen. It can have complications, such as local spread of infection which may lead to periorbital cellulitis, orbital cellulitis and meningitis. It needs to be treated with antibiotics.

Latex Allergy

Natural rubber latex allergy is caused by the sensitisation to proteins in the sap-like fluid from the tree *Hevea brasiliensis.* Most individuals are sensitised after exposure to latex gloves, dental dams or balloons.

The prevalence of latex allergy is higher in patients sensitised to other allergens and those with eczema or a fruit/vegetable allergy. Children with spina bifida are at high risk of latex sensitisation because they undergo multiple surgeries, frequent bladder catheterisations and manual rectal evacuation.

Symptoms depend on the route of exposure, the amount of allergen in the rubber and the mechanism of the reaction. Common presentations include:

- Dry, crusted, irritated skin with/without erythema and vesicle formation (a form of irritant contact dermatitis – non-IgE mediated reaction)
- Urticaria, rhinoconjunctivitis, asthma and anaphylaxis i.e. IgE-mediated reactions

The diagnosis is made based on a strong suggestive history and significant association between exposure and symptoms. Management includes avoidance, pharmacotherapy, immunotherapy and anti-IgE therapy.

Insect Venom Allergy

Pathophysiology

It is similar to that of food allergy. Insects commonly involved include mosquitoes, fleas, flies, bees, wasps, hornets, and fire and harvester ants.

Clinical presentation

The child will present with history of:

- A sting or bite from an insect
- Localised pain, swelling and redness
- Anaphylactic symptoms

Examination findings:

- Localised tenderness, swelling, erythema and blisters
- Signs of anaphylaxis

Investigations

One should attempt to identify the insect and perform venom testing.

Management

Non-pharmacological management includes cleaning the wound and applying a cold compress.

Pharmacological management includes the use of antihistamines, analgesia and steroids (if there is significant swelling). Anaphylaxis management should be performed, as needed.

Mastocytosis

This is a group of conditions in which there is accumulation of mast cells in various tissues, and it can be divided in two categories:

- Cutaneous – limited to the skin
- Systemic – there is accumulation of cells in organs; can have cutaneous involvement

There may be various skin findings with pruritus being common. The child may also have symptoms related to the effects of mast cell mediators (e.g. hypotension, nausea, diarrhoea, vomiting) and the organ that has been infiltrated.

Chapter 15:

HAEMATOLOGICAL AND ONCOLOGICAL CONDITIONS

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This chapter covers the following topics:

- Anaemia
- Idiopathic thrombocytopenic purpura (ITP)
- Haemophilia
- Disseminated intravascular coagulopathy (DIC)
- Von Willebrand disease (vWD)
- Leukaemia
- Lymphoma
- Wilms tumour (nephroblastoma)
- Neuroblastoma
- Retinoblastoma
- Rhabdomyosarcoma

ANAEMIA

It is defined as haemoglobin (Hb) or haematocrit (Hct) below the normal value for age and sex. The cut-off values for anaemia for the different age groups are shown in table 15.1 and are based in WHO/Integrated Management of Childhood Illness (IMCI) guidelines).

Table 15.1: Anaemia Cut-off Values

Age (years)	Hb (g/dl)
0.5 - 4.9	< 11
5 - 11.9	< 11.5
12 - 14.9	<12

Severe anaemia is diagnosed in the child with Hb <5 g/dl.

Iron-Deficiency Anaemia (IDA)

Iron deficiency is the most common cause of anaemia in early childhood, ranging in prevalence from 5% in Western societies to 50% in developing countries. It develops when body iron stores are too low to support erythrocyte production.

Term neonates have enough iron reserves for 3 months, after which they get iron from their food. This is not so for preterm neonates. Thus, iron supplementation is required from birth weight for these neonates.

Aetiology and Predisposing Factors

Iron deficiency may be caused by:

- Inadequate dietary intake
- Increased requirements (as in infancy, adolescence and pregnancy)
- Impaired absorption e.g. gluten enteropathy, *H. pylori* infection
- Blood loss e.g. menses in females, GIT bleeding (as with helminthiasis, peptic ulcers, diverticulosis or colonic malignancy)
- Chronic loss of body iron in urine

Bacterial, viral and parasitic infections impair iron uptake and utilisation or cause chronic blood loss.

Prenatal predisposing factors (factors which result in depleted iron stores at birth) for IDA include:

- Maternal multiparity
- Multifoetal pregnancies e.g. twin births
- Low birth weight
- Blood loss

Clinical Features

They include:

- Initial symptoms:
    - Fatigue and lethargy (caused by depletion of tissue enzyme and myoglobin iron)
    - Irritability
    - Anorexia or pica
- Long-term manifestations:
    - Cognitive dysfunction
    - Growth impairment
    - Impaired immunity
- Examination findings:
    - Pallor
    - Koilonychia
    - Angular stomatitis
    - Glossitis
    - Moderate splenomegaly
    - Soft ejection systolic murmur

Assessment and Investigations

When one suspects IDA, one must ask the mother about the factors and causes listed above. The following blood results will be found in the child with IDA:

- Low serum iron (<40 μg/dl)
- High iron binding capacity (>450 μg/dl)
- Low ferritin (due to the low serum iron and transferrin saturation)
- Low transferrin saturation (<16%)
- Low serum ferritin (<10ng/mL)
- High free erythrocyte protoporphyrin level (FEP)
- High RDW

- Microcytosis (mean corpuscular volume; MCV <70 fL)
- Hypochromia (mean corpuscular Hb; MCH <26 pg)
- Pencil cells, target cells and reactive thrombocytosis on the peripheral blood smear (PBS)

The reticulocyte count will be low for the degree of anaemia, unless the anaemia is caused by acute blood loss.
Measurement of bone marrow iron is the gold standard for assessing iron stores. One will see reduced iron stores on Perl's Prussian blue stain. However, it is an invasive test and is, thus, not routinely done.

- To determine another cause of microcytic anaemia:
  - stool testing
  - incubated osmotic fragility testing
  - measurement of lead in tissue

Diagnosis and Differential Diagnosis
IDA is diagnosed based on the presence of supporting clinical features and investigations. Response to iron supplementation (improvement of lethargy and fatigue) usually confirms the diagnosis. Differential diagnoses for the hypochromic microcytic anaemia in children aged 6 months to 3 years are:

- Thalassaemia
- Chronic infections or inflammatory conditions
- Lead poisoning

Management
One must identify and treat the cause, and correct the deficiency with oral or parenteral supplementation. Attempts to prevent iron deficiency in the at-risk child must be made, including:

- Encouraging breastfeeding
- Encouraging the intake of citrus fruits (only if >6 months) as they increase the availability of dietary iron
- Giving supplemental iron (may be given in the form of iron-fortified food)

Pharmacological management includes:

- Oral ferrous sulphate supplementation:

    - A dose of 6 mg elemental Fe^{2+}/kg/day will correct nutritional iron deficiency in 4 weeks (in >90% of patients).
    - The minimum acceptable rise in Hb is 2 g/dl in 3 weeks.
- Parenteral iron:
    - It is usually reserved for genuine oral intolerance e.g. gastrointestinal disease, malabsorptive state.
- Blood transfusion:
    - It is only indicated in the patient with very severe anaemia (Hb <4 g/dl) and cardiopulmonary symptoms, continuing blood loss or severe infection.
    - 5-10 mL/kg of packed red blood cells (RBCs) is given slowly with a diuretic.

Haemolytic Anaemia

It is anaemia which results from:

- Increased RBC destruction (intravascular haemolysis)
    - There is a compensatory increase in bone marrow extramedullary (liver and spleen) erythropoiesis.
- Excessive removal of RBCs by the macrophages within the reticuloendothelial system (RES), mainly the spleen (extravascular haemolysis)

Clinical Features
The patient will have:

- Pale mucous membranes
- Mild, fluctuating jaundice
- Splenomegaly
- Gallstones and cholecystitis (present at younger ages)
- Lower leg ulcers
- Aplastic crises precipitated by parvovirus B19 infection
- Bone marrow hyperplasia

Investigations
Laboratory tests may show:

- Anaemia
- High unconjugated bilirubin levels
- Haemosiderinuria, haemoglobinuria and urobilinogenuria
- Reticulocytosis
- Low serum haptoglobin levels
- Evidence of RBC damage on PBS (spherocytes, fragments, bite cells)
- Heinz bodies (aggregates of denatured Hb which are seen in glucose-6-phosphate-dehydrogenase deficiency; G6PD) (see related image here)

Aetiology
The causes of haemolytic anaemia may be hereditary or acquired.

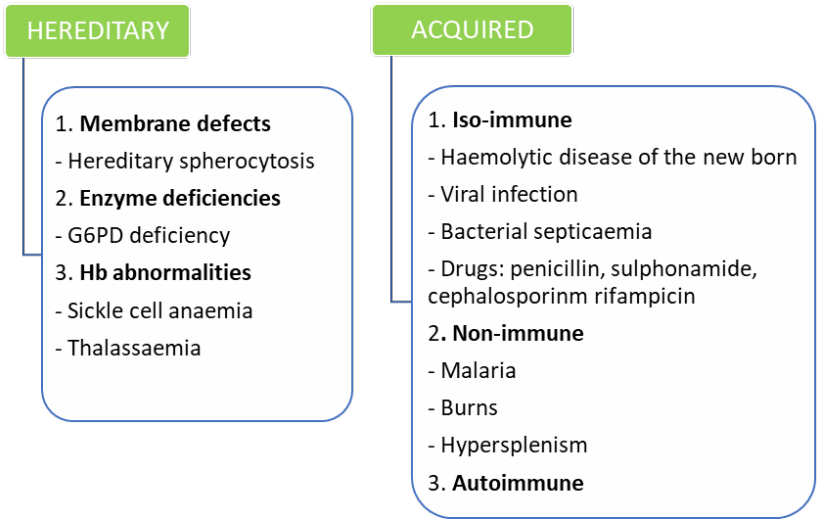

Figure 15.1: Hereditary and Acquired Causes of Haemolytic Anaemia

Hereditary Spherocytosis

It is an autosomal dominant condition that is often the result of de novo mutation (25% of cases). The resultant deficiency in spectrin is associated with increased permeability of the cells to sodium. The degree of spectrin deficiency is directly proportional to the severity of disease and degree of spherocytosis.
Due to the deficiency, the RBC membrane becomes round and unusually rigid, causing the RBCs to become less pliable. As a result, the cells are unable to pass through the splenic microcirculation and become trapped and destroyed in venous sinuses i.e. the cells' lifespans are shortened. Thus, a splenectomy will cure the anaemia.

Clinical Features
The clinical presentation in hereditary spherocytosis varies. The patient may be asymptomatic, have compensated haemolysis or have severe recurrent anaemia and require transfusion. The age at presentation is also variable (infancy to old age). Generally, the patient will present with:

- Anaemia with episodes of haemolysis and jaundice
- Splenomegaly (typical)
- Gallstones (in the long term)

Investigations
Laboratory tests will show:

- Spherocytes with polychromasia on PBS (see related image here)
- Reticulocytosis
- Negative Coombs test
- Increased osmotic fragility

Management
Most patients do not require specific therapy and are treated with routine folate supplementation. Patients with severe anaemia may need to be considered for splenectomy, however this does not change the intrinsic cause of the condition. Post-splenectomy risk of pneumococcal septicaemia is decreased when surgery is deferred until the child is older than 5 years, and giving the pneumococcal vaccine and prophylactic penicillin post-operatively.

Hereditary Elliptocytosis

Hereditary elliptocytosis is an autosomal dominant condition in 85-90% of cases and is autosomal recessive in the remaining 10-15% of cases (see related image here). It is characterised by oval-shaped RBCs caused by an abnormality in the RBC skeletal membrane. Patients may be symptomatic or have mild, compensated anaemia. A splenectomy is offered for severe disease.

Glucose-6-Phosphate Dehydrogenase (G6pd) Deficiency

It is most prevalent in people originating from areas with endemic *P. falciparum* malaria as the deficiency provides limited protection against malaria. The resultant

glutathione deficiency makes the RBC susceptible to oxidative stress and shortens its lifespan.

G6PD deficiency is a sex-linked disorder, with the gene being carried on the X chromosome. Thus, full expression of the disease occurs in males and females are carriers (but females are rarely homozygous). Enzyme levels are lower in Caucasian populations than in African populations. Thus, the former may have compensated haemolytic anaemia with increased reticulocytosis and splenomegaly, while the latter display few or no symptoms until exposed to oxidant stress.

Clinical Features and Diagnosis

Neonatal jaundice is a common presenting feature (likely triggered by substances in breast milk). Jaundice and haemoglobinuria are followed by a sharp drop in Hb, brisk reticulocytosis (present on days 3-7) and a return of Hb to normal (in 1-2 weeks). The child may present with:

- Favism (expression of the disease can be triggered by eating fava beans)
- Chronic non-spherocytic haemolytic anaemia
- Drug-induced acute haemolysis
- Neonates may develop haemolysis from

The diagnosis of G6PD deficiency is confirmed by screening tests and a quantitative assay of RBCs.

Management

It includes:

- Avoidance of oxidant drugs
- Blood transfusion in acute haemolytic episodes
- Prompt management of infection

Patients should apply for a MedicAlert bracelet and this should be worn at all times.

Pyruvate Kinase Deficiency

It is an autosomal recessive condition which mainly occurs in northern European people. The diagnosis is confirmed by an enzyme screening test or on RBC assay. Haemolysis may be precipitated by infection.

Glucose-6-Phosphate Isomerase and Hexokinase Deficiency

It is a rare, autosomal recessive condition which is diagnosed on RBC enzyme assay. It is managed with a splenectomy.

Table 15.2: Pathophysiology of Haemoglobinopathies and Thalassaemias

HAEMOGLOBINOPATHIES AND THALASSAEMIAS
Normal Hb is composed of three components: HbA ($\alpha 2\beta 2$ chains), HbA2 ($\alpha 2\delta 2$ chains) and HbF ($\alpha 2\gamma 2$ chains). HbA accounts for >95% of circulating Hb. HbF is the major Hb type at birth and decreases by 3-4%/week until adult levels are reached ($\sim$6 months old). α-chains are common to all normal Hb. Thus, defects of these chains will manifest before birth. α-chain disorders include Hb Barts, hydrops fetalis, Hb H disease, trait and silent carriers. Defects of β-chains only manifest at 3-6 months of age when β-chain synthesis occurs. Sickle cell disease is a common β-chain haemoglobinopathy. Other β-chain defects cause less severe haemolysis (Hb C, D and E).

Sickle Cell Disease

This inherited autosomal codominant condition is caused by a substitution of valine for glutamic acid. This renders Hb less soluble on deoxygenation. Tactoids form within the RBCs, distorting their shape, impeding their passage through small capillaries and causing vaso-occlusive crises and haemolytic anaemia. Both parents will show sickle cell trait and patients may be homozygous (HbSS), heterozygous (HbAS) or compound heterozygous (HbSC, HbS/ β-thalassaemia) Sickle cell disease is the most common and most severe inherited disease in Africa. The highest prevalence of the disease is in in West Africa because sickle cell trait offers protection against *P. falciparum* malaria in endemic areas.

Clinical Features

Intravascular sickling may be caused by acute infections, hypoxia, shock, dehydration, acidosis, or exposure to cold and leads to:

- Painful vaso-occlusive episodes – intense pain in the abdomen, chest or long bones and dactylitis (swelling of hands and feet); may require analgesia (morphine)

- Infarction of the viscera e.g. stroke, acute kidney injury, mesenteric ischemia, acute chest syndrome, splenic auto-infarction with progressive splenic hypofunction and atrophy by about 5 years
- Haemolytic crises with varying degrees of anaemia and jaundice
- Splenic sequestration with severe anaemia and thrombocytopaenia

Other problems may include aplastic crises following infection with parvovirus B19, gallstones and high risk of pneumococcal and haemophilus influenza infection.

Investigations
Laboratory tests will show

- Anaemia (see related image here)
- Sickle cells on blood smear
- Increased osmotic fragility

The diagnosis is confirmed by Hb electrophoresis (will show that the total Hb is comprised of 80% HbS and HbF).

Management
It includes:

- Folate supplementation
- Penicillin VK prophylaxis
- Hydroxyurea 15 mg/kg daily (to stimulate HbF production)
- Prompt treatment of any infections
- Treatment of painful crises with liberal IV or oral fluids and adequate analgesia
- Blood transfusion; considered in the following settings – severe anaemia, splenic sequestration, or aplastic or hyperhaemolytic crises.

Newer treatments include gene therapy and bone marrow transplantation. One should consider enrolling patients with Moya Moya syndrome in a hypertransfusion programme.
In terms of prevention, prenatal testing of parents and/or foetuses in areas with a high prevalence should be offered, as should termination of pregnancy.

Thalassaemia

Thalassaemia is the result of defective mRNA translation and the defective production of mRNA-controlling globin chains, leading to decreased synthesis of α-, β-, δ- or γ-chains. The most common form is β-thalassaemia (no β-chains are synthesised, HbA is absent and HbF predominates). β-thalassaemia is prevalent in people with Middle Eastern and Asian heritage e.g. the Indian community in South Africa. Thalassaemia major (Cooley's anaemia) is homozygous β-thalassaemia and thalassaemia minor is heterozygous β-thalassaemia (usually asymptomatic), see related image here.

β-thalassaemia is characterised by abnormal haem synthesis, which results in:

- Microcytic, hypochromic erythropoiesis
- Chronic, progressive hemosiderosis

Clinical Features

Patients typically present at 4-6 months with:

- Anaemia – severe, microcytic, hypochromic anaemia with poikilocytes, target cells, stippled cells and increased reticulocytes
- Jaundice
- Fever
- Impaired growth
- Hepatosplenomegaly

Skull bossing and maxillary hypertrophy develop in the first 2 years due to extramedullary erythropoiesis. Progressive haemosiderosis leads to hepatic, cardiac and endocrine dysfunction. The child will develop chronic, transfusion-dependent haemolytic anaemia and experience frequent infections. Few survive beyond a decade without treatment (see related image here).

Investigations

Laboratory tests will show elevated serum iron, transferrin saturation, serum ferritin and bone marrow iron (all due to chronic transfusions). The diagnosis is confirmed with Hb electrophoresis.

Management
The patient is treated with regular transfusions (reduces the phenotype) and oral iron chelators. Desferrioxamine is given overnight by continuous subcutaneous infusion to promote urinary iron excretion and delay progressive haemosiderosis. A splenectomy is performed in patients with gross splenomegaly and increasing need for transfusions.
Primary prevention involves screening high-risk populations, offering premarital counselling and making a prenatal diagnosis (via amniocentesis).

Acquired Haemolytic Anaemia

These anaemias can be categorised depending on the mechanism of destruction of the RBCs:

- Immune haemolytic anaemia:
    - Autoimmune:
        - Warm antibody – idiopathic, autoimmune diseases, infections, cancer and drugs (Coombs positive)
        - Cold antibody – infection, lymphoma or autoimmune disorder
    - Alloimmune – haemolytic disease, post-stem cell transplant, transfusion reactions
- Non-immune haemolytic anaemia:
    - Infection e.g. malaria, haemophagocytic lymphohistiocytosis (HLH), HIV, other viruses
    - Chemicals and physical causes, e.g. drugs, burns, drowning, lead poisoning
    - Fragmentation, e.g. march haemoglobinuria, microangiopathic haemolytic anaemia (MAHA), cardiac haemolysis
    - Acquired membrane disorder, e.g. paroxysmal nocturnal haemoglobinuria

These conditions are managed by identifying and treating the underlying cause. The mainstay of treatment in autoimmune haemolytic anaemia is steroids, given intravenously or orally. Splenectomy, rituximab, chemotherapy and immunosuppressants are second-line treatments. Some patients with acquired haemolytic anaemia may require emergency blood transfusions.

IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)

Thrombocytopenia is diagnosed when the platelet count is <100 x10^9/L and patients become symptomatic with platelet counts <20 x10^9/L. Thus, ITP is a quantitative platelet disorder which may be acute (<1 year duration) or chronic (>1 year duration).

Aetiology

ITP is idiopathic but is associated with:

- Autoimmune disease e.g. SLE
- HIV infection
- Viral infection 2-3 weeks prior
- Lymphoproliferative disorder e.g. lymphoma, chronic lymphocytic leukaemia (CLL)
- Adverse drug reaction e.g. after immunisation

Pathophysiology

ITP platelet antibodies often cross-react, resulting in platelet sensitisation. Sensitised platelets are cleared from circulation by the macrophages of the RES, reducing the lifespan of the platelets to just a few hours.

Clinical Features

The patient may present with:

- Bleeding – mucosal bleeding (e.g. purpura), nose bleeding, menorrhagia, gum bleeding, bleeding from the urinary or GI tract
- Acute-onset of spontaneous bruising or generalised petechiae
- Intracranial bleeding (<1% of cases; can be life-threatening)

Investigations

The platelet count will be <50x10^9/L, and the PBS will show megakaryocytes (see related image here) and normal RBCs and white blood cells (WBCs). The bone marrow aspirate will be normal or show increased megakaryocytes and normal white and RBC precursors (the other preserved cell lines and normal lactated

dehydrogenase (LDH) and uric acid help one decide between leukaemia and ITP). If the patient is >10 years old, s/he should be investigated for SLE and HIV.
The platelet count should be rechecked one hour post-platelet transfusion. If it demonstrates thrombocytopaenia, peripheral platelet consumption is confirmed i.e. ITP. However, this would be an expensive diagnostic investigation and should not be routinely done.

Management

In most cases this is a self-limiting condition and does not require treatment. However, the patient should avoid drugs which may interfere with platelet function e.g. aspirin and NSAIDS.
Platelets should not be routinely transfused unless the patient is suffering from a life-threatening haemorrhage e.g. intracerebral bleeding. Even then, a transfusion should only be done in consultation with a haematologist. When there is moderate-to-severe bleeding, one should give prednisone (4 mg/kg/day) for 4 days and then repeat the FBC after 4 days.
Other therapies include:

- High-dose IV immunoglobulin (IVIg) 0.5-1 g/kg
- Alternative forms of immunosuppression e.g. azathioprine, cyclophosphamide, rituximab (anti-CD20 monoclonal antibody)
- Splenectomy (for resistant chronic ITP):
    - This could be considered in children >5 years.
    - The patient should receive the pneumococcal vaccine prior to splenectomy and prophylactic penicillin until the age of 18.

HAEMOPHILIA

It is an inherited coagulation disorder (see related image here) that is X-linked recessive (females are rarely affected). The partial thromboplastin time (PTT) is prolonged, while the prothrombin time (PT) and bleeding time are normal. The severity of disease is inversely proportional to factor levels.

Classification

It can be classified according to the factor deficiency:

- Haemophilia A:
    - It is caused by a deficiency of factor VIII.
    - Carrier females have some evidence of decreased factor VIII and lyonisation (inactivation of the second X chromosome) can result in a symptomatic female.
    - Haemophilia A is most common (4-5-fold more common than haemophilia B).

30% of patients have no family history.

- Haemophilia B – caused by a deficiency of factor IX.
- Haemophilia C:
    - It is caused by a deficiency of factor XI.
    - It occurs equally in both sexes and is most prevalent in Jewish populations.

Haemophilia can also be classified according to the severity of the bleeding that occurs:

- Mild (occasional bleeds; 5-25% of cases)
- Moderate (less frequent bleeds post trauma or dental extraction; 1-5% of cases)
- Severe (spontaneous bleeding into joints and muscles; <1% of cases)

Clinical Features

The patient may present with a minor or major bleed.

Table 15.3: Features of Minor and Major Bleeds

Minor Bleeds	Major Bleeds

● Bleeding into soft tissue
● Gum bleeds
● Epistaxis
● Hemarthrosis (pain or swelling in joint)
● Intramuscular haematoma
● Haematuria
	● Intracranial haemorrhage (most severe)
	● Retroperitoneal bleeding
	● Soft tissue bleeding resulting in:
	  ○ Compression of the femoral nerve (bleeding into the groin)
	  ○ Volkmann's contracture (bleeding into the forearms causing neurovascular compression)

Investigations

Blood tests will show a prolonged PTT and factor levels <25% of normal.

Management

Non-Pharmacological Management
It includes:

- Genetic counselling
- Applying for a MedicAlert bracelet
- Addressing dental care
- Applying ice packs 5 min on and 10 min off in the acute bleed
- Health education for the patient (e.g. avoidance of aspirin and NSAIDs) and family on how to monitor and treat patients
- Management of knee haemarthrosis:
    - Admit and avoid weight-bearing
    - Immobilising the knee in slight flexion (with a backslab or plaster of Paris; POP)
    - Refer to physiotherapy and occupational therapy to decide on splinting

Pharmacological Management
Bleeding episodes are treated and prevented by replacing the missing clotting factors with factor concentrate. Fresh frozen plasma (FFP) (see related image here) may be given as an alternative in an emergency situation should factor concentrate not be available. In severe haemophilia, one may consider offering 2-3-times weekly prophylactic replacement of the deficient factor. This may be continued lifelong. Patients with mild haemophilia A and some patients with Von Willebrand disease (vWD) can be treated with desmopressin (DDAVP®) prior to surgery or during bleeding episodes.
Mucous membrane bleeds can be treated with tranexamic acid (contraindicated in haematuria as may cause obstructive uropathy). Surgical and dental procedures should be done under factor cover and a multidisciplinary approach is mandatory. The patient may become refractory to replacement of coagulation factor, as a result of developing high levels of circulating inhibitors. These may be managed through inhibitor eradication by immune tolerance induction (ITI) or the use of bypass agents e.g. anti-inhibitor coagulant complex (FEIBA®) or emicizumab.

DISSEMINATED INTRAVASCULAR COAGULOPATHY (DIC)

It is an acquired condition characterised by simultaneous bleeding diathesis and microvascular thrombosis.

Aetiology

DIC may be caused by:

- Septicaemia and shock
- Trauma e.g. burns, head injury, post-operative states
- Malignancy e.g. promyelocytic leukaemia
- Perinatal complications e.g. birth asphyxia, necrotising enterocolitis
- Viraemia

DIC is also associated with Kaposiform haemangio-endothelioma (Kasabach-Merritt syndrome).

Pathophysiology

The inciting event induces endothelial damage and activates the coagulation cascade, which consumes clotting factors and platelets and inhibits natural anticoagulants and fibrinolysis. This process continues uncontrollably, resulting in DIC. Depending on the extent of the thrombosis, end-organ failure may develop (kidney, liver, lung, brain, adrenals, heart or extremities).

Clinical Features and Investigations

Haemorrhage is the most prominent clinical feature with the most common sites of bleeding being the skin (purpura), venipuncture sites, GIT, lungs (intrapulmonary bleeding) or brain (intraventricular haemorrhages).

The patient will also have abnormal coagulation studies (PTT, low fibrinogen levels and elevated D-dimer levels).

Management

One must treat the underlying cause and give supportive care, including FFP and cryoprecipitate transfusions. Blood and platelet transfusions may also be given, as

needed. Anticoagulation is generally not indicated unless there is significant thrombosis e.g. purpura fulminans.

VON WILLEBRAND DISEASE (vWD)

It is the most common congenital bleeding disorder. Von Willebrand factor (vWF) is a large multimeric protein that is essential for primary haemostasis and is the carrier for factor VIII.

Low levels of vWF affect up to 1% of the population, however individuals are rarely symptomatic. vWD may be autosomal dominant or recessive.

Pathophysiology

The deficiency of vWF (due to a quantitative deficiency or qualitative deficiency i.e. abnormal vWF) results in lower platelet adhesiveness and an impairment of primary haemostasis.

Clinical Features

The patient may present with:

- Family history or significant personal history of bleeding
- Recurrent epistaxis and mucosal bleeding e.g. easy gum bleeding, easy bruising, prolonged bleeding from injuries
- Heavy menstrual bleeding at the onset of menarche in girls

Investigations

Blood tests will show

- Prolonged bleeding time
- Prolonged PTT
- screening tests – may be normal
- Decreased vWF antigen
- Decreased ristocetin cofactor and/or collagen binding activity
- Decreased factor VIII coagulant activity

Management

Non-pharmacological management includes first aid (especially for epistaxis) and the application of pressure to bleeding areas e.g. using tranexamic acid-impregnated gauze to apply pressure for tooth socket bleeds.

Pharmacological management includes

- For mild bleeds – IV desmopressin (maximum 3 doses)
- For severe bleeds – factor VIII or vWF concentrate
- For mucous membrane bleeds – tranexamic acid
- For menorrhagia – low-dose combined oral contraceptive

ONCOLOGY

At the link is a mnemonic for the early paediatric oncological signs by the Childhood Cancer Foundation of South Africa (CHOC), based on Saint Siluan's early warning signs of childhood cancer (see related link here).

Classification

Childhood cancers may be classified as blood-forming tumours and solid tumours; see related image to lymph nodes here.

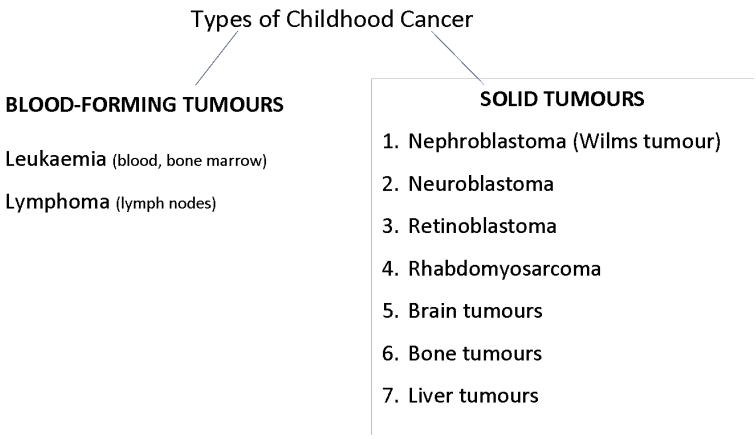

Figure 15.2: Types of Childhood Cancers

LEUKAEMIA

Acute leukaemia is the most common cancer in childhood. The leukaemia can either have a lymphoid- or myeloid-precursor origin – ALL or acute myeloid leukaemia (AML), respectively (see related image here). ALL can either have a B-cell lineage (B-ALL) or T-cell lineage (T-ALL).

Pathophysiology

Leukaemia is caused by uncontrolled replication of a single, immature, haematopoietic WBC with arrested or abnormal differentiation. It is, therefore, a clonal disease. Proliferation of the cells leads to the infiltration of bone marrow by blasts and replacement of normal haematopoietic cells. The abnormal cells circulate in the bloodstream and infiltrate other tissues.

Clinical Features

Leukaemia peaks in children aged 1-5 years and is slightly more common in males. The child may present with an acute history (days to weeks) of:

- Pallor
- Fatigue, lethargy and irritability
- Headache
- Generalised lymphadenopathy
- Hepatosplenomegaly
- Bone pain
- Fever
- Bleeding (epistaxis or gingival), bruising and petechiae
- Chloroma
- Gingival hypertrophy
- Testicular enlargement
- Focal neurological signs and/or seizures (if there is CNS involvement)
- Dyspnoea, orthopnoea and/or tachypnoea (if there is a mediastinal mass)

Investigations

They should include:

- FBC – will show:

    - High, normal or low WCC
    - Normochromic, normocytic anaemia
    - Thrombocytopaenia
- RFTs – will show:
    - High LDH
    - High urate
- PBS – will show blasts
- Bone marrow aspirate and trephine biopsy (BMAT)
    - A sample should be sent for morphology, immunophenotyping (flow cytometry) and cytogenetics.
- CXR – to exclude a mediastinal mass
- Abdominal ultrasound scan (USS) – to demonstrate hepatosplenomegaly
- LP – to demonstrate the presence of blasts and confirm CNS disease

Management

Treatment is adapted based on prognostic factors. One must treat infections and manage bleeding and tumour lysis syndrome (TLS).
Steroids (prednisone and dexamethasone) and chemotherapeutic agents (vincristine, daunorubicin and asparaginase) are the mainstays of treatment.
Intrathecal chemotherapeutic agents may also be used (methotrexate is used to prevent or treat CNS disease).
Maintenance chemotherapy, with mercaptopurine, methotrexate, vincristine and dexamethasone, is continued for two years in girls and three years in boys. A bone marrow transplant is indicated for high-risk or relapsed leukaemia (see related image here).

SOLID TUMOURS

LYMPHOMA

Paediatric lymphomas can be divided into Hodgkin's lymphomas (HLs) and non-Hodgkin's lymphomas (NHLs). HLs can be further subdivided into classical and nodular, lymphocyte-predominant HLs. NHLs can either have a T-cell origin (e.g.

anaplastic large cell lymphoma) or B-cell origin (e.g. Burkitt lymphoma, diffuse, large B-cell lymphoma).

Clinical Features

The child will present with:

- Lymphadenopathy:
  - Painless nodal enlargement
  - Often chronic lymphadenopathy in HLs
- Presence of B symptoms:
  - Anorexia and weight loss
  - Fever
  - Drenching night sweats

Children with Burkitt's lymphoma may have:

- Jaw mass (endemic Burkitt's lymphoma)
- Abdominal mass (sporadic Burkitt's lymphoma)
- Acute abdomen with intussusception and bowel obstruction or acute bowel perforation
- Ascites and/or kidney infiltration
- Disseminated disease (bone marrow and/or CNS involvement)

Patients with HLs may present with:

- Painless lymphadenopathy (usually spreads to contiguous nodes in a predictable sequence)
- Generalised pruritus (may indicate the presence of immune haemolytic anaemia)
- Mediastinal lymphadenopathy (may manifest as airway compression or superior vena cava obstruction)

Investigations

They should include:

- Fine needle aspiration biopsy (FNAB) and/or excision biopsy for histology:
  - HLs will show Reed-Sternberg cells on a background of other inflammatory cells.

    - Burkitt's lymphoma will have a 'starry sky' appearance and a high Ki-67 proliferation index (indicating a high mitotic rate).
- Chest X-ray (to exclude a mediastinal mass)
- Abdominal USS (to exclude an abdominal mass and/or lymphadenopathy)
- Bone marrow aspirate (to investigate for bone marrow involvement)
- LP (to investigate for CNS involvement)

NHLs will then be staged using the St Jude/Murphy staging system and HLs using the Ann Arbor staging system.

Management

Table 15.4: Management of Non-Hodgkin's and Hodgkin's Lymphomas

NHLs	HLs
● For Burkitt's lymphoma, tumour debulking should not be performed. Instead chemotherapy should be performed as it responds well to chemotherapy alone. ● Radiotherapy is rarely indicated for NHLs. ● Good supportive care measures must be implemented to prevent TLS.	● Surgery is limited to excisional biopsy. These cancers are sensitive to both chemotherapy and involved field radiotherapy.

WILMS TUMOUR (NEPHROBLASTOMA)

It is the most common renal malignancy in children and remains one of the most common malignancies in Africa. It usually occurs in children <5 years old and is more common in females. In 5-10% of cases, both kidneys are affected.
Wilms tumour is associated with genetic conditions in which there is a WT-1 gene deletion or mutation, such as:

- WAGR syndrome (Wilms tumour, aniridia, genito-urinary abnormalities and mental retardation)
- Beckwith-Wiedemann syndrome (characterised by macroglossia, macrosomia, omphalocele and hemi-hypertrophy)
- Denys-Drash syndrome (characterised by diffuse mesangial sclerosis leading to progressive renal failure, male pseudohermaphroditism and Wilms tumour)

Clinical Features

They may include:

- Incidental finding of an abdominal mass by the parent or doctor
- Associated congenital anomalies (present in 20% of cases)
    - Aniridia
    - Hemihypertrophy
    - Urogenital anomalies
- Fever
- Abdominal pain
- Haematuria
- Hypertension
- Anaemia (may be caused by intratumoural bleeding or rupture)
- Acquired vWD and associated bleeding
- Severe malnutrition (may be present in advanced disease)

5% of affected children present with bilateral tumours.

Investigations

One should order:

- FBC
- RFTs
- LFTs
- Coagulation screen
- Urinalysis:
    - It is done to look for blood and protein and to look for urine catecholamines to exclude neuroblastomas.
- Ultrasound:
    - This non-invasive investigation is done to identify the tumour site and characteristics, bilateral or hepatic involvement, nephrogenic rests, abdominal lymphadenopathy, and renal vein or IVC thrombosis.
- MRI abdomen (to better delineate the renal mass)
- Chest X-ray or CT lung (to detect lung metastases)
- FNAB:

- It is done to confirm the diagnosis and determine the prognosis.
- Focal or diffuse anaplasia is associated with a worse prognosis and will require radiotherapy.

Management

Treatment is determined by the stage of the disease but multimodal therapy is often required (chemotherapy, surgery and radiotherapy).

NEUROBLASTOMA

It is the most common extracranial solid tumour in children. The median age of onset is 2 years. The neoplastic cells are derived from primordial neural crest cells which develop into sympathetic ganglia and the adrenal medulla. The abdomen is the most frequent location for this cancer (suprarenal mass) but the disease can manifest anywhere along the sympathetic chain (from neck to pelvis).
There is great heterogeneity in this disease, with some patients undergoing spontaneous regression and others having resistant and aggressive disease.

Clinical Features

The patient will have general clinical features (fever, anorexia, lethargy, pallor, weight loss and irritability) and organ-specific clinical features.

- Abdominal disease – abdominal mass associated with pain, anorexia, vomiting or constipation
- Thoracic disease – posterior mediastinal mass associated with dyspnoea, orthopnoea or dysphagia
- Head and neck – Horner's syndrome
- Pelvic – difficulty micturating and defecating
- Paraspinal disease (extension to the neural foramen) – spinal cord compression with associated symptoms dependent on the level of compression e.g. pain, paralysis and issues with bladder and bowel function
- Disseminated disease (common) – swellings on the skull, proptosis and raccoon eyes (blue periorbital discolouration), skin metastasis (blueberry muffin rash), painful skeletal metastasis, distant lymph node metastasis or liver metastasis

- Paraneoplastic phenomena – chronic diarrhoea, opsoclonus-myoclonus ataxia syndrome (dancing eyes) and hypertension

Investigations

They should include:

- FBC (to assess for bone marrow infiltration)
- Tumour markers (raised LDH and ferritin)
- Abdominal USS (to assess for an abdominal mass)
- Chest X-ray (to assess for a mediastinal or paraspinal mass)
- Bone scan (to look for skeletal metastasis)
- BMAT (to look for BM involvement)
- Biopsy (to assess the histology and biology of the tumour; MYCN amplification is associated with a very poor prognosis)
- Urine catecholamines (homovanillic acid and vanillylmandelic acid)
- CT/MRI (to better delineate an abdominal mass from a paraspinal mass)
- Metaiodobenzylguanidine (MIBG) scan (to assess uptake in the primary mass and assess for skeletal deposits)

Management

A multimodal approach is used, with chemotherapy, surgery and radiotherapy all being used. An autologous stem cell transplantation may also be performed. Maintenance therapy is with anti-GD2 immunotherapy and cis-retinoic acid.

RETINOBLASTOMA

It is the most common intraocular tumour in childhood and occurs in children <5 years old. The tumour can be unilateral or bilateral, unifocal or multifocal, and sporadic or hereditary. Bilateral, multifocal, hereditary retinoblastoma is associated with RB1 gene mutations or deletions. In hereditary retinoblastoma there is an increased risk of developing secondary malignancies, including the development of an asynchronous brain tumour (trilateral RB) (see related image here).
Genetic counselling is indicated in all patients. Patients should be screened for the development of retinoblastoma in the contralateral eye and for the development of

an asynchronous brain tumour. Siblings and future offspring should be screened for retinoblastoma.

Clinical Features

Patients may present with leukocoria (absent red reflex on flash photography) and/or strabismus early in the disease process.

Children with locally advanced disease present with a painful, red eye, proptosis and/or glaucoma. In metastatic disease, there is extension to the optic nerve (causing blindness) or cerebrum (causing localising neurological signs, seizures or raised intracranial pressure).

A thorough ophthalmological examination should be performed. One may need to use a RetCam® or examine the child under anaesthesia.

Investigations

They should include:

- USS of the eye (to look for a hyperechoic mass and calcifications)
- CT/MRI of brain and orbit (to assess for extension to the optic nerve, orbit or cerebrum)
- Bone marrow aspiration (to assess for BM involvement)
- LP (to assess for CNS involvement)

Management

A well-coordinated, multidisciplinary team approach is required. One's priorities are to preserve life, preserve vision and preserve the eye. Treatment is dependent on the stage and the extent of the disease.

For small tumours, one should consider local therapies (photocoagulation, cryotherapy, intralesional or intra-arterial chemotherapy and/or brachytherapy). For larger tumours which are limited to the eye, enucleation is the intervention of choice. For advanced or metastatic disease, chemotherapy and external beam radiotherapy are required. CNS disease may require intrathecal chemotherapy and craniospinal irradiation.

RHABDOMYOSARCOMA

It is the most common soft-tissue sarcoma of childhood, and is generally diagnosed ~5 years old. Approximately half of the tumours occur in the head and neck region (orbit, nasopharynx, middle ear or face), a quarter in the genitourinary system (bladder, prostate, vagina, uterus or paratesticular space) and the remaining quarter in the extremities, trunk, or retroperitoneum. Metastases occur early and are to regional lymph nodes, lungs, bones, and bone marrow.

Clinical Presentation

Tumours of the ear, nose, bladder, uterus or vagina may present as polypoid lesions, which cause obstruction or secrete a bloodstained, offensive discharge. On the trunk and extremities, the tumours present as soft-tissue masses (may be tender and easily confused with an acute abscess). Orbital swelling may be mistaken for a retinoblastoma, neuroblastoma or Burkitt's lymphoma. The brain and cerebrospinal fluid may be infiltrated with parameningeal tumours.

Investigations

One should perform a FNAB or incisional/excisional biopsy of the lesion. The extent of metastatic spread must also be investigated (CT, CXR, PET scan, etc.).

Management

A multimodal approach must be followed (chemotherapy, surgical resection and radiotherapy). Primary total surgical resection followed by chemotherapy or chemotherapy followed by complete resection of residual tumour offers the best chance of cure. Radiotherapy must be done at tumour sites where surgical removal has not produced a microscopically complete tumour resection.

Prognosis

Children with limited disease which has been completely excised have a good prognosis. Those with advanced disease, with incomplete resection or who are <1 year or >10 years old have a worse prognosis.

Chapter 16:

POISONINGS

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This chapter covers the following topics:

- Epidemiology of poisonings and toxidromes
- Approach to the child with suspected poisoning
- Iron poisoning/overdose
- Organophosphate poisoning
- Paraffin poisoning (hydrocarbons)
- Tricyclic antidepressants (TCAs) overdose
- Caustic and corrosive substance ingestion
- Neuroleptic overdose
- Salicylate poisoning
- Snake bites
- Oral contraceptive overdose

EPIDEMIOLOGY OF POISONING AND TOXIDROMES

Children may be exposed to a large spectrum of potentially harmful substances. Most poisoning cases are in children <6 years old. Internationally, poisoning is responsible for 3.9% of injury-related deaths, with children in low- and middle-income countries making up the greatest proportion of these cases. A study of poisoning cases encountered at Red Cross War Memorial Children's Hospital revealed that pharmaceuticals are responsible for most poisoning cases, followed by paraffin, pesticides, household products and cosmetics.

Below are important toxidromes which can help one identify the class of the implicated toxin:

Table 16.1: Clinical Features of Important Toxidromes

Toxidrome	Clinical Features	Examples
Anticholinergic	Agitation, hallucinations, dilated pupils, dry mouth, dry skin, fever, urinary retention	Antihistamines, atropine, *Amanita pantherina*
Cholinergic	Pinpoint pupils, bradycardia, respiratory secretions (bronchorrhoea), fasciculations, salivation, wheezing, diarrhoea	Organophosphates
Sympathomimetic	Agitation, hallucinations, dilated pupils, sweating, tremor, seizures, tachycardia, hypertension	Cocaine, amphetamines, nasal decongestants
Sedative/hypnotic	Coma, hypothermia, hypotension	Alcohol, benzodiazepines
Opioid	Coma, pinpoint pupils, hypothermia, hypotension, respiratory depression	Codeine

APPROACH TO THE CHILD WITH SUSPECTED POISONING

One must:

- Resuscitate
- Identify the poison
- Prevent further absorption of the poison
- Enhance and support elimination of the poison

Resuscitate

Assess airway, breathing, circulation and disability, noting the child's mental status, heart rate, respiratory rate, temperature, pupils, skin colour and temperature, and the presence of fasciculations.

Identify the Poison

One must take a history from the child (if possible) and caregiver, and read the drug name and concentration of the suspected poison from its bottle or container. In South Africa, one may call the Poisons Information Helpline (0861 555 777; a 24-hour emergency line) to find out if the symptoms correspond with any toxidromes.

Prevent Absorption

Decontaminate the skin or mucous membranes by washing or irrigating them with water for 15-20 mins (use saline to irrigate the eye, if possible). Gut decontamination is performed if a potentially life-threatening poison is ingested and the patient presents within 1 hour of ingestion. One can consider using multiple doses of activated charcoal to adsorb the poison if the child has an intact gag reflex or the airway is protected. Activated charcoal binds certain toxins (e.g. carbamazepine, theophylline) in the GIT to prevent absorption. Haemodialysis may also be of benefit in some poisonings e.g. ethylene glycol poisoning.

Support and Enhance Elimination of the Poison

One may support elimination preventing and reversing complications:

- Monitor the child
- Support respiration
- Treat hypotension or arrhythmias and give fluids
- Control convulsions
- Manage hypoglycaemia and hypothermia

If possible, one should measure the drug levels.

The effect of the drug may be limited by administering an antidote, such as:

- Desferrioxamine for iron poisoning
- Atropine for organophosphate poisoning
- Naloxone for opioid overdose

- Flumazenil for benzodiazepine overdose
- N-acetylcysteine for paracetamol overdose

Urine alkalinisation (administer IV sodium bicarbonate to increase the pH of the urine) is done to enhance the elimination of acids, such as salicylates.

IRON POISONING/OVERDOSE

Children are usually exposed to iron because their parents have iron supplements in the medicine cabinet. Risk of serious poisoning is dependent on the child's exposure to elemental iron. Doses of more than 20 mg/kg may result in symptoms and doses of 40-60 mg/kg may result in symptoms of serious toxicity. See related image here.

Clinical Features

The clinical picture progresses through five phases which often overlap. They are:

- Gastrointestinal phase (30 mins to 6 hours)
- Latent phase (6-24 hours)
- Shock (6-72 hours)
- Hepatotoxicity (12-96 hours)
- Bowel obstruction (2-8 weeks)

The presentation varies and may include:

- Mild abdominal symptoms e.g. abdominal tenderness, vomiting and diarrhoea
- Tachycardia
- Altered mental state
- Hypotension suggestive of shock
- Liver failure after about 48 hours (the loss of synthetic function results in coagulopathy, INR >1.5 and encephalopathy)

Investigations

Special investigations should include serum iron levels (at least 4 hours post-ingestion and may need to be repeated) and abdominal X-ray (may demonstrate ingested pills).

Management

Iron poisoning is a medical emergency and must be treated with urgency. Delay in starting therapy may prove fatal. Treatment is based on three principles which must be simultaneously applied in all patients with iron poisoning:

- Maintain an effective circulating blood volume
- Eliminate as much iron from the gut as possible, before it can be absorbed
- Chelate absorbed iron with desferrioxamine before it can cause mitochondrial damage

General and Supportive Measures

Resuscitate the patient as needed. Should the child have a reduced level of consciousness, secure the airway and consider ventilation.

Specific Management

If the child presented early and mainly has gastrointestinal manifestations, gastrointestinal decontamination should be considered. However, activated charcoal is not recommended (has poor iron binding capacity) and gastric emptying and lavage are not indicated (the child will most likely be vomiting and adult iron preparations cannot be removed with an orogastric tube). Whole bowel irrigation therapy can be performed.

Desferrioxamine is an IV antidote which is given in serious overdose at a rate of 15 mg/kg/hour (maximum total dose of 80 mg/kg). It chelates iron and, thus, limits exposure. Desferrioxamine may be used in conjunction with sodium bicarbonate (if the child is acidotic).

ORGANOPHOSPHATE POISONING

Children are mainly exposed to organophosphates in the form of insecticides (used in rural or farming communities) or rat poison (in urban communities). Toxicity is the result of inhibition of the acetylcholinesterase enzyme, which causes the accumulation of acetylcholine.

Clinical Features and Diagnosis

Acute toxicity presents with a cholinergic toxidrome:

- Sweating
- Salivation
- Lacrimation
- Urination
- Diarrhoea
- Constriction of pupils
- Bradycardia
- Respiratory symptoms e.g. bronchospasm, bronchorrhoea, respiratory depression
- Muscle weakness

The diagnosis is made based on clinical features and suggestive history. If there is doubt surrounding the diagnosis, an atropine challenge may be done (give 0.01-0.02 mg/kg of atropine) and the patient watched for the development of anticholinergic symptoms. The plasma acetylcholinesterase level may be measured to confirm the diagnosis.

Management

General and Supportive Measures

One must first secure the child's airway. Decontamination is guided by history. The person who is performing the decontamination must wear the appropriate protective clothing. If the child’s skin is contaminated, discard the child’s clothes and thoroughly wash the child.

If the organophosphate was ingested, activated charcoal may be given (within 2 hours of ingestion). A gastric lavage should not be performed.

Intravenous benzodiazepines (e.g. diazepam 0.3 mg/kg; to a maximum of 10 mg) should be used in all but the mildest cases to relieve anxiety and treat or prevent breakthrough seizures. Doses should be repeated as necessary.

Organophosphate poisoning is a notifiable condition (as are all symptomatic poisonings), thus a form should be filled out and sent to the relevant local health authority.

Specific Treatment

One may administer:

- Atropine antidote:
    - One should give an initial bolus dose of atropine (0.05 mg/kg) and then double the atropine (see related image here) bolus dose every 5 minutes until some signs of atropinisation occur i.e. clearing of secretions (the most important sign of adequate atropinisation; improving heart rate and BP, drying of skin and dilating of pupils are late signs).
    - Once there is clinical improvement and signs of atropinisation, one should start an atropine infusion (10-20% of the total bolus dose of atropine given, administered hourly). Regularly monitor the patient and give additional bolus doses of atropine if any deterioration occurs until the patient is re-atropinised.
- Inhaled ipratropium:
    - 0.5 mg inhaled ipratropium can be given to help resolve bronchospasms.

PARAFFIN POISONING (HYDROCARBONS)

Hydrocarbons are found in a wide range of industrial and domestic products. Paraffin is the most ubiquitous of the hydrocarbons and is often stored in unmarked cooldrink bottles in unsecure locations, giving children easy access to it (see related image here). Toxicity depends on the route of exposure:

- Direct contact (local toxicity) – causes local irritation of the skin and mucous membranes due to leaching of oils and fat from skin
- Inhalation/aspiration – even small amounts can cause necrotising and haemorrhagic pneumonitis i.e. chemical pneumonitis
- Ingestion – causes systemic toxicity, CNS depression, cardiac sensitisation to catecholamines and even liver and kidney damage

Clinical Features

Clinical features suggestive of inhalation or aspiration include coughing, tachypnoea or dyspnoea with nasal flaring, wheezing and cyanosis. Air in the alveoli is displaced by vaporised hydrocarbons causing oedema and worsening hypoxia.
Systemic toxicity is typified by CNS effects – headache, dizziness, blurred vision, lethargy progressing to seizure and coma. Myocardial sensitisation results in arrhythmia.

Investigations

Important special investigations include arterial blood gas, FBC, RFTs and serum glucose. If respiratory symptoms develop, take a chest X-ray 6-8 hours after ingestion (or sooner if clinically indicated). The X-ray may demonstrate small patchy opacification.

Management

There is no role for gastrointestinal decontamination in patients with paraffin poisoning, as activated charcoal (see related image here) does not adsorb hydrocarbons and induced emesis/gastric lavage are contraindicated.
There is no specific treatment for paraffin poisoning, therefore the mainstay of treatment is supportive (careful monitoring of respiratory symptoms and pulse oximetry). If the child is severely distressed or has a decreased level of consciousness, one should intubate. Give oxygen and bronchodilators (β_2-antagonists) for distress. Closely monitor the child's oxygen to detect late-onset respiratory failure. If seizures develop, treat with benzodiazepines. Keep the child hydrated; monitor input and output.

TRICYCLIC ANTIDEPRESSANTS (TCAs) OVERDOSE

There is a high potential for toxicity with TCAs because of their narrow therapeutic indices (>5 mg/kg in children).

Clinical Features and Investigations

The symptoms are predominantly neurological (altered mental state, seizures) but also include cardiotoxicity, acidosis and respiratory depression. The child will also have anticholinergic features, such as decreased GI motility and urinary retention.

Management

Monitoring

It is important to monitor input and output, arterial blood gas results (for acid-base levels) and RFTs (especially potassium) because of the anticholinergic effects of TCAs. One must also monitor drug levels. Baseline and continuous 12-lead ECGs should be done because cardiac toxicity may occur. BP should also be monitored.

Treatment

Gastrointestinal decontamination with activated charcoal is helpful up to several hours after exposure because of delayed gastric emptying. However, one must always ensure that the airway is protected before using activated charcoal due to the risks of rapid CNS depression, loss of airway control and seizure.

One should consider ventilation if the patient becomes hypoxic (pCO_2 >6.7 kPa or pO_2 <8 kPa). Sodium bicarbonate is the mainstay of treatment and 0.5-2 mmol/kg sodium bicarbonate by slow IV infusion with 5% dextrose should be administered. This should be followed by an infusion to keep the pH around 7.50. Wide QRS arrhythmias may develop and must be treated with sodium bicarbonate as above. Hypotension should be treated and normotension maintained through volume expansion (give Ringer's lactate or normal saline). Torsades de Pointes should be managed with magnesium sulphate (25-100 mg repeated every 10 mins to a maximum of 2 g). Convulsions are managed with benzodiazepines. Phenytoin is contraindicated.

CAUSTIC AND CORROSIVE SUBSTANCE INGESTION

Corrosive or caustic injury occurs as the result of the ingestion of acid or alkaline substances. Acids that have a corrosive effect include hydrochloric acid and battery acid. Alkalis which have corrosive effects include sodium hydroxide, calcium

hydroxide and potassium permanganate. Potassium permanganate is a commonly ingested or corrosive substance. See related image here.

Clinical Features

The main clinical feature is pain. Younger children who are unable to give a history of pain will present with crying, refusal to swallow, drooling or vomiting. Other symptoms include stridor or hoarseness. On examination, oral burns may be seen.

Management

If the child has been asymptomatic for 12 hours and is able to tolerate oral fluids, no intervention is necessary. All symptomatic patients will be investigated by endoscopy, which will influence further management.
Symptomatic patients should be kept nil per mouth and thoroughly examined to exclude an oesophageal perforation. If airway involvement is suspected, endotracheal intubation is indicated. A gastrointestinal bleed or oesophageal perforation should be surgically managed.

NEUROLEPTIC OVERDOSE

Neuroleptics are a group of antipsychotic and sedating agents. Commonly used neuroleptic drugs include chlorpromazine, haloperidol and phenothiazine antiemetics e.g. promethazine.

Clinical Features

The main clinical symptoms of neuroleptic overdose are:

- Decreased level of consciousness
- Respiratory difficulty/depression e.g. dyspnoea, cyanosis, apnoea
- Hypotension
- Extrapyramidal side effects

These agents also have antimuscarinic effects, namely dry mouth, urinary retention, dilated pupils and blurred vision.

Management

Monitoring

The child must be attached to an ECG monitor to detect arrhythmias. Other routine monitoring which should be performed are temperature, blood pressure and heart rate monitoring (tachycardias are common). Arterial blood gases should be done to monitor urea, electrolyte and glucose levels.

The child's level of consciousness must be regularly evaluated to ensure the child can maintain his/her own airway. If not, intubation is indicated.

General and Supportive Measures

If the child presents early (within two hours) and a significant overdose is suspected, give activated charcoal.

The associated hypotension should be managed with fluids and placing the child in Trendelenburg position to increase venous return. Occasionally, neuroleptic malignant syndrome (NMS) can develop. It causes:

- Hyperthermia
- Altered level of consciousness
- Muscle rigidity
- Abnormal U&E
- Features of autonomic disturbance (fluctuating BP, sweating incontinence)

NMS is an emergency and must be differentiated from dystonia for appropriate clinical management.

Specific Treatment

Children are prone to extrapyramidal side effects e.g. dystonia (prolonged, painful muscle contraction with abnormal postures and movements). This is managed with anticholinergics e.g. biperiden (Akineton®) given IM/IV at an aged-dependent dose which is repeated 6-8 hourly over 48-72 hours:

- Age <1 year – 1 mg
- 2-6 years – 2 mg
- 7-10 years – 3 mg
- >10 years – 5 mg

If there is no response, one should consider giving diazepam (0.1-0.4 mg/kg).

SALICYLATE POISONING

Salicylates are found in many over-the-counter medications, such as aspirin, Grand-Pa headache powders®, Tylenol®, Compral® and wintergreen ointment.

Clinical Features

Patients will commonly present with tachypnoea, hyperventilation and metabolic acidosis. They may also have nausea, vomiting, diarrhoea or tinnitus. With more severe intoxication they may have altered mental states, fever or pulmonary oedema, and may die.

Investigations

The plasma salicylate concentration should ideally be measured in anyone suspected of salicylate poisoning, and should be measured in 2-4-hour intervals. The results should be interpreted in the context of the patient's clinical condition. Doctors should continue careful monitoring of patients, even if salicylate concentrations are on the decline.

Management

As with any emergency patient, the Advanced Life Support (ALS) algorithm should be followed. One must pay special attention to and correct electrolyte imbalances, particularly glucose and potassium imbalances.

GIT decontamination with activated charcoal is recommended in acute overdose (1 g/kg; maximum single dose of 50 g). This should be reconsidered or omitted in patients with altered mental states who cannot maintain their airways (unless intubated). Urinary alkalinisation is recommended in addition to gastrointestinal decontamination with activated charcoal. This is done by administering an IV bolus of 1-2 mL/kg 8.4% sodium bicarbonate, followed by an infusion of sodium bicarbonate (add 100 mL of 8.4% sodium bicarbonate to 900 mL of 5% dextrose) at a rate approximately double the maintenance requirement. Potassium levels should be monitored and replaced as needed.

SNAKE BITES

There are about 35 venomous snake species in South Africa, but only ~10 of these are potentially fatal. These include cobras, mambas, adders, vipers, boomslangs and vine snakes.

Classification of Venom and Associated Syndromes

There are three types of venom – neurotoxic, cytotoxic and haemotoxic.

Table 16.2: Snake Venom Types

Neurotoxic Venom e.g. black mambas, small adders and non-spitting cobras	**Cytotoxic Venom** e.g. puff adders and some vipers	**Haemotoxic Venom** e.g. boomslangs and vine snakes
• Mainly acts in the synaptic clefts • Patients may present with dizziness, slurred speech, impaired coordination, hypersalivation and ptosis • Can cause hyponatremia, respiratory failure and paralysis of skeletal muscles • Associated syndrome – progressive weakness (PW) syndrome	• Contains proteolytic enzymes, therefore directly injures tissues (causes local tissue damage with necrosis) • Patients may present with tender lymphadenopathy, rash, low-grade fever and headaches • Associated syndrome – painful progressive swelling (PPS) syndrome	• Activate certain clotting factors (II and X), causing a consumptive coagulopathy • Patient may present with profuse bleeding, swelling and necrosis • May lead to DIC and multi-organ failure • Associated syndrome – bleeding (B) syndrome

Management

Identifying the type of snake is not always accurate and is not recommended. Instead, treatment should be given based on clinical presentation i.e. syndromic management. Management should always start with resuscitation (ABCDE). Tourniquets should not be used. Instead the patient must be kept still and the

affected limb may be gently splinted. One must check that the child's tetanus immunisation is up-to-date.

90% of envenomations are treated with supportive measures alone, unless severe envenomation is suspected. This includes:

- For PW syndrome – airway and ventilator support
- For PPS syndrome (90% of envenomation in SA) – elevate the bitten limb, remove tight clothing, give adequate analgesia and IV fluids, and mark the area of swelling and monitor hourly to assess progression and whether antivenom will be required.
- For B syndrome – perform coagulation studies; give blood and other blood products

Specific Treatment

Antivenom is only indicated in ~10% of snakebite patients. The antivenom may be polyvalent or monovalent. Polyvalent antivenom is used most commonly, as it covers ten types of snake bites e.g. for patients with PW. Monovalent antivenom is given to patients with a bleeding syndrome (as it may be due to a boomslang bite).

ORAL CONTRACEPTIVE OVERDOSE

Depending on the specific product, ingested oral contraceptives (see example here) are generally comprised of a mix of synthetic progesterones (progestins) and oestrogens, which have different ways of causing toxicity.

Clinical Features

Progestins do not cause acute toxicity; however, chronic exposure has been known to cause thromboembolic phenomena, jaundice and altered liver function. It also potentially precipitates porphyria attacks.

Oestrogens do have the potential to cause acute toxicity, but hospitalisation is rarely required. Symptoms of oestrogen toxicity include nausea, vomiting, diarrhoea and lethargy. Theoretically, a withdrawal vaginal bleed can occur in girls 1-3 days post-exposure but this is not supported by evidence. One must identify chronic exposure in children as it may lead to premature closure of epiphyseal plates and stunting growth.

Chapter 17:

RENAL DISORDERS

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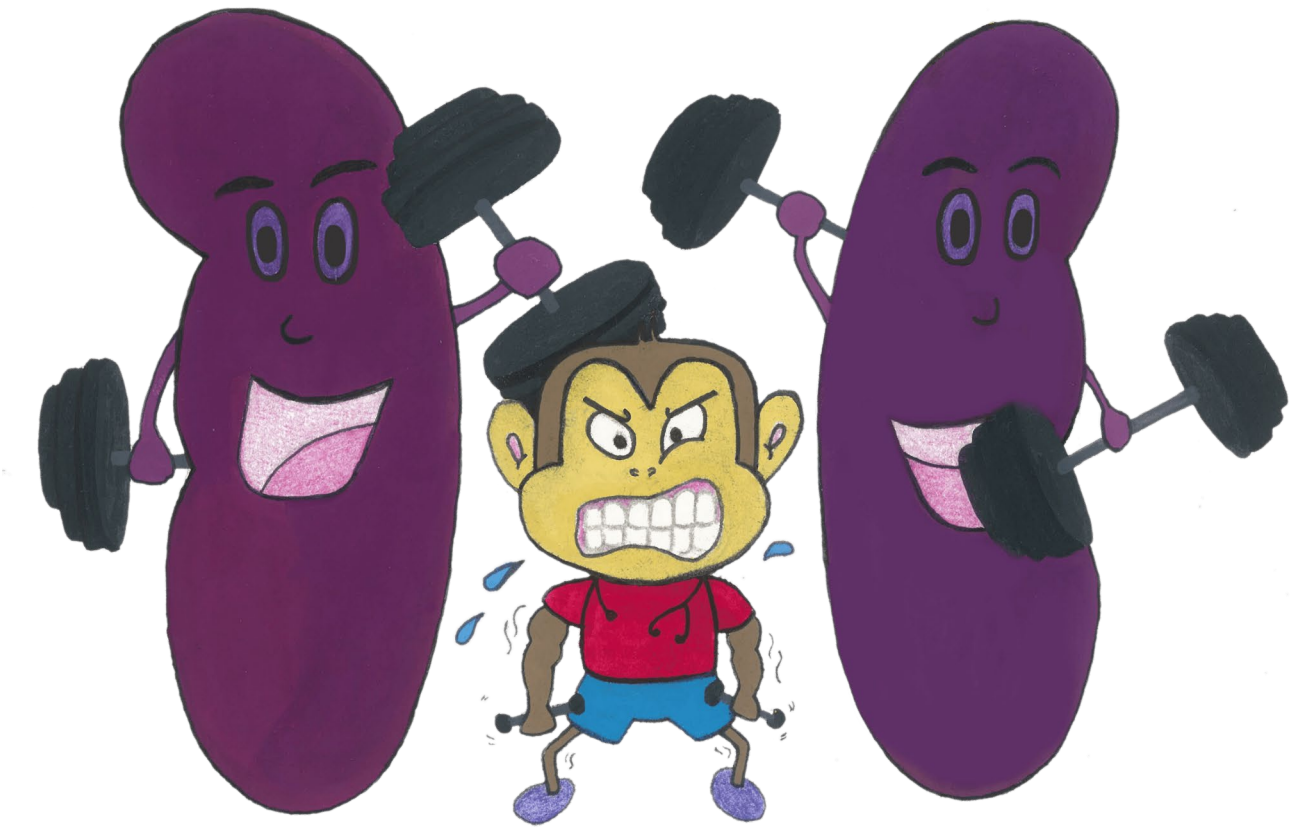

This chapter covers the following topics:

- Renal anatomy and physiology
- Urinary tract infections (UTIs)
- Nephritic syndrome
- Nephrotic syndrome
- Acute kidney injury (AKI)
- Haemolytic uraemic syndrome (HUS)
- Urinary tract obstruction
- Nephrolithiasis (renal stones)
- Hypospadias
- Chronic kidney disease (CKD)
- Paediatric hypertension (HPT)

RENAL ANATOMY AND PHYSIOLOGY

The kidneys are paired organs located between the T12 and L3 vertebrae. They are both retroperitoneal with the left kidney situated more superiorly than the right.

Gross Anatomy of the Kidney

The functional unit of the kidney is the nephron. The nephron is comprised of:

- Glomeruli – filter blood as it travels through the afferent and efferent arterioles
- Proximal convoluted tubule (PCTs) and Loops of Henle (LoHs) – play important roles in absorption
- Distal convoluted tubules (DCT) – play important roles in dilution
- Collecting tubules – fine-tune the pH of the urine

The functions of the kidney are to maintain homeostasis, which includes:

- Fluid balance (via the renin-angiotensin-aldosterone-system; RAAS)
- Electrolyte balance
- Waste excretion e.g. nitrogen, urea, ammonia, creatinine
- Acid-base balance
- Endocrine functions:
    - Erythropoietin production by the interstitial cells of the renal medulla in response to decreased O_2 delivery
    - Renin production by the juxtaglomerular apparatus
    - Metabolism of vitamin D and its constituents

Pathology

Renal pathology can either be primary or secondary. Primary disease refers to an intrinsic structural or functional kidney abnormality that is symptomatic e.g. minimal change nephrotic syndrome, polycystic kidney disease, renal tumour. Secondary disease refers to a systemic condition that affects the kidney function e.g. HPT, post-infectious glomerulonephritis, Wegener's granulomatosis, use of nephrotoxic drugs.

URINARY TRACT INFECTIONS (UTIs)

UTIs are quite common in children and occur more in females (30% of girls) than in boys (1%), except in the <1 year age group. They range from lower urinary tract disease (e.g. urethritis, cystitis) to more severe and complicated upper UTIs (e.g. pyelonephritis, renal abscesses).
The UTI may be uncomplicated (lower UTI in a generally well child) or complicated (upper UTI or a systemically unwell child).

Aetiology

Urine is normally sterile but there is sometimes colonisation of urine and proliferation of disease-causing organisms. 90% of the bacteria which cause UTI form normal flora of the GIT. Common causative organisms include:

- *E. coli* sp.
- Enterococcus sp.
- Klebsiella sp.
- Pseudomonas sp.
- Proteus sp.

Risk Factors

Children at greater risk of developing a UTI are:

- Females (as they have shorter urethra)
- Uncircumcised males (at risk of recurrent UTIs)
- Those with anatomical urogenital anomalies
- Chronically constipated children
- Those with poor hygiene or ablution habits

Clinical Features

They include:

- Lethargy
- Dehydration
- Pyrexia
- Abdominal tenderness

- Renal angle tenderness
- In neonates and infants:
    - FTT
    - Irritability
    - Vomiting
    - Diarrhoea
- In older children (classical symptoms):
    - Dysuria
    - Frequency
    - Urgency
    - Abdominal/flank pain or mass

Investigations

The following investigations should be done:

- Urinalysis:
    - The urine may be collected by suprapubic aspiration or catheterisation for younger, ill and uncooperative children, or a midstream sample may be collected in older children.
    - Urine dipsticks:
        - They are done to look for leucocytes and nitrites – diagnostic of a UTI.
        - The test is more sensitive if both leucocytes and nitrites are detected.
    - Urine MC&S (UMCS):
        - It is done to identify pyuria and grow colony forming units.
        - The antibiotic choice is adjusted based on UMCS results.
- Serum urea and electrolyte levels (U&E; if the child is systemically unwell, dehydrated or has recurrent UTI)
- Abdominal USS (all children with UTIs must have an initial USS to rule out anatomical causes)
- Voiding cystourethrogram or MAG3 scan (if ultrasound is abnormal)

Management

It includes:

- Excluding and managing risk factors
- Prescribing analgesia (give paracetamol and avoid NSAIDs)

For the child with an uncomplicated UTI:

- Prescribe 5-7 days of amoxicillin/clavulanic acid (adjust antibiotic based on urine culture)
- Encourage feeding and hydration
- Review in a week with urine culture, if necessary

For the child with a complicated UTI:

- Admit the child to hospital
- If there is severe disease, start ceftriaxone or amoxicillin/clavulanic acid. The enteral route (oral or via NGT) is preferred over the parenteral route
- Maintain fluids, feeds and electrolytes
- Review the child's response to treatment in 24-48 hours. If responsive, switch to oral antibiotics and continue treatment for 7 days (10-14 days in neonates) and adjust antibiotic choice according to culture results. If unresponsive, add gentamicin with trough level monitoring and review again.
- Follow up in 1-2 weeks with a urine culture. More frequent follow-up is required if the child has recurrent episodes.

NEPHRITIC SYNDROME

It is caused by glomerular damage and is characterised by a triad of symptoms – macro-/microscopic haematuria**,** oligo-/anuric renal failure and HPT.

Pathophysiology and Aetiology

Nephritic syndrome is caused by damage to the glomerulus of any cause:

- Bacteria
- Toxins
- Stones
- Trauma
- Tumours

- Immunological responses that cause inflammation
- Cell proliferation and glomerular dysfunction

Nephritic syndrome is most commonly due to post-streptococcal glomerulonephritis i.e. there is a group A streptococcus throat infection 5-21 days prior to the nephritis (more common than after impetigo). Glomerular damage is due to deposition of circulating immune complexes or as a result of bacterial protein deposition within the basement membrane, leading to in-situ immune activation.

Clinical Features

The child may present with:

- Haematuria (usually the reason for presentation at a healthcare facility)
- Oliguria/anuria
- HPT (examine target organs e.g. eyes and heart)
- Proteinuria
- Oedema
- Inflamed throat, impetigo or history of recent throat or skin infection (with associated fever, lethargy or rash)
- Palpable purpura (vasculitis of the skin)
- Family history of sickle cell, renal stones or haematuria
- Abdominal or flank pain/tenderness
- Dysuria and urinary frequency
- History of trauma
- Arthritis

Complications

Nephritic syndrome may be complicated by:

- Hypertensive crisis
- Seizures
- Encephalopathy
- Pulmonary oedema
- Heart failure

Investigations

They should include:

- Urinalysis:
    - Urine dipstick (will show haematuria and may show proteinuria)
    - UMCS (will contain casts and crystals, and show microscopic haematuria and proteinuria)
- Blood tests:
    - Creatinine and U&E
    - Calcium
    - Protein (albumin)
    - FBC
    - C3 and C4
    - Anti-DNAse B, ASOT and ANA (only request if there are other features of autoimmune disease or low C3 and C4)
- Throat or skin swab (for culture; not routinely performed)
- Imaging:
    - Renal USS
    - CXR
    - ECG (if indicated)
- Biopsy (often unnecessary)

Management

One must:

- Identify the cause and remove or treat it e.g. treat underlying streptococcal infection with IM benzyl benzathine penicillin or oral phenoxymethylpenicillin
- Restrict fluids (give diuretics if the child is fluid overloaded), sodium and potassium
- Perform daily weight, dipsticks and BP checks
- Start antihypertensives:
    - Furosemide is usually given as the HPT is due to fluid overload.
    - Amlodipine may be given if the BP remains uncontrolled.
    - Labetalol may be used in hypertensive urgencies or emergencies.
- Monitor and manage complications

Table 17.1: Approach to Coloured Urine

Approach to Coloured Urine

Urine may be coloured because of:

- Haematuria:
  - Patients with glomerular haematuria will have positive dipsticks and abnormal RBCs or RBC casts on urinalysis. Causes include:
    - Post strep GN
    - IgA nephropathy
    - Infections
    - Toxins
    - Trauma
  - Patients with non-glomerular haematuria will have positive dipsticks and normal RBC on urinalysis. Causes include:
    - Urolithiasis
    - Pyelonephritis
    - Obstruction
    - Cystitis
    - Menstruation
    - Strenuous exercise
    - Tumours
    - Iatrogenic
- Haemoglobinuria; causes include:
  - DIC
  - Intravascular haemolysis (e.g. sickle cell)
- Myoglobinuria; causes include:
  - Rhabdomyolysis
  - Trauma
  - Burns
  - Myositis
- Pigmenturia; causes include:
  - Porphyria
  - Urate
  - Beets
  - Drugs e.g. rifampicin

NEPHROTIC SYNDROME

It is characterised by proteinuria, oedema, hypoalbuminaemia and hypercholesterolaemia.

Pathophysiology

Nephrotic syndrome is due to glomerular or tubular disruption which impairs the basement membrane proteins and effects of their negative charge, making the basement membrane more permeable to serum proteins. This leads to a decrease in serum protein, decreased oncotic pressure and the shift of fluid into the interstitium. The effective decrease in plasma volume results in the activation of RAAS, which retains more fluid and leads to the shifting of even more fluid into the interstitium. Lastly, hepatic lipoprotein synthesis is activated and there is a resultant increase in triglycerides and cholesterol.

Aetiology

Nephrotic syndrome may be:

- Primary (idiopathic nephrotic syndrome):
    - Minimal change nephrotic syndrome
    - Focal segmental glomerulosclerosis
    - Membranoproliferative glomerulonephritis
- Secondary:
    - SLE
    - Granulomatosis with polyangiitis
    - Infection
    - DM

Clinical Features

The child may present with:

- Sudden-onset pitting oedema or ascites
- Pleural effusion
- Anorexia
- Malaise
- Abdominal pain
- Diarrhoea (because of the oedematous bowel)
- Respiratory distress
- Heart failure

Investigations

The following investigations should be performed:

- Urinalysis:
    - It will show proteinuria and an elevated spot urine protein:creatinine ratio (UPCR >0.2 g/mmol).
- Blood tests:
    - U&E
    - Cholesterol
    - Albumin and total protein
- Renal USS
- Renal biopsy (if a secondary cause is suspected)

Other tests which may be performed to diagnose a secondary cause:

- ASOT and anti-DNAseB
- HBV and HCV antibodies
- HIV, syphilis, CMV
- Anti-dsDNA

Management

General Measures

The child should be put on a diet with restricted sodium and saturated fat restriction. However, fluids should not be restricted. The diet must maintain nutrition and contain sufficient multivitamins, calcium and folic acid. Daily weights, BP, dipsticks and UPCRs should be done.

Prophylaxis against secondary infections should be given. If the child has anasarca, phenoxymethylpenicillin should be administered, as these patients are at risk of pneumococcal peritonitis. The child should also be given the routine vaccinations against pneumococcus, VZV and HBV according to the EPI, once s/he is in remission and not on steroids or immunosuppressive therapy.

Specific Management

The child with idiopathic nephrotic syndrome should be started on empiric steroid therapy (prednisone 2 mg/kg up to maximum of 60 mg) for a minimum of 4-6 weeks. In secondary nephrotic syndrome, the underlying illness needs to be treated.

Mild oedema will improve with conservative management and steroids (if the nephrosis is steroid-responsive). Resistant oedema may be cautiously treated with diuretics and severe anasarca may require an albumin infusion. Enalapril, chronic diuretics and statin therapy are only indicated in steroid-resistant cases and should be given under specialist supervision.

ACUTE KIDNEY INJURY (AKI)

Pathophysiology

AKI is characterised by an abrupt decline in the glomerular filtration rate (GFR) and tubular function, resulting in decreased excretion of creatinine, urea, nitrogen, phosphate and fluid. This child will, therefore, be azotaemic and fluid overloaded with normal, decreased or increased urine output.

Aetiology

AKI may have a pre-, intra- or post-renal cause.

Table 17.2: Pre-, Intra- and Postrenal Causes of AKI

Pre-Renal AKI	Intrarenal AKI	Post-Renal AKI
● Dehydration ● Septic shock ● Heart failure ● Haemorrhage ● Burns ● Renal artery or vein issues	● Acute tubular necrosis ● Nephrotoxins ● Glomerulonephritis ● Acute cortical necrosis ● Interstitial nephritis ● Infection	● Urethral obstruction ● Ureteral obstruction ● Extrinsic compression of outlet e.g. tumour ● Neurogenic bladder

Clinical Features

The child may present with:

- History of any cause of hypoperfusion e.g. vomiting, diarrhoea, bleeding
- History of use of a nephrotoxic drug
- Family history of coagulopathy or tumours
- Anuria or polyuria

- Flank or abdominal mass/pain
- Haematuria
- Proteinuria
- Hypotension or other signs of dehydration (examine the eyes, oedema, skin)
- Bleeding
- Signs of heart failure
- Distended bladder

One must examine the child for features of genetic syndromes associated with renal disease e.g. Down syndrome, FASD

Investigations

They should include:

- Urinalysis:
    - Dipsticks to screen for infection (proteinuria, haematuria, leukocytes and nitrites).
    - UMCS to assess RBC dysmorphology, attempt to grow bacteria and look for RBC/WBC/protein casts.
    - Fractional excretion sodium percentage to distinguish between pre-renal AKI (<1%) and intrarenal failure (>1%).
    - Blood urea nitrogen:creatinine ratio >20:1 suggests pre-renal failure.
    - Spot UPCR to assess for proteinuria.
- Blood tests:
    - Creatinine and U&E
    - Creatinine clearance and GFR
- Imaging:
    - Perform an USS and, if abnormal, further imaging e.g. voiding cystourethrogram (VCUG), CT scan, MRI.
- Renal biopsy (if indicated)

Management

General Measures

One must identify and manage the cause(s) e.g. relieve obstruction in post-renal AKI, treat active infection. Adequate perfusion and fluid balance must be maintained

(replace fluid losses and restrict fluid intake as needed). Feeding must be maintained and the child placed on sodium-, potassium- and phosphate-restricted, high-protein diet. Daily weights, BP and dipstick checks should be done.

Specific Management

One must manage:

- Fluid balance:
    - Restrict fluids if the patient is fluid overloaded.
    - Replace fluids if the patient is fluid depleted.
    - Consider furosemide if the patient remains anuric despite fluid administration.
- Electrolytes:
    - If the patient is hyperkalaemic, shift according to emergency guidelines and restrict potassium.
    - If the patient has metabolic acidosis, correct the acidosis with sodium bicarbonate.
    - If the patient has symptomatic hypocalcaemia or hyperphosphataemia, administer 10% calcium carbonate if the patient.
    - If the patient has severe anaemia, give a slow transfusion of packed RBCs (administer with caution and only if necessary as it can lead to fluid overload, HPT and hyperkalaemia).
- Seizures:
    - Causes may include HPT, uraemia, hypocalcaemia and hyponatraemia.
    - Treat with diazepam and investigate for the cause (may be due to ARF or an unrelated cause).
- Pulmonary oedema:
    - Treat with furosemide, morphine and oxygen.

Dialysis (peritoneal dialysis or haemodialysis) is indicated when the above-mentioned issues become refractory or the child has been poisoned with a dialysable agent.

HAEMOLYTIC URAEMIC SYNDROME (HUS)

Pathophysiology and Aetiology

There are many types of HUS but the most common type is associated with a prodromal diarrhoeal phase. HUS typically occurs 7-10 days after a diarrhoeal illness caused by bacteria which secrete Shiga or verotoxins e.g. Shigella sp. or *E. coli*, respectively. The toxin binds to and damages glomerular endothelial cells, resulting in coagulation.

If severe, glomerular and interstitial thrombosis and haemolysis result (RBCs are squeezed through the narrowed vessel lumens). Thus, HUS presents with the triad of microangiopathic haemolytic anaemia, thrombocytopenia and acute renal injury (haematuria or renal failure).

Clinical Features

The child may present with:

- Haemorrhagic diarrhoea (dysentery)
- Lethargy and irritability
- Fever
- Dehydration
- Features of renal failure e.g. haematuria, proteinuria, HPT, oedema
- Petechiae
- Hepatosplenomegaly (occasionally)

Investigations

They should include:

- Urinalysis:
    - A dipstick is done to identify haematuria and proteinuria.
    - The UMCS is used to assess for casts and organisms.
- Blood tests:
    - U&E
    - The FBC will show elevated reticulocytes, decreased haptoglobin and, possibly, leucocytosis.
    - LDH will be elevated.

    - INR/PTT will be normal (done to exclude sepsis-related DIC).
    - A PBS is done to look for evidence of intravascular haemolysis (e.g. schistocytes, helmet and burr cells, fragmented erythrocytes).
- Stool tests:
    - A stool culture may show vero- or Shiga toxin-producing strains of *E. coli* or *Shigella.*

Management

It is supportive and includes:

- Managing fluid status and electrolyte levels
- Maintaining BP control with anti-hypertensives
- Performing a RBC transfusion (as needed)
- Platelet transfusion (if still actively bleeding)
- Maintaining nutrition
- Managing complications e.g. pulmonary oedema, seizures, hypertensive crisis

URINARY TRACT OBSTRUCTION

It is a common condition which can occur at any anatomical level of the genitourinary tract.

Aetiology and Pathophysiology

Common congenital causes of urinary tract obstruction are:

- Pelvi-ureteric junction (PUJ) obstruction
- Posterior urethral valves (PUVs)
    - PUVs are the most common cause of bladder outlet obstruction in males.
    - The valves are present because of persistence of the urogenital membrane or abnormal integration/involution of embryonic structures.
- Vesico-ureteric junction (VUJ) obstruction (much less common)

The obstruction may be:

- Intraluminal e.g. stones, clots, stenosis
- Intramural e.g. tumours, uterocoeles

- Extramural e.g. tumours, other masses

Clinical Features

The child may present with:

- Fever
- Irritability
- Poor stream strength
- Dribbling
- Straining
- Recurrent UTIs
- Lower abdominal pain/mass
- Flank mass/pain
- Stunted growth
- Renal scarring
- Urinary reflux hydronephrosis
- Chronic renal impairment
- History of intrauterine concerns
    - Oligohydramnios
    - Facial distortion
    - Lung hypoplasia
    - Rupture of the ureter leading to urine ascites in the neonate
- Congenital syndromes/facies
- Anaemia
- Features of renal impairment e.g. oedema, haematuria, proteinuria, HPT
- Features of UTI e.g. dysuria, fever, frequency, irritability

Investigations

They should include:

- Urinalysis
    - Urine dipsticks
    - UMCS
- Blood tests:
    - U&E

    - FBC
- Imaging:
    - Kidney, ureter and bladder (KUB) USS (useful for identifying anomalies).
    - VCUG (can show elements of reflux or obstruction).
    - MAG3 (can assess PUJ severity and for renal scars).
    - MRI/CT scan (if indicated).

Management

The obstruction must be relieved as soon as possible with a catheter. One must exclude or manage dysfunctional voiding or a neurogenic bladder. Current infections should also be treated. Prophylactic antibiotics may be indicated in patients with recurrent infections and/or abnormal anatomy.
Regular dipsticks and RFTs should be done. Surgery may be required to correct any anatomical anomalies.

NEPHROLITHIASIS (RENAL STONES)

Nephrolithiasis is the formation of a precipitate in the genitourinary system.

Pathophysiology

It may be due to:

- Recurrent UTIs
- Neurogenic bladder
- Presence of sutures (act as a nidus)
- Obstruction
- Metabolic causes:
    - Familial hypercalciuria
    - Cystinuria

Clinical Features

The child may present with:

- Acute obstruction

- Renal colic
- Flank, lower abdominal or groin pain/mass
- Vomiting
- Features of infection – fever, irritability, lethargy
- Haematuria
- Fever
- Renal angle tenderness
- Tachycardia
- Tachypnoea

Investigations

They should include:

- Urinalysis:
    - Urine dipstick
    - Urine MCS
    - Urine biochemistry
- Blood tests:
    - U&E and uric acid levels
    - Calcium, phosphate and parathyroid hormone levels
- Imaging:
    - Abdominal X-ray and CT scans are more helpful than USS as the stones can be radio-opaque (e.g. calcium stones) or radio-lucent (e.g. magnesium/ammonium/phosphate stone or struvites due to infective causes).

Management

General management includes:

- Relieve acute obstruction
- Give analgesia
- Start antibiotics (if there are signs of infection)
- Alkalinise urine with oral agents
- Keeping the child hydrated
- Making dietary changes (decrease salt, protein and oxalate intake)

HYPOSPADIAS

It forms part of a triad of congenital anomalies:

- Urethral meatus that is ventral and proximal to its normal opening (hypospadias)
- Dorsal hood
- Chordee

It is associated with genital ambiguity rather than urinary anomalies.

Clinical Features

The child may have:

- Meatal opening on the glans, corona or distal third of the shaft
- Phimosis or paraphimosis
- Ventral hood
- Chordee
- Undescended testes (10% of patients)
- Inguinal hernia

Investigations

The diagnosis is clinical and investigations are usually unnecessary.

Management

Surgical intervention before 18 months of age is best.

CHRONIC KIDNEY DISEASE (CKD)

It refers to continuous injury to the kidneys that results in progressive decline in kidney function until end stage renal failure develops.

Aetiology

Causes include congenital and obstructive diseases. After puberty, acquired conditions and the inability to support the growing body become more common causes of chronic renal failure.

Clinical Features

They may include:

- FTT
- Pallor
- Hypertension (may have headaches and heart failure)
- Polyuria
- Dehydration
- Oedema
- Anaemia
- Renal osteodystrophy
- Rickets (pigeon chest, curved weight bearing bones, etc.)
- Uraemic symptoms (nausea, vomiting, confusion, convulsions)
- Delayed puberty
- Impaired learning and poor school performance

Investigations

They should include:

- Urinalysis:
    - Urine dipstick (to look for proteinuria and haematuria)
    - UPCR
    - UMCS
- Blood tests:
    - U&E
    - FBC
    - Creatinine clearance and eGFR (to grade severity)
- Imaging:
    - X-ray (to look for osteomalacia)
    - Ultrasound to exclude anatomical anomalies

Management

A multidisciplinary approach should be used. Treatment should include:

- Daily weight, BP and dipstick checks
- Dietary management:
    - The child should be put on a high-energy diet with supplemental multivitamins and folic acid.
    - Salt- and potassium-intake should be restricted but not protein-intake.
- Fluid management
- Avoidance of nephrotoxic drugs
- Managing electrolyte dysfunction (metabolic acidosis and hyperkalaemia), anaemia, HPT and dyslipidaemia
- Following the appropriate immunisation schedule (especially for pneumococcus, VZV and HBV)

The child must be assessed for the need for chronic dialysis or renal transplantation.

PAEDIATRIC HYPERTENSION (HPT)

This is defined as systolic or diastolic BP >95th percentile for age, sex and height.

There is an increased risk of sequelae with severe or chronic hypertension.

The HPT may be due to:

- Primary cause (essential HPT)
- Secondary cause (renal disease is the most common cause)

Clinical Features

Children are usually asymptomatic but can present with target organ damage. The child may have:

- Family history of HPT
- Truncal obesity and poor dietary history
- Headache
- Blurry vision
- Stroke
- Heart attack or heart failure

- Bruits
- Diminished leg pressure
- Flank masses
- Signs of Cushing syndrome

Investigations

One should perform investigations which help one assess target organ damage, assess cardiovascular risk factors and identify causes. Further focused investigation should be done based on initial findings.

Management

It includes:

- Finding and treating identifiable causes
- Adjusting risk factors and making lifestyle changes
- Initiating anti-hypertensive therapy (start with a single agent and add other agents as required)
- Managing hypertensive crises

ABOUT THE EDITORS

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Dr Lehlohonolo Ntlatlapo is a community service medical doctor at Themba hospital, Mpumalanga. He completed his matric at Phumulani Secondary school in Katlehong, Gauteng, in 2012. He obtained his MBChB in 2018 from University of Cape Town (UCT). As a student, Dr Ntlatlapo was actively involved in student organisations, such as SHAWCO Health and Rural Support Network, that offer free health care services to disadvantaged communities.

His passion for education landed him in the ‘Mail & Guardian 200 Young South Africans’ 2020 list for his foundation (Help Me Up) which assists high school learners apply for tertiary education.

PROF. CAROL HLELA

Prof. Carol Hlela was born and bred in KwaMashu, which is near Durban, KwaZulu Natal. She has a Master's degree in Global Health Science (MSc GHS) and completed her PhD in Clinical Medicine at Oxford University in England.

As one of only two paediatric dermatologists in South Africa, Prof. Hlela now heads the Department of Dermatology at Red Cross War Memorial Children’s Hospital. She has a private practice in the southern suburbs of Cape Town and is also employed by UCT, where she teaches medical students, and supervises PhD candidates.

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Prof. Rannakoe Lehloenya completed a BSc at the National University of Lesotho and The Medical University of South Africa, now Sefako Makgatho Health Sciences University (MBChB). He specialised in dermatology at UCT in 2008.

Prof. Lehloenya is a clinician researcher with special interests in phototherapy, TB, HIV and other infectious diseases and has several publications to his name. He works as a senior lecturer at UCT, has a private practice ad serves as the Director at the Dermatology Treatment and Phototherapy Clinic in Century City, Cape Town.

CHRISTINE ILE

Christine Ile is a final-year medical student at UCT. She served as the Head of Research for UCT PaedSoc in 2019/20 and Vice-Chairperson of PaedSoc in 2020/21. Over these two years, Ms Ile also served as the co-ordinating editor for the Paeds in a Pinch study guide.

She has special interests in paediatrics, radiology and ophthalmology and hopes to explore these interests while pursuing her passion for public service.

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