

MALAWI PAEDIATRIC NON-COMMUNICABLE DISEASES GUIDELINES 2024

FOREWORD

Malawi has adopted the life course approach to health in the Health Sector Strategic Plan III and the child health strategy. This approach looks beyond the traditional causes of under-five mortality which are mainly infectious diseases extending to children aged nineteen years where non-communicable diseases (NCDs) are an important cause of morbidity and mortality.

Malawi's Package of Essential Non-communicable Disease Interventions-Plus (PEN-Plus) operational plan outlines the pathway for improving the diagnostics and management of NCDs in Malawi. It has however recognised the urgent requirement to address the unique needs and approach required to improve the management of paediatric NCDs. Some of the important common NCDs include chronic respiratory conditions like asthma, cardiovascular diseases like congenital heart disease and rheumatic heart disease, neurological conditions like epilepsy, sickle cell disease and renal diseases. Despite recognition of the problem posed by these non-communicable diseases, most health workers and health facilities may not be adequately prepared to manage children who present with non-communicable diseases mainly because of lack of human resources, knowledge, skills and supplies required to manage these patients.

In order to improve the provision of quality health care in children presenting with NCDs, the non-communicable disease treatment guidelines have been developed by experts both nationally and reviewed by international experts to aid health workers in managing such conditions. The guidelines are tailored towards helping health workers at various healthcare levels in Malawi including primary, secondary and tertiary care levels. They also include promotion and preventive messages where applicable.

The NCDs treatment guideline for children is aligned with the Child Health Strategic Plan and Health Sector Strategic Plan III priority 1, priority 4 and priority 6. The guideline will ensure that all paediatric patients access quality equitable health care provided by knowledgeable and skilled professionals regardless of the level at which they access the care. The guidelines will also be accessed by an interactive application which will increase accessibility of the information by health professionals who manage these children.

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The implementation of these guidelines should follow the Malawi PEN-Plus Operational Plan 2021

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CHAPTER 1: TRAUMA AND EMERGENCY

TRAUMA

AETIOLOGY

- Road traffic accidents: pedestrian vs. vehicle, cyclist vs. vehicle, passenger in vehicle (restrained or unrestrained)
- Falls: out of trees, off walls, into septic tanks
- Crush injuries: buildings collapsing
- Burns: fire, scalds, immersion, electrical, lightening
- Drowning: rivers, water, septic tanks
- Animal bites: dog, snake, hyena, crocodile
- Inflicted injuries: beatings, stabbing, gunshot

IMPORTANT POINTS IN HISTORY

- Age, name
- Location where accident occurred, if others involved, number of casualties, any deaths at the scene
- Date and time of injury
- Mechanism of injury: e.g. road traffic accidents: speed of vehicle, contact point, distance thrown, dragged by vehicle, ridden over by vehicle; or fall: height of fall, how landed, what landed on
- If drowning: length of immersion time
- If animal bite: what animal, vaccine history (TTV, RABIES),
- Events after injury:
 - Clinical: loss of consciousness and duration, seizure, vomiting, confusion, abnormal behaviour, bleeding, respiratory arrest
 - Treatment prior to presentation (including local medicines / herbs)
- Last meal
- Past medical history, social history, family history
- Regular medication, immunisations
- Allergies
- Suspicion of non-accidental injury

IMPORTANT DIFFERENCES BETWEEN CHILDREN AND ADULTS

During resuscitation, it is important to note anatomical / physiological differences between a child and an adult. A child has: -

- A relatively large head compared to the body therefore has more shearing type injuries with head trauma.
- Weaker neck muscles so cervical spine injuries occur at higher spinal levels.
- Cartilaginous ribs result in more compliant chest wall; pulmonary contusion and haemopneumothorax may occur without rib fractures.
- Low respiratory reserves and higher metabolic rate result in greater risk of hypoxic injury compounding trauma.
- Intra-abdominal organs are less protected therefore more likely to have solid organ injury.
- Small blood volume – haemorrhage may be life threatening.
- Bladder abdominal rather than pelvic – increased risk of bladder injury.
- Possibility of non-accidental injury.
- Relatively large skin surface to body mass and loses heat rapidly.

PRIMARY SURVEY AND EMERGENCY MANAGEMENT (cAcBCDE)

The primary survey is a systematic approach to evaluating and managing trauma cases, and to identify and treat the most life-threatening injuries first. The initial evaluation of injured children has two main goals:

1. Identify and immediately treat potentially life-threatening injuries
2. Determine the trauma resuscitation

It is important to use a standardised approach (cAcBCDE) when assessing trauma cases, to avoid omission of potentially life-saving interventions. It is key to treat life threatening problems as identified. Deal with each problem as found in a step-by-step process. Cut off all clothes to facilitate full assessment.

cAcBCDE:

c: catastrophic external haemorrhage - stop bleeding by firm compression on the site.

A: Airway and c-spine stabilisation

B: Breathing - if necessary with ventilatory support

C: Circulation with haemorrhage control

D: Disability with prevention of secondary insult

E: Exposure with temperature control

c – Catastrophic haemorrhage

If evident apply direct pressure immediately. Use of a tourniquet is not recommended.

Ac - Airway + cervical spine stabilisation

Two categories of children need to be identified.

- a. Those with a patent airway requiring no support.
- b. Those who will need an intervention to establish a patent airway.
 - o Suctioning of secretions / blood / vomit
 - o Airway manoeuvres – in trauma cases this is done using the jaw thrust.
A chin lift and head tilt is NEVER advised in trauma patients with a suspected injury of the cervical spine.

Use of adjuvants

A Guedel airway is the main adjuvant used. This is measured from the middle of the incisors to the angle of the jaw. Under 1-year of age this is inserted directly (the right way up). Over 1-year of age it is inserted upside down and then turned round.

Cervical spine protection

- Assume a cervical spine injury in any significant trauma.
- Manual inline stabilisation: should be commenced immediately when there is a high suspicion of cervical spine injury.
- In-line immobilisation: triple immobilisation comprises fluid bags or sandbags either side of the head with tape / twisted chitenje then fixed to the hard surface of the bed or trolley (see diagram below).

Rigid collars are NOT used!

- If uncooperative / combative c-spine immobilisation can be harmful.
- If significant concern about c-spine injury maintain in-line immobilisation during any movement of the patient. When assessing the back a log-roll should be used. If the patient vomits then they should be turned to the side using a log-roll.



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B- Breathing

- In trauma a full assessment of breathing is crucial.
- Respiration rate and oxygen saturations should always be assessed.
- Inspect for any evidence of chest wall trauma.
- Examine for symmetry of chest movements and signs of respiratory distress.
- Perform percussion and assess for tracheal deviation.
- Auscultate the chest to identify likely pathology.
- Exclude tension pneumothorax, open pneumothorax, flail chest, pulmonary contusions and massive haemothorax.

Tension pneumothorax

- Clinical diagnosis: Tracheal deviation away from the side of pneumothorax; absence of breath sounds over the involved lung and hyper resonant on percussion; neck vein distension, tachycardia and hypotension with respiratory distress. ***When the clinical diagnosis is made, the chest should immediately be decompressed by placing a large bore canula into the second intercostal space, mid clavicular line, above the rib.***
- Ensure IV access.
- Chest drain insertion will be needed after decompression. Call for HELP!!! While this is being arranged continue with cAcBCDE assessment and management.

Open pneumothorax

- This is also referred to as a sucking chest wound.
- This injury can cause mediastinal shift, decreased venous return and cardiopulmonary collapse.
- A non-occlusive dressing should be applied over the injury and fixed on three sides. This enables air to escape on expiration but inhibits air entry on inspiration. Gauze does not work as it becomes adherent to the wound.

Flail chest

- This occurs when a segment of chest wall has lost continuity with the movement of the thoracic cage occurring when two or more ribs are fractured in two or more positions.
- First line management is adequate pain relief, but these patients may also require ventilatory support.

Massive haemothorax

- Presentation includes decreased breath sounds and dullness to percussion on the affected side. The trachea may be deviated away from the affected side.
- The patient will usually be in shock: Insert 2 large bore cannula, send blood for urgent group and crossmatch and commence fluid resuscitation prior to chest drain insertion.
- Treatment is by chest drain insertion.
- Consider the possibility of cardiac tamponade. If clinically evident, do an urgent echocardiogram, but if not feasible then perform pericardiocentesis.
- Consider other mediastinal injuries, disruption of great vessels, diaphragmatic rupture etc.
- If respiratory effort is inadequate – call for help, consider need for intubation and ventilation, consider starting bag mask ventilation.
- If bag valve mask ventilation is indicated use the right size mask and if possible, the right sized self-inflating mask according to weight [neonatal (volume 200-250 ml), paediatric up to 25-30 kg (volume 500-600 ml), adult for large child/adolescent (volume 1500-2000 ml)]
- If bag and mask ventilation are not successful one can consider more invasive procedures e.g. endotracheal intubation or surgical airway.
- In this case anticipate a difficult airway as some may have had facial injuries, swollen oral structures, loose teeth.
- During these invasive airway manoeuvres, the cervical spine needs to be maintained in-line.

Indication for intubation and ventilation

- Persistent airway obstruction.
- Predicted airway obstruction (e.g., inhalational burn, severe facial trauma).
- Loss of airway reflexes / loss of consciousness.
- Inadequate respiratory effort or increasing fatigue.
- Disrupted ventilator mechanism e.g., flail chest.
- Persistent hypoxia despite oxygen administration.

- Severe traumatic brain injury (GCS <8).

Note: Resources for mechanical ventilation are limited. Decision to intubate and ventilate should be made in consultation with a paediatrician / anaesthetist / paediatric intensivist, so CALL FOR HELP!!

Note on the usage of drugs for intubation: ketamine (1mg/kg) and vecuronium (0.1mg/kg) or rocuronium (1mg/kg) are used as induction agents.

C- Circulation

- Objective assessment of circulation is made by measuring heart rate, blood pressure and capillary refill time and feeling the peripheries.
- **Note:** Tachycardia alone cannot be used for assessing circulation as this can be a sign of pain or distress. Also, hypotension is a very late sign of severe shock.
- All potential sites of bleeding must be examined as part of the circulation assessment including: on the floor (catastrophic bleeding), chest, abdomen, pelvis, long-bones and in a baby with an open fontanelle the head.
- Two main interventions for managing cardiovascular compromise are controlling external haemorrhage and fluid resuscitation.
- Fluid resuscitation requires insertion of two large bore cannula. In the event of failure to establish percutaneous IV access call for HELP and consider other options:
 - Intraosseous – avoid injured limb
 - Central vein – external jugular, femoral
 - Cut down: cephalic vein (elbow) / long saphenous vein (ankle)
- Take samples for FBC, crossmatch, blood sugar, MPS & PCV
- Perform a FAST scan.

If in shock:

- Ideally give blood.
- If not available administer 10ml/kg of normal saline or ringers lactate over 20 minutes. **Do not** give fluids as a rapid bolus as this can exacerbate bleeding.
- Reassess and if necessary, repeat up to a total of 40ml/kg.
- Consider type specific or O-negative blood in extreme emergencies.
- Contact surgical / orthopaedic team early.
- Blood loss in case of femur fractures can be massive - alignment and traction is needed.

Catastrophic external hemorrhage - Simple direct pressure, specialized haemostatic dressing or a tourniquet must be applied instantly.

Activation Criteria for a Paediatric Massive Transfusion Protocol (PMTP)

- Critical bleeding with coagulopathy
- Anticipated, or estimated blood loss > 1/2 blood volume
- Critical bleeding continuing after transfusion of 1/2 blood volume
- Any child requiring more than 20mL/kg of packed red blood cells (PRBC) in 2 hours and/or anticipated ongoing blood loss
- Any child requiring more than 40mL/kg of PRBC in a 24-hour period with ongoing blood loss
- Consider Tranexamic acid (15mg/kg)

D - Disability

- Use AVPU or GCS to assess consciousness.
- Establishment of baseline GCS may have prognostic value among children with evolving intracranial injury. The motor score has been shown to be the best predictor of outcome after injury.
- Check pupils for size, equality and reactivity.
- Check child can move all 4 limbs.
- Please note that the accurate assessment of disability will help establish the need for airway support.
- All children with neurologic injury must be referred to the neurosurgical team for assessment and for surgical interventions if needed.

A Alert

V responds to voice

P responds to pain

U unresponsive

Glasgow Coma Scale (GCS)

| >5 years | <5 years |
|--|--|
| Motor | |
| Obeys commands (6) | Normal spontaneous movements (6) |
| Localises pain (5) | Withdraws to touch (5) |
| Withdraws to pain (4) | Withdraws to pain (4) |
| Flexion to pain (decorticate) (3) | Abnormal flexion (decorticate) (3) |
| Extension to pain (decerebrate) (2) | Abnormal extension (decerebrate) (2) |
| No response (1) | No response (1) |
| Verbal | |
| Orientated (in person or place or address) (5) | Alert, babbles, words or sentences to usual ability (normal) (5) |
| Confused (4) | Less than usual ability, irritable cry (4) |
| Inappropriate words (3) | Cries to pain (3) |
| Incomprehensible sounds (2) | Moans to pain (2) |
| No response to pain (1) | No response to pain (1) |
| Eyes | |
| Spontaneous (4) | Spontaneous (4) |
| To voice (3) | To voice (3) |
| To pain (2) | To pain (2) |
| None (1) | None (1) |

- Basic management of traumatic brain injury to prevent secondary brain injury:
 - Adequate oxygenation. Saturations should be kept above 94%. Consider need for intubation if ICU is available.
 - Control of CO₂ tension – intubation & ventilation might be needed. Do not hyperventilate. Keep CO₂ between 40-45 mmHg.
 - Maintenance of adequate cerebral perfusion pressure (CPP) by maintaining good blood pressure: aim for target mean arterial pressure (MAP) above 99th percentile for age to maintain a good CPP.
 - Maintain normovolaemia. Fluid resuscitate as required to correct shock. May need inotropes. Use normal saline & glucose for maintenance fluids at 2/3 maintenance.
 - Head up position (around 30 degrees), midline position.
 - Control of potentially raised ICP: consider mannitol: 250-500mg/kg (1.25-2.5ml / kg of 20% Mannitol) IV over 30-60 minutes or hypertonic saline if available.
 - Maintain normoglycaemia.
 - Treat convulsions.
 - Maintain normal temperature.
 - Avoid aspiration: insert OGT and keep on free drainage.
 - Avoid electrolyte imbalance (especially hyponatraemia).
- All patients with a GCS of 5-8 should be discussed with the neurosurgical and ICU teams, for possible referral and safe transfer to a tertiary level facility.

Exposure

Fully expose the child to assess for other injuries. This should include examination of the back using a log roll if a cervical spine injury is suspected.
It is important to keep the child covered to minimise heat loss.

THE SECONDARY SURVEY

- This occurs once the child has been successfully resuscitated. It includes a medical and events history, a more complete physical examination and additional interventions.
- The acronym AMPLE is useful for remembering these key elements.
 - **A** – Allergies
 - **M** – Medications
 - **P** – Past medical history
 - **L** – Last meal
 - **E** – Environment and events detailed history leading up to injury
- The physical examination comprises a full head to toe examination to identify any other injuries.
 - Reassess ABCD
 - Start at the head: check for signs of a head injury and examine the face including ears, eyes, nose, mastoid, maxilla, mandible and oral cavity.
 - Re-examine the chest, abdomen and pelvis.

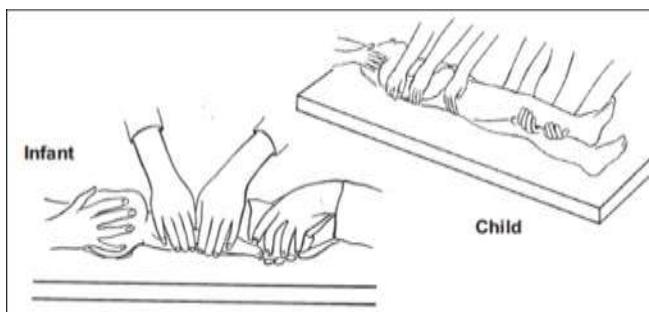
- Examine the genitalia.
- Perform a neurological examination including level of consciousness, pupils, fundoscopy, tone, power, reflexes, sensation.
- Examine all limbs, including hands, feet, fingers and toes for evidence of fractures, wounds, vascular injury, compartment syndrome.
- Examine the back. In case of a potential spinal injury, the child should be log-rolled (see below).
- Check the back of the head, the cervical, thoracic, lumbar spine and sacral region.
- Examine the bottom and perform a rectal exam.
- Also examine the back of the limbs.

Examining and clearing a cervical spine

- Remember despite normal x-rays the child can have a Spinal Cord Injury Without Radiological Abnormalities (e.g. haematomas, ligament injuries) – **SCIWORA**
- To clear the c-spine
 - The child should be co-operative and alert
 - Have no midline cervical tenderness on direct palpation
 - Have no focal neurological deficit
 - Have no painful distracting injuries

Log Roll

- Keep the head in a neutral position.
- Keep the head and body straight, avoid rotation or flexion/extension.
- The person holding the head is in charge: maintain in-line stabilisation of the c-spine (do not cover the ears).
- Assistants hold the arms and legs (see below) to keep the body in line.
- On the instructions of the lead person turn the patient onto their side to allow the back to be examined.



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Positioning an unconscious child

- If there is no neck trauma consider putting the child in the recovery position
- Turn the child on to their side to reduce the risk of aspiration
- Keep the neck slightly extended and stabilise by placing the cheek on one hand
- Bend one leg to stabilise the body

DIAGNOSTIC ASSESSMENT

1. Full blood count
2. Group and crossmatch
3. Random blood sugar
4. Arterial/venous/capillary blood gas
5. Radiographic imaging as indicated per patient. Please note there is no such thing as a trauma series in paediatric trauma. X-ray requests should be based on clinical findings. FAST scans are a useful adjunct in trauma. CT if indicated.

TRANSFER & FURTHER MANAGEMENT

- Reassess cAcBCDE regularly.
- Ensure adequate analgesia.
- Consider need for tetanus toxoid and IV antibiotics.
- Transfer to HDU, theatre, ICU, radiology department.
- Critically ill children need to be accompanied by nurse +/- doctor
- Take resuscitation equipment with you
- Use oxygen cylinder for transfer of sick children
- Handover to receiving team: using SBAR is a useful approach to handing over emergency patients
- Regular monitoring, including "neuro-observations" in severely injured child.
- Signs of raised ICP due to cerebral oedema or intracranial haematomas (e.g., extradural) can present even hours after initial presentation.
- Encourage parents to alert nurses or medical team in case of any concern.

PAEDIATRIC SHOCK

Definition

Shock is a life-threatening disorder of the circulatory system that results in inadequate organ perfusion and tissue hypoxia, leading to metabolic disturbances and ultimately irreversible organ damage.

Types of shock

- Hypovolaemic shock (dehydration, acute blood loss)
- Distributive shock (anaphylaxis, sepsis)
- Dissociative shock (anaemia)
- Cardiogenic shock (valvular disease, congenital heart disease, cardiac ischaemia, arrhythmias, toxins)
- Obstructive shock (tension pneumothorax, cardiac tamponade, pulmonary embolism)

Risk factors / causes

- Diarrhoea / vomiting
- Infections
- Trauma
- Bleeding
- Underlying conditions e.g., congenital / acquired cardiac disease
- Known allergies and recent allergen exposure

Signs and symptoms

- Cold extremities
- Peripheral capillary refill time > 3 seconds
- Weak, fast pulse
- Low systolic blood pressure (late sign)
- Other signs of underlying cause:
 - Signs of severe dehydration (sunken eyes, skin pinch goes back slowly, lethargy)
 - Bleeding
 - Fever
 - Non-blanching rash (petechiae / purpura)
 - Oedema or urticaria
 - Engorged neck veins and hepatomegaly

Health promotion / prevention

- Early health seeking behaviour when unwell
- Educating the public on basic life support measures

Investigations

- Are dependent on cause, but may include, FBC, Blood culture, Blood glucose, Arterial/venous/capillary blood gas e.t.c

Differential diagnosis

- Are dependent on history and examination (see risk factors / causes)

Management

Primary / Secondary Level

CALL FOR HELP!!!

Keep the child calm.

A = Clear airway

B = Start oxygen, check for breathing.

C = Circulation

- Check heart rate. If absent / < 60 bpm initiate CPR
- Establish IV access - 2 x large bore IV cannulas according to the child's size.
 - If IV access unsuccessful after 2 attempts (maximum 5 mins) insert intraosseous needle
- **Hypovolaemic shock**
 - **Trauma:** Stop bleeding. 10ml/kg over 20 minutes and reassess. Repeat up to a maximum of 40ml/kg. Aim to get blood as soon as possible.
 - **Dehydration:** 30 ml/kg over 30 minutes / 1 hour depending on age. Reassess. Repeat if necessary or continue with 70 ml/kg over 2.5 / 5 hours depending on age.
- **Distributive shock**
 - **Septic shock:** 10 ml/kg over 1 hour and reassess. Repeat up to a maximum of 40ml/kg. Give antibiotics. May need inotropic support.
 - **Anaphylactic shock:** 10 ml/kg over 20 minutes and reassess. Repeat up to a maximum of 40 ml/kg. Definitive treatment is IM adrenaline (0.01ml/kg 1:1000). Other treatment includes steroids, antihistamines, adrenaline nebulisers and salbutamol nebulisers
- **Dissociative shock**
 - **Anaemia:** Do not give fluid resuscitation. Needs blood transfusion. If no blood available put on IV maintenance fluids.
- **Cardiogenic shock**
 - Avoid IV fluid if possible, but if evidence of preload insufficiency give 10ml/kg over 1 hour.
- **For shock with severe acute malnutrition and diabetic ketoacidosis follow local guidelines, but it is important to avoid aggressive fluid resuscitation.**

Note: Patients who remain in shock despite adequate treatment of the underlying cause need to be discussed with a consultant.

C = Coma

- AVPU/GCS/BCS
- Treat hypoglycaemia

C = Convulsion

- Treat hypoglycaemia
- Treat convulsions

D = Dehydration

- Assess severity and treat with Plan C

E = History and thorough examination

- Obtain relevant blood samples
- Manage other associated conditions

REFER after initial stabilisation if still unwell.

Tertiary Level

Manage as above

Refractory shock

- Patients who remain in shock despite adequate treatment of the underlying cause need to be discussed with the consultant.
- Other alternative treatments include:
 - Vasoactive agents (adrenaline, noradrenaline)
 - Corticosteroids (hydrocortisone) - for suspected critical illness-related adrenal insufficiency
 - Bicarbonate - for correction of metabolic acidosis
 - ICU admission

Follow up

- Depends on cause.

DROWNING

Definition

Drowning is respiratory impairment after the head is submerged in liquid. Drowning can be fatal, have subsequent morbidity or cause no harm.

- Pulmonary oedema encountered after drowning is due to acute respiratory distress and not from fluid overload.
- Central nervous system injury is by far the most important cause of death and long-term functional impairment among drowning survivors.
- The outcome of drowning victims depends largely on the success of resuscitation measures at the scene of injury.

Pathophysiology

After initial panic and fight, comes breath holding and aspiration of large amounts of water. Laryngospasm, hypoxia and convulsions immediately follow resulting in death.

RESPIRATORY SYSTEM

- Aspirated fluid results in reduced O₂ uptake, CO₂ elimination and surfactant disruption resulting in hypoxia and hypercarbia.
- Approximately 15% of drowning victims have severe laryngospasms after submersion and die without aspirating water.
- The drowned victims will usually have a combined respiratory acidosis (hypercarbia) and metabolic acidosis (hypoxia-anaerobic aspiration).
- Pneumonia and pulmonary oedema develop as the aspirated fluid washes out surfactant, disrupting the alveolar-capillary membrane leading to increased permeability and aspirated debris/bacteria from contaminated water.

CARDIOVASCULAR SYSTEM

- Cardiovascular effects result from hypoxia causing poor myocardial perfusion, contractility and cardiac output.
- The hypoxia can also lead to life threatening dysrhythmias i.e., ventricular fibrillation, ventricular tachycardia or asystole.

CENTRAL NERVOUS SYSTEM

- Hypoxia, if sufficiently prolonged, causes profound disturbances of the central nervous system. The severity of brain injury depends on the magnitude and duration of hypoxia and cerebral perfusion.
- However, if promptly rescued and successfully resuscitated this can be reversed.

MANAGEMENT

- All drowning victims should receive aggressive basic and advanced life support as necessary. This applies for both at the scene and in the emergency department.
- The right management in the immediate post drowning period is very important.
- The fundamentals of basic life support are the same as for any other patient requiring resuscitation.
- The following are other things to consider.

1. Remove from water as soon as possible (at the scene)
2. Airway, breathing and circulation as well as cervical spine stabilisation.
 - a. If the child is very cold on arrival, resuscitation efforts should theoretically be continued until the body temperature is normalised. However, this can be challenging. Body temperature should be raised slowly.
 - b. Prolonged attempts to remove water from the lungs are futile and may delay attempts to establish breathing manoeuvres.
 - c. Beware of patients regurgitating aspirated contents into the airway as they have swallowed a lot of water. Insert an OGT.
 - d. Any debris seen on the mouth / oropharynx must be removed.
3. The need for admission should be determined by the severity of the drowning episode.
4. All patients with history of drowning with mild symptoms should be observed in the hospital for 4-6 hours
5. If evidence of persistent hypoxia and hypercapnia, consider intubation and ICU referral.
6. It is advisable to cover the drowned patient on antibiotics if there is a history of having drowned in contaminated water.

SNAKE BITE

Clinically snake bites can cause:

- Bleeding from decreased blood coagulability
- Oedema
- Tissue damage
- Pain

There are four main types of envenoming:

1. ***Cytotoxic envenoming***: very painful and progressive swelling. Blistering and bruising on the bite.
2. ***Haemorrhagic envenoming***: bleeding from gums, gastrointestinal and genitourinary tracts.
3. ***Neurotoxic envenoming***: moderate or absent local swelling. Progressive descending paralysis starting with the drooping of eyelids and later paralysis of eye movement. Can progress to difficult swallowing and breathing.
4. ***Myotoxic envenoming***: Negligible local swelling, generalised muscle pain and tenderness. Can also have features of neurotoxic envenoming.

Clinical Assessment

History

A precise history of the time and circumstances of the bite and the progression of local and systemic symptoms and signs is vital:

1. Where is the bite located on the body?
2. When did the incident happen?
3. Was the snake seen, what did it look like?
4. How is the patient feeling now, what symptoms is the patient experiencing?

Examination

1. Check for fang marks, note if scarification present or not
2. Look for evidence of use of a tourniquet
3. Check bitten limb for swelling, pulses, colour and viability
4. Mark with a pen, the level of swelling on a limb so that further swelling can be assessed
5. Bleeding (puncture wound, venepuncture sites, gums)
6. Shock (blood pressure, cold, cyanosed, sweaty skin, reduced coma score)
7. Paralysis (blurred vision, drowsiness, heavy eyelids, paradoxical breathing, drooling, poor cough)

Clinical Sign of Envenoming

Local Symptoms and signs

Immediate localised pain, oedema and bruising at the site of the bite, persistent bleeding from fang puncture wounds. Enlarged and swollen regional lymph nodes. Blisters (blood or fluid filled).

Generalised symptoms and signs

Signs of hypotensive shock, neurotoxic symptoms, acute renal failure (secondary to

hypotension or rhabdomyolysis)

Please note: mixed types of envenoming may occur i.e., mixed cytotoxic and neurotoxic; mixed haemorrhagic and cytotoxic.

Note: not all bites, even from the deadliest of snakes, always cause envenoming. Up to 50% of bites may be un-envenomed i.e. 'dry bites'.

Some of the presenting symptoms and signs can result from fear and treatment (first aid/traditional).

Investigations

- FBC: leucocytosis, low haemoglobin, low platelets
- Coagulation studies:
 - 20 min whole blood clotting test (see how long it takes for blood to clot in a plain tube)
 - prothrombin time, thrombin and activated partial thromboplastin times, D-dimer, INR.
- Biochemistry: creatine kinase, LFTS, U&E, blood gas
- Group and crossmatch

First Aid Management

1. Move the patient away from the place where the bite has occurred.
2. Remove anything tight from the bitten part of the body e.g. rings, bracelets, bands from bitten limbs
3. Reassure the victim
4. Immobilise the victim, splint the limb to keep it still
5. Never use a tight arterial tourniquet
6. Avoid traditional first aid methods, herbal medicines. The following are discouraged:
 - Tattooing around the area, suctioning out venom by mouth, ice packs.
 - Do not wash, rub or massage or tamper with the bite wound in any way. These interventions may encourage systemic absorption of venom from the site and/or they may introduce infection.

Management

Primary Level

- Snake bite is a medical emergency, so use the ABCCDE approach.
- Place on maintenance fluids.
- Check that tetanus toxoid immunisation is up to date, if not give it.
- Treat pain
- REFER PATIENT

Secondary / Tertiary Level

- As above
- Treat pain appropriately – oral paracetamol is our first line, but morphine may be

needed.

- Elevate the limb if there is extensive swelling and monitor for compartment syndrome.
- If local circulation is threatened, inform the surgical team on call as compartment syndrome may need fasciotomy.
- The following are signs and symptoms that may indicate a need for anti-snake venom:
 - Neurotoxicity
 - Spontaneous systemic bleeding
 - Incoagulable blood
 - Cardiovascular instability
 - Extensive swelling (involving more than half the bitten limb)
 - Rapidly progressive swelling
 - Bites on fingers and toes
 - If anti venom is needed:
 - Give 40mls in 200mls of normal saline IV over 1hr but have adrenaline standing by: anaphylactic reactions are not uncommon.
- If any signs of necrotic tissue, surgical debridement is vital

TOXICOLOGY

The incidence of poisoning is highest among children 1 to 3 years of age. Boys slightly outnumber girls as victims of unintentional exposures. A second peak occurs in adolescence due to suicide attempts or accidental overdose during substance abuse. The most common agents involved in preschool poisonings are medications, household products (cleaning agents, soaps, detergents), pesticides

History

- REMEMEBER THERE MAY BE NO CLEAR HISTORY!!!
- *Route of exposure:* Ingestion, inhalation, dermal, ocular or parenteral.
- *Time of the exposure/incident:* The delay between the time of ingestion and the onset of symptoms is important.
- *Toxin involved:* Important to establish the precise ingredients of what has been ingested. Parents must be encouraged to bring the product container or label.
- *Estimated volume/quantity ingested:* For estimations of liquid toxins, the average swallow of a young child is approximately 5 to 10 mL while that of the older child and adolescent is 10 to 15 mL
- *Initial symptoms post ingestion if any.*
- *Prehospital attempts at decontamination*
- Include the patient's past medical history, allergies, current medications, last meal and events surrounding the ingestion.

Physical Examination

- May be asymptomatic
- Drowsiness / coma
- Convulsions (severe organophosphate poisoning)
- Diarrhoea (if a child is dehydrated, but salivating ++ consider organophosphate poisoning, with pin point pupils)
- Pupillary abnormalities - pin-point pupils (organophosphate poisoning, sometimes mushrooms); dilated pupils (barbiturates)
- Ataxia
- Tachypnoea / tachycardia or flushing / bradycardia (organophosphate poisoning, atropine)
- Wheezing (paraffin inhalation)
- Cardiac arrhythmia or hypotension
- Presence of burns within the mouth (bleach or acid with oesophageal injury)
- Stridor (laryngeal damage)
- Abdominal distension (local medicine intoxication)
- Hypersecretions and noisy wet breathing: organophosphate poisoning
- Acidotic

Investigations

Investigations should be done after stabilising patient:

- Blood glucose: rapid identification and treatment of hypoglycaemia is crucial.
- Urea and Electrolytes
- Arterial / venous / capillary blood gas: identify hypercapnia, acid base disturbances.
- Electrocardiogram (ECG)

Management

Primary Level

- Primary assessment (ABCCCDE) to recognise and treat life-threatening emergencies
- Many toxins are rapidly absorbed from the gastrointestinal tract, skin and respiratory system. The development of severe toxicity may be avoided if further absorption can be prevented. **Dermal and ocular decontamination should consist of flushing the skin and eyes with tepid water and removal of all exposed clothing.**
- REFER

Secondary Level

- As above
- The adequacy of the airway and breathing should be addressed immediately.
- Supplemental oxygen should be administered for any degree of hypoxaemia.
- Stabilisation of vital physiological functions takes priority over the diagnosis of the specific toxin.
- Often, supportive measures are adequate, and no specific therapy is required.
- Supportive measures include the evaluation and treatment of cardiopulmonary, neurologic and metabolic abnormalities.
- REFER

Tertiary Level

- As Above
 - Endotracheal intubation and mechanical ventilation should be considered in any child with progressive neurologic deterioration
 - Definitive management of specific condition once stabilised.
- REFER TO TREATMENT OF SPECIFIC POISONS BELOW**

Treatment of Specific Poisons

1. ORGANOPHOSPHATES AND CARBAMATES

Found in many insecticides, pesticides and most exposures are accidental. They can occur both via oral ingestion and transdermal route. Most accidental ingestions are seen around the time of maize harvest and treatment for storage.

Patients often present with a constellation of signs that create a toxicome of cholinergic findings. The mnemonic "**DUMBELLS**" refers to **D**iarrhoea, **U**rination, **M**iosis, **B**ronchorrhea and **B**ronchospasm, **E**mesis, **L**acration, **L**ethargy and **S**alivation.

The nicotinic signs include alteration in mental status, seizures, sweating, muscle fasciculations, weakness and paralysis. Other symptoms include bradycardia, hypotension, and hypothermia.

Management:

- Get rid of poison and control ongoing absorption hence if the toxin was absorbed through the skin remove all clothing and wash the patient. Oral ingestion is much more common in children.
- Atropine is a selective muscarinic receptor blocker and therefore will reverse only muscarinic effects. It will not improve weakness or paralysis.
 - Doses of **20 micrograms/kg** IV or IM every 15 minutes may be required to achieve "atropinisation", (no secretions, clear chest).
- Monitor regularly (secretions, respiratory rate, heart rate, coma score).
- Atropine is stopped when the chest is dry. It is NOT determined by pupil size.
- Continuous infusions of atropine may be required (0.02–0.08 mg/kg/h) if there is no improvement with initial treatment. Atropine infusion may need ICU admission.

2. IRON POISONING

- Ingestion of 40–60 mg/kg of elemental iron in children places them at risk for significant toxicity.
- Five classical stages described.
 - ***GIT phase:*** occurs within 30 minutes to 6 hours post ingestion. Secondary to the corrosive effect of iron. Vomiting, diarrhoea, haemorrhagic necrosis and shock are symptoms described.
 - ***Latent or relative stable phase:*** 6-24 hours after ingestion.
 - ***Shock and metabolic acidosis:*** 6-72 hours after ingestion.
 - ***Hepatotoxicity/hepatic necrosis:*** 12-96 hours after ingestion
 - ***Bowel obstruction:*** 2-8 weeks after ingestion.

Management:

- IV fluid resuscitation.
- May need potassium and glucose supplementation.
- Chelation therapy with deferoxamine should be initiated if there is evidence of hypovolaemia, shock, lethargy, persistent vomiting, diarrhoea, positive anion gap, metabolic acidosis, large number of pills on abdominal radiograph, or a serum iron level > 500 µg/dL.

- Desferrioxamine is most effective as an infusion at 15-35mg/kg/hr based on severity of clinical severity.

3. PARACETAMOL POISONING

- Doses greater than 140–200 mg/kg have been associated with toxicity in children.

- There are four clinical stages in paracetamol poisoning:

Stage 1: first 24 hrs post ingestion. Most appear normal. They may exhibit anorexia, pallor, nausea and vomiting. Biochemical evidence is usually absent.

Stage 2: 24-72 hours post ingestion, right upper quadrant pain. Biochemical evidence with aspartate aminotransferase (AST) as the most sensitive marker. High bilirubin and prothrombin time are also noted.

Stage 3: 72-96 hours post ingestion: patient develops hepatic necrosis and encephalopathy. Nausea and vomiting reappear, and patients may develop jaundice, myocardial dysfunction, haemorrhage and renal failure. Laboratory values for AST and alanine transferase (ALT) are above 10,000 IU/L. PT (INR) and bilirubin are raised. Hypoglycaemia and metabolic acidosis may occur and are important prognostic indicators

Stage 4: 4 days to 2 weeks. If irreversible damage has occurred, complete hepatic failure ensues, and transplantation is required for survival.

Management:

- Supportive care (ABCCCDE)
- **Activated Charcoal:** Paracetamol is completely absorbed from the gastrointestinal tract in the first few hours after drug ingestion Therefore, activated charcoal (1 g/kg body weight) is recommended only in the first 4 hours after acetaminophen overdose
- **N-acetylcysteine:** Best outcome if given within 8-10 hours of ingestion. But it - can be beneficial up to 36 hours after ingestion. Can be given either orally or parenterally.

Oral

Use 10% NAC (100 mg/mL) and dilute 2:1 in water or juice to make a 5% solution (50 mg/mL).

Initial dose: 140 mg/kg

Maintenance dosage: 70 mg/kg every 4 h for 17 doses

Intravenous

Use 20% NAC (200 mg/mL) for each of the doses below and infuse in 150 mg/kg in 200 mL D5W over 60 min

50 mg/kg in 500 mL D5W over 4 h

100 mg/kg in 1000 mL D5W over 16 h

4. SALICYLATES POISONING

Common medications containing salicylates are aspirin and oil of wintergreen. Acute ingestions of 150–300 mg/kg of salicylates are associated with mild symptoms and greater than 500 mg/kg with severe symptoms and death.

Presentation

Patients will present initially with nausea, vomiting, mild tachypnoea and tinnitus. They develop hyperpnoea and hyperventilation due to direct stimulation of the respiratory centre. Confusion, agitation, seizures and coma may also develop. Respiratory alkalosis predominates early but later there is respiratory acidosis plus specific electrolyte disturbances (hypokalaemia, hyperglycaemia, hypoglycaemia). An anion gap metabolic acidosis occurs in severe cases.

Management:

- ABCCCDE
- Correct fluid and electrolyte abnormalities
- Salicylate excretion:
 - Activated charcoal is beneficial (each gram of charcoal absorbs 550g of salicylate acid).
 - Alkalisation of urine ($\text{PH} > 7.5$) by giving sodium bicarbonate (1-2 mmol/kg with maximum dose of 100 mmol) increases salicylate excretion through ion trapping.
- Dialysis in severe cases.

5. CAUSTICS

- Caustics consist of acidic and alkali compounds often used as cleaning materials (e.g. bleach), or compounds used to make soap or detergents.
 - Acids produce damage by coagulating proteins and causing tissue necrosis.
 - Alkalies dissolve proteins and cause liquefaction necrosis.
- Patients often present with burns to the eyes, skin, mouth, oropharynx, oesophagus and stomach. Symptoms include pain, vomiting, drooling or difficulty swallowing.
- Injuries to the oesophagus may result in perforation and later strictures while damage to the stomach may lead to ulceration and gastric outlet obstruction secondary to scarring of the pylorus.
- Respiratory symptoms may predominate if pulmonary aspiration has occurred.

Management:

- ABCCCDE
- Decontamination: If the fluid was on the skin, remove all clothing, and wash skin immediately. If in the eyes, wash continuously for 15-30 minutes.
- DO NOT induce vomiting, NO gastric lavage, NO activated charcoal.
- If any evidence of airway involvement, alert ICU or anaesthesia as they are at risk of obstruction with worsening oedema.
- For careful assessment of GI tract, endoscopy may be indicated.
- Important to follow these children long term as they can have late complications with strictures weeks after initial injury.

6. HYDROCARBONS

- Hydrocarbons are organic compounds that consist solely of carbon and hydrogen molecules. Examples are fuels, household cleaners.
- They are classified based on viscosity (ability to flow against friction) and volatility (ability to vaporise). This classification can aid in determining expected clinical effects.
- Aspirations of low viscosity can cause chemical pneumonitis and surfactant denaturing. Resulting in acute respiratory distress.

Management:

- Stabilisation of ABCCCDE.
- Supportive treatment
- DO NOT induce vomiting.
- NO activated charcoal / gastric lavage

7. LOCAL MEDICINE

- This is usually noted in children that have diarrhoea and vomiting. It is also given to neonates and its use is influenced by cultural practices.
- In children with burns the medicine may be given either topical and/or orally.
- The most common presentation is severe metabolic acidosis not in keeping with the history. Some may also have acute kidney injury.

Management:

- Supportive management is the most effective management as the constituents of traditional medications are usually not known.

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CHAPTER 2. CARDIOLOGY

ACUTE RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

Definition

Acute Rheumatic Fever (ARF) is an inflammatory disease of childhood resulting from *Streptococcus pyogenes* (group A streptococcus) pharyngeal or skin infections. Rheumatic Heart Disease (RHD) results from recurrent attacks of acute rheumatic fever causing scarring of mitral and aortic valves. It commonly presents with congestive cardiac failure (CCF) and mitral regurgitation. It commonly occurs between the ages of 5 to 18 years, with a female predominance.

Risk factors

- Over crowding
- Low social economic status
- Genetic predisposition

Prevention / Promotion

- Four weekly intramuscular benzathine penicillin prophylaxis up to 21 years of age in mild cases of rheumatic heart diseases and life long in moderate to severe cases
- Oral penicillin VK or macrolides in people with elevated risk of adverse reactions i.e.
 - Severe aortic insufficiency,
 - Severe mitral stenosis,
 - Severe aortic stenosis,
 - Ventricular dysfunction (EF <50%), or
 - Severe symptoms (NYHA class III or IV)
- Health education & advocacy
- Screening (as health system permits)

Signs and symptoms

| Acute Rheumatic Fever* | Rheumatic Heart Disease |
|---|--|
| <ul style="list-style-type: none"> • Fever • Carditis (presence of a murmur) • Arthritis or arthralgia (joint pain/swelling) • Skin rash • Nodules • Chorea (abnormal movement) | <ul style="list-style-type: none"> • Clinical features of cardiac failure <ul style="list-style-type: none"> ○ Respiratory distress ○ Tachypnoea ○ Hepatomegaly |

* also see Modified Jones Criteria below

Diagnosis of Acute Rheumatic Fever

Modified 2015 Jones criteria for High-Risk population

| Major Criteria |
|---|
| 1. Carditis (clinical or subclinical) 2. Arthritis (Monoarthritis or Polyarthritis or polyarthralgia) 3. Sydenham's chorea 4. Erythema marginatum 5. Subcutaneous nodules |
| Minor Criteria |
| <ul style="list-style-type: none">• Monoarthralgia• Fever ($\geq 38.0^{\circ}\text{C}$)• ESR $\geq 30\text{mm/h}$ or CRP $\geq 3.0\text{mg/dl}$• Prolonged PR interval (after taking into account the differences related to age, if there is no carditis as a major criterion) |
| Making a Diagnosis |
| <ol style="list-style-type: none">1. Initial episode of ARF: Evidence of preceding group A β-hemolytic streptococcal infection + 2 major criteria or 1 major and 2 minor criteria2. Recurrent attack of ARF (Past ARF or known RHD): 2 major criteria or 1 major and 2 minor criteria or 3 minor criteria |

In the Malawi setting, it is reasonable to make a diagnosis of ARF without evidence of preceding group A strep infection or supporting lab criteria given the lack of access to lab tests.

Investigations

- *Acute Rheumatic fever*
 - C-reactive protein (CRP)
 - Erythrocyte sedimentation rate (ESR)
 - Antistreptolysin O Titre (ASOT)
 - Throat swab
 - Cardiac echo
 - Electrocardiogram (ECG)
- *Rheumatic Heart Disease*
 - Electrocardiogram (ECG)
 - Cardiac echo

Differential diagnosis

- Juvenile idiopathic arthritis
- Septic arthritis
- Post streptococcal reactive arthritis
- Malaria

Management

Primary Level

- Give a stat dose of I.M. benzathine penicillin, stabilize, and refer

Secondary Level

- Anti-streptococcal therapy *
 - STAT dose IM Benzathine Penicillin (600,000 IU IM < 25kg; 1,200,000 IU IM > 25kg) then 4-weekly
- Ibuprofen 10 mg/kg TDS for 7 days (until joint pains resolve)
- Chorea
 - Severe/ distressing chorea: Haloperidol 0.02mg/kg once daily (Max 1mg) or sodium valproate 5mg/kg twice daily (Max 600mg/day). Mild cases of chorea do not require specific treatment.
 - Steroids e.g prednisone can be added in severe/distressing chorea (prednisone 2mg/kg daily for 2 weeks then taper over 1 to 2 weeks)
- If signs of heart failure give Furosemide 1 mg/kg BD

Duration of prophylaxis

21 years of age in mild cases of rheumatic heart diseases and life long in moderate to severe cases.

ALL PATIENTS SHOULD BE REFERRED TO A TERTIARY FACILITY

Tertiary Level

- Treat as above
- Referral for cardiology review

FOLLOW UP

- Regular follow up for benzathine penicillin prophylaxis and management of cardiac failure in PEN-Plus Clinic

MYOCARDITIS

Definition

Inflammation of myocardium causing poor contractility of heart muscle.

Risk factors/causes

- Idiopathic
- Viruses eg. Adenovirus, coxsackie,
- Bacterial infections
- Fungal infections

Promotion / Prevention

- Health education

Symptoms / signs

- Signs of heart failure
- A low grade fever
- Other features of a viral infection, e.g. rhinorrhoea
- Regurgitant murmurs (e.g. pansystolic murmur of mitral regurgitation)
- Myocarditis in children presents with unexplained shortness of breath

Investigations

- Chest X-Ray
- Echocardiogram
- Electrocardiogram
- HIV test
- Viral screening
- Blood culture

Management

Primary level

- Stabilize the patient and refer

Secondary level

- Stabilize the patient
- Treat as heart failure if symptoms present
- Start antibiotics, if any signs of bacterial infection,
- Refer to tertiary level

Tertiary level

- Stabilize the patient
- Treat as heart failure if symptoms present.
- Start antibiotics, if any signs of bacterial infection,
- Cardiology review

Follow up

- Medication
- Growth
- Review symptoms

DILATED CARDIOMYOPATHY

Definition

Dilated cardiomyopathy (DCMO) is defined as left ventricular dilation with systolic dysfunction

Risk factors / causes

- Idiopathic
- Drugs e.g., Doxorubicin, HAART
- Infections e.g, HIV and other viruses
- Malnutrition
- Hypertension
- Genetic causes

Promotion / Prevention

- Health education

Symptoms / signs

- Signs of heart failure
- Regurgitant murmurs (e.g. pansystolic murmur of mitral regurgitation)

Investigations

- Chest X-Ray
- Echocardiogram
- Electrocardiogram
- HIV test

Management

Primary level

- Stabilize the patient and refer

Secondary level

- Stabilize the patient
- Treat as heart failure if symptoms present. See section on heart failure
- Refer to tertiary level

Tertiary level

- Stabilize the patient
- Treat as heart failure if symptoms present. See section on heart failure
- Cardiology review

Follow up

- Medication
- Growth
- Review of symptoms

PULMONARY HYPERTENSION

Definition

Pulmonary hypertension (PH) is a disease characterized by elevated pulmonary arterial pressure, which can result in right ventricular (RV) failure.

Risk factors / causes

The NICE (2013) Updated Classification of Pulmonary Hypertension

| |
|---|
| 1. Pulmonary arterial hypertension (PAH) <ul style="list-style-type: none"> – Idiopathic PAH – Heritable PAH – Drug and toxin induced – Associated with connective tissue disease, HIV infection, congenital heart diseases, schistosomiasis |
| 2. PH due to left heart disease <ul style="list-style-type: none"> – Left ventricular systolic dysfunction. – Left ventricular diastolic dysfunction. – Valvular disease |
| 3. Chronic thromboembolic PH |
| 4. PH with unclear multifactorial mechanisms <ul style="list-style-type: none"> – Haematological disorders e.g. chronic haemolytic anaemia – Metabolic disorders e.g. thyroid diseases – Systemic diseases and Others e.g. chronic renal failure |

Promotion / Prevention

- Appropriate management of treatable diseases
- Surgical management of congenital heart diseases in children
- Health awareness and advocacy

Signs and symptoms

The presentation of PH varies considerably based upon the following; age of the patient, presence and absence of associated medical conditions, and severity of PH and right ventricular function. Symptoms and signs include:

- Difficulty feeding or shortness of breath on activity
- Fatigue
- Syncope
- Cyanosis
- Failure to thrive
- Cough
- Chest Pains
- Signs of heart Failure
- Right ventricular dilatation/dysfunction: Loud P2, left parasternal heave, systolic/diastolic murmurs, hepatomegaly

Investigations

Investigations are aimed at identifying the underlying cause and include:

- Echocardiogram: Most helpful in the initial assessment and follow-up of PH
- Chest X-ray
- ECG

Management

Primary Level

- Stabilize patient
- REFER TO SECONDARY/TERTIARY FACILITY FOR PULMONOLOGIST AND/OR CARDIOLOGIST REVIEW

Secondary Level

- Stabilize the patient
- Bedrest: avoid strenuous exercise
- Supplemental oxygen
- If presents with signs of heart failure, manage appropriately (see section on Heart failure Management)
- Treat underlying cause of pulmonary hypertension if possible
- Refer to tertiary facility for pulmonology and/or cardiology review

Tertiary level

- Manage as above.
- Pulmonologist and/or Cardiologist review
- Treat underlying cause of pulmonary hypertension if possible. Vasodilators e.g. Sildenafil can be considered with pulmonology and/or cardiology consultation
- Involve palliative care

Follow up

- Regular pulmonology and/or cardiology review

CONGENITAL HEART DISEASES

Definition

Congenital heart diseases (CHD) encompass a spectrum of structural abnormalities of the heart or intrathoracic vessels.

Risk factors / causes

- Majority of the cases occur sporadically
- Exposure to teratogenic drugs (e.g. warfarin, sodium valproate)
- Maternal illness: diabetes mellitus and rubella
- Advanced maternal age
- Family history
- Genetic syndromes

Promotion / Prevention

- Avoid drugs that predispose to development of heart defects during pregnancy
- Antenatal screening
- Health education
- Increased awareness of common presentations of congenital heart disease

Signs and symptoms

- Sweating and / or difficulties breast feeding
- Respiratory distress
- Wheeze / crepitations
- Poor weight gain
- Squatting
- Recurrent chest infections
- Cyanosis
- Effort intolerance e.g during play.
- Finger clubbing
- Chest deformity
- Differential saturations (SpO_2 lower limbs < upper limbs)
- Oedema
- Weak or unequal pulses.
- Heart murmur
- Hepatomegaly

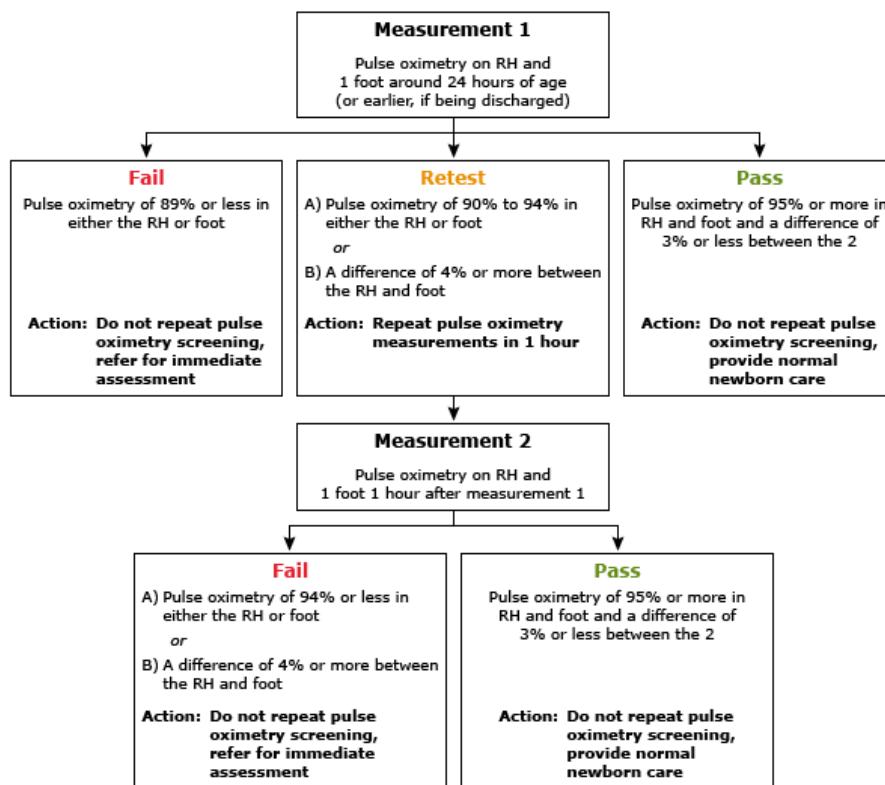
Investigations

- Full blood count
- Chest X-ray
- Electrocardiogram
- Echocardiography

New Born Screening

Congenital heart defects (CHD) are the most common and severe types of congenital anomalies. Pulse oximetry is an effective and reliable tool for screening and early detection of cyanotic congenital cardiac defects with a sensitivity of 75-83% and specificity of 99%. Pulse oximetry may not detect severe acyanotic lesions in the new-born period. Cardiac auscultation may detect these lesions if a murmur is present.

Algorithm for New-born screening



A FAILED PULSE OXIMETRY SCREEN SHOULD BE REFERRED TO A SECONDARY/TERtiARY LEVEL FACILITY FOR FURTHER EVALUATION

PRESENCE OF A MURMUR ON AUSCULTATION SHOULD PROMPT REFERRAL TO SECONDARY/TERtiARY LEVEL FACILITY FOR FURTHER EVALUATION.

Management

Primary Level

- Stabilize using ABCDE
- Refer to secondary level

Secondary level

- Stabilize using ABCDE
- Treat heart failure if present (see section on heart failure)
 - Furosemide 1-2 mg / kg / dose IV BD (use oral furosemide if IV not available)
AND
 - Spironolactone 1-2 mg / kg / dose PO BD (max 25mg / dose)
- Virtual consultation and refer to tertiary center

Tertiary level

- Stabilize using ABCDE
- Can use CPAP if severely distressed / hypoxic
- Treat heart failure if present (see section on heart failure)
 - Furosemide 1-2 mg / kg / dose IV BD (use oral furosemide if IV not available)
AND
 - Spironolactone 1-2 mg / kg / dose PO BD (max 25mg / dose)
- Nutritionist / Dietician review
- Cardiologist review and possible corrective surgery referral
- Palliative care team when necessary

Follow up

- Once diagnosis is confirmed, the child must be followed up in a PEN-Plus clinic regularly
- Ensure child has adequate stock of medications for home use at each visit
- Monitor growth and development
- Ongoing counseling and education

HYPERCYANOTIC SPELL IN TETRALOGY OF FALLOT

Definition

Sudden severe episodes of intense cyanosis caused by reduction of pulmonary flow in patients with underlying Tetralogy of Fallot or other cyanotic heart lesions.

Risk factors for spells

- Hypovolaemia e.g. diarrhea and vomiting
- Febrile illness
- Pain / Agitation
- Anemia
- Crying, feeding, defaecation
- Cold weather

Promotion and prevention

- Educate parent / guardian on home measures when child is in spell (knee chest position)
- Early health seeking behavior if acutely unwell
- Avoid unfavorable conditions (pain, cold, agitation, dehydration)
- Adherence to prescribed medications

Signs and symptoms (clinical features)

- Severe hypoxia / cyanosis
- Hyperpnoea
- Syncope
- Seizure
- Stroke
- Reduced intensity or absence of systolic murmur during spell.

Management

Primary Level

- Keep the child with the parent / guardian and place in a knee chest position
- Place the baby on the mother's shoulder with the knees tucked up underneath.
 - This provides a calming effect, reduces systemic venous return and increases systemic vascular resistance.
- Stabilize with ABCDE approach
- Place on oxygen (preferably 100% oxygen)
- Give bolus RL or NS 20 ml/kg rapid IV over 30 minutes to increase preload. Can repeat another bolus if not improving (max 2 boluses)
- CONSULT and REFER

Secondary Level

- As Above
- Give PO morphine 0.1 mg/kg to reduce distress and hyperpnoea.

- Propranolol 0.5 - 1 mg /kg /dose PO TDS
- CONSULT and REFER TO TERTIARY LEVEL FACILITY

Tertiary Level Facility

- Put on knee chest position
- Place on oxygen (preferably 100% oxygen)
- Give bolus RL or NS 20 ml/kg rapid IV over 30 minutes to increase preload. Can repeat another bolus if not improving (max 3 boluses)
- Give PO/IV morphine 0.1 mg/kg to reduce distress and hyperpnoea.
- Do arterial blood gas. If there is severe metabolic acidosis:
 - Give IV sodium bicarbonate 1 mEq/kg STAT to correct.
- In resistant cases consider PICU admission for IV Phenylephrine / IV Ketamine in consultation with cardiologist
- Long Term medical management
 - Propranolol 0.5 - 1 mg /kg /dose PO TDS
 - Aspirin 3-5 mg / kg PO daily
 - Fefol supplement according to weight
- Cardiology and dietician / nutritionist review
- Refer for surgical repair if appropriate

Follow up

- Once diagnosis is confirmed, the child must be followed up in a PEN-Plus clinic regularly
- Ensure child has adequate stock of medications for home use at each visit
- Monitor growth and development
- Ongoing counseling and education

CONGESTIVE HEART FAILURE

Definition

Congestive heart failure (CHF) is a clinical condition in which the heart is unable to pump enough blood to the body to meet its needs, to dispose of systemic or pulmonary venous return adequately, or a combination of the two.

Risk factors/causes

- Cardiac causes
 - Congenital heart diseases
 - Acquired heart diseases
 - Arrhythmias
- Non-cardiac causes:
 - Anemia
 - Sepsis
 - Chronic kidney disease
 - Auto-immune

Promotion / Prevention

- Health education on early health seeking behavior
- Early referral of patients with suspected heart disease with or without heart failure.
- Early detection and treatment of anemia

Signs and symptoms

- ***IN INFANTS tachycardia, tachypnoea and hepatomegaly are the most common signs***
- Respiratory distress
- Cardiomegaly (displaced apex beat)
- Exertional dyspnoea / sweating during breastfeeding in infants
- Presence of bibasal crepitations
- Signs of shock; reduced pulse volume, delayed capillary refill time, tachycardia, hypotension
- Gallop rhythm
- Raised JVP (older child)
- Peripheral/ sacral oedema (oedema will be in dependant area)
- Failure to thrive / severe malnutrition

Investigations

- Imaging
 - Chest x-ray
 - Echocardiogram
 - ECG
- Blood tests
 - HIV test
 - Full blood count
 - Urea and electrolytes
 - Liver function tests
- Urine dipstick

- Other investigations according to suspected etiology

Differential diagnosis

- pneumonia
- bronchiolitis
- asthma
- Nephrotic / nephritic syndrome
- Renal failure
- Chronic liver failure

Management

Primary Level

- Stabilize using ABCDE
 - If available give a single dose of Frusemide 1 mg / kg IV stat (use oral furosemide if IV not available)
- Refer to secondary

Secondary Level

- Stabilize using ABCDE
 - Oxygen supplementation
 - Propped up position
 - Keep warm, gentle handling
 - Treat concomitant chest infections
 - Optimize caloric intake; low threshold for nasogastric feeding
 - Anti-failure medications:
 - Furosemide 1-2 mg / kg / dose IV BD or TDS (use oral furosemide if IV not available)
- AND**
- Spironolactone 1-2 mg / kg / dose PO BD (max 25mg / dose)
- Refer to tertiary center

Tertiary Level

- As Above
- Correct anemia (cautious transfusion, ideally with packed red blood cells)
- Correct electrolyte imbalance
- Treat concomitant chest infections
- Anti-failure medications (FIRST LINE)

Frusemide (loop diuretic)

- Dose: 1 - 2 mg/kg/dose OD to QID, oral or IV

- Continuous IV infusion at 0.1 – 0.5 mg/kg/hour if severe fluid overload
- Use with potassium supplements (1 - 2 mmol/kg/day) or add potassium sparing diuretics.

Spironolactone (potassium sparing diuretic, modest diuretic effect)

- Dose: 1 mg/kg/dose BD

- Afterload reduction: SECOND LINE

(Discuss with Paediatrician before use)

Angiotensin converting enzyme inhibitor

Enalapril 0.1mg / kg / dose PO OD

OR

Captopril 0.1 mg/kg/dose PO TDS, gradually increase up to 1 mg/kg/dose TDS

Monitor blood pressure and potassium level (risk of hyperkalemia)

- THIRD LINE DRUGS

Digoxin (Discuss with Paediatrician / Cardiologist before use)

- Useful in heart failure with excessive tachycardia, supraventricular tachyarrhythmias.
- In practice: Don't "digitalize" with high-dose digoxin. Start with maintenance dose:
 - 2-17 years: 10 mcg / kg / day OD (max 0.25 mg daily)

IV inotropic agents - Adrenaline, dobutamine (DISCUSS WITH CARDIOLOGIST)

Beta blockers (Carvedilol) - To be considered in acute heart failure with cardiogenic shock (DISCUSS WITH CARDIOLOGIST)

- **Pericardiocentesis**- May be necessary if:

- Large pericardial effusion (>3cm on ECHO) and / or
- Signs of cardiac tamponade (Tachycardia, elevated JVP, hypotension, pulsus paradoxus muffled heart sounds)
- PERICARDIOCENTESIS SHOULD ONLY BE DONE IN CONSULTATION WITH THE CARDIOLOGIST

- Nutritionist / Dietician review
- Cardiology review and possible corrective surgery referral
- Palliative care team when necessary
 - Palliative care involvement early if in terminal chronic cardiac failure
 - Morphine is a venodilator reducing preload in children in cardiac failure and improves pulmonary oedema (Morphine dosing: 200-400 mcg/kg every 4 hours)

FOLLOW UP

- Once diagnosis is confirmed, the child must be followed up in a PEN-Plus clinic regularly
- Ensure child has adequate stock of medications for home use at each visit
- Monitor for complications of medications
- Monitor growth and development
- Ongoing counseling and education

PAEDIATRIC ARRHYTHMIAS

1. ATRIOVENTRICULAR BLOCKS

Definition

An interruption or delay of electrical conduction from the atria to the ventricles leading to abnormally slow heart rate and irregular rhythm.

Criteria for bradycardia

| Age Group | Heart Rate |
|-----------------------|------------|
| Infants to < 3 years | < 100 bpm |
| Children 3-9 years | < 60 bpm |
| Children 9-16 years | < 50 bpm |
| Adolescents > 16years | < 40bpm |

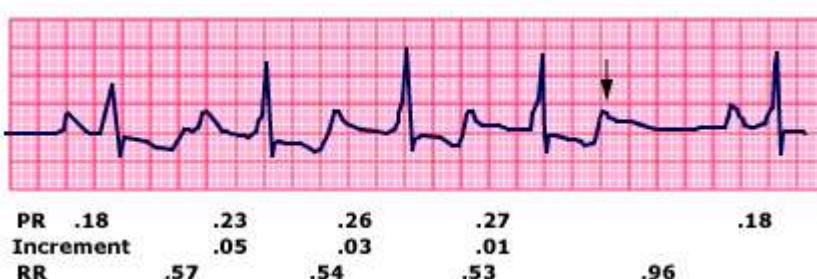
Types of conduction defects

1st degree - prolonged PR interval

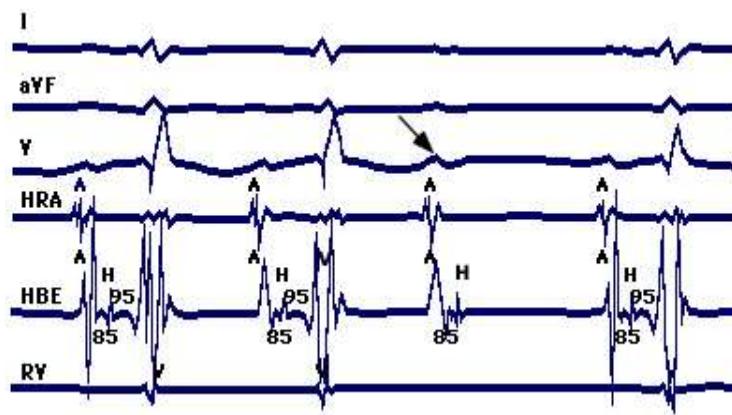


2nd degree

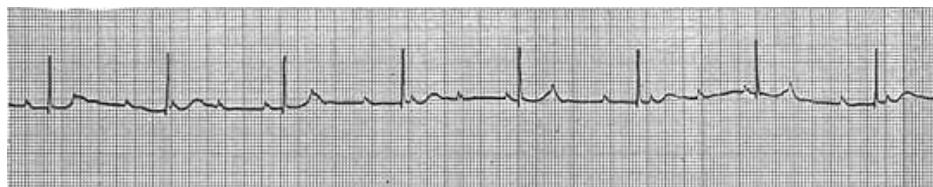
- Mobitz type 1 (Wenckebach): progressive PR prolongation before
 - Dropped AV conduction.
 - Generally not pathologic.



- Mobitz type 2: abrupt failure of AV conduction without prior PR prolongation.



- 3rd degree (complete heart block): AV dissociation with no atrial impulses conducted to ventricles.



Note: 2nd degree (Type 2 and above) and 3rd degree heart block are always pathological!

Risk factors / causes

- Hypoxia
- Sepsis
- Acidosis
- Hypothyroidism
- Electrolyte abnormalities i.e. hypokalaemia, hypocalcaemia
- Maternal Lupus(anti Ro /La positive) ; mother frequently asymptomatic
- Structural heart diseases: AVSD, congenital corrected transposition of great arteries (L-TGA), left atrial isomerism
- Long QT syndrome
- Surgical trauma: Especially in VSD closure, TOF repair, AVSD repair
- Infection: Rheumatic fever, endocarditis, viral myocarditis
- Drugs e.g. quinine

Health promotion

- Education and awareness of risk factors
- Screening of immediate family members of a person who suffered sudden cardiac death

Signs and symptoms

- most patients are asymptomatic
- Syncope
- hypotension

- exercise intolerance
- fatigue
- Dyspnoea
- dizziness
- Palpitations
- Cardiac arrest

Investigations

- ECG
- Chest X Ray
- Cardiac Echo
- Urea and Electrolytes
- Other tests as clinically indicated

Differential diagnosis

- See causes

MANAGEMENT

Primary / Secondary Level

- If unstable, manage ABC then REFER to a tertiary center
- Hemodynamically stable patients – REFER

Tertiary Level

- Treat the underlying systemic causes of bradycardia.
- Hemodynamically stable patient with normal blood pressure:
 - No medical management for the bradycardia.
 - Refer to a cardiology specialist.
- Symptomatic Bradycardia with Haemodynamic Instability
- Manage ABCDE
 - Cautious fluid resuscitation. Give 10mls /kg bolus if in shock or hypotensive with close monitoring for signs of fluid overload.
- Medical management of bradycardia:
 - IV Atropine 0.02mg /kg/ dose (max 0.6mg) - can repeat doses if remains bradycardic (max 3mg)
 - If atropine not working, add IV Adrenaline infusion at 0.02 mcg/kg/min and / or dopamine 2-10 mcg / kg / min
- Cardiologist review

Followup

- Once diagnosis is confirmed, the child must be followed up in a PEN-Plus clinic regularly
- Monitor growth and development
- Ongoing counseling and education

b. SUPRAVENTRICULAR TACHYCARDIA

Definition

Abnormally rapid heart rhythm originating above the ventricles, often (but not always) with a narrow QRS complex

Causes / risk factors

- Wolff-Parkinson-White (WPW)
- Congenital heart disease
- Pericarditis
- Idiopathic
- Infections (e.g. sepsis, pneumonia)

Signs and symptoms / clinical features

- Severe tachycardia (> 220bpm)
- Heart palpitations
- Respiratory distress
- Shock

Management

Primary Level

- Manage ABCDE
- Consult / refer to secondary level

Secondary Level

- Manage ABCDE
- Haemodynamically stable patients, do:
 - Vagal manoeuvres:
 - Icepack/iced water for infants: apply to face for a max of 30 seconds.
 - Valsalva maneuvers if the child is old enough (blow into a pinched straw).
- Refer to tertiary hospital

TERTIARY LEVEL

- **Haemodynamically stable patients**
 - Vagal manoeuvres:
 - Icepack/iced water for infants: apply to face for a max of 30 seconds.
 - Valsalva manoeuvres if child is old enough (blow into a

- pinched straw).
- For the performance of the following call the paediatric consultant or the cardiologist
 - IV Adenosine: 0.1mg/kg (max 6mg) rapid push into a big vein and follow with a flush. Increase by 0.1mg/kg every 2 mins until tachycardia terminated or up to a maximum of 0.5mg/kg/dose (maximum: 18 mg total)
 - IV Amiodarone: 25mcg/kg/min for 4 hours then 5 -15mcg/kg/min until conversion.
 - PATIENT NEEDS TO BE ON A CONTINUOUS CARDIAC MONITORING IN HDU / ICU
 - **Hemodynamically unstable (IN SHOCK)**
 - Synchronized DC conversion at 0.5 to 1 joule/kg.
 - CARDIOLOGIST REVIEW

Follow up

- Once diagnosis is confirmed, the child must be followed up in a PEN-Plus clinic regularly if SVT persistent
- Ensure child has adequate stock of medications for home use at each visit.
- Ongoing counseling and education

CHEST PAIN

A complaint of chest pain is frequently encountered in children. Although chest pain does not indicate serious disease of the heart or other systems in most pediatric patients, the clinician should be aware of the differential diagnosis for chest pain.

Causes/Risk factors

Non-Cardiac causes:

- Psychogenic
 - Life stressor (death in family, family discord, divorce, failure in school, nonacceptance from peers, sexual molestation)
- Musculoskeletal e.g.
 - Costochondritis,
 - Trauma to chest wall
 - Muscle strains
- Abnormalities of the rib cage or thoracic spine
- Respiratory e.g.
 - Reactive airway disease
 - Pneumonia
 - Pleural irritation
 - Pneumothorax or pneumomediastinum
 - Foreign bodies in the airway
- Gastrointestinal e.g.
 - Gastroesophageal reflux
 - Peptic ulcer disease
 - Esophagitis
 - Gastritis
 - Foreign bodies (e.g., coins)
 - Cholecystitis

Cardiac Causes:

- Structural abnormalities of the heart
 - severe aortic or pulmonary stenosis, hypertrophic obstructive cardiomyopathy, Eisenmenger's syndrome, MVP
- Coronary artery abnormalities
 - Previous Kawasaki disease, congenital anomaly, coronary heart disease, hypertension, sickle cell disease
- Inflammatory Conditions
 - Pericarditis, Myocarditis, Kawasaki disease

Health promotion

- Health education
- Early health seeking behavior for persistent chest pain

Investigations

The investigations should be done according to the suspected underlying cause. If cardiac cause is suspected do the following:

- Electrocardiogram
- Chest Xray
- Cardiac Echo (*There is no need to do an echo if a cardiac cause is not suspected by history and physical exam.*)

Differential diagnosis

- See causes

Management

Primary Level

History and physical examination

The initial history should be directed at determining the probable cause and should include the following;

- nature of the pain, in terms of the duration, intensity, frequency, location, and points of radiation.
- Physical examination should include a complete cardiovascular examination to rule out probable cardiac causes.

Refer to secondary facility:

- When history reveals that chest pain is triggered or worsened by physical activities
- When there are abnormal findings in the cardiac examination

Secondary / Tertiary Level

- History and physical examination as above.
- Refer to a cardiologist:
 - When history reveals that chest pain is triggered or worsened by physical activities
 - When there are abnormal findings in the cardiac examination or when abnormalities occur in the chest radiographs or ECG, cardiology referral is clearly indicated.
 - When there is a positive family history for cardiomyopathy, long QT syndrome, sudden unexpected death, or other hereditary diseases commonly associated with cardiac abnormalities.

Follow - up

- If cardiac cause, patient should be followed up in a PEN-Plus clinic.
- Medication use and side effects

SYNCOPE

Definition

Syncope is a transient loss of consciousness and muscle tone that results from inadequate cerebral perfusion.

Presyncope is the feeling that one is about to pass out but remains conscious with a transient loss of postural tone. It is usually less serious than syncope and is often a manifestation of a benign condition. Dizziness is the most common prodromal symptom of syncope.

Causes/Risk factors

- Autonomic
 - Vasovagal syncope
 - Orthostatic (postural) hypotension
 - Situational syncope
 - Postural orthostatic tachycardia syndrome (POTS)
- Cardiac arrhythmias
 - Tachycardia: SVT, atrial flutter or fibrillation, ventricular tachycardia
 - Bradycardia: sinus bradycardia, asystole, complete heart block
- Cardiac obstructive lesions
 - Outflow obstruction: Severe Aortic/Pulmonary Stenosis, Hypertrophic Cardiomyopathy, pulmonary hypertension
 - Inflow obstruction: Severe Mitral Stenosis, cardiac tamponade, constrictive pericarditis
- Metabolic
 - Dehydration
 - Hypoglycaemia
 - Electrolyte disorders
- Pregnancy

Investigations

- Investigate for underlying conditions.
- Measure Blood pressure in the supine and upright position to check for postural hypotension and heart rate changes
- ECG
- Echocardiogram

Differential diagnosis

- Neuropsychiatric disorders
 - Anxiety disorders: panic disorders, phobia
 - Hyperventilation
 - Seizure disorders
 - Brain tumors
 - Conversion disorders (malingering, hysteria etc)

Management

Primary / Secondary Level

- Refer to tertiary level facility for cardiology / neurology review

Tertiary Level

- Investigate for underlying cause and manage as appropriate.
- Consult cardiologist.

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CHAPTER 3. CHILD PROTECTION

Definitions

Child protection refers to prevention and response to violence, exploitation and abuse of children in all contexts including child marriage, violence in all forms, female genital mutilation (FGM), child labor, trafficking, and lack of official recording of births.²

A **child** is defined as a person below the age of 18 years.⁴

Child Sexual abuse is the involvement of a child in sexual activity that:

- The child does not fully comprehend,
- The child is unable to give informed consent to,
- The child is not developmentally prepared and cannot give consent,
- Violates the laws or social taboos of society.

Child sexual abuse is evidenced by sexual activity between a child and an adult or another child who by age or development is in a relationship of responsibility, trust or power, the activity being intended to gratify or satisfy the needs of the other person. This may include but is not limited to:

- The inducement or coercion of a child to engage in any unlawful sexual activity;
- The exploitative use of a child in prostitution or other unlawful sexual practices;
- The exploitative use of children in pornographic performance and materials.⁵

Sex with a child (formerly known by the outdated term of ‘defilement’) and indecent assault are defined according to the Laws of Malawi in the Penal Code (Cap 7:01,138) as any person having sexual intercourse, or attempting to have sexual intercourse or indecently assaulting a girl / boy under the age of eighteen years.⁶

Physical abuse means any act or omission which causes or is intended to cause physical injury or reasonable apprehension of physical injury.⁷ Physical abuse includes physical acts ranging from those which do not leave a physical mark on the child to physical acts which cause permanent disability, disfigurement, or death.⁸

Emotional / Psychological Abuse consists of intentional caregiver behavior that conveys to a child that he/she is worthless, flawed, unloved, unwanted, endangered, or valued only in meeting another’s needs.⁸ Psychological abuse can be continual (e.g., chronic and

pervasive) or episodic (e.g. triggered by specific context or situation: caregiver substance use/abuse).⁸

Child Neglect is the failure to provide for a child's basic physical, emotional, or educational needs or to protect a child from harm or potential harm. Child neglect involves acts of omission for example:

- Failure to provide (physical neglect, emotional neglect, medical neglect and educational neglect).
- Failure to supervise.
- Exposure to violent environments.⁸

Parent includes an adoptive parent, foster parent or any person acting in whatever way as parent.³

Guardian means a person who has lawful or legitimate custody, care or control of a child in place of a parent.

Place of safety means an appropriate place where a child in need of care and protection can be kept temporarily and includes a safety home or a foster home.³

RISK FACTORS

Individual Risk Factors

Caregivers:

- misusing drugs or alcohol
- with mental illness, including depression
- who don't understand children's needs or development
- who were abused or neglected as children, or witnessed domestic violence
- experiencing high levels of parenting stress or economic stress
- who use spanking and other forms of corporal punishment for discipline
- who are not a biological parent
- Who have ungoverned access to children in their care (for instance teachers, or religious leaders)

Children:

- Disabled children
- Street children
- Female children (sexual abuse, emotional abuse)
- Male children (physical abuse, trafficking for work)

Family Risk Factors

- Families that have household members in jail or prison
- Families that are isolated from and not connected to other people (extended family, friends, neighbors)
- Families experiencing other types of violence, including relationship violence
- Families with high conflict and negative communication styles

Community Risk Factors

- Communities with embedded hierarchical misogynistic (oppressive) views of the relationship between men and women
- Communities with high rates of poverty and limited educational and economic opportunities
- Conflict, or any event resulting in an increase in refugees

PREVENTION, ADVOCACY AND HEALTH PROMOTION

- A child is determined to be in need of care and protection if there has been or there is substantial risk that the child will be physically, psychologically, emotionally or sexually abused, or neglected by a member of the family or any other person.³
- Healthcare workers play a role in the protection of children, and should ensure that they do not send a child back to a dangerous / harmful environment. Involvement of Social Workers, Child Protection Officers and Law Enforcement officers is key before discharging a survivor out of medical care.
- Malawi has several guiding documents that specifically relate to child protection, namely:
 - Constitution of Malawi (2017)
 - Childcare, Protection and Justice Act number 22 of (2010)
 - Malawi prevention of Domestic Violence Act Chapter 7:05 (2006)
 - National Guidelines for Provision of Services for Physical and Sexual Violence (2021)
 - Malawi Penal Code Ammendment Act (2023)
- Rights of the child are outlined in section Section 23 of the Constitution of Malawi
- If a health care worker encounters a parent / guardian who is denying care for the child, they should consult social welfare and other required stakeholders. Guidance for procedures to follow are outlined in the Malawi - Child Care, Protection and Justice Act; Act No. 22 of 2010.
- A medical practitioner is required by law to immediately inform the social welfare officer / police officer if he / she believes on reasonable grounds that a child being examined or treated is physically, psychologically or emotionally injured as a result of being ill-treated, neglected, abandoned or exposed, or is sexually abused.

| PREVENTING CHILD ABUSE AND NEGLECT | |
|---|--|
| Strategy | Approach |
| Strengthen economic support to families | <ul style="list-style-type: none"> • Strengthening household financial security • Family-friendly work policies |
| Change social norms to support parents and positive parenting | <ul style="list-style-type: none"> • Public engagement and education campaigns • Legislative approaches to reduce corporal punishment |
| Female empowerment | <ul style="list-style-type: none"> • Legislative approaches such as increasing the age of consent to marry • Female empowerment programmes in schools including self-defence lessons |
| Provide quality care and education early in life | <ul style="list-style-type: none"> • Preschool enrichment with family engagement • Improved quality of child care through licensing and accreditation |
| Enhance parenting skills to promote healthy child development | <ul style="list-style-type: none"> • Early childhood home visitation • Parenting skill and family relationship approaches |
| Intervene to reduce harms and prevent future risk | <ul style="list-style-type: none"> • Enhanced primary care • Behavioral parent training programs • Treatment to lessen harms of abuse and neglect exposure (such as via a One-Stop Centre) • Treatment to prevent problem behavior and later involvement in violence |

- One Stop Centers (OSC) are deliberately designed spaces offering multi-sectoral services to survivors of abuse.⁶ These centers are located at several health facilities across the country and comprise of a standard multidisciplinary team which includes:
 - medical practitioners,
 - social welfare,
 - mental health,
 - police and prosecutors,
 - court,
 - Ministry of Gender, Community Development and Social Welfare
 - Civil Society Organizations.
- In the absence of one stop centers, survivors should access the appropriate care and support through the various health facilities namely central hospitals, district hospitals, community hospitals, health centers and clinics.

Signs and symptoms

- Findings that raise the suspicion of child abuse include:
 - Injuries with patterns that suggest deliberate injury.
 - Slap, belt, loop of cord, and other shaped bruises.
 - Cigarette, iron, spatula, and other shaped burns.
 - Immersion burns.
 - Multiple fractures in various stages of healing or different types of injuries coexisting (e.g. bruises, burns, and fractures).
 - Metaphyseal fractures of long bones.
 - Bruises of the trunk, ear, neck, angle of the jaw, fleshy cheek, and eyelid.
 - Bruises in children who cannot cruise.
 - Frenulum tears and subconjunctival hemorrhages, especially in children <2 years old and those who are not yet walking independently.
 - Long bone fractures in children who do not walk.
 - Rib fractures in infants younger than one year of age.
 - Subdural hematoma in infants younger than one year of age.
 - Hollow viscus injury in children younger than four years of age.
 - Injuries that are epidemiologically or biomechanically unlikely to arise from the reported trauma event.
 - Evidence of poor caretaking (a child who is dirty or inadequately clothed) may raise suspicion of abuse; however, these factors correlate more strongly with neglect or poverty than with abuse, and abuse may be present in the absence of these signs.
 - Sudden onset of altered mental status not attributable to

- medical illness or other signs of poisoning.
- A history which is out of keeping with the injury and changes.
 - Injuries to the genitalia – bruising, bleeding, grazes, lacerations to the posterior fourchette or/and hymen

Investigations

- HIV test after counseling
- Urine dipstick if concern for renal injury.
- Pregnancy test if post-menarche
- Imaging
 - Skeletal survey radiographs: Humeri (AP), Forearms (AP), Hands (PA), Femurs (AP), Lower legs (AP), Feet (AP), Thorax (AP, Lateral, R & L oblique), Abdomen with pelvis (AP), Lumbosacral spine (Lateral), Skull (Frontal & lateral) and C-spine (lateral). Indications are:
 - All children <2yrs
 - Children with neurological impairment OR distracting injury OR suspicious index fracture.
 - Concern for abuse in children with impaired mobility or impaired communication skills.
 - Neuroimaging (cranial USS / head CT) indications are:
 - All infants < 6 months old regardless of physical findings.
 - Infants 6m - <12m old with external head injuries on examination OR skull fracture OR fracture highly suggestive of abuse (e.g. rib fractures or metaphyseal fractures).
 - Child of any age with signs suggesting intracranial injury.
- Serum and urine toxicology screen in children with suspected drug exposure, poisoning, or symptoms suggesting drug toxicity.
- Fundoscopy + ophthalmology consult in children with abusive head trauma, periorbital bruising, or eye injury.
- OPTIONAL - Swab fluid/ pus for microscopy for STI or sperm if available (rarely useful)
- Other tests if indicated:
 - PT, INR, aPTT, VWF, Factors VIII/IX/XIII, D-dimer, Fibrinogen
- Screening for bleeding disorder in children with bruising / bleeding
 - AST, ALT, Lipase
 - Screening for abdominal injury
 - Serum electrolytes and osmolality
 - In the setting of abusive head trauma, dehydration, water intoxication or drowning
 - Calcium, phosphorous, alkaline phosphatase, PTH level, 25-OH vitamin D level
 - Screening for metabolic bone disease in children with multiple fractures
 - Osteogenesis imperfecta genotype / phenotype testing

DIFFERENTIAL DIAGNOSIS

| TYPE OF ABUSE | SIGN OR SYMPTOM | DIFFERENTIAL DIAGNOSIS |
|------------------------|---|---|
| Physical abuse | Bruising | Coagulopathies e.g Von Willebrand disease |
| | Fractures | osteogenesis imperfecta, metabolic bone diseases |
| | Scalp swelling | Subdural hematoma, Subgaleal hemorrhage |
| Sexual abuse | Vaginal / urethral discharge Genital Ulcers / Sexually transmitted infections | Allergies to fabric, pinworms, foreign bodies, Urinary tract infections |
| | Bruising / bleeding / discharge / pain from genital areas. Difficulty in sitting / walking | Trauma, urethral prolapse |
| Emotional Abuse | Lack of energy, sadness, sleeping and eating changes | Mood disorders, Anxiety disorders, substance use/abuse |
| Child Neglect | Poor appearance and hygiene; change in behaviour; developmental problems; frequent absent from school | Poverty, Rule out medical conditions e.g., malnutrition |

MANAGEMENT APPROACH IN SUSPECTED CHILD ABUSE

General Principles

- A survivor of sexual or physical abuse must be attended to as soon as possible upon arrival in the health facility.
 - *The survivor is NOT REQUIRED BY LAW to produce a letter from the police before they can be attended to. Insisting on a police letter will cause a great burden on the survivor and cause unnecessary delays, and must be avoided at ALL TIMES!*
- *It is not the health care worker's responsibility to determine whether or not a person has been abused, this is a legal determination.* The

health care worker's responsibility is to provide appropriate care, to record the history, examination and other relevant information which can be provided to the police and used for their investigations.

- Service providers are also encouraged to provide suitable temporary shelter to survivors of abuse, as well as ensuring that the survivor has access to information about the range of service providers and the kind of support that may be provided by any service provider.
- All survivors who are suspected victims of abuse should receive a medical evaluation by a health provider who has received training in the diagnosis and treatment of sexual and physical abuse.
- It is rarely possible to definitively conclude that physical abuse has occurred in the first few hours of an evaluation. When physical child abuse is suspected, clinicians should emphasize the need for further evaluation and avoid making accusations.

History taking

- ***In most cases, the history will be more important than the examination!!***
- History and examination should take place in a place of privacy
 - Aim to limit the number of health care workers attending to the survivor: 'one-on-one' care works best in sexual assault cases during interviewing.
- Interview the parent alone, then the child alone (if possible) as the adult's presence might influence the child.
 - In the setting of acute trauma, it may be difficult to separate the child from the caregiver, and the questioning of the child can be deferred till later.
 - Age appropriate questioning of the child needs to be instituted to avoid misleading information.
 - Ask the survivor if she/he wants to have a specific person present for support.
- Introduce yourself and build rapport (e.g. "tell me about school")
- Maintain eye contact. Be empathetic and non-judgmental as your survivor recounts her/his experiences.
- Interview rules (optional) –

Establish the need to tell the truth:

"If I ask you something, and you don't know the answer – that's o.k. just say 'I don't know.'"

Introducing the topic of concern e.g.

- “Do you know why you are here today?”

“I am and I talk to children about things that happen to them. Do you want to talk to me about things that happened to you?”

Older children: “Part of my job is to take care of children who had really bad things happen to them... so don’t worry that you will say something that will surprise me – I won’t be surprised. And don’t worry that you will say something that will make me think bad of you”

Free narrative

“Tell me everything that happened, starting from the beginning” DO NOT INTERRUPT!

Open questioning

Who/ when/ where/ what.

“How did you know it was over?”

Avoid ‘multiple choice’ questions, or one-word answer questions.

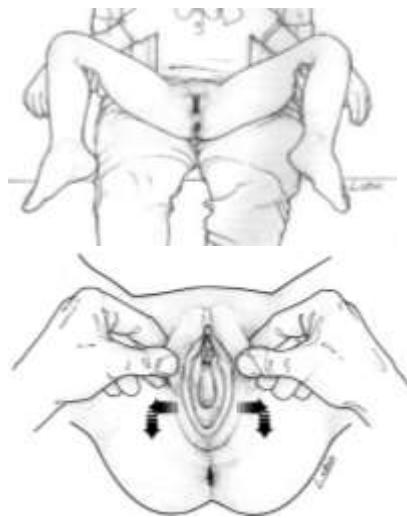
- Probe for behavioral or emotional problems and physical symptoms which may occur after abuse and can act as corroborating evidence in court (fill this in the appropriate section on the medical report):
 - Change in behavior
 - Suicidal thoughts
 - Headaches
 - Abdominal pain
 - Dysuria
 - Vaginal discharge
 - Constipation
 - Anal bleeding
 - Secondary enuresis
- When physical injury is identified, the history should ascertain how the injury came about. Detailed history of events should include:
 - Preceding activity, elevation and motion.
 - Events leading up to the trauma event.
 - Mechanics of the injurious circumstances.
 - Subsequent actions and symptoms of the patient.
- While an accurate summary or paraphrasing of given answers may be adequate, *when particularly important statements are made, quoting the exact words of the reporter will avoid concerns of inaccurate interpretation by the clinician and serve any subsequent*

legal proceeding better.

- Ask the survivor if she/he has any questions.
- Conclusion of interview – assure them of safety
- Red flags in the history include:
 - Caregiver offering no history or specifically denies history of trauma despite severe injury.
 - The history is inconsistent with the degree or type of injury.
 - Unexplained or excessive delay in seeking care.
 - Injury attributed to in-home resuscitation efforts.
 - Caregiver histories that change with re-telling or conflict with versions from other observers.
 - Severe injury explained as self-inflicted or blamed on other young children or pets.
 - The history is inconsistent with the developmental stage of the child e.g. a 4 month old who reaches for hot water and gets burnt.
 - History of prior bruising or orofacial injury in an infant who is not cruising.
- *The behavior of the parents/caregivers and the interaction between family/household members should be observed carefully during the evaluation of the child. Certain behaviors and/or types of interaction may increase the level of suspicion for child abuse. Such behaviors include:*
 - Arguing, roughness, or violence.
 - Aloofness and lack of emotional interaction between parents/caregivers or between parents/caregivers and children.
 - Negative characterization of the child by the parent.
 - Inappropriate response to the severity of the injury (e.g. lack of appropriate concern).
 - Inappropriate delay in seeking medical care
 - A partial confession by the parent (e.g. "I hit them, but not that hard") or a frank admission by a parent that injury was inflicted. Such confessions occur occasionally and are an indication that the parent realizes that abuse is a problem and is seeking help.

Physical Examination^{5,6} (Secondary / Tertiary Health Facilities only)

- Should be done by somebody **who has been trained** in the evaluation of such cases.
- *While a careful physical examination can raise the level of concern for abuse, many abusive injuries remain hidden. Occult abdominal injuries, fractures, and brain injury have been well described in children with normal examinations.*
- The examination room should have a table and chairs, a lockable door, examination couch with a light source and hand washing facilities.
- Ideally, blood drawing, HIV testing, history taking, physical examination and treatment provision should all be conducted in the same room.
- During examination it is recommended to have another health care provider or family member of the same sex as the client present.
- If the child is seen shortly after the assault and still wearing the same clothes as at that time, then all clothes should be carefully examined for stains of semen or blood and for rips and tears suggestive of aggression.
- Remove the child's clothing to fully expose all areas (can be done sequentially).
 - Examine the whole body for signs of injury – not just the perineum.
 - Look for evidence of finger imprints in arms and/or legs where the child may have been held down or stopped from screaming.
 - Look in the mouth for evidence of injury from forced oral-penile penetration and the breasts which may have been bitten or squeezed.
 - Characteristic skin lesions, swelling/deformity, bone tenderness or reluctance to use an extremity should be looked for.
- Technique for perineal exam:
 - The hymen can be viewed by gently separating the labia majora. For young children, the examination can be performed while they lay on their family member's lap in a frog leg position (see below).



*Frog – Leg position
Labial separation*

- The hymen shape, size and edges should be recorded.
- Anal findings may vary from no physical abnormality, to a wheel of oedema around the recently injured anus with anal incontinence, to a dilated, somewhat incontinent anus.
- Findings suggesting or confirming sexual abuse in females include:
 - acute abrasions, lacerations or bruising of the labia, perihymenal tissues, penis, scrotum, or perineum.
 - hymenal notch / cleft extending through more than 50% of the width of the hymenal rim, usually in 4 o'clock to 8 o'clock
 - scarring or fresh laceration of the posterior fourchette
 - presence of sperm confirmed on microscopy
 - presence of sexually transmitted disease
- Normal and non-specific vaginal findings include:
 - Hymenal bumps, ridges and tags
 - v-shaped notches located superior and lateral to the orifice, **not** extending to the base of the hymen
 - vulvovaginitis
 - labial agglutination
 - vaginal discharge

The presence of multiple types of injuries suggests abuse because conditions that mimic abuse typically only cause one type of finding.

Primary Level

- ABCDE approach if patient is unstable.
- Brief history.
- Refer all patients. **DO NOT EXAMINE!**

Secondary / Tertiary Level

- ABCDE approach if patient is unstable.
 - History and examination as above.
 - Identify and treat all injuries. Hospitalize for serious injuries or if the child does not have a safe space to go back to.
 - Involve available seniors in the evaluation and management.
 - For suspected sexual abuse give:
 1. Post-exposure prophylaxis
 - The child is eligible for PEP if the child has presented within 72 hours of the assault **and** they are HIV negative **and** the family agrees to comply with the treatment.
 - ***The survivor should be given PEP regardless of the sero-status of the assailant, as the assailant may be in the window period during the time of a negative test outcome.***
 - Test for HIV and give PEP at THE SAME TIME THE CHILD IS SEEN – DO NOT DELAY.
 - Give **ABC/3TC + DTG** according to body weight
OR
TDF/3TC/DTG (for those >30kg)
 - Treat for 30 days. A repeat HIV test is required at 1, 3 and 6 months.
 2. Antibiotics to prevent or treat STI
 - Metronidazole 5mg/kg PO, TDS for 7 days (max 2g/day)
- AND**

- Erythromycin 12.5 mg/kg PO, QID for 7 days (max 500mg / dose) or Azithromycin 20 mg/kg PO, daily for 3 days **AND**
 - Gentamicin 7.5 mg/kg STAT IM (max 240mg) **AND**
 - Intramuscular Benzathine penicillin STAT
($< 25 \text{ kg} = 0.6 \text{ MU}$; $> 25\text{kg} = 1.2 \text{ MU}$)
- 3. Tetanus Toxoid Vaccine 0.5ml IM STAT if indicated
- 4. Consider emergency contraception if post-menarchal and $<72\text{h}$
 - Postinor (Levonorgestrel 750mcg) 2 tablets STAT
 - OR**
 - Lofemenal / Microgynon 4 tablets STAT then 4 tablets 12 hrs later
- Inform and involve social workers and police early. Refer to other medical specialties as indicated e.g paediatric surgery, urology etc.

GUIDANCE FOR COMPLETING THE MEDICAL REPORT FOR THE POLICE (PHYSICAL / SEXUAL)

- Use the 'Medical examination for suspected physical/sexual abuse' forms (see below) and keep copies of the records.
 - These documents may be used as evidence so WRITE LEGIBLY.
- Briefly summarise the history.
 - Use the child's words if possible.
 - Recording of history should be factual.
 - Statements from the child / parent / caregivers should be recorded as direct quotations.
- Summarise and document the physical findings
 - Injuries should be described in as much detail as possible.
 - Sketches of injuries are helpful in documenting extensive injuries.
 - Avoid terms such as 'hymen intact' or 'hymen perforated' – better 'no signs of injury to hymen' or 'evidence of injury to the

hymen'.

- WRITE A CONCLUSION/ OPINION:
 - 'In my opinion.....'
 - State if you think the child's history is clear, logical and credible
 - **If the physical findings are normal, remember this does not exclude the possibility of physical abuse or sexual penetration** e.g. '*the examination is normal, but this does not rule-out the possibility of penetration, and these findings are consistent with the history given to me by the child*'
 - If there are physical findings present, state if they are consistent with the history given to you.
 - If there is clear physical evidence of penetration in sexual abuse, state this clearly '*these findings are highly suggestive of penetration/ confirm that penetration has taken place*'.
 - Be cautious of interpreting the ages of injuries.
 - Do not be afraid of stating your uncertainty '*the child was unable to provide any details in her history that would confirm that physical contact occurred*'.
 - **YOU ARE NOT THE 'JUDGE AND JURY' BUT THE PROSECUTOR AND COURT WILL BENEFIT FROM A CLEAR STATEMENT OF YOUR OPINION.**
- Any person working with people who have been sexually/physically assaulted should be aware of the differences between myth and fact, and personal beliefs and attitudes towards abuse need to be examined and challenged.
- ***It is essential that healthcare workers understand the need for impartiality. It is not the role of the health care worker to make judgments about the veracity of sexual / physical abuse allegations, nor about the innocence or guilt of the alleged perpetrator, this is for the investigators and the courts to decide!***

MEDICAL REPORT FORM

Medical Report for Suspected Physical /Sexual Abuse in Malawi

Name: _____ DOB: _____ Age: _____

Address: _____

Phone: _____ Source of referral: _____

Local Police station: _____ Referring officer (if applicable): _____

I _____ being the client, or the mother / father / guardian of the above named child hereby give consent for myself/ him / her to be examined and for a written report of the findings to be given to the police and / or social welfare. Signature: _____

Witness Name: _____ Witness signature: _____

Date and time of incident:

1st occasion? Yes / No If 'No' approximate dates of previous incident (s):

History / details of incident:

(Use patient's words if possible. Distinguish child's statement from guardian's statement):
(E.g. When, where, what happened, witnesses, condom, ejaculation, name of assailant, threats made, gifts)

Clinician's Impression / Opinion after History and Examination:

Name / title of clinician: _____ Signature: _____

Health Facility: _____ Date: _____

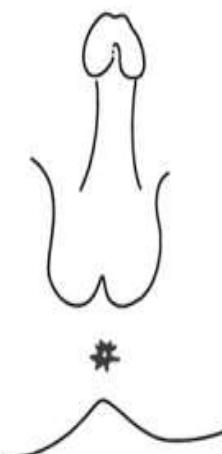
Date of Examination:

Time:

General Examination:

(signs of other injury, clothing – document multiple injuries on physical assault form)

WEIGHT: KG

Genital (*Speculum in adults only*):

Past Medical History of Note:

Regular Periods: Y / N LMP:

Pregnant? Y / N

Previous consensual intercourse? Y / N

- If 'Y' in last 2 weeks? Y / N

Previous genital trauma? Y / N

Examining Clinician:

Name _____ Position _____ Sign _____

| Any symptoms? | Prior to incident | Following incident |
|-------------------|-------------------|--------------------|
| Behaviour change | | |
| Problems sleeping | | |
| Headaches | | |
| Suicidal thoughts | | |
| Abdo pains | | |
| Dysuria | | |
| Vaginal discharge | | |
| Vaginal bleeding | | |
| Constipation | | |
| Blood PR | | |

FOLLOW-UP PROCEDURES

Procedures and services for child protection in Malawi are evolving quickly and the up-to-date guidelines should always be adhered to. Currently:

- The guardians should be given the stamped medical report form to take back to the referring police station (they should get all the pages – history, examination and report). A copy of the medical report should be stored securely at the health facility.
- After initial evaluation, all children should be seen / referred at the OSC as soon as possible – preferably the same or next working day.
 - Each district or catchment area should have an approved referral system by the multi-disciplinary team made in collaboration with the community with clear communication plans.
 - Information to have ready when you make the referral:
 - The survivor's name, sex, age, date of birth, address.
 - Phone numbers (preferably 2, if possible) of the survivor and/or the accompanying family member
 - Name of the family member who is accompanying them who is helping provide the details
 - Type of abuse: sexual or physical or both.
 - Location where the abuse occurred.
 - Date and approximate time if/when the sexual assault occurred.
- Make the referral to the health facility OSC as soon you identify the need – even if the survivor does not need to go immediately. This way, the OSC team can be aware of the survivor and contact them sooner to ensure a successful referral and prompt medical, legal and social services.
- For sexual abuse, make sure the alleged perpetrator is not bringing the survivor to the appointment. Survivors will not feel comfortable disclosing abuse when the abuser is the one who brought them to the OSC and is just sitting in the other room.
- Keep a copy of all the report forms in a safe space for future reference.

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CHAPTER 4. DERMATOLOGY

ATOPIC DERMATITIS / ECZEMA

Definition

Atopic dermatitis, or eczema, is a chronic inflammatory skin disease that causes dry skin, severe itching, and heightened sensitivity to various environmental stimuli.

Risk Factors / Causes

- Genetic risk factors – A family history of atopy (eczema, asthma, or allergic rhinitis) is the strongest risk factor for atopic dermatitis.
- Environmental Exposures – climate, urban dwellers, early exposure to non-pathogen microorganisms

Promotion / Prevention

- Health education
- Avoid anything that causes the skin to itch, because scratching triggers flare-ups
- Moisturize the skin at least twice a day
- Use a gentle non soap cleanser
- Avoid irritants such as soaps, detergents, including shampoo, bubble bath, environmental factors or allergens such as cold and dry weather and more specific things like house dust mites, pet fur, pollen and molds

Signs and Symptoms

- Infants and Young children
 - Marked by red, scaly, and crusty lesions on the scalp, cheeks, and body's extensor surfaces
 - The diaper area is usually spared
 - Severe cases may show vesicles, serous exudates, and crusting.
- Older children and Adolescents
 - Appears as lichenified plaques in flexural areas, such as the antecubital and popliteal fossae, wrists, ankles, and neck
 - The neck may show reticulate pigmentation, known as "atopic dirty neck".

Investigations

- No specific investigations are required
- It is diagnosed based on clinical evaluation, including history, morphology and distribution of skin lesions, and associated clinical signs.

Differential diagnosis

- Seborrheic dermatitis
- Ichthyosis
- Psoriasis
- Drug eruptions

Management

Effective management includes:

- Educating the patient
- Maintaining skin hydration
- Restoring skin barrier function
- Using pharmacological treatments to address skin inflammation
- Identifying and eliminating exacerbating factor

Primary / secondary level

Mild-To-Moderate Atopic Dermatitis

- Patient / guardian education
 - Avoid known triggers.
 - Reduce bathing frequency and avoid using irritant soaps / products. Non-fragranced aqueous cream can be used as a soap substitute if necessary.
 - Rinse clothes thoroughly after washing to remove all soap residue.
- Nonpharmacological therapy such as emollients administered as monotherapy.
 - Emollients need to be used liberally and multiple times a day to keep the skin moisturized always.
- Add topical pharmacotherapy if nonpharmacological therapy is insufficient such as topical steroids (preferred).
 - Topical steroids should not be used for prolonged periods of time, but should only treat acute flare-ups
 - Use low potency topical corticosteroids (TCS) on affected areas once daily for 2-4 weeks.
- Assess for concomitant skin infection (*staph aureus*) and treat as necessary.
- Refer severe cases to tertiary level facility

Tertiary level

Moderate / Severe Atopic Dermatitis

(with significant functional impairment)

- Patient education as above
- Consider alternative non-pharmacological therapy (e.g., wet wrap therapy with emollients)
- Topical steroids
 - Use medium – to – high potency TCS on affected areas once or twice daily for 2 – 4 weeks

N.B. Only low potency steroids should be used on the face, neck and skin folds
- Assess for and treat concomitant infections.
 - If refractory disease, consult a dermatologist and consider:
 - Increasing potency of topical agents
 - Topical calcineurin inhibitors
 - Adding systemic therapy to topical agents if the disease is refractory.

- Use of phototherapy (UV light)
 - Non-corticosteroid systemic immunomodulatory medications

FOLLOW-UP

- Dermatology clinic every 1-3 months.
- Ongoing education
- Review of medication and side effects

MILIARIA

Definition

Eccrine miliaria, commonly referred to as "sweat rash," "prickly heat," or "heat rash," is a temporary skin condition that occurs when the eccrine sweat duct is obstructed. There are three types of eccrine miliaria, including:

- **Miliaria crystalline** – also known as sudamina, is very common in neonates. Incidence peaks at approximately one week of age
- **Miliaria rubra** – the most common type. It has been reported in 4 percent of neonates and in up to 30 percent of people of all ages
- **Miliaria profunda** – also known as tropical anhidrosis

Risk factors / causes

Anything that causes sweating can lead to miliaria including:

- A hot and humid environment
- Intense exercise or physical activity
- Febrile Illness
- Occlusion of the skin with non-porous dressings or synthetic clothing against the skin

Promotion / Prevention

- Avoid excessive wrappings / woollen hats in infants
- Avoid tight clothing

Signs and Symptoms

- **Miliaria crystalline** – Presents as 1-2 mm superficial clear blisters that easily break leaving a bran like scale. There is no inflammation. The blisters are usually widely spread on the head, neck and upper trunk.
- **Miliaria rubra** – Results in red 2-4 mm non-follicular papules and papulo-vesicles. They are very itchy. Background erythema is often present. It involves the trunk and the skin folds of the neck, axilla and the groin. Miliaria Pustulosa is a variant of miliaria rubra with pustules.
- **Miliaria profunda** – Presents as asymptomatic deep papules. The flesh coloured 1-3mm diameter papules develop on the trunk and extremities.

Investigations

- Clinical diagnosis.
- Tzanck smear can be taken from the vesicles to distinguish miliaria from herpes simplex or toxic erythema of the newborn.

Differential Diagnosis

- Herpes simplex
- Bacterial folliculitis
- Acute generalized exanthematous pustulosis (AGEP)

Management

Primary / Secondary / Tertiary Level

- Minimize heat and humidity exposure to reduce sweating and irritation of the skin
- Calamine lotion
- Emollients
- Mild topical steroids
- Reassurance - usually resolves within 2 days after changing to a cooler environment.
- Refer to a dermatologist if the condition persists.

FOLLOW-UP

- The condition is generally self-limiting thus will not require routine follow-up unless other concerns are flagged by the diagnosing physician.

URTICARIA

Definition

Refers to a group of conditions in which wheals (hives) or angioedema (swelling) develop in the skin. It is very common in children.

Occurs as a result of mast cell and basophil activation causing release of histamine (which causes itching) and vasodilatory mediators (which cause localized swelling).

- A **wheal** is a superficial swelling, usually pale or skin coloured. It is often surrounded by an area of erythema and can last from a few minutes to 24 hours.
- **Angioedema** is a deeper swelling from within the skin or mucous membranes. It usually looks red and puffy. The most common areas for angioedema in children are the lips, tongue, and eyelids.

Risk factors / causes

In many cases, no specific cause can be identified. Other potential causes are:

- Infections (viral and bacterial infections)
- Food allergy (such as eggs, milk, soy, peanut and wheat)
- Drug induced urticaria such as antibiotics, NSAIDs
- Bee or wasp sting

Prevention / promotion

- Choosing mild or fragrance-free soaps, skin creams, and detergents
- Antihistamines
- Keeping a record of any possible triggers, such as a food diary.

Signs and Symptoms

- Wheals
 - Appear on any part of the body.
 - Usually red, raised plaques with a central pale area and can be itchy.
 - Can be round, oval, or serpentine and vary in size from small to large.
- Angioedema
 - It most commonly affects the face. The child may have a swollen tongue, eyelids, or lips.
 - Usually localized to a single area such as the hands, feet, and genitalia.
 - Is often tender or painful.
- Inducible urticaria
 - Due to a physical stimulus: the wheals will be localized to the exposed site.
 - Often comes on within minutes after exposure and resolves in less than an hour.
- Anaphylaxis (severe allergic response)
 - Shortness of breath, wheezing, collapse, hypotension.

Investigations

- Urticaria is usually diagnosed history and physical examination.
- If food or drug allergy is suspected skin prick or immunoglobulin E (IgE) tests can be helpful.

Differential Diagnosis

- Insect bites – Presents on exposed sites, as asymmetrical clusters of itchy papules or wheals, often with a central fluid filled blister
- Contact dermatitis – Presents on areas in contact with a causative irritant or allergen with irregular red, blistered, scaly sometimes swollen plaques. Dermatitis persists for days or weeks, much longer than urticarial wheals
- Erythema multiforme – Erythematous plaques usually located on acral sites. Target lesions (a pattern of concentric rings) are characteristic, sometimes with central blistering
- Urticular vasculitis (uncommon) – It resembles urticaria with the exception that the wheals last longer than 24 hours and are followed by bluise-like discolouration

Management

Primary Level

- Mild Urticaria
 - Initial treatment of new-onset urticaria should prioritize short-term relief of symptoms.
 - About two-thirds of cases self-resolve.
 - The itch may be reduced by cooling with a fan, ice pack or moisturizing lotion such as calamine lotion.
 - Antihistamine pharmacotherapy (cetirizine / promethazine / piriton). These are not curative, but often controls the itch and the spread of wheals until the urticaria settles on its own
 - In cases that are unresponsive to antihistamines, a short course oral prednisolone 0.5 - 1mg/kg / day x 3 days
- Severe/Life-threatening anaphylaxis (urticaria with angioedema)
 - Remove inciting allergen if still present.
 - Place patient in recumbent position and elevate the lower extremities
 - 100% Oxygen therapy via non-rebreather mask at 15 litres/ min
 - Give adrenaline 0.01mg/kg IM STAT (1:1000 solution)
 - Repeat dose in 5 - 15 minutes if not responding
 - Normal Saline rapid bolus 10mls/kg. Repeat if necessary to maximum 40mls/kg
 - Intramuscular promethazine 0.5mg/kg IM TDS (maximum 25mg/dose) for children more than 2 years old
 - Refer
 - patients with severe anaphylaxis,
 - those requiring more than one dose of adrenaline,

- those who received adrenaline only after a significant delay (>60 minutes)

Secondary / Tertiary Level

- Manage mild / moderate as above
- Severe / life threatening anaphylaxis:
 - As above but can add:
 - Salbutamol nebuliser 2.5 - 5 mg if bronchospasm is not responding to IM epinephrine - can repeat every 15 minutes if required
 - H1 antihistamine
 - IV Diphenhydramine 1 mg/kg over 5 minutes (max 50mg/dose)
OR
 - IV Cetirizine 2.5mg (6mo-5yrs) or 5 - 10 mg (6-11 yrs) over 2 minutes
OR
 - IM Promethazine 0.5 mg /kg (max 25mg / dose) for children > 2 years old
 - Glucocorticoids
 - Methylprednisolone 1 mg/kg (maximum 125mg)
OR
 - IV hydrocortisone 1 - 2 mg/kg
OR
 - Prednisone 1-2 mg/kg PO
- Refractory anaphylaxis
 - Intubation and admission to ICU if airway compromise.
 - Adrenaline infusion 0.1-1 mcg/kg/min, titrated to effect if refractory shock
 - Some patients may require a second vasopressor in addition to epinephrine if not responding.

Follow-up

Patients with a history of life threatening anaphylaxis should be followed up bi-annually for:

- Ongoing education / counselling on avoidance of triggers.
- Anaphylaxis emergency action plan including EPIPEN dosage and administration technique.
- Detect and manage co-morbidities

PSORIASIS

Definition

- Psoriasis is an immune-mediated disease that causes red patches with silvery scales.
- It can occur at any age and in different forms, but chronic plaque psoriasis is common in children.

Risk Factors / Causes

- Genetic Risk Factors – i.e., early-onset psoriasis (onset under the age of 40 years) is the human leukocyte antigen (HLA) type Cw6 (PSOR1)
- Environmental Exposures
 - Skin trauma (Koebner phenomenon), sun exposure, certain medications
- Infections
 - Streptococcal, staphylococcal, varicella zoster
- Autoimmune / inflammatory diseases
- Psychological and physical stress

Promotion / Prevention

- Use emollient/moisturizing creams
- Use gentle cleansers and perfumes
- Avoid dry, cold weather
- Avoid medications that cause flare-ups
- Avoid scrapes, cuts, bumps, and infections
- Stress management

Signs and Symptoms

- **Diaper Area Psoriasis** – Presents with shiny, red patches in diaper area with minimal or absent scaling. Affect infants.
- **Chronic Plaque Psoriasis** – Presents as red, scaly patches with well-defined edges, typically on the elbows, knees, scalp, and lower back. Auspitz sign may be observed when scales are removed. Children may have thinner scales, less distinct edges, and may develop psoriasis in facial, intertriginous, and diaper areas.
- **Guttate Psoriasis** – Presents with numerous, small, "drop-like," erythematous papules and plaques, particularly when involving the trunk and proximal extremities. Plaques are erythematous.
- **Generalized Pustular Psoriasis and Erythrodermic Psoriasis** – Acute generalized pustular psoriasis presents with widespread erythema, pustules, and scale. Erythrodermic psoriasis presents with widespread erythema and scale. Patients with these disorders often appear systemically ill.
- **Inverse psoriasis** – Presents with well-demarcated, shiny, erythematous, thin plaques within skin folds and/or on anogenital skin. Scale is minimal or absent.

Investigations

- The diagnosis of psoriasis in children usually can be made based upon the clinical features.
- A skin biopsy is not necessary for the diagnosis of most patients.

Differential diagnosis

- Atopic dermatitis
- Pityriasis rosea
- Pityriasis lichenoides chronica
- Pityriasis rubra pilaris

Management

Primary / secondary / tertiary levels

- **All Patients** – Assess disease severity: e.g., based on estimated body surface area (BSA) affected and provide supportive care
- **Mild psoriasis (below 3–5% BSA involvement)**
 - Topical pharmacotherapy (e.g., corticosteroids, calcipotriene, retinoids) and/or targeted phototherapy.
 - Systemic agents if treatment response is insufficient.
- **Moderate to severe psoriasis (above 3–5% BSA involvement)**
 - Systemic pharmacotherapy and/or phototherapy.
 - Narrowband UV-B therapy.

ALL SUSPECTED PSORIASIS CASES MUST BE DISCUSSED WITH THE DERMATOLOGY DEPARTMENT!!

Follow up

Biannual follow-up in dermatology clinic for long-term psoriasis

OCULOCUTANEOUS ALBINISM

Definition

A collection of congenital disorders of melanin synthesis resulting in hypopigmentation, 2 main distinctions:

1. **Partial albinism** – A genetic condition characterised by the partial absence of melanin pigment from melanosomes in the body due to defects in the biosynthesis of melanin. Ocular albinism (OA) only affects the visual system (e.g. iris, retina), but not the skin or hair.
2. **Total albinism:** A genetic condition characterised by the total absence of melanin pigment from melanosomes. Oculocutaneous albinism (OCA) consists of an absence of melanin in the skin, hair, and iris.

Risk Factors / Causes

- Inheritance is autosomal recessive trait

Promotion / Prevention

- Albinism is a genetic condition that is inherited and cannot be prevented.
- It is not an illness.
- While it presents unique physical characteristics, acceptance, understanding and love among family members can be fostered.
- Health education to decrease co-morbidities associated with albinism.
- Increase awareness and understanding to create safer lives for those living with this condition.
- A heightened awareness of albinism is necessary for early diagnosis and management, providing the best opportunity for the child's vision to develop to its fullest potential.

Signs and Symptoms

- **Ocular Albinism**
 - Eyes are translucent with hypo-pigmented blue, grey, or green irides.
 - Marked photophobia, with decreased visual acuity.
 - Other ocular manifestations such as strabismus, nystagmus and amblyopia.
 - Abnormalities of the optic nerve (e.g., hypoplasia, abnormal crossing of optic fibers at the optic chiasm).
- **Oculocutaneous Albinism**
 - Along with ocular plus milky white skin color which is photosensitive and sunburns easily
 - Predisposition to skin cancer.

Investigation

- Diagnosis based on physical examination including comprehensive ophthalmologic examination.
- Molecular testing using a multigene panel or comprehensive genome sequencing can be done for precise diagnosis.

Differential diagnosis

- Disorders associated with hair and skin hypopigmentation
 - Waardenburg syndrome type II
 - Tietz albinism-deafness syndrome
 - Chediak-Higashi syndrome

Management

Primary / Secondary Level

- **Lifelong photoprotection**
 - Seeking shade and avoiding ultraviolet exposure during the peak hours of sunlight.
 - Use of protective clothing, such as wide-brimmed hats, ultraviolet protective factor (UPF)-labelled clothing, shirts with a collar, long sleeves, long pants, and socks.
 - Liberal and frequent (every two hours) application of sunscreen of at least sun protection factor (SPF) 30 when in the sun.
 - Avoiding medications that increase photosensitivity whenever possible. NSAIDS, antihistamines, oral contraceptives, Sulphonylureas, Thiazide diuretics and Tetracycline.
- **Skin cancer surveillance**
 - Skin examination at 6- to 12-month intervals starting in adolescence.
 - Educated about the importance of skin self-examination including awareness of concerning skin lesions, such as new lesions in sun-exposed areas, non-healing lesions or lesions undergoing changes, and lesions associated with symptoms like pain, itching, or bleeding.
- **Management of eye abnormalities**
 - Optometry and/or ophthalmology review for correction of refractive errors and provision of low vision aids
- Refer to tertiary level for review by ophthalmologist / dermatologist.

Tertiary Level

- Manage as above
- Review by dermatologist and ophthalmologist.

FOLLOW-UP

- Dermatology review every 6-12 months for early cancer detection.
- Ophthalmology follow-up in the first 2 years of life, then annually during school age.
- On-going education, psychosocial counselling and social support.

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CHAPTER 5. ENDOCRINOLOGY

DIABETES IN CHILDREN

Definition

Diabetes mellitus (DM) is a complex metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, action, or both which leads to abnormalities of carbohydrate, fat, and protein metabolism.

The most common type in children is type 1 DM, usually diagnosed from age 6 months to 36 years.

Risk / Causes factors

- Genetics - family history in parent or sibling of type 1 DM
- Age- Type 1 diabetes can appear at any age, but it appears at two noticeable peaks. The first peak occurs in children between 4 and 7 years old. The second is in children between 10 and 14 years old
- Environmental factors
 - The environmental triggers include infections, nutritional, changes in the microbiome and chemicals.
 - Infections include Enterovirus infection (during pregnancy, infancy, childhood, and adulthood), congenital rubella syndrome, CMV, mumps, influenza, rotavirus, and H1N1, possibly SARS-CoV
- Idiopathic and sporadic

Prevention / Promotion

- Early diagnosis
- Health education and advocacy

Signs and symptoms

| | |
|--|---|
| <ul style="list-style-type: none"> ● Polyuria ● Polydipsia ● Nocturia ● Changing enuresis ● Weight loss ● Polyphagia ● Fatigue ● Frequent UTIs ● Frequent fungal and bacterial infections | <ul style="list-style-type: none"> ● Abdominal pain (pseudo-appendicitis diabetica) ● Behavioral disturbance, including reduced school performance, and blurred vision ● Impairment of growth and susceptibility to perineal candidiasis ● In its most severe form, DKA or (rarer) non-ketotic hyperosmolar syndrome may develop and lead to stupor, coma and, in the absence of effective treatment, death |
|--|---|

CRITERIA FOR THE DIAGNOSIS OF TYPE 1 DIABETES MELLITUS

- Classic symptoms of diabetes or hyperglycemic crisis with plasma glucose concentration ≥ 11.1 mmol/L (≥ 200 mg/dl), **OR**
- Fasting plasma glucose ≥ 7.0 mmol/L (≥ 126 mg/dl). Fasting is defined as no caloric intake for at least 8 hrs, **OR**
- Two-hour post-prandial glucose ≥ 11.1 mmol/L (≥ 200 mg/dl) during an oral glucose tolerance test (OGTT). The OGTT should be performed using a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g, **OR**
- HbA1c $\geq 6.5\%$ (important indicator of glycemic control)

Investigations

- Random blood glucose
- Fasting blood sugar
- Oral glucose tolerance test
- HbA1c
- Serum electrolytes
- Urine dipstick (ketones)
- Insulin & C-peptide levels
- Antibodies- Islet cell cytoplasmic autoantibodies (ICA); Glutamic acid decarboxylase (GADA); Insulinoma associate-2 autoantibodies (IA-2A); Insulin autoantibodies (IAA)

Differential diagnosis

- Type 2 diabetes mellitus
- Maturity onset diabetes of the young (MODY-dm)
- Psychogenic polydipsia
- Diabetes insipidus
- Stress hyperglycemia
- Long standing steroid therapy
- Renal tubular acidosis type-1
- Glucagonoma
- Cushing's syndrome
- Hypothyroidism

Management

- Management follows a multidisciplinary approach which involves dieticians, nutritionists, psychologists, nurses, doctors and endocrinologists.
- Diabetes education is a cornerstone.

Primary Level

- Relevant history and physical exam
- Investigations
 - Random blood sugar
 - Fasting blood sugar
 - Urine dipstick (ketones)
- Treatment (stabilize the patient)
 - Check hydration status and manage as per protocol
- Refer for secondary level care

Secondary Level

- Relevant history and physical exam
- Investigations
 - Random blood sugar
 - Fasting blood sugar
 - Urine dipstick
- Treatment
 - Rehydrate patient
 - Screen for and treat for DKA. Refer to DKA section of guideline.
 - Prepubertal and pubertal children usually require 0.5 to 1.0 IU/kg/day of insulin. The daily dose is divided and administered as demonstrated below using the glucose- and meal-adjusted injection regimen.

| Type of Insulin and dosing ratio | AM | Noon | PM |
|--|--|--|--|
| Soluble <ul style="list-style-type: none"> • 1/3 of total daily insulin dose • Administered before main meals | 1/3 of total daily dose of soluble insulin | 1/3 of total daily dose of soluble insulin | 1/3 of total daily dose of soluble insulin |
| NPH <ul style="list-style-type: none"> • 2/3 of total daily insulin dose | 2/3 of total daily dose of NPH | | 1/3 of total daily dose of NPH |

- Glycemic targets:
 - Achieving target glucose levels assessed through HbA1c, and/or SMBG reduces risks of acute and chronic complications of diabetes. This minimizes the detrimental effects of hypoglycemia and hyperglycemia on brain development, cognitive function, mood and quality of life.
 - Finger capillary glucose should be assessed at least 3 times a day for a person with diabetes taking insulin.

- Finger capillary glucose- recommended target glucose values are between 4 and 10 mmol (70–180 mg/dl), with a narrower fasting target range of 4–8 mmol/L (70–144 mg/dl).

Tertiary Facility

- Relevant history and physical exam
- Investigations
 - Random blood sugar
 - Fasting blood sugar
 - Urine dipstick
 - HbA1c every 3 months
 - Antibody tests (gold standard for T1D diagnosis) – in new diagnosis
 - Screen for other autoimmune diseases
 - Screen for thyroid disease and celiac disease.
- Treatment
 - Rehydrate patient
 - Screen for and treat for DKA or Hk
 - Prepubertal children usually require 0.5 to 1.0 IU/kg/day and during puberty. The daily dose is divided and administered as demonstrated in the table above using the Glucose- and meal-adjusted injection regimen.
- Glycemic targets as above
- Adherence to insulin treatment even on sick days. Do not stop insulin even on sick days. Adjust up by 10 to 20% of total dose and taper after recovery to previous dosage before illness.

Follow up

Short term Follow up

- In patients with new diagnosis of type 1 DM, schedule a 2-weekly visit in which checking of glucose diary and health education are re-enforced
- Thereafter subsequent clinics can be scheduled monthly.

Long term Follow-up

- Dietary education on every visit.
- 3-monthly HbA1c.
- Screen on every visit peripheral neuropathy (3-5years after diagnosis or from age of 9-11 years)
- Screen for diabetic nephropathy annually (3-5years after diagnosis or from age of 9-11).
- Screen for diabetic retinopathy annually (3-5years after diagnosis or from age of 9-11).

DIABETIC KETOACIDOSIS (DKA)

Definition

A state of absolute or relative insulin deficiency resulting in hyperglycemia, dehydration and metabolic acidosis. Leading cause of morbidity and mortality in children with T1DM but can also occur in patients with type 2 DM.

Risk factors

- New onset T1DM especially due to missed diagnosis
- Omission of insulin or inadequate administration in a known patient with T1DM
- Infection
- Trauma, surgery emotional stress
- Being a young child and/or adolescent

Prevention

- Early diagnosis
- Diagnose and treat underlying infections / triggers early
- Adherence to insulin treatment even on sick days. Do not stop insulin even on sick days. *Adjust up by 10 to 20% of total dose and taper after recovery to previous dosage before illness.*
- Regular reviews in diabetic clinic
 - Assess for signs of puberty
 - Review insulin dosages
 - Intensify diabetes education (drug storage, drug administration / injection technique, injection site care, nutrition and diet, identifying complications)
- On-going psychosocial counselling

Promotion and advocacy

- Health education and advocacy
- Screening of patients at risk
- Advocate for consistent availability of insulin

Causes

- Missing insulin doses
- New diagnosis of T1DM
- Stress secondary to an acute illness e.g Infection and surgery

Signs and symptoms

- Any patient with T1DM who presents with abdominal pain, nausea, fatigue and/or dyspnea should be evaluated for DKA

| Symptoms of hyperglycemia | Symptoms of acidosis | Signs of Dehydration |
|--|--|----------------------|
| Polyuria | Abdominal pain | Poor skin turgor |
| Polydipsia | Vomiting, nausea | Dry mucous membranes |
| Fatigue | Rapid or deep respiration (Kussmaul's) | Sunken eyes |
| Nocturia in a previously continent child | Confusion and coma | Tachycardia |
| | Muscle pains and cramps | |
| | Fruity Smelling breath | |

Investigations

- Random blood glucose
- Urine dipstick
- Full blood count (FBC) with differential
- Serum electrolytes (with calculation of the anion gap), blood urea nitrogen (BUN), and plasma creatinine
- Arterial blood gas
- Plasma osmolality
- Serum beta-hydroxybutyrate
- Electrocardiogram – to look for signs of hypokalemia/hyperkalemia

Differential diagnosis

- Gastroenteritis
- Sepsis
- Pneumonia
- Encephalitis
- Acute abdomen
- Metabolic acidosis
- Severe malaria
- Meningitis

Management

Principles of DKA management

- Correct dehydration
 - Correct acidosis and reverse ketosis (bicarbonate is contraindicated)
 - Normalize blood glucose
 - Minimize DKA complications
- Provide education for DM

Primary Level

- DKA is an emergency, follow ABC approach in managing patient.
- Obtain relevant history and examination.
- Collect relevant investigations: RBS and urine dipstick.
- Assess airway & breathing status and support accordingly
- Assess **circulation**: Assess level of dehydration status and start fluid replacement based on the dehydration status.
 - ***Estimate 5% dehydration for mild/moderate dehydration and 7% in severe dehydration***
 - Two peripheral intravenous (IV) catheters should be inserted.
 - If unable to give IV rehydration place NGT and use ORS for rehydration (if not vomiting) and for severely dehydrated patients, consider intraosseous fluid replacement if available
 - Fluid replacement should begin before starting insulin therapy.
 - ***Every patient with DKA is always dehydrated and should get an initial fluid resuscitation volume of 0.9% saline/RL 10ml/kg over 1 hour***

- If in shock give 20mls/kg of 0.9% saline/RL IV infused over 20 to 30 mins to restore peripheral circulation
- Start maintenance fluid 0.9% saline and refer.
- Refer to the next level of care once a patient has stable vital signs, refer whilst on fluid rehydration.
- **CLEARLY DOCUMENT AMOUNT OF FLUIDS GIVEN**

Secondary / Tertiary Level

- As above
- If in shock or severely dehydrated expand volume using boluses 20mls/kg of 0.9% saline or RL infused over 20–30 min to restore peripheral circulation. **Reassess after every bolus.** If the patient is not responding after 2 boluses consult paediatrician
- After initial bolus, calculate the subsequent rate of fluid administration which should include maintenance and fluid deficit (**Use 5% deficit for dehydration fluid calculation**). Deficit should be given over 48hrs. SEE EXAMPLE OF FLUID CALCULATION (Box below).
- If needing more fluid replacement, discuss with a paediatrician.
- Monitor for signs of fluid overload.
- Assess **disability**
 - GCS, pupillary exam
 - Draw samples: blood glucose, beta-hydroxybutyrate blood or urine ketones, serum electrolytes and blood gases.

Manage the child in an HDU or a designated area where close monitoring can take place.

- Monitor **electrolytes** / arterial blood gas every 6 to 8 hours. Correct accordingly
- Continue with **fluid replacement** and assess for signs of fluid overload every hour
- **Catheterize** and monitor urine output
- Hourly **glucose** check
- **Insulin therapy:**
 - Begin with 0.05U/kg at least 1hr AFTER starting fluid replacement therapy.
 - Check blood sugars hourly after initiation of insulin.
 - RBS should drop by 88 – 100mg/dL every hour.
 - If the RBS consistently declines by less than 88mg/dL/hr over the 1st 4 - 5 hours, consult paediatrician for dose adjustment.
 - If there is rapid drop of RBS by > 100mg/dL/hr reduce dose of insulin by 10-20% and **CONSULT** paediatrician.
- **Potassium:** All children with DKA have a relative hypokalemia. Start Potassium therapy after confirming urine void. Begin with 40 mmol potassium added in 1 L of fluid (0.9% NS / RL)

- 6 Hourly **ketones** check.
- Treat the underlying cause of DKA.
- Keep the patient nil per os during DKA management.
- **Manage other complications**
 - Cerebral oedema is the most common cause of mortality among children with DKA and symptoms include:
 - ◆ Onset of headache or vomiting after beginning treatment or progressively worsening or severe headache,
 - ◆ slowing of heart rate not related to sleep or improved intravascular volume,
 - ◆ change in neurological status (irritability, lethargy, confusion, incontinence),
 - ◆ specific neurological signs (e.g. cranial nerve palsies),
 - ◆ decreased oxygen saturation.
 - ◆ Risk factors for developing cerebral oedema are:
 - elevated blood urea nitrogen (BUN) concentration (>20 mg/dl)
 - severe acidosis ($\text{pH} < 7.1$)
 - severe hypcapnia ($\text{pCO}_2 < 21$ mmHg)
 - age < 5 years)
 - ◆ If neurologic status deteriorates acutely, hyperosmolar therapy with mannitol or hypertonic saline should be given immediately
 - If signs of cerebral edema refer to the management guideline of cerebral edema.
- Transitioning to fixed dosing of insulin:
 - Clearing of beta-hydroxybutyrate (blood ketones) is the gold standard for resolution of DKA.
 - Stable patients with overall improvement of clinical picture should be considered to have resolved DKA, urine ketones take longer to clear therefore should not be the only measure to determine resolution of DKA.
 - Once DKA has resolved, the patient is ready to transition to subcutaneous insulin. Give the child the subcutaneous insulin dose then feed the child. ***Continue IV insulin for 30 minutes after administering subcutaneous insulin then stop.***

FLUID CALCULATION IN DKA

Formulae for fluid deficit calculation

Weight in kg x % dehydrated

Percentage dehydrated is 5% for mild dehydration and 7.5% for moderate/severe dehydration and shock)

Total fluid for patients in DKA: Maintenance fluid + Fluid deficit

Note that in DKA fluid calculation, the maintenance volume needs to be doubled as correction occurs over 48hours

Example of fluid calculation

A child weighing 20kg on admission in shock

1 x 20mls/kg bolus needed to correct shock = 400mls

Maintenance = 1500ml/day (1.5L)

Deficit = 20 kg x 5% = 1L

Requirement (over 48 hours) = Maintenance (1.5L + 1.5L) + Deficit (1L) =
4 liters/48hrs = 83mls/hr

HOW TO PREPARE AND ADMINISTER INSULIN

- Mix insulin and fluids in a 1:1 ratio, e.g. 20units insulin in 20mls normal saline / ringers lactate
 - This gives a concentration of 1 unit insulin / ml
- Start insulin infusion (via infusion pump) at a rate of 0.05u / kg / hr e.g for a 20kg child
$$20\text{kg} \times 0.05 \text{ u/kg} = 1\text{ml/hr}$$
- If infusion pump is not available, use burette and use a drop rate calculation depending on giving set available.

THYROID DISORDERS

CONGENITAL HYPOTHYROIDISM

Definition

Congenital hypothyroidism (CH) is caused by inadequate thyroid hormone production in newborn infants resulting from an absent or under-developed thyroid gland (a-/dysgenesis) (80-85% of cases) or one that has developed but cannot produce thyroid hormone because of a 'production line' problem (dys-hormonogenesis) (10-15% of cases).

Risk factors / Causes

- Maternal perinatal factors such as advanced maternal age, gestational complications, maternal iodine deficiency, mother on antithyroid drugs, with antithyroid antibodies or excess iodine exposure.
- Neonatal perinatal factors such as female sex, preterm birth, post term birth, low birth weight, presence of other birth defects, and multiple gestation.
- Down's syndrome.
- Predominantly sporadic.
- 2% genetic or familial.

Prevention / promotion

- Newborn screening (TSH): blood (heel prick or cord blood) for screening is collected from full-term infants, the sample is usually collected one to two days after birth.
- Advocate for neonatal screening to prevent intellectual and physical disability.
- Health education.

Signs and symptoms

- Can be asymptomatic.
- Symptoms usually develop over the first few months of life: lethargy, hoarse cry, feeding problems (often needing to be awakened to nurse), constipation, puffy (myxedematous) and/or coarse facies, macroglossia, umbilical hernia, large fontanelles, hypotonia, dry skin, hypothermia, and prolonged jaundice (primarily unconjugated hyperbilirubinemia).
- Later problems: profound intellectual disability, growth retardation.
- 3-7% have other birth defects e.g. ASD, VSD, micropenis, undescended testes, hearing loss.

Investigations

- T4 and TSH assays.

| | |
|-----------------------------------|--------------------------------------|
| Primary hypothyroidism | High TSH, low free T4 |
| Subclinical hypothyroidism | High TSH, normal free T4 or total T4 |
| Central hypothyroidism | Low or normal TSH, low free T4 |

- Cardiac echo and audiology screening
- Additional testing (may be helpful for selected infants)
 - Thyroid imaging
 - Thyroid ultrasonography and color flow Doppler
 - Thyroid radionuclide uptake and scan
 - Thyroid autoantibodies

- Serum thyroglobulin concentration
- Urinary iodine concentration
- Genetic testing
- Imaging of left lower extremities: absent distal left femoral epiphysis in 54% of patients.

Differential diagnosis

- Spinal muscular atrophy
- Muscular dystrophies
- TORCH infections
- Hirschsprung's disease
- Panhypopituitarism
- Beckwith-Wiedemann syndrome

Management

PRIMARY HEALTH CARE FACILITY

- Identify key diagnostic features (Refer to signs and symptoms above)
- Manage acute illnesses like hypoglycemia as per ETAT protocol.
- Refer patient to tertiary level of care.

SECONDARY HEALTH CARE FACILITY

- Proceed as on primary level of care.
- Refer patient to tertiary level of care.

TERTIARY HEALTH CARE FACILITY

- Identify key diagnostic features as highlighted above
- Carry out baseline tests
 - T4 and TSH assays
 - Random blood sugar
 - Serum electrolytes and liver function tests
 - Manage symptoms of acute illness such as hypoglycemia as per ETAT protocol
- Treatment
 - Plot growth chart for length, weight, and head circumference. Follow growth charts on every visit.
 - 0-3 months of age: levothyroxine dose of 10 to 15 µg/kg/day.
 - Administration: The tablet should be crushed and mixed with 5-10mls of breastmilk, formula (except soy protein formula), or water and fed to the infant. Give immediately, do not store. Avoid administration with Soy formula, supplements with iron or calcium and antacids (aluminum hydroxide) or infant "colic" drops (simethicone) may reduce absorption
 - Treatment goals — ensure normal growth and neurodevelopmental outcome. This is achieved by restoring the serum fT4 (or T4) and TSH concentrations to the normal range as rapidly as possible, followed by dose adjustment to ensure continued clinical and biochemical euthyroidism.
 - Target is serum T4 concentration in the upper one-half of the reference range for age.

- Target for serum TSH should be in the lower end of the reference range.
 - For infants with congenital central hypothyroidism, serum free T4 should be used to guide treatment because measurement of serum TSH is not helpful.
- Monitoring schedule – For infants with congenital primary hypothyroidism, monitor serum T4 and TSH at the following intervals:
 - Two weeks and at 4 weeks after the initiation of levothyroxine treatment.
 - Every one to two months during the first 6 months of life
 - Every three to six months between six months and three years of age.
 - Every 6 to 12 months thereafter until growth is complete.
 - 4 weeks after any change of dose.
- Once diagnosis is confirmed and treatment is started refer patient to endocrinologist.

ACQUIRED HYPOTHYROIDISM IN CHILDHOOD AND ADOLESCENCE

Definition

Abnormally low activity of the thyroid gland, resulting in slowing of growth, mental development and metabolic changes in children.

Risk factors/Causes

- Chromosomal disorders such as Down syndrome, Williams syndrome, or Turner syndrome.
- An autoimmune disorder such as type 1 diabetes or celiac disease.
- Too little or too much iodine intake.
- Injury to the thyroid gland.
- Radiation to the head and neck
- Nutritional
 - Iodine Deficiency
 - Excess exposure (e.g. Herbal supplements, drugs [amiodarone, expectorants])
- Drugs
 - Antithyroid drugs (eg, methimazole, propylthiouracil)
 - Antiseizure medications (eg, phenytoin, phenobarbital, valproate)

Promotion

Health education

Signs and symptoms

- Initial symptoms: constipation, sluggishness, lethargy, cold intolerance, dry skin, brittle hair, facial puffiness, muscle aches and pains.
- Declining school performance
- Delayed pubertal development.
- Declining growth velocity/short stature.
- Encephalopathy
- Hypothalamic or pituitary disease will cause headaches, visual symptoms, or manifestations of other pituitary hormone deficiencies.

Investigations

- T4 and TSH assays

| | |
|----------------------------|--------------------------------------|
| Primary hypothyroidism | High TSH, low free T4 |
| Subclinical hypothyroidism | High TSH, normal free T4 or total T4 |
| Central hypothyroidism | Low or normal TSH, low free T4 |

- Additional testing (may be helpful for selected infants)
 - Thyroid imaging - Thyroid ultrasonography and color flow Doppler
 - Serum thyroglobulin concentration
 - Thyroid autoantibodies - antithyroid peroxidase antibodies (TPO-Ab) and antithyroglobulin antibodies (TrAb)
 - Urinary iodine concentration
 - Genetic testing

Differential diagnosis

- Autoimmune thyroid disease
- Iodine deficiency/malnutrition
- Constipation
- Growth hormone deficiency

Management

Primary Level

- Identify key diagnostic indicators
 - Check random blood glucose
 - Symptoms and signs: as stated above
 - Manage acute illnesses as per protocol
- Refer patient to next level of care

Secondary Level

- Identify key diagnostic factors as highlighted above
- Carry out baseline tests including Random blood glucose
- Serum electrolytes and liver function tests
- Stabilize patient, manage acute illness as per protocol.
- Refer patient to next level of care

Tertiary Level

- History and physical exam as above.
- Baseline investigations
- T4 and TSH.
- Treatment

Levothyroxine dose — Initial treatment is started with levothyroxine at the following doses, given by mouth, once daily and administered in the morning 30minutes before food and adapt as necessary:

- Age 1 to 3 years – 4 to 6 µg/kg body weight
- Age 3 to 10 years – 3 to 5 µg/kg
- Age 10 to 16 years – 2 to 4 µg/kg
- Monitoring and dose adjustment —
 - Serum TSH and free T4 should be checked six to eight weeks after initiation of treatment and then every 6 to 12 months.
 - Thyroid function tests should be obtained six to eight weeks after any dose change or if the patient develops any clinical manifestations suspicious for hypo- or hyperthyroidism.
 - The levothyroxine dose is adjusted to maintain TSH and free T4 in the normal reference range for age.
- Once diagnosis is confirmed and treatment is started refer patient to endocrinologist.

Follow up

Medication review and side effects
Growth and development

HYPERTHYROIDISM

Definition

Hyperthyroidism is defined as an inappropriately high production of thyroid hormones from the thyroid gland leading to various systemic clinical manifestations.

Risk factors/causes

- Drugs (levothyroxine, lithium)
- Having a personal or family history of autoimmune disease
- Viral infections (e.g mumps, influenza)
- Autoimmune dysfunction (eg. Graves' disease)
- Tumours (thyroid carcinoma)
- Excess iodine intake

Prevention / Promotion

- Early diagnosis in patients at risk
- Health education and advocacy

Signs and symptoms

| | Symptoms | Signs |
|---------------------------------|--|--|
| Constitutional | Weight loss despite increased appetite; heat-related symptoms (heat intolerance, sweating) | Weight loss |
| Neuromuscular | Tremor; nervousness; anxiety; fatigue; weakness; disturbed sleep; poor concentration | Tremor of the extremities; hyperactivity; hyperreflexia; pelvic and girdle muscle weakness |
| Cardiovascular | Palpitations | Tachycardia; systolic hypertension; irregular heartbeat (atrial fibrillation) |
| Pulmonary | Dyspnoea, shortness of breath | Tachypnoea |
| Gastrointestinal | Diarrhea; nausea, vomiting | Abdominal tenderness |
| Skin | Increased perspiration | Warm and moist skin |
| Reproductive | | Menstrual disturbances |
| Ocular (Graves' disease) | Diplopia; sense of irritation in the eyes; eyelid swelling; retro-orbital pain or discomfort | Proptosis; eyelid retraction and lag; periorbital oedema; conjunctival injection and chemosis; ophthalmoplegia |

Investigations

- Full blood count
- Serum thyroid function tests (T4, TSH)
- Serum thyroid antibody tests (TPOs and Trab)
- Ultrasound
- Radionuclide uptake and scan

Differential diagnosis

- Graves' disease
- Subacute thyroiditis

- Hashimoto toxicosis
- Autonomously functioning thyroid nodule
- Factitious hyperthyroidism (intake of exogenous hormone)
- TSH-secreting pituitary tumor (rare)
- Pituitary resistance to thyroid hormone

Management

Primary Level

- Identify key diagnostic indicators
- Symptoms and signs: as stated above
- Manage acute illnesses as per protocol
- Refer patient to next level of care

Secondary Level

- Identify key diagnostic factors as highlighted above
- Carry out baseline tests
- Random blood sugar
- Serum electrolytes and Liver function tests
- Stabilize patient: manage acute illness as per protocol
- Manage hypertension (see section on Hypertension)
- Refer patient to next level of care

Tertiary Level

- History and physical exam as above.
- Baseline investigations
- T4 and TSH assays
- Treatment with antithyroid drugs
 - Carbimazole 15mg daily as starting dose
- Once diagnosis is confirmed and treatment is started refer patient to endocrinologist.

Follow up

- FBC-look for evidence of bone marrow suppression
- Blood pressure monitoring
- Nutrition and growth

APPROACH TO DISORDERS OF SEX DEVELOPMENT (AMBIGUOUS GENITALIA)

Definition

Patients born with genitalia that do not appear typically male or female, or that have an appearance discordant with the chromosomal sex, are classified as having a difference (or disorder) of sex development (DSD).

Risk factors / Causes

- Autosomal recessive and X-linked.
- Caused by mutations of genes associated with sex determination.

Prevention/Promotion

- Genetic counselling of family members
- Advocacy
- Reducing stigma associated with DSD
- Health education for health staff and affected families

Signs and symptoms

| General symptoms | |
|---|--|
| Overt genital ambiguity | |
| Discordance between genital appearance and (pre-/postnatal) karyotype | |
| +Newborns and infants | |
| Apparent Male | Apparent female |
| Largely male appearance of the external genitalia and any of the following: <ul style="list-style-type: none">- Bilaterally nonpalpable gonads- Severe hypospadias- Any degree of hypospadias accompanied by unilateral or bilateral cryptorchidism and/or micropenis- Genital appearance discordant with sex chromosomes | Largely female appearance of the external genitalia and any of the following: <ul style="list-style-type: none">- Clitoromegaly- Posterior labial fusion- Gonads palpable in the labioscrotal folds or inguinal region- Genital appearance discordant with sex chromosomes |
| Children and adolescents | |
| Male | Female |
| Largely male appearance of the external genitalia and any of the following: <ul style="list-style-type: none">- Bilaterally nonpalpable gonads- Severe hypospadias- Any degree of hypospadias accompanied by unilateral or bilateral cryptorchidism and/or micropenis- Breast development- Genital appearance discordant with sex chromosomes | Largely female appearance of the external genitalia and any of the following: <ul style="list-style-type: none">- Clitoromegaly- Posterior labial fusion- Gonads palpable in the labioscrotal folds or inguinal region- Lack of breast development- Genital appearance discordant with sex chromosomes- Absence of menarche |

Investigations

- Biochemistry
 - Urea and electrolytes (Sodium and potassium)
 - Blood glucose
 - Hormonal levels, i.e. cortisol, testosterone, estradiol, progesterone, 17-hydroxy-progesterone, LH – luteinizing hormone, FSH – follicle stimulating hormone, and anti-mullerian hormone (AMH)
- Abdomen and pelvic USS
- Karyotyping
- Laparoscopy and gonadal biopsy

Differential diagnosis

- Hypospadias
- Congenital adrenal hyperplasia (CAH)
- Androgen insensitivity
- Ovo-Testicular DSD (True hermaphroditism)

Management

- ***DO NOT ASSIGN SEX before full evaluation at tertiary level and encourage parents to give unisex name.***

Primary Level

- History - Pregnancy and birth + Family history of consanguinity
- Conduct physical examination
- Management - Supportive care, correct dehydration and hypoglycemia
- Referral

Secondary Level

- History and examination as above
- Investigations
 - Electrolytes
 - Abdomen and pelvic USS (if available)
- Management - Supportive care, correct dehydration and hypoglycemia
- Referral

Tertiary Level

- History and examination as above
- Thorough investigations (see investigation section)
- Management
 - Supportive care, correct dehydration and hypoglycemia
 - Specific treatment according to underlying disease
- Refer to endocrinologist
- Management requires multidisciplinary team that includes: paediatric endocrinologist, Pediatrician, geneticist, urologist, gynecologist, psychologist, nurses, social worker.

Follow up

- Medication review and side effects
- Ongoing social counseling

CONGENITAL ADRENAL HYPERPLASIA (CAH)

Definition

Congenital adrenal hyperplasia (CAH) is a family of autosomal recessive disorders that occurs because of a defect in adrenal steroidogenesis caused by a mutation in one or more enzyme-encoding genes, leading to dysfunctional cortisol and aldosterone production and excessive levels of androgens.

The most common form is 21-alpha-hydroxylase deficiency (21-OHD).

Risk factors / Causes

Factors that increase the risk of having CAH include:

- Parents who both are known to be heterozygous for one of the severe mutations
- Parents who both have CAH
- Having an affected sibling

Prevention / Early diagnosis

- Neonatal screening for elevated 17-hydroxy-progesterone (where screening facilities are available in patients with the above risk factors)
- Genetic testing of other family members
- Early detection and management to prevent complications

Promotion

- Advocacy
- Health education

Signs and symptoms

- Symptoms depend on severity of enzyme deficiency, type of enzyme deficiency and age.

| Infants | |
|--|--|
| Atypical genitalia/ ambiguous genitalia | <p><u>Females</u></p> <ul style="list-style-type: none">• Clitoral enlargement,• Labial fusion• Formation of a urogenital sinus caused by the effects of in-utero androgen excess on the development of the external genitalia.• Virilization may be so profound that genital atypia is unrecognized, and male sex assignment (with undescended testes) is made at birth in a 46XX patient. |
| | <p><u>Males</u></p> <ul style="list-style-type: none">• Normal-appearing genitalia at birth but may have subtle findings such as hyperpigmentation of the scrotum or an enlarged phallus.• In some rare enzyme defects, ambiguous genitalia may be present due to impaired androgen production |
| Adrenal crisis | <ul style="list-style-type: none">• Vomiting, diarrhea, hypotension, and hypovolemic shock can occur, typically between 10 to 20 days of age |

| | |
|---------------------------------|--|
| | <ul style="list-style-type: none"> Laboratory findings suggesting adrenal crisis include hyperkalemia with or without hyponatremia, metabolic acidosis, and hypoglycemia. |
| Children and adolescents | |
| | <ul style="list-style-type: none"> Pubic hair appears early, acne may be excessive, and the voice may deepen. Excessive pigmentation may develop. Signs of virilization in girls, early growth of penis and testicles in boys. Isosexual central precocious puberty may occur and bone age is significantly advanced if patient is not adequately treated. Final adult height is often compromised. |

Differential Diagnosis

- Other forms of DSD
- Metabolic diseases of the newborn
- Addison's Disease
- Sepsis

Management

Primary Level

- Identify key diagnostic indicators (signs and symptoms).
- Manage acute illnesses like dehydration and hypoglycemia as per protocol.
- Refer patient to the next level of care.

Secondary Level

- Identify key diagnostic indicators.
- Carry out baseline tests
 - Random blood sugar
 - Serum electrolytes
 - Abdominal and pelvic ultrasound scan
- Stabilize patient, manage dehydration and hypoglycaemia.
- Refer patient to next level of care.

Tertiary Level

- History and physical exam as above.
- Stabilize patient, manage dehydration and hypoglycaemia as per protocol.
- Baseline investigations (**Ordered with guidance from Endocrinologist**)
 - Random blood sugar (hypoglycaemia)
 - Serum electrolytes (hyperkalemia, hyponatremia)
 - Serum 17-hydroxyprogesterone (elevated in CAH)
 - Cortisol at a minimum (decreased)
 - Abdominal and pelvic ultrasound scan
- Other tests
 - ACTH stimulation test
 - Genetic testing

- Medical management
 - Supportive management
 - Treat adrenal crisis (refer to adrenal crisis management)
 - Correct dehydration and manage hypoglycaemia
 - Specific management
 - Newborns:

Glucocorticoid therapy should be initiated in newborns with:

 - Confirmed CAH – Initiate treatment with hydrocortisone, fludrocortisone and sodium supplements indefinitely.
 - Suspected CAH (eg, in an infant presenting with a positive newborn screen or atypical genitalia) need treatment with hydrocortisone, fludrocortisone, and sodium chloride supplements at standard starting doses. Continue this treatment until the diagnosis of CAH is either confirmed or excluded.
 - Initial dosing for newborns — In the absence of adrenal crisis, a typical starting regimen for an infant includes:
 - Hydrocortisone at 20 to 30 mg/m²/day, divided three times daily (ie, 2.5 mg three times a day), with rapid dose reduction when target hormone levels are reached.
 - Fludrocortisone 100 µg (0.1 mg) once or twice daily and sodium chloride, 1 to 2 g or 17 to 34 mEq/day (2 to 4 mEq/kg/day), divided in several feedings.
 - Infants and children
 - Hydrocortisone (cortisol) in a dose of 10 to 15 mg/m²/day, divided into three doses.
 - Hydrocortisone should be increased 3-5 fold in severe infection, high fever and surgery.
- Consult endocrinologist.

Follow up

- Medication review and side effects
- Patients/guardians should be educated on sick day management

PUBERTY DISORDERS

PRECOCIOUS PUBERTY

Definition

Onset of secondary sexual characteristics before the age of 8 in girls and 9 years in boys.

Much more common in girls than in boys.

Other forms of premature sexual maturation

- **Premature thelarche** - Premature breast development (as early as first year of life) that can be unilateral or bilateral and is self-limiting usually by age of 4 years.
- **Adrenarche** - Premature development of pubic hair and axillary hair. If isolated, it is not a sign of puberty in either sex.
- **Precocious pseudopuberty** - When signs of sexual maturation occur due to sex steroid secretion which has a different mechanism from normal puberty. Usually recognized by abnormal sequence of events of sexual maturation.

Risk Factors

- Females
- Obesity
- Sex hormone exposure (estrogen or testosterone cream or ointment, or other substances that contain these hormones such as medication or dietary supplements)
- Other medical conditions (McCune-Albright syndrome or congenital adrenal hyperplasia, hypothyroidism and neural tube defects).
- Radiation therapy of the central nervous system.
- Pituitary hamartomas
- Pituitary adenomas

Causes

- Idiopathic
- CNS irradiation
- Females
 - Ovarian cysts
 - Ovarian tumors
- Males
 - Leydig cell tumors
 - Human chorionic gonadotropin secreting germ-cell tumors
- Primary hypothyroidism
- Adrenal pathology

Prevention / Promotion

- Early diagnosis and treatment
- Health education and advocacy

Signs and symptoms

Male

- Testicular enlargement ($=/ > 4\text{mls}$)
- Growth of testis correlates well with growth of penis and pubic hair
- Size of penis (if obese, retract the pubic fat pad to obtain an accurate estimation of size). Use penile growth chart.
- Presence of anatomical variants of the penis e.g. hypospadias
- Easy foreskin retractability
- Scrotal pain or swelling

Female

- Breast development
- Colour and size of the area around the nipples
- Presence of pubic hair
- Presence of anatomical variants, labial adhesions, vulvar ulcers.
- Vaginal discharge / bleeding (early menarche)

TANNER STAGING FOR SEXUAL DEVELOPMENT

| Tanner stage | Girls | Boys |
|--------------|-------|------|
| 1 | | |
| 2 | | |
| 3 | | |
| 4 | | |
| 5 | | |

Investigations

- Medical history
- Physical exam
- Plot height, weight, BMI and bone age on growth chart
- Imaging
 - Bone age (x-ray of left hand)
 - Abdominal USS and pelvis USS (r/o cryptorchidism)
 - CT/MRI brain
- Hormones
 - Testosterone and estrogen
 - LH, FSH
 - LH:FSH ratio

Differential diagnosis

- Premature adrenarche
- Premature thelarche
- Exogenous androgens
- Testicular mass

Management

Primary / Secondary Level

- Identify and refer

Tertiary Level

- History, physical exam and investigations as above.
- Treatment
 - Psychosocial support to the family
 - Treat the underlying cause.
 - Medical Management
 - Gonadotropin analogues
 - Leuproride acetate
- Refer to endocrinologist

Follow up

- Medication review and side effect
- Growth and development

DELAYED PUBERTY

Definition

Absence of secondary sexual characteristics by 13 years in a girl and 14 years in a boy. Pubertal arrest is also considered as delayed puberty.

Risk factors

- Being male
- Family history
- Excessive exercise
- Chronic disease
- Radiation
- Malnutrition
- Eating disorders (eg anorexia nervosa)
- Pituitary surgery
- Pheochromocytoma
- Chemotherapy

Causes

- Chronic disease
- Poor nutrition
- Psychosocial deprivation
- Steroid therapy
- Tumors adjacent to the hypothalamus eg craniopharyngioma
- Congenital anomalies
- CNS irradiation and trauma
- Testicular torsion / trauma
- Cryptorchidism
- Mumps
- Female DSDs
- Polycystic Ovarian Syndrome (PCOS)
- Gonadal dysgenesis eg Turner syndrome, Klinefelter syndrome
- Chemotherapy

Prevention / Promotion

- Early diagnosis
- Health education and advocacy

Signs and symptoms

Girls

- No breast development and / or pubic hair by age 14 years
OR
- No Menstruation by age 16 years
OR
- First signs of puberty appeared > 5 years before menarche

Boys

- No enlargement of penis or testes by age 15 years
OR
- No pubic hair by age 15 years

Investigations

- Medical history including family history of delayed puberty
- Physical exam - Plot height, weight, BMI and bone age on the growth chart.
- Imaging studies
 - Bone age
 - Abdominal USS and pelvis USS
 - CT/MRI brain
- Hormones
 - LH, FSH
 - LH:FSH ratio

Differential diagnosis

- Constitutional delay of growth and puberty
- (Congenital) hypergonadotropic hypogonadism
- (Congenital) hypogonadotropic hypogonadism

Management

Primary / Secondary Level

- Identify and refer

Tertiary Level

- Treatment
- Psychosocial support to the family
- Investigate and treat underlying cause
- Medical Management
 - Male - Testosterone
 - Female - Estrogen and Progestin
- Refer to endocrinologist

Follow up

- 3 monthly follow-up in endocrinology clinic
- Medication review and side effects
- Growth and development

OVERWEIGHT AND OBESITY IN CHILDREN AND ADOLESCENTS

Definition

The definition refers to an excess of body fat.

- Overweight – BMI between >85th and 95th percentile for age and sex.
- Obesity – BMI \geq 95th percentile for age and sex.
- Severe obesity – Severe (class II or greater) obesity is defined as BMI \geq 120 percent of the 95th percentile values or a BMI \geq 35 kg/m² (whichever is lower).

Risk factors/Causes

Environmental factors

- Glycemic index of foods
- sugar-containing beverages
- large portion sizes for prepared foods
- fast food service
- diminishing family presence at meals
- decreasing structured physical activity
- shortened sleep duration
- changes in elements of the built environment (e.g. availability of sidewalks and playgrounds)
- Excessive television viewing
- Medications (e.g. certain psychoactive drugs, steroids)
- Genetic factors
- Endocrine causes e.g. Hypothyroidism and Cushing syndrome

Prevention / Promotion

- Lifestyle modification
- Health education and advocacy

Signs and symptoms

- Striae distensae
- acanthosis nigricans (darkening of the neck, armpits and groin)
- sleep apnoeas
- joint pains
- fatigue
- infections in skin folds
- shortness of breath
- heat intolerance
- excessive sweating
- depression

Investigations

- Plot height and weight on a growth chart
- Calculate and plot BMI
- Assess for dysmorphic features
- Neurodevelopmental assessment
- Blood pressure
- Random blood glucose
- Urea and electrolytes
- LFTs, LDL, HDL

Management

Primary Level

- Relevant history, physical exam and anthropometric measurements as above
- RBS
- Management
 - Lifestyle modification
 - Exercise
 - Reduction of intake of food with high glycemic index
 - Screen for diabetes and hypertension and manage accordingly
- Refer to next level of care

Secondary Level

- Relevant history, physical exam and anthropometric measurements as above
- Measure blood pressure
- RBS, U&Es, LFTs
- Management
 - Lifestyle modification
 - Exercise
 - Reduction of intake of food with high glycemic index
 - Screen for diabetes and hypertension and manage accordingly
- Refer to next level of care

Tertiary Level

- Relevant history, physical exam and anthropometric measurements as above.
- Measure blood pressure
- RBS, U&Es, LFTs, LDL, HDL
- Management
 - Lifestyle modification
 - Exercise
 - Reduction of intake of food with high glycemic index
 - Screen for diabetes and hypertension and manage accordingly
- Psychosocial counseling
 - Refer to the endocrinologist.
- Multidisciplinary involvement including nurses, dieticians, nutritionists, paediatricians, psychosocial counselors.

Follow up

- Monthly follow-up in endocrinology clinic
- Medication review for side effects
- Monitor growth and development
- Ongoing education / counselling

GROWTH DISORDERS

SHORT STATURE

Definition

Short stature is a term applied to a child whose height is 2 standard deviations (SD) or more below the mean for children of that sex and chronologic age (and ideally of the same racial-ethnic group).

Risk factors/Causes

- Chronic disease
- Chronic malnutrition
- Psychosocial deprivation
- Family history of short stature
- Delayed growth and puberty
- Chronic steroid use
- Genetic syndromes (e.g. down's syndrome, turners syndrome)

Prevention / Promotion

- Early detection and treatment of underlying causes.
- Health education.

Signs and symptoms

- Shorter than peers of same age and sex.
- May have dysmorphic features
- Signs of underlying disease

Investigations

- Bone age
- Full Blood Count (FBC)
- Erythrocyte Sedimentation Rate (ESR)
- Urea and Electrolytes
- Thyroid-Stimulating Hormone (TSH), free thyroxine (T4)
- If available: IGF-1, IGFBP-3, Transglutaminase IgA

Differential diagnosis

- Familial short stature
- Constitutional delay of growth and puberty
- Undernutrition
- GI disease (especially Crohn disease and celiac disease)
- Renal disease (CKD, renal tubular acidosis)
- Endocrine causes of growth failure (hypothyroidism, isolated growth hormone deficiency, cushings disease)
- Cardiac disease
- Genetic diseases with primary effects on growth eg down's syndrome, Turner syndrome

Management

Primary Level

- History and physical examination
- Plot height and weight on growth chart
- Random blood Glucose (RBS) and urine dipstick
- Refer to next level of care

Secondary Level

- As above
- RBS, FBC, erythrocyte sedimentation rate (ESR)
- Refer to next level of care

Tertiary Level

- History and physical exam
- Calculate height velocity
- Plot parents' height and calculate mid-parental height
- Investigations
- Bone age
- FBC
- ESR
- Electrolytes, creatinine
- Thyroid-stimulating hormone (TSH), free thyroxine (T4)
- If available and appropriate: IgF-1, IgFBP-3, IgA, Tissue Transglutaminase IgA
- Refer to paediatric endocrinologist

Follow up

- 3 monthly follow - up in endocrinology clinic
- Monitor growth and development
- Ongoing education / counselling

TALL STATURE

Definition

Tall stature is a term applied to a child whose height is 2 standard deviations (SD) or more above the mean for children of that sex and chronologic age (and ideally of the same racial-ethnic group).

Risk factors/Causes

- Growth hormone excess
- Hyperthyroidism
- Family history of tall stature
- Overweight/obesity
- Accelerated growth and puberty
- Genetic syndromes (e.g. Marfan's syndrome, Klinefelter syndrome)

Prevention / Promotion

- Early detection
- Health education and advocacy

Signs and symptoms

- Taller than peers of same age and sex.
- May have dysmorphic features

Investigations

- Bone age
- Complete Blood Count (CBC)
- Erythrocyte Sedimentation Rate (ESR)
- Urea and Electrolytes
- Thyroid-Stimulating Hormone (TSH), free thyroxine (T4)
- If available and appropriate: IgF-1, IgFBP-3

Differential diagnosis

- Familial tall stature
- Hyperthyroidism
- GH-secreting tumours
- Precocious puberty (temporary tall stature)
- Genetic diseases with primary effects on growth eg Klinefelter syndrome

Management

Primary / Secondary Level

- History and physical examination
- Plot height and weight on growth chart
- Refer to next level of care

Tertiary Level

- History and physical exam
 - Calculate height velocity
 - Plot parents' height and calculate mid-parental height
- Investigations
 - Bone age
 - Thyroid-stimulating hormone (TSH), free thyroxine (T4)

- If available and appropriate: IgF-1, IgFBP-3
- Refer to paediatric endocrinologist

Follow up

- 3 monthly follow up in endocrinology clinic
- Monitor growth and development
- Ongoing education / counselling

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CHAPTER 6. GASTROENTEROLOGY AND FOOD ALLERGY

CHRONIC ABDOMINAL PAIN

Definition

It is intermittent or constant abdominal pain (either organic or functional) with a duration of at least 2 months.

Risk factors/Causes of Functional Abdominal pain

- Genetic factors are thought to increase the likelihood that a child develops an FAPD.
- Physical stressors in infancy and childhood predisposes the development of FAPDs later in childhood, adolescence, and adulthood (e.g., history of cow's milk protein intolerance, allergic proctocolitis in infancy, gastrointestinal infection, Henoch-Schönlein purpura, abdominal surgery early in life, urinary tract infection in infancy).
- Psychosocial events and conditions throughout the patient's life (e.g., stressful life events, anxiety, and depression)
- Psychological stressors early in life e.g., sexual, emotional, and physical abuse in childhood.
- Parental deprivation such as unsatisfactory relationship between parents and losing a parent through death, divorce, or separation.
- Consider gynaecological causes in girls who have achieved menarche.

Promotion/Prevention

- Deworming
- Health Education

Signs and symptoms

- Depends on the cause

Red flags in chronic abdominal pain

- Historical findings
 - Involuntary weight loss (malabsorption)
 - Unexplained fever
 - Dysphagia, odynophagia
 - Significant vomiting (protracted, bilious, projectile etc.)
 - Chronic severe diarrhoea or nocturnal diarrhoea
 - Urinary symptoms (change in bladder function, dysuria, haematuria, flank pain)
 - Persistent right upper or right lower quadrant pain
 - Back pain
 - Family history of inflammatory bowel disease, coeliac disease, peptic ulcer disease
 - Gastrointestinal blood loss (bloody diarrhoea / melena)
 - Skin changes (rash, eczema, hives)
 - Arthralgia

- Examination findings
 - Deceleration in linear growth
 - Delayed puberty
 - Oral aphthous ulcerations
 - Abdominal tenderness
 - Hepatomegaly and/or splenomegaly
 - Costovertebral angle tenderness
 - Perianal abnormalities (e.g skin tags, fissures, fistulae)
 - Abdominal mass
 - Jaundice
 - Pallor
 - Psoriasis
 - Signs of arthritis

Differential diagnosis

Functional Abdominal Pain:

- Functional dyspepsia
- Functional abdominal pain not otherwise specified
- Irritable bowel syndrome
- Abdominal migraine

Organic causes:

- Peptic Ulcer disease
- Inflammatory bowel disease
- Coeliac disease
- Constipation
- Gastroesophageal reflux

Rome IV Diagnostic Criteria for Functional Abdominal Pain Disorders

| Disorder | Diagnostic criteria |
|-----------------------------------|--|
| Functional dyspepsia (H2a) | <p>Must include at least 1 of the following for at least 4 days per month:</p> <ul style="list-style-type: none"> • Postprandial fullness • Early satiation • Epigastric pain or burning not associated with defecation (Criteria must be fulfilled for at least 2 months.) <p>H2a1. Postprandial Distress Syndrome Includes bothersome postprandial fullness or early satiation which prevents finishing a regular meal. Supportive features include upper abdominal bloating, postprandial nausea, or excessive belching.</p> <p>H2a2. Epigastric Pain Syndrome Includes all of the following: bothersome (severe enough to interfere with normal activities)</p> |

| | |
|--|--|
| | <p>pain or burning localized to the epigastrium. The pain is not generalized or localized to other abdominal or chest regions and is not relieved by defecation or passage of flatus. Supportive criteria can include:</p> <ul style="list-style-type: none"> (a) burning quality of the pain but without a retrosternal component, (b) commonly induced or relieved by ingestion of a meal but may occur while fasting. |
| Irritable bowel syndrome - IBS (H2b) | <p>Must include all of the following:</p> <ul style="list-style-type: none"> • Abdominal pain at least 4 days per month associated with at least 1 of the following: Related to defecation, a change in stool frequency, or a change in appearance of stool • In children with constipation, pain continues despite resolution of constipation (if pain resolves, the child has functional constipation) <p>(Criteria must be fulfilled for at least 2 months)</p> |
| Abdominal migraine (H2c) | <p>Must include all of the following occurring at least twice:</p> <ul style="list-style-type: none"> • Sudden episodes of intense, acute abdominal pain lasting at least 1 hour • Episodes are separated by weeks to months of mild or no abdominal pain • Typical pattern for each child • Pain is associated with at least 2 of the following: Anorexia, nausea, vomiting, headache, photophobia, or pallor <p>(Criteria must be fulfilled for at least 6 months)</p> |
| Functional abdominal pain—not otherwise specified - FAP-NOS (H2d) | <p>Must include all of the following for at least 4 days per month:</p> <ul style="list-style-type: none"> • Episodic or continuous abdominal pain not solely related to physiologic events (like eating or menses) • Does not meet criteria for other functional abdominal pain disorders (FAPD) <p>(Criteria must be fulfilled for at least 2 months.)</p> |

Investigations

Investigate those with red flags based on underlying possible diagnosis.

- Full blood count
- Peripheral blood film
- ESR, CRP
- Liver Function Tests
- Urea & Electrolytes
- Urinalysis and culture
- Stool microscopy
- Stool occult blood testing

- Abdominal ultrasonography

Management

- Treatment strategies need to be individualised based on the child's presentation.

Primary level

- Deworming therapy
- Refer all cases with red flags

Secondary Level

- Investigations as above
- Treat underlying causes
- Refer if cause not identified

Tertiary Level

- Investigate as above + other additional investigations as indicated
- Treat the underlying causes

Follow up

- Nutrition and growth monitoring
- Follow up for underlying disease

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Definitions

Gastroesophageal reflux (GER) refers to passage of gastric contents into the oesophagus

GERD refers to reflux with pathological consequences such as oesophagitis, nutritional complications with weight loss or respiratory complications.

Causes / Risk factors

- Overweight, obesity
- Neurologic disorders (due to delayed gastric emptying)
- Cerebral palsy
- Hiatal hernia
- Asthma
- Stress
- Functional constipation
- Delayed gastric emptying
- Gastric outlet obstruction

Prevention / Promotion

- Caregivers and older children should be informed that excessive body weight is associated with an increased prevalence of GERD.
- Massage therapy, lifestyle interventions, or complementary treatments such as prebiotics, probiotics, or herbal medications should not be used to treat GERD.
- For patients on NGT feeding - Education of parents on NGT care.
- For patients on gastrostomy feeding - Education of parents on gastrostomy care.

Signs and symptoms

General

- Excessive irritability/pain
- Refusal of feeding
- Dental erosion
- Anemia
- Weight loss or poor weight gain
- Dystonic neck posturing (Sandifer syndrome)

Gastrointestinal

- Recurrent regurgitation with/without vomiting in the older child
- Heartburn/chest pain
- Epigastric pain
- Hematemesis
- Dysphagia/odynophagia
- Ruminant behavior
- Esophagitis
- Esophageal stricture
- Barrett esophagus

Airway

- Wheezing
- Stridor
- Cough
- Hoarseness
- Apnea spells
- Apparent life-threatening events
- Asthma
- Recurrent pneumonia associated with aspiration
- Recurrent otitis media

Investigation

- Full Blood count
- Urea and electrolytes
- Ultrasound
 - Look for signs of hiatal hernia, pyloric stenosis (first few months of age) and other disorders mimicking GER.
- Endoscopy
 - For direct visual examination and biopsy of the esophageal mucosa to rule out macroscopic lesions such as esophagitis, erosions, exudate, ulcers, strictures, hiatal hernia, and others.
- Barium studies
 - To diagnose anatomic abnormalities such as malrotation, duodenal web, and stenosis; can also diagnose functional abnormalities such as achalasia.

Differential diagnosis

- Cow's milk protein allergy
- Eosinophilic esophagitis
- Foreign body ingestion
- Irritable bowel syndrome
- Esophageal motility disorders
- Helicobacter pylori infection
- Hiatal Hernia
- Intestinal motility disorders
- Other disorders associated with vomiting e.g. UTI, increased intracranial pressure, cyclic vomiting syndrome and metabolic disorders

MANAGEMENT**Primary Level**

- Physiologic GER and regurgitation do not need medical treatment.
- Most will need parental reassurance, observation
- Lifestyle modifications
 - Weight loss
 - Avoid large meals (eat small frequent meals)
 - Wait 3 hours after a meal before lying down
 - Refrain from eating food (except liquids) within 3 hours of bedtime.
 - Elevate head of bed by 20 cm
- In infants, dietary treatment helps to decrease regurgitation. This includes:

- Thickened formula and thickening agents
- The addition of rice cereal (1 tablespoon) decreases the volume and frequency of regurgitation
- Upright position after feeding
- Advise against overfeeding babies.
- If persists, refer to next level

Secondary Level

- As above
- Pharmacotherapy:
 - Antacids (Not recommended for routine use in infantile GERD)
 - Proton Pump Inhibitor (omeprazole, esomeprazole): 1-2 mg/kg/day for 4 – 8 weeks. First line
 - If PPIs not available, use H₂ receptor antagonists (cimetidine)
- *DO NOT ROUTINELY USE prokinetic agents such as domperidone, metoclopramide, erythromycin, cisapride, and bethanechol as there is insufficient evidence to support their use.*
- ***The goal for medical therapy is to use the lowest doses for the shortest time possible***

If persists, refer to the next level

Tertiary Level

- As above
- Surgery indications include:
 - GERD with life-threatening complications such as apnea or an apparent life-threatening event (ALTE) after failure of optimal medical treatment.
 - Symptoms refractory to optimal therapy after appropriate evaluation
 - Chronic conditions (i.e., neurologic impairment, CP) with a significant risk of GERD-related complications
 - Need for chronic pharmacotherapy to control signs and/or symptoms of GERD beyond the age of 2 to 3 years
 - Poor compliance to medication
 - Barrett's esophagus
- Refer to gastroenterologist

Follow up

- Nutrition and growth
- Monitor complications of treatment

PEPTIC ULCER DISEASE (PUD)

Definition

PUD is a spectrum of acid-related disorders that can affect the esophagus, stomach, and duodenum leading to mucosal barrier injury.

Risk factors / causes

- Extreme physiologic stress, including trauma and sepsis
- Use of medications such as steroids, nonsteroidal anti-inflammatory drugs (NSAIDs)
- Hypersecretory state as in Zollinger-Ellison syndrome
- H. pylori infection
- Alcohol abuse (especially in the setting of psychiatric disorders)
- Smoking
- Psychological and work-related stress

Prevention and Health Promotion

- Early diagnosis
- Avoid prolonged use of NSAIDs or steroids without health practitioner guidance
- Proton pump inhibitor use in cases of chronic use of NSAIDs or steroids.
- Promote health literacy, and key health messages

Signs and symptoms

- Irritability
- Generalized abdominal pain
- Poorly localized abdominal pain (children will often have difficulty describing their symptoms)
- Epigastric abdominal pain
- Dyspepsia
- Vomiting
- Emesis
- Hematemesis
- Gastroesophageal reflux

Red flags in PUD (should alert the physician that a child may truly have gastritis or PUD)

- Hematemesis
- Involuntary weight loss
- Nocturnal awakening
- Poor appetite or early satiety
- Anemia (iron deficient)
- Epigastric tenderness

Investigations

- FBC
- H. pylori test (stool antigen test or endoscopic biopsy with rapid urea testing)
- Endoscopy with biopsy
- Occult blood in stool examination

Differential diagnosis

- Oesophagitis
- Functional dyspepsia
- Gastritis
- Gastroenteritis
- Gastroesophageal disease

Management

Primary Level

- Stabilize patients
- Discontinue aggravating medications e.g NSAIDs, aspirin
- Administer antacids
- Refer all patients with suspected PUD to next level of care

Secondary Level

- As above
- Treat underlying conditions.
- H. Pylori eradication if confirmed.
- Pharmacotherapy:
 - Antacids
 - Proton Pump Inhibitor (omeprazole, esomeprazole) in older children: 1-2 mg/kg/day – FIRST LINE
 - H₂ receptor agonists (cimetidine)
- Refer all bleeding patients

Tertiary level

- Stabilize patient
- Investigations as above
- Pharmacotherapy as above
- Endoscopy in bleeding patients
- Gastroenterologist review

Follow up

- Follow up endoscopy if indicated.
- Confirmation of H.pylori eradication 4 weeks after eradication therapy.
- Medication and side effects.

CHRONIC DIARRHEA

Definition

Chronic diarrhea is defined as three or more watery stools per day that persist for more than 2 weeks.

Risk factors

- History of infectious diarrhea
- Impaired immune function, primary or secondary immunodeficiency
- Underlying disease with fecal loading, such as Hirschsprung disease
- Young age < 5 years
- Malnutrition
- Lack of breastfeeding
- Previous antibiotic use
- Food allergies

Causes

Secretory diarrhea

- Infections (rotavirus, adenovirus, cholera, entero-toxigenic escherichia coli (ETEC), clostridium, giardia, cryptosporidium)
- Neuroendocrine disorders (Vasoactive intestinal peptide (VIP) secreting tumors e.g. neuroblastoma, pheochromocytoma)
- Endocrine disorders (hyperthyroidism, addison disease,)
- Congenital diarrheas (congenital sodium diarrhoea, congenital chloride diarrhea, Tufting enteropathy, Microvillous inclusion disease)

Malabsorption / maldigestion

- Infections (giardiasis, small intestinal bacterial overgrowth (SIBO), tropical sprue, whipple disease)
- Galactosemia
- Ileal resection
- Exocrine pancreatic insufficiency e.g. cystic fibrosis
- Coeliac disease
- Causes of protein losing enteropathies (infections e.g. Tb, structural anomalies eg intestinal lymphangiectasia)

Inflammatory diarrhea

- Infections (shigella, salmonella, E.coli, e.t.c)
- Inflammatory bowel disease (Ulcerative Colitis, Crohn disease)
- Food allergy

Osmotic diarrhea

- Lactose intolerance
- Osmotic laxatives
- Fructose intolerance

Functional Diarrhoeal disorders

- Irritable bowel syndrome
- Toddler diarrhea

Prevention / Promotion

- Promote breastfeeding
- Water and sanitation hygiene (WASH)
- Vaccination
- Avoid unnecessary antibiotic use
- Restrict ingestion of large amounts of fruit juices

Signs and symptoms

- Abdominal pain
- Weight loss / failure to thrive
- Fever
- Alternating diarrhea and constipation
- Increased flatulence
- Abdominal bloating
- Other findings related to the specific etiology

Investigations

- Assess for malnutrition and other comorbid conditions e.g TB
- Stool studies
 - Stool microscopy (WBC, bacteria stain, parasite identification)
 - Stool culture
 - Perform fecal leukocyte, calprotectin, and lactoferrin studies and a Fecal Occult Blood Test.
 - Consider further studies to help classify diarrhea: e.g., fecal fat estimation, stool osmotic gap (differentiates osmotic from secretory diarrhea. Stool osmolar gap <50 indicates secretory diarrhea), stool pH (if < 6 suggests carbohydrate malabsorption).
 - Stool alpha 1 antitrypsin >0.5mg/g suggests a protein losing enteropathy
 - Stool elastase level <200mcg/g suggest pancreatic insufficiency (note loose stool may have a dilution effect and give a false low elastase level)
- Blood tests:
 - HIV test
 - FBC & differential count & diagnostic studies for anemia, acanthocytes on peripheral smear may suggest fat malabsorption
 - Serum electrolytes including calcium, magnesium, phosphates, liver blood profile
 - ESR / CRP
 - Blood gas, random blood sugar
- Imaging studies - Use imaging studies to evaluate red flags in diarrhea and consider initially to rule out structural disease.
 - CT abdomen or MRI abdomen with enterography
- Endoscopy / colonoscopy with biopsy for suspect inflammatory bowel disease, Coeliac disease and congenital diarrheas
- Other investigations specific to the suspected etiology, including immunoglobulin levels (IgA, IgG, IgM as basic screen for primary immune deficiencies)

Management

Primary level

- Correct dehydration and refer

Secondary

- Investigations as above
- Correct dehydration
- Treat infectious causes / malnutrition
- Refer if diarrhea persists or non-infectious etiology identified

Tertiary

- Investigate as above
- Correct dehydration and electrolyte imbalances
- Treat the underlying causes
- Consult gastroenterologist for complex conditions

Follow up

- Nutrition and growth
- Refer to relevant clinics

CONSTIPATION

Definition

Constipation is a delay or difficulty in defecation, for 2 or more weeks, which is sufficient to cause significant distress to the patient.

Risk Factors / Causes

Usually multifactorial:

- Includes environmental conditions e.g. diet
- Physical disabilities, e.g. cerebral palsy
- Painful or frightening defecation
- Age difference risk factors are as below:
 - Toddlers
 - Dietary changes (breastmilk to formula or cow's milk) lead to dry hard stools with fissures and pain.
 - Toilet training: Excessive parental pressure, anxiety
 - Older children
 - Unpleasant toilet facilities away from home
 - Sexual abuse
 - Trauma to the perianal area
 - Voluntary withholding while playing

Prevention and Promotion

- Encourage a high fibre diet, including beans, vegetables, fruits, whole grain cereals.
- Encourage the child to eat fewer foods with low fiber such as processed food.
- Encourage the child to drink plenty of fluids.
- Encourage the child to stay active and get regular exercise.
- Schedule time for toilet visits.

Signs and symptoms

- A history and physical examination are usually sufficient to distinguish functional constipation from constipation caused by an organic condition.
- The Rome IV criteria are the most accepted criteria for diagnosing childhood constipation.

Rome IV diagnostic criteria for diagnosing functional constipation in children

At least two of the following in a child with a developmental age younger than four years*

- Two or fewer bowel movements per week
- At least one episode of incontinence per week
- At least one episode of incontinence per week after the acquisition of toileting skills
- History of excessive stool retention
- History of painful or hard bowel movements
- Presence of a large fecal mass in the rectum
- History of large diameter of stools that may obstruct the toilet

At least two of the following in a child with a developmental age of 4 years or older with insufficient criteria for irritable bowel syndrome[#]

- Two or fewer bowel movements in the toilet per week
- At least one episode of fecal incontinence per week
- History of retentive posturing or excessive voluntary stool retention
- History of painful bowel movement
- Presence of a large stool mass in the rectum
- History of large diameter of stool that may obstruct the toilet

*Criteria must be fulfilled for at least 1 month.

Criteria must be fulfilled at least once a week for a least 1 month

Further evaluation may be warranted in children with red flags that might suggest an organic etiology *as below:*

| Red Flags | Suggested diagnoses |
|--|--|
| <i>Age of onset ≤ 1 month</i> | Anorectal malformation or spine malformation, Hirschprung's Disease (HD), allergy, metabolic/endocrine condition |
| <i>Delayed passage of meconium more than 48hrs after birth</i> | HD, cystic fibrosis, anorectal malformation, spine malformation, congenital hypothyroidism |
| <i>Failure to Thrive</i> | HD, malabsorption, cystic fibrosis, metabolic condition |
| <i>Abdominal distention</i> | HD, impaction |
| <i>Sacral dimple covered by a tuft of hair abnormal neurological exam</i> | Spinal cord abnormality |
| <i>Extra-intestinal symptoms like vomiting, and ill appearance, anaemia, jaundice, clubbing, respiratory problems, joint disease</i> | May indicate an organic cause, e.g. HD, Coeliac ds |
| <i>Gushing of stool with rectal examination</i> | HD |
| <i>No response to conventional treatment</i> | HD, spinal cord problem |

Investigations

- Review growth chart to assess growth
- FBC
- TSH and T4 can screen for hypothyroidism
- Contrast enema to evaluate for Hirschsprung disease (HD)
- Abdominal ultrasonography (if not available then X-ray abdomen) to show fecal impaction (in a child whose abdominal examination is difficult but is not done routinely)
- Magnetic resonance imaging of the spine may be necessary to evaluate for a tethered cord, spinal cord tumor, or sacral agenesis.
- Rectal biopsy

Differential Diagnosis

- Functional constipation
- HD
- Anatomical malformation (colon/rectal stenosis/ imperforate anus)
- Spinal cord abnormalities (MMC)
- Cerebral palsy
- Hypothyroidism
- Hypercalcemia, hypokalaemia, other electrolyte abnormalities
- Breast fed children or formula fed children
- Drugs e.g. opioids, phenobarbital
- Cow's milk protein intolerance
- Coeliac disease
- Inflammatory bowel disease

Management

Primary level

- Health promotion steps
- Patients with red flags or suspected organic causes should be referred to the Secondary and Tertiary Level of Care

Secondary / Tertiary Level

- Algorithms for the evaluation and management of constipation in infants and older children are presented in Figures 1 and 2.

Disimpaction (enema)

- The first phase of treatment is to empty the hard stool from the colon, also known as disimpaction.
- In the past, manual removal, suppositories, and enemas were common methods during this phase of treatment. Polyethylene glycol (PEG 3350) has become the first treatment of functional constipation due to its efficacy, safety profile, and because it is well tolerated.
- A reasonable dose is 1 to 1.5 grams per kilogram PEG 3350 mixed with 200 mL water or juice.
- Patients should be encouraged to drink this over 3 hours, if possible.
- If there has not been a significant response to this treatment, the patient can repeat the dose the next day.
- If there is no response after two days of treatment or significant abdominal discomfort, persistent vomiting, or any other concerns, the family should present for follow-up and reevaluation.
- Below is a summary of therapies for dis-impaction in children:

Therapies for disimpaction in children

| Therapy | Dose |
|----------|------|
| Osmotics | |

| | |
|----------------------------------|---|
| Polyethylene glycol 3350 | 1.5g/kg/day |
| Lactulose | 1-3 ml/kg/day of 3.3g/5ml solution |
| Stimulants | |
| Bisacodyl | Over 2 years: 5 – 15 mg (1 – 3 tablets) per day in a single dose |
| Enema (one per day) | |
| Saline | 5 – 10 mL per kg |
| Mineral oil | 15 – 30 mL per year of age up to 240 mL |
| Suppository (one per day) | |
| Bisacodyl | ≥ 2 years: 5 to 10 mg (½ to 1 suppository) |
| Glycerin | ½ to 1 infant suppository Adult suppository for those older than 6 years |

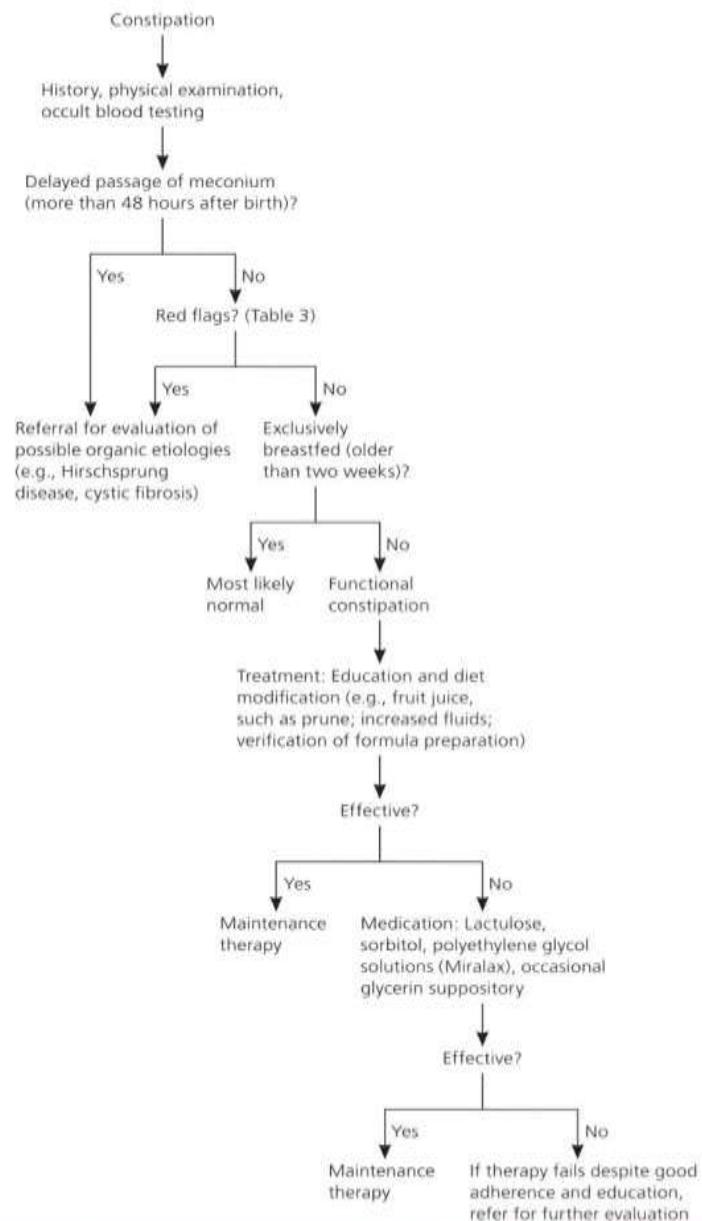
Maintenance Therapy

- In the second phase of treatment, the goal is to keep the stool very soft, preventing re-accumulation of hard stool while the colon returns to normal size and function. Drugs in this phase are oral medications.
- Osmotic laxatives
 - Polyethylene glycol (PEG) 3350 at 0.2-0.8 g/Kg/day
 - Lactulose at 1- 3 mL /kg/day
 - Magnesium hydroxide at 0.5-3 mL/kg/day
- Stool Softeners
 - Docusate sodium at 5 mg/kg/day
 - Mineral oil (lubricant) at 1-3 mL/Kg/day
- Stimulant laxative for rescue therapy in addition or alone (duration less than 30 days)
 - Senna at 2.5-7.5 mL/day
 - Bisacodyl at 5-10 mg/day
- Non-Pharmacological - Same as preventative measures outlined above.

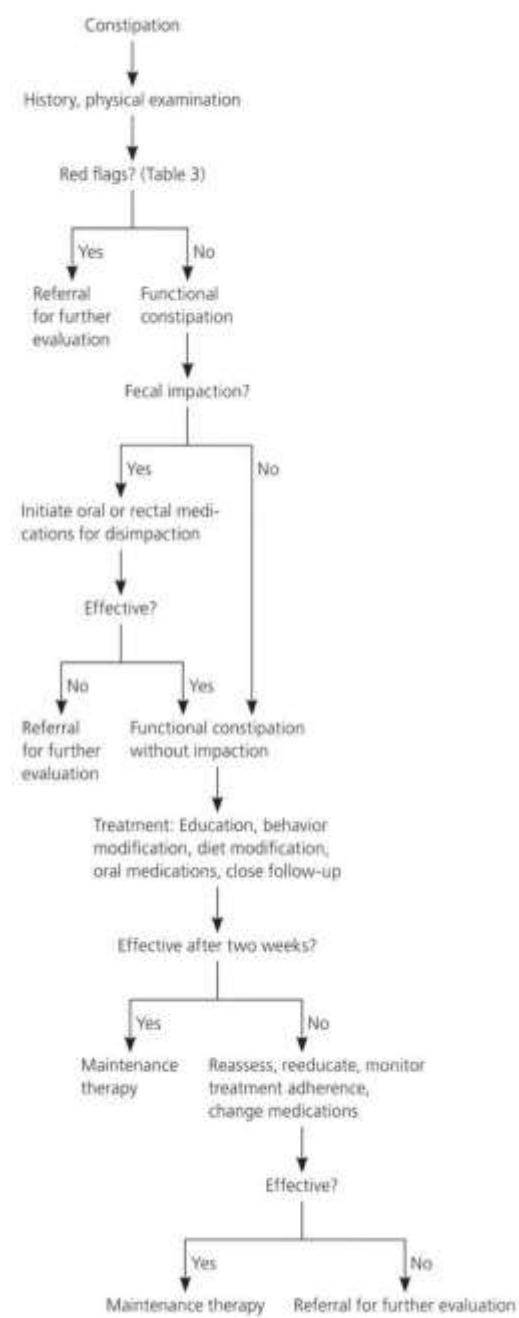
Follow up

- Assessing for complications
- Medication side effects
- Growth and development

Constipation in Infants Younger than Six Months



Constipation in Children Six Months and Older



FOOD ALLERGY

Definition

- Food allergy is an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food. Can be:
 - IgE mediated Type 1 hypersensitivity reaction (immediate onset within minutes - 2hrs of ingestion)
 - OR**
 - Mixed IgE/non-IgE mediated reactions (delayed onset hours to days after ingestion)
- Food intolerance is an adverse reaction to food or a food component that lacks an identified immunologic pathophysiology.

Risk Factors / Causes

- Peanuts / tree nuts
- Fish / Seafood
- Milk (bovine / soy)
- Eggs
- Seeds (maize) and other foods
- Fruits
- Positive Family history

Prevention / Promotion

- Education of children, parents and carers is the mainstay of dietary avoidance advice. Educate on:
 - Avoidance of known food allergens by checking common ingredients and reading food labels.
 - Appropriate safe, cost-effective, freely available and nutritionally adequate substitutes for the avoided foods.
- Encourage exclusive breastfeeding for the first 4-6 months.
- Early introduction of complementary foods (including potential allergens) by 4-6 months of age (not applicable to infants experiencing allergic reactions).
- Health talks and increased awareness.
- Encourage susceptible children not to eat food which is not prepared by a person who is aware of their conditions.
- Advocate for availability of epi-pens and teach the parents / child / caregiver how to administer.

Signs and symptoms

IgE mediated food allergy

- Symptoms usually recur on exposure to the food on every occasion. They may be mild or severe, associated with anaphylaxis.
 - Skin (most common): pruritus, urticaria, atopic dermatitis, exanthem, angioedema
 - Respiratory: rhinitis, sneezing, nasal congestion, dyspnoea, wheezing, laryngeal edema (**CAN BE FATAL**)
 - Gastrointestinal: nausea, vomiting, abdominal pain, diarrhoea, oral itching/swelling

- Cardiovascular: hypotension, tachycardia, dysrhythmias
- CNS: Headache

Non-IgE / mixed food allergy

- Symptoms typically limited to skin and gastrointestinal tract.
 - Skin: atopic dermatitis
 - Gastrointestinal: abdominal pain, vomiting, diarrhoea, bloody stools, failure to thrive, eosinophilic oesophagitis, food protein-induced enterocolitis syndrome, allergic proctocolitis and enteropathy syndromes.
- A clear cause-effect relationship between exposure to the suspected food and symptoms is not always possible, as symptoms develop over time and are more chronic in nature.

Investigations

- Patient History VITAL in establishing diagnosis
- FBC
- *Suspected IgE mediated food allergies*
 - Skin prick testing
 - Serum specific IgE antibodies to suspected foods are used to prove sensitization. Diagnosis requires a clear correlation between the test result and clinical reaction (by positive history or food challenge).
 - Total IgE antibody serum levels
 - If above tests are inconclusive try elimination diet: the suspected allergens are eliminated from the patient diet while being observed for an improvement in symptoms without the need for medication.
- *Non IgE mediated food allergies*
 - No validated tests exist to confirm non-IgE- or mixed IgE- / non-IgE-mediated food allergies.
 - In certain cases endoscopy with biopsy is indicated to evaluate the response to dietary changes.

Differential diagnosis

- psychological reactions (food aversion)
- organic reactions (e.g. peptic ulcer disease)
- anatomical reactions (e.g. strictures)
- toxic reactions (e.g. food poisoning)
- non-toxic reactions

Management

Primary / secondary level

- ABCDE approach if acutely unstable
- Manage anaphylaxis (refer to section in emergency chapter)
- Perform thorough history
- REFER all patients with suspected food allergy

Tertiary Level

- ABCDE approach if acutely unstable
- Manage anaphylaxis (refer to section in emergency chapter)

- Perform thorough history
- Eliminate offending food from diet
- Provide with auto injectable epinephrine (EPI-PEN) for emergency home treatment
 - 8 - 25 kg 0.15mg/dose
 - >25 kg 0.3mg/dose
- Refer to dietician / allergologist / gastroenterologist for further management tailored to each child

Follow-up

- Continued counselling and education.
 - Severity of future allergic reactions is not accurately predicted by past history or allergy test results.
- Refill of EpiPen and continued family training
- Provision of individualised written instructions / care plan on the indications for and method of administration of emergency medication.
- The diagnosis of food allergy should, with permission, be communicated to all relevant caregivers, including school teachers.
- Patients should be encouraged to join an appropriate patient support organisation.

INFLAMMATORY BOWEL DISEASE

Definition

- Inflammatory bowel diseases (IBD) is a spectrum of diseases characterised by recurrent inflammation of the intestine.
- Can be categorised into three main subtypes:
 - Crohn's Disease is characterised by transmural, granulomatous inflammation affecting any part of the gastrointestinal tract from the mouth to the anus, often discontinuously.
 - Ulcerative Colitis (UC) is limited to the colon and consists of superficial ulceration of the bowel mucosa.
 - Inflammatory bowel disease unclassified (IBDU) describes patients with chronic colitis within the spectrum of IBD but in the absence of distinguishing features of either CD or UC.
 - <10 years: early onset IBD
 - <6 years: very early onset IBD (VEO-IBD) – higher likelihood of underlying monogenic aetiology or primary immune deficiency

Risk factors / Causes

- Low-fibre, high-sugar diets
- Sedentary lifestyle
- Diets poor in fruits and vegetables and high in animal fats and sugar
- Emulsifiers commonly found in processed food
- Antibiotic use in early childhood and dysbiosis of the gut microbiota
- Vitamin D deficiency
- Intestinal infections
- Stress
- Sleep deprivation
- Other autoimmune diseases e.g. enthesitis arthritis
- Genetics - having a first- or second-degree relative with IBD
 - Onset below 6 years of age

Prevention / Promotion

- Health Education
- Over-the-counter and prescription medicines should be avoided
- Avoid taking ibuprofen or other NSAIDs.
- Avoid unnecessary antibiotic use

Signs and symptoms

Intestinal Manifestations:

- Abdominal pain
- Abdominal distension (UC > CD)
- Right iliac fossa mass (CD)
- Diarrhea ± blood/mucus; urgency and tenesmus (proctitis)
- Rectal bleeding
- Perirectal disease, fistula
- Nausea/vomiting
- Anorexia; weight loss; lethargy (CD > UC)
- Aphthous oral ulcers (CD > UC)
- Fever

- Growth retardation (CD >> UC)
 - May begin before the development of specific gastrointestinal symptoms
 - May be the only presenting clinical symptom

Extraintestinal manifestations:

- Arthralgia; arthritis; ankylosing spondylitis
- Enthesitis; myositis; erythema nodosum; pyoderma gangrenosum
- Uveitis; episcleritis; iritis; conjunctivitis
- Finger clubbing
- Anemia
- Thromboembolism; vasculitis
- Urinary tract obstruction; renal stones
- Delayed puberty; hepatic disease
- Nutritional deficiencies; iron, vitamin D, vitamin B₁₂ and folic acid deficiency
- Depression and anxiety
- Hepatobiliary manifestations: primary sclerosing cholangitis

Table: Differential diagnosis of presenting symptoms of inflammatory bowel disease

| Primary presenting symptom | Diagnostic consideration |
|--|---|
| <i>Right lower quadrant abdominal pain, with or without mass</i> | Appendicitis, abscess, infection (e.g., <i>Campylobacter</i> , <i>Yersinia</i>), lymphoma, intussusception, mesenteric adenitis, Meckel diverticulum, ovarian cyst |
| <i>Chronic perumbilical or epigastric abdominal pain</i> | Irritable bowel syndrome, constipation, lactose intolerance, peptic disease, coeliac disease |
| <i>Rectal bleeding, no diarrhea</i> | Fissure, polyp, Meckel diverticulum, rectal ulcer syndrome, vascular abnormalities |
| <i>Bloody diarrhea</i> | Infection (intestinal TB, amoeba, CMV), hemolytic-uremic syndrome, Henoch-Schönlein purpura, Cow Milk Protein Allergy |
| <i>Watery diarrhea</i> | Irritable bowel, lactose intolerance, giardiasis, <i>Cryptosporidium</i> , sorbitol, laxatives |
| <i>Perirectal disease</i> | Fissure, hemorrhoid (rare), streptococcal infection, condyloma (rare) |
| <i>Growth delay</i> | Coeliac disease, endocrinopathy |
| <i>Anorexia, weight loss</i> | Anorexia nervosa |

| | |
|----------------------------|--|
| <i>Arthritis</i> | Collagen vascular disease, infection |
| <i>Liver abnormalities</i> | Chronic hepatitis (Infection, Autoimmune hepatitis, Coeliac ds, Wilsons Disease) |

Investigations / Evaluation

- Urinalysis
- Blood tests
 - Full blood count
 - ESR / CRP
 - ALT, AST, GGT
 - Total protein / Albumin
- Stool tests
 - Microscopy, culture and sensitivity
 - Stool for occult blood
 - Stool calprotectin or lactoferrin
- TB screening tests
- Imaging (for localization of small bowel disease)
 - Upper GI series / small bowel follow through
 - Abdominal CT with oral contrast
 - Magnetic resonance enterography (MRE)
- Endoscopy
 - Ileo-colonoscopy with biopsies
 - Upper endoscopy with biopsies
- Specialised tests depending on clinical findings:
 - Perinuclear antineutrophil cytoplasmic antibody (P-ANCA) - UC
 - anti-saccharomyces cerevisiae (ASCA) - CD
 - Lactose/glucose hydrogen breath test
 - 72hr fecal fat quantification
 - Stool alpha-1 antitrypsin
 - Cholinesterase
 - Serum iron, calcium, magnesium, folate, zinc, vitamins A/E/B12

Treatment

Primary / Secondary Level

- Refer suspected cases

Tertiary level

- Supportive treatment
- If severely ill, keep nil by mouth with IV hydration +/- parenteral nutrition
- Provide adequate pain relief
- Pharmacologic treatment
 1. Oral 3-aminosalicylic acid (ASA) dimers (mesalazine and sulfasalazine)

- Can be used to induce and maintain mild-moderate CD colonic inflammation.
2. Corticosteroids (induction therapy)
- Oral prednisone 1 mg/kg daily (maximum of 40 mg but up to 60 mg/day), intravenous therapy for severe disease: methylprednisolone at 1 to 1.5 mg/kg (maximum daily dose of 60 mg)
OR
Budesonide 9 mg/day (Compared with prednisone, it has fewer corticosteroid side effects so can be used for a longer period)
For 6 weeks tapered over 2 weeks for the treatment of ileocecal disease.
 - Corticosteroid enemas can be used to treat rectal disease.
 - *Glucocorticoids are not effective as maintenance therapy and are associated with significant side effects.*
3. Biological Therapy
- Anti-TNF α antibodies (Infliximab, Adalimumab, Certolizumab). Indications are:
 - Moderate-to-severe luminal CD
 - Corticosteroid-dependent or corticosteroid-refractory disease
 - Failure of response to immunomodulators
 - Fistulizing disease, especially perianal fistulas
 - Superior outcomes may be achieved if used within 3 months of diagnosis
4. Antibiotics (Ciprofloxacin or metronidazole may be helpful, especially in fistula disease)
5. Dietary treatment
- Modular/elemental diets to induce remission (CD > UC)
 - Dietary supplementation to minimise poor growth and correct specific nutritional deficiencies: vitamin D, vitamin B12, folic acid, mineral supplements like iron
 - Consult gastroenterologist / dietician / surgeon.

Follow-up

- Adherence to the prescribed medications for IBD is critical for disease control
- Advise on appropriate diet
- Patients should drink enough fluids to be well hydrated
- If patients are on steroids, they should get plenty of calcium in the diet to maintain healthy bones. Consider taking a calcium supplement with vitamin D
- Patients should keep a food diary to identify foods that make symptoms better or worse, and avoid foods that cause symptoms

COELIAC DISEASE

Definition

Coeliac disease (CD) is an immune-mediated enteropathy due to intolerance to gluten protein (present in wheat, barley and rye).

Causes / risk factors

- Consumption of wheat, rye and barley-containing grains by genetically susceptible individuals.
- Genetic factors: increased incidence in girls, higher prevalence of CD among first-degree relatives (occurrence of multiple cases in families)
- Associated conditions: Down syndrome, insulin-dependent type 1 diabetes mellitus, Hashimoto thyroiditis, Addison disease, selective IgA deficiency

Prevention and Promotion

- Avoid gluten exposure
- Family members should get screened for early signs of CD
- Educate on appropriate diet

Clinical features.

- Failure to thrive
- Chronic diarrhea
- Pale, bulky, floating stools
- Constipation
- Abdominal distension
- Vomiting
- Anorexia
- Irritability
- Later manifestations
 - Anaemia (iron deficiency)
 - Apathy
 - Ascites
 - Peripheral oedema
 - Short stature
 - Delayed puberty
 - Arthralgia
 - Hypotonia, muscle wasting
 - Specific nutritional disorders (vitamin D, iron)
 - Coeliac crisis: Life threatening dehydration due to diarrhoea accompanying malabsorption

Investigations

Diagnosis is confirmed by positive tissue transglutaminase IgA antibodies + positive mucosal histology and full recovery on gluten-free diet.

- Serum
 - Antiendomysial antibodies, e.g tissue transglutaminase and antireticulin IgA antibodies (beware of false negatives in IgA deficiency)
 - Total IgA
 - Antigliadin antibody
- Endoscopy with biopsy of duodenum
 - shows lymphocyte infiltration, diffuse subtotal villous atrophy, crypt hyperplasia

Differential diagnosis

- Transient gluten intolerance post gastroenteritis
- Cow's milk protein intolerance
- Giardiasis
- Crohn's disease

Management

Primary Level

- Manage dehydration and refer

Secondary / Tertiary level

- Supportive management
 - Treat life threatening dehydration or anaemia (refer to emergency section)
- Gluten-free diet under supervision of a dietician
 - Rice, maize, and buckwheat are nontoxic and are usually used as wheat substitutes. Chestnut, cassava, sorghum, millet, teff, quinoa, and amaranth are other safe starchy foods.
 - Gluten avoidance should be lifelong.
- Nutritional supplements (vitamin D, iron) may be required
- Consult Gastroenterologist

ACUTE LIVER FAILURE

Definition

- Coagulopathy with INR ≥ 1.5 with encephalopathy or INR ≥ 2 without encephalopathy due to a liver cause, not correctable by intravenous vitamin K, with biochemical evidence of acute liver injury and no evidence of chronic liver disease.

Subtypes:

- Hyperacute liver failure (0 - 1 weeks)
- Acute (fulminant) liver failure (8 - 28 days)
- Subacute liver failure (4 - 12 weeks)

Risk factors / Causes

- Idiopathic (20-45% of cases)
- Viral Infections (Hepatitis A/B/B+D/E, CMV, EBV, HSV, Adenovirus, varicella, measles)
- Non-viral infections (Salmonella, TB, Malaria, gram negative sepsis, Toxoplasmosis)
- Hepatotoxic medications
 - Acetaminophen
 - Antimicrobials (amoxicillin, ciprofloxacin, cephalosporins, TB treatment, Ketoconazole, antiretrovirals)
 - Anticonvulsants (phenytoin, carbamazepine, valproic acid)
 - Chemotherapy
- Other toxins (herbal supplements, alcohol, aflatoxins, cocaine, mushroom poisoning)
- Malignant infiltration (HLH, Leukemia, lymphoma)
- Ischaemia
 - Acute circulatory failure (shock, cardiac failure, myocarditis)
 - Tissue hypoxia due to respiratory failure
 - Budd-Chiari syndrome
 - Ischemic hepatitis
- Genetic / metabolic (galactosaemia, Wilson disease, inborn urea cycle defects)
- Autoimmune hepatitis
- Gestational Alloimmune liver disease (neonatal acute liver failure, with haemachromatosis)

Signs and symptoms

Presentation mostly non-specific and clinicians should maintain a high level of suspicion. Signs / symptoms include:

- Fatigue, lethargy, malaise
- Jaundice
- Anorexia
- Nausea, vomiting
- Abdominal pain (RUQ pain or generalised pain)
- Signs of hepatic encephalopathy
 - Altered level of consciousness
 - Asterixis
- Symptoms of cerebral oedema
- Pruritus
- Features of underlying etiology

Health Promotion / prevention

- Vaccination
- Educate on danger of herbal remedies
- Drug and toxin storage in appropriate places away from children
- Careful medication use in communities and hospitals
- Educate on danger of alcohol abuse
- Education on appropriate storage of groundnuts and maize for consumption to reduce aflatoxin exposure

Investigations

- Blood tests
 - Random blood sugar
 - HIV test
 - Malaria screen
 - Full blood count
 - CRP
 - Liver chemistries - ALT, AST, GGT, ALP, Bilirubin, Albumin, Total protein
 - Coagulation Tests - PT / INR
 - Serum Electrolytes, Urea, Creatinine
 - Blood gas with lactate
 - Serum ammonia
 - Hepatitis A, B, C, E, HSV, , syphilis
 - Toxicology screen (e.g. acetaminophen levels)
 - Other tests if indicated:
 - Older children: autoimmune screen and Wilson Diseases screen (caeruloplasmin)
 - ferritin level and transferrin saturations, triglycerides and metabolic screen- urine reducing substances, urine organic acids, serum amino acids (In babies <6 months with liver failure)
- Imaging (findings vary as liver failure progresses)
 - Abdominal USS
 - heterogeneously decreased liver echogenicity (liver necrosis), ascites
 - In patients who have been sick for at least 7 days, Ultrasound may show a nodular surface which can be mistaken for cirrhosis.
 - Doppler ultrasound - to identify underlying cause e.g portal vein thrombosis / hepatic ischemia
- Liver biopsy indications
 - To distinguish between acute liver failure and chronic liver disease if the diagnosis is uncertain
 - If the suspected underlying aetiology requires specific management e.g. autoimmune hepatitis
- Other tests for specific etiologies can be done based on clinical suspicion.

Differential diagnosis

- Other encephalitis or encephalopathy e.g. drugs and toxins, uremic encephalopathy
- Sepsis
- Other coagulation disorders

Management

Primary Level

- Emergency Stabilisation ABCDE approach
 - Volume repletion (Normal Saline 20mls/kg bolus)
 - Treat hypoglycaemia
- REFER

Secondary Level

- ABCDE approach
- Aggressive supportive care
 - Volume repletion (Normal Saline 20mls/kg bolus - repeat if necessary)
 - Treat hypoglycaemia
 - Treat electrolyte disturbances
 - Optimise Nutrition (maintain 1-2 mg/kg/day protein intake)
 - Stress ulcer prophylaxis to prevent GI bleeding
- Control Hyperammonemia
 - Lactulose 0.5mls/kg/dose - titrate to produce 2-4 loose stools daily
- Neuroprotective measures
 - Elevate head of bed to 30°
 - Maintenance of normoxia, normocapnia, normotension, normothermia, euglycemia
- Correct coagulopathy
 - IV Vitamin K (300 mcg/kg/day, [max 10mg] for at least 3 days)
 - FFP transfusion (15mls / kg) recommended if active bleeding
- Infection control - antibiotic prophylaxis (ceftriaxone 50 mg/kg/day)
- Refer to tertiary facility

Tertiary Level

- ABCDE approach
 - Early intubation in patients with rapidly progressing encephalopathy
- Aggressive supportive care
 - Volume repletion (Normal Saline 20mls/kg bolus - repeat if necessary)
 - Start vasopressors if not responsive to fluids
 - Treat hypoglycaemia
 - Treat electrolyte disturbances
 - Optimise Nutrition (maintain 1-2 mg/kg/day protein intake)
 - Stress ulcer prophylaxis to prevent GI bleeding
- Neuroprotective measures
 - Maintenance of normoxia, normocapnia, normotension, normothermia, euglycemia
 - Elevate head of bed to 30°
- Manage high ICP
 - Mannitol (0.5 - 1g / kg) IV over 30 minutes. Repeat 8hrly.
 - 3% Hypertonic saline (0.5-3mls/kg/hr)

- Control Hyperammonemia
 - Lactulose 0.5mls/kg/dose - titrate to produce 2-4 loose stools daily
- Correct coagulopathy
 - IV Vitamin K (300 mcg/kg/day, [max 10mg] for at least 3 days)
 - FFP transfusion (15mls / kg) if bleeding actively
- Infection control - antibiotic prophylaxis (ceftriaxone 50 mg/kg/day)
- Manage kidney injury
 - optimise hemodynamic support
 - renal replacement therapy if necessary
- N-acetylcysteine in acetaminophen toxicity and when cause unknown
- Treat underlying cause

Follow up

- Check for progress of disease / complications

LIVER CIRRHOSIS

Definition

Liver cirrhosis is the advanced stage of liver fibrosis and is the common endpoint of many different liver diseases.

Risk factors / causes

- Cholestatic liver disease e.g. biliary atresia, choledochal cyst
- Metabolic liver disease e.g. Wilsons disease, glycogen storage disease
- Vascular disease e.g. heart failure
- Drugs
- Herbal medication
- Toxins
- Infections
- Autoimmune hepatitis

Promotion / Prevention

- Avoid exposure to risk factors that are associated with acute liver injury / disease.
- Encourage vaccination according to Extended Programme on Immunization (EPI)
- Routine screening of pregnant women for Hepatitis B and appropriate treatment of exposed babies.
- Alcohol education for adolescents
- Early referral of infants with congenital liver diseases.

Signs and symptoms

- Patients initially asymptomatic.
- Fatigue, malaise, anorexia
- Weight loss / malnutrition / signs of micronutrient deficiency (fat soluble vitamins A, D, E, K)
- Peripheral oedema / anasarca
- Fetur hepaticus
- Abdominal features (Jaundice, nausea, vomiting, abdominal distension, hepatomegaly, splenomegaly, ascites, pale stools, dark urine) - liver can be shrunken, small and impalpable in advanced cirrhosis.
- Skin features (spider naevi, palmar erythema, and prominent periumbilical veins, caput medusae, petechiae, purpura, dry and atrophic skin, scratch marks)
- Digital clubbing, leukonychia, asterixis
- Variceal bleed with hematemesis, coffee ground vomitus, and/or melena
- Recurrent epistaxis and spontaneous bruising/ bleeding
- Signs of hyperestrogenism
 - Males - gynaecomastia, hypogonadism, feminisation
 - Females - amenorrhoea

Investigations

- Blood tests
 - Random blood sugar
 - HIV test
 - Full blood count and grouping and cross matching if indicated
 - Liver chemistries - ALT, AST, GGT, ALP, Bilirubin, Albumin, Total protein
 - Coagulation Tests - PT / INR
 - Serum Electrolytes including calcium, magnesium, phosphate
 - Urea, Creatinine

- Hepatitis B, C, Tb, Syphilis, Schistosomiasis
 - Toxicology screen (e.g. acetaminophen levels)
 - *Alpha-fetoprotein (AFP), LDH*
- Imaging (findings vary as liver failure progresses)
 - Abdominal USS with doppler
 - Heterogeneous nodular liver with fibrous septae. May be enlarged and shrunken, portal hypertension, ascites, splenomegaly, increased portosystemic collateral flow.
 - Cardiac echo to exclude cirrhotic cardiomyopathy
 - Plain radiographs of the wrist and knee to demonstrate bone age and/or the development of osteopenia or osteomalacia (rickets/hepatic osteodystrophy)
- Endoscopy
 - Upper GI Endoscopy to identify esophageal varices and peptic ulcer
 - Lower GI Endoscopy to identify source of bleeding
- Liver biopsy (gold standard). Indications are:
 - In cases of uncertain diagnosis
 - Grading and staging of inflammation and fibrosis
 - Monitoring treatment response e.g. in autoimmune hepatitis
 - Evaluation of focal lesions
- Other tests for specific etiologies can be done based on clinical suspicion

Differential diagnosis

See section on risk factors and causes

Management

Primary / secondary level

- Stabilise the patient
- check RBS and correct any hypoglycaemia
- Manage bleeding with Vitamin K (2.5–10 mg/day)
- Nutritional assessment (mid-arm circumference) and provide nutritional support.
- Involve palliative care team
- Refer all undiagnosed chronic cases

Tertiary level (consult a pediatric gastroenterologist)

- Stabilise the patient as above
- Management will depend on underlying cause
- Encourage breastfeeding with supplementation with high-caloric-density feeds (involve dieticians)
- Nasogastric tube if oral feeding cannot meet caloric need.
- Fat soluble vitamin supplementation (age dependent)
 - Vitamin D (3,000–10,000 IU/day)
 - Vitamin K (2.5–10 mg/day)

- Vitamin E (10–20mg/kg/day)
 - Vitamin A (5,000–10,000 IU/day)
- Restrict protein intake in children with end-stage liver disease (approximately 2 to 3 g/kg/day)
- Pruritus (multidrug therapy is often required)
 - Cholestyramine (1 to 4 g daily)
 - Phenobarbitone (5 to 10 mg/kg/day)
- Emesis
 - Ondansetron 2 to 4 mg twice daily (<12 years) or 4 to 8 mg twice daily (12 to 18 years). *Side effects include worsening of liver function tests.*
- Coagulopathy
 - Vitamin K provision and use of FFP, cryoprecipitate, and platelets as required.
- Manage fluid balance and circulatory change (including ascites)
 - Spironolactone (1 to 9 mg/kg/day in two to three divided doses) and furosemide (0.5 to 2 mg/kg/day)
 - Salt and water restriction (70% to 80% of maintenance)

Note: Avoid vigorous diuretic administration or therapeutic paracentesis as these can further decrease the circulating plasma volume, thereby reducing renal perfusion and increasing sodium retention.

- Electrolyte changes and renal failure
 - Correct hypoglycaemia, hypo/hyperkalemia, hyponatremia, hypocalcemia and hypomagnesemia
- Family and psychologic Support
 - Physiotherapy may improve gross motor development
 - Ongoing family education

Palliative care consultation

Follow up

- Check for progress of disease / complications

PORTAL HYPERTENSION (PH)

Definition

PH is defined as a portal venous pressure of greater than 10 mm Hg and occurs when there is increased portal resistance or/and portal blood flow.

It is characterized by splenomegaly, ascites, gastrointestinal varices and encephalopathy.

Causes / Risk factors

Prehepatic:

- Extrahepatic portal venous obstruction (e.g thrombus formation following umbilical venous access)
- Omphalitis
- intra-abdominal infections in the neonatal period

Intra-hepatic:

- congenital hepatic fibrosis or veno-occlusive disease
- infectious hepatitis (hepatitis B and C, schistosomiasis)
- toxin injury (hypervitaminosis A, valproate, methotrexate, phenytoin, alcohol)
- hemochromatosis
- metabolic disease

Posthepatic:

- Hepatic venous outflow obstruction (Budd-Chiari syndrome, extrinsic compression of the hepatic vein from a tumor)
- Hypercoagulable state (myeloproliferative states, polycythemia vera, tumors, hereditary thrombophilia)

Promotion / Prevention

- Vaccination
- Reduction of alcohol intake
- Early treatment of schistosomiasis

Signs and symptoms

See section on cirrhosis

Investigations

- FBC
- LFTs
- Stool microscopy and occult blood
- Ultrasonography of the liver
- Doppler ultrasonography
- Esophagogastroduodenoscopy (EGD); gold standard for the diagnosis of GI lesions from PH
- If indicated, carry out investigations for causes of liver failure and its consequences (see section on cirrhosis)

Differential diagnosis

- Mallory Weiss tears
- PUD

- Nephrogenic ascites
- Tuberculosis
- Sickle Cell disease

Management

Primary / Secondary level

Stabilize the patient and refer

Tertiary level

- Manage acute variceal bleed
 - Nasogastric tube placement to monitoring for ongoing bleeding and to prevent encephalopathy
 - 0.9% saline or Ringer's Lactate and packed red blood cells (Hb goal 7-9gm/dL). Avoid overzealous fluid replacement as this will provoke further bleeding
- Lactulose oral therapy
 - infants: 2 to 6 g/day (2.5 to 10 mL/day) in 2-3 divided doses; adjust dosage to produce 2 to 3 stools/day.
 - Children and Adolescents: 26 - 60 g/day (40 to 90 mL/day) in 2-3 divided doses; adjust dosage to produce 2 to 3 stools/day.
- Intravenous vitamin K, platelets, and fresh frozen plasma (FFP) as required
- Octreotide infusion 1-2mcg/kg bolus followed by 1-2mcg/hr i.v infusion
- Omeprazole 500mcg/kg/day intravenously
- Intravenous ceftriaxone 50mg/kg/day
- Measure prothrombin time (PT) with an internationalized normalized ratio (INR). Administer vitamin K if PT/INR is elevated
- Prophylactic angiotensin II receptor antagonists e.g losartan should be considered for those requiring frequent intervention.

Follow up

- Medication dosing and side effects
- Monitoring PT/INR
- Monitoring variceal haemorrhage

ASCITES

Definition

Ascites is the pathologic accumulation of fluid within the peritoneal cavity.

Risk factors / Causes

Noncirrhotic Ascites:

- Peritoneal inflammation (infections, malignancies, chemical peritonitis [pancreatic and bile-induced ascites])
- Portal venous or lymphatic obstruction (chylous ascites)
- Rupture of intra-abdominal viscera
- Renal (nephrotic syndrome, renal failure)
- Cardiac (pericardial disease, heart failure)
- Hepatic (portal hypertension)

Cirrhotic ascites:

- α1-antitrypsin deficiency, biliary atresia, congenital hepatic fibrosis, neonatal or viral hepatitis, inborn errors of metabolism, storage diseases, autoimmune hepatitis

Prevention / Promotion

- Vaccination
- Reduction of alcohol intake
- Early treatment of schistosomiasis

Signs and symptoms

- Respiratory distress present in severe cases.
- Protuberant abdomen, bulging flanks, or dullness to percussion in the flanks, and everted umbilicus
- Scrotal edema.

Investigations and diagnostic testing

- HIV test
- FBC
- LFTs
- Electrolytes, Urea & Creatinine
- CRP, ESR
- AFP and LDH
- Serum amylase and lipase
- Blood and urine culture
- Screen for TB, Schistosomiasis and syphilis
- Viral serologies (hepatitis A, B, and C, cytomegalovirus, and Epstein–Barr virus).
- Diagnostic paracentesis (10-20mls).
- Abdominal Ultrasonography
- Abdominal CT or MRI is useful in suspected malignancies

Ascites fluid analysis studies

| Condition | Appearance | Protein** | WBCs/ μ L | Other tests |
|----------------------|--|---------------------|---------------|--|
| Cirrhosis | Straw-colored or bile-stained | <25 (95%) | <250 | |
| Heart Failure | Straw-colored | Variable, 15–53 | 1000 | |
| Nephrosis | Straw-colored or chylous | <25 (100%) | <250 | Sudan staining if chylous |
| Neoplasm | Straw-colored, hemorrhagic, or chylous | >25 (75%) | >1000 | Cytology, cell block, peritoneal biopsy |
| Pancreatic ascites | Turbid, chylous, or hemorrhagic | Variable, often >25 | variable | Increased amylase in fluid and serum |
| Biliary ascites | Bile-stained | Variable, <25 | Variable | Increased bilirubin in fluid |
| TB peritonitis | Clear, turbid, hemorrhagic, or chylous | >25 (50%) | >1000 | Stain and culture for acid-fast bacilli, peritoneal biopsy |
| Pyogenic peritonitis | Turbid or purulent | If purulent, >2.5 | >250* | Positive gram stain, culture |

* Normal ascitic fluid contains less than 500 leukocytes/ μ L with less than 250 polymorphonuclear neutrophils (PMN)/ μ L. An elevated PMN count greater than 250 cells/ μ L is a predictor of spontaneous bacterial peritonitis in the absence of bowel perforation.

** Measures in grammes/dL

Differential diagnosis

- Mesenteric cysts
- Omental cysts
- Intestinal duplications
- Fluid-filled intestinal loops
- Large ovarian cysts
- Urinary ascites

Management

Primary level

Stabilise and refer all cases

Secondary level

- Investigate for cause of ascites and manage appropriately
- If no cause established / complicated diagnosis refer to tertiary level for investigations and work up described above.

Tertiary level

- Stabilise
- Salt restriction
- Restrict fluids when the serum sodium level decreases below 125 mEq/L.
 - If fluid resuscitation is indicated, enteral fluids are preferred. **DO NOT give hypertonic intravenous fluids** as these will increase total body sodium and lead to worsening ascites and fluid overload.
- Diuretics
 - Spironolactone
 - 0.5 to 1 mg/kg in infants and 1 to 3 mg/kg in older children (up to 100 mg). It can be increased by 2 mg/kg every 5 to 7 days up to a maximum of 4 to 6 mg/kg/day.
 - Furosemide
 - Added if there is not an adequate response to spironolactone
 - 1 mg/kg (up to 40 mg). Increase dose by 1 mg/kg to a maximum dose of 4 mg/kg until a response is seen
 - Response to diuresis can be assessed by trending daily weights.
- Therapeutic paracentesis
 - Is used in patients unresponsive to medical therapy or if in respiratory distress.
 - Can be used periodically to treat refractory ascites.

Consult gastroenterologist in refractory cases

Follow up

- Review in gastroenterology / general clinic every 3 months
- May need routine ascitic taps if chronic ascites

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CHAPTER 7. HAEMATOLOGY AND ONCOLOGY

NON-TRAUMA BLEEDING

Definition

It is the spontaneous loss of blood into the skin, muscle or mucous membranes.

Risk Factors / Causes

- Factor deficiency
- Malignancy
- Drugs
- Infections- viral infections, bacterial
- Drugs- chemotherapy
- Radiotherapy

Promotion / Prevention

- Early detection and treatment of infections
- Monitor full blood count following radiotherapy and chemotherapy
- Screening of individuals with family history of bleeding
- Prophylactic Factor replacement in Factor deficient individuals

Signs and Symptoms

Thrombocytopenia

- Epistaxis
- Mucus membrane bleeding
- Petechiae
- Small bruises
- Gastrointestinal bleeding
- Menorrhagia

Coagulation disorders

- Deep seated haematomas
- Haemarthrosis
- Renal bleeding
- Intracerebral bleeding

Differential Diagnosis

Decreased platelet production

- Aplastic anaemia
- Marrow infiltration
- Infections (hepatitis, HIV)
- Drugs
- Micro thrombocytopenia
- Bernard -Soulier syndrome

Increase platelet destruction

- Immune thrombocytopenic purpura
- Infection
- Drugs
- Disseminated intravascular coagulation
- Cavernous haemangioma

Ineffective thrombopoiesis

- Vitamin B 12 deficiency
- Folic acid deficiency

Platelet sequestration

- Hypersplenism

Assessment

HISTORY

- Age
 - neonatal: vitamin K, coagulation defects
- Sex
 - male with swollen joints: haemophilia,
 - adolescent females with menorrhagia: Von Willebrand's Disease(VWD)
- Duration
 - Long duration: Factor deficiency, VWD
 - Short duration: ITP, Leukaemia
- Type:
 - petechiae suggests platelet disorder
 - haematoma suggests Factor deficiency
- Site:
 - Joint or muscle bleeding suggests Factor deficiency
 - mucus membrane bleedings suggest low platelets or VWD.
- History of jaundice: Vitamin K deficiency
- History of multiple blood transfusions may suggest bone marrow failure
- History of fever, anaemia, lethargy: bone marrow failure
- Recent history of immunisation: immune thrombocytopenic purpura (ITP).
- Recent history NSAIDS, methylphenidate: thrombocytopenia
- Involvement of male siblings and maternal uncles: Factor deficiency

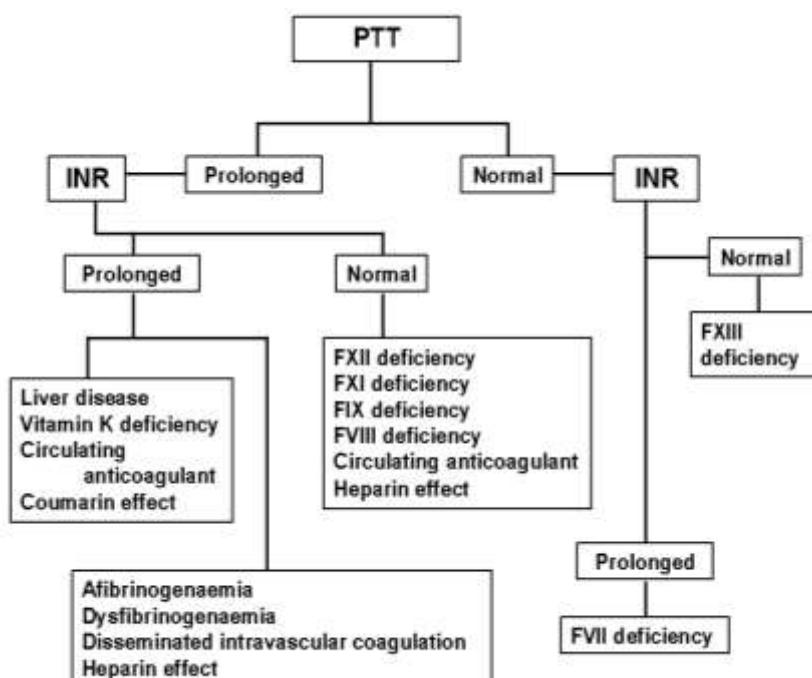
EXAMINATION

- Are there any dysmorphic features?
- Type and Site of bleeding
- Severity of bleeding
- Signs of haemodynamic instability
- Evidence of jaundice
- Signs of systemic illness may suggest disseminated intravascular coagulopathy (DIC)
- Signs and severity of anaemia
- Presence of lymphadenopathy
- Presence hepatosplenomegaly
- Presence of limb defects

Investigations

- Full blood count
 - Pancytopenia: leukaemia, bone marrow failure syndromes
 - Thrombocytopenia: disseminated intravascular coagulation, itp.
- Activated partial thromboplastin time (aptt)
 - Refer to flow chart below
- Prothrombin time (pt)
 - Refer to flow chart below
- Mixing study
 - This test checks for presence of inhibitors (antibodies) to factors. Blood of a patient with abnormal aptt is mixed with normal plasma in a ratio of 1:1. If aptt corrects the patient has factor deficiency. If it doesn't correct, the patient has inhibitors.
- Bleeding time
 - This test is no longer used.

Laboratory flow diagram



Management

Primary Level

- Manage according to ABCDE
- Refer

Secondary Level

- As in primary but also:
 - Take blood samples for FBC, Blood group, Coagulation, Factor levels
 - Transfuse whole blood 20ml/kg
- REFER

Tertiary Level

- As in secondary but also:
 - Transfuse whole blood
 - Investigate for cause of bleeding
 - Factor deficiency must be corrected
 - Appropriate counselling
 - Sibling test
- Provide follow up plan
- Multidisciplinary care may be done in Factor deficiency

Follow up

- All patients to be followed up in the haematology oncology clinic at the tertiary level
- Monitor FBC
- Monitor for complications of underlying disease

HAEMOPHILIA

Definition

- Haemophilia A: inherited deficiency of factor VIII
- Haemophilia B: inherited deficiency of factor IX

Note: mainly in male children

CAUSES OF SEVERE HAEMOPHILIA IN FEMALES

- Extreme degree of X chromosome inactivation
- Loss of part or all of X chromosome that contains FVIII or Factor IX
- Inheritance of pathogenic variants from both parents

Severity

- Severe: < 1% factor activity
- Moderate: >1% to < 5% factor activity
- Mild: > 5% to < 40% factor activity

Prevention / Promotion

- Early identification
- Sibling testing
- Lifestyle counselling (self-protection from trauma)

Signs and symptoms

- Infants
 - Cephalohaematoma
 - Bleeding post circumcision
 - Bleeding post venepuncture
- Children
 - Bruising
 - Joint bleeds
 - Muscle bleeding
 - Forehead bleeding (from minor falls)

Laboratory

- Aptt is prolonged
- Reduced levels of factor viii or factor ix activity

Management

Primary / Secondary Level

- Stabilise patient then refer to tertiary

Tertiary Level

- Stabilise patient
- Transfuse 20ml/kg of whole blood if indicated

- Factor VIII concentrate
 - The half-life is 8-12 hours
 - Treatment of choice for haemophilia a
 - Vials available in dosages ranging from 250 units to 3000 units
 - Consult haematologist for dosing
- Factor IX concentrate:
 - The half-life is approximately 18-24 hours
 - Used in treatment of haemophilia b
 - Consult haematologist for dosing
- Fresh frozen plasma 10mls / kg iv over 1hr
- Cryoprecipitate
 - This is preferable to fresh frozen plasma in the treatment of haemophilia a.
 - 5 – 10mls / kg iv
- Desmopressin (ddavp)
 - Synthetic analogue of vasopressin that boosts plasma levels of fviii and vwf
 - It does not affect factor ix levels and is of no value in haemophilia b.
 - A single dose of 0.3 µ/kg intravenously or subcutaneously can be very effective.
 - Rapid infusion may result in tachycardia, flushing, tremor and abdominal discomfort.
- Tranexamic acid
 - 15 - 25mg/kg, given 3 to 4 times daily
- Emicizumab (consult haematologist before use)
 - Monoclonal antibody that binds factor ix and x and activates factor x.
 - It is used in patients with haemophilia a
 - It is also used in patients with inhibitors to factor viii
 - Dose
 - Loading: 3mg/kg subcutaneous per week for 4 weeks
 - Maintenance: 1.5mg/kg sc per week

Consult haematologist

Follow up

- Follow up in haematology-oncology clinic
- Follow-up for complications

EARLY WARNING SIGNS OF CHILDHOOD CANCER

Introduction

World-wide there are more than 400000 new cases of childhood cancer and more than 70% of these will occur in the developing world. Despite this high incidence, childhood cancer is not a priority in the developing world, where other health needs are more immediate. In Malawi, the paediatric cancer registry recorded 500 new cases in 2022. The commonest malignancy recorded was Burkitt's Lymphoma followed by leukaemia, retinoblastoma and nephroblastoma. Survival from these tumours is often poor due to late presentation and late diagnosis.

Why do we need to make early diagnosis?

If patients are diagnosed early the prognosis is improved. Patients with stage 1 or 2 disease have better prognoses than those with stage 3 or 4 disease. The survival rates for childhood cancer are better in well-resourced parts of the world than in poorly resourced parts mainly because patients present and are diagnosed early.

How do we make early diagnosis?

- High index of suspicion
 - Childhood cancer is rare, and unless you think of the diagnosis, it is going to be missed
- Recognising the high-risk groups
 - Patients with neurocutaneous syndromes
 - Patients with chromosomal disorders e.g., Down syndromes
 - Children with immunodeficiency states
 - Children with previous history of malignancy or radiotherapy
 - Children with congenital malformations e.g. Beckwith-Wiedemann syndrome
- Recognising the 'red flag signs' of childhood cancer.

What are the "red flag signs" of childhood cancer?

These are signs and symptoms that are not exclusive to malignancy, but should alert a clinician to the possibility of malignancy.

- PALLOR AND BLEEDING
 - Anaemia and bleeding in malignancy is due to bone marrow infiltration.
 - Malignancy associated with anaemia and bleeding include leukaemia, neuroblastoma and lymphoma.
 - Bleeding is usually from the nose or gum, gut or into the skin (petechiae)
 - Bleeding is due to thrombocytopenia
 - Intracranial bleeding may also occur
- BONE AND JOINT PAIN
 - Common in primary and secondary bone tumours
 - Bone pain usually wakes children at night
 - 20-30% of patients with leukaemia will present with bone pain
 - Other malignancies that present with bone pain include neuroblastoma, retinoblastoma, rhabdomyosarcoma and histiocytosis
 - Backache in children must be taken seriously and may be due to spinal and vertebral tumours

- LYMPHADENOPATHY
 - Considered enlarged if > 1 cm
 - Most causes are benign and related to infection and inflammation
But may be a presenting sign and symptom of leukaemia, lymphoma, neuroblastoma or Kaposi's sarcoma.
 - Malignant nodes are firm, rubbery and non-tender
- UNEXPLAINED MASSES
 - Mass in any area may be the first clinical sign or symptom of malignancy.
 - Masses may be a group of nodes or may arise from any organ in the body.
 - Masses in the abdomen may be renal (nephroblastoma, neuroblastoma) hepatic (hepatoblastoma, hepatocellular carcinoma), pelvic (germ cell tumour, rhabdomyosarcoma, lymphoma).
 - Testicular masses are commonly due to leukaemia and rhabdomyosarcoma
 - Head and neck masses are commonly due to neuroblastoma, rhabdomyosarcoma, leukaemia and lymphoma
 - Mediastinal masses can be life threatening and often due to lymphoma, leukaemia and neuroblastoma
- HEADACHE
 - Fairly common in children
 - Rarely caused by intracranial tumours
 - Headache associated with early morning vomiting or coordination difficulties needs to be evaluated urgently.
- CHANGES IN THE ORBIT OR EYE
 - Loss of vision and development of a squint are often indicative of a malignant process
 - A squint in a child over 3 months may be due to retinoblastoma or neuroblastoma
 - A white pupil may be suggestive of retinoblastoma or cataract
 - Proptosis may be suggestive of neuroblastoma, lymphoma, leukaemia, rhabdomyosarcoma and extraocular retinoblastoma
- PERSISTENT FEVER AND WEIGHT LOSS
 - Fever is a common complaint in children and usually due to infection
 - Fever that does not respond to routine treatment should arouse suspicion of malignancy
 - Lymphoma is the classic malignancy that causes fever and weight loss
 - TB and HIV should be considered in the differential diagnosis and be excluded

Who should you refer?

All children or adolescents under the age of 15 years with a suspected malignancy should be referred.

What should you do before referral?

- Discuss with the referral centre
- Avoid invasive procedures
- Make sure the patient is stable and safe

If you must give lifesaving treatment e.g. a blood transfusion, take a blood sample and make unstained peripheral blood films to send with the child.

ONCOLOGICAL EMERGENCIES

Definition

These are emergencies that occur at any point in the care of the child with cancer.

- Some of the emergencies are the initial manifestation of cancer
- They must be recognized, triaged or treated quickly and appropriately

1. FEBRILE NEUTROPENIA

Definition

- Neutropenia is an absolute neutrophil count < 1500/microL
- Severe neutropenia is an absolute count of <500/ microL
- Fever is elevation of a single oral temperature > 38 degrees Celsius for over 1 hour or 2 elevations > 38% degrees Celsius over 12-hour period

Risk Factors

- Advanced malignancy suppressing the bone marrow
- Radiotherapy
- Chemotherapy

Causes

- *Bacteria:* Streptococcus, Staphylococcus, E.coli, Pseudomonas, Enterobacter Species
- *Viruses:* Respiratory viruses, Herpes simplex, varicella zoster
- *Fungi:* Candida species, aspergillus, cryptococcus
- *Protozoa:* Pneumocystis Jirovecii pneumoniae

Promotion / Prevention

- Early recognition
- Infection prevention
- Regular monitoring of haematological parameters

Signs and Symptoms

- Fever
- Cough
- Diarrhoea
- Mucositis

Investigations

- Full blood Count: to estimate degree of neutropenia
- Electrolytes and liver function tests: to look for co-morbidity
- Microbiology testing (Blood culture, urine MC&S, CSF MC&S if indicated)
- Imaging: Chest X-ray and CT Chest (if indicated)

Management

Primary / Secondary Level

- Stabilise patients and refer to tertiary

Tertiary Level

- Stabilise using ABCDE
- Investigations as above
- Start IV antibiotics (**should be given as early as possible within 30 minutes of presentation**)
 - IV Benzylpenicillin 50000 IU/kg 6 hourly
 - IV Gentamicin 7.5mg/Kg once daily
 - Fluconazole 12mg/kg IV/PO daily
 - Acyclovir 10mg/kg PO/IV 8 hourly
 - Antibiotics should be changed, if necessary, after culture and sensitivity results
- Manage anaemia and thrombocytopenia

Follow up

- Follow up in haematology-oncology clinic at tertiary level

TUMOUR LYSIS SYNDROME (TLS)

Definition

- Oncologic emergency characterised by massive abrupt release of cellular components into the blood following rapid lysis of malignant cells which overwhelm normal physiological pathways resulting in end organ damage
- Can occur spontaneously or after initiation of cytotoxic therapy
- Associated with the following metabolic disorders
 - Hyperkalaemia
 - Hyperphosphatemia
 - Hypocalcaemia
 - Hyperuricaemia

Diagnosis of Tumor Lysis Syndrome

Laboratory tumor lysis syndrome plus 1 or more of the following:

- Creatinine > 1.5 times the upper limit of normal
- Seizures
- Cardiac arrhythmia or sudden death

Risk factors/Causes

- High tumour burden
- Tumours with high rates of proliferation
- Tumours with high sensitivity to chemotherapy
- Preexisting renal disease or impairment in the patient
- Preexisting hyperuricaemia
- Dehydration

Stratification of tumours based on their risk of developing tumour lysis syndrome

| High risk | Intermediate risk | Low risk |
|---|---|-------------------------------------|
| Acute Lymphoblastic Leukaemia with WBC>100,000 | Acute Lymphoblastic Leukaemia with WBC<100,000 | Acute myeloid leukaemia WBC <25,000 |
| High grade Non-Hodgkin Lymphoma e.g. Burkitt Lymphoma | Acute Myeloid Leukaemia with WBC 25,000-100,000 | Chronic myelogenous Leukaemia |
| Acute Myeloid Leukaemia with WBC>100,000 | Chemosensitive solid tumours NHL, Neuroblastoma | Solid tumours |

Promotion / Prevention

- Anticipate TLS
- Hyperhydration (Crystalloids 3L/m² /day)
- Urine alkalinization
- Diuresis to maintain urine output ≥100ml/m²/hour

- Intermediate to high risk of developing tumour lysis syndrome: prophylactic allopurinol

Signs and symptoms

- Signs and symptoms of underlying disease
- Oliguria or anuria, flank pain, haematuria
- Nausea and vomiting
- Seizures
- Tetany
- Altered mental status
- Lethargy
- Heart palpitations
- Signs of fluid overload- facial and pedal oedema, abdominal distension

Investigations

- Blood chemistry: Urea, creatinine, electrolytes and uric acid
- Identify underlying cause e.g., FBC, Chest Xray, abdominal USS, biopsy etc.
- Laboratory diagnosis of Tumour Lysis syndrome Requires 2 or more of the following:
 - Uric acid 25% increase from baseline or $\geq 476\mu\text{mol}/\text{L}$
 - Potassium 25% increase from baseline or $\geq 6.0 \text{ mmol}/\text{L}$
 - Phosphorus 25% increase from baseline or $\geq 2.1 \text{ mmol}/\text{L}$
 - Calcium 25% decrease from baseline or $\leq 1.75\text{mmol}/\text{L}$

Management

Primary level

- Discuss with secondary level and refer patient to secondary level

Secondary level

- Identify patients at risk of tumour lysis syndrome
- Stabilise patient
- Start **Potassium free IV maintenance fluids (Normal Saline)**

Discuss patient with tertiary level and refer

Tertiary Level

1. Treat hyperuricaemia
 - Allopurinol 10mg/kg/ day divided in 8 hourly doses PO
 - Rasburicase 0.15-0.2mg/kg IV
2. Hyperhydration
 - **Potassium free IV fluid** - Normal saline 3litres/m²/day
 - Monitor urine output, aim for urine output 100ml/m²/hour
 - If not meeting urine output, give furosemide 1mg/kg to drive diuresis
3. Monitor and treat electrolyte imbalances
 - Monitor electrolytes 4-6 hourly

Hyperkalaemia

- Avoid and stop all exogenous Potassium
- Calcium gluconate 0.5ml/kg of 10% solution slow IV

- Nebulised Salbutamol
- IV insulin and dextrose
- Kayexalate
- Dialysis

Hyperphosphatemia

- Avoid IV phosphate administration
- Phosphate binders
 - Aluminium hydroxide 12.5 - 37.5mg/kg 6 hourly with meals
 - Calcium carbonate 30-40mg/kg with each meal

Hypocalcaemia

- Treat only if symptomatic and hyperphosphatemia is resolved to prevent calcium-phosphate precipitation
- Calcium gluconate 0.5ml/kg of 10% solution slow IV push

Indications for renal replacement therapy

- Severe oliguria or anuria
- Intractable fluid overload
- Persistent hyperkalaemia
- Hyperphosphatemia induced symptomatic hypocalcaemia
- A calcium-phosphate product $\geq 70\text{mg}^2/\text{dL}^2$

Follow-up

All patients to be followed up in oncology clinic

SPINAL CORD COMPRESSION

Definition

Mass compromising the spinal cord, conus medullaris or cauda equina.

Risk Factors / Causes

- Burkitt lymphoma
- Ewing's sarcoma
- Neuroblastoma
- Osteogenic sarcoma
- Rhabdomyosarcoma

Promotion / Prevention

- Early detection of malignancy

Clinical Features

| SIGN | SPINAL CORD | CONUS MEDULLARIS | CAUDA EQUINA |
|------------------------------|---------------------|-----------------------------------|---------------|
| Weakness | Symmetric | Symmetric | Asymmetric |
| Tendon reflexes | Increased or absent | Increased knee Decreased ankle | Decreased |
| Babinski | Extensor | Extensor | Plantar |
| sensory | Symmetric | Symmetric | Asymmetric |
| Sphincter abnormality | Spared | Early involvement | May be spared |
| Progression | Rapid | May be rapid | May be rapid |

Investigations

- Full blood count
- Urea and electrolytes
- Liver function tests
- USS abdomen
- Biopsy of the lesion
- MRI

Management

Primary Level

- Secure the airway, breathing and circulation
- Start IV fluids normal saline plus 5% dextrose
- Urgent referral to secondary centre

Secondary Level

- Ensure the airway, breathing and circulation
- Continue IV fluids
- Catheterise the patient

Tertiary Level

- Maintain airway, breathing and circulation
- Continue IV fluids and urine output monitoring
- Start Dexamethasone 1-2mg/kg stat then 0.5mg/kg hourly
- Monitor for development of tumor lysis syndrome
- If Burkitt's lymphoma is suspected, Give allopurinol or rasburicase
- Epidural mass may require decompression with surgery or radiotherapy

Follow up

- All patients to be followed up in oncology clinic

SUPERIOR VENA CAVA COMPRESSION SYNDROME

Definition

Symptoms and signs arising from obstruction of superior vena cava (SVC) e.g. compression or thrombosis.

- Tumour or infection in the mediastinum can compress the SVC causing venous stasis and reducing venous return from the head and neck leading to facial oedema and distended neck veins.
- SVC compression, thrombosis and oedema combined decrease tracheobronchial airflow leading to dyspnoea.

Risk Factors / Causes

- Anterior Mediastinal mass: T-cell lymphoma, T-cell leukaemia
- Posterior Mediastinal mass: Hodgkin lymphoma, neuroblastoma, germ cell tumours.

Promotion / Prevention

- Early detection and treatment of malignancy

Signs and Symptoms

- Cough
- Dyspnoea
- Orthopnoea
- Dysphagia
- Wheezing
- Hoarseness
- Chest pain
- Distended neck veins
- Face appears 'swollen'

Investigations

- Full blood count
- LDH
- Uric acid
- Chest X-ray (AP+Lateral)
- CT chest
- Ultrasound and Doppler

Management

Primary / Secondary Level

- Secure and manage airway, breathing and circulation. If in shock, treat as cardiogenic shock (see emergency chapter)
- Do not make the patient lie flat, keep in a 45° angle
- Start maintenance fluids.
- Refer to Tertiary Centre

Tertiary level

- Manage airway, breathing and circulation as above
- Start empirical steroids prednisolone 2mg/kg in two divided doses and allopurinol 10mg/kg in 3 divided doses
- Consult oncologist for chemotherapy and further management

Follow up

- All patients to be followed up in the oncology clinic

HYPERLEUKOCYTOSIS

Definition

White blood count > 50,000 or 100,000/ μL

Risk Factors / Causes

- Infant ALL
- Infant AML
- Blast Phase of CML
- T-Cell Leukaemia
- Acute Promyelocytic Leukaemia
- Leukaemia with 4;11, 11q23, 9;22

Promotion / Prevention

- Early detection of malignancy

Signs and Symptoms

- Clinical features as a result of leukostasis

| ORGAN | SYMPTOMS |
|------------------------|--|
| Brain | Seizures Confusion Headache Visual impairment Gait abnormalities |
| Cardiac | Myocardial infarction Cardiac failure |
| Pulmonary | Hypoxia Dyspnoea |
| Renal | Acute kidney injury |
| Haematological | DIC |
| Musculoskeletal | Acute limb ischaemia |
| Genitalia | Priapism |

Management

Primary Level

- Secure and maintain airway, breathing, and circulation.
- Start maintenance IV Normal Saline (avoid potassium containing fluids)
- Refer for further management to a higher level of care.

Secondary Level Management

- Continue to maintain airway, breathing, and circulation.
- Discuss the case with the referral center.
- Start IV normal saline with 5% dextrose at 2 times the normal maintenance rate.
- Refer the patient to the Tertiary Center.

Tertiary Level

- Maintain airway, breathing, and circulation.
- Continue IV normal saline with 5% dextrose at 2 times the patient's maintenance fluid rate.
- Administer allopurinol at 10 mg/kg in 3 divided doses or rasburicase at 0.2 mg/kg.
- Ensure urine output is between 1-2 ml/kg/hour.
- Transfuse platelets at 10 units/kg if platelet count is less than 20,000/microL.
- **Avoid** transfusion of packed cells as they can increase blood viscosity.

Follow up

- All patients to be followed up in haem-oncology clinic.

WILMS TUMOUR (WT) / NEPHROBLASTOMA

Definition

Wilms tumour or nephroblastoma is an embryonal tumour of the kidney.

Risk Factors / Causes

These tumours are often 'found' when a mother is bathing her toddler and feels a large hard mass in the abdomen.

a. WT1 RELATED SYNDROMES

- WAGR (Wilms tumour Aniridia Genital Urinary anomaly, Mental retardation).
- Denys-Drash Syndrome.

b. WT2 RELATED SYNDROME

- Beckwith-Wiedemann syndrome

c. OTHER SYNDROMES

- Perlman syndrome
- Bloom syndrome
- Neurofibromatosis
- Li-Fraumeni

Promotion / Prevention

- Wilms tumour surveillance aims to improve survival. This is achieved through earlier detection of small and localised tumours.
- Screening usually targets patients with overgrowth syndromes and genetic mutation. Screening is done with ultrasound from the age of 3 months till 8 years.
- Do not assume a hard mass in a child's abdomen is a spleen until WT is excluded

Signs and Symptoms

- Abdominal mass
- Abdominal pain in 40% of the patients but this is not a prominent symptom
- Haematuria, often microscopic, in 25% of the patients
- Hypertension
- Fever, anorexia and weight loss occur in 10% of the patients

Investigations

- Full blood count
- Blood pressure measurement
- Urinalysis
- Chest radiography
- Ultrasound of the abdomen
- CT scan of the chest / abdomen
- Coagulation studies (transient von Willebrand like syndrome is recognized in 1% of the cases)

Staging

| Stage | Description |
|-------|---|
| I | Limited to the kidney but completely resected with intact capsule |
| II | Extends beyond the kidney but completely resected |
| III | Residual post-surgical tumour but confined to the abdomen |
| IV | Haematogenous spread to the liver, lung, bone and brain |
| V | Bilateral disease |

Differential Diagnosis

- Neuroblastoma
- Renal cell carcinoma
- Clear Cell Sarcoma
- Rhabdoid tumours of the kidney
- Congenital mesoblastic nephroma

Management

Primary Level

- Appropriate counselling on suspected diagnosis
- Early referral

Secondary Level

- Nutritional support
- Counselling on diagnosis and treatment which is often lengthy
- Referral

Tertiary Level

- Ongoing counselling
- Definitive treatment: Chemotherapy and surgery +/- radiotherapy

Follow Up

- Review every 3 months in oncology clinic at tertiary level
- Ultrasound abdomen at each follow-up to look for recurrence or metachronous tumours

RETINOBLASTOMA

Definition

Retinoblastoma is a common tumour of childhood that arises from the retina.

Risk Factors

- The tumour can be inherited (25%-30%) or spontaneous (70%-75%). The inherited form of disease occurs due to germline mutation while non-herited form occurs due to a somatic mutation. Mutations occur in RB1 gene.

Promotion / Prevention

- Infants and children who are at increased risk of retinoblastoma on the basis of positive family history should be screened for retinoblastoma.
- Patients aged zero to three years.
 - Screening should occur during the first 8 weeks then every 3 months by looking for a red eye reflex
- Patient aged three to seven years
 - Screening examinations are performed 6 monthly

Signs and Symptoms

- Early
 - Leukocoria
 - Strabismus (squint)
- Late
 - Proptosis
 - Orbital mass
 - Destruction of the eyeball
 - Cervical lymphadenopathy
 - Bone metastases
 - Bone marrow failure
 - Seizures due to intra-cerebral disease

Investigations

- Full blood count
- Urea and electrolytes
- Liver function tests
- Bone marrow and cerebral spinal fluid examination
- Biopsy of the lesion if feasible
- Ocular ultrasound- B-scan
- Examination under anaesthesia
- CT or MRI brain
- Slit lamp exam

NB: Always check both eyes

Staging

The international classification of intraocular retinoblastoma grouping system

| GROUP | DESCRIPTION | DEFINING FEATURE |
|----------|---|--|
| A | Small tumour away from fovea and disc | < 3mm in size |
| B | Tumour confined to retina | Subretinal seeds < 3mm |
| C | Local subretinal fluid or seeding | Subretinal seeds > 3mm and < 6mm |
| D | Diffuse subretinal fluid or seeding | Subretinal seeds > 6mm |
| E | Presence of any one or more of the following poor prognostic features | <ul style="list-style-type: none"> -Tumour touching lens -Diffuse infiltrating tumour -Neovascular glaucoma - Opaque media due haemorrhage -Tumour necrosis |

International Retinoblastoma Staging System

| STAGE | DESCRIPTION |
|------------|---|
| 0 | Conservative treatment, eye preserved |
| I | Eye enucleated, complete resection (See subclassification below) |
| II | Eye enucleated, microscopic residual (See subclassification below) |
| III | Regional extension <ul style="list-style-type: none"> -Orbit -Preauricular or cervical lymph nodes |
| IV | Metastatic disease <ul style="list-style-type: none"> - Haematogenous metastasis (without CNS involvement) - CNS extension <ul style="list-style-type: none"> -Pre-chiasmatic lesion - CNS mass - Leptomeningeal spread |

| Sub-classification of stages I and II |
|---|
| N0: No tumour in optic nerve N1: Pre or intra-laminar invasion N2: Retro-laminar invasion, margin clear of tumour N3: Resection margin or subarachnoid invasion Nx: Unknown |
| C0: Choroid negative C1: Focal choroid invasion C2: massive choroid invasion |
| S0: No scleral involvement S1: Scleral invasion S2: Microscopic extension through sclera into orbit |

Management

Primary Level

- Counselling on possible diagnosis
- Discuss the case with ophthalmology at secondary centre
- Refer to secondary level

Secondary Level

- Discuss the case with tertiary centre and refer to tertiary centre
- Counselling on diagnosis and treatment

Tertiary Level

- Counselling on further investigations and treatment
- The primary goal of treatment is to preserve life
- Chemotherapy
- The following drugs are often used: vincristine, etoposide and carboplatin.
- The number of chemotherapy cycles depend on the stage of disease. Early staged disease may require 2-3 cycles. Extraocular disease requires six cycles; three are given preoperatively and the remaining three cycles are given postoperatively.
- Palliative chemotherapy may be offered in patients with metastatic disease
- Surgery
- Enucleation is the main surgery in advanced disease. It is done when there is no chance of preserving vision in the affected eye.
- Cryotherapy can be used for small primary anteriorly located tumours
- Photocoagulation can be used as primary therapy for posteriorly located tumours
- Exenteration is considered when the tumour has spread or reoccurred
- Radiotherapy

- External Beam Radiation therapy: this is considered in tumours with significant vitreous seeding, progression of disease during chemo-reduction and for tumours extending beyond cut margin of optic nerve.
- Radioactive Plaques -
- Use of radioactive rods placed adjacent to the tumours has replaced external beam radiation therapy where it is available

Follow Up

- All patients to be followed up in oncology clinic
- Regular eye examination for recurrence
- Full blood count
- Sibling examination for tumours

LYMPHOMA

Definition

Malignant disease of the lymphoid cells in both primary (bone marrow and thymus) and secondary lymph organs (lymph nodes, spleen and mucosa associated lymphoid tissue).

- There are two types of lymphoma, Hodgkin and Non-Hodgkin lymphoma

NON-HODGKIN LYMPHOMA (NHL)

- Aggressive, high grade or rapidly proliferating malignancies originating from mature B or T cells. NHL occurring in childhood and adolescents falls into three categories
 - Aggressive mature B cell NHL: (Burkitt lymphoma, diffuse large B cell lymphoma and mediastinal B cell lymphoma)
 - Lymphoblastic lymphoma
 - Anaplastic large cell lymphoma

Risk Factors

- Epstein-Barr Virus (EBV)
- Age: rare in children less than 3 years
- Sex: more common in males than females
- Immunodeficiency
 - Primary immunodeficiency syndromes
 - Acquired immunodeficiency
 - HIV
 - Post transplant lymphoproliferative disease (PTLD)
- DNA repair syndromes e.g., ataxia telangiectasia, Nijmegen breakage syndrome and constitutional mismatch syndrome

Promotion / Prevention

Screening in at risk population

Signs and symptoms

- NHL is characterised by a short history of symptoms with a rapidly growing mass
 - Remember Burkitt lymphoma has doubling time of 24 hours
- Enlarged lymph nodes (>1cm)- cervical, axillary, abdominal
- Jaw swelling
- Abdominal mass
- Paraplegia
- Mediastinal mass +/- pleural effusion
- Superior Vena Cava (SVC) syndrome
- Constitutional symptoms: fever, weight loss
- Signs of Tumour lysis syndrome (refer to tumour lysis syndrome section)

St Jude Children's Research Hospital (Murphy) staging

| Stage | Description |
|--------------|--|
| I | Single tumour or nodal area involved, excluding the abdomen and mediastinum |
| II | Single tumour with regional node involvement Or Two or more tumours or nodal areas involved on one side of the diaphragm |
| III | Tumours or involved lymph node areas occur on both sides of the diaphragm Or Primary intrathoracic (mediastinal, pleural or thymic) disease Or Extensive intrabdominal disease Or Any paraspinal or epidural tumours |
| IV | Tumours involving the bone marrow and/or CNS |

Investigations

- Full Blood count and differential
- Urea and electrolytes, creatinine,
- Uric acid
- LFT, LDH
- HIV test
- Imaging: Chest Xray
- Abdominal Ultrasound scan
- CT neck, chest and abdomen, where available MRI abdomen instead of CT
- Biopsy of lesion
- Bone marrow aspirate and trephine biopsy
- CSF analysis

Differential diagnosis

- Tuberculosis
- Neuroblastoma
- Rhabdomyosarcoma

Management

Primary level

- Discuss patient and refer to secondary level

Secondary level

- Discuss patient with tertiary level
- Do not perform any invasive procedures
- Stabilise patient
- Start potassium free fluid, normal saline full maintenance

Tertiary level

- Treat medical emergencies
 - a) Mediastinal Masses
 - Patients are at risk of tracheal compression, SVC syndrome, large pleural and pericardial effusions and right and left ventricular outflow compression.
 - They are at risk of cardiac and/or respiratory arrest if placed in supine position
 - Perform procedures while patient is on their side or prone e.g Bone Marrow Aspiration and Trehpene biopsy (BMAT), CT scans,
 - Use the least invasive procedure to establish diagnosis e.g Lymph node biopsy, thoracocentesis, BMAT
 - b) Treat and/or prevent tumour lysis syndrome
 - Refer to tumour lysis section
 - Treat or prevent hyperuricaemia
 - Vigorous IV hydration with potassium free fluids
 - Monitor and treat electrolyte imbalances
 - c) Spinal cord compression
 - Early identification is paramount
 - Dexamethasone 1-2mg/kg IV stat then 0.5mg/kg 6 hourly IV
 - Monitor neurology
 - Give chemotherapy if no improvement in neurology on steroids
- Initiate Chemotherapy as per facility protocol
 - Initial pre-phase of low dose chemotherapy
 - Multi agent high dose chemotherapy and CNS directed therapy

Follow up

- All patients to be followed up in oncology clinic

SICKLE CELL DISEASE

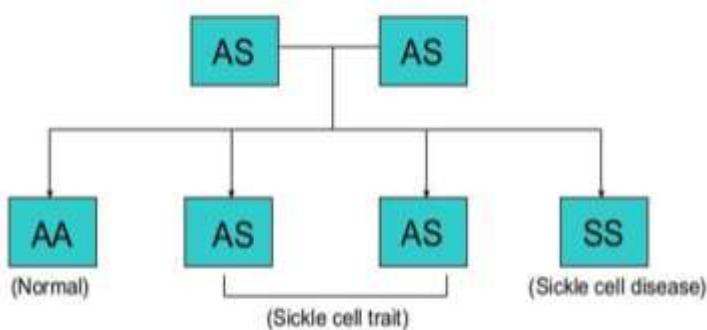
Definition

- Sickle Cell Disease is a haemoglobinopathy.: a genetic blood disorder in which red blood cells become deformed into crescent sickle shaped when exposed to low oxygen tension.
 - This is an inherited genetic mutation causes abnormal beta chain of haemoglobin (HbS) in RBCs and is the commonest genetic blood disorder.

Risk Factors

- Genetic predisposition
 - SCD is transmitted as an autosomal recessive or codominant trait. Both parents must be carriers in order for the children to be at risk of SCD as shown below:

Inheritance pattern :-



Possible genotype of the offspring of parents with the sickle cell trait

Prevention / Promotion

- Health education & advocacy
 - Genetic counselling of at-risk populations
 - Screening

Signs and Symptoms

Suspect SCD in patients with a haemoglobin level of <10mg/dl with one of the following clinical features:

- History of multiple transfusions (≥ 2 in lifetime)
 - Recurrent acute non-traumatic bone and joint pains with or without swelling
 - History of dactylitis (pain and swelling in hands and/or feet) as an infant
 - History of stroke
 - Full sibling with SCD
 - Frontal bossing
 - Persistent scleral icterus
 - Osteomyelitis
 - Splenomegaly
 - Unexplained pulmonary hypertension

Investigations

- Point of care test (sickle SCAN)
 - PBF in absence of Sickle SCAN
- High Performance Liquid Chromatography (HPLC), Hemoglobin Electrophoresis (HbE)
- FBC
- Depending on the presentation of the child and clinical suspicion: U&Es and LFTs may be indicated.
- Before starting hydroxyurea (HU) do the following tests: creatinine, ALT, and total bilirubin as a minimum

Differential Diagnosis

- Leukaemia
- Thalassemia
- Juvenile Arthritis
- Septic Arthritis

Management

- Sickle cell disease care pillars
 1. Use of hydroxyurea
 2. Infection Prevention
 3. Folic Acid supplementation
 4. Blood Transfusions
 5. Management of acute crises in SCD
 6. Management of chronic crises in SCD

Primary Level

- Manage pain crisis and treat any underlying infections
- REFERRAL FOR SECONDARY LEVEL REVIEW

Secondary Level

1) USE OF HYDROXYUREA

STARTING HYDROXYUREA

- Universal initiation of hydroxyurea regardless of clinical severity
- Can be started in children older than 12 months of age. (Refer to tertiary centre if you are considering starting it in children less than 12 months)
- Start at 20 mg/kg PO daily (see the dosing table below).
- Always re-weigh at every clinic visits and adjust dose as needed.
- Conduct a full blood count and liver function test to ensure that the criteria below are met for initiation:
 - Absolute neutrophil count (ANC)> 1,500/ μ l, platelet > 100,000/ μ l, and ALT is < X2 the upper limit of normal
 - Normal creatinine
- Check FBC at 1 month and 3 months after initiation of HU, then every 6 Months

| PATIENT WEIGHT (kg) | 20mg/kg/dose | | |
|---------------------|------------------------------|----------------|-----------------|
| | # HU 500mg capsules per week | 1 month supply | 3 months supply |
| 4kg - 5kg | 1 | 4 | 12 |
| 6kg - 8kg | 2 | 8 | 24 |
| 9kg - 12kg | 3 | 12 | 36 |
| 13kg - 16kg | 4 | 16 | 48 |
| 17kg - 19kg | 5 | 20 | 60 |
| 20kg - 23kg | 6 | 24 | 72 |
| 24kg - 26kg | 7 | 28 | 84 |
| 27kg - 30kg | 8 | 32 | 96 |
| 31kg - 33kg | 9 | 36 | 108 |
| 34kg - 37kg | 10 | 40 | 120 |
| 38kg - 41kg | 11 | 44 | 132 |
| 42kg - 44kg | 12 | 48 | 144 |
| 45kg - 48kg | 13 | 52 | 156 |
| 49kg - 51kg | 14 | 56 | 168 |

- CONSIDER WITHHOLDING HYDROXYUREA WHEN:
 - HGB <4.0 g/dL
 - ANC < 1.0 x 10⁹ /L
 - PLT < 80 x 10⁹ /L
 - Recheck counts every 2 weeks: If, recovery within 2 weeks, start same dose
 - If >2 weeks to recover or history of previous toxicity at same dose, then decrease dose by 5mg/kg
 - Refer to tertiary centre if persistent toxicity to hydroxyurea.
- HYDROXYUREA DOSE ESCALATION
 - Firstly, before considering dose escalation check adherence to hydroxyurea.
 - A pill count may reveal some adherence issues in addition to a clinical history.
 - Secondly, prior to dose escalation do an FBC to ensure that the MCV is ≥100fl.
 - Dose escalation is indicated in children on HU fixed dose with:
 - Cerebral vascular accident (stroke)
 - Any acute chest syndrome (ACS) event in the preceding 24 months
 - More than one previous pain crisis requiring hospital care & admission in the previous 24 months.
 - High conditional (> 170 cm/sec) or abnormal (> 200 cm/sec) velocities on transcranial Doppler (TCD)
 - Refer to tertiary centre for hydroxyurea dose escalation

2) INFECTION PREVENTION

- Daily Penicillin V is recommended for all children less than 5 years.

| Penicillin V Dosing Table | |
|----------------------------------|----------------|
| Age | Dose |
| < 3 years old | 125mg BD Daily |
| 3-5 years old | 250mg BD Daily |

Alternatives if PCN V not available: Amoxicillin - 10 mg/kg/dose BD (max 250 mg BD); Azithromycin - 5 mg/kg once daily (max 250 mg)

- Malaria Prophylaxis: SP monthly for all children and use Chloroquine for those with Sulphur Allergy

| SP Dosing Table | |
|------------------------|-------------------------------|
| Weight (kg) | No. of tablets/monthly |
| <10kg | 0.5 |
| 10 - <20 | 1 |
| 20 - <30 | 1.5 |
| 30 - 45 | 2 |
| > 45 | 3 |

- If a SCD patient is noted to have repeated infections, refer to tertiary centre.
- Patients to receive all vaccines as per Malawi National EPI schedule. Ideally should also get PCV13 (PCV23 where available), Influenza, Meningococcal, and COVID vaccines.
- Pneumococcal (PCV13) Recommendations:
 - Age 2 – 5 years: < 3 PCV doses: Give 2 doses of PCV (8 weeks after the most recent dose and administered 8 weeks apart)
 - Only 3 PCV doses: Give 1 dose of PCV at least 8 weeks after last dose
 - Age 6 -18 years: No history of PCV13: Give 1 dose of PCV13

3) NUTRITIONAL SUPPLEMENTATION

- Folic acid: 2.5mg OD.
- Iron: Avoid iron therapy unless iron deficiency is documented

4) BLOOD TRANSFUSION IN SICKLE CELL DISEASE

Indications for blood transfusion:

- Haemoglobin <6g/dL in all patients
- Haemoglobin 6-8g/dL and/or >2 points below patient's baseline Hb (check health passport) and if the patient has the following;
 - Laboured breathing or impaired consciousness
 - Stroke - aim for Hb of ~10g/dL

- Note: If stroke and Hb >8g/dL, then perform red cell manual exchange transfusion
- Acute Chest Syndrome (ACS) with laboured breathing and/or requiring oxygen
 - aim for a Hb of ~10g/dL
 - Note: If ACS and Hb >8g/dL with laboured breathing, poor oxygenation (O₂sats <95%) despite oxygen therapy, and/or escalating oxygen/respiratory support, then perform red cell manual exchange transfusion
- Acute splenic or hepatic sequestration - aim for Hb of ~8g/dL
- Before surgery requiring general anaesthesia that is expected to last more than 30-60 minutes - aim for Hb of ~10g/dL
- Severe complicated malaria
- Organ failure present (ex: lungs, liver, kidney, brain, heart)

Safety measures while blood transfusion is running:

- Ensure that blood is prescribed at 20cc/kg whole blood or 10cc/kg packed cells.
- Document a clear rate of transfusion for giving the blood over 4 hours. If this needs to be administered faster, discuss with consultant.
- Check with guardian and patient if there is a history of previous blood transfusion and /or any reactions to it.

5) MANAGEMENT OF ACUTE COMPLICATIONS OF SCD

Pain Crisis

- It is important to determine the cause. It can be difficult to distinguish between a vaso-occlusive crisis and osteomyelitis or septic arthritis. History and clinical exam is important.

Management

- Collect lab samples for FBC & group and crossmatch. Place IV cannula.
- Hydration: The aim is to have the patient on 100% maintenance fluids orally and wean IV fluids as able.
- If dehydrated, correct appropriately.
- NB: hyperhydration can lead to pulmonary compromise.
- Give pain medicine as per Faces Score grading for pain.
- If in mild to moderate pain, give paracetamol 15mg/kg/dose PO 4-6 hourly or ibuprofen 10mg/kg/dose PO 6 hourly.
- If in severe pain, in addition to the paracetamol and ibuprofen, you can give Morphine 0.1mg – 0.2mg/kg/dose orally 4 hourly and escalate cautiously. This is as per WHO analgesic ladder.
- Constipation is a common adverse effect of morphine. Stool softeners (liquid paraffin) should be prescribed. The patient should be assessed daily for stooling and constipation regimen escalated as necessary.
- Blood transfusion is indicated if Hb is =<6g/dL or 2 below the patient's normal baseline Hb (check in health passport).
- If febrile (defined as >38.5C), see fever guidelines section.

Fever

- Take samples for:
 - FBC, blood culture (obtain prior to the first dose of antibiotics, but do not delay initiation of antibiotics >30 min), malaria test, group and crossmatch, and creatinine as indicated
 - Urine dipstick. Add urinalysis if <2 years or symptoms suggestive of infection.
 - Lumbar puncture if sign and symptoms of meningitis
 - Malaria: If malaria test positive, start anti-malarial treatment per national guidelines.
- Imaging Studies:
 - CXR if respiratory signs & symptoms (Refer to Acute Chest Section)
 - Bone X-rays if concerned for osteomyelitis (Refer to Pain section)

Management

- Antibiotics
 - Treat with antibiotics ceftriaxone 50mg/kg IV every 24 hours
 - If very sick treat for 7 to 10 days with antibiotics
 - If not improving at 48 hours re-examine patient and refer to tertiary centre
- Inpatient Hospital Admission:
 - Indications:
 - Age less than 6 months or not up to date with immunizations
 - Family lives far from a health facility
 - Temperature > 40.0°C
 - Patient is tachycardic, tachypnoeic, hypotensive, poorly perfused, or drowsy
 - WBC >30,000 or <5,000 or if significantly different from patient's baseline
 - Hb < 6g/dL or Hb which is 2 g/dL lower than patient's baseline. (Check previous Hbs in the health passport or file.)
 - Previous history of sepsis
 - Any concerning signs or symptoms
 - Monitor closely as such patients can deteriorate quickly.
 - Continue ceftriaxone 50mg/kg IV every 24 hours. Malaria treatment if malaria tests positive as per national guidelines.
 - If in septic shock, needs a minimum of every 30 min observations (heart rate, pulse rate, O₂ saturation, blood pressure, GCS) until the patient stabilises.
 - Give IV fluid bolus of 10ml/kg and re-evaluate in 15 min, repeat x 2 (total of 30ml/kg) within 1 hour or until BP/ HR stabilise.
 - If vital signs are stable on admission, then check vital signs (heart rate, pulse rate, O₂ saturation, blood pressure) 1 hour after the first dose of antibiotics given, and every 6 hours for the first 48 hours.

- Start O₂ therapy if increasing RR or O₂sats <92% (see Acute Chest section)
- Hydration: The aim is to have the patient on 100% maintenance fluids; orally and wean IV fluids as able. If dehydrated, correct appropriately. Pre-hydration can lead to pulmonary compromise.
- Blood transfusion is indicated if Hb is =<6g/dL or 2 below baseline the patient's normal baseline Hb (check-in health passport)

Acute chest syndrome

Diagnosis:

- A new infiltrate seen on CXR (not required in our setting)
- PLUS, one or more of the following:
 - Chest pain
 - Fever >38.5C
 - Tachypnoea, wheezing, cough, or increased work of breathing.
 - Hypoxaemia (SaO₂ <92% on air or 3-5% below their baseline).

Management

- If requiring oxygen or increased work of breathing, admit patient as it is life threatening and patients can decompensate quickly. Place on a monitor.
- Collect samples for FBC, malaria test (if febrile), creatinine, group and crossmatch
- Obtain chest radiograph
- Continuous monitoring of vital signs- heart rate, respiratory rate and oxygen saturations
- If O₂ saturations <95% on room air, administer supplemental O₂ and consider blood transfusion (see below)
- Aim for oxygen saturations > 95%. If low oxygenation, then refer.
- Simple blood transfusion if Hb <=6g/dL in all patients with ACS. If laboured breathing is present or the patient is requiring oxygen then give a simple blood transfusion for Hb <=8g/dL, with goal of 10 g/dL.
 - If Hb is >8 g/dL and persistent respiratory insufficiency despite oxygen therapy. Refer to tertiary centre
- Initiate antibiotics with ceftriaxone IV 50mg/kg every 24 hours PLUS an oral macrolide such as azithromycin (10mg/kg OD on day 1 followed by 5mg/kg on days 2-5 days; or 10mg/kg OD for 3 days)
- Pain relief as appropriate (See Pain section)
- Hydration with caution: The aim is to have the patient on 75% maintenance (oral + IV fluids). If tolerating oral fluids can give all fluids orally.
 - If one needs to support with IV fluids consider adding 5% dextrose if limited oral intake. Use of an infusion pump is preferred when giving IVF.
 - Encourage oral fluid intake and wean IV fluids as able.
 - If dehydrated, correct appropriately in discussion with a senior colleague.
 - Note that hyperhydration can be detrimental in SCD and can lead to pulmonary oedema and respiratory decompensation.

- Give furosemide if signs/symptoms for fluid overload and/or pulmonary oedema
- Start chest physiotherapy.

Splenic Sequestration

Signs and symptoms:

- Pallor, lethargy, signs of hypovolemic shock
- Diffuse abdominal pain
- Abdominal distension with acute splenomegaly, often tender
- +/- fever
- Sudden drop in Hb of >2g/dL
- Thrombocytopenia

Management

- If patient is in shock needs minimum of every 30 min observations (heart rate, pulse rate, O₂ saturations, blood pressure, GCS) until patient stabilises
- Investigations: FBC, reticulocyte count (if available), urgent group and crossmatch
- Give fluid bolus to restore circulatory volume while awaiting blood, depending on clinical condition.
 - Give IV fluids bolus of 10ml/kg and re-evaluate in 15min, repeat x 2 (total of 30ml/kg) within 1 hour or until BP/ HR stabilises.
- Refer to tertiary centre as soon as patient has been stabilised

Stroke

- Stroke in children with SCD is defined as the occurrence of any new neurological symptoms in a patient with SCD. It could also be the presentation of a new diagnosis of SCD.

Management

- Stabilise Airway Breathing Circulation Coma Convulsions (ABCCC) approach.
- Blood sample for labs: rapid bedside glucose. FBC, U&Es including creatinine, LFTs. group and cross-match.
- If fever, obtain blood culture (and malaria test and initiate ceftriaxone 50mg/kg IV (Refer to Fever section)).
- Refer to tertiary centre once stabilised
- Oxygen therapy should be initiated to ensure oxygen saturations of >95% (If hypoxia present, refer to Acute Chest Syndrome Section).
- The treatment for stroke in SCD is a simple whole blood transfusion of 20ml/kg, if haemoglobin = <8 g/dL or manual red cell exchange transfusion if Hb >8 g/dL.
 - This should be performed as soon as possible and preferably within 6 hours of recognition of acute neurological symptoms.
 - Simple transfusion should be performed with a goal of an Hb of 10 g/dL.
- Hydration with caution: The aim is to have the patient on 75% maintenance oral + IV fluids.

- This can be all orally if tolerated or as IV fluids 0.9% normal saline (consider adding 5% dextrose if limited oral intake) if necessary.
 - Encourage oral fluid intake and wean IV fluids as able.
 - If dehydrated, correct appropriately.
 - Note that hyperhydration can be detrimental in SCD and can lead to cerebral oedema.
 - Use of an infusion pump is preferred when giving IVF.
- For long term management of stroke, priapism and transient red cell aplasia refer to tertiary centre for continued management.
 - Management of chronic complications and end-organ damage of SCD - Refer to tertiary centre.

Tertiary Level

USE OF HYDROXYUREA

- STARTING HYDROXYUREA- as in secondary level
- WITHHOLDING HYDROXYUREA- as in secondary level
- HYDROXYUREA DOSE ESCALATION
 - Firstly, before considering dose escalation check adherence to hydroxyurea. A pill count may reveal some adherence issues in addition to a clinical history. Secondly, prior to dose escalation do an FBC to ensure that the MCV is ≥ 100 .
 - Dose escalation is indicated in children on HU fixed dose with:
 - Cerebral vascular accident (stroke)
 - Any acute chest syndrome (ACS) event in the preceding 24 months
 - More than one previous pain crises requiring hospital care & admission in the previous 24 months.
 - High conditional (> 170 cm/sec) or abnormal (> 200 cm/sec) velocities on transcranial Doppler (TCD)
 - Dose escalation should be
 - An increase in hydroxyurea dose by not more than 5 mg/Kg/day every 8 weeks
 - The minimum interval between dose increases is 8 weeks
 - After each escalation check a FBC at 1 month and 3 months after escalation of HU, then every 6 months
 - We can escalate the dose of hydroxyurea up to a maximum dose of 30mg/Kg.

INFECTION PREVENTION- Refer to secondary level

NUTRITIONAL SUPPLEMENTATION- Refer to secondary level

BLOOD TRANSFUSIONS- Refer to secondary level

MANAGEMENT OF ACUTE COMPLICATIONS

Pain Crisis

- Refer to secondary level guidelines
- If localised pain not improving after 48-72 hours of analgesics and concerning for osteomyelitis, consider imaging of affected limb (Note that x-ray changes associated with osteomyelitis may take 10-14 days to appear)
 - If persistent localised signs and symptoms concerning for osteomyelitis or septic arthritis, obtain a blood culture, start ceftriaxone (per fever protocol), and add cloxacillin or clindamycin
- **A painful crisis without fever does not require antibiotics.**
- Blood transfusion is not indicated in the management of uncomplicated pain episodes. It is indicated if Hb is =<6g/dL or 2 below baseline the patient's normal baseline Hb (check in health passport).
- All patients should be encouraged to mobilise and to do incentive spirometry to prevent the development of Acute Chest Syndrome. Ensure the head of the bed is elevated at all times. Where possible involve the physiotherapy team in the management of all SCD patients.
- At discharge ensure that the patient receives counselling on avoiding the triggers of vaso-occlusive crisis such as keeping warm, and continuing to have good oral intake so as to ensure good hydration. Additionally, supply the patient with 48 – 72 hours supply of pain medication. Always consult the paediatric oncology team prior to discharge and organise follow up.

Fever

- Refer to secondary level guidelines

Acute chest syndrome

- Refer to secondary level guidelines.
- Simple blood transfusion if Hb <=6g/dL in all patients with ACS.
- If laboured breathing is present or the patient is requiring oxygen then give a simple blood transfusion for Hb <=8g/dL, with goal of 10 g/dL.
- If Hb is >8 g/dL and patient has laboured breathing, poor oxygenation (sats <95%) despite oxygen therapy, and/or escalating oxygen/respiratory support, then a manual red cell exchange transfusion may be considered after discussion with Paeds Haem-Oncology consultant.

Splenic sequestration

- Splenic sequestration is one of the most common cases of death in SCD children under the age of 2 years old. It results from the rapid sequestration of red blood cells by the spleen and may cause an abrupt drop to half of baseline Hb within a few hours of onset resulting in hypovolaemic shock. It is the second most common cause of death in the first decade of children with SCA.

- Signs and symptoms
 - Pallor, lethargy, signs of hypovolaemic shock
 - Diffuse abdominal pain
 - Abdominal distension with acute splenomegaly, often tender
 - +/- Fever
 - Sudden drop in Hb of >2g/dL
 - Thrombocytopenia

Immediate action

- If patient is in shock, admit to HIGH DEPENDENCY UNIT/ RESUSCITATION if available as this is an EMERGENCY. Alert the consultant on call and haematology consultant.
- Needs minimum of every 30min observations (heart rate, pulse rate, O₂ saturations, Blood Pressure, GCS) until patient stabilises
- Investigations: FBC, reticulocyte count (if available), urgent group and crossmatch
- Give fluid bolus may be given to restore circulatory volume whilst awaiting blood depending on clinical condition. Give IV fluids bolus of 10ml/kg and re-evaluate in 15min, repeat x 2 (total of 30ml/kg) within 1 hour or until BP/ HR stabilizes.

Management

- If febrile, obtain blood culture and MRDT malaria test. Give broad spectrum antibiotics with ceftriaxone 50mg/kg IV every 24 hours (Refer to Fever section).
- IMMEDIATE blood transfusion with packed red cells 10cc/kg or whole blood 20cc/kg to be given over 3-4 hours to a goal Hb of 8 g/dL.
 - Care must be given not to over-transfuse as subsequent release of pooled blood from spleen to the circulation can lead to hyper viscosity
 - Check Hb 4-6 hours after transfusion. Repeat transfusion as appropriate.
- Monitor spleen size for the first 12-24 hours until it is seen to be reducing in size
- Give supportive oxygen therapy if O₂sats <95%
- At discharge ensure that the patient receives counselling. Always consult the oncology team prior to discharge and organise follow up.

Stroke

- Admit patient to HIGH DEPENDENCY UNIT/ RESUSCITATION. Airway Breathing Circulation Coma Convulsions (ABCCC) approach. Call the on-call consultant and haematologist consultant.
- Blood Sample for labs: Rapid bedside glucose. FBC, U&Es including creatinine, LFTs, group and cross-match.
- If fever, obtain blood culture (obtain prior to first dose of antibiotics, but do not delay initiation of antibiotics >30 min) and malaria test and initiate ceftriaxone 50mg/kg IV (Refer to Fever section).
- **Oxygen therapy** should be initiated to ensure oxygen saturations of >95% (If hypoxia present, refer to Acute Chest Syndrome Section).

- The treatment for stroke in SCD is a simple whole blood transfusion of 20ml/kg, if haemoglobin =<8 g/dL or manual red cell exchange transfusion if Hb >8 g/dL. This should be performed as soon as possible and preferably within 6 hours of recognition of acute neurological symptoms.
 - Simple transfusion should be performed with a goal of an Hb of 10 g/dL. The goal of red cell exchange is to reduce the HbSS concentrations to less than 30%.
- **Hydration with caution:** The aim is to have the patient on **75% maintenance oral + IV fluids**. This can be all orally if tolerated or as IV fluids 0.9% normal saline (consider adding 5% dextrose if limited oral intake) if necessary. Encourage oral fluid intake and wean IV fluids as able.
 - If dehydrated, correct appropriately.
 - Note that hyperhydration can be detrimental in SCD and can lead to cerebral oedema. Use of an infusion pump is preferred when giving IVF.
- In the presence of **fever**, obtain blood culture and malarial test and initiate ceftriaxone 50mg/kg IV every 24 hours (See Fever Section).
 - In addition, if signs and symptoms of meningitis are present, obtain lumbar puncture and treat as per hospital/national guideline for meningitis e.g. IV ceftriaxone high dose (100mg/kg).
 - Antipyretics should be given to reduce fevers which has potential to accelerate ischaemic neuronal injury.
- **Dexamethasone** should be considered if features of raised intracranial pressure after discussing with haematology consultant, and other neuroprotective measures such as raise the head of the bed to 30 degrees.
- **Anticonvulsants** should be administered if patient is having seizures, as per seizure guideline.
- Obtain a **CT scan of the head**, if possible, but stabilising patient and blood transfusion or red cell exchange should be prioritised over this. CT may be helpful to identify haemorrhagic stroke which is less common in children
- Refer early to physiotherapy and occupational therapy.
- At discharge ensure that the patient receives counselling. Always consult haematology team prior to discharge and organise follow up.
- **Primary prevention** (prevention before ever having a stroke)
 - Annual transcranial doppler (TCD) screening is recommended for children aged 2-16 years
 - Children with abnormal TCD velocities (defined as >200cm/sec) if not already on hydroxyurea should be initiated at a dose of 20mg/kg/day and escalated as tolerated to a maximum dose of up to 35mg/kg/day.
- **Secondary prevention** (prevention measures after having a stroke)
 - The aim is to prevent a repeat stroke.
 - Hydroxyurea dosage should be escalated to maximum tolerated dose (up to 35mg/kg/day as per the guidelines of dose escalation of hydroxyurea).

- Annual TCD screening to assess for risk of recurrence.

Priapism

- Priapism is a prolonged and painful penile erection, often not associated with sexual stimulation. Male children, especially adolescents, with SCD should be made aware of this and advised to inform parents/doctors as it can lead to impotence if left untreated. It can also be triggered by sexual activity or a full bladder.
- Signs and symptoms
 - Stuttering
 - Lasts <4 hours and tends to resolve spontaneously
 - Major/Fulminant
 - Lasts >4 hours;
- Assessment: Clinically assess whether the patient has urinary retention and whether or not the glans penis is soft or turgid. This determines treatment.

Management

- Requires URGENT urological assessment and management - **Contact urology team on call.**
- Consult haematology consultant.
- Document time of onset of the episode and any precipitating factors e.g. trauma, sexual stimulation, infection, medication.
- If less than two hours from the onset, **give fluids** - IV NS 10-20 ml/kg bolus followed by IV + PO goal of 100% maintenance rate.
- Check Hb. If Hb = <6 g/dL or 2 points below baseline (check health passport) and priapism is persisting beyond 4 hours and/or recurring, then consider simple blood transfusion.
- **Analgesia** (refer to Pain section) and anxiolytic agents should be prescribed as needed.
 - This can be very painful, so please ensure adequate pain management
- Have the patient take a warm bath and/or apply **warm compresses** to the penis.
- **Micturition** (urination) should be encouraged once priapism starts as this may provide detumescence.
- If no relief/ detumescence after 2 hours from onset:
 - Give tablets of **pseudoephedrine**. Start with 0.5mg/kg bd for 3 days. If this is successful in achieving detumescence, then it can be stopped.
 - Alternatively, it can be continued at a dose of 0.5mg/kg/day for seven days. A dose of 0.25mg/kg/day for one month can be considered for stuttering priapism.
- If the priapism persists >4-6 hours from onset:
 - Fluid intake should be increased - IV NS 10-20ml/kg bolus followed by IV + PO goal of 100% maintenance rate. Consider blood transfusion. (See management above)
 - Consult the **urologist** as penile aspiration, intra-corporeal injection of phenylephrine, and washout might be necessary. If

these procedures fail to relieve the priapism, a shunting procedure will be necessary by urology.

- If no urinary retention and glans penis is soft, then the corpus spongiosum is likely unaffected, and a glans-cavernosa shunt can be performed.
- In the presence of urinary retention and a turgid glans penis, the corpus spongiosum is likely to be affected, and a glans-cavernosa shunt is unlikely to be of benefit. In this situation, a surgical shunt between the dorsal vein of the penis and the corpora cavernosa is indicated.
 - All the surgical interventions should be done by an experienced surgeon.
- Management of chronic complications and end-organ damage of scd
 - Consult haematology consultant to coordinate care

Follow up

- Patients should be followe dup in PEN-Plus clinic.
- Investigations on routine visit
 - Hb at every Visit [If receiving HU:do FBC every 6-12 months]
 - MRDT if clinical findings/complaints suggestive of malaria
 - Transcranial Doppler for stroke (annually starting at age 2yo)
 - Fundoscopy for retinopathy (every 2 years starting at age 10 yr)
 - Creatinine for nephropathy (every 2 years starting at age 10 yr)
 - Echocardiogram as clinically indicated

ANAEMIA

Definition

Anaemia is defined as a reduction in haemoglobin concentration, haematocrit, or red cell mass by more than two standard deviations below the mean for age and sex for the normal population.

- “Reduction in red blood cell mass or blood haemoglobin concentration”
- Physiologic: haemoglobin level too low to meet cellular oxygen demands.
- Practical: haemoglobin >2s.d. below the mean for age, gender, and race.

Table I. Normal values of the red series according to age and gender (various sources)

| <i>Age</i> | | <i>Hb (g/dl)</i> | <i>Hct (%)</i> | <i>MCV (fl)</i> |
|--------------|--------|---------------------|----------------|-----------------|
| 1-3 days | | 19,5 (14.5-23.5) | 58 (45-72) | 98-118 |
| 7 days | | 17,5 (14-22) | 55 (43-67) | 88-126 |
| 14 days | | 16,5 (13-20) | 50 (42-66) | 86-119 |
| 1 month | | 14 (10-18) | 43 (31-51) | 85-123 |
| 2 months | | 11,5 (9-14) | 35 (28-42) | 77-118 |
| 3-12 months | | 11,5 (9.5-13.5) | 35 (29-41) | 74-108 |
| 12-24 months | | 12,5 (11-14) | 37 (32-42) | 71-89 |
| 2-3 years | | 12,6 (11-14.2) | 37 (33-41) | 74-89 |
| 4-6 years | | 12,9 (11.7-14.1) | 38 (34-42) | 77-91 |
| 7-10 years | | 13,5 (12-15) | 40 (35-45) | 78-91 |
| 11-14 years | Female | 13,7 (12.3-15.1) | 40 (36-44) | 80-94 |
| | Male | 14,3 (12.6-16) | 46 (40-52) | 80-94 |
| 15-18 years | Female | 13,7 (11.5-15.9) | 40 (34-46) | 81-96 |
| | Male | 15,4 (13.7-17.1) | 46 (40-52) | 81-96 |

- Anaemia can be an isolated abnormality or be a part of multiple cell line abnormalities (red cells, white cells, and platelets). Abnormalities of two- or three-cell lines may indicate one of the following:
 - a. bone marrow involvement (e.g., infections, aplastic anaemia, leukaemia, toxicity from medications);
 - b. autoimmune disorders (e.g., connective tissue disease, Evans syndrome);
 - c. sequestration (e.g., hypersplenism) or intravascular trapping and destruction (e.g., thrombotic microangiopathy).

Risk Factors

- Worldwide the most common cause of anaemia is **iron deficiency**
- Causes of anaemia in children vary based upon age at presentation and sex
- Age:
 - Birth to three months –*
 - The most common cause of anaemia in young infants is "physiologic anaemia," which occurs at approximately six to nine weeks of age. Pathologic anaemia in newborns and young infants is distinguished from physiological anaemia by any of the following:
 - Anaemia (Hgb <13.5 g/dL) within the first month of life
 - Anaemia with lower Hgb level than typically seen with physiological anaemia (ie, <9 g/dL)
 - Signs of haemolysis (eg, jaundice, scleral icterus, or dark urine) or symptoms of anaemia (eg, irritability or poor feeding) due to immature liver function.
 - Prematurity
 - Infants three to six months –*
 - Anaemia detected at three to six months of age suggests a haemoglobinopathy. Nutritional iron deficiency is an unlikely cause of anaemia before the age of six months in term infants.
 - Toddlers, children, and adolescents –*
 - In toddlers, older children, and adolescents, acquired causes of anaemia are more likely, particularly iron deficiency anaemia.
 - Sex:
 - Some inherited causes of anaemia are X-linked (eg, G6PD deficiency and X-linked sideroblastic anaemia) and occur most commonly in males.
 - In postmenarcheal girls, excessive menstrual bleeding is an important cause of anaemia, and clinicians should suspect and evaluate for an underlying bleeding disorder.

Prevention / Promotion

- Health education & advocacy
- Genetic counselling of at-risk populations
- Screening **where applicable**
- Micronutrient supplementation,
- Parasitic infection control,
- Promotion of key dietary behaviours,
- Food fortification

Signs and Symptoms

- Symptoms attributable to anaemia – common symptoms of anaemia include:
 - Lethargy
 - Tachycardia
 - Pallor
 - Infants may present with irritability and poor oral intake.
- However, because of the body's compensatory abilities, patients with chronic anaemia may have few or no symptoms compared with those with acute anaemia at comparable haemoglobin (HGB) levels.
- Symptoms of haemolysis – Changes in urine colour, scleral icterus, or jaundice may indicate the presence of a haemolytic disorder.
- Bloody stools, haematemesis, severe epistaxis, or severe menstrual bleeding suggest anaemia from blood loss and/or iron deficiency
- Pica – The presence of pica, the intense craving for non-food items, should be assessed given its strong association with iron deficiency.
- Infectious symptoms (e.g., fevers, cough) suggest an infectious aetiology of anaemia
- Prior episodes of anaemia suggest an inherited disorder
- Anaemia in a patient with previously documented normal FBC suggests an acquired aetiology
- Hyperbilirubinemia in the new-born period suggests a haemolytic aetiology; microcytosis at birth suggests chronic intrauterine blood loss or thalassaemia
- Underlying renal disease, malignancy, or inflammatory/autoimmune disorders may be associated with anaemia
- Anaemia following exposure to oxidant drugs or fava beans suggests G6PD deficiency
- Exposure to paint, home renovations, or use of imported or glazed ceramics suggest lead toxicity
- Family members with jaundice, gallstones, or splenomegaly suggests an inherited haemolytic anaemia
- In infants and young children, iron deficiency is suggested by the following:
 - Use of low iron formula
 - Introduction of unmodified cow's milk before the age of 1 year
 - Excessive milk intake (>24 ounces per day)
 - Poor intake of iron-rich foods (meats or fortified infant cereal)
- Developmental delay is associated with iron deficiency, vitamin B12/folic acid deficiency, and Fanconi anaemia
- Hyperpigmentation
- Petechiae, purpura
- Jaundice
- Ulcers on lower extremities
- Frontal bossing, prominence of the malar and maxillary bones
- Glossitis
- Angular stomatitis
- Splenomegaly

Investigations

- The FBC, RBC indices, blood smear, and reticulocyte count are used to focus the diagnostic considerations and guide further testing to confirm the aetiology of anaemia
- FBC (Hb, Haematocrit, MCV, MCH, MCHC, Platelets, RDW)
- Peripheral Blood Film (microcytic, normocytic, macrocytic)
- Reticulocyte count: High (haemolysis), Low (hypoplastic)
- ESR, CRP (chronic disease)
- Serum Ferritin, Serum Iron (Iron deficiency, chronic inflammation)
- Haemoglobin Electrophoresis (Haemoglobinopathies)
- Bone Marrow Examination (hypoplasia, leukaemia)
- RBC morphology
 - Normocyte normal size ($MCV = 75 - 105 \text{ fl}$)
 - Microcyte small cells ($MCV < 75 \text{ fl}$)
 - Macrocyte large cells ($MCV > 105 \text{ fl}$)

Diagnosis

Anaemia classification according to MCV and reticulocytosis

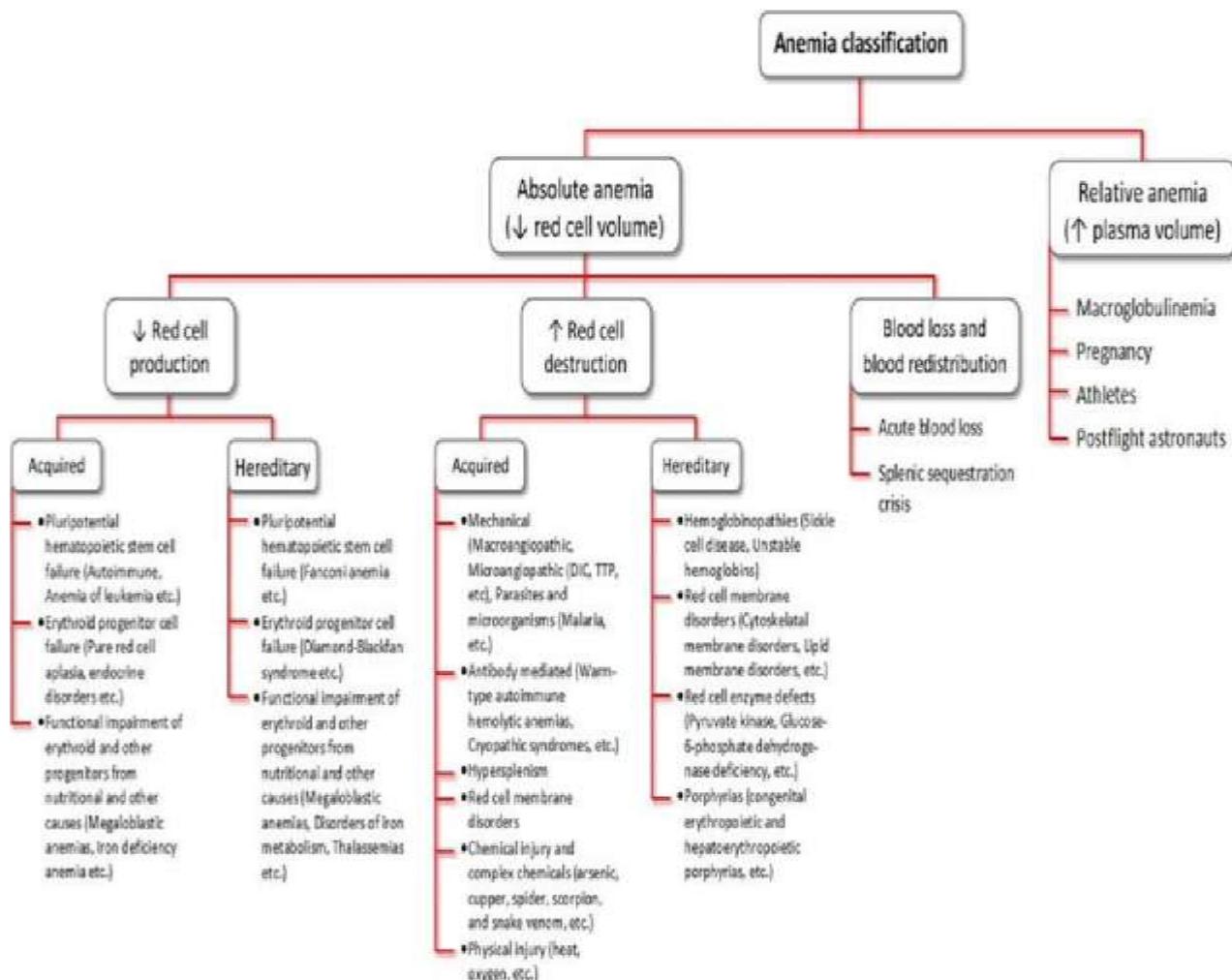
| | <i>Regenerative (RPI ≥ 3)</i> | <i>Arregenerative (RPI <2)</i> |
|-------------|---|--|
| Microcytic* | <ul style="list-style-type: none"> - Iron deficiency anemia under treatment - Congenital or corpuscular hemolytic anemias (spherocytosis, thalassemia, sickle cell disease) | <ul style="list-style-type: none"> - Iron deficiency anemia - Chronic infection / inflammation - Lead poisoning |
| Normocytic* | <ul style="list-style-type: none"> - Extracorporeal hemolytic anemia (hypersplenism, microangiopathy, drugs, infections) - Corpuscular hemolytic anemia - Acute bleeding | <ul style="list-style-type: none"> - Medullary aplasia - Spinal infiltration - Aplastic crisis or transient erythroblastopenia in corpuscular hemolytic anemia - Infectious anemia - Chronic kidney disease |
| Macrocytic* | <ul style="list-style-type: none"> - Hemolytic crisis in AIHA with marked reticulocytosis | <ul style="list-style-type: none"> - Folic acid or vitamin B12 deficiency - Fanconi anemia - Blackfan-Diamond anemia - Liver disease - Myelodysplastic syndrome - Sideroblastic anemia - Hypothyroidism |

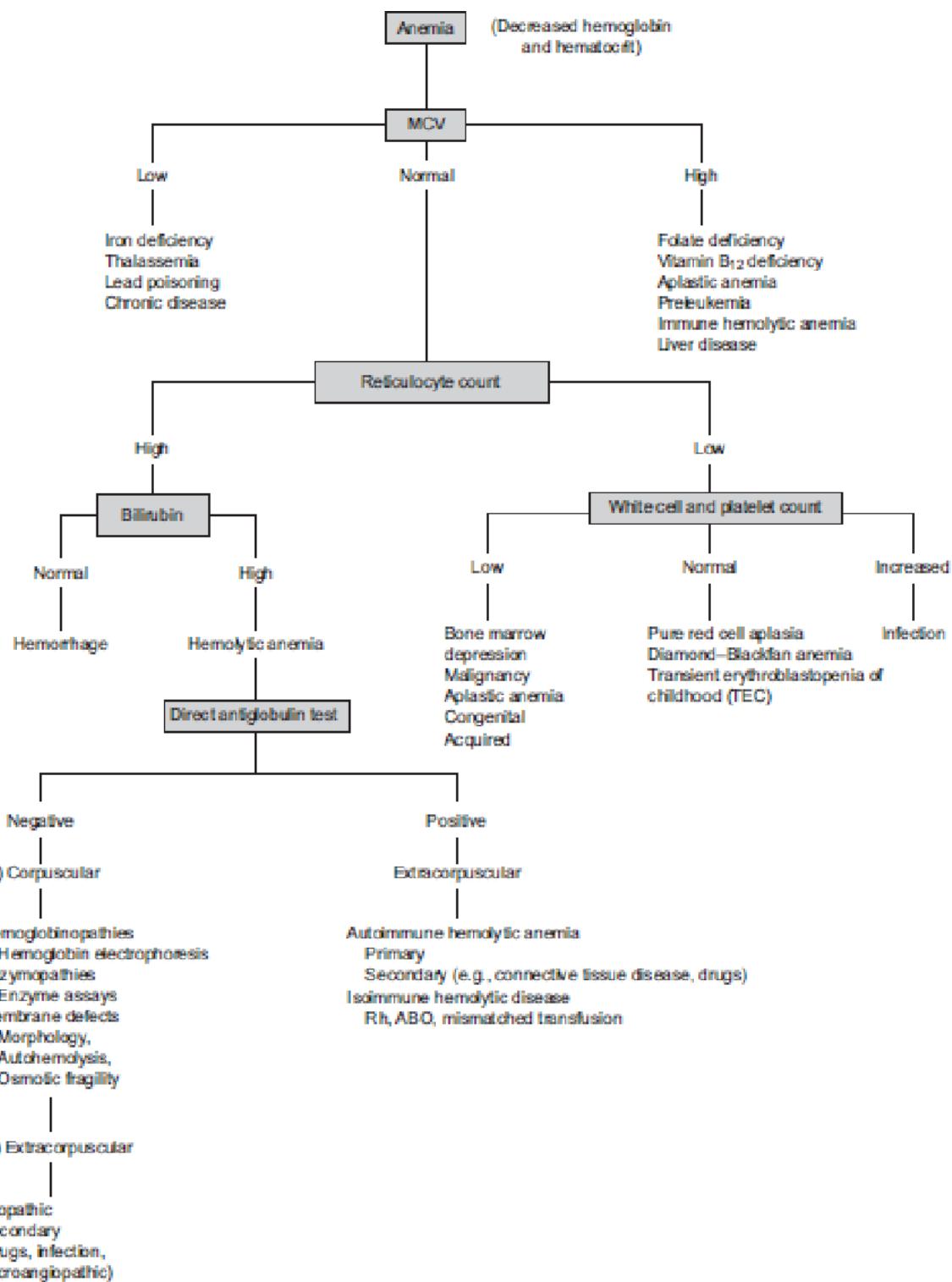
*Always adjust MCV according to age and sex for each patient.

AIHA: Autoimmune hemolytic anemia

Adapted from: San Roman S, Mozo Y, 2017

Pathologic Classification of Anemia





Management

Primary Level

- Supportive management
- Treat any underlying infections or parasites
- REFERRAL FOR SECONDARY LEVEL REVIEW

Secondary Level

Non-severe anaemia

- Young children (aged < 6 years) are anaemic if their Hb is < 9.3 g/dl (approximately equivalent to an Hct of < 27%).
- If anaemia is present, begin treatment, unless the child has severe acute malnutrition
 - Give (home) treatment with iron (daily iron–folate tablet or dose of iron syrup) for 14 days.
 - Ask the parent to return with the child in 14 days. Treat for 3 months, when possible, as it takes 2–4 weeks to correct anaemia and 1–3 months to build up iron stores.
 - If the child is ≥ 1 year and has not received mebendazole in the previous 6 months, give one dose of mebendazole (500 mg) for possible hookworm or whipworm infestation.
 - Advise the mother about good feeding practice.

Severe anaemia

- Give a blood transfusion as soon as possible (see below) to:
- All children with an Hct of ≤ 12% or Hb of ≤ 4 g/dl
- Less severely anaemic children (Hct, 13–18%; Hb, 4–6 g/dl) with any of the following clinical features:
 - Clinically detectable dehydration
 - Shock
 - Impaired consciousness
 - Heart failure
 - Deep, laboured breathing
 - Very high malaria parasitaemia (> 10% of red cells with parasites).
- If packed cells are available, give 10 ml/kg over 3–4 h in preference to whole blood. If not available, give fresh whole blood (20 ml/kg) over 3–4 h.
- Check the respiratory rate and pulse rate every 15 min. If either rises or there is other evidence of heart failure, such as basal lung crepitations, enlarged liver or raised jugular venous pressure, transfuse more slowly. If there is any evidence of fluid overload due to the blood transfusion, give IV furosemide at 1–2 mg/kg, up to a maximum total of 20 mg.
- After the transfusion, if the Hb remains as low as before, repeat the transfusion.
- In children with severe acute malnutrition, fluid overload is a common and serious complication. Give packed cells when available or whole blood at 10 ml/kg (rather than 20 ml/kg), and do not repeat transfusion based on the Hb level, or within 4 days of transfusion
- If the cause is unknown, do a PBF for microscopy
- TREAT THE CAUSE!

Iron deficiency anaemia

- If female and menorrhagia identified, refer for gynae evaluation
- If occult bleeding identified, refer for GI evaluation
- Following diagnosis, treat with oral iron supplementation - ferrous sulphate, ferrous gluconate or liquid iron preparations.
- If patient intolerant to one form of oral iron it can be switched to an alternative as they may tolerate it better.
- Refer to tertiary centre if there is intolerant response or sub-optimal response to oral iron after 6-8 weeks

Sickle Cell Disease- see SCD guidelines

- Refer to tertiary centre if:
 - Recurrent or persistent anaemia
 - Intolerant response or sub-optimal response to oral iron after 6-8 weeks trial.
 - Unexplained anaemia
 - Anaemia with other cell lines affected on FBC
 - Neonatal Anaemia

Tertiary Level

Non-severe anaemia

- Young children (aged < 6 years) are anaemic if their Hb is < 9.3 g/dl (approximately equivalent to an Hct of < 27%).
- If anaemia is present, begin treatment, unless the child has severe acute malnutrition
 - Give (home) treatment with iron (daily iron-folate tablet or dose of iron syrup) for 14 days.
 - Ask the parent to return with the child in 14 days. Treat for 3 months, when possible, as it takes 2–4 weeks to correct anaemia and 1–3 months to build up iron stores.
 - If the child is ≥ 1 year and has not received mebendazole in the previous 6 months, give one dose of mebendazole (500 mg) for possible hookworm or whipworm infestation.
 - Advise the mother about good feeding practice.

Severe anaemia

- Give a blood transfusion as soon as possible (see below) to all children with an Hct of ≤ 12% or Hb of ≤ 4 g/dl
- Give a blood transfusion to less severely anaemic children (Hct, 13–18%; Hb, 4–6 g/dl) with any of the following clinical features:
 - Clinically detectable dehydration
 - Shock
 - Impaired consciousness
 - Heart failure
 - Deep, laboured breathing
 - Very high malaria parasitaemia (> 10% of red cells with parasites).
- If packed cells are available, give 10 ml/kg over 3–4 h in preference to whole blood. If not available, give fresh whole blood (20 ml/kg) over 3–4 h.

- Check the respiratory rate and pulse rate every 15 min. If either rises or there is other evidence of heart failure, such as basal lung crepitations, enlarged liver or raised jugular venous pressure, transfuse more slowly. If there is any evidence of fluid overload due to the blood transfusion, give IV furosemide at 1–2 mg/kg, up to a maximum total of 20 mg.
- After the transfusion, if the Hb remains as low as before, repeat the transfusion.
- In children with severe acute malnutrition, fluid overload is a common and serious complication. Give packed cells when available or whole blood at 10 ml/kg (rather than 20 ml/kg), and do not repeat transfusion based on the Hb level, or within 4 days of transfusion
- **TREAT THE CAUSE!**

Iron deficiency anaemia

- If female and menorrhagia identified, refer for Gyn evaluation
- If occult bleeding identified, refer for GI evaluation
- Following diagnosis, treat with oral iron supplementation - ferrous sulphate, ferrous gluconate or liquid iron preparations.
- If patient is intolerant to one form of oral iron it can be switched to an alternative as they may tolerate it better.
- Refer to tertiary centre if there is intolerant response or sub-optimal response to oral iron after 6-8 weeks

Sickle Cell Disease - see SCD guidelines

Neonatal anaemia

- a. *haemorrhage: acute or chronic;*
 - Blood loss may occur during the prenatal, intrapartum, or postnatal periods.
 - Prenatal blood loss may be transplacental, intraplacental, or retroplacental or may be due to a twin-to-twin transfusion.
 - The clinical and laboratory manifestations of haemorrhage depend on the volume of the haemorrhage and the rapidity with which it occurs.
 - Clinical Findings
 - Anaemia—pallor, tachycardia, and hypotension (if severe, e.g., 20 mL/kg blood loss). Nonimmune hydrops can occur in severe anaemia.
 - Liver and spleen not enlarged (except in chronic transplacental bleed).
 - Jaundice absent (except after several days in entrapped haemorrhage).
 - Laboratory findings:
 - reduced haemoglobin (as low as 2 g/dL)
 - increased reticulocyte count,
 - polychromatophilia,
 - nucleated RBCs are raised,
 - foetal cells in maternal blood (in foetomaternal bleed), and direct antiglobulin test (DAT) negative.
 - Treatment
 1. Severely affected

- a. Transfusion of packed red blood cells.
- b. Crossmatch blood with the mother. If unavailable, use group O Rh-negative blood or intravenous fluids, temporarily for shock, while awaiting available blood.

2. Mild anaemia due to chronic blood loss

- a. Ferrous sulphate (4-6 mg elemental iron/kg body weight per day) for 3 months.
- o b. *haemolysis*:
 - Congenital haemolytic anaemias or due to immune haemolytic anaemias;
 - Refer to neonatologist and haematologist
- o c. *hypoplasia*:
 - Failure of red cell production in inherited bone marrow failure syndromes, for example, Diamond-Blackfan anaemia (pure red cell aplasia) (see bone marrow failure syndromes below)
- o d. *congenital infections*:
 - Refer to neonatologist
 - Test for syphilis in mother and child

Aplastic anaemia

- o Aplastic anaemia is characterised by a marked decrease or absence of blood-forming elements with resulting pancytopenia and can be inherited or acquired.
- o Various degrees of lymphopenia may be present.
- o Splenomegaly, hepatomegaly, and lymphadenopathy do not generally occur in aplastic anaemia.
- o Severe aplastic anaemia (SAA) is defined by:
 - Bone marrow cellularity of less than 25% **and** at least two of the following cytopenias:
 - granulocyte count <500/ μ L (<200 μ L defines very SAA),
 - platelet count <20,000/ μ L, and/or
 - reticulocyte count <20,000/ μ L.
- o Refer to haematologist

Inherited bone marrow failure syndromes

- o The key shared clinical manifestations of IBMFs are as follows:
 - bone marrow failure
 - congenital anomalies
 - cancer predisposition
- o Refer to haematologist

Other Haemolytic Anaemias

- o Refer to Haematologist

Follow up

- Non severe anaemia cases can be followed up at secondary level PEN-Plus clinic
- Severe cases of anaemia should be followed up at the tertiary level

BLOOD TRANSFUSION

Storage of blood

- Use blood that has been screened and found negative for transfusion-transmissible infections.
- Do not use blood that has passed its expiry date or has been out of the refrigerator for more than 2 h.
- Large-volume, rapid transfusion at a rate > 15 ml/kg per h of blood stored at 4 °C may cause hypothermia, especially in small infants.

Problems in blood transfusion

- Blood can be the vehicle for transmitting infections (e.g. malaria, syphilis, hepatitis B and C, HIV).
- Therefore, screen donors for as many of these infections as possible.
- To minimise the risk, give blood transfusions only when essential.

Indications for blood transfusion

There are five general indications for blood transfusion:

- acute blood loss, when 20–30% of the total blood volume has been lost, and bleeding is continuing
- severe anaemia
- septic shock (if IV fluids are insufficient to maintain adequate circulation; transfusion to be given in addition to antibiotic therapy)
- clotting factor deficiencies - whole fresh blood is required to provide plasma and platelets for clotting factors, if specific blood components are not available
- Neonatal hyperbilirubinemia exchange transfusion in neonates with severe jaundice.

Giving a blood transfusion

Before transfusion, check that:

- the blood is the correct group, and the patient's name and number are on both the label and the form (in an emergency, reduce the risk for incompatibility or transfusion reactions by cross-matching group-specific blood or giving O-negative blood if available)
- the blood transfusion bag has no leaks
- the blood pack has not been out of the refrigerator for more than 2 h, the plasma is not pink nor has large clots, and the red cells do not look purple or black
- the child has no signs of heart failure. If present, give 1 mg/kg of furosemide
- IV at the start of the transfusion to children whose circulating blood volume
- is normal. Do not inject into the blood pack.
- Make baseline recordings of the child's temperature, respiratory rate and pulse rate.
- The volume of whole blood transfused should initially be 20 ml/kg, given over 3–4h.

During transfusion:

- If available, use an infusion device to control the rate of transfusion.
- Check that the blood is flowing at the correct speed.

- Look for signs of a transfusion reaction (see below), particularly carefully in the first 15 min of transfusion.
- Record the child's general appearance, temperature, pulse and respiratory rate every 30 min.
- Record the times the transfusion was started and ended, the volume of blood transfused and any reactions.

After transfusion:

- Reassess the child. If more blood is needed, a similar quantity should be transfused and the dose of furosemide (if necessary) repeated.

Transfusion reactions

- If a transfusion reaction occurs, first check the blood pack labels and the patient's identity. If there is any discrepancy, stop the transfusion immediately and notify the blood bank.
- **Mild reaction** (due to mild hypersensitivity)

Signs and symptoms:

- itchy rash

Management

- Slow the transfusion.
- Give chlorphenamine at 0.1 mg/kg IM, if available.
- Continue the transfusion at the normal rate if there is no progression of symptoms after 30 min.
- If the symptoms persist, treat as a moderately severe reaction (see below).

- **Moderately severe reaction** (due to moderate hypersensitivity, non-haemolytic reactions, pyrogens or bacterial contamination)

Signs and symptoms:

- severe itchy rash (urticaria)
- Flushing
- fever $> 38^{\circ}\text{C}$ ($> 100.4^{\circ}\text{F}$) (Note: fever may have been present before the transfusion.)
- rigor
- restlessness
- raised heart rate

Management:

- Stop the transfusion, remove the IV line but not the cannula. Set up a new infusion with normal saline.
- Give 200 mg hydrocortisone IV or 0.25 mg/kg and chlorphenamine IM, if available.
- Give a bronchodilator if wheezing (see respiratory section)
- Send the following to the blood bank: the blood-giving set that was used, a blood sample from another body site and urine samples collected over 24 h.
- If there is improvement, restart the transfusion slowly with new blood and observe carefully.

If there is no improvement in 15 min, treat as a life-threatening reaction (see below), and report to the senior doctor in charge and to the blood bank.

- **Life-threatening reaction** (due to haemolysis, bacterial contamination and septic shock, fluid overload or anaphylaxis)

Signs and symptoms:

- fever $> 38^{\circ}\text{C}$ ($> 100.4^{\circ}\text{F}$) (Note: Fever may have been present before the transfusion.)
- rigour
- restlessness
- raised heart rate
- fast breathing
- black or dark-red urine (haemoglobinuria)
- unexplained bleeding
- confusion
- collapse
- Note that in an unconscious child, uncontrolled bleeding or shock may be the only signs of a life-threatening reaction.

Management:

- Stop the transfusion, take out the IV line, but keep in the cannula. Set up an IV infusion with normal saline.
- Maintain airway and give oxygen (see emergency section).
- Give adrenaline 0.15 ml of 1:1000 solution IM.
- Treat shock (see GIT section).
- Give 200 mg hydrocortisone IV or chlorphenamine 0.1 mg/kg IM, if available.
- Give a bronchodilator, if there is wheezing.
- Report to the senior doctor in charge and to the blood laboratory as soon as possible.
- Maintain renal blood flow with IV furosemide at 1 mg/kg.
Give antibiotics as for septicaemia

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CHAPTER 8. NEONATOLOGY

BASIC DEFINITIONS

Categorization of neonates by maturity

- Term babies: Born at 37+0 - 41+6 weeks gestational age (GA)
- Preterm babies: Born at < 37+0 weeks GA
- Extremely preterm: < 28+0 weeks GA
- Very preterm: 28+0 - 31+6 weeks GA
- Moderate to late preterm: 32+0 - 36+6 weeks GA
- Post-term babies: Born at 42+0 weeks GA or more

Categorization of neonates by birth weight

- Macrosomia: >3999g
- Normal birth weight: 2500g - 3999g
- Low birth weight (LBW): <2500g
- Very low birth weight (VLBW): <1500g
- Extremely low birth weight (ELBW): <1000g
- Appropriate for GA (AGA): 10th - 90th centile
- Large for GA (LGA): > 90th centile
- Small for GA (SGA)/small for date (SFD): < 10th centile

Determining Gestational Age

- If the mother's last-known menstrual period (LNMP) is known and correct, use the LNMP for estimating GA
- If the LNMP is unknown or deemed to be incorrect, use the early antenatal ultrasound to estimate the GA
- If neither correct LNMP nor early ultrasound is available, use the *New Ballard Score* (or a similar maturity score) to estimate the baby's GA soon after stabilization (see figure)

The new Ballard Score

MATURATIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballard Score)

NAME _____ SEX _____
 HOSPITAL NO. _____ BIRTH WEIGHT _____
 RACE _____ LENGTH _____
 DATE/TIME OF BIRTH _____ HEAD CIRC. _____
 DATE/TIME OF EXAM _____ EXAMINER _____
 AGE WHEN EXAMINED _____
 APGAR SCORE: 1 MINUTE _____ 5 MINUTES _____ 10 MINUTES _____

NEOMUSCULAR MATURITY

| NEUROMUSCULAR Maturity SIGN | SCORE | | | | | | | RECORD SCORE HERE |
|------------------------------------|-------|---|---|---|---|---|---|-------------------|
| | -1 | 0 | 1 | 2 | 3 | 4 | 5 | |
| POSTURE | | | | | | | | |
| SQUARE WINDOW (Wrist) | | | | | | | | |
| ARM RECOIL | | | | | | | | |
| POPLITEAL ANGLE | | | | | | | | |
| SCARF SIGN | | | | | | | | |
| HEEL TO EAR | | | | | | | | |
| TOTAL NEUROMUSCULAR MATURITY SCORE | | | | | | | | |

SCORE
 Neuromuscular _____
 Physical _____
 Total _____

MATURITY RATING

| SCORE | WEEKS |
|-------|-------|
| -10 | 20 |
| -5 | 22 |
| 0 | 24 |
| 5 | 26 |
| 10 | 28 |
| 15 | 30 |
| 20 | 32 |
| 25 | 34 |
| 30 | 36 |
| 35 | 38 |
| 40 | 40 |
| 45 | 42 |
| 50 | 44 |

PHYSICAL MATURITY

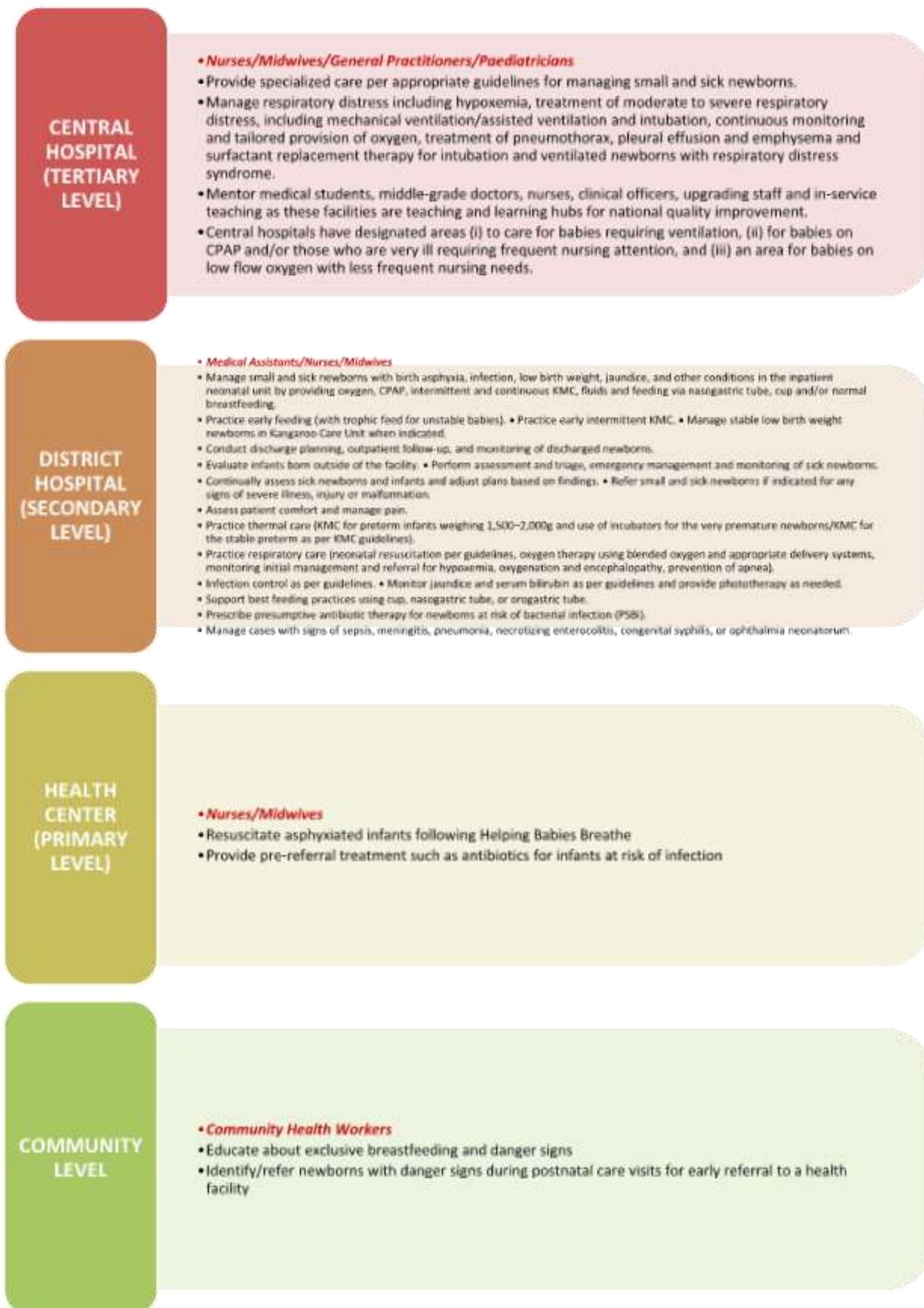
| PHYSICAL Maturity SIGN | SCORE | | | | | | | RECORD SCORE HERE |
|-------------------------------|---------------------------------------|---|---------------------------------------|--|--------------------------------|------------------------------------|---------------------------|-------------------|
| | -1 | 0 | 1 | 2 | 3 | 4 | 5 | |
| SKIN | sticky friable transparent | gelatinous red translucent | smooth pink visible veins | superficial peeling &/or rash, few veins | cracking pale areas rare veins | parchment deep cracking no vessels | leathery cracked wrinkled | |
| LANUGO | none | sparse | abundant | thinning | bald areas | mostly bald | | |
| PLANTAR SURFACE | heel-toe 40-50 mm: -1 <40 mm: -2 | >50 mm no crease | faint red marks | anterior transverse crease only | creases ant. 2/3 | creases over entire sole | | |
| BREAST | imperceptible | barely perceptible | flat areola no bud | stippled areola 1-2 mm bud | raised areola 3-4 mm bud | full areola 5-10 mm bud | | |
| EYE / EAR | lids fused loosely: -1 tightly: -2 | lids open pinna flat stays folded | sl. curved pinna; soft; slow recoil | well-curved pinna; soft but ready recoil | formed & firm instant recoil | thick cartilage ear stiff | | |
| GENITALS (Male) | scrotum flat, smooth | scrotum empty faint rugae | testes in upper canal rare rugae | testes descending few rugae | testes down good rugae | testes pendulous deep rugae | | |
| GENITALS (Female) | clitoris prominent & labia flat | prominent clitoris & small labia minora | prominent clitoris & enlarging minora | majora & minora equally prominent | majora large minora small | majora cover clitoris & minora | | |
| TOTAL PHYSICAL MATURITY SCORE | | | | | | | | |

GESTATIONAL AGE (weeks)
 By dates _____
 By ultrasound _____
 By exam _____

Reference
 Ballard JL, Khoury JC, Wedig K, et al: New Ballard Score, expanded to include extremely premature infants. *J Pediatr* 1991; 119:417-423. Reprinted by permission of Dr Ballard and Mosby—Year Book, Inc.

TOTAL PHYSICAL MATURITY SCORE

Levels of Newborn Care: Services by provider at each level of care in Malawi



Source: A case study in establishing care for small and sick newborns in Malawi, PATH 2022

NEONATAL RESUSCITATION

Introduction

- Birth asphyxia is a major problem, causing around 25% of neonatal deaths globally.
- Neonatal resuscitation is one of the most important interventions in newborn care.
- 90% will not require any assistance at birth.
- 10%, will require some assistance
- About 1% will need active resuscitation.

Anticipation for a neonatal resuscitation

- Alertness and preparedness for a resuscitation at all times is crucial.

Risk factors for a newborn requiring resuscitation

| Mother | Fetus/Neonate | Peri-partum |
|---|---------------------------------|---------------------------------|
| 40 years of age | Prematurity or | Prolapsed cord |
| Lower socioeconomic status | Postmaturity | Utero-placental |
| Smoking, alcohol/drug abuse | Macrosomia | bleeding |
| Chronic/untreated medical conditions (e.g., diabetes, preeclampsia) | Intrauterine growth retardation | Breech presentation |
| Worrisome obstetric/gestational issues (e.g., premature rupture of membranes (PROM), placenta previa) | Multiple gestation | Chorioamnionitis |
| | Congenital anomalies | Meconium-stained amniotic fluid |

Prevention and promotion

- Improved Antenatal Care (ANC) and intrapartum care
- Awareness on effect of maternal age, drugs, underlying illnesses etc on birth outcomes

Goals of resuscitation

- Early identification of risk factors
- Anticipation of problems
- Early recruitment of equipment and qualified personnel
- Early formulation of a care plan
- Assist with the initiation and maintenance of adequate ventilation, oxygenation, cardiac output, tissue perfusion, normal core temperature and serum glucose

Preparing for a resuscitation:

- Anticipate >> Prepare >> Evaluate risk factors >> Communicate >> Plan >> Initiate.
- Team work: Each member must have a clear role!

Requirements for a resuscitation

- Radiant warmer / resuscitaire (this must be on before the baby is delivered)
- Sterile, warm linen for receiving, drying and carrying the baby
- Thin plastic wrap if available

- Sterile procedure trays
- Sterile cord ties
- Glucometer
- Suction machine and catheters
- Pulse oximeter
- Feeding tube (8F catheter), - Syringe, catheter tipped, 20 mL
- Meconium aspirator, suction catheters
- IV catheters (22 g) - tape and sterile dressing material
- Fluids and drugs: Isotonic sodium chloride solution saline, 10% Dextrose water, adrenaline
 - Intermittent Positive Pressure Ventilation IPPV equipment and accessories
 - Intubation accessories
- Timer
- Umbilical catheters (2.5F, 5F)
- Chest tube (10F catheter)

ASSESS ALL NEWBORNS

- ***The 2021 AHA/AAP/*ILCOR (*ILCOR = International liaison committee on resuscitation) guidelines include a rapid assessment of the neonate's clinical status based on the following questions:***
 - Doe(l)s the infant
 - Full-term?
 - Have good muscle tone?
 - Breathing or crying?
- If the answer to all three questions is yes, the newborn does not need resuscitation, should not be separated from the mother, and is managed by routine neonatal care.

ILCOR 2021 – Order of approach to a neonatal resuscitation

Initial stabilization >> Provide warmth, dry, stimulate >> Open airway for patency if necessary >> Assess breathing >> Ventilation and oxygenation if necessary >> Assess circulation >> Chest compressions if necessary >> Inotropes and/or volume expansion if necessary

A. Airway

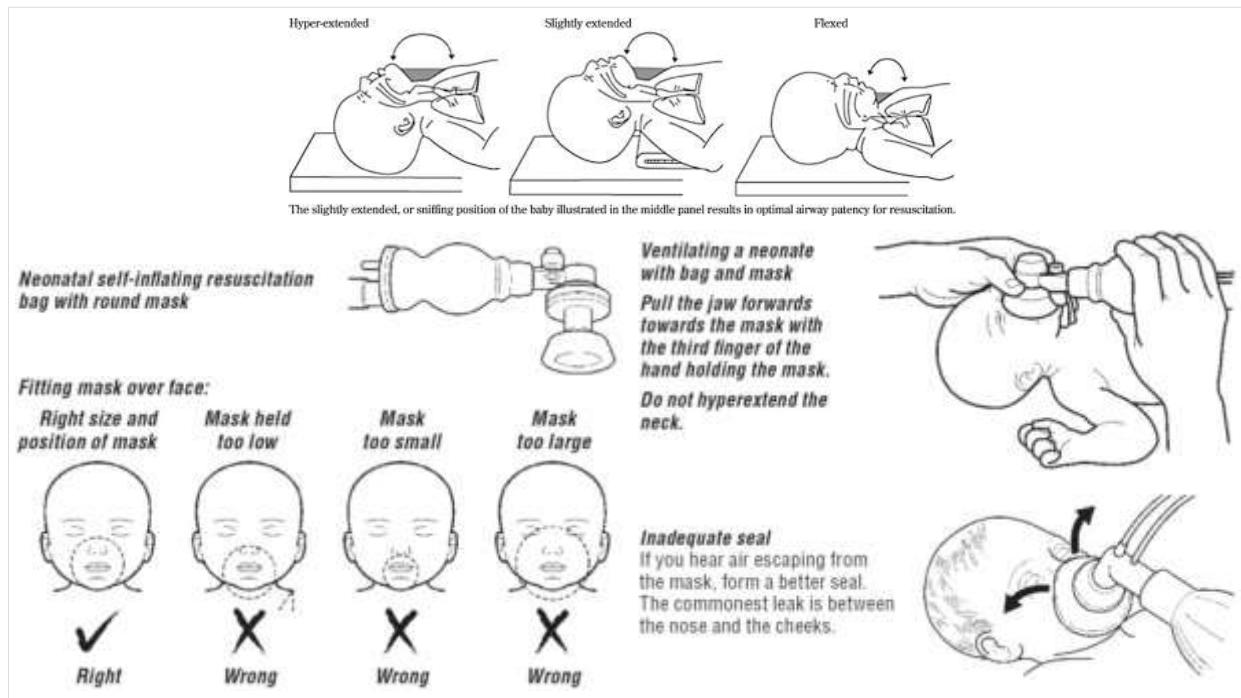
- Positioning – place the baby in neutral position
- Routine suctioning NOT recommended, unless obvious obstruction from secretions
- Meconium staining NOT indication for suctioning if it is not blocking the airway
- Wiping or light suctioning should be done if copious secretions impair the airway

B. Breathing

- Look, Listen, Feel
- Start bag and mask (IPPV) if:
 - Gasping or apnoeic
 - HR < 100/min
 - Choosing mask size: 1 for > 2.5kg, 0 for < 2.5kg

- Ventilation: BMV at ~30 breaths/minute (1 breath every 2 seconds)
- Make sure there is chest movement
- Avoid overinflating the lungs

Correct procedure for neonatal bag-mask ventilation



Source: WHO

Oxygen during neonatal resuscitation:

- For $\geq 35/40$ GA, initiate resuscitation with room air
- For $< 35/40$ GA, initiate resuscitation with 21 to 30 % oxygen
- Monitor SpO₂ by pulse oximetry
- Adjust the O₂ concentration (FiO₂) to achieve targeted SpO₂ levels.
- If HR < 60 bpm after 90 s of IPPV, increase the FiO₂ to 100% until normal heart rate.

Normal range for SpO₂ levels after birth:

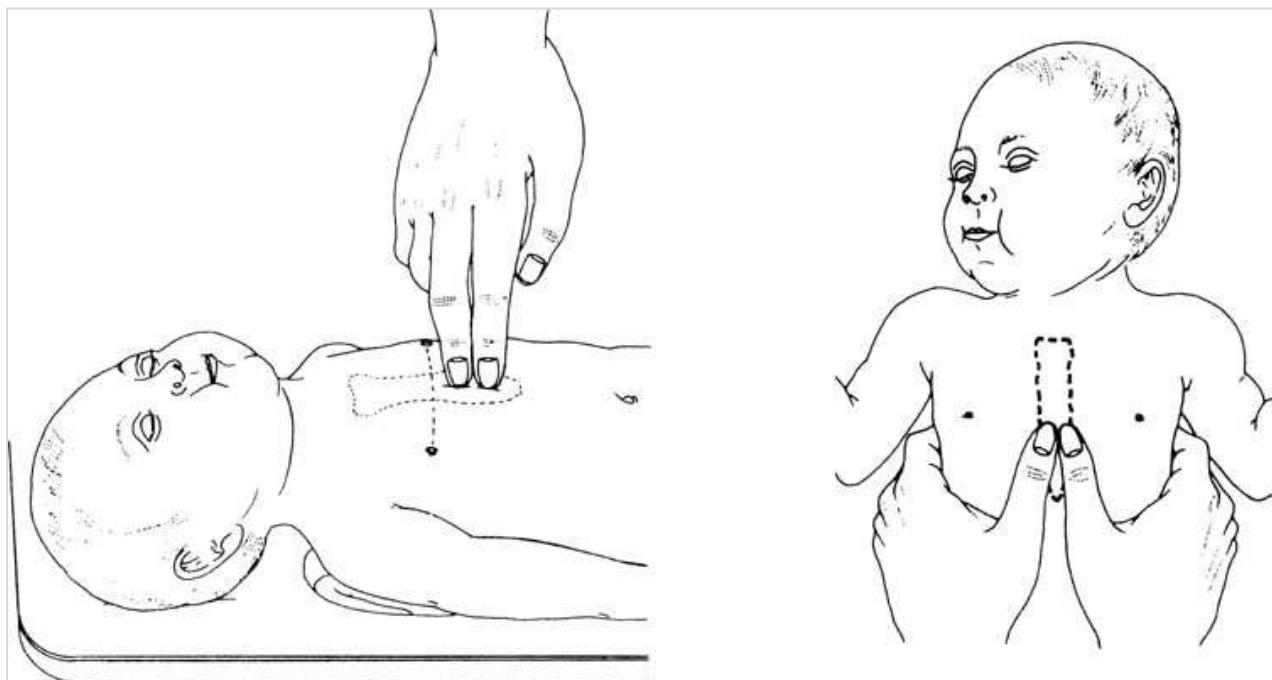
- 1 minute – 60 to 65 percent
- 2 minutes – 65 to 70 percent
- 3 minutes – 70 to 75 percent
- 4 minutes – 75 to 80 percent
- 5 minutes – 80 to 85 percent
- 10 minutes – 85 to 95 percent

C: Circulation

- Assess colour, central pulses, umbilical pulsation, capillary refill time.
- Chest compressions:
 - If HR remains < 60 beats per minute despite adequate ventilation for 30 seconds.
 - 90 compressions to 30 breaths /min (3 to 1)

- 1/3 the A-P diameter of the chest (1-1.5cm)
- Evaluate the heart rate and breathing every 30 sec.
- If shock – IVF N/S 10ml/kg over 10 minutes. Can repeat once, then O-Rh-negative blood

Correct positioning for neonatal chest compressions



(Source: WHO)

Medications during resuscitation

- **Drugs are rarely indicated in neonatal resuscitation!**
- Fluids
 - N/S (volume expander), 10ml/kg over 5 to 10 minutes if hypovolaemic
 - 10% D/W, 2ml/kg if hypoglycaemic
- Adrenalin (1:10,000) 0.1ml/kg
 - Indicated when HR < 60 despite adequate ventilation & compressions
 - Repeat every 3 minutes
- Naloxone
 - 0.1mg/kg IM, if documented exposure to opioids
 - Give once adequate supportive ventilation has been established
- Sodium bicarbonate (0.5mEq/ml)
 - Not shown to change the outcome, therefore not routinely recommended
- Calcium gluconate
 - Does not change the outcome, therefore not recommended

Reasons for failure to respond to positive pressure ventilation (PPV)

- Poor technique
- Mechanical block (eg, meconium, choanal atresia, malformations)
- Impaired lung functioning (pneumothorax, pleural effusions, Congenital Diaphragmatic Hernia, pulmonary hypoplasia)
- Congenital heart disease – central cyanosis

- Heart block – persistent bradycardia
- Brain injury (hypoxic ischaemic encephalopathy)
- Congenital neuromuscular disorder
- Respiratory depression - from maternally administered opioids

Counselling of the mother and guardians

- Counselling of the mother and the guardian must be continuous right from the beginning.
- To the best of our ability, the mother and guardians must be regularly updated on progress
- Allow the mother, as much as possible, to be part of the decision making process as the care continues.

Difficult decisions

- Currently there is no routine ventilation available, therefore only babies who are able to breathe by themselves can survive.
- Babies not responding to full resuscitation after 10 minutes are unlikely to survive.
- Discuss with senior colleagues on further decision making for a newborn undergoing resuscitation.

Cessation of resuscitation

- If after 10 minutes of effective resuscitation, the baby is not breathing and pulse is absent.
- If after 20 minutes of effective resuscitation, there is no spontaneous breathing and pulse is not reaching 60/minute.

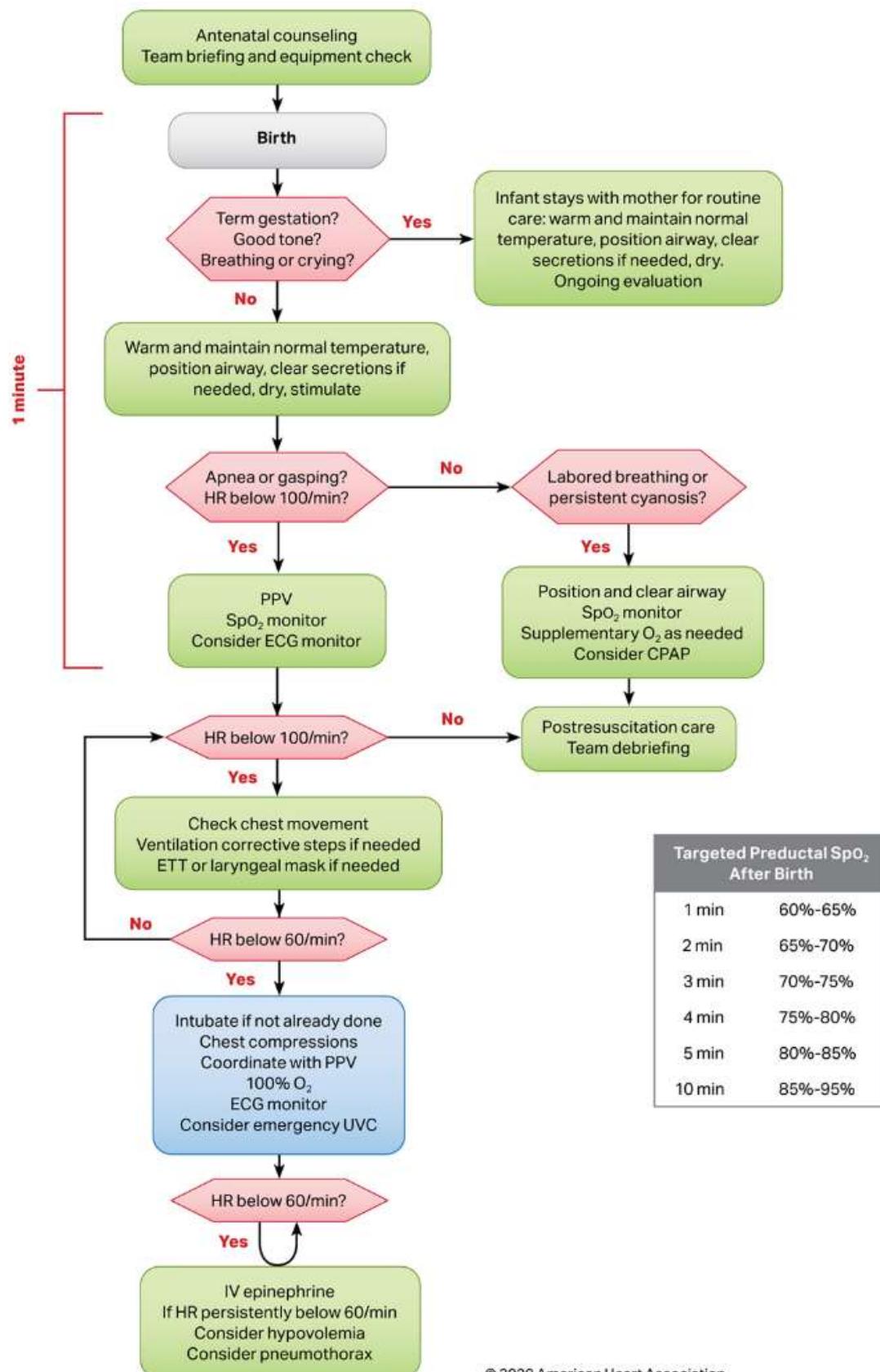
Referral

- Primary level
- All newborns who have required bag and mask ventilation for more than 5 minutes, or have signs of encephalopathy must be referred to the secondary level hospital
- Secondary Level
- All newborns with clinical features of moderate to severe HIE must be referred to the tertiary level hospital

Follow up

- All neonates with a diagnosis Birth Asphyxia should be followed up at secondary or tertiary level for Neurodevelopmental assessment, audiology and visual assessments.
- Refer to specific central hospital guidelines for scheduling.

Neonatal resuscitation algorithm



- Our recommendation is to secure the airway and provide ventilation, using bag and mask or neopuff, throughout the resuscitation.

BIRTH ASPHYXIA / LOW APGAR SCORE / HYPOXIC ISCHAEMIC ENCEPHALOPATHY

Definition Birth Asphyxia

- Failure to establish regular spontaneous respiration within 1 minute of birth. Results from failure of normal physiological processes at the time of labour and delivery.
- Therefore, commonest cause is compromised fetal or maternal oxygenation or perfusion.
- In some cases, longstanding adverse effects on the fetal brain, which can also present as birth asphyxia.

Definition Low Apgar Score

- A low APGAR score is a score of less than 7/10 at 5 minutes.

APGAR Score Chart

| Factor | 0 | 1 | 2 |
|--------------------|---------------------------|--------------------------------|--------------------------------------|
| <u>Appearance</u> | Blue or pale | Body pink; limbs blue | Body and limbs pink |
| <u>Pulse</u> | No pulse | Less than 100 beats per minute | Greater than 100 beats per minute |
| <u>Grimace</u> | No reaction | Grimacing or frowning | Coughing, sneezing or crying |
| <u>Activity</u> | No movement; limp | Weak; some arm & leg movement | Strong movement; flexing arms & legs |
| <u>Respiration</u> | Not breathing; not crying | Weak cry or whimper | Crying well and loudly |

Definition Hypoxic Ischaemic Encephalopathy (HIE)

- Abnormal neurological state seen after birth asphyxia.
- Affected infants may have problems with the pulmonary, CVS, GIT and renal systems.
- Organ damage in latent phase: 6-24 hours after insult (up to >72 hours)
- HIE secondary phase: 6-72 hours
 - Usually results in chronic brain and other organ injury.
 - Therefore, the first 6 hours are crucial in the management of HIE.

Risk factors

| Preconceptual | Antepartum | Intrapartum |
|--------------------------|----------------------|------------------------------|
| Primigravida | Placenta praevia | Malpresentation |
| Teenager | Abruptio placentae | Maternal illness |
| Advanced maternal age | IUGR | Induction |
| Chronic maternal illness | Severe pre-eclampsia | Prolonged labour |
| | Other causes of APH | Instrumental delivery |
| | Fetal distress | Severe prematurity |
| | Maternal collapse | Maternal drugs |
| | In utero infection | Born outside health facility |

- As HIE manifests end organ injury due to significant asphyxia, the risk factors for HIE are the same as those for birth asphyxia.

Prevention and promotion

- Improvements in the antepartum and intrapartum care of pregnant women
- Immediate and effective neonatal resuscitation.
- Awareness on risk factors for birth asphyxia
- Empowerment of health workers on early anticipation and diagnosis and effective resuscitation of asphyxia babies.
- Early diagnosis and management of HIE

Clinical Presentation

- HIE is a multi-systemic pathology.
- Refer to figure below

HIE staging (Thompson, Sarnat & Sarnat)

| | |
|-------------------------------|--|
| Stage 1 (Mild) | <ul style="list-style-type: none">• Hyperalert, irritable, overactive reflexes, Sympathetic effects (tachycardia, large pupils)• Outcome – very good• Duration of symptoms - < 24 hrs |
| Stage 2 (Moderate) | <ul style="list-style-type: none">• Obtunded, lethargic, hypotonia, decreased spontaneous movements with or without seizures• Outcome – 80% normal• Symptoms lasting > 5 days increases the probability of neurological deficit |
| Stage 3 (Severe) | <ul style="list-style-type: none">• Stupor, flaccidity, continuous seizures, suppressed brain stem and autonomic functions, apnoeas• Outcome – 50% mortality, remainder with lasting neurological impairment |

Differential diagnosis

- Brain trauma: haemorrhage, thrombo-embolism ("neonatal stroke")
- Drugs eg. opioids
- Infections: meningitis, encephalitis, TORCH infections
- Metabolic and electrolyte abnormalities: hypoglycaemia, hypocalcaemia, hypokalaemia, hyponatraemia, hypernatraemia, hypophosphataemia
- Endocrine: hypothyroidism
- Inborn errors of metabolism
- Syndromes: Down Syndrome, muscular dystrophies, Prader-Willi, Marfan, etc.

Relevant investigations

- Arterial blood gas (ABG)
- Blood sugar: Hypoglycaemia is common and needs appropriate management.
- Consider septic screen as above and if sepsis risk factors
- Specific tests for organ damage can be done to determine the degree of damage such as to the liver and kidneys
- Consider cranial USS to exclude intraventricular haemorrhage or other intracranial abnormalities.

Management

Important points in the history:

- Last menstrual period of mother (if known)
- Any complications/ illnesses in pregnancy
- Maternal risk factors for infection e.g. fever, prolonged rupture of membranes.
- History of labour – length of 1st + 2nd stage, any drugs administered to the mother.

Important points in the examination:

- Assess and manage ABCDE
- Assess gestational age
- Any clinical seizures?
- Tone, reflexes, including ability to suck

Indications for admission:

- Low APGAR score (< 7) at 5 minutes of age
- Term babies with a low APGAR score at 5 minutes but who are active and vigorous at 10 minutes do not need admission.
- Stabilize the patient (Refer to neonatal resuscitation section).

Primary Level

- Resuscitate according to HBB protocol
- Manage hypoxia, stabilize
- Provide pre-referral antibiotics if indicated
- Refer All newborns who have required bag and mask ventilation for more than 5 minutes, or have signs of encephalopathy to the secondary level hospital

Secondary Level

- Resuscitate according to the COIN protocol/HBB
- Manage hypoxia, hypoglycaemia, fluid balance
- Manage convulsions
- If poor suck or reduced gag reflex will require NG feed as at high risk of milk aspiration.
- Monitor blood sugar and temperature.
- Temperature instability is common but infection must always be considered and a full septic screen carried out if persistent temperature >38°C.
- Refer to the tertiary level if persistent seizures, cardio-respiratory or metabolic instability or signs of hepatic, renal impairment.
- All newborns with clinical features of moderate to severe HIE must be referred to the tertiary level hospital

Tertiary Level

- Resuscitate
- Manage hypoxia, acidosis, electrolyte and metabolic derangements
- Provide supportive management.
- Observe for convulsions/ apnoeas; if present treat as per protocol.
- If poor suck or reduced gag reflex will require NG feed as at high risk of milk aspiration.
- Monitor blood sugar and temperature.
 - Temperature instability is common but infection must always be

- considered and a full septic screen carried out if persistent temperature $>38^{\circ}\text{C}$.
- Therapeutic hypothermia has not been proven to be effective in low resource countries.

Complications

- Moderate or severe on the Thompson score above is associated with neurodevelopmental impairment or death.
- Residual brain injury may not be apparent on discharge examination
 - Disabilities such as cerebral palsy or learning difficulties may only manifest as the child develops.
 - The parents should be counselled about this on discharge.
- Periventricular leukomalacia
- Seizure syndromes
- Blindness; Hearing impairment

When to discharge

- The baby can cup / breast feed safely and is gaining weight.
- When seizures have resolved.
- Mother and family have been thoroughly counselled

Follow up

- Babies with HIE should be reviewed after 1 week at either the secondary or tertiary level.
- Refer for audiology, and visual acuity assessments on discharge
- Refer for neurodevelopmental, physio, speech, occupational and physiotherapy follow up on discharge
- Refer to specific central hospital guidelines for scheduling.

CARE OF PREMATURE, SMALL FOR GESTATIONAL AGE AND LOW BIRTH WEIGHT (<2.5KG) BABIES

Definitions

- Refer to definitions above
- Low birth weight, SGA and premature babies are at risk of a number of problems – it is important to try and anticipate these, and to recognize and treat.

Causes / Risk factors for prematurity and their prevention

| Type | Risk factors | Examples | Prevention strategies |
|----------------------------------|---|---|--|
| Spontaneous preterm birth | <i>Age at pregnancy and pregnancy spacing</i> | Adolescent pregnancy, advanced maternal age, short inter-pregnancy interval | Preconception care, including access to family planning from adolescence, after birth and throughout reproductive years |
| | <i>Multiple pregnancies</i> | Increased rates of twin and higher-order pregnancies with assisted reproduction | Introduce and monitor policies for best practice in assisted reproduction |
| | <i>Infection</i> | Urinary tract infections, asymptomatic bacteriuria, malaria, HIV, syphilis, chorioamnionitis, bacterial vaginosis | Sexual health programmes aimed at prevention and treatment of infections prior to and during pregnancy. Intermittent preventive treatment of malaria (context-specific), antenatal screening for lower genital tract infections and asymptomatic bacteriuria |
| | <i>Underlying chronic medical conditions</i> | Diabetes, hypertension, anaemia, asthma, thyroid disease, HIV | Maximize preconception control for pre-existing conditions, as well as screening and prompt management during pregnancy |
| | <i>Nutritional</i> | Undernutrition, micronutrient | Assess and treat low nutritional status prior |

| | | | |
|---------------|---|--|--|
| | | deficiencies | to conception and in early pregnancy. Consider supplementation (e.g. iron folate and zinc supplementation) for pregnant women without systemic illness |
| | <i>Lifestyle and work-related</i> | Smoking, excess alcohol consumption, recreational drug use, excess physical work and activity | Adopt laws and rights-based approaches to protect pregnant women, and ensure maternity leave. Behavioural and community public health interventions targeting pregnant women and women of reproductive age, e.g. pharmacological interventions for smoking cessation |
| | <i>Environmental</i> | Exposure to indoor and ambient air pollution, heat stress | Public health measures, antenatal counselling, avoidance of air pollution and excessive heat where possible |
| | <i>Maternal psychological health</i> | Depression, violence against women | Antenatal screening where capacity to provide a supportive response is available |
| | <i>Genetic and other</i> | Genetic risk (e.g. family history), cervical incompetence, intrauterine growth restriction, congenital abnormality | Individual-specific interventions, e.g. cervical cerclage for women with singleton pregnancy and high risk of preterm birth |
| Health | <i>Induction or caesarean birth for</i> | Common indications include: pre- | Not applicable |

| | | | |
|--|--|---|---|
| professional -initiated preterm birth | <i>maternal indication</i> | eclampsia/eclampsia, placental abnormalities (e.g. placenta accrete) and pre-existing maternal conditions | |
| | <i>Induction or caesarean birth for fetal indication</i> | Common indications include severe fetal growth restriction | Not applicable |
| | <i>Induction or caesarean birth without medical indication</i> | Non-medically indicated, due to physician or patient preferences or incentives | Programmes and policies to reduce the practice of non-medically initiated preterm birth. Midwifery-led continuity models of care have proved effective |

(Source: 'Born too soon, decade of action on preterm birth', WHO 2023)

Prevention / promotion

- Awareness on risk factors for preterm delivery
- Strengthening ANC and post-natal care
- Improvement in obstetric care
- Antenatal steroids
- Strengthening KMC / IKMC

Clinical presentation and complications of prematurity

Preterm babies present with complications related to the immaturity of their physiological systems.

- **Respiratory:** Respiratory Distress Syndrome (RDS), aspirations, Bronchonco Pulmonary Dysplasia(BDP)
- **Cardiovascular:** Hemodynamic instability
- **CNS:** Apnoea of prematurity, intraventricular haemorrhage, PVL
- **Ophthalmology:** Retinopathy Of prematurity(ROP)
- **CNS / Endocrine /Skin:** Temperature dysregulation, glucose dysregulation
- **GIT:** Feeding intolerance, reflux, NEC, Jaundice
- **Immunity:** Sepsis
- **Renal:** Fluid acid-base and electrolyte dysregulation.
- **Haematology:** Anaemia of prematurity

Investigations

- Thorough clinical examination
 - Quick examination – ABC
 - Maturity assessment, anthropometry and classification of growth
 - Systemic examination for pathology or complications of prematurity
 - Eg. FBC, blood cultures, U&Es, CXR etc
 - Head to toe examination for congenital anomalies

Management

- Stable babies:
 - >2000g: Counsel mothers and followed up at primary health care level.
 - 1500g – 2000g: Admit at secondary care level for KMC and follow up
 - <1500g: Admit at tertiary care level for KMC and follow up
- All unstable preterm newborns should be stabilized, then discussed and referred to the next level care facility.
- Preterm babies must be started on KMC as soon as possible after birth (Immediate KMC).
- Manage specific complications of prematurity (see specific chapters in the COIN manual)

Primary Level

- ABCDE, stabilize, keep warm and refer all premature babies to the secondary level in KMC position

Secondary / Tertiary Level

- Unstable babies
 - Stabilize and refer all preterm babies who are unstable
- Stable babies
 - Birth-weight 1500g – 2000g admit to the KMC ward
 - Birth-weight <1500g – refer to the tertiary level for care including KMC

Follow up:

- A baby, whose weight is less than 1800g, is followed up at the discharging facility or the nearest health facility every week until the baby reaches 1800g.
- Once 1800g is attained, subsequent follow-up is done every 2 weeks until the baby is 2500g.
- Ensure the mother is linked to the HSA in the community for continued KMC support.
- Provide nutritional supplements – refer to the COIN guidelines.

SMALL FOR GESTATIONAL AGE

Definition

- Refer to Basic Definitions on page 212

Causes / Risk factors / Clinical presentation

Symmetrically small:

- low weight, short length and small head circumference
- Signifies early onset growth restriction e.g. intrauterine infection i.e. CMV, severe placental insufficiency, chromosomal abnormality, severe maternal disease such as renal disease or hypertension

Asymmetrically small:

- Discordance in plots between anthropometric measures; eg. low weight but relative sparing of length and head circumference
- Due to onset in the last few weeks e.g. placental insufficiency, pre-eclampsia or maternal smoking, drug addiction or alcohol ingestion

Prevention / Promotion:

- Early treatment of maternal disease
- Counselling
- Family planning

Investigations

- Take a good history
- Consider blood sugar test if unwell, jittery or poor feeding
- Consider checking for congenital infections and chromosomal disorders

Differential diagnoses

- Low birth weight
- Prematurity

Management

Primary Level

- Feed as soon after birth as possible – NG / cup / breast
- Refer unstable babies to secondary level

Secondary / Tertiary Level

- Feed as soon after birth as possible – NG / cup / breast
- Consider iv fluids if too sick to tolerate oral feeds
- Give warmth (dry, nurse near heater, hat, IKMC)
- Consider antibiotics if symptomatic / risk factors – see sepsis protocol
- Secondary can refer to tertiary level upon discussion with consultants

Complications

- Hypoglycaemia
- Thermal instability (increased surface area, immature skin, low subcutaneous fat)
- Polycythaemia secondary to intrauterine hypoxia – exacerbates respiratory problems, hypoglycaemia and necrotizing enterocolitis.

KANGAROO MOTHER CARE (KMC/ (IKMC))

Definition

- **KMC:** When the baby is nursed on the mother's or surrogate's chest, in skin-to-skin contact.
- **IKMC:** Immediate KMC is when skin to skin care is provided to the newborn as soon as possible after birth, irrespective of the baby's clinical condition, and continued in hospital or at home.
- KMC and IKMC are provided together with counselling and support for exclusive breast feeding.

Risk factors for KMC / IKMC

- See risk factors for prematurity

Benefits of KMC / IKMC

- When compared with conventional neonatal care, KMC in our setting leads to
- Better weight gain
- Less temperature dysregulation
- Less infection
- Possibly less apnoea
- Better short- and long-term survival (40% improvement in survival)

Implementing KMC

- Current WHO guidelines recommend Kangaroo mother care (KMC) as routine care for all preterm or low-birth-weight infants. KMC can be initiated in the health-care facility or at home and should be given for 8–24 hours per day (as many hours as possible).
- Kangaroo mother care (KMC) for preterm or low-birth-weight infants should be started as soon as possible after birth and continued thereafter (IKMC).
- Preterm babies being admitted to the neonatal unit must be transferred from the delivery area in skin-to-skin position either by the mother or available surrogate.
- KMC must continue for the LBW in the neonatal ward, as much as possible, depending on the availability of a stable mother or surrogate, and space for keeping the baby and the mother / surrogate together in the NICU (adapting towards IKMC).

Admission to the KMC ward

- The KMC ward remains a place for implementing skin to skin care for stable low birth weight babies (Refer to the Malawi KMC guidelines).
- Babies weighing >2000g and <2500g and being stable, are not admitted.
- The mother should be referred to the KMC ward for counselling on outpatient KMC and the baby kept with the mother. (Please refer to the levels of care for premature babies to decide on the appropriate level of in-patient KMC).
- All babies with a weight <2kg, who are stable, should be admitted to the KMC ward.
- Babies who weigh 1800g – 2000g can be admitted briefly in the KMC ward, and discharged as soon as the baby is stable, tolerating feeds, gaining weight, and the mother is confident and competent to continue KMC at home.
- All babies with a weight <2kg, who are unstable, should be admitted to the neonatal ward, and KMC provided as much as possible when the mother / surrogate is

available.

- Babies in the KMC ward should be weighed daily.
- Babies can be NGT fed when on KMC position.

Discharge from the KMC ward

- The following criteria must be met before a baby can be discharged from the KMC ward
- Baby has at least regained birth weight and has a minimum weight of 1500g
- Baby has gained at least 15g/kg/day for three consecutive days
- Kangaroo position is well tolerated by baby and mother
- The baby remains in respiratory and haemodynamic stability
- Temperature of the baby is stable
- No other illnesses exist
- Mother is capable of breast feeding and expressing breast milk
- Mother is willing to continue with KMC at home, and has support of the family
- For a baby with birth weight of 1800g; they can be discharged, as long as they remain stable and gaining weight, without necessarily regaining the birth weight.

Primary Level

- ABCDE, stabilize, keep warm and refer all premature babies to the secondary level in KMC position
- Stabilize and refer all preterm babies who are unstable to tertiary care facilities.

Secondary Level

- Unstable babies - Refer unstable babies to Tertiary level
- Stable babies
 - Birth-weight 1500g – 2000g admit to the KMC ward
 - Birth-weight <1500g – require tertiary level care including KMC

Tertiary Level

- As above
- Consider iv fluids if too sick to tolerate oral feeds
- Give warmth (dry, nurse near heater, hat, IKMC)
- Consider antibiotics if symptomatic / risk factors – see sepsis protocol

Follow up

- A baby, whose weight is less than 1800g, is followed up at the discharging facility or the nearest health facility every week until the baby reaches 1800g.
- Once 1800g is attained, subsequent follow-up is done every 2 weeks until the baby is 2500g.
- Ensure the mother is linked to the HSA in the community for continued KMC support.

NEWBORN FEEDING

Scheduling of feeds

- All babies must be weighed at delivery, on admission to the neonatal ward, and daily subsequently.
- For babies > 1500g, feeds are given every 3 hours
- Small babies (<1500g) should be fed every 2 hours (by breast or EBM by cup/NGT)
- For detail on insertion of feeding tubes, refer to the **NEST 360 Clinical modules** (<https://nest360.org/project/clinical-modules/>)

Calculation of feeds

- The daily feed volume should be calculated as below, and divided by 8 to give the 3-hourly feed volume, or by 12 to give the 2-hourly feed volume
- In general start daily feeds at 60ml/kg/day for >1500g and 90ml/kg/day for <1499g
- On average, increase total daily feeds daily by 24-30ml/kg/day

Use the birth weight for calculations until the actual weight is above the birth weight!

Newborn fluid requirements in ml/kg/day

| Day | 1 | 2 | 3 | 4 | 5 onwards |
|---------------|--------------|--------------|---------------|---------------|-------------------|
| 1500g & above | 60 ml/kg/day | 80 ml/kg/day | 100 ml/kg/day | 120 ml/kg/day | 150-200 ml/kg/day |
| <1500g | 90 ml/kg/day | 110ml/kg/day | 130 ml/kg/day | 150 ml/kg/day | 150-200 ml/kg/day |

- These numbers are for oral feeds
- These numbers can also be used for IV fluids
- If on IV fluids, discuss with seniors once the total fluid intake reaches 120ml/kg/day to plan further management.

Example for feed calculation:

A baby with birth weight 1.6kg, now on day 3 of life with 1.5 kg, requires
 $100 \text{ ml} \times 1.6 \text{ kg} = 160 \text{ ml/day} \div 8 = 20 \text{ ml/feed}$

Monitoring of feeds

- Monitor feed tolerance and weight gain and adjust the feeds appropriately.
- Once 150ml/kg/day is reached, do not automatically increase the feed intake, adjust feeds based on weight gain and as tolerated.
- If feed volumes are not sufficient, supplemental IV fluids may be started where clinically indicated.
 - There is no need for supplementation with IV fluids if the baby is taking at least 120ml/kg/day feed volumes.

Cautious feeds in sick and unstable patients

Feeds should be started cautiously and after discussion with registrar or consultant in-charge in the following patients:

- Severe HIE
- Severe hydrops fetalis
- Severe metabolic acidosis
- Extreme prematurity or ELBW
- Abdominal distension with soft abdomen
- Shocked patients, post-resuscitation
- Any cardio-respiratory instability

Stopping feeds (Nil per mouth)

Patients with the following should be kept NPO:

- NEC
- Bile-stained NGT aspirates
- Tracheo-oesophageal fistula / atresia
- Tense abdominal distension
- Abdominal tenderness
- Suspected GIT bleed
- Persistent vomiting
- Any intestinal atresia
- Ileus
- Severe metabolic acidosis
- Septic shock

HYPOTHERMIA

Definition

Hypothermia is defined as rectal temperature <36.5°C.

- It is one of the biggest killers of newborn babies.
- With each 1°C reduction in temperature, there is up to 28% increase in mortality.
- Therefore, at all costs, effort must be made to prevent and treat hypothermia in newborns, particularly the preterm and low birth weight.

Risk factors

- Premature baby
- Small for gestational age
- Intra-uterine growth restriction
- Sepsis
- Hypothermia
- HIE
- Maternal illness / Orphaned baby
- In-born errors of metabolism
- Born before arrival/ in transit

Prevention / Promotion:

- Awareness
- Manage risk factors of prematurity
- Early diagnosis and treatment of underlying conditions
- Improvement in delivery and transfer of neonates
- Optimizing nutrition

Prevention of hypothermia in the delivery room

- Keep a warm delivery room. Avoid draughts and open windows; room temperatures must be >26°C.
- Deliver the baby onto the mother's abdomen in skin-to-skin position
- Use warm linen to dry and wrap the baby and resuscitate the baby under a radiant warmer
- For very preterm babies (<32 weeks), use sterile plastic wraps for heat conservation if available
- Follow optimal thermal care during delivery, resuscitation, transfer and care.
- Start IKMC in the delivery room

Prevention of hypothermia during transfer from delivery area

- The baby must be warmed up and normothermic before being transferred from the delivery area.
- The baby must be placed on the chest of the mother or surrogate in KMC position, and wrapped over with warm linen when being transferred (IKMC).
- Alternatively, a pre-warmed transfer incubator should be used.
- Communicate with the receiving ward team before transfer, and confirm that the radiant warmer is on in the 'pre-warm' mode on the receiving ward.

Admission in the neonatal ward

- There must always be a reserved radiant warmer on in readiness for the next admission.
- There must always be a nurse assigned to the admission station ready to receive new admissions as soon as they arrive.
- There must always be sufficient handover from the transfer team / person and the admitting team / person.
- It is the responsibility of the admitting person to ensure that they receive clear and sufficient handover, and that the transfer team has thoroughly completed the relevant maternal information on the admission sheet.
- On arrival in the ward, place the baby under a warmer already switched on and remove any cool or wet surfaces/linen.
- Place the temperature probe and monitor the baby's temperature, making sure that the baby does not warm up too fast.
- Once normothermia is achieved, put the settings on the radiant warmer in 'servo,' mode, to maintain the temperature within normal set limits.
- Every new admission must be seen by the clinician as soon as they arrive, and not more than an hour after admission.
- Every new admission must have a gestational age assessed by the admitting clinician, using the Ballard (or similar) score.
- Every new admission must have gestational age assigned by the admitting clinician using the scheme under the section "Categorization of neonates admitted to the Neonatal Unit by maturity."

Ongoing thermal management

- Ongoing specific management of the admitted neonate will proceed depending on the assessment on admission and in subsequent monitoring or reviews. These are covered under specific sections of this guideline.
- Keep the ward warm, ambient temperature $>26^{\circ}\text{C}$.
- Ensure the baby is well wrapped and wearing a hat.
- Initiate intermittent early KMC in all low birthweight babies where possible, when the mothers come for feeding, until the baby has been moved to the KMC ward.
- All babies $<1500\text{g}$ must be nursed under a radiant warmer, a working enclosed incubator or in continuous KMC position.
- All babies $1500\text{g} - 2000\text{g}$ must be nursed in KMC position or if this is not possible, should be nursed well covered in open cot (room temperature $> 26^{\circ}\text{C}$).
- If a baby is cold don't warm up faster than 1°C per hour.
- Start feeding early, unless there is a contraindication for enteral feeds.
- Keep the baby well hydrated
- Investigate and manage any risk factors, underlying causes and associated problems.

To minimize the risk of burn injuries to babies:

DO NOT USE WARMED IV FLUID BAGS TO WARM THE BABY!

Monitor temperature of radiant warmers regularly.

*For further information on the use of radiant warmers, see the NEST 360 clinical and technical modules on this link: <https://nest360.org/project/clinical-modules/>

Referral

- Primary level: Refer persistent hypothermia or hypothermia with underlying co-morbidity to the secondary level
- Secondary level: Refer severe or persistent hypothermia to the tertiary level

Follow up

- Follow up will be decided depending on the baby's clinical condition during admission, response to treatment and underlying pathologies.

NEONATAL HYPOGLYCAEMIA

Definition

A random blood glucose level <45mg/dl (< 2.5 mmol/l)

Risk factors / Causes

Hypoglycaemia is common and must be suspected in the following newborn infants:

- Premature baby
- Small for gestational age
- Postmature
- Intra-uterine growth restriction
- Infant of a diabetic mother
- Macrosomic / Large for gestational age
- Dysmorphic/Syndromic baby (especially with hemihypertrophy and visceromegaly)
- Severe Rhesus disease
- Prolonged labour
- Polycythaemia
- Sepsis
- Hypothermia
- HIE
- Maternal illness / Orphaned baby
- Maternal antihyperglycaemic drugs
- In-born errors of metabolism

Prevention / Promotion

- Early diagnosis and management of underlying pathologies
- Community awareness on KMC and breastfeeding
- Optimize nutrition
- Improvement in maternity and newborn care infrastructure

Signs and symptoms

Asymptomatic:

- Any asymptomatic neonate who has a risk factor for hypoglycaemia must have glucose level checked on first contact.

Symptomatic:

- Lethargy, floppiness, sweating, convulsions, apnoea, abnormal neurological behaviour.
- Any sick looking neonate must be investigated for hypoglycaemia.

Examination

Perform a complete head to toe examination of the newborn and examine for:

- Signs of growth disorders (PT, LBW, SGA, IUGR, LGA, Post-maturity)
- Stigmata of endocrine or inborn errors of metabolism.
 - Syndromic features
 - Neurological impairment

Investigations

- RBS
- FBC
- Urine for reducing substances.
- A blood gas analysis may help if there is unexplained hyperlactataemia.
- Insulin and cortisol levels.

Management

Primary Level

- **Emergency treatment for RBS < 45 mg/l / < 2.5 mmol/l**
 - Give 2 ml/kg of 10% dextrose IV (slow bolus) **OR**,
 - 1 ml/kg of 50% dextrose PO/NGT (bolus) **OR**,
 - 40% buccal glucose gel (200 mg/kg) = 0.5 ml/kg/dose (bolus)
- Follow with regular feeds (breastfeeding/NGT) or, if not tolerating oral intake, with an IV infusion 10% dextrose.
- Repeat RBS after 30 minutes.
- Stabilize and refer all neonates diagnosed with hypoglycaemia to the secondary level

Secondary Level

Emergency treatment as above PLUS

- Repeat RBS after 30 minutes. If RBS remains < 2.5 mmol/l repeat treatment as above
- If RBS remains < 2.5 mmol/l after 2 doses of bolus treatment, start IV infusion with 10% dextrose, optimize feeds
 - Start at 90 ml/kg/day and monitor RBS every two hours. Calculate the glucose infusion rate*

*Calculation of glucose infusion rate (GIR):

$$\text{GIR (mg/kg/min)} = \text{Fluid Rate (ml/kg/day)} \times \%D / 10 \times 0.07$$

(e.g., if giving 100 ml/kg/day of 10% D, $\text{GIR} = 100 \times 10 / 10 \times 0.07 = 7.0 \text{ mg/kg/min}$)

- NB: If GIR is more than 10mg/kg/min to keep RBS >45mg/dl, suspect hyperinsulinaemia.
- Monitor RBS every 2 hours. Adjust the dextrose infusion (glucose delivery rate) as appropriate.
- Feed the infant whenever possible. Increase the volume by 30 ml/kg/day until normal RBS is achieved
- REFER all patients with persistent hypoglycaemia see below) to tertiary level

Tertiary Level

- Manage as primary and secondary above
- Once 130 ml/kg/day reached, increase the dextrose concentration to 12.5%.
 - A central line will be needed if dextrose concentration exceeds 12.5%

- Once the RBS level has normalized, start weaning the glucose delivery by 2 mg/kg/min every 6 hours
- If the infant is still hypoglycaemic after reaching the glucose infusion rate of 12 mg/kg/min, consider endocrine or inborn errors of metabolism. Discuss with the consultant for possible further investigations
- In addition to managing the hypoglycaemia, thorough examination must be done to look for risk factors and underlying causes.
- Appropriate investigations will depend on the differential diagnoses. All sick babies with hypoglycaemia should be investigated and presumptively covered for sepsis.

Persistent hypoglycaemia

- Hypoglycaemia lasts beyond 72 hours
- May be caused by an underlying metabolic or endocrine condition.
- In our setting IUGR and sepsis are the commonest cause, but other causes are:
 1. *Hepatic enzyme deficiencies:*
 - Hepatic glycogen storage diseases (type 1 etc.)
 - Glycogen synthase deficiency
 - Disorders of galactose metabolism (galactosaemia)
 - Disorders of fructose metabolism (fructose intolerance, fructose-1,6-diphosphatase deficiency)
 2. *Disorders of amino-acid metabolism:*
 - Maple syrup urine disease, propionic and methylmalonic acidaemia
 - Tyrosinaemia
 - 3-OH 3-methylglutaryl CoA lyase deficiency
 3. *Mitochondrial, fatty acid oxidation and ketogenesis defects*
 - Carnitine/acylcarnitine defects
 - Acyl-CoA dehydrogenase defects
 - Very long / long / medium / short chain acyl-CoA dehydrogenase
 - Long chain 3-OH-acyl-CoA dehydrogenase
 4. *Endocrine disorders*
 - Hyperinsulinism
 - Primary - Nesidioblastosis
 - Secondary - Infant of diabetic mother, Beckwith-Wiedemann syndrome, Erythroblastosis fetalis
 - Hypopituitarism - Growth hormone deficiency
 - Adrenal disorders - Cortisol deficiency
 - Glucagon deficiency
 5. *Lack of substrate (neonatal growth)*
 - Intrauterine growth retardation
 - Small for gestational age
 - Prematurity
 6. *Medical*
 - Sepsis
 - Asphyxia

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring

NEONATAL HYPERGLYCAEMIA

Definition

Random blood glucose > 140mg/dl (> 7.8 mmol/l)

Most times hyperglycaemia is associated with an underlying problem, such as sepsis. Treatment of the underlying problem can result in the resolution of the hyperglycaemia.

Causes / Risk factors

- Prematurity <35 weeks' gestation
- SGA / IUGR
- Sepsis
- Severe dehydration
- Other stress (eg intraventricular haemorrhage)
- Iatrogenic (eg dextrose infusion), drugs
- Maternal steroids
- Inborn errors of metabolism
- Rarely neonatal diabetes mellitus

Prevention / Promotion

- Optimal antenatal care
- Appropriate prescription and use of IV dextrose
- Prevention, early detection and management of sepsis

Examination

- Perform a complete head to toe examination of the newborn.
- Look for signs of shock, dehydration, sepsis growth restriction, IVH.

Investigations

- Check blood glucose (preferably whole blood)
- Urine dipstick for glucosuria and ketonuria
- Blood gases for ketosis and electrolyte abnormalities
- Investigate for underlying causes (see specific chapters)

Management

Primary level

- Stabilize the patient (ABCD), refer to secondary level

Secondary Level

- Resuscitate and stabilize the patient: ABCD
- Stop any glucose infusions.
- Treat dehydration and start maintenance **glucose-free IV fluids** (N/S or RL)
- Monitor glucose levels 2 hourly
- Target glucose levels 95mg/dl – 135mg/dl
- Investigate for common aetiologies
- Refer to tertiary level, if the hyperglycaemia persists beyond 6 hours or the baby is clinically sick

Tertiary level

- Treat any dehydration, acidosis and electrolyte abnormalities
- Monitor glucose 2-hourly
- Investigate and treat underlying causes and complications
- Discuss with consultant on further management.
- Insulin
 - Not routinely indicated
 - If blood glucose > 200mg/dl AND glycosuria AND osmotic diuresis

If glucose persistently >190mg/dl for more than 3 days with no other causes of the hyperglycaemia, neonatal diabetes mellitus could be a possibility.

Complications of neonatal hyperglycaemia:

- Retinopathy of prematurity
- Intraventricular Haemorrhage (IVH)
- Necrotising Enterocolitis (NEC)
- Bronchopulmonary Dysplasia (BPD)

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring

NEONATAL SEPSIS

Introduction

- Newborns are a vulnerable group, prone to developing infection.
- Premature babies, are exposed to additional risk factors for infection.
- Clinical features of infection in newborns are non-specific
- Need to maintain a low threshold for making a presumptive diagnosis of and starting treatment for sepsis in sick newborns.
- In every baby being admitted to the neonatal ward, assess for risk of infection by evaluating exposure to antenatal and postnatal risk factors of infection and for signs of clinical instability / disease.

Classification of neonatal sepsis

- ***Early onset sepsis:***
 - presents within the first 3 days (72hrs) of life
- ***Late onset sepsis:***
 - Presents after the first 3 days (72hrs) of life
 - Presentation of sepsis will be non-specific.
 - Presume every feature of instability presenting or persisting after the first 72 hours of life as a possible presentation of late onset neonatal sepsis.
 - Perform sepsis diagnostics in these babies and start appropriate antibiotics as per the guideline above.

Risk factors / Causes

- Spontaneous preterm labour (SPTL)
- Pre-labour rupture of membranes (PROM)
- Prolonged ROM >18 hours (> 12 hours in preterm infants)
- Foul smelling amniotic fluid
- Positive antenatal GBS
- Positive Group B Streptococcus(GBS) in previous pregnancy or baby
- Maternal chorio-amnionitis
- Maternal fever

Prevention / Promotion

- Avoidance of risk factors
- Antenatal antibiotic treatment
- Infection prevention measures

Signs and symptoms

- Non-specific
- Abnormal neurology (irritability, seizures, lethargy)
- Respiratory distress (tachy-dyspnoea, cyanosis, grunting, intercostal recessions, apnoea)
- Abnormal heart rate
- Abnormal acid-base balance
- Abnormal glucose
- Abnormal temperature (hypothermia, fever)
- Poor or refusal to feed, vomiting, diarrhoea
- Jaundice

- Any other features can be included as discussed and agreed with registrar or consultant.

Differential Diagnosis

- Congenital heart disease (especially coarctation of the aorta)
- Inborn error of metabolism
- Gastroenteritis with dehydration
- Non accidental injury

Investigations

- **Every (sick) newborn suspected of having sepsis must have:**
 - Full blood count
 - Blood culture
 - CSF (If the baby is too sick to tolerate an LP this should be clearly documented)
 - Sterile urine culture (where possible),
 - Blood Sugar
- Consider Malaria screen
- Ideally the above investigations should be performed before antibiotics are given, but treatment should not be delayed if this is not possible!

Management

Primary Level

Stable newborns in the first 72 hours of life

- ABCDE
- Give single dose of IV / IM antibiotic.
- Refer to the secondary or tertiary level

Sick / unstable newborns in the first 72 hours of life

- ABCDE

(A)irway

- If necessary, position the airway in the 'neutral position'. Proceed with airway manouvres as per the resuscitation guidelines (see chart)

(B)reathing

- Bag and mask if apneic. Proceed as per the resuscitation guidelines (see chart)
- Monitor SPO₂, RR, HR and for signs of respiratory distress
- Give O₂ if there is significant respiratory distress or cyanosis
- Scale up to CPAP if necessary.

(C)irculation

- If the baby is shocked, give 10 mls/kg IV bolus Normal Saline or Ringers Lactate slowly over 10 minutes
- Reassess and repeat until there are no signs of shock
- Monitor HR, BP
- After 3 boluses give blood
- Consider inotropes if no improvement; discuss with consultant

(D)isability

- If blood sugar is 45mg/dl or less: treat as per the hypoglycaemia

- management guideline
- Keep the baby warm rectal temperature 36.5-37.5 C).
- Paracetamol should be used where necessary to relieve fever (15mg/kg tds). Paracetamol should not be continued more than 3 days without discussion with the consultant.
- Observe for and treat any seizures

Secondary Level

Stable newborns in the first 72 hours of life

- ABCDE
- Screen for sepsis (Blood culture, CSF analysis and Urine culture) and give antibiotics for 5 days if the following risk factors are present:
 - Evidence of suspected or confirmed maternal infection
 - Evidence of suspected or confirmed infection in the other twin
 - Any other factors, as discussed and agreed with registrar or consultant

Sick / unstable newborns in the first 72 hours of life

- ABCDE as above
- Screen for sepsis and start antibiotics (see antibiotics choices below) if any of the following are present:
 - Respiratory distress requiring CPAP in a term baby
 - Any baby who has a clinical deterioration, having been stable in the first few hours after birth
 - Shocked patients
 - Convulsions
 - Ileus or suspected NEC
 - Suspected meningitis
 - Any other features as discussed and agreed with registrar or consultant
- Manage any complications or co-morbidities
- Refer to the tertiary level if sepsis is suspected and the baby is deteriorating or not improving on treatment, or a neonate who through other criteria should not be managed at a secondary level facility.

Tertiary Level

Stable newborns in the first 72 hours of life

- Stable newborns with one risk factor should screened for infection as above and treatment started:
 - If cultures available, stop antibiotics once blood culture is negative at 72hrs.
 - Where cultures are not available, continue antibiotics for 5 days.

Sick / unstable newborns in the first 72 hours of life

- ABCDE as above
- Start antibiotics if the conditions below are present:
 - Respiratory distress requiring CPAP in a term baby
 - Any baby who has a clinical deterioration, having been stable in the first few hours after birth
 - Shocked patients
 - Convulsions
 - Ileus or suspected NEC
 - Suspected meningitis

- Any other features as discussed and agreed with registrar or consultant

Antibiotic choice

- We currently categorize antibiotics or combinations of antibiotics into first-line, second-line and third-line antimicrobials.
- Guidance on these combinations is bound to depend on prevailing organisms and sensitivity patterns.
 - Current first-line: X-pen / Ampicillin and Gentamicin.
 - Current second-line: Ceftriaxone
 - Current third line: Meropenem
- First-line antibiotics can be started by the nurses, clinicians, junior doctors and senior doctors at all levels of care
- Second-line antibiotics should be started by the registrar or a junior doctor (in consultation with registrar or consultant) at secondary and tertiary care levels
- Third-line antibiotics should be started by the consultant or registrar (in consultation with the consultant) at tertiary care level.
- Antibiotics outside these categories should be started by consultant or registrar in discussion with microbiology or infectious disease experts at tertiary care level.

Early onset sepsis

- The likely causative organisms will be antenatally or perinatally acquired organisms.
- Start with the ***first-line antibiotics*** and subsequently evaluate based on clinical response and culture results in the first 72 hours of life.
 - IV Penicillin (Xpen) 50 000 IU/kg BD if < 7days, QDS if older
 - Double the dose (Xpen 100,000 IU/kg) if meningitis is suspected
 - **OR** IV Ampicillin 50mg/kg B.D for <2000g; 50mg/kg TDS for >2000g
 - **Plus** IV Gentamicin 5 mg/kg OD if < 7days, 7.5 mg/kg OD if older
- IM antibiotics should only be given if IV access has failed.
 - Steps should be taken to gain IV access for the subsequent doses.
 - It is the doctor's responsibility to check and confirm that there is good IV access in every newborn on antibiotics.
- Consultation should be made with ward registrar / consultant or with anaesthetic department if a newborn on antibiotics has failed IV access

Late onset sepsis

- Likely caused by nosocomially acquired organisms.
- Klebsiella spp., S. aureus, and Enterobacter spp. are the most common organisms found.
- S. aureus joint/ bone infection present with reduced limb movement.
- Coagulase negative staphylococcal septicaemia presents with non-specific signs, often in a baby who has been admitted for several days.
- Include non-typoidal Salmonella in your differential diagnosis

- Start with the second line antibiotics and subsequently evaluate based on clinical response and culture results.
 - Other antibiotic choices will depend on clinical and microbiological considerations. These require discussion with the consultants.
- All culture results must be reviewed at around 72 hours after sampling, and a decision made about continuing, stopping or changing antibiotics depending on the clinical picture and culture and sensitivity results.
- These decisions must be made with the involvement of the paediatric registrar or consultant.
- ***The dosing, frequency and duration of antibiotics will be determined by the clinical picture, site of infection, the organism and sensitivity pattern.***

Continued Treatment/ When to Discharge

- This will be guided by the progress of the baby and results available.
- Consult a senior colleague for further advice.
 - If **blood culture and CSF are negative** and the baby is well, stop antibiotics then discharge.
 - If **both are negative** but the baby remains sick, then antibiotics should be continued. Further attempts to localize a source of infection (e.g. urine sample) or further diagnoses may need consideration. Consult a senior colleague.
 - If the **LP is positive** give high dose antibiotics for 10 to 14 days.
 - If the **blood culture is positive**, give **7 to 10 days** of IM/IV antibiotics (depending upon organism).

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring

APNOEA OF PREMATURITY

Definition

Neonatal apnoea is defined as cessation of breathing in a newborn, lasting 20 seconds or more.

- Very premature babies have immature respiratory centers in the brain and sometimes "forget" to breath.
- However, a newborn who stops breathing and is followed by hypoxia and bradycardia can be considered to have apnoea.

Risk factors / Causes

- (Extreme) prematurity
- IVH
- Sepsis / Meningitis
- Hypothermia
- Hypoglycaemia
- Anaemia
- Acidosis
- PDA
- NEC
- Electrolyte abnormalities

Prevention / Promotion

- Prevention of prematurity
- Administration of prenatal steroids to a mother with imminent preterm delivery
- Preterm babies should be started on prophylactic treatment with Aminophylline or caffeine
- Early diagnosis and management of underlying illness

Clinical presentation

- Cessation of breathing for more than 20 seconds
- Followed by hypoxia (desaturation) and (not always) bradycardia (< 100 bpm)
- Central: due to brain immaturity or disease
- Obstructive: obstructed airways (secretions, positioning, hypotonia)
- Combined: both components

Differential diagnosis

- IVH, meningitis, encephalitis
- Increased intracranial pressure
- Seizures
- Pulmonary disease
- Cardiac disease

Management

Prophylactic Treatment

- Give prophylaxis for newborns <34/40 corrected gestation OR <1500g using aminophylline / caffeine as a respiratory stimulant (see box below).

Primary Level

- Stabilize symptomatic patient (ABCDE)
- Give loading dose of either Aminophylline or Caffeine:
 - Use aminophylline
 - Loading dose: 6mg/kg STAT, then maintenance dose 2.5mg/kg BD.
 - Alternatively, if available, use Caffeine
 - Loading Dose: 10 mg/kg of Caffeine Base
- Refer neonates with apnoea to the secondary level

Secondary Level

- Stabilize symptomatic patient (ABCDE)
- Give loading dose of either Aminophylline or Caffeine
- Pulse oximetry or cardiac monitoring
- Start on CPAP
- Treat every preterm baby who has presented with apnoeas, irrespective of gestation or weight.
- Use aminophylline as a respiratory stimulant for babies <34/40 gestation
 - Loading dose: 6mg/kg STAT, then maintenance dose 2.5mg/kg BD.
- Alternatively, if available, use Caffeine
 - Loading Dose: 10 mg/kg of Caffeine Base
 - Maintenance dose: 2.5 mg/kg/dose. If indicated, can be increased up to 5 mg/kg/dose.
 - Higher doses may be considered but must be approved by a Consultant.
- All babies presenting with apnoea must be assessed for possible infection and managed appropriately
- Rule out other underlying causes (eg IVH)
- Refer babies with recurrent apneas or apneas with instability to the tertiary level

Tertiary Level

- Manage as in secondary above.
- For recurrent apneas
 - Repeat loading dose of the treatment and continue as per schedule.
 - Investigate possible underlying causes
 - Discuss with paediatric consultant

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring

NEONATAL JAUNDICE

Definition

Yellow discolouration of the skin and visible mucous membranes resulting from accumulation of bilirubin in the blood.

- Very common in newborns, especially the premature babies.

Types of Jaundice

Physiological jaundice: Consider physiological jaundice if:

- Presentation after 24 hours of life
- Resolving within 14 days in term babies and 21 days in preterm babies
- Unconjugated bilirubinaemia
- Well baby with no associated abnormalities on examination

Pathological jaundice: Consider pathological jaundice in the following:

- Presentation within 24 hours of birth
- Rapid increase in bilirubin levels ($> 0.5 \text{ mg/dl/hr} = > 9 \text{ mmol/l/hr}$)
- Presentation or persistence of jaundice beyond 14 days in term and 21 days in preterm babies
- Persistence of hyperbilirubinaemia despite treatment
- Ill-looking baby
- Associated anaemia, acidosis, hypoglycaemia, temperature dysregulation
- Associated hydrops
- Associated organomegaly and / or ascites
- Maternal blood group O or Rhesus negative.
- Conjugated bilirubinaemia
- Pale stools
- Dysmorphic or syndromic baby

Common causes of pathological jaundice:

- ABO or Rhesus incompatibility
- Infections, including TORCH infections such as syphilis.
- Enzyme defects such as G6PD deficiency.
- Big haematomas, particularly subgaleal haematoma

Jaundice presenting in the first 24 hours is PATHOLOGICAL and babies must be treated!!

Prevention and Health promotion

- Optimal antenatal care
- Increased community awareness
- Anti – D antibodies
- Optimal fluid and nutrition management

Investigations

Thorough examination to exclude other causes of pathological jaundice.

- Check baseline bilirubin level (TSB or TCB)
- FBC and differential count; reticulocytes if possible
- Blood culture, TORCH screen
- Blood grouping for mother and baby
- If the mother's blood group is O or Rhesus negative;
 - Coombs test
 - Peripheral smear

Management

Primary Level

- Refer any baby with significant jaundice to the secondary level, after stabilization

Secondary / Tertiary Level

- Stabilize the patient (ABCDE)
- Check baseline bilirubin level (TSB or TCB)
 - If a bilirubinometer (TCB) or serum Bilirubin is not available, assign clinical severity grade to the jaundice, using the chart below:

Clinical grading of neonatal jaundice

| Score | Area of body | Serum bilirubin levels | |
|-------|--------------------------------|------------------------|--|
| 1 | Face (blue) | 4–6 mg/dl | |
| 2 | Chest, upper abdomen (green) | 8–10 mg/dl | |
| 3 | Lower abdomen, thighs (yellow) | 12–14 mg/dl | |
| 4 | Arms, lower legs (pink) | 15–18 mg/dl | |
| 5 | Palms, soles (red) | 15–20 mg/dl | |

- If bilirubin levels are available, use the table for treatment thresholds. Note that the treatment thresholds are different for preterm, low birth weight and sick or unstable newborns.

Jaundice treatment thresholds for jaundiced babies

| | Phototherapy levels; healthy term baby | Phototherapy levels; Preterm, LBW, sick baby | Exchange transfusion levels; healthy term baby | Exchange transfusion levels; Preterm, LBW, sick baby |
|---------------|--|--|--|---|
| Day of life | μmol/L (mg/dl) | μmol/L (mg/dl) | μmol/L (mg/dl) | μmol/L (mg/dl) |
| Day 1 | Treat any visible jaundice with phototherapy | | 17 (1.00) | 14 (0.80) |
| Day 2 | 15 (0.85) | 13 (0.75) | 22 (1.28) | 17 (0.95) |
| Day 3 | 18 (1.00) | 16 (0.90) | 24 (1.40) | 18 (1.00) |
| Day 4 & after | 20 (1.20) | 17 (0.95) | 25 (1.45) | 20 (1.20) |

- If the bilirubin is not high enough to warrant phototherapy, but is close to the threshold (within 3mg/dl), please check it again the following day.
- Start phototherapy. Once on phototherapy:
 - The baby's eyes should be covered with a gauze pad to protect them from the light.
 - Babies on phototherapy must be fully exposed, including removal of nappies.
 - Ensure the baby is feeding well - top up with EBM via cup or NGT if necessary.
 - Add 10% of the daily requirement to the fluids/ feeds the baby is getting to account for transpiration due to phototherapy.
 - The baby should be turned at least every 6 hours, but ideally every 2-3 hours to ensure the whole body is exposed to the blue light.
 - Babies under phototherapy should have their bilirubin level checked on a daily basis. Those with pathological jaundice due to severe haemolysis must have at least a TCB every 6 hours.
 - The bilirubinometer should be used on the chest and the forehead (which is not directly exposed to the phototherapy) and whichever value is highest used.
 - For a successful treatment, the bilirubin should be falling by at least 1mg/dl every 6 hours.
 - Phototherapy should be stopped when the value is more than 3mg/dl below the threshold shown above
 - Monitor for **complications of phototherapy:**
 - Diarrhoea
 - Dehydration
 - Hypothermia
 - Hyperthermia
 - Retinal damage
 - Eye infections
 - Bronze baby syndrome
 - Double phototherapy
 - Check bilirubin 6 hourly (TSB or TCB)
- Transfuse for anaemia, based on the transfusion guidelines and the clinical picture.
- Exchange transfusion if meeting criteria, and where facilities are available.
 - All patients who are in the exchange transfusion range should be referred to the tertiary level. Stabilization and phototherapy should continue, while waiting for transfer.
- For all jaundiced babies, consider whether infection may be the cause.
 - Examine and investigate (blood culture, lumbar puncture) and treat appropriately.
- Investigate for the cause of pathological jaundice as outlined in the investigations above.

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring
- Palliative care

ACUTE BILIRUBIN ENCEPHALOPATHY / KERNICTERUS

Definition and pathophysiology

- Results from neuronal damage due to bilirubin crossing over to the brain parenchyma at extremely high levels.
- Occurs in hyperbilirubinaemia (if bilirubin > around 350 µmol/l (or less in preterms or sick infants), more commonly if >500 µmol/l).

Clinical presentation

- Stage 1: sleepy, reduced suck, lethargy
- Stage 2: increased temperature, restless, lid retraction, odd mouth movements, seizures, high pitched cry, opisthotonus
- Stage 3: death or latent period
- Stage 4: cerebral palsy (esp. choreo-athetoid), deafness, reduced IQ

Management

- If the jaundice is not promptly and appropriately treated with adequate phototherapy light, permanent brain damage may occur.
- In addition to phototherapy, exchange transfusions are required for serious jaundice.
- Long-term neurodevelopmental follow up and palliative care will be required after discharge
- Arrange for screening for hearing, and visual acuity

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring
- Palliative care

PROLONGED JAUNDICE

Definition

Diagnose prolonged jaundice in a baby whose jaundice persists beyond 14 days for a term baby, and 21 days for a preterm baby.

- Remember that sepsis must always be suspected in a newborn with prolonged or late onset jaundice.

Causes of prolonged jaundice

| Prehepatic (Haemolysis) | Hepatic Disease | Posthepatic (Obstructive) |
|---|---|--|
| <ul style="list-style-type: none"> Sepsis Enzyme defects (eg G6PD deficiency) Hb abnormalities (eg Thalassaemia) Membrane defects eg hereditary spherocytosis | <ul style="list-style-type: none"> TORCH Syphilis Infective Hepatitis Inborn errors of Metabolism | <ul style="list-style-type: none"> Choledochal cyst Biliary atresia Allagille's syndrome Bowel obstruction |

Important points in history

- Family history of hereditary haemoglobinopathy, liver disease
- Previous need for transfusion (transfusion suggests risk for contracting hepatitis)
- Colour of stool and urine - normal colour of stools suggests unconjugated jaundice and haemolysis, **tea-coloured urine and pale stools suggests obstructive causes of jaundice**

Important points on examination

A full physical examination is necessary. Particular signs may point to a diagnosis or may be important in different conditions.

- Assess growth and nutritional state - poor in chronic liver disease
- Pallor-suggests haemolysis if acute
- Bruising, bleeding, skin rashes, snuffles
- Hepatosplenomegaly (syphilis, prolonged haemolysis)
- Liver tenderness - suggestive of acute hepatitis
- Abdominal masses - choledochal cyst
- Look for pale stools

Investigations

- Urine dipstick for bilirubin and urobilinogen - suggests prehepatic disease
- PCV/FBC
- Malaria parasites
- VDRL, TORCH screens
- Hepatitis B serology if hepatitis is considered
- Sickle cell test in older newborns or infants
- Blood film
- Thyroid test
- Liver function tests
 - Conjugated bilirubin** in liver disease or biliary obstruction
 - Unconjugated bilirubin** in haemolysis or hepatitis

- Transaminases raised in hepatitis
- If bleeding tendency, a clotting screen should be done
- Abdominal ultrasound (shrunken liver in cirrhosis, large bright inflamed liver in hepatitis, tumours of liver, biliary atresia, choledochal cysts or gallstones)

Management

Primary / Secondary Level

- Refer any neonate with prolonged jaundice to the tertiary level

Tertiary Level

Pre-hepatic (Haemolysis)

- Blood transfusion if anaemic; see guideline on anemia
- Treat underlying cause of haemolysis including infections
- IV fluids – hyperhydration
- Oxygen
- Screen and treat for presumed sepsis

Hepatic disease

- Blood sugar level - daily and more frequently if the child has a decreased conscious state - maintain RBS between 65-155mg/dl.
- Vitamin K: iv if bleeding actively or persistent jaundice
- Vitamin A - if chronic liver disease is suspected.
- Diet: Feed 2 hourly.
- Fluid balance monitoring if encephalopathic- need approximately 2/3 maintenance fluid requirement. Monitor daily weight.
- Antibiotics if febrile and jaundiced and MPS are negative.
- Avoid Paracetamol.

Post hepatic disease

- Monitor the colour of the stool
- Perform abdominal ultrasound
- Stabilize the patient as per guideline
- Consult the surgeons for surgical management for structural obstruction

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring
- Palliative care

NEONATAL SEIZURES

Definition

Paroxysmal alterations in neurologic function in a newborn (motor, behavioural, autonomic).

Epileptic seizure: Clinical seizure associated with EEG seizure activity

Non-epileptic seizure: Clinical seizures without EEG changes

EEG seizures: Abnormal EEG changes without clinical correlation

Causes / Risk Factors

- Perinatal
 - HIE (40-50%)
 - Intracranial haemorrhage (IVH, trauma, subarachnoid haemorrhage)
- Metabolic and endocrine causes
 - Hypoglycaemia, hypocalcemia, hypomagnesemia, hypo/hypernatraemia, pyridoxine deficiency, inborn errors of metabolism
- Infections
 - Sepsis, meningitis, encephalitis, TORCH, tetanus
- Congenital brain malformations
- Cerebro-vascular-malformation and disease
- Drugs and alcohol
- Familial seizures
- Syndromes: Sturge-Weber, benign familial, myoclonic epilepsy of the infant
- Idiopathic

Prevention

- Neonatal seizures can be prevented by early detection and management of underlying pathologies.

Clinical presentation

- Neonates commonly present with unusual and subtle seizures:
 - Ocular – sustained eye deviation, ocular fixation
 - Oral-facial-lingual movements – chewing, tongue-thrusting, lip-smacking etc.
 - Limb movements – cycling, paddling, boxing-jabs
 - Autonomic manifestations – tachycardia or bradycardia, apnoea
 - Tonic, clonic, myoclonic seizures
- EEG seizures may present sub-clinically and will only be picked up on EEG of a comatose patient.

Investigations

- Blood glucose, ABG
- FBC
- B/C
- Electrolytes (especially sodium, calcium, and magnesium, if available)
- CSF
- Consider cranial ultrasound
- EEG where available
- Metabolic panel screen if available

Differential diagnoses

- See under causes / risk factors

Management

Primary Level

- Manage ABCDE
 - Administer oxygen
 - Check blood glucose – correct by iv dextrose bolus if < 45mg/dl (see hypoglycaemia management)
- Refer every newborn who presents with a seizure to the secondary or tertiary level for investigation and management.

Secondary Level

- Stabilize patient (ABCDE)
- If fits are occurring more than twice an hour or lasting more than 3 minutes:
 - Phenobarbitone 20mg / kg IM Stat
 - If still fitting after 10 minutes repeat phenobarbitone
- Refer any neonate with persistent seizures or seizures with an underlying pathology

Tertiary Level

- Stabilize as above
 - If still no seizure control, give a loading dose of IV Phenytoin 20mg/kg OR Levetiracetam (Keppra) 20mg/kg PO or IV
 - Screen for infection and start antibiotics
 - Perform a lumbar puncture as soon as the baby is stable
 - If seizures are difficult to control despite adequate doses of anticonvulsants give:
 - Calcium gluconate at 1mmol/kg or pyridoxine 100mg IV
- Consult neurologist/neonatologist

Follow up

- Neurodevelopmental follow up.
- Visual and hearing assessments.
- Growth monitoring

APPROACH TO A DYSMORPHIC NEONATE

Definition

Dysmorphic features: ranging from unusual appearance to major malformation

The definition of terms used in description of birth defects/dysmorphic features.

| Terminology | Meaning |
|------------------------------|--|
| Malformation | Morphologic abnormality that arises because of an abnormal developmental process. A primary error in morphogenesis e.g. cleft lip |
| Malformation sequence | Pattern of multiple defects resulting from a single primary malformation e.g. talipes and hydrocephalus can result from a lumbar neural tube defect |
| Malformation syndrome | Pattern of features, often with a unifying underlying cause, that arises from several different errors in morphogenesis e.g. trisomy 21 |
| Deformation | Distortion by a physical force of an otherwise normal structure e.g. club foot |
| Disruption | Destruction of a tissue that was previously normal e.g. amniotic band sequence |
| Dysplasia | Abnormal cellular organisation within a tissue resulting in structural changes e.g. within cartilage and bone in skeletal dysplasias |
| Association | Group of anomalies that occur more frequently than would be expected by chance alone but that do not have a predictable pattern or unified etiology e.g. VACTERL association |

Epidemiology: 1 in 40 neonates (2.5%)

Risk Factors / Causes

- Single gene disorders (including inborn errors of metabolism which may be progressive) e.g. Zellweger syndrome, congenital adrenal hyperplasia, Smith-Lemli-Opitz syndrome
- Chromosomal disorders (non-progressive) e.g. Down syndrome
- Microdeletion syndromes e.g. Prader-Willi syndrome
- Polygenic disorders e.g. club foot
- Environmental causes (teratogenesis) e.g. Rubella, congenital viral infection, infant of diabetic mother (IDM), fetal alcohol syndrome

Prevention / Promotion

- Genetic causes are not preventable.
- Promote awareness of risk of consanguinity.
- Prevent congenital infections via maternal immunization and hygiene measures.

Clinical presentation

Suspect a genetic cause if:

- Congenital anomalies present: one or more major anomaly or more than two minor anomalies (see tables below)
 - Major anomaly: cause dysfunction or require surgical correction
 - Minor anomaly: neither cause significant dysfunction nor require surgical correction
- Poor growth: symmetric intrauterine growth restriction or postnatal growth failure
- Developmental delay or developmental regression
- Craniofacial dysmorphism
- Ambiguous genitalia

Common clinical signs in dysmorphic syndromes

| Sign | Definition |
|-----------------------------------|--|
| Brachycephaly | A condition in which head shape is shortened from front to back along the sagittal plane; the skull is rounder than normal |
| Brachydactyly | A condition of having short digits |
| Brushfield spots | Speckled white rings about two thirds of the distance to the periphery of the iris of the eye |
| Camptodactyly | Permanent flexion of one or more fingers associated with missing inner phalangeal creases indicating lack of finger movement from before 8 wk of gestation |
| Clinodactyly | A medial or lateral curving of the fingers; usually refers to incurving of the 5th finger |
| Hypoplastic nail | An unusually small nail on a digit |
| Low-set ears | This designation is made when the helix meets the cranium at a level below a horizontal plane that is an extension of a line through both inner canthi |
| Melia | A suffix meaning "limb" (e.g., amelia—missing limb; brachymelia—short limb) |
| Ocular hypertelorism | Increased distance between the pupils of the two eyes |
| Plagiocephaly | A condition in which head shape is asymmetric in the sagittal or coronal plane; can result from asymmetry in suture closure or from asymmetry of brain growth |
| Posterior parietal hair whorl | A single whorl occurs to the right or left of midline and within 2 cm anterior to the posterior fontanel in 95% of cases. The whorl represents the focal point from which the posterior scalp skin was under growth tension during brain growth between the 10th and 16th wk of fetal development. Aberrant position of the whorl reflects an early defect in brain development. |
| Postaxial polydactyly | Extra finger or toe present on the lateral side of the hand or foot |
| Preaxial polydactyly | Extra finger or toe present on the medial side of the hand or foot |
| Prominent lateral palatine ridges | Relative overgrowth of the lateral palatine ridges secondary to a deficit of tongue thrust into the hard palate |

| | |
|--------------------------|--|
| Scaphocephaly | A condition in which the head is elongated from front to back in the sagittal plane; most normal skulls are scaphocephalic |
| Shawl scrotum | The scrotal skin joins around the superior aspect of the penis and represents a mild deficit in full migration of the labial-scrotal folds |
| Short palpebral fissures | Decreased horizontal distance of the eye based on measurement from the inner to the outer canthus |
| Syndactyly | Incomplete separation of the fingers. It most commonly occurs between the 3 rd and 4 th fingers and between the 2 nd and 3 rd toes. |
| Synophrys | Eyebrows that meet in the midline |
| Telecanthus | Lateral displacement of the inner canthi. The inner canthal distance is increased, but the inner pupillary distance is normal. |
| Widow's peak | V-shaped midline, downward projection of the scalp hair in the frontal region. It represents an upper forehead intersection of the bilateral fields of periocular hair growth suppression. It usually occurs because the fields are widely spaced, as in ocular hypertelorism. |

Minor anomalies seen in various systems

| System | Minor anomaly |
|--------------|---|
| Craniofacial | Large fontanel Flat or low nasal bridge Saddle nose, upturned nose Mild micrognathia Cutis aplasia of scalp |
| Eye | Inner epicanthal folds Telecanthus Slanting of palpebral fissures Hypertelorism Brushfield spots |
| Ear | Lack of helical fold Posteriorly rotated pinna Preauricular with or without auricular skin tags Small pinna Auricular (preauricular) pit or sinus Folding of helix Darwinian tubercle Crushed (crinkled) ear Asymmetric ear sizes Low-set ears |
| Skin | Dimpling over bones Capillary hemangioma (face, posterior neck) Mongolian spots (African Americans, Asians) Sacral dimple Pigmented nevi Redundant skin Cutis marmorata |

| | |
|---------------|--|
| Hand | Simian creases Bridged upper palmar creases Clinodactyly of fifth digit Hyperextensibility of thumbs Single flexion crease of fifth digit (hypoplasia of middle phalanx) Partial cutaneous syndactyly Polydactyly Short, broad thumb Narrow, hyperconvex nails Hypoplastic nails Camptodactyly Shortened fourth digit |
| Foot | Partial syndactyly of second and third toes Asymmetric toe length Clinodactyly of second toe Overlapping toes Nail hypoplasia Wide gap between hallux and second toe Deep plantar crease between hallux and second toe |
| Others | Mild calcaneovalgus Hydrocele Shawl scrotum Hypospadias Hypoplasia of labia majora |

Evaluation / Investigations

Approach to a neonate with dysmorphism

- History including perinatal details and family history (consanguinity, previous pregnancy losses)
- Physical examination detailing the major and minor anomalies
 - Major anomaly: cause dysfunction or require surgical correction
 - Minor anomaly: neither cause significant dysfunction nor require surgical correction
- Growth recording and measurements
- Examination of previous records and photographs
- Making a diagnosis based on the above details
 - Ballpark diagnosis: an ‘approximation’ of the diagnosis based upon the clinical features
 - Diagnosis by Gestalt: identifying the syndrome by ‘pattern recognition’
 - Syndrome search: searching a dysmorphology database using the key anomalies noted in the neonate
- Investigations to confirm the diagnosis and to evaluate the neonate for affected organ systems
 - Methods of genetic analyses
 - Karyotype
 - Fluorescence in situ hybridization (FISH)
 - DNA microarray
 - Comparative genomic hybridization (CGH)
 - Single nucleotide polymorphism (SNP) or oligonucleotide arrays
 - Molecular analysis
- Other diagnostic procedures

- Biochemical testing
- Metabolic investigations
- Rarely histology
- Imaging studies
 - Ultrasound
 - X-ray
 - CT
 - MRI

Differential diagnosis of common genetic syndromes

- A list of common dysmorphic syndromes encountered during the neonatal period and the lab test for confirming the diagnosis:

| Condition | Presenting feature | Diagnostic test |
|---------------------------------------|--|--|
| Trisomy 21 Down syndrome | Brachycephaly, low set ears, flat nasal bridge, epicanthic folds, hypertelorism, macroglossia, brachydactyly, hypotonia, AVSD, single palmar crease, sandal gap, Hirschsprung disease | Karyotyping |
| Trisomy 18 Edward syndrome | Overlapping fingers, globular head, dysplastic ears, low birth weight, heart defects, short great toes, radial aplasia, rocker bottom feet, IUGR | Karyotyping |
| Trisomy 13 Patau syndrome | Holoprosencephaly, cleft palate, heart defect, polydactyly, renal abnormalities, microphthalmia, umbilical hernia | Karyotyping |
| Turner syndrome | Only female neonates Wide or weblike neck, low-set ears, broad chest with widely spaced nipples, high, narrow roof of the mouth (palate), arms that turn outward at the elbows, fingernails and toenails that are narrow and turned upward, swelling of the hands and feet, especially at birth, slightly smaller than average height at birth, slowed growth, cardiac defects, low hairline at the back of the head, receding or small lower jaw, short fingers and toes | Karyotyping, cardiac and abdominal echo |
| Noonan syndrome | Characteristic facial appearance: Broad forehead, drooping eyelids (ptosis), wider-than-usual distance between the eyes (ocular hypertelorism), short, broad nose, low-set ears that are rotated towards the back of the head, small jaw, short neck with excess skin folds, lower-than-usual hairline at the back of the head and neck Lymphoedema Cardiac defects, single kidney Short stature at later stage | Mutation analysis, cardiac echo |
| 4p-Wolf-Hirshorn syndrome | Hypertelorism, prominent glabella (Greek helmet), cleft lip and palate, short philtrum, large ears | May be visible on standard karyotype. More reliably detected by FISH or MLPA |

| | | |
|---|--|--|
| 5p-Cri du Chat syndrome | Mewing cry, microcephaly, round face, prominent epicanthic folds, cleft palate, ear anomalies | Usually visible on routine karyotype. FISH will detect smaller deletions |
| 22q11 deletion DiGeorge syndrome Velocardiofacial syndrome | Cardiac defects especially outflow tract, Cleft palate, micrognathia, prominent nose, overturned helix of ear, hypocalcaemia, absent thymus | FISH for 22q11 deletion, few have smaller deletions detectable on MLPA of 22q11 |
| Prader-Willi syndrome | Neonatal hypotonia Bitemporal narrowing, Almond-shaped eyes, Tube feeding required | DNA for 15q11-13 methylation (15q11-13 FISH will miss infants with uniparental disomy (UPD) of chromosome 15) |
| Achondroplasia | Proximal limb shortening, relatively large head, trident hand, extra skin creases, depressed nasal bridge, lumbar kyphosis | Skeletal survey shows square ilia, translucent proximal femur, narrow sacrosciatic notch. Analysis of FGFR3 gene shows characteristic mutation |
| Williams-Beuren syndrome | Distinct facial appearance: broad fore-head, bitemporal narrowing, periorbital fullness, stellate and/or lacy iris pattern, short upturned nose with bulbous tip, long philtrum, wide mouth, full lips and mild micrognathia Cardiac anomalies (most frequently supravalvular aortic stenosis) Connective tissue abnormalities (e.g., joint laxity); later in life cognitive and developmental abnormalities | Mutation analysis, micro-deletion on chromosome 7q11.23, cardiac echo |
| Myotonic dystrophy | Hypotonia , Tented upper lip, Elevated diaphragm, Mother has myotonia | Examine mother DNA for expansion in myotonic dystrophy gene on chromosome 19 |
| Beckwith-Wiedemann syndrome | Exomphalos, High birth weight, Large tongue, Facial naevus flammeus | DNA to assess methylation of 11p15 Parental DNA for UPD studies. Not all have 11p abnormality |
| Cornelia De Lange syndrome | Low birth weight, Synophrys, hirsutism, Beaked philtrum, Heart defects, Limb defects but may be subtle Diaphragmatic hernia | Primarily a clinical diagnosis. Some have mutations in NIPBL gene on chromosome 5 or other genes. Genetic abnormality not found in every patient |
| Neonatal Marfan syndrome | Long limbs, arachnodactyly, contractures, enophthalmos, dislocated lenses, wrinkly skin, heart murmur | Cardiac echo and follow-up as aortic dilatation may not be present at birth. Eye examination, FBN1 mutation analysis |
| Rubinstein-Taybi syndrome | Broad medially deviated thumbs and great toes, long columella, hirsutism, microcephaly, heart defects, glaucoma | Clinical diagnosis, FISH 16p13 deletion in 15-20%, some have mutations in |

| | | |
|---|--|---|
| | | CRBBP gene. Many have no genetic abnormality identified |
| Goldenhar syndrome (Hemifacial microsomia) | Findings usually unilateral. Mandibular hypoplasia, dysplastic or absent ear, pre-auricular tags, macrostomia, epibulbar dermoid. May be vertebral and cardiac defects | Clinical diagnosis. Heterogeneous condition with both genetic and environmental causes |
| 12p tetrasomy Pallister Killian syndrome | High birth weight, macrocephaly, diaphragmatic hernia, coarse face, hypotonia, long philtrum, sparse hair over temples | Always in mosaic form. Unlikely to be detectable on blood chromosome analysis. Need skin biopsy or FISH cells from buccal mucosa |
| Stickler syndrome | Pierre Robin sequence with cleft palate and micrognathia. Flat nasal bridge, prominent eyes, joint laxity | Eye examination shows myopia and vitreous abnormalities (not often apparent at birth). Mild platyspondyly on spinal X-. Genetic testing complex May be mutation in Type 2 or Type 11 collagen genes |

Management

- Depends on the underlying condition
- Wide range from medical and/or surgical interventions with the aim of curative care to purely palliative care
- Best handled at tertiary care level

Prognosis

- Depends on the underlying condition
- Range from normal life-span to early death

PRINCIPLES OF POSTNATAL CARE AND POST-DISCHARGE FOLLOW-UP

WHO Recommendations

Healthy mother, healthy newborns

- Care for healthy mothers and newborns in the health facility is recommended for at least 24 hours after vaginal birth.
- Prior to discharging mothers and newborns after birth from the health facility to the home, health workers should assess the following criteria to improve maternal and newborn outcomes:
 - The mother's and baby's physical well-being and the mother's emotional well-being;
 - The skills and confidence of the mother to care for herself and the skills and confidence of the parents and caregivers to care for the newborn; and
 - The home environment and other factors that may influence the ability to provide care for the mother and the newborn in the home, and care-seeking behaviour.
- A minimum of four postnatal care contacts is recommended.
 - If birth is in a health facility, healthy mothers and newborns should receive postnatal care in the facility for at least 24 hours after birth.
 - If birth is at home, the first postnatal contact should be as early as possible within 24 hours of birth.
 - At least three additional postnatal contacts are recommended for healthy mothers and newborns, between 48 and 72 hours, between 7 and 14 days, and during week six after birth.
- Home visits during the first week after birth by skilled health personnel or a trained community health worker are recommended for the postnatal care of healthy mothers and newborns.
- Where home visits are not feasible or not preferred, outpatient postnatal care contacts are recommended.

Preterm or low-birth-weight infants

- Families of preterm or low-birth-weight infants should be given extra support to care for their infants, starting in health-care facilities from birth, and continued during follow-up post-discharge.
- The support may include education, counselling and discharge preparation by health workers, and peer support.
- If preterm or low-birth-weight infants are born at home, immediate kangaroo mother care should be provided.
- Extra home visits (in addition to routine home visits) by trained health workers (e.g. community health workers, nurses, midwives, or doctors) are recommended to support families to care for their preterm or low-birth-weight infant.

Focus on

- Nutrition (breastfeeding)
- Weight gain
- Prevention of hypoglycaemia
- Thermal care
- Hygiene, prevention of infections
- Early detection of signs of infection

- Respiratory problems

Look for danger signs (if present indication for hospitalization)

- History of difficulty feeding
- Movement only when stimulated
- Lethargic
- Temperature $< 35.5^{\circ}\text{C}$
- Temperature $\geq 37.5^{\circ}\text{C}$
- Prolonged capillary refill
- Respiratory rate $\geq 60/\text{min}$
- Grunting
- Cyanosis
- Severe chest indrawing
- History of convulsions
- Stiff limbs
- Jaundice
- Infected umbilical stump

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CHAPTER 9. NEPHROLOGY

Acronyms

| | |
|--------|--|
| ADH | Antidiuretic hormone |
| AKI | Acute kidney injury |
| ANP | Atrial natriuretic peptide |
| BUN | Blood urea nitrogen |
| CCF | Congestive Cardiac failure |
| CKD | Chronic Kidney disease |
| CRRT | Continuous renal replacement therapy |
| DIC | Disseminated intravascular coagulopathy |
| ECG | Electrocardiography |
| FRNS | Frequently relapsing nephrotic syndrome |
| GFR | Glomerular Filtration rate |
| GN | Glomerulonephritis |
| HD | Haemodialysis |
| HSP | Henoch-schonlein purpura |
| KUB | Kidney ureter bladder ultrasound |
| MCS | Microscopy culture and sensitivity |
| MPs | Malaria parasites |
| MRDT | Malaria rapid diagnostic test |
| NAC | N-acetyl cysteine |
| NSAIDs | Non-steroidal anti-inflammatory drugs |
| PBF | Peripheral blood film |
| PD | Peritoneal dialysis |
| PSGN | Post-streptococcal glomerulonephritis |
| RBS | Random blood sugar |
| RFT | Renal function test |
| SIADH | Syndrome of inappropriate antidiuretic hormone release |
| TTP | Thrombotic thrombocytopenic purpura |
| UTI | Urinary tract infection |

ACUTE KIDNEY INJURY (AKI)

Definition

Acute Kidney Injury is a syndrome characterized by rapidly declining kidney function that results in a decline in glomerular filtration rate (GFR), retention of urea and other nitrogenous waste products, and dysregulation of extracellular volume and electrolytes.

If untreated, AKI is associated with increased mortality during hospitalization and increased risk of developing Chronic Kidney Disease (CKD). In critically ill children up to 50% have AKI.

AKI is classified into pre-renal, renal and post-renal failure.

AKI is defined as any of the following

- Increase in SCr by $\geq 0.3 \text{ mg/dl}$ ($\geq 26.5 \mu\text{mol/l}$) within 48 hours;
- Increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days;
- Urine volume $<0.5 \text{ ml/kg/h}$ for 6 hours.

| Stage | Serum creatinine (SCr) criteria | Urine output criteria |
|--------------|---|--|
| 1 | Increase $\geq 26 \mu\text{mol/l}$ within 48 hours or increase ≥ 1.5 to $1.9 \times$ baseline SCr | $<0.5 \text{ ml/kg/hour}$ for 6–12 hours |
| 2 | Increase 2 – $2.9 \times$ baseline SCr | $<0.5 \text{ ml/kg/hour}$ for ≥ 12 hours |
| 3 | Increase $\geq 3 \times$ baseline SCr or increase $354 \mu\text{mol/l}$ or commenced on renal replacement therapy, irrespective of stage | $<0.3 \text{ ml/kg/hour}$ for ≥ 24 hours or anuria for ≥ 12 hours |

KDIGO (2012)

Estimated (e)GFR can be calculated using the formula below:

Counahan-Barrat height formula for calculating eGFR in children

$$\frac{\text{Height (cm)} \times 40}{\text{Serum creatinine } (\mu\text{mol/L})} = \text{creatinine clearance } (\text{ml/min}/1.73\text{m}^2)$$

Normal ranges of eGFR in children

| Age | Mean eGFR (ml/min/1.73/ m²) | Range |
|------------------|--|---------------|
| Birth | 20 | |
| 7 days | 40 | 25-60 |
| 1 months | 50 | 30-70 |
| 6 months | 75 | 40-100 |
| 12 months | 115 | 65-160 |

Causes / Risk factors of AKI

| Types | Causes/risk factors |
|--|--|
| Pre-renal | <ul style="list-style-type: none"> • Most common form • Hypovolaemia (bleeding (e.g. from surgery) or gastrointestinal, urinary or cutaneous losses) • Reduction of effective circulation (heart failure, septic shock) |
| Renal – structural damage to the renal parenchyma | <ul style="list-style-type: none"> • Acute Tubular Necrosis (Epithelial cell casts): Ischemia (severe hypotension), malaria, nephrotoxic drugs, e.g. aminoglycosides, NSAIDS, amphotericin B, radio-contrast, cisplatin, acyclovir, traditional medicine etc. • Thrombotic thrombocytopenic purpura (TTP/HUS): Shiga-like toxin (E. coli), drugs, HIV, malignancy etc. • Rapidly Progressive Glomerulonephritis: Anti-GBM antibodies, immune-complex deposition (IgA, post-strep, lupus), pauci-immune (Granulomatosis with polyangiitis /microscopic polyangiitis) etc. • Acute Interstitial Nephritis: Drugs (NSAIDs, Abx, allopurinol, PPI), infections (CMV, strep, legionella), immune (lupus, sarcoidosis, Sjögren syndrome) • Tubular Obstruction: Cast nephropathy, urate crystals - Tumour lysis syndrome, calcium oxalate (Ethylene glycol), multiple myeloma (uncommon in children) etc. |
| Post-Renal or obstructive – | Obstruction/hydronephrosis: Constipation, urolithiasis, posterior urethral valves, vesicoureteral junction obstruction/reflux, schistosomiasis, e.t.c. |

Prevention / Promotion

- Early health seeking behaviour
- Appropriate fluid management
- Early recognition of AKI, especially if prerenal and rapid (fluid) treatment
- Early use of inotropes to treat hypotension, especially in sepsis
- Avoid/stop all nephrotoxic drugs
- Pre-hydration in children going for major surgery or pre- chemotherapy for huge tumours
- Discourage use of traditional medicine

Symptoms and signs

Paediatric AKI can present with a wide range of clinical features which include:

- Raised Serum Urea and creatinine

- Renal failure patient may present with clinical features of the underlying pathology eg Sepsis/infection, HUS (hx of bloody diarrhoea three to seven days prior to onset of oliguria), poststreptococcal glomerulonephritis (hx of pharyngitis or impetigo a few weeks prior to onset of gross hematuria or oedema), shock e.t.c.
- Edema (nephrotic syndrome or glomerulonephritis)
- Hypertension (in glomerulonephritis)
- Rash (IgA vasculitis (Henoch Schönlein Purpura) Reduced urine output –
- Anuria or oliguria
 - Neonates and infants – output < 1ml/kg/hr.
 - Older children < 0.3 ml/kg/hr.
- Polyuria: Urine output >3 ml/kg/h, particularly with acute tubular necrosis and nephrotoxic AKI
- In pre-renal renal failure patients often present with dehydration and/or shock.
- In post renal failure patients present with obstruction with abdominal distension and a palpable bladder.
- In intra renal disease the patient can present with oedema, signs of fluid overload, hypertension, acute weight gain, gross (or microscopic) hematuria
- Other associated symptoms may include
 - Acid base and electrolyte imbalance (especially hyperkalemia)
 - Uraemic encephalopathy
 - Uraemic coagulopathy
 - Uraemic frost

Investigations

- Malaria Rapid diagnostic test (MRDT)
- Random Blood sugar (RBS) test.
- Urine dipstick – Haematuria, proteinuria (Glomerular disease); leukocytes and nitrites (Pyelonephritis). May be normal in prerenal AKI!
- Urine microscopy, culture and sensitivity–
- Serum creatinine and BUN.
- Serum electrolytes, Calcium, Magnesium and Phosphate (CMP) + blood gas - typical biochemistry may show hyperkalemic metabolic acidosis, hypocalcaemia, hyperphosphataemia
- Drug levels of nephrotoxic drugs (if available)
- ECG to look for signs of life-threatening hyperkalaemia (spiked T wave and/or arrhythmias)
- CXR – cardiomegaly, pleural effusion, pulmonary oedema as signs of fluid overload
- Abdominal ultrasound – Kidney-ureter-bladder (KUB), size of the kidneys according to the length of the child (normal or large in AKI), and renal doppler
- FBC and differential
- Peripheral blood smear if suspecting HUS – look for schistocytes and RBC fragments
- Blood culture if febrile
- Clotting profile and disseminated intravascular coagulopathy (DIC) workup if septic
- Further investigations should be guided by the underlying pathology that is suspected

Monitoring

- Monitor BP and other vital signs
- Monitor daily and cumulative fluid balance

- Monitor input - all IV- Fluids , medication and all Oral intake
- Catheterise to monitor urine output (at least 6 hrly)
- Document any other losses (e.g. vomitus)
- Daily weight

Remember to adjust the daily input and medication dose based on the patient's current weight and kidney function!

Management

Primary level

- Refer all patients with oedema, hypertension, hematuria, proteinuria and oliguria/anuria to secondary level

Secondary level

- Discuss +- refer all patients with oedema, hypertension, hematuria, proteinuria and oliguria/anuria to tertiary facility for referral after acute management and stabilisation of the patient

Tertiary level

- Manage all cases in conjunction with a general paediatrician, paediatric/nephrologist, Urologists, Dieticians.

Fluid management

- Assess and treat dehydration if the patient presents with dehydration and in shock (see management of dehydration)
- During treatment of dehydration monitor urine output and presence of extra renal losses.
- ***Do not use potassium containing fluids in anuric patient.***
- Use intravenous (IV) fluids only if oral intake is not possible.
- Diagnostic fluid challenge 20 ml/kg IV over 30 minutes in patients presenting with an decreasing urine output and a history and physical findings consistent with prerenal etiology.
 - If urine output increases, it is likely a prerenal pathology.
 - **Fluid challenge is contraindicated if patient has signs of fluid overload and/or heart failure!! START INOTROPES**
- **In a patient with pulmonary oedema plus oliguria/anuria:**
 - DO NOT GIVE FLUIDS!!
- **In a patient who is anuric with no dehydration or extra renal fluid losses –**
 - Fluid replacement should be for insensible losses only if they require fluids for nutrition.
 - If patient cannot take oral fluids, then prescribe parenteral fluids with electrolyte-free solution i.e. (dextrose 5% or 10%) with caution

Insensible losses calculation:

Neonate and young infant – 30-40ml/kg/day

Older children – 25ml/kg/day (400ml/m²/day)

- **If a patient has normal hydration and oliguria:**
 - Give oral fluids to replace insensible water loss plus urine output of previous 24 hours.
- **If the patient is dehydrated and has on-going extra-renal fluid losses:**
 - Replace fluid according to losses. Replace losses with appropriate fluid solution similar to the losses e.g.
 - Diarrhoea losses give $\frac{1}{2}$ strength Darrows or Dextrose 5% IV or oral rehydration solution (ORS)
 - Vomiting/gastric fluid losses give normal saline (0.9%)/dextrose 5%.
- **If the patient is normally hydrated with normal urine output:**
 - Give normal intake
- **If the patient is in shock:** (see management of shock)
- **If the patient has polyuria with urine output >4ml/kg/hr:**
 - Commonly seen in patients who are recovering (diuretic phase) from acute tubular necrosis (ATN)
 - Give fluid and electrolyte losses with $\frac{1}{2}$ strength Darrows / Dextrose 5% IV.
 - The volume calculated is equal to urine output of preceding 4-6 hours.
 - Therefore, assess 4-6 hours to make appropriate fluid replacement plan to achieve normal fluid balance.

Nutritional support

- High-energy diet (infants 120 kcal/kg/d, older children 150 kcal/kg/d), supplement via nasogastric tube is needed.
- Encourage breast milk for infants if not enough add formula feeds.
- Daily requirements
 - Protein – 1g/kg/d maximum
 - Carbohydrate - 2-3 g/kg/d
 - Fats – 2g/kg/d
- Restrict salt intake
- Do not give potassium or phosphorus containing fluids to patients with oligo-anuric AKI unless they have significant hypokalaemia or hypophosphatemia
- Restrict protein intake when serum urea > 25mmol/L (450mg/dl)

Electrolyte and acid base management

- Replace electrolyte deficit according to monitored serum levels of electrolytes
- Note that once correcting acidosis, calcium levels are affected
- Manage hyperkalaemia (see management of hyperkalaemia)
- Manage Metabolic acidosis (serum pH ≤ 7.1)
- IV fluid therapy with Ringers Lactate instead of Normal Saline
- give sodium bicarbonate 4.2% IV 4ml/kg administered over 2-4 hours. Do not mix calcium and sodium bicarbonate containing solutions.

Manage hypertension

- Four limb blood pressure (BP) measurement
- If BP has systolic or diastolic measurements $\geq 95^{\text{th}}$ percentile for gender and age, patient has hypertension and must be managed for hypertension – see management of hypertension in children

Manage any concurrent infections and avoid nephrotoxic drugs

- Antibiotic treatment if poststreptococcal GN is suspected
- Adjustment of drug dosing in renal failure
- Discuss with Paediatrician / Nephrologist and / or Pharmacist concerning the possible nephrotoxic drugs
- Stop the offending drug or adjust the drug dose to renal friendly doses if the benefit outweighs the risk

Avoid nephrotoxic or renally excreted medicines e.g. NSAIDS, aminoglycosides, Vancomycin, cough and cold mixtures, radio-contrast

Manage uraemic convulsions

- (see management of seizures)
- Refer the patient for urgent dialysis
- Exclude other treatable causes of convulsions e.g. hypoglycaemia, hyper- or hyponatraemia, hypocalcaemia, hypertension etc.

Manage and treat anaemia

- For acute blood loss/active haemolysis and Hb $< 7\text{g/dl}$ give packed red blood cells 10ml/kg administered over 6 hours

Manage and treat pulmonary oedema, fluid overload and hypertension

- Do not give fluids to anuric patients with pulmonary oedema
- Refer for urgent dialysis
- Provide respiratory support as soon as possible.
 - Give oxygen, 100%, 2-3L/minute by nasal prongs escalate to face mask if needed for comfort.
 - CPAP
 - Intubate and initiate positive pressure ventilation as soon as possible where indicated.
- Furosemide, IV, 2 - 5mg/kg given over 5 minutes (maximum daily dose is 8mg/kg/24 hours)
 - Closely monitor electrolytes, especially in high doses
 - Care must be taken, as furosemide can also deteriorate the renal function
 - If oliguria and / or creatine worsen – think about renal replacement therapy
- Morphine, IV, 0.1mg/kg 4 hourly (with caution and close monitoring)

Renal replacement therapy (RRT)

- Think about RRT early as some conditions are rapidly progressing (e.g. HUS)
- The choice of RRT depends on the clinical status of the patient, the expertise of the clinician, and the availability of resources.
 - Hemodialysis (HD)
 - Peritoneal dialysis (PD)
 - Continuous RRT (CRRT)

Indications for RRT: AEIOU

- ACIDOSIS not responsive to medical management
- ELECTROLYTES: Refractory hyperkalemia (serum or plasma potassium >6.5 mEq/L) unresponsive to non-dialytic therapy (See "Management of hyperkalemia in children".)
- INTOXICATIONS: Drug toxicity (not for all drugs, please check if appropriate)
- OVERLOAD FLUID : refractory to diuretics
- URAEMIC complications: pericarditis, encephalopathy
- **Involve palliative care team from the onset if considering RRT!!!**

Follow up

- Follow up in PEN-Plus clinic in 1 month

CHRONIC KIDNEY DISEASE (CKD)

Definition

This is a clinical condition characterised by progressive, irreversible loss of kidney function due to abnormalities of the kidney structure or function (measured by proteinuria and /or reduction of estimated GFR, present for more than 3 months).

The diagnosis requires fulfilment of one of the two criteria which is clearly documented or inferred for more than 3 months: either GFR <60 mL/min/1.73m² or presence of markers of kidney damage including albuminuria (proteinuria).

Staging of chronic kidney disease (KDQOI)

| Stage | Estimated GFR (mL/min/1.73 m ²) | Features |
|-------|---|--|
| 1 | ≥90 | Renal parenchymal disease present |
| 2 | 60-89 | Usually asymptomatic – biochemical abnormalities present |
| 3 | 30-59 | Biochemical abnormalities and poor growth, poor appetite |
| 4 | 15-29 | |
| 5 | <15 (ESRF) | End stage renal failure. |

Risk Factors / Causes

There is increased risk of CKD in patients with the following:

- Congenital renal abnormalities (eg obstructive uropathy, PUV, polycystic kidney disease) – 60% of Pediatric CKD
- History of acute kidney injury
- Medical conditions that can affect kidney function
- Nephrotic syndrome
- Vasculitides/autoimmune disorders – eg. Immunoglobulin A vasculitis previously called HSP, Takayasu arteritis
- Infections and infestations – eg HIV, malaria, syphilis, schistosomiasis, TB
- Genetic disorders – eg. sickle cell, polycystic kidney disease
- Diabetes
- Cardiovascular disease - high blood pressure
- Family history of kidney disease
- Exposure to nephrotoxins (consider herbal remedies)

**ALL PATIENTS PRESENTING WITH RISK FACTORS MUST BE
SCREENED FOR CKD!!**

Promotion / Prevention

- Early health seeking behaviour
- Education and advocacy
- Early screening and detection in patients with high risk of CKD

- Scheduled follow up of at-risk patients, especially after AKI, with congenital abnormalities
- Appropriate fluid management
- Avoid/Stop all nephrotoxic drugs
 - stop early if cannot be avoided
- Antibiotic prophylaxis and early operation if possible, for congenital UT abnormalities
- Discourage use of traditional medicine
- Confirm drug doses for children based on their weight and adjust accordingly

Signs and symptoms

Key point in history

- Thorough history on previous renal diagnoses. Children can present with acute or chronic renal failure during episodes of an acute illness.
- Antenatal history (polyhydramnios?), postnatal history, family history and ask of possible exposure to traditional or complimentary herbal medicines and nephrotoxic drugs
- Hypertension
- Recurrent UTI
- Early UTI in infancy – needs screening for UT abnormalities
- Incomplete voiding (abnormal stream)
- Dysuria
- Haematuria
- Anuria or oliguria
- Chronic anaemia, chronic constipation, polyuria, polydipsia.

Key points on examination

- Thorough physical examination which must include dysmorphic features (especially looking at the ears, genitourinary system, back and spine deformities, and the skin).
- Anthropometric measurement and assessment
 - Poor growth – failure to thrive (FTT), severe stunting and poor weight gain
- 4 limb blood pressure if systolic or diastolic blood pressure is $\geq 95\%$ for gender and age, the child has hypertension. Refer to management of hypertension in children
- General body swelling
- Flank abdominal pain
- Signs and symptoms of salt wasting in children with renal tubular disorders or bilateral renal dysplasia.
 - These patients lose the ability to concentrate urine. The patient will present with dehydration and metabolic acidosis.
- Bone pain and skeletal deformities e.g. signs suggestive of rickets or osteomalacia
- Signs of fluid overload
 - Oedema, hypertension, heart failure and pulmonary oedema
- Signs and symptoms of raised Urea
 - Nausea, vomiting pruritus, brownish skin pigmentation, Uraemic frost
- Bleeding tendency
- Convulsions due to hyponatraemia, hypernatraemia, hypocalcaemia, uraemia or hypertension

Investigations

- Calculated estimated Glomerular filtration rate (eGFR) assesses kidney function and albuminuria / proteinuria assesses kidney injury
- Urine dipstick, Urine Microscopy, culture and sensitivity
- FBC
- Serum Urea and creatinine.
- Serum electrolyte
 - Hyperkalaemia, hyperchloraemia and decreased bicarbonate are common in CKD
 - Hypocalcaemia, hyperphosphataemia and increased ALP are common manifestation of CKD)
- 25-hydroxyvitamin D
- Parathyroid hormone (PTH)
- Liver function test
- Imaging:
 - CXR- pulmonary oedema?
 - Cardiac echo
 - Abdominal USS, KUB and renal artery Doppler.
 - Renal USS can reveal obstruction.
 - Small shrunken kidneys are suggestive of CKD.
 - Abdominal CT angiography in cases presenting with hypertension
- No biopsy is indicated in cases of CKD.

Management

Primary Level

- Manage any emergency signs and refer every patient to secondary level when CKD is suspected

Secondary Level

- Stabilise the patients if acutely unwell with supportive therapy as indicated

General and supportive care

- Identify and treat the underlying cause of CKD.
- Avoid further kidney damage – treat hypoperfusion early, detect and treat infections early, strict BP control
- Start oxygen support if indicated
- Do not give blood unless the child has symptomatic or severe anaemia <7g/dl
- Monitor BP and other vital signs
- Daily weight
- Monitor input
- Monitor output
 - Document any losses
 - Monitor Urine output
 - Catheterize only if indicated - Catheter placement may not always be needed (infection risk)

Initiate management of complications

- Manage pulmonary oedema (see management of pulmonary oedema)

- Manage hypertension (see management of hypertension)
- Manage UTI with antibiotics
- Manage diabetes complications (see management of diabetes)
- Discuss then refer patient to tertiary level

Tertiary Level

- Stabilise the patients with supportive therapy
 - Start oxygen support
 - Do not give blood unless the child has symptomatic severe anaemia
 - Catheterise and monitor urine output
- Identify and treat underlying cause

Fluid Management

- Assess and treat dehydration. (see management of dehydration).
 - During treatment of dehydration consider urine output and presence of extra renal losses. Do not use potassium containing fluids in anuric patient.
 - Use intravenous (IV) fluids only if oral intake is not possible (refer to the section on AKI)
- **In a patient with pulmonary oedema plus oliguria/anuria:**
 - DO NOT GIVE FLUIDS!!
- **In a patient who is anuric with no dehydration or extra renal fluid losses –**
 - Fluid replacement should be for insensible losses only (see AKI section for calculation).
 - If patient cannot take oral fluids, then prescribe parenteral fluids with electrolyte-free solution i.e. dextrose 5% or 10%
- **If a patient has oliguria, oedema and hypertension**
 - give oral fluids to replace insensible water loss plus urine output of previous 24 hours plus extra-renal losses.
 - When the patient improves calculate the losses within the previous 12 hours and replace for the next 12 hours to give a total of 100% fluid loss replacement.
- **If the patient is dehydrated and has on-going extra-renal fluid losses:**
 - Replace fluid according to losses. Replace losses with appropriate fluid solution similar to the losses e.g.
 - Diarrhoea losses give $\frac{1}{2}$ strength Darrows or Dextrose 5% IV or oral rehydration solution (ORS)
 - Vomiting/gastric fluid losses give normal saline (0.9%)/dextrose 5%.
- **If the patient is normally hydrated with normal urine output:**
 - Give normal intake
- **If the patient is in shock:** (see management of shock)

Manage Pulmonary Oedema (see management of pulmonary oedema)

Manage hypertension (see management of hypertension in children)

Manage Chronic Metabolic Acidosis and Electrolyte Abnormalities

- If serum bicarbonate is <18mmol/L give sodium bicarbonate, orally, 1 mmol/kg/dose 2-3 doses per day after meals.
 - Adjust according to response. The intravenous formulation can be given orally.
- If patient has severe metabolic acidosis with serum pH ≤ 7.1
 - give sodium bicarbonate 4.2% IV 4ml/kg administered over 2-4 hours. *Do not mix calcium and sodium bicarbonate containing solutions!*
- Replace electrolyte deficit according to monitored serum levels of electrolytes
- Manage hyperkalaemia (see management of hyperkalaemia)

Manage and treat anaemia

- Give iron supplements which include iron, folic acid or vitamin B12 and ensure that there are adequate iron stores by measuring ferritin, transferrin and transferrin saturation and total iron binding capacity regularly.
- If patient has persistent Hb <8g/dL despite correction of possible deficiencies of iron, folic acid or vitamin B12 treatment, start recombinant human erythropoietin (rHEPO).

- Give EPO, SC, 75units/kg/week in divided doses 2–3 times per week.
- Increase dose gradually whilst monitoring Hb levels every 4 weeks. Aim to increase Hb to 10-12g/dL.
 - If the Hb level is increasing with the initial dose, do not change dose.
 - If Hb level increases > 12 g/dL, stop treatment for one week. Thereafter continue with 25% less than previous dose per week.
 - If Hb level increase is not satisfactory adjust dose until target haemoglobin level of 12 g/dL is reached, then maintain the same EPO dose.
 - Increase by 25% at 4-week intervals until maximum dose of 300units/kg/week is reached.

- Avoid unnecessary transfusions due to risk of developing antibodies in patients who may be a potential candidate for renal transplant.
- For patients with symptomatic anaemia and Hb < 7g/dl give packed red blood cells 10ml/kg administered over 6 hours

Manage Infections & Review Prescribed Medications

- Manage any concurrent infections and avoid nephrotoxic drugs

Avoid nephrotoxic or renal excreted medicines e.g. NSAIDS, aminoglycosides, Vancomycin, cough and cold mixtures, radio-contrast drugs

- Manage UTI with antibiotics
- Adjustment of drug dosing in renal failure
- Discuss with pharmacist concerning the possible nephrotoxic drugs
- Stop the offending drug or adjust the drug dose to renal friendly doses if the benefit outweighs the risk

Manage diabetes complications (see management of diabetes)

Provide nutritional support

- Involve the dietician as soon as possible (e.g. salt restriction, high calorie, high protein, low potassium diet)
- High-energy diet (aiming for 120%), supplement via nasogastric tube is needed.
- Encourage breast milk for infants - if not enough add formula feeds.
- Do not restrict protein intake in all patients with CKD.
- If potassium is >5.5 mmol/L reduce potassium intake.
 - Restrict fruit juices, dried fruit, all citrus fruits, bananas, guavas and tomatoes. These foods have high potassium content.
 - All vegetables should either be soaked for 24 hours before cooking or water should be decanted twice during cooking.
- If phosphate is >1.8 mmol/L with a GFR <70 ml/min/1.73m² reduce phosphate intake.
- Reduce salt intake - no salt should be added during food preparation or during meals.
 - Do not allow eating salt preserved foods. No salt intake in all patients with hypertension and oedema.
 - **Note: Do not restrict salt intake in patients with salt loosing nephropathies.**

Provide vitamin and mineral supplements

- Give multivitamin, orally, 5 ml/day - Choose formulations that have pyridoxine, other B vitamins, Vitamin C-30mg and vitamin D- 400IU.
- Give folic acid, orally, 5mg/day.
- For management of hyperphosphataemia / osteodystrophy and hyperparathyroidism:
 - Restrict foods rich in phosphate
 - Give calcium carbonate, orally, 1-4 chewable tablets 8 hourly with meals. 1 tablet = 1.68g elemental calcium.
 - Give Alfacalcidiol, orally, 0.25mcg daily- discuss with seniors/paediatrician or specialist if available.
 - In patients with serum calcium <2.2 mmol/L start alfacalcidiol 0.25mcg twice weekly and increase dose as instructed by specialist or senior medical personnel present to maintain normal calcium range.
 - If serum phosphate >2.5 mmol/L treat hyperphosphataemia first to decrease to <1.8 mmol/L before starting alfacalcidiol to avoid metastatic calcification

Manage dyslipidaemia in CKD

- Dyslipidaemia may contribute to the progression of chronic kidney disease, particularly in children with nephrotic syndrome.
- Hypertriglyceridaemia and abnormal apolipoprotein metabolism is a feature of CRF.
- Dietary intervention includes reducing foods with saturated fats and cholesterol.
- For children > 8 years with persistent total cholesterol levels > 7 mmol/L, give statins - HMGCoA reductase inhibitors, e.g. Simvastatin, oral, 10 mg (maximum dose of 20 mg) at night. Discuss with seniors before initiation.

Provide reno-protective treatment

- All children with persistent nephrotic range proteinuria and GFR > 30 mL/minute give ACE inhibitor e.g. Enalapril, oral, 0.1 mg/kg/dose, once daily.
 - Increase dose to 0.5 mg/kg/day, as a single dose or two divided doses.
 - Monitor for adverse effects which include hyperkalaemia (increased risk when potassium sparing diuretic is used simultaneously) and acute renal failure (increased risk in children with impaired renal function or volume depletion) and cough (which is often main reason why patients would stop taking the drug)
 - ACEi may worsening metabolic acidosis and cause a decline in renal function while reducing proteinuria. Therefore, monitor serum urea and electrolytes, i.e. serum potassium, bicarbonate, and renal function within 7 days of starting the drugs.
 - If serum creatinine has doubled, check hydration status, stop diuretics and halve the dose of ACE inhibitors.
 - If renal function does not improve, or hyperkalaemia > 5.5 mmol/L persists, stop ACE inhibitor treatment.

Other Management considerations

- Consult the urology (surgical) team if the patient has confirmed obstructive uropathy
- Consider haemodialysis where the patient meet criteria and services are available (see indications for dialysis)
- Start palliative care support soon after diagnosis of CKD
- Ensure that the child is fully vaccinated and provide catch up immunisations as appropriate

Follow up

- Follow up in PEN-Plus clinic regularly

NEPHROTIC SYNDROME

Definition

Nephrotic syndrome is a clinical syndrome associated with heavy proteinuria due to increased permeability of the glomerular basement membrane.

The diagnostic criteria include the following:

- Oedema
- Proteinuria (at least 3+ on urine dipstick)
- Hypoalbuminaemia (<30g/L)
- Hyperlipidaemia

Causes / Risk factors

- Primary
 - Idiopathic (minimal change; focal segmental glomerulonephritis (GN) - most frequent, usually responds to corticosteroids)
- Secondary
 - Infections (e.g., post infectious glomerulonephritis, malaria, HIV, TB, hepatitis B & C, schistosomiasis, syphilis)
 - Drugs (NSAIDs)
 - Autoimmune disease (SLE)
 - Mechanical (obstructive neuropathy)
 - Malignancy (lymphoma)
- Congenital/infantile (present at birth or in children less than 1 year)
 - Immune disorders (infantile systemic lupus erythematosus)
 - Infective (TORCH, Hep B,)

Prevention / Promotion

- Vaccination against common medical conditions associated with NS e.g. Malaria, Hepatitis B, *streptococcus pneumonia* infections etc.
- Health education and advocacy
- Early identification
- Averting complications (e.g. preventing infections of encapsulated organisms, and thromboembolic events, malnutrition and progress to chronic kidney disease)

Symptoms and signs

- Oedema
 - Often starting under the chin and around the eyes which may become generalised (anasarca, genitals, ascites and pleural oedema)
 - Dependent on position and activity of the child – upon awaking usually periorbital or facial oedema, decreases over the day while anasarca and pretibial oedema increase

Differential Diagnosis

- Other causes of oedema e.g.
 - malnutrition (bilateral pitting oedema that do not vary with position), cardiac failure, liver cirrhosis, allergies, severe anaemia
- Other renal causes of oedema – e.g. glomerulonephritis, renal failure

Investigations

- Blood pressure (Usually normal)

- Urine dipstick – ($\geq +3$ proteinuria, trace to +1 haematuria)
- Spot random urine sample for protein: creatinine ratio ($> 0.2\text{g}/\text{mmol}$).
- Urine microscopy – hyaline and lipid casts seen. Occasionally, red and white blood cell casts seen.
- FBC
- HIV, Malaria, Syphilis, CMV antibody, hepatitis B and C serology,
 - to exclude secondary causes of NS
- Stool microscopy for schistosomiasis
- Urea and creatinine – often within normal range
- Electrolytes
- Liver Function Tests
- Raised Cholesterol levels
- Hypoalbuminaemia (Serum albumin $< 3 \text{ g/dL}$)
- Complement levels
- TB workup
 - Montoux
 - CXR: to Rule out TB.

NOTE: Other more advanced investigations including kidney biopsy should be taken in consultation with a paediatric nephrologist and histopathologist.

All patients with clinical signs of steroid resistant nephrotic syndrome should have renal biopsy. Please refer to the Nephrologist.

Management

- Hospitalize for initial therapy
- General supportive measures
 - Monitor fluid balance. Do not fluid restrict
 - Monitor urine output
 - Daily weight and adjust the medication dosages according to current weight
 - Assess hydration status.
 - Suspect hypovolaemia if patient has hypotension, small pulse volume and cold extremities.
 - Encourage ambulation
 - Replace on-going renal losses. (See management of dehydration in children).
- Nutritional support
 - Do not restrict oral fluid intake
 - Restrict salt intake in all patients
 - Ensure normal calorie and protein intake (for patients with normal renal function)

Primary Level

- Refer all patients with nephrotic range proteinuria ($\geq 3+$) \pm oedema to secondary level

Secondary Level

Supportive management

- Fluid balance – daily weight, urine output monitoring, BP monitoring

- Do not restrict oral fluids (risk of thrombosis due to hypercoagulopathy)
- Diet – salt and fat diet restriction, involve dietician if available
- Encourage ambulation to prevent thromboembolic events
- Treat infections as soon as they appear (NS patients are more prone to infection. Also infections are often a trigger for relapses)

Pharmacological Treatment

- Treat intercurrent infection before starting steroids
- Exclude active tuberculosis
- Start steroids:
 - Prednisolone 2mg/kg/d with maximum dose 60mg/d for 4 weeks
 - Review after 4 weeks. Check urine dipstick and
 - if in complete remission: **steroid sensitive nephrotic syndrome.** Wean prednisolone 1.5mg/kg on alternate days for 4 weeks
 - if not yet in complete remission at 4 weeks
 - Continue prednisone upto 6 weeks
 - if goes into remission : **steroid sensitive late responder.** Wean prednisolone 1.5mg/kg alternate days for 6 weeks.
 - if not in remission after 6 weeks of prednisolone ; **steroid resistant nephrotic syndrome.** Wean prednisolone as above

For all patients taking steroids, monitor, check and manage complications of steroids (e.g. eye cataracts, adrenal insufficiency, reflux, poor growth, cushing's syndrome etc.)

prescribe calcium and vitamin D supplements for all children on steroids for nephrotic syndrome

- **Do not use furosemide unless a child has signs of pulmonary oedema or respiratory distress** (see pulmonary oedema treatment guidelines)
 - Treat with the lowest possible dose, e.g. 0.5 mg/kg BD).
 - Children with nephrotic syndrome even with gross oedema may be intravascularly depleted and frusemide can result in acute kidney injury
- Look for and initiate management of complications and refer for tertiary level care. Complications include the following;
 - Thrombotic events (eg stroke, DVT)
 - Spontaneous bacterial peritonitis
 - Hypovolaemic shock

- Electrolyte imbalances
- Refer if gaining weight or has oliguria/anuria or not in remission at 6 weeks (i.e. urine dipstick with protein trace for ≥ 3 days in a row)

Tertiary Level

- Management as above
- If critically low albumin with oedema causing symptoms :
 - IV albumin 0.5-1g/kg slowly over 4 hours with frusemide half way. (please ensure the patient is passing urine)
 - if Albumin not Available consider using FFPs 15ml/kg over 4 hours
- For steroid dependant or frequently relapsing nephrotic syndrome
 - Low dose prednisolone
 - 0.5mg/kg alternate days (max 20mg alt daily)
 - 0.25mg/kg daily (max 10mg)
 - Cyclophosphamide
 - 2mg/kg/day for 12 weeks
 - 3mg/kg/day for 8 weeks
 - Nb: maximum dose 150mg and follow up FBC 14 days after starting treatment then monthly
 - Other steroid sparing agents : cyclosporine, MMF, Rituximab
- For steroid resistant nephrotic syndrome
 - RAAS inhibitors to decrease proteinuria
 - Calcineurin inhibitors if available : cyclosporine or tacrolimus

Follow – up

- Follow up in PEN-Plus clinic. During the initial part of treatment, follow-up has to be frequent to monitor response.

Definitions:

| Term | Definition |
|--|---|
| Nephrotic-range proteinuria* | Urinary protein creatinine ratio (UPCR) $\geq 200 \text{ mg/mmol}$ (2 mg/mg) in a spot urine, or proteinuria $\geq 1000 \text{ mg/m}^2$ per day in a 24-h urine sample corresponding to $3+$ ($300\text{--}1000 \text{ mg/dL}$) or $4+$ ($\geq 1000 \text{ mg/dL}$) by urine dipstick |
| Nephrotic syndrome | Nephrotic-range proteinuria and either hypoalbuminemia (serum albumin $< 30 \text{ g/L}$) or edema when serum albumin is not available |
| Complete remission | UPCR (based on first morning void or 24 h urine sample) $\leq 20 \text{ mg/mmol}$ (0.2 mg/mg) or $< 100 \text{ mg/m}^2$ per day, respectively, or negative or trace dipstick on three or more consecutive days |
| Partial remission | UPCR (based on first morning void or 24 h urine sample) > 20 but $< 200 \text{ mg/mmol}$ ($> 0.2 \text{ mg/mg}$ but $< 2 \text{ mg/mg}$) and serum albumin $\geq 30 \text{ g/L}$ |
| Steroid-sensitive nephrotic syndrome (SSNS) | Complete remission within 4 weeks of PDN at standard dose ($60 \text{ mg/m}^2/\text{day}$ or 2 mg/kg/day , maximum 60 mg/day) |
| Steroid-resistant nephrotic syndrome (SRNS) | Lack of complete remission within 4 weeks of treatment with PDN at standard dose |
| Confirmation period | Time period between 4 and 6 weeks from PDN initiation during which responses to further oral PDN and/or pulses of IV MPDN and RAASi are ascertained in patients achieving only partial remission at 4 weeks. A patient not achieving complete remission by 6 weeks, although partial remission was achieved at 4 weeks, is defined as SRNS |
| SSNS late responder | A patient achieving complete remission during the confirmation period (i.e. between 4 and 6 weeks of PDN therapy) for new onset NS |
| Relapse | Urine dipstick $\geq 3+$ ($\geq 300 \text{ mg/dL}$) or UPCR $\geq 200 \text{ mg/mmol}$ ($\geq 2 \text{ mg/mg}$) on a spot urine sample on 3 consecutive days, with or without reappearance of edema in a child who had previously achieved complete remission |
| Infrequently relapsing nephrotic syndrome | < 2 relapses in the 6 months following remission of the initial episode or fewer than 3 relapses in any subsequent 12-month period |
| Frequently relapsing nephrotic syndrome (FRNS) | ≥ 2 relapses in the first 6-months following remission of the initial episode or ≥ 3 relapses in any 12 months |
| Steroid-dependent nephrotic syndrome (SDNS) | A patient with SSNS who experiences 2 consecutive relapses during recommended PDN therapy for first presentation or relapse or within 14 days of its discontinuation |
| Steroid toxicity | New or worsening obesity/overweight, sustained hypertension, hyperglycemia Behavioral/psychiatric disorders, sleep disruption Impaired statural growth (height velocity $< 25^{\text{th}}$ percentile and/or height $< 3^{\text{rd}}$ percentile) in a child with normal growth before start of steroid treatment Cushingoid features, striae rubrae/distensae, glaucoma, ocular cataract, bone pain, avascular necrosis |
| Sustained remission | No relapses over 12 months with or without therapy |
| SSNS controlled on therapy | Infrequently relapsing NS or sustained remission while on immunosuppression in the absence of significant drug-related toxicity |
| SSNS not controlled on therapy | Either frequently relapsing NS despite immunosuppression or significant drug-related toxicity while on immunosuppression |
| Secondary steroid resistance | SSNS patient who at a subsequent relapse does not achieve complete remission within 4 weeks of PDN at standard dose |
| Complicated relapse | A relapse requiring hospitalization due to one or more of the following: severe edema, symptomatic hypovolemia or AKI requiring IV albumin infusions, thrombosis, or severe infections (e.g., sepsis, peritonitis, pneumonia, cellulitis) |

GLOMERULONEPHRITIS / NEPHRITIC SYNDROME

Definition

This is a clinical manifestation of glomerular injury due to massive inflammation, which is characterized by haematuria, hypertension and oedema. (can also have proteinuria). It can lead to impaired kidney function

Causes

Primary glomerulonephritis (GN)

- Isolated Kidney Disease
 1. Membranoproliferative glomerulonephritis
 2. Immunoglobulin A (IgA) nephropathy
 3. Anti-glomerular basement membrane (GBM) disease
 4. Idiopathic crescentic GN

Secondary GN

- Systemic disease
 1. Post-streptococcal GN (most common cause)
 2. Other postinfectious GN (Staph aureus, E.coli, Mycoplasma, Salmonella typhi, EBV, Parvo B19, Varizella, Hep B, Schistosomiasis, Malaria, .)
 3. IgA vasculitis (Henoch-Schönlein purpura)
 4. Systemic lupus erythematosus nephritis
 5. ANCA-associated vasculitis
 6. Nephritis associated with infective endocarditis
 7. Good pasture syndrome

Risk factors

- Upper respiratory tract infection/pharyngitis (Group A streptococcal infection - GAS); common between 2-6 years of age
- Bacterial infection (streptococcal and staphylococcal) e.g. pyoderma, impetigo, abscesses, atypical pneumonia etc.
- Viruses e.g. Hepatitis B infection
- Vasculitis disorders eg Autoimmune disorders and others
- Alport Syndrome

Promotion / Prevention

- Early health seeking behaviour
- Early detection and treatment of sore throat and skin infections including scabies
- Adhere to the national EPI program for vaccines

Signs and Symptoms

- Sudden onset of haematuria (microscopic or gross) ±Proteinuria
- Oliguria
- Oedema (fluid retention) with facial swelling, dyspnoea,
- Abdominal pain
- Rapid weight gain
- Hypertension which can cause headache, seizures and visual impairment
- Rash secondary to HSP, IgA nephropathy, infected scabies.

Investigations

- 4 limb blood pressure if systolic and diastolic blood pressure is >95th percentile for age and gender the patient has hypertension.
- Urine appearance – smoky, brown or bloody.
- Urine dipstick – +1 to +3 haematuria ± trace to +2 proteinuria.
- Urine Microscopy – including red cells that are dysmorphic with or without red and granular casts.
- Urine culture
- Decreased C3 and normal C4 complement levels
- Anti-streptolysin (ASO) anti-DNAse B titre if available. ASO is usually positive in the absence of prior antibiotic treatment. It is often negative in preceding skin infections.
- Urea and creatinine – mildly elevated in acute phase of the disease
- Electrolytes – (hyponatraemia, hyperchloraemic hyperkalaemic metabolic acidosis is common)
- FBC – anaemia with normal platelet count
- Blood cultures
- Hepatitis B virus
- Abdominal USS and KUB plus Renal artery Doppler
- Cardiac echocardiography if hypertensive or signs of fluid overload
- ESR
- Kidney biopsy

Differential Diagnosis

- Other causes of oedema e.g. malnutrition, cardiac failure, liver cirrhosis, allergies, severe anaemia
- Other renal causes of oedema – eg. Nephrotic syndrome, renal failure
- Other causes of hypertension eg coarctation of aorta, Aortic stenosis, brain tumors, Takayasu arteritis
- Malignancy eg Wilm's Tumor
- Drugs (rifampicin, ibuprofen)
- Hemoglobinurias and Myoglobinuria

Management

Primary Level

- Manage emergencies eg. Manage ABCDE, administer frusemide 1-2 mg/kg stat dose if fluid overload
- Manage seizures according to seizure protocol
- Refer all patients presenting with oedema, hypertension and haematuria to secondary level

Secondary Level

- Manage ABCDE
- Manage seizures according to seizure protocol
- Manage pulmonary oedema and hypertension
 - Hypertension develops acutely due to fluid overload and normalizes after treatment.
 - Measure BP regularly – at least 6hrly but preferred to be in HDU if hypertensive for more frequent monitoring
 - Give Furosemide 1-2 mg / kg

- (see pulmonary oedema and hypertension management)
- Bed rest for patients with severe hypertension or pulmonary oedema (semi-seated position)
- Fluid balance
 - Daily weight, urine output monitoring, BP monitoring
 - Fluid management according to fluid state
 - Strict fluid intake
 - Avoid using IV fluids - if IV fluids need to be administered, then a potassium free fluid is ideal.
- Diet
 - Restrict salt intake in all patients presenting with GN
 - Restrict potassium intake until results of potassium is available
- Antibiotic therapy (post-streptococcal glomerulonephritis)
 - Amoxycillin 15mg / kg / dose 8hrly (max 500mg/dose) for 10 days
OR
 - Benzylpenicillin 50,000 MU / kg IV, 6 hourly for 10 days
OR
 - Benzathine penicillin STAT dose
 - 600,000 IU if \leq 25kg / 1,200,000 IU if $>$ 25kg
OR
 - Alternative drugs if there is history of penicillin sensitivity is oral erythromycin 10 mg/kg/dose 6 hourly for 10 days
- All patients with complications (refractive seizures, hypertensive encephalopathy), those not improving after antibiotic and supportive treatment must be discussed and referred to tertiary hospital
- Involve palliative care and psychosocial support

Tertiary Level

- Manage as above
- Supportive therapy
- Manage pulmonary oedema (see pulmonary oedema management)
- Manage hypertension (see hypertension management)
- Manage electrolyte and acid base derangements
- Dialysis if indicated should be commenced as soon as possible (see indications for dialysis)
- Involve palliative care team if the disease becomes chronic or requires dialysis
- In rapidly progressive GN (rapid decline in GFR of atleast 50% over a few days to 3 months)
 - high dose steroids
 - Methylprednisolone 10mg/kg for 3 days then 2mg/kg prednisone and wean over 4 weeks if not available 2mg/kg prednisolone for 5 days and wean
 - Cyclophosphamide IV.
- Management of the patient should be in conjunction with a general paediatrician, paediatric nephrologist if available and infectious disease specialist.

Follow up

- Follow up in PEN-Plus clinic
- Most cases of acute GN are due to PSGN- symptoms resolve within one or two weeks of presentation. - adapt antihypertensive drugs. Usually only needed initially
- If unsure of diagnosis of PSGN then do a kidney biopsy (nephrologist consultation).

HAEMOLYTIC URAEMIC SYNDROME (HUS)

Definition

It is a clinical syndrome of thrombotic microangiopathy characterized by the following triad;

- 1 Micro-angiopathic haemolytic anaemia (fragmented erythrocytes)
- 2 Thrombocytopenia
- 3 Acute Kidney Injury (AKI)

Subtypes

Shiga Toxin-producing Escherichia Coli HUS (STEC-HUS)- 90%

Non STEC-HUS

Risk Factors / Causes

1 *Acquired Infectious*

- STEC – usually 5-10 days after onset of diarrhea
- Shigella
- Streptococcus pneumoniae
- HIV Infection
- Malaria
- H1N1 influenza A
- Parvovirus B19

2 *Acquired non-infectious*

- Autoantibodies to complement factors
- Drug toxicity, particularly in patients with cancer or solid organ transplant recipients
- Pregnancy
- Autoimmune disorders e.g. systemic lupus erythematosus

3 *Heredity*

- Complement gene mutations in children
- Inborn errors of cobalamin C metabolism
- Diacylglycerol kinase epsilon (DGKE) gene mutations

Promotion / Prevention

- Promote hygiene and sanitation
- Vaccination
- Early recognition and treatment

Signs and Symptoms

- Petechiae and easy bruising
- Fever
- Abdominal pain
- Bloody diarrhoea
- Pallor
- Hypertension – common!
- Oliguria or anuria
- CNS manifestations – reduced level of consciousness or seizures
- **Severe AKI in ½ of the HUS cases!**

Differential diagnosis

- DIC – Disseminated Intravascular Coagulopathy
- TTP – Thrombotic thrombocytopenic purpura
- Systemic vasculitis
- Immunoglobulin A vasculitis

Investigations

- Urine dipstick and urinalysis
- Full Blood count – Hb usually less than 8g/dl
- Peripheral Blood Film
 - schistocytes (RBC fragmentation) in up to 10% of erythrocytes
- Findings of hemolysis: high indirect bilirubin concentration, reduced serum haptoglobin, raised LDH
- HIV tests
- Urea and Creatinine (raised)
- Electrolytes.
- Stool microscopy, culture and sensitivity
- Stool Shiga toxin ELISA
- Blood culture
- Additional laboratory tests may be needed in case by case basis to exclude other possible diagnoses that present in a similar manner (differential diagnosis):
 - Coagulation profile
 - Autoimmune workup (Coombs test , ANA, Anti-dsDNA, ANCA)

Management

Primary Level

- Manage emergency conditions – ABCDE
- Refer to next level of care

Secondary Level

- Manage emergency conditions – ABCDE
- Transfuse blood transfusion in anaemic patients haemoglobin level below 6 or haematocrit <18 percent (see Malawi Blood Transfusion Guidelines)
- Refer urgently to next level of care

Tertiary Level

- **Manage emergency conditions – ABCDE**
- **Transfuse blood transfusion** in anaemic patients haemoglobin level below 6 or haematocrit <18 percent (see Malawi Blood Transfusion Guidelines) – aim for an HB of 8-9 g/dl (not higher due to risk of fluid overload)
- **Transfuse Platelet** for patients who have low platelets with significant active clinical bleeding
- **Supportive therapy**
 - Manage pulmonary oedema (see pulmonary oedema management)
 - Manage hypertension (see hypertension management)
 - Manage fluid and electrolyte to maintain adequate intravascular volume and correct/avoid electrolyte imbalances (See management of electrolyte imbalances).
 - Manage seizures

- **STOP** nephrotoxic drugs or those drugs associated with HUS e.g. gentamicin, vancomycin,
 - A trial of frusemide in severe fluid overload can be performed, but stop diauretics if no effect
- **START** dialysis therapy (see indication for AKI)
- **PROVIDE** adequate nutrition

Follow up

- Follow up the patient in PEN-Plus clinic as appropriate

ELECTROLYTE IMBALANCES

HYPERKALAEMIA

Definition

Serum or plasma potassium greater than 5.5 mmol/L.

- Potassium levels > 7 mmol/L is an emergency requiring immediate treatment!!

Risk factors / Causes

Excessive potassium intake:

- IV Fluids with high potassium content
- Massive blood transfusion
- Parenteral nutrition e.g. TPN
- IV medications with high potassium content e.g. NSAIDS
- Rarely diet intake e.g. bananas

Transcellular movement of intracellular potassium into the extracellular space

- Cellular injury: Rhabdomyolysis, burns, trauma, extreme exercise (exertional heat illness), tumour lysis syndrome, gut necrosis and severe haemolytic disorders.
- Metabolic/respiratory acidosis
- Hyperglycaemia

Decreased renal excretion of potassium

- Acute and chronic kidney disease: Decreased glomerular filtration rate (GFR) below 30ml/min per 1.73 m²
- Tubular dysfunction: Urinary tract infections (UTI), sickle cell disease and Type 4 renal tubular acidosis (hypoaldosteronism)

Decreased effective arterial blood volume

- Functional renal tubular acidosis (RTA)
- Severe dehydration in infants and young children

Decreased activity of the renin-angiotensin-aldosterone system:

- Congenital adrenal hyperplasia (CAH)
- Primary adrenal insufficiency – Addison's disease or crisis
- Pseudohypoaldosteronism
- Medications: potassium sparing diuretics eg. spironolactone, angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB).

Pseudohyperkalemia

- This is not a TRUE hyperkalemia - it is most commonly caused by haemolysed blood samples due to difficulties in obtaining or handling blood samples. Always question the results if obtaining blood has been difficult.

Health Promotion/prevention

- Promote healthy normal diet
- Avoid over the counter medication
- Early health seeking behaviour
- Appropriate and accurate fluid and electrolyte management in cases with dehydration

- Avoid haemolysis when acquiring blood sample for potassium assessment

Signs and symptoms

- A thorough clinical assessment and evaluation with history and clinical examination should be conducted to ascertain the cause.
- Asymptomatic:
 - Mild elevation with serum potassium <6mmol/L
 - Moderate elevation with serum potassium between 6-7mmol/L
- Symptomatic
 - Severe elevation with serum potassium > 7mmol/L
 - Ascending muscle weakness/flaccid paralysis, decreased deep tendon reflexes
 - Constipation, abdominal distension
 - Palpitations, bradycardia, syncope, or asystole depending on the severity of cardiac conduction disturbances
- ECG changes:
 - Potassium level between 5.5 to 6.5 – Tall peaked T waves (more than 2/3 of the R wave) with a narrow base and shortening of the QT interval
 - Potassium level between 6.5 to 8.0 – Peaked T waves, prolonged PR interval, decreased or disappearing P wave, widening QRS complex, and amplified R wave
 - Potassium level above 8.0 – Absent P wave, bundle branch block, progressive widening of QRS complex that eventually merges with the T wave to form a sinusoidal pattern. This is followed by ventricular fibrillation or asystole.

ECG TRACING WITH HYPERKALAEMIA

| Serum potassium | Typical ECG appearance | Possible ECG abnormalities |
|--------------------------|---|--|
| Mild (5.5–6.5 mEq/L) |  | Peaked T waves Prolonged PR segment |
| Moderate (6.5–8.0 mEq/L) |  | Loss of P wave Prolonged QRS complex ST-segment elevation Ectopic beats and escape rhythms |
| Severe (>8.0 mEq/L) |  | Progressive widening of QRS complex Sine wave Ventricular fibrillation Asystole Axis deviations Bundle branch blocks Fascicular blocks |

EpoMedicine

Investigations

- History – pointing towards AKI (Oliguria/Anuria)
- Laboratory investigations depending on presentation and availability should be conducted and may include:
 - Full blood count, PBF, urinalysis
 - Serum electrolytes - to exclude pseudohyperkalemia repeat the blood sample using a free flowing or arterial blood

- sampling
- Arterial blood gas analysis
 - BUN and creatinine.
 - Serum lactate dehydrogenase – see haemolysis
 - Serum creatinine kinase – Rhabdomyolysis
 - ECG
 - Abdominal USS and KUB

Differential diagnosis

Ascending muscle weakness / paralysis:

- Polio and West Nile virus infection, toxins (e.g. botulism), hypocalcaemia and hypermagnesaemia, and Guillain-Barré syndrome

Palpitation and syncope

- Life threatening cardiac conduction abnormalities. (See section on syncope)

Management

Primary Level

- Stabilize the patient and refer

Secondary Level

- Stop all potassium containing fluids, feeds and/or drugs
- Start managing hyperkalaemia depending on availability of resources
 - Stabilize the cardiac membrane with Calcium gluconate
 - Give Salbutamol nebulisation
- Discuss and refer the patient for tertiary level care

Tertiary Level

- Confirm the patient truly has hyperkalaemia by obtaining venous or arterial blood sample that is not haemolysed for rapid analysis
- Admit patient in HDU or ICU

1.a. Stop all potassium containing fluids, feeds and/or drugs

1.b. Stabilize the cardiac membrane with

- 10% calcium gluconate – 60mg/kg given as a 0.5mls/kg diluted in equal volumes of Normal saline. Maximum 2g (20ml, 4.5mmol) per dose IV or IO over 5 minutes.
- May repeat in 10 minutes if arrhythmias or ECG changes persist
- DO NOT mix with sodium bicarbonate!

1.c. Decrease extracellular potassium levels with

- Salbutamol nebulisation
 - Neonates - 0.4mg in 2ml of saline
 - <5 years - 2.5mg in 2ml saline
 - >5 years – 5mg in 2ml saline
- Give 2 back to back nebs and repeat after 20 minutes

If no response after 30 minutes:

- Give insulin 0.1IU/kg bolus subcutaneously with glucose 0.5g/kg (2.5mls/kg 20% glucose or 5ml/kg of 10% glucose) bolus.
- Monitor glucose after 30minutes, then 1 hourly
- If no response after 30 minutes, repeat insulin and glucose dose

If no response after another 30 minutes:

- Insulin infusion 0.05 – 0.2IU/kg/hr. Give with 2-4ml/hr 10% dextrose. Monitor glucose after 30mins then 1 hourly
- Salbutamol IV 4 μ g/kg in 5mls water for injection over 20 min (repeat as necessary)
- Consider 10ml/kg bolus normal saline plus 1mg/kg frusemide if patient euvoalaemic or hypovolaemic

1.d Treat metabolic acidosis

Sodium bicarbonate 1-2mmol/kg IV over 30 min

1.e Reduce potassium body stores by

Peritoneal dialysis

Treating the underlying cause

- Start initial management whilst consulting ICU, nephrologists, urologist as needed.
- Refractory hyperkalaemia may need to be managed with dialysis.

HYPOKALAEMIA

Definition

Serum or plasma potassium less than 3 mmol/L.

- Moderate hypokalaemia with serum potassium levels between 2.5 to 3mmol/L
- Severe hypokalaemia with serum potassium levels below 2.5mmol/L

Risk factors/causes

Gastrointestinal losses:

- Profuse vomiting or diarrhoea.
- Infective gastroenteritis including cholera
- Pyloric stenosis
- Pancreatitis
- Malabsorption e.g. HIV enteropathy

Urinary losses: e.g. Osmotic diuresis in DKA, glomerulonephritis, pyelonephritis, tubulopathy etc.

Drugs: diuretic therapy e.g. furosemide use, aminoglycosides and/or steroids

Decreased intake:

- Malnutrition
- Prolonged IV fluids especially post-operation surgical patients on nil per os (NPO)

Intracellular shift:

- Metabolic alkalosis
- Acute stress
- Insulin therapy
- High dose salbutamol

Promotion / Prevention

- Health education on balanced diet which include food rich in potassium
- Early health seeking behaviour
- Timely and appropriate fluid and electrolyte management
- Avoid prolonged fluid administration in post-operated cases, encourage early feeding as soon as tolerated

Signs and symptoms

- Lethargy or coma
- Muscle weakness: Generalized muscle weakness, respiratory muscle weakness and GIT hypo-motility leading to paralytic ileus or constipation
- Hyperglycaemia
- Hypotension
- Cardiac arrhythmias
- ECG changes: Flat T-waves and ST depression
- Cardiac arrest

Diagnosis

- Clinical assessment and evaluation should include thorough history and physical examination

- Laboratory investigations should depend on presentation and availability as follows:
 - Full blood count, MRDT/MPs, electrolytes, RBS, arterial blood gas analysis
 - BUN and creatinine
 - ECG
 - Abdominal X-ray, abdominal USS
 - Urine dipstick, urinalysis (MCS)

Management

Primary Level

- Stabilize the patient (ABCDE) and refer to next level of care

Secondary Level

- Stabilize the patient (ABCDE) and manage losses if present
- Initial laboratory investigations to find the underlying cause depending on availability
- If potassium > 2.5 mmol/L and able to feed and not having on-going losses
 - Oral potassium supplement slow K 1 - 4mmol/kg/day
 - Potassium rich diet with bananas, cooked Irish potatoes, nuts, oranges etc.
- If severe hypokalaemia (<2.5mmol/L) / persistent hypokalaemia despite treatment, discuss the patient and refer to tertiary level

Tertiary Level

- Start initial management whilst consulting ICU, nephrologists, urologist
- Admit patient to HDU or ICU as indicated
- Stabilise the patient and manage losses if present
- Initial laboratory investigations to find the underlying cause
- If potassium > 2.5 mmol/L and able to feed and not having on-going losses
 - Oral potassium supplement slow K 1 - 4 mmol/kg/day
 - Potassium rich diet with bananas, cooked Irish potatoes, nuts, oranges etc.
- If potassium < 2.5 mmol/L and/or symptomatic
 - IV potassium chloride 2mmol / kg **plus** the deficit (3.5 – measured serum potassium in mmol/L)/kg.
Do not exceed 0.2mmol/L/kg /h.

Example:

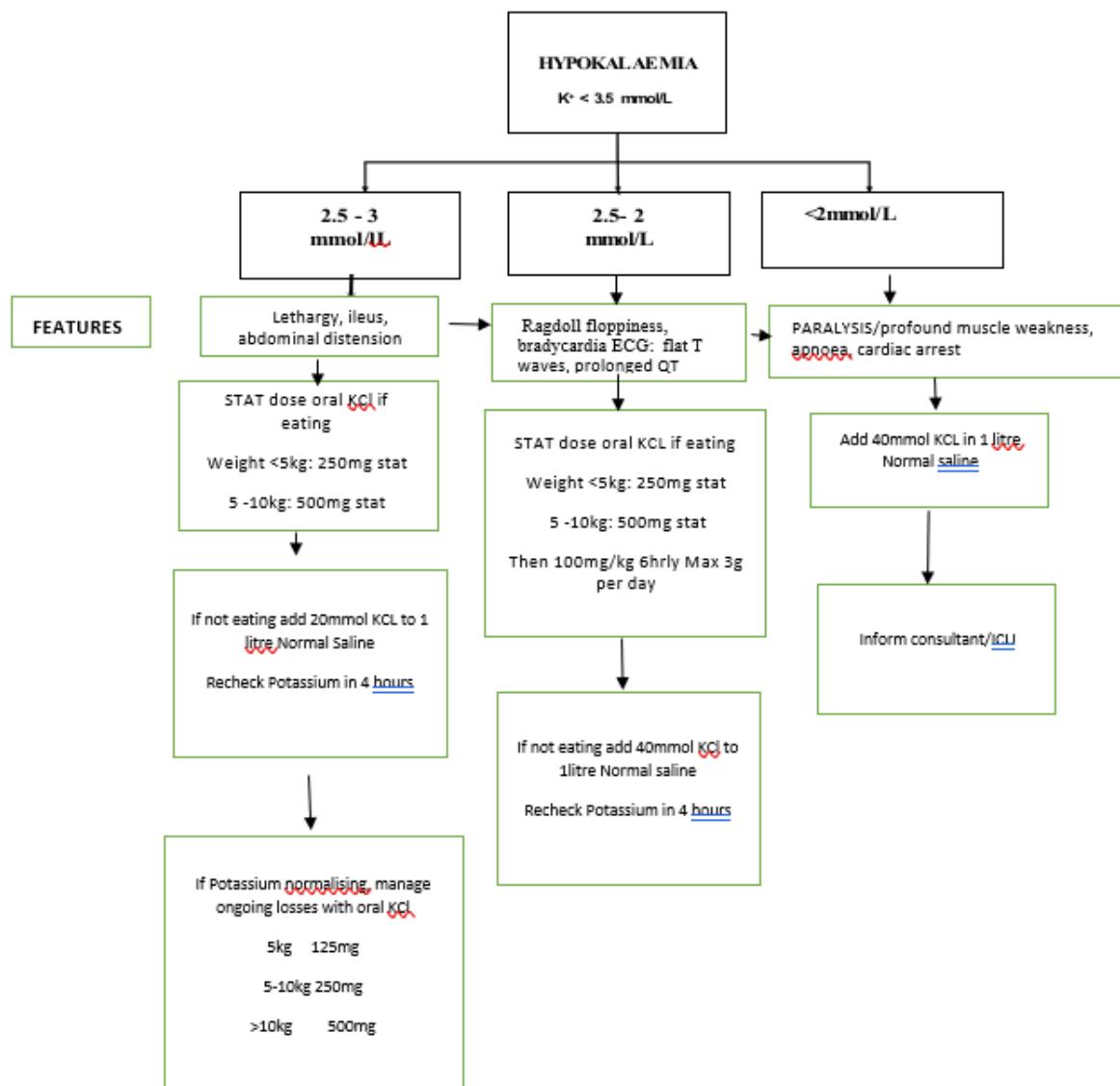
7kg infant with serum potassium of 1.5mmol/L, IV potassium will be:

$$\begin{aligned} &(2\text{mmol} \times 7\text{kg}) + [(3.5 - 1.5\text{mmol}) \times 7\text{kg}] \\ &= 28 \text{ mmol in 24hrs} \end{aligned}$$

Dont give it as a pure infusion! Add the calculated potassium to the calculated daily maintenance fluid for the child e.g in 700mls of fluid for the 7kg child and give at normal maintenance rate.

- **Emergency: Arrhythmias – call paediatric consultants for help!!!**
 - Discuss the patient with seniors
 - Start 0.5 mmol/kg potassium chloride in 20mls normal saline over 30 min (Concentration should not exceed 80mmol/L)
- Monitor potassium regularly because supplemental potassium can cause hyperkalaemia
- Treat the underlying cause

Flow chart for management of hypokalaemia



HYPERNATRAEMIA

Definition

It is clinical disorder characterized by serum or plasma sodium greater than 150mmol/L.

Risk factors / causes

Inadequate water intake

- Premature infants
- Inadequate breast feeding
- Poor fluid intake during illness
- Drought

Gastrointestinal losses

- Excessive vomiting
- Profuse diarrhoea
- Loss from stomas

Urinary losses

- Central Diabetes Insipidus: inadequate production or release of ADH

Congenital Central DI

- Congenital central nervous system malformation
- Genetic syndromes associated with CNS abnormalities
- Congenital hydrocephalus

Acquired Central DI

- Brain tumours
- Acquired hydrocephalus
- Infiltrative processes of the hypothalamic-pituitary stalk
- Neurological sequelae from neurosurgery and trauma

- Nephrogenic Diabetes Insipidus: inadequate response to circulating ADH

Hereditary Nephrogenic DI

- Bardet-Biedl and Bartter syndromes
- Nephronophthisis
- Cystinosis, and
- Familial hypomagnesemia with hypercalciuria and nephrocalcinosis

Acquired Nephrogenic DI

- Drug toxicity is the most common cause of acquired DI: Amphotericin, demeclocycline, ifosfamide, foscarnet, and cidofovir, lithium toxicity etc.
- Chronic diseases: Obstructive uropathy, sickle cell disease, acute or chronic kidney disease
- Hypercalcemia and Hypokalaemia

Other causes of osmotic diuresis

- Renal excretion of nonelectrolyte, nonreabsorbed solutes, such as mannitol or glucose
- DKA and Hyperglycaemia

Excess skin losses

- Burns
- Excessive sweating
- Excessive heat
- Significant febrile illness
- Vigorous exercise
- Severe premature infants

Excessive salt intake/iatrogenic causes

- Diet
- IV fluids -Normal saline
- Sodium bicarbonate infusion during correction of metabolic acidosis
- Use of hypertonic saline
- Inappropriate preparation of home made ORS

Salt poisoning:

- Intentional increased salt intake in a child's diet as a form of child abuse

Signs and symptoms

1 Acute Hypernatraemia

- Irritability
- restlessness
- weakness
- muscular twitching
- In young infants high pitched cry
- Fever and tachypnoea
- Doughy skin
- Severe symptoms with serum sodium > 160mEq/L.
- Altered mental status, lethargy, coma, and seizures

2 Chronic Hypernatraemia

- Hypernatraemia present more than 1 day
- There are no symptoms due to cerebral adaptation which occurs within 1 to 3 days of presentation
- Most patients with chronic hypernatraemia have underlying neurologic conditions e.g. mid-brain abnormalities

In severe cases, e.g. salt poisoning, hypernatraemia causes demyelinating and irreversible neurological brain injury.

If clinical manifestation includes insensible losses, there will be clinical signs of severe dehydration “see Dehydration”.

Investigations/Diagnosis

- Elevated serum or plasma sodium level above 150 mEq/L
- Serum or plasma electrolytes
- Serum or plasma BUN and creatinine
- Urine electrolytes
 - Low urine sodium <25 mEq/L - Hypernatraemic hypovolaemia due to GIT losses
 - High urine sodium exceeding 200 mEq/L - suspect salt poisoning
- Fraction excretion of Sodium (FENa)

$$\text{FENa} = \frac{\text{Serum Cr } (\mu\text{mol/l}) \times \text{Urinary Na } (\text{mmol/L})^*}{\text{Serum Na } (\text{mmol/L}) \times \text{Urine Cr } (\mu\text{mol/l})^*} \times 100$$

*From morning void collection

FENa = > 2% - Suspect salt poisoning

FENa = < 1% - Suspect hypernatraemia caused by water loss

- Urine osmolality

| | |
|--|---|
| Urine osmolality > plasma osmolality | Normal ADH response suspect water losses from GIT or skin |
| Urine osmolality < plasma osmolality | Abnormal ADH response causing urine concentration defect manifested by polydipsia, polyuria and less concentrated urine |

Management

Primary level

- Assess the hydration status
- Refer
 - All cases with history of vomiting and diarrhoea not tolerating Plan A with oral rehydration solution (ORS) to secondary hospital facilities (see management of dehydration - plan A)
 - All cases with signs of severe dehydration
 - All cases with history of losses and clinical signs suggestive of hypernatraemia
- Refer the cases after inserting an IV line and commenced on intravenous maintenance fluid (see calculation of maintenance fluids in management of dehydration).
 - The prescribed fluids should be Ringers lactate or 0.9 percent (normal) saline
 - If IV access is not possible, insert NGT for ORS and give ORS according to Plan A or B depending on level of dehydration (see management of dehydration)

Secondary level

- Assess hydration status
- Start initial management of severe dehydration as per protocol (see management of dehydration)
- Initial investigations: MPs/MRDT, FBC, BUN and creatinine, serum or plasma electrolytes
 - Blood culture and Lumbar puncture if suspected sepsis or meningitis
- Start treating underlying cause and cover for sepsis or meningitis if suspected.
- Catheterize and monitor input and output
- Once a diagnosis of hypernatraemia is made, discuss and refer the patient to a tertiary level facility

Tertiary level

- Initial management as in secondary above.
- **N.B. Fluid resuscitation with isotonic fluid to restore intravascular volume and tissue perfusion takes precedence over correction of the hypernatremia!!**

Correction of Hypernatraemia

- When managing hypernatraemia in paediatrics these questions must be addressed:
 - 1 What is the volume status of the patient?
 - 2 Is there an emergent need for fluid resuscitation to restore intravascular volume and tissue perfusion?
 - 3 What is the magnitude of the water deficit that needs to be restored?
 - 4 At what rate should the hypernatremia be corrected (as lowering the sodium concentration too rapidly may lead to neurologic injury)?
 - 5 Is there a concurrent ongoing fluid loss that needs to be addressed?
 - 6 What is the underlying cause of hypernatremia and are there specific interventions that need to be considered?
- Calculating the free water deficit and rate of administration:
 - The volume of free water to be provided can be calculated using one of two common approaches:

METHOD 1:

Free water deficit (mL) =

Current total body water x ([current plasma Na/140] - 1)

- Estimating total body water (TBW) as 60% of the child's body weight (kg) (0.6 L/kg)
- Thus, in a 6 kg infant with a plasma sodium of 160, the free water deficit is:

$$(0.6 \text{ L/kg}) \times (6 \text{ kg}) \times ([160/140] - 1) = 0.5\text{L or } 510 \text{ mL.}$$

METHOD 2:

Free water deficit (mL) =

$$(4 \text{ mL/kg}) \times (\text{weight in kg}) \times (\text{desired change in plasma Na})$$

Thus, for this the 6 kg infant described above with plasma sodium elevated 20 mEq/L above desired (160 – 140), his or her water deficit would be:

$$(4 \text{ mL/kg}) \times (6 \text{ kg}) \times (20 \text{ mEq/L}) = \underline{480 \text{ mL}}$$

- Estimate that the provision of 4 mL/kg of free water will lower plasma sodium by approximately 1 mEq/L.

- **NOTE:** The variation in free water needed between the two calculations is generally clinically negligible. The calculated volumes are estimates and correction requires laboratory results and clinical exams to guide ongoing changes.

In children with chronic hypernatremia (plasma sodium ≥ 150 mEq/L for greater than 24 hours) or those with acute severe hypernatremia (plasma sodium > 160 mEq/L), it is recommended that a rate of correction does not exceed a fall of sodium greater than 0.5 mEq/L per hour (i.e., 10 to 12 mEq/L/day).

- **Prescribed fluids:**
 - The total fluids given should be the daily maintenance **plus** the free water deficit.
 - The deficit should be corrected over 24 - 48hrs to avoid complications.
 - Most administered fluid contains sodium, but IT is hypotonic to the patient's plasma, thereby providing free water.
 - Can use 0.45 percent saline which is hypotonic to the patient's plasma
 - Normal saline (0.9 percent saline) is isotonic in patients with normal plasma sodium, BUT, it is a hypotonic fluid for children with hypernatremia, therefore it can be used as initial rehydration fluid for patients with Hypernatraemic hypovolaemia.
 - Enteral fluids including oral rehydration solution (ORS) are also typically hypotonic fluids.
- **Ongoing losses and maintenance needs**
 - The above calculations correct free water losses that have occurred up to the time of presentation.
 - Children have ongoing normal maintenance needs and may also have excess free water losses not accounted for by calculations for maintenance fluids (e.g. continuing diarrhea or persistent fever),

therefore, should receive replacement of these ongoing losses to prevent further electrolyte derangement.

- Calculate the water deficit
- Calculate maintenance fluids accounting for insensible losses

● Monitoring

- Monitor clinical progress regularly every 30 minutes for the first 2 hours then 4 hourly regularly for improvement or deterioration (check mental status, seizures or coma, dehydration status, neurological status, fluid intake and urine output)
- Monitor serum/plasma electrolytes every 6 hours if blood gas analyser is available; BUN and creatinine every 24 hours. If not available monitor every 24 hours
- Consult paediatric nephrologist in all cases with no improvement or with clinical deterioration including development of AKI after 24 hours

Clinical example:

A 10 kg child (TBW 0.6 x body weight) is estimated to have a 10 percent hypovolemic loss (approximately 1 L of fluid) and a serum/plasma sodium concentration of 156 mEq/L. The following calculations can be made:

Total fluid deficit: 10 percent of 10 kg = 1 L (1000 mL)

Free water deficit: 6 L $[(156/140 \text{ mEq/L}) - 1] = 0.686 \text{ L (}686 \text{ mL)}$

Isotonic loss: Total fluid deficit - Water deficit = 1000 mL - 686 mL = 314 mL

During resuscitation:

Received 20ml/kg bolus = 20ml x 10 kg = 200mls

Remaining isotonic fluid loss = 314 mL - 200 mL = 114 mL

Replace the remaining fluid deficit over 36 hours so that the sodium is lowered at a rate below 0.5mEq/L per hour:

Free water deficit replacement is 686 mL in 24 hours = $(686 \text{ mL}/3) \times 2 = \text{about } 460 \text{ mL}$

Maintenance fluid is 100 mL x 10kg = 1000 mL/day

Remaining isotonic fluid loss = 314 mL - 200 mL = 114 mL (excess on going losses of fluid and electrolyte)

Therefore, the rate of fluid replacement using 0.45 percent saline = 65 mL / hour

Follow up

- Follow up all uncomplicated cases in general clinic in a month
- Follow up all complicated cases in renal clinic if they had AKI
- Follow all complicated cases with neurological sequelae in neurology clinic

HYPONATREMIA

Definition

Hyponatraemia is defined as serum or plasma sodium is < 135 mEq/L.

- Mild hyponatraemia – Serum concentration between 130 and 134 mEq/L
- Moderate hyponatraemia – Serum concentration between 120 to 129 mEq/L
- Severe hyponatraemia – Serum concentration <120 mEq/L

- Hyponatraemia is further classified as:

- Acute hyponatraemia developing over a period of less than 48 hours – risk of cerebral oedema
- Chronic hyponatraemia is defined as hyponatraemia that has been present for more than 48 hours

Causes / Risk Factors

A Hypotonic hyponatraemia

Hyponatraemia due to loss of sodium as well as free water or excess free water retention

Hypovolaemia and persistent antidiuretic hormone (ADH) levels:

- Hyponatraemia due to loss of sodium in excess of water
- Urinary salt wasting in obstructive uropathy
- Skin losses in cystic fibrosis

Normovolaemia and inappropriate ADH levels:

- Excess water intake (suppresses ADH release, allowing free water excretion and the generation of a dilute urine)
- Pulmonary and oncologic disorders
- Recent surgery
- Central nervous system (CNS) injury or infection
- Endocrine disorders
- Medications e.g. some anticonvulsants and chemotherapeutic drugs

Normovolaemia

- Primary polydipsia
- Reset osmostat (a condition with a lower-than-normal plasma osmolality threshold for ADH release)

Hypervolaemia

- Excess water retention, promoted by a decrease in kidney perfusion and urine output leading to a drop in serum sodium leading to decreased effective circulating volume (ECV).
 - Nephrotic syndrome
 - Liver cirrhosis
 - Heart failure
- Kidney failure with a decrease in GFR results in water retention, leading to a drop in serum sodium.

B Hyponatraemia without Hypotonicity

Increased tonicity

- Endogenous sources e.g. Hyperglycaemia and increased urea (Azotaemia)
- Exogenous sources e.g. mannitol and sorbitol

C Pseudohyponatraemia

- Common in patients with hyperlipidaemia or hyperproteinaemia.
 - Total parenteral nutrition (TPN)
 - Hyperproteinaemia is uncommon in children
- check with the clinical laboratory staff, what method is used to measure sodium levels before interpreting the results of patients with confirmed hyperlipidaemia or hyperproteinaemia

Promotion / Prevention

- Avoid administration of unrestricted hypotonic fluids to at risk paediatric population intravenously or by mouth. They are at risk of developing syndrome of inappropriate anti-diuretic hormone secretion (SIADH).
- At risk population include postoperative cases, central nervous system injury or illness (e.g. meningitis or encephalitis etc.) and respiratory disorders (e.g., pneumonia or bronchiolitis).
- Prescribe fluids accurately and correct any electrolyte imbalance to avoid giving excessive free water

Signs and symptoms

- History and physical examination with focus on the following:
 - Fluid loss e.g. vomiting and diarrhea, excess water intake, excess salt loss, medications, administration of TPN
 - Medical conditions associated with unsuppressed ADH release e.g. CNS injury or infection, pulmonary diseases, immobilization etc.
 - Anuria or oliguria, oedema and ascites with reduced ECV e.g. Nephrotic syndrome, liver failure and heart failure
- **Acute hyponatraemia:**
 - Patients are more likely to be symptomatic and symptoms dependent on the severity of hyponatraemia
 - Sodium >125 mEq/L: minimal specific symptoms related to hyponatraemia
 - Sodium below 125 mEq/L: some neurologic symptoms observed e.g. nausea and malaise
 - Sodium below 120 mEq/L: may present with headache, lethargy, obtundation, and seizures.
 - In severe cases, brain herniation and death may occur.
- **Chronic hyponatraemia:**
 - Usually asymptomatic
 - May present with subtle neurologic manifestations such as restlessness, weakness, fatigue, or irritability
 - If some acute event causes rapid decreases in sodium level in chronic hyponatraemia the patients may present as in severe acute hyponatraemia (Acute-on-chronic presentation)

Investigations

Laboratory investigations should include:

- RBS, serum BUN, creatinine and electrolytes
 - Hyponatraemia and hyperkalaemia may be a sign of adrenal insufficiency
- Urine dipstick
- Other tests:
 - Lipemic plasma and serum tests to exclude pseudohyponatraemia
 - Serum osmolality and tonicity – hyponatraemic children are hypotonic with serum osmolality lower than the normal <275 Posm/kg
 - Urine Osmolality
 - **Hyponatraemia and Hypotonicity**, urine osmolality >100 mosmol/kg is indicative of impaired water excretion - SIADH and Renal impairment
 - **Hyponatraemia and increased total body water (oedema)**, urine osmolality >100 mosmol/kg is indicative of reduced ECV, leading to ADH release - Nephrotic syndrome, heart failure, and liver cirrhosis
 - **Hyponatraemia and dilute urine**, urine osmolality <100 mosmol/kg, the differential diagnosis includes:
 - Psychogenic polydipsia
 - Reset osmostat
 - Salt-losing nephropathy

Plasma and Urine osmolality and Plasma tonicity measurement

Plasma osmolality (Posm)

It is the **ratio** of plasma solutes and plasma water. The normal Posm is 275 to 290 mosmol/kg.
Estimated Posmo calculation:

If glucose and urea reported in mg/dL:

$$\text{Posm} = 2 \times [\text{Na}] + [\text{Glucose}]/18 + \text{Blood urea nitrogen}/2.8$$

If Glucose and urea reports in mmol/L:

$$\text{Posm} = 2 \times [\text{Na}] + [\text{Glucose}] + [\text{Urea}]$$

Urine osmolality (Uosm)

Uosm can be calculated from the urine concentrations of sodium (Na), potassium (K), and urea when there is no marked glucosuria and metabolic acidosis:

If urea reported in mg/dL:

$$\text{Uosm} = 2 (\text{Urine Na} + \text{Urine K}) + \text{Urine [Urea} \div 2.8]$$

If urea is reported in mmol/L the formula is:

$$\text{Uosm} = 2 (\text{Urine Na} + \text{Urine K}) + \text{Urine [Urea]}$$

Plasma Tonicity

It is the **effective** plasma osmolality.

If glucose is measured in mg/dL:

$$\text{Plasma tonicity} = 2 \times [\text{Na}] + [\text{Glucose}]/18$$

If glucose is measured in mmol/L:

$$\text{Plasma tonicity} = 2 \times [\text{Na}] + [\text{Glucose}]$$

Management

- Relieve the symptoms of hyponatraemia
- Avoid too rapid correction to prevent central nervous system (CNS) complications
- Prevent a further decline in sodium concentration
- Determining and treating the underlying cause
- Treatment approach depends on:
 - Duration of hyponatraemia – Acute versus chronic hyponatraemia
 - Severity of hyponatraemia based on the presence and severity of symptoms
- Frequent monitoring to reassess and adjust therapy based on clinical examinations and follow-up laboratory evaluation, including subsequent assessment of sodium levels.

Primary Level

- Assess the hydration status
- Refer to secondary hospital facilities:
 - All cases with history of vomiting and diarrhoea not tolerating Plan A with ORS (see management of dehydration - plan A)
 - All cases with signs of severe dehydration
 - All cases with clinical signs suggestive of hyponatraemia
- Refer the patient after inserting an IV line and after commencing intravenous maintenance fluid: Normal saline (0.9%)
- If I.V access not possible, insert NGT and commence Plan B with ORS and refer as soon as possible.
- Replace on going losses with ORS as in plan A using NGT if the child is not able to drink

Secondary Level

- Assess hydration status
- Start initial management of severe dehydration (see management of dehydration)
- Initial investigations: MPS, FBC, BUN and creatinine, serum or plasma electrolytes
 - Blood culture and Lumbar puncture if suspect sepsis or meningitis
- Start treating underlying cause and cover for sepsis or meningitis if suspected
Catheterize and monitor input and output

Sodium Correction

Asymptomatic hyponatraemia:

- Treat underlying cause
- If hyponatraemia is not being corrected, then concurrently give Normal Saline and correct any associated electrolyte imbalance

Mild to Moderate symptomatic hyponatraemia:

- If no hypovolemia: Fluid restriction
- If hypovolemia present: correct hydration with Normal saline IV
- Aim to not exceed increase in serum Sodium concentration by 0.5 mmol/L/hour
- Monitor clinical progress regularly every 30 minutes for the first 2 hours then 4hourly regularly for improvement or deterioration (check mental status, seizures or coma, dehydration status, neurological status, fluid intake and urine output)

- Monitor serum/plasma electrolytes; BUN and creatinine regularly at least every 24 hours if blood gas analyser is not available
- Refer all cases with no improvement or with clinical deterioration including development of AKI after 24 hours
- Refer all cases with severe hyponatraemia

Tertiary Level

- Manage mild and moderate hypernatraemia as in secondary level above.

Acute hyponatraemia

- There is inadequate cerebral adaptation. Saline therapy is given to all symptomatic patients to prevent development of complications of hyponatraemia

Severe hyponatraemia (seizures, obtundation, and coma):

- Give hypertonic saline (3% saline) at rate of 1-2ml/kg/hour. Aim to raise sodium by 8-9mmol/L over the initial 24 hours.
- If hypertonic saline not available give homemade NaCl via NGT
 - 1 teaspoon of salt = 17mmol
 - Mix 1 teaspoon of salt in 15mL of water and give 5mL= 5.7mmol
 - This dose should be given once daily.
 - Aim to increase serum sodium by 3mmol/L.
- Check serum Sodium 6 hourly after administration of oral dose. If there is no increase in sodium or further reduction in sodium, repeat the oral dose.

Sodium correction in chronic hyponatraemia

- Cerebral adaptation has occurred therefore if plasma sodium is corrected too quickly, the patient is at risk of osmotic demyelination
- Identify and treat the underlying cause
- ***In cases where the patient has chronic hyponatraemia with acute exacerbation leading to symptomatic presentation then initiate therapy as for acute hyponatremia to increase serum sodium levels.***

Sodium correction in unknown classification

- Duration of hyponatraemia is unknown.
- Treat patients as in chronic hyponatraemia
- If symptomatic then correct hyponatraemia by giving Normal saline (0.9%) to increase the concentration of sodium
- Monitor clinical progress regularly every 30 minutes for the first 2 hours then 4 hourly regularly for improvement or deterioration (check mental status, seizures or coma, dehydration status, neurological status, fluid intake and urine output)
- Monitor serum/plasma electrolytes every 6 hours if available, BUN and creatinine every 24 hours.
- Consult paediatric nephrologist/endocrinologist (as appropriate) if no improvement or with clinical deterioration including development of AKI after 24 hrs

Follow up

- Follow up all uncomplicated cases in general clinic in a month
- Follow up all complicated cases with AKI in renal clinic
- Follow all complicated cases with neurological sequelae in neurology clinic

CALCIUM

The normal ranges of ionized serum or whole blood varies with age.

Normal ranges of calcium according to age

Neonates 1 month of age: 5.2 to 6.1 mg/dL (1.29 to 1.52 mmol/L)

Infants 3 months of age: 5.2 to 6.0 mg/dL (1.30 to 1.49 mmol/L)

Infants 12 months of age: 5.0 to 5.6 mg/dL (1.24 to 1.39 mmol/L)

After 12 months of age:

Ionized calcium – 4.65 to 5.25 mg/dL (1.2 - 1.3 mmol/L)

Total calcium – 8.5 to 10.5 mg/dL (2.12 - 2.62 mmol/L)

Distribution of total serum calcium

- 15 percent of serum calcium is bound to multiple organic and inorganic anions such as sulphate, phosphate, lactate, and citrate
- 40 to 45 percent of serum calcium is bound to proteins, primarily albumin
- The remaining 40 to 45 percent serum calcium circulates as physiologically active ionized (or free) calcium

HYPERCALCAEMIA

Definition

Hypercalcaemia is a clinical condition in which serum or plasma calcium concentration >11 mg/dL (2.75 mmol/L)

- **Mild hypercalcemia** – Serum or plasma calcium above the upper limit of normal but <12 mg/dL [3 mmol/L]
- **Moderate hypercalcemia** – serum or plasma calcium concentration between 12 to 14 mg/dL (3 to 3.5 mmol/L)
- **Severe hypercalcemia** – serum or plasma calcium concentration >14 mg/dL [3.5 mmol/L]
- Serum or plasma calcium concentrations >15 mg/dL (3.75 mmol/L) are life threatening

Risk Factors / Causes

1 Parathyroid mediated

- Primary hyperparathyroidism
- Secondary hyperparathyroidism e.g severe CKD
- Familial hypocalciuric hypercalcaemia (Autosomal dominant disorder)
- Metaphyseal chondrodysplasia: A rare form of dwarfism -Jansen-type metaphyseal chondrodysplasia

2 Non-parathyroid mediated

- Malignancy e.g most solid tumors and leukemia
- Hypervitaminosis D
- Immobilization: occurs due to a non-parathyroid-mediated increase in bone resorption
- Medications e.g. Lithium, Thiazide diuretics, PTH or PTHrP analogs
- Increased calcium intake
 - Chronic kidney disease treatment
 - Milk alkali syndrome: Excess calcium carbonate supplementation to treat osteoporosis or dyspepsia
- Hypervitaminosis A: Retinoic acid causes a dose-dependent increase in bone resorption
- Theophylline toxicity

3 Endocrine disorders

- Thyrotoxicosis - thyroid hormone-mediated increase in bone resorption
- Pheochromocytoma - Tumour production of PTH-related protein (PTHrP)
- Adrenal insufficiency – there is increased bone resorption, increased proximal tubular calcium reabsorption and increased binding of calcium to serum proteins

4 Miscellaneous causes

- Rhabdomyolysis associated with acute renal failure - mobilization of calcium that had been deposited in the injured muscle
- Congenital lactase deficiency - increase in calcium absorption in the ileum in the presence of non-hydrolyzed lactose.

Promotion / Prevention

- Early detection and treatment
- Appropriate dosing of calcium, vitamin D and vitamin A

Signs and symptoms

- Asymptomatic
- GIT symptoms e.g. anorexia, nausea, vomiting, and constipation, pancreatitis and Peptic ulcer disease (PUD)
- Cardiovascular system symptoms e.g. hypertension, bradycardia, short QT interval
- Renal system symptoms e.g. polydipsia, polyuria, nephrocalcinosis, renal insufficiency, renal tubular acidosis
- Dermatological symptoms e.g., pruritus
- Neurologic symptoms e.g. headache, irritability, weakness, and lethargy, seizures, confusion, stupor, coma and death
- Neuropsychiatry symptoms e.g. behavioral changes, delirium, anxiety, depression

Investigations

- Exclude malaria with MPS and MRDT
- Blood culture
- Lumbar puncture for CSF analysis
- BUN and creatinine, Serum electrolytes including calcium, magnesium and phosphate (CMP)
- Parathyroid hormone
- Vitamin D

- Serum albumin, total protein and liver function tests
- Urine dipstick, Urine MCS
- Plain abdominal x-ray
- Cardiac echocardiography and electrocardiography (ECG)
- Abdominal USS and KUB
- Abdominal CT scan or MRI
- Brain CT scan or MRI

Differential diagnosis

- Acute gastroenteritis
- Sepsis, Meningitis, Encephalitis
- Hyperparathyroidism
- Chronic kidney disease
- Hypervitaminosis D and A
- Pancreatitis
- Addison Crisis
- Malignancies
- Neonatal subcutaneous fat necrosis

Management

- Treat the presenting symptoms
- Treat the underlying cause
- Mild and moderate hypercalcium do not need immediate treatment but should avoid aggravating factors e.g
 - Thiazide diuretics,
 - Lithium,
 - Volume depletion,
 - Prolonged bedrest/inactivity,
 - High calcium diet >1000mg/day,
 - Calcium supplements,
 - Vitamin D supplements > 800u/day
 - Ensure adequate hydration

Primary Level

- Thorough clinical assessment
- Treat emergency presenting symptoms
- Refer all complicated cases to secondary level

Secondary Level

- Thorough clinical assessment
- Initial lab work up to exclude Malaria, sepsis or meningitis, BUN and creatinine, serum electrolytes and CMP, liver function test, total protein and albumin level
- Urine work up
- Initial imaging:
 - CXR, plain abdominal x-ray, abdominal USS and KUB
- Start treatment for possible sepsis or meningitis if suspected
- Start treating for hypercalcaemia with furosemide
 - Start furosemide 1-2mg/kg/dose (maximum 6mg/kg/day in divided doses twice or three times a day) to increase calcium excretion.
- Reassess and monitor regularly the clinical and laboratory improvement of hypercalcaemia
- Refer to tertiary level if no signs of improvement.

Tertiary Level

- Thorough clinical assessment
- Initial lab work up to exclude Malaria, sepsis or meningitis, BUN and creatinine, serum electrolytes and CMP, liver function test, total protein and albumin level
- Urine work up
- Initial imaging:
 - CXR, plain abdominal x-ray, abdominal USS and KUB, cardiac echo, ECG
- Start treatment for possible sepsis or meningitis if suspected.
- Start treating for hypercalcaemia with furosemide
 - Start furosemide 1-2mg/kg/dose (maximum 6mg/kg/day in divided doses twice or three times a day) to increase calcium excretion.
 - Reassess and monitor regularly the clinical and laboratory improvement of hypercalcaemia
- **Consult paediatric nephrologist or endocrinologist as needed for severe hypercalcaemia.**

HYPOCALCAEMIA

Definition

Hypocalcaemia is a clinical condition characterized by physiologic reduction of calcium concentration in the body.

- Serum ionized free calcium < 4.4mg/dL (1.1 mmol/L)
- Total serum calcium < 8mg/dL (2 mmol/L)

Causes / Risk factors

1 Decreased Calcium intake or Vitamin D intake

2 Neonatal Hypocalcaemia: Early/late transient neonatal hypocalcaemia and persistent neonatal hypocalcaemia

3 Decreased PTH

Genetic:

- DiGeorge syndrome
- HDR syndrome (hypoparathyroidism, deafness, renal anomaly),
- Mutations interfering with parathyroid gland development (X-linked)
- Mitochondrial disorders e.g., MELAS syndrome, Kearns-Sayre syndrome)

Autoimmune:

- APS1, Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) syndrome

Other:

- Parathyroid or thyroid gland surgery or Infiltration of parathyroid gland (e.g., iron overload, copper deposition in patients with Wilson disease etc.)

4 Decreased Vitamin D

- Defects in vitamin D metabolism
- Hepatic dysfunction
- Renal dysfunction
- Genetic disorders e.g 25-hydroxylase deficiency, 1-alpha-hydroxylase deficiency (previously known as vitamin D-dependent rickets type 1 or pseudovitamin D-deficient rickets)
- Defects in vitamin D action: Hereditary resistance to vitamin D (previously known as vitamin D-dependent rickets type 2)

5 Decreased Calcitonin hormone

6 Drugs

- Bisphosphonates, denosumab, calcimimetics (cinacalcet), foscarnet, and some chemotherapeutic drugs

7 Miscellaneous:

- Hungry bone syndrome, osteopetrosis, sepsis or acute severe illness, Gram-negative sepsis, toxic shock syndrome, HIV infection, hyperphosphatemia, alkalosis, intravenous products with citrate or lactate (e.g. transfusion with any blood products), pancreatitis, fluoride poisoning and hypomagnesemia etc.

Promotion / Prevention

- Early detection and treatment
- Appropriate drug prescription and drug dosing
- Health education
- Advocate for a balanced diet with food rich in calcium and vitamin D
- Advocate for food fortification with calcium and vitamin D
- Advocate for breast milk fortification with vitamin D

Signs and symptoms

- Hypocalcaemia presentation is divided into acute and chronic hypocalcaemia.
- ***Acute manifestations of hypocalcaemia***
 - Tetany - increased peripheral neuromuscular irritability, electromyographically (EMG), shows repetitive, high-frequency discharges after a single stimulus
 - Trousseau's sign - induction of carpal spasm by inflation of a sphygmomanometer above systolic blood pressure for three minutes. Carpal spasm, is characterized by adduction of the thumb, flexion of the metacarpophalangeal joints, extension of the interphalangeal joints, and flexion of the wrist
 - Chvostek's sign - contraction of the ipsilateral facial muscles elicited by tapping the facial nerve just anterior to the ear
 - Cardiovascular – Hypotension, ECG with prolongation of the QT interval and Congestive cardiac failure (CCF)
 - Papilledema – in severe hypocalcaemia
 - Seizures
- ***Chronic manifestations of hypocalcaemia:***
 - Extrapyramidal signs, Parkinsonism, dementia and subcapsular cataracts, abnormal dentition and dry skin.
- ***Disease specific presentation:*** features of the underlying disease e.g
 - Hypoparathyroidism (see hypothyroidism)
 - Pseudohypoparathyroidism (see Pseudohypoparathyroidism)
 - Vitamin D deficiency
 - Autosomal dominant hypocalcaemia

Investigations

- Exclude hypoglycaemia: RBS
- Exclude infections: FBC, MPS, Blood culture, Lumbar puncture
- Liver function test: Liver enzymes (AST, ALT, GGT)
- Total protein and albumin
- Renal function test: BUN + creatinine
- Blood gas: calcium, acid base balance
- Serum electrolytes + Calcium, Magnesium, Phosphate
- Serum PTH, serum vitamin D levels
- ECG, EMG (if available)
- Imaging:
 - Cranial USS
 - Cardiac Echo
 - abdominal USS + KUB
 - CT-brain or MRI

Calculation of corrected calcium

Calcium is mainly bound to albumin in the blood. In cases of hypoalbuminaemia, measurement of total calcium may not reflect the true levels of ionized or free calcium in the blood. Therefore, free or ionized calcium is the recommended measurement for clinical decisions (gold standard). The calcium correction formula is used when there is hypocalcaemia in the setting of hypoalbuminaemia. The formula assumes that for every 1g/dl (10g/L) fall of albumin is equal to 0.8mg/dl fall in serum calcium.

E.g. Serum total calcium concentration = 8 mg/dL (2 mmol/L)

Serum albumin concentration = 2 g/dL (20 g/L) below normal,

The corrected calcium = 8mg/dL + (2x 0.8 mg/dL) = 9.6 mg/dL (2.4 mmol/L) which is normal

Differential diagnosis

- Sepsis or meningitis
- Renal failure or CKD
- Liver failure
- Congestive cardiac failure
- Hypoparathyroidism
- Pseudohypoparathyroidism
- Vitamin D deficiency

Management

Primary Level

- Assess the patient for signs of hypocalcaemia
- Treat the emergency presenting symptoms
- Refer all patients suspected of hypocalcaemia

Secondary Level

- Assess the patient for signs of hypocalcaemia
- Treat the emergency presenting signs
- Start the initial investigations
- Start treating for acute hypocalcaemia aim to stabilize the patient:

Mild symptomatic acute or chronic hypocalcaemia:

- Give 1 to 2 g of elemental calcium using calcium carbonate or calcium citrate daily in divided doses
- Refer to tertiary level for further management and investigations

Tertiary Level

- Assess the patient for signs of hypocalcaemia
- Treat the emergency presenting signs
- Start the initial investigations
- Start treating for acute hypocalcaemia aim to stabilize the patient

Mild symptomatic acute or chronic hypocalcaemia management:

- Give 1 to 2 g of elemental calcium using calcium carbonate or calcium citrate daily in divided doses

Severe symptomatic and / or acute hypocalcaemia management:

- Intravenous calcium dosing:
 - 1-2ml/kg intravenous 10% calcium gluconate over 10 minutes (dilute 1: 1 with normal saline). Repeat dose if necessary.
- Monitor for bradycardia on a monitor.
- Give maintenance dose of 5ml/kg/day in maintenance intravenous fluids or divided into 4-6 doses orally with feeds.
 - If given orally dilute at least 50% by feeds or water.

Check for hypomagnesaemia:

- Hypomagnesaemia is a common cause of hypocalcaemia by inducing PTH resistance and secretion
- Correct hypomagnesaemia first before correcting hypocalcaemia. If magnesium levels are not possible, give one dose of the magnesium sulphate.
 - If magnesium is low, give 2 g (16 mEq) of magnesium sulfate bolus by adding to 10% dextrose solution and infuse over 10 to 20 minutes, then give 1 gram (8 mEq) in 100 mL 10% dextrose per hour.
 - Continue magnesium slow infusion as long as the serum magnesium concentration is less than 0.8 mEq/L (1 mg/dL or 0.4 mmol/L).
- Persistent hypomagnesemia as seen in patients with ongoing GIT losses (e.g., malabsorption) or renal losses requires oral magnesium supplementation of 300 to 400 mg daily divided into three doses.

Hypocalcaemia due to hypoparathyroidism:

- Patients with hypoparathyroidism require lifelong calcium and vitamin D supplementation (see management of hypoparathyroidism)

Hypocalcaemia due to vitamin D deficiency:

- Hypocalcaemia due to vitamin D deficiency is treated with ergocalciferol (vitamin D2) or cholecalciferol (vitamin D3).
- Give oral vitamin D2 and D3 50,000 IU weekly for 6 to 8 weeks if available.

Hypocalcaemia due to Chronic kidney disease:

- Few patients with chronic kidney disease have symptomatic hypocalcaemia
- Treat with oral calcium to bind intestinal phosphate and to prevent bone disease

Chronic liver disease:

- Give vitamin D metabolites to treat hypocalcaemia especially when there is abnormal vitamin D metabolism (renal or liver disease)
- Hemodialysis is often indicated in patients with symptomatic hypocalcaemia
- Involve the dietitian in the management of the case
- Consult the Paediatric Endocrinologist, Gastroenterologist, Nephrologist and Infectious disease specialist if available

Follow up

- Follow up in Paediatric General Clinic
- Follow up in Renal clinic if the patient has renal disease
- Follow up in Gastroenterology clinic if has a malabsorption complication if available

MAGNESIUM

Normal serum or plasma magnesium concentration ranges from 1.7 to 2.1 mg/dL (0.70 to 0.85mmol/L).

HYPOMAGNESEAEMIA

Definition

- Hypomagnesaemia is serum or plasma concentration below 1.7mg/dL (0.7mmol/L)

Causes / Risk factors

Gastrointestinal losses:

- Diarrhea, malabsorption and steatorrhoea, and small bowel bypass surgery
- Acute pancreatitis
- Medications – PPIs
- Genetic disorders - Intestinal hypomagnesemia with secondary hypocalcaemia

Renal losses:

- Medications
 - Diuretics e.g. loop and thiazide
 - Antibiotics e.g. Aminoglycoside, amphotericin, pentamidine etc.
 - Cancer drugs e.g. Calcineurin inhibitors, cisplatin etc.
 - Antibodies targeting epidermal growth factor (EGF) receptor e.g. cetuximab, panitumumab, matuzumab etc.
- Volume expansion
- Uncontrolled diabetes mellitus
- Hypercalcaemia
- Acquired tubular dysfunction
 - Recovery from acute tubular necrosis
 - Post obstructive diuresis
 - Post-kidney transplantation
- Genetic disorders
 - Bartter/Gitelman syndrome
 - Familial hypomagnesemia with hypercalciuria and nephrocalcinosis
 - Renal malformations and early-onset diabetes mellitus

Health promotion

- Health education
- Early screening and treatment

Signs and symptoms

- **Neuromuscular manifestations** - Neuromuscular hyperexcitability (e.g. tremors, tetany and convulsions), weakness, apathy, delirium, and coma.
- **Cardiovascular manifestations** - ECG changes - widening of the QRS and peaking of T waves with moderate magnesium depletion and widening of the PR interval, diminution of T waves, and atrial and ventricular arrhythmias with severe depletion.
- Signs and symptoms of associated hypocalcaemia, hypoparathyroidism, parathyroid hormone (PTH) resistance, and decreased synthesis of calcitriol.
- Signs and symptoms of hypokalaemia

Differential diagnosis

- Sepsis
- Acute gastroenteritis
- Malabsorption disorders
- Electrolyte imbalance especially hypokalaemia and hypocalcaemia
- Hypercalcaemia
- Acute pancreatitis
- Diabetes mellitus
- Acquired tubular dysfunction
- Genetic disorders associated with hypomagnesaemia
- Fluid overload and drug induced hypomagnesaemia

Investigations

- Exclude diabetes mellitus: RBS
- Exclude infection: FBC, MPS, blood culture, urine culture, lumbar puncture
- Renal function tests: BUN and creatinine
- Electrolytes + CMP + ECG
- Measure 24-hour urinary magnesium excretion or
- Measure Fractional excretion of magnesium (FEMg) on a random urine specimen
 - A 24-hour urine collection with Mg excretion of 10 to 30 mg or a FEMg above 3 to 4 percent in a person with hypomagnesaemia and normal kidney function indicates renal magnesium wasting.

Calculation of FEMg

$$\text{FEMg} = \frac{\text{UMg} \times \text{PCr}}{(0.7 \times \text{PMg}) \times \text{UCr}} \times 100\%$$

U = Urinary, P = Plasma, Mg = Magnesium, Cr = Creatinine

Management

Primary Level

- Assess the patient and refer

Secondary Level

- Thorough history and examination
- Exclude hypoglycaemia: RBS
- Exclude infection: FBC, blood culture, urine culture, lumbar puncture
- Renal function tests: BUN and creatinine
- Electrolytes + CMP + ECG
- Start treating symptomatic hypomagnesaemia
 - Give 1 to 2 grams of magnesium sulfate [8 to 16 mEq (4 to 8 mmol)] in 50 to 100 mL of 5% dextrose over 30 to 60 minutes.
 - Repeat bolus if still symptomatic.
- Refer to tertiary level after initial stabilization

Tertiary Level

- Thorough history and examination
- Exclude hypoglycaemia: RBS
- Exclude infection: FBC, blood culture, urine culture, lumbar puncture

- Renal function tests: BUN and creatinine
- Electrolytes + CMP + ECG
- Start treating for hypomagnesaemia
 - Give 1 to 2 grams of magnesium sulfate [8 to 16 mEq (4 to 8 mmol)] in 50 to 100 mL of 5% dextrose over 30 to 60 minutes.
 - Repeat bolus if still symptomatic.
 - If still hypomagnesaemic give magnesium infusion of 4 to 8 g of magnesium sulfate [32 to 64 mEq (16 to 32 mmol)] slowly over 12 to 24 hours.
 - Aim to maintain serum or plasma magnesium concentration above 1 mg/dL (0.4 mmol/L or 0.8 mEq/L)
- Look for other possible associated disorders
- Involve Paediatric nephrologists, gastroenterologist and endocrinologist

Follow up

- In general clinic after 2 weeks
- In renal clinic if presence of renal disease
- Endocrinology clinic if the patient has associated endocrine disorder (if available)

HYPERMAGNESEAEMIA

Definition

Hypermagnesaemia is serum or plasma concentration above 2.1 mg/dL (0.85mmol/L).

Causes / risk factors

- Neonatal hypermagnesaemia that results from maternal administration of magnesium sulphate due to eclampsia.
- Iatrogenic hypermagnesaemia caused after administration of magnesium sulphate during management of life threatening asthma

Promotion / Prevention

- Early screening and treatment
- Appropriate dosing of Magnesium containing medications.

Signs and symptoms

- Reduced level of activity
- General hypotonia
- Respiratory depression with apneas in severe cases

Investigations

- RBS
- FBC, Blood culture and urinalysis
- Cranial USS, cardiac echo, renal and KUB USS
- Electrolytes and CMP

Differential diagnosis

- Commonly seen in neonates
- Neuromuscular junction disorders: Transient acquired neonatal myasthenia, congenital myasthenia, aminoglycoside toxicity and infantile botulism
- Anterior horn cell disorders: Acute infantile spinal muscular atrophy, traumatic myelopathy, hypoxic-ischemic myelopathy, arthrogryposis multiplex congenita
- Congenital motor or sensory neuropathies: Charcot-Marie-Tooth disease, congenital hypomyelinating neuropathy
- Congenital myopathies:
- Muscular dystrophies: e.g Duchenne and Becker muscular dystrophy
- Inborn errors of Metabolic disorders

Management

Primary Level

- Manage ABCDE and refer

Tertiary Level

- Thorough history and examination
- History of magnesium sulphate administration in a child or maternal use for eclampsia
- Supportive treatment and close monitoring ABCDE approach

Follow up

- Follow up in general clinic or nursery for neonates after 2 weeks

PHOSPHATE

Normal ranges of phosphate in the body varies with age

0 to 3 months of age: 4.8 to 7.4 mg/dL (1.55 to 2.39mmol/L)

1 to 5 years of age: 4.5 to 6.5 mg/dL (1.45 to 2.1mmol/L)

6 to 12 years of age: 3.6 to 5.8 mg/dL (1.16 to 1.87mmol/L)

13 to 20 years of age: 2.3 to 4.5 mg/dL (0.74 to 1.45mmol/L)

HYPERPHOSPHATAEMIA

Definition

It is a clinical condition characterized by increased serum phosphate levels above normal levels. See ranges above.

Causes/risk factors

- Excess intake of phosphate:
 - Infants fed cows milk or formula with high phosphate levels
 - Use of phosphate enemas
- CKD with phosphate retention
- Tumour lysis syndrome
- Hypophosphatemia associated with hypocalcaemia

Health promotion

- Early screening and treatment
- Adequate prehydration of children with malignancies at risk of tumor lysis syndrome
- Promote breastfeeding
- Avoid use of cow's milk products in early infant feeding.

Signs and symptoms

- Hypomagnesaemia leads to secondary hypocalcaemia result into tetany and or seizures. See signs and symptoms of hypocalcaemia
- AKI due to Calcium phosphate deposition in the renal tubules. See signs and symptoms of AKI.
- Cardiac arrhythmia; due to calcium deposits in the cardiac conducting system
- In children with CKD, hyperphosphatemia and hypocalcaemia occur when the GFR falls below 30 mL/min per 1.73 m² (stage G4 disease and beyond), (See signs and symptoms of CKD).

Investigations

- Exclude hypoglycaemia: RBS
- Exclude infections: FBC, MPs, blood culture, urine culture and lumber puncture
- Serum electrolytes + CMP
- ECG + Cardiac echo

Differential diagnosis

- Hypoglycaemia
- Sepsis/ meningitis
- Hypocalcaemia
- CKD
- Tumour lysis syndrome

Management

Primary Level

- Assess the patient and refer

Secondary Level

- Assess the patient
- Start initial investigations
- Supportive treatment and refer when stable

Tertiary Level

- Assess the patient
- Start initial investigations
- Start treatment of hyperphosphataemia
 - Low phosphate diet, consult dietitian
 - Calcium containing phosphate binders can be used if there is associated hypocalcaemia (calcium carbonate, calcium acetate, calcium gluconate)
 - If hyperphosphataemia is not associated with hypocalcaemia use Sevelamer carbonate

Do not use the following phosphate binders in patients with CKD:

Aluminium hydroxide can cause aluminium bone toxicity

Magnesium-containing antacids e.g. magnesium hydroxide can cause hypermagnesaemia and diarrhoea.

Calcium citrate can increase absorption of dietary aluminium.

- Involve dieticians
- Consult Paediatric Haem-oncologists, nephrologists, endocrinologist.

Follow up

- Follow up in general clinic in 1 month
- Follow up in renal clinic if presenting with CKD in 1 months
- Follow up in Haem-onco clinic if present with Tumour lysis syndrome (as advised by the oncology team if available)

HYPOPHOSPHATAEMIA

Definition

Clinical condition characterized by physiological reduction of serum or plasma concentration in circulation. See normal ranges above.

Causes / Risk factors

- Hereditary hypophosphataemic rickets: X-linked hypophosphataemic rickets (XLHR), autosomal dominant or recessive hypophosphataemic rickets,
- Hypophosphatemia with hypercalciuria: Hereditary hypophosphataemic rickets with hypercalciuria (HHRH),
- Acquired disorder: Tumour-induced osteomalacia (TIO)

Promotion / Prevention

- Early screening and treatment

Signs and symptoms

- Presentation is based on the underlying clinical condition:

X-linked hypophosphataemic rickets:

- Musculoskeletal abnormalities seen soon after birth when the infant starts weight bearing there is evidence of hypophosphataemia, slow growth, rickets and osteomalacia

Autosomal dominant hypophosphataemia rickets (ADHR):

- Clinical course is similar to XLHR, however, ADHR is especially notable for its variable age of onset and incomplete penetrance.
- The disease starts at 1 or 3 years of age with evident phosphate wasting, rickets, and lower extremity deformities.

Autosomal recessive hypophosphataemia rickets (ARHR):

- Presentation similar to XLHR
- ARHR1, 2 and 3.
- ARHR 2 can present with hearing loss

Hypophosphatemia with hypercalciuria:

- Hereditary hypophosphataemic hypercalciuria rickets (HHHR): Disease onset is in childhood and presents with rickets and/or osteomalacia that is associated with hypophosphatemia, short stature, and secondary absorptive hypercalciuria.
- Dent disease: Proximal tubular solute wasting, hypercalciuria, nephrocalcinosis, kidney stones, renal failure, and, in some cases, rickets.
- Idiopathic hypercalciuria: Risk factor for kidney stone formation, mild hypophosphatemia and elevated levels of calcitriol.

Tumour-induced osteomalacia (TIO):

- clinical features of rickets, including gait disturbances, growth retardation, and skeletal deformities.

Differential diagnosis

- See conditions in signs and symptoms above

Investigations

- Serum electrolytes + CMP
- CXR looking for signs of rickets
- X-rays of the wrist bones and long bones looking for signs of rickets
- Serum PTH and vitamin D levels
- Genetic tests (if available)

Management

Primary Level

- Stabilize the patient and refer

Secondary Level

- Start initial investigations
- Stabilize the patient and refer

Tertiary Level

- Assess the patient
- Start investigations
- Start management
 - Oral phosphate 40 mg of elemental phosphorus/kg per day.
 - Vitamin D 10 to 20 ng/kg per dose, twice daily (20 to 40 ng/kg/day).
 - Add calcimimetics to prevent secondary hyperparathyroidism e.g. cinacalcet.
- Involve dietician
- Consult Paediatric nephrologist, Haem-oncologist, Paediatric (genetics if available)

Follow up

- Follow up in general clinic in 1 month
- Follow up in renal clinic if has kidney disease in 1 month
- Follow up in Haem-onco clinic if has a Tumour

RENAL REPLACEMENT THERAPY (RRT)

Definition

- It is the treatment directed towards removal of toxins, metabolites, and water from the body if kidney function is transiently or persistently lost.
- Therapy can also be used in cases of poisoning or overdose.

Indications

- Various causes of AKI and Uraemic symptoms (see causes of AKI)
- Various causes of CKD (see causes of CKD)
- Complications due to medical management
 - Refractory fluid overload
 - Electrolyte imbalances
 - Acid-base disturbances
- Acute poisoning e.g. by ethylene glycol, etc. (see management of acute poisoning)

Modalities of RRT

- Three main modalities used to replace renal function:
 - Dialysis (either peritoneal dialysis or haemodialysis)
 - Haemofiltration
 - Kidney transplantation

Promotion / Prevention

- Advocate for training of health workers to become certified providers of RRT
- Avoid nephrotoxic medications and adjust medications accordingly.

Contact nephrologist and/or a pharmacist for all medication dosing and if clinical management may affect or be affected by RRT

- Discuss with nephrologist on vaccination requirements for the patient
 - Likely to be vaccine non-responders; additional and/or higher doses and serological testing may be needed
 - Avoid live vaccines in immunosuppressed patients.
- Avoid unnecessary blood transfusions

A. PERITONEAL DIALYSIS (PD)

Basic Principles of peritoneal dialysis

- PD is the RRT modality that uses diffusion and ultrafiltration to remove solutes and water from the blood across the peritoneum that acts as a semipermeable membrane.
- Decision to manage the patient with peritoneal dialysis should be made in conjunction with Paediatrician and a paediatric nephrologist
- Patient and guardians need to be given enough information and education before initiation of RRT.
- Signed informed consent should be obtained.

Procedures in PD

- Peritoneal catheter placement
 - Consult paediatric urology / paediatric surgical team/ any trained health personnel for PD catheter placement.

- The peritoneal catheter is inserted into the peritoneal cavity and tunnelled to an exit site. (Anti-septic procedure).
- Initiation of dialysis
 - Dialysate is infused into the abdominal cavity and left for a set period of time (dwell time) to allow diffusion.
 - The dialysate draws water and electrolytes / waste products across the peritoneal membrane.
 - The fluid in the abdominal cavity (effluent) is removed at the end of the dwell time.

Complications of peritoneal dialysis

- Metabolic disturbances: weight gain, hyperglycemia
- Infections e.g exit site and catheter tunnel infections
- Peritoneal dialysis-associated peritonitis
- Protein loss: hypoalbuminaemia
- Abdominal hernias: umbilical and inguinal hernias are most common
- Leakage of dialysate
- Pleural effusion - rare
- Catheter blockage

Frequently examine the peritoneal dialysis catheter and exit site for signs of infection. Signs of infection include swelling and erythema around the catheter tunnel and exit site and purulent/ pus drainage at the exit site. Consider ultrasound for a more detailed assessment if infection is suspected.

Peritoneal dialysis-associated peritonitis

Definition: Peritonitis arising as a complication of peritoneal dialysis.

Risk factors:

- Peritoneal dialysis being performed in unclean environment, inadequate peritoneal dialysis training,
- Invasive procedures performed during dialysis e.g. colonoscopy, cholecystectomy etc.
- Patient factors include hypoalbuminaemia, staphylococcus aureus nasal carriage, previous exit site infection etc.

Prevention:

- Antibiotic prophylaxis prior to insertion of the peritoneal dialysis catheter
- Systemic prophylaxis prior to certain invasive procedures e.g. dental procedures, invasive abdominal procedures etc.
- Daily application of topical antibiotics to the catheter exit site.
- Health care providers and patient education on peritoneal dialysis catheter care
 - Keeping the exit site clean
 - Practicing thorough hand hygiene prior to dialysis exchange
 - Prompt treatment of exit site infections
 - Addressing modifiable risk factors
- Monitor effluent dialysis fluid characteristics when draining after dwell time.

Signs and symptoms:

- Mostly asymptomatic and identified by cloudy peritoneal effluent
- Clinical features of peritonitis which include abdominal pain, distension, and fever. On physical examination the patient may have rebound tenderness, rigidity, and guarding. (See management of Acute Abdomen – Peritonitis)

Investigations:

- Collect a peritoneal fluid sample for microscopy, culture and sensitivity (MCS).
- If the effluent is cloudy, initiate empiric antibiotic therapy.

Start empiric antibiotic therapy for presumed peritonitis in all patients with cloudy peritoneal effluent, even if they are asymptomatic!
- Systemic signs of infection: Initiate diagnostic workup for sepsis.
- Confirm peritonitis if ≥ 2 of the following are present:
 - Clinical features of peritonitis
 - Peritoneal fluid with > 100 WBCs/mcL (typically $> 50\%$ polymorphonuclear cells)
 - Positive peritoneal fluid culture

Management:

Tertiary Level

- Admit the patient in an isolated high dependence unit (HDU) if available
- Start management and treatment for sepsis if clinical features are suggestive of sepsis (see management of sepsis) including empiric systemic antibiotics.
- If the patient present with no systemic signs of infection
 - Consult nephrology and infectious diseases specialists if available
 - Initiate broad-spectrum empiric intraperitoneal antibiotics.
 - Adjust the dose based on renal function per hospital protocol.
 - Recommended regimens include: Vancomycin or cephalosporin e.g. Ceftriaxone (gram-positive cover) or aminoglycoside (gram-negative cover)
 - Adjust antibiotics based on culture and susceptibility results.
- Start antifungal prophylaxis (oral nystatin or fluconazole).
- Provide supportive treatment as needed e.g. oxygen therapy, pain management, antiemetics etc.
- Patients with relapsing or refractory peritonitis or confirmed fungal peritonitis: Consider removal of the peritoneal dialysis catheter and advocate for temporary hemodialysis.
- Involve palliative care team
- Involve renal dietician in management of patients with renal disease requiring dialysis

B. HAEMODIALYSIS

- Not routinely recommended or performed in Malawian paediatric patients
- Adolescent patients transitioning to adult care can be considered
- Discuss all patients requiring dialysis with nephrologist

Basic principles

- Haemodialysis uses diffusion and ultrafiltration to remove solutes and water from the blood.
- More effective at removing small molecules (e.g., urea, creatinine, ammonia) than larger molecules
- Blood is pumped through the dialysis unit on one side of a semipermeable membrane and dialysate in the opposite direction on the other side of the membrane.
- Molecules diffuse across the semipermeable membrane down their concentration gradient.

Procedure

- Intermittent renal replacement therapy
 - RTT may occur over 3–5 hours; may be prolonged as per patient requirement lasting 6–18 hours (prolonged intermittent renal replacement therapy)
 - Most common option for outpatient administration in patients with CKD but it can also be used for acute RRT
- Continuous renal replacement therapy
 - Gradual fluid and solute clearance over 24 hours
 - Used almost exclusively for acute RRT
 - Preferred if fluid shifts are contraindicated

Complications of haemodialysis

Venous Access complications:

- Loss of access due to thrombosis or stenosis
- Infections e.g., skin and soft tissue infection, central line-associated bloodstream infection
- Local aneurysm
- AV access steal syndrome: painful ischemia of the hand secondary to the AV fistula or graft shunting blood away from the distal limb
- Dialysis vascular access haemorrhage
 - Apply firm pressure for 15–20 minutes; avoid occluding the vessel.
 - If the patient is haemodynamically unstable:
 - Manage as hemorrhagic shock
 - Place tourniquets above and below the site and attempt a figure of 8 or purse-string suture.
 - Determine time of last dialysis and consider anticoagulant reversal.
 - Urgently consult vascular surgery if bleeding is heavy, persists, or recurs.

Cardiovascular complications:

- Hypotension and heart failure
- Increased bleeding risk caused by platelet dysfunction due to CKD and/or platelet contact with the dialysis membrane. Avoid systemic anticoagulation solely to maintain or improve haemodialysis catheter patency.

Dialysis disequilibrium syndrome:

- It is a clinical syndrome characterized by development of acute cerebral oedema secondary to the rapid extraction of osmotically active substances e.g. urea, NaCl from the blood.

Other complications:

- Acquired cystic kidney disease
- Cramps
- Electrolyte abnormalities e.g. hypophosphatemia
- Dialysis-related amyloidosis, which can cause carpal tunnel syndrome
- Allergic reaction to the equipment or dialysate

C. RENAL TRANSPLANT

For further enquiries on renal transplant discuss with nephrologist.

- Not routinely recommended or performed in Malawian paediatric patients
- Discuss all patients who can benefit from renal transplant with nephrologist
- Renal transplant cases will be discussed at external referral meetings where final decision is made
- Involve renal dietitian and palliative care team

Indications

- All patients with ESRD can benefit from renal transplant

Contraindications

Absolute:

- Unsuitable vascular anatomy
- Aorto-bifemoral bypass or an aorto-iliac stent graft that extends to both external iliac arteries
- Circumferential calcification of the iliac vessels
- Thrombosis of iliac vein and inferior vena cava
- Active infection (e.g., tuberculosis, invasive fungal infections, osteomyelitis)
- Malignancy in the past 2 years
- Obesity
- Lack of adequate social support (e.g., patient in a nursing home, homeless patient)

Relative:

- Age < 1 year or > 75 years
- Diseases of the lower urinary tract
- For female paediatric patients in reproductive age range, pregnancy is a contraindication
- Psychiatric diseases or psychosocial problems
- Systemic diseases potentially leading to kidney damage
- Proteinuria > 300 mg/day
- Hypertension that does not respond to treatment
- Diabetes mellitus

HYPERTENSION IN CHILDREN

Definition

- Hypertension (HTN) is the increase of systolic or diastolic blood pressure above 95th percentile for age, gender and height.
- Several HTN Categories have been developed to classify HTN according to the national population.
- Below is a table of 2017 American Academy of Paediatrics (AAP) updated definitions for paediatric blood pressure categories which is widely used for reference in many countries.

2017 American Academy of Paediatrics updated definitions for paediatric blood pressure categories

| | For children 1 to <13 years | For children ≥ 13 years |
|--------------------|---|--|
| Normal BP | Systolic and diastolic BP <90th percentile | Systolic BP <120 and diastolic BP <80 mmHg |
| Elevated BP | Systolic and diastolic BP \geq 90th percentile to <95th percentile, OR 120/80 mmHg to <95th percentile (whichever is lower) | Systolic BP 120 to 129 and diastolic BP <80 mmHg |
| Stage 1 HTN | Systolic and diastolic BP \geq 95th percentile to <95th percentile+12 mmHg, OR 130/80 to 139/89 mmHg (whichever is lower) | 130/80 to 139/89 mmHg |
| Stage 2 HTN | Systolic and diastolic BP \geq 95th percentile+12 mmHg, OR \geq 140/90 mmHg (whichever is lower) | 140/90 mmHg |

- Paediatric HTN is further classified into primary and secondary HTN, where primary HTN there is no identifiable cause whilst in secondary HTN the underlying cause is identified.
- It is also important to note another classification which is based on ambulatory BP monitoring. This classification classifies BP into white coat HTN and Masked HTN.
 - White coat HTN or Office HTN is an isolated BP \geq 95 percentile for age and sex determined within clinical setting but normal values outside the clinical settings.
 - Masked HTN is characterized as normal BP in clinical or office setting but a high ambulatory BP outside clinical setting. Mostly commonly, it is associated with obesity and increased left ventricular load, which are all risk factors for early adult cardiovascular disease..

Risk factors

Modifiable risk factors

- Obesity
- Increased dietary sodium intake
- Obstructive sleep apnoea (OSA)
- Decreased physical activity
- Breast feeding is protective. There are studies that indicate that breastfeeding lowers BPs in childhood posing a big risk of developing HTN in those children who were never breastfed.
- Tobacco exposure
- Adverse childhood experiences (ACEs) including traumatic events in childhood, abuse, neglect, parental mental health problems and household dysfunction increase the risk of overweight and obesity (in Malawi it would depend on social background), cardiovascular disease (coronary heart disease and stroke) and HTN. The ACEs are associated with increased mortality and morbidity.
- Prenatal and neonatal factors e.g. low birth weight and in utero exposure to preeclampsia has been associated with development of primary HTN.

Non-modifiable factors

- Sex: increased risk of developing HTN is seen more in boys than girls
- Family history of HTN mostly seen in patients with primary HTN
- Race and ethnicity – there is increased risk shown in Black and Hispanic children compared with White and Asian children in studies done in United States.

Causes of HTN

Primary HTN

- There is no underlying cause identified.
- This is a diagnosis of exclusion

Secondary HTN

- There is an identified underlying cause identified.
- The identified disorder can be curable with complete resolution of HTN

Causes of secondary HTN in children and adolescents

| Kidney disease | Pharmacologic causes |
|---|----------------------|
| Pyelonephritis | Sympathomimetics |
| Kidney parenchymal disease | Corticosteroids |
| Congenital anomalies | Stimulants |
| Reflux nephropathy | Oral contraceptives |
| Acute glomerulonephritis | Anabolic steroids |
| IgA Vasculitis (Henoch-Schönlein purpura) | Cocaine |
| Kidney trauma | Phencyclidine (PCP) |
| Hydronephrosis | Licorice |
| Hemolytic uremic syndrome | Nicotine |
| Kidney stones | Caffeine |
| Nephrotic syndrome | |

| | |
|---|---|
| Wilms tumor Hypoplastic kidney Polycystic kidney disease | |
| Endocrine disease Hyperthyroidism Congenital adrenal hyperplasia Cushing syndrome Primary aldosteronism Primary hyperparathyroidism Diabetes mellitus Hypercalcemia Pheochromocytoma | Vascular disease Renal artery abnormalities Renal vein thrombosis Coarctation of the aorta Patent ductus arteriosus Arteriovenous fistula |
| Neurologic causes Increased intracranial pressure Guillain-Barré syndrome | Psychologic causes Mental stress Anxiety |
| Other causes Neuroblastoma Heavy metal poisoning Acute pain Collagen vascular diseases Neurofibromatosis Tuberous sclerosis | |

Promotion / Prevention

- Early enrolment into antenatal care services to avoid complications of preeclampsia and premature delivery
- Promote exclusive breastfeeding
- Promote healthy eating diet
- Reduce sedentary lifestyle
- Promote physical education in schools
- Increase community screening health posts and refer appropriately
- Early identification and treatment by advocating for supplying appropriate sized cuffs for all age groups including neonates in the health facilities.
- Early identification and treating of all conditions that are associated with HTN
- Discourage indoor smoking
- Health promotion messages targeting teenagers who are at risk of indulging in risky behaviours of smoking and drinking which can predispose them to early development of HTN and cardiovascular diseases.

Signs and symptoms

- Can be asymptomatic only detected on a hospital consultation
- Non-specific hypertension symptoms
 - Headaches (early morning or waking up headache), dizziness, tinnitus, blurred vision, flushed appearance, epistaxis, chest discomfort, heart palpitations, nervousness, fatigue, sleep disturbance
 - Bounding pulses on palpation
- Symptoms of underlying disease
- Suspect secondary hypertension in the following:
 - Severe hypertension
 - Resistant hypertension

- Target organ damage disproportionate to the degree of hypertension
 - Hypertensive emergency
- Unusual onset of hypertension especially in all children and adolescent patients
- Drug induced hypertension
- Unprovoked or significant hypokalaemia

| Signs and Symptoms | Possible cause of hypertension |
|---|--|
| CNS: History of Head Trauma, headache, visual disturbance, lethargy, seizures, tremors, morning vomiting | Elevated intracranial pressure |
| Hearing: Hearing loss | Renal disease (e.g. Alport syndrome) Lead poisoning |
| Cardiovascular: Palpitations, irregular pulse | Catecholamine excess |
| Renal: Oedema, history of UTI or unexplained fever, abnormal urine colour, enuresis, flank pain, dysuria | Renal disease or condition (eg, pyelonephritis, acute glomerulonephritis, acute kidney injury, and chronic kidney disease) |
| Skin: Rash, sweating, pallor | Catecholamine excess Thyroid dysfunction Renal vasculitis |
| Recent medical history: Recent pharyngitis or impetigo, exposure to sources of enterohemorrhagic E. coli | Post-infectious glomerulonephritis Hemolytic uremic syndrome |
| Medications: Sympathomimetics, oral contraceptives, corticosteroids | Side effect of medication |
| Substance use: Cocaine, amphetamines, anabolic steroids, phencyclidine, ephedra-containing alternative medications, caffeine | Drug-mediated effects |
| Family history: Hypertension, early MI, diabetes, stroke | Essential hypertension |
| Sexual history: Postmenarchal female actively engaged in sexual intercourse | Preeclampsia |
| Neonatal history: Use of umbilical artery catheters | Renovascular hypertension |
| Growth history: Excessive weight gain or loss, change in growth percentiles | Obesity, thyroid dysfunction |
| Dietary history: Types and amount of food ingested; salt craving | Obesity, essential hypertension |
| Social history: Stress factors at home and school | Stress |

Distinguishing clinical features between primary (essential) and secondary pediatric hypertension

| Clinical features | Primary HTN | Secondary HTN |
|--|---|---|
| Age: | | |
| Prepubertal | | Secondary HTN is more likely in younger children, especially those less than six years of age |
| Postpubertal | Older children and adolescents are more likely to have primary HTN | |
| Diastolic HTN | | Diastolic HTN is more likely to be associated with secondary HTN |
| Nocturnal HTN | | Nocturnal HTN is more likely to be associated with secondary HTN |
| Overweight/obesity | Overweight or obese children/adolescents are more likely to have primary HTN | |
| Family history of HTN | Children with a positive family history of primary HTN are more likely to have primary HTN. | Family history may be positive in some cases of secondary HTN due to a monogenic cause (eg, autosomal dominant polycystic kidney disease) |
| Symptoms of underlying disorder | Patients with primary HTN are typically asymptomatic. | Patients with secondary HTN often have other symptoms related to the underlying cause (eg, headache, sweating, and tachycardia due to catecholamine excess in patients with pheochromocytoma) |

Promotion / Prevention

- Early screening and detection
- Advocate for community blood pressure screening e.g. at the market centres, churches and other public functions
- Advocate for screening of hypertension during all hospital consultations
- Advocate for 4 limb blood pressure measurement
- Advocate for screening of secondary hypertension causes in all children presenting with elevated blood pressures

Investigations

- The main goal of doing extensive investigation is to:
 - Differentiate between primary and secondary HTN.
 - Identify any treatable condition contributing to HTN. See table on causes.
 - Identify other comorbid conditions or risk factors for early cardiovascular disease (CVSD).
- Serum urea and creatinine to assess for possible renal disease causing HTN
- Serum electrolytes and blood gas analysis - hypokalaemia and metabolic alkalosis indicate excess mineralocorticoids (e.g. aldosterone) secretion.
 - Do serum renin and aldosterone level, if available, to confirm mineralocorticoid excess.
 - Examples of excess mineralocorticoid secretion disorders include Congenital Adrenal hyperplasia, Aldosterone secreting tumours, Liddle syndrome, pseudohypoaldosteronism (Gordon syndrome) etc.
- CMP
- Urinalysis
 - To assess if there is renal disease
 - Glucosuria may be suggestive of diabetes mellitus
- Lipid profile to look for dyslipidaemia. In obese children do the following additional tests
 - Haemoglobin A1c, fasting blood glucose to exclude diabetes mellitus
 - Serum alanine transaminase to screen for fatty liver disease
- Plasma and urine catecholamines – catecholamine excess as seen in Pheochromocytoma and neuroblastoma.
- Kidney ultrasound- recommended in all patients with HTN.
 - Kidney ultrasound – looks for presence of structural abnormalities or abnormally small kidney size which may indicate scarring.
 - If kidney ultrasound is suggests of renal scarring do Dimercaptosuccinic acid (DMSA) scan if available.
- Renovascular imaging
 - Standard digital subtraction angiography (DSA) previously called renal angiography is gold standard for investigating renovascular diseases in children
 - Magnetic resonance angiography (MRA) AND computed tomography angiography can be used.
 - Duplex doppler can be used if the above are not available but has low sensitivity.
 - Indicated in patients with predisposing factors or findings associated with renal artery stenosis e.g. prior umbilical artery catheter placements, family history or findings for neurofibromatosis, an abdominal bruit, or a significant size discrepancy on renal ultrasonography
- Cardiac echo – Left ventricular hypertrophy (LVH) is common end organ damage from HTN and can be detected on a cardiac echo
- Sleep study in OSA
- Drug screening e.g. cocaine, methamphetamine

A: Management of chronic hypertension in children and adolescents

- The target BP goal for children diagnosed with hypertension treated with non-pharmacologic and/or pharmacologic therapy is a **reduction of systolic and diastolic BP below the 90th percentile for age and sex or <130/80 in adolescents 13 years or older**
- Screen all patients for cardiovascular disease risk factors and treat as necessary.

Primary Level

- Refer all suspected cases of hypertension to secondary level for further management

Secondary Level

- Screen all cases for HTN
- Screen all cases of HTN for possible non-complicated causes of secondary HTN and start treatment
- Confirm the diagnosis of HTN and start treatment

Non-pharmacological management of hypertension

- Lifestyle modification
- Weight loss in obese patients - maintain BMI < 25 kg/m².
- Restrict salt with increased potassium intake from fresh fruits and vegetables involve the dietician
- Dietician's advice recommended.
- Reduce alcohol intake & stop smoking.
- Follow a healthy eating plan i.e. low fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables. Involve dietician if available.
- Regular moderate aerobic exercise, e.g. 40 minutes brisk walking at least 3 times a week.

Pharmacological management of chronic hypertension for infants, children, and adolescents:

- Antihypertensive drugs for outpatient management of chronic hypertension for infants, children, and adolescents
- First line treatment with ACE inhibitors (ACEI) or Angiotensin receptor blockers (ARBs) or Calcium channel blockers (CCB)
 - Calcium Channel Blockers
 - Nifedipine 0.25mg/kg BD increase to QID if no response maximum dose 1mg/kg/day.
- Refer and discuss all suspected cases with complicated primary or secondary HTN
- Refer and discuss all cases with acute severe HTN to tertiary level
- Follow up all cases of HTN in NCD / General clinic

Tertiary Level

- Screen all patients for HTN and investigate for secondary causes.
- Confirm the diagnosis of HTN and start treatment
- Manage all cases referred with acute severe hypertension

Non-pharmacological management of hypertension

- See Secondary Level above.

Pharmacological management of chronic hypertension for infants, children, and adolescents:

- Antihypertensive drugs for outpatient management of
- First line treatment with ACE inhibitors (ACEI) or Angiotensin receptor blockers (ARBs) or Calcium channel blockers (CCB)
 - Calcium Channel Blockers
 - Nifedipine 0.25mg/kg BD increase to QID if no response maximum dose 1mg/kg/day.
 - Amlodipine 0.05 to 0.2mg/kg od.
 - ACE inhibitors
 - Enalapril dose infant \geq 1 month of age 0.08mg/kg/day; children 0.1 mg/kg/day (maximum 40mg) daily to twice a day.
 - Captopril dose infants 0.05mg/kg/dose daily to 4 times a day; children 0.05mg/kg/dose (maximum 6mg/kg) three times a day.
 - Contraindications: Pregnancy, angioedema.
 - Common adverse effects: Cough, headache, dizziness, asthenia.
 - Severe adverse effects: Hyperkalemia, acute kidney injury, angioedema, fetal toxicity.
 - ARBs
 - Losartan dose > 6 years old 0.7mg/kg (maximum 50mg) daily
 - Candesartan dose 1 to 5 years old 0.02mg/kg/day (maximum 4mg/day) daily or twice a day. <50kg 4 mg per day
- If target BPs not achieved add Thiazide diuretics

Other management considerations:

Stage 1 primary hypertension (HTN) without evidence of end-organ damage or CVD risk factors

- Non-pharmacologic therapy is the initial intervention.
- If BP target goals are not met within four to six months after initial therapy (ie, BP below the 90th percentile), pharmacologic therapy is initiated.

Stage 2 primary HTN

- Treat with both non-pharmacologic and pharmacologic therapy.
- Patients with stage 2 HTN and neurologic symptoms including headache, mental status changes, and neurologic findings should be emergently evaluated and treated

Secondary HTN

- Start to treat underlying cause if treating the cause is adequate to treat HTN.
- If treating underlying cause does not treat hypertension, start pharmacologic and non-pharmacologic therapy dependent on the elevation of BP

HTN with Chronic kidney disease (CKD)

- Start both non-pharmacologic and pharmacologic therapy

Diabetes mellitus (DM) patients with HTN

- Start both non-pharmacologic and pharmacologic therapy.
- Involve paediatric nephrologist, endocrinologist, paediatric cardiologist, Paediatric oncologists, Paediatric surgeons and other needed specialised care as indicated
- Involve allied medical departments as indicated e.g. physiotherapy, palliative care, psychosocial support etc.

B: Management of acute severe hypertension in children and adolescents

Definitions:

Hypertensive emergency: An acute severe elevated BP (above the level of stage 2 hypertension) with evidence of life-threatening symptoms or target-organ damage e.g. hypertensive encephalopathy, heart failure, or acute kidney injury.

Hypertensive urgency: An acute severe elevation in BP without life-threatening symptoms or evidence of acute target-organ damage.

Note: *Symptoms or target organ damage is more important than the absolute BP level!!*

For example, a child with chronic hypertension with very high BP measurements without symptoms.

Another child with an acute moderately high in BP with hypertensive emergency because the child has symptomatic or has signs of end organ damage.

Primary Level

- Manage ABCDE
- Refer all patients

Secondary Level

- Manage ABCDE
- Give supportive oxygen therapy
- Stop all medications that lead to hypertension
- Manage the hypertension:
 - Start hydralazine 0.1 to 0.2 mg/kg/dose every 4 to 6 hours, titrate as needed in consultation with paediatricians
 - If hydralazine not available, give nifedipine 0.25mg/kg PO
 - **Target BP systolic at 95th percentile for age and sex**

Short-acting oral nifedipine is not recommended in children due to difficulties with dosing, prolonged and unpredictable action, risk of hypotension, and rebound hypertension.

The onset of action for other calcium channel blockers is too slow to recommend them for children with hypertensive urgencies.

- Provide continuous cardiorespiratory monitoring, plus pulse oximetry and ECG monitoring if available.
- Treat seizures with anticonvulsants (see management of seizures)

Tertiary Level

- Provide continuous cardiorespiratory monitoring, plus pulse oximetry and ECG monitoring if available.
- Stop all medications that lead to hypertension
- Place 2 IV lines. One for administration of antihypertensive drugs, the other one for general use
- Treat seizures with anticonvulsants (see management of seizures)
- Start IV antihypertensive medications

Hypertensive emergency

- Start labetalol bolus 0.2 to 1 mg/kg/dose (maximum dose: 40 mg/dose) **then**
- Labetalol IV infusion (0.25 to 3 mg/kg/hour) or repeated as a boluses every 10 minutes until reaching desired BPs.
- start with lower dose and titrate upwards according to response
- **Target BP systolic at 95th percentile for age and sex!!**

OR

- Start nicardipine 0.5 to 1 mcg/kg/minute continuous IV infusion **or**
- Nicardipine boluses 30 mcg/kg (up to 2 mg) of until reaching desired BPs.
- Start with low dose and titrate upwards

If no response to initial treatment above within 30 minutes:

- Start continuous IV infusion of both labetalol and nicardipine
- Alternative drugs include hydralazine and sodium nitroprusside have adverse effects that make them less suitable for the initial treatment of severe hypertension in children
 - Start hydralazine 0.1 to 0.2 mg/kg/dose (maximum dose: 20 mg/dose) every 4 to 6 hours, titrate as needed OR
 - Start Sodium nitroprusside 0.3 - 0.5 mcg/kg/minute titrate every 5 minutes to desired effect (maximum dose 10 mcg/kg/minute). Severe side effect is cyanide toxicity.

Do not lower the BP by more than 25 percent of the planned BP in the first eight hours of treatment in patients with chronic hypertension!!!

This will cause irreversible target-organ damage, including permanent neurologic sequelae, visual defects, myocardial infarction, and renal insufficiency. This is because of abnormal autoregulatory responses in circulatory beds of these organs.

Hypertensive urgency

- Target BPs <90th percentile for age, sex and height
- Start Labetolol IV bolus (preferred), or
- Start hydralazine or nicardipine IV bolus

Management of Chronic condition with Hypertensive urgency

- Do not lower BPs quickly
- Give oral medications if can take medications orally. If the patient cannot take oral medications:
 - Give IV labetalol bolus doses (preferred)
 - In infants < 1 year of age or for children with asthma, give IV doses of hydralazine or nicardipine (give slowly to lower the BP)
- Treat any associated conditions appropriately e.g. pulmonary oedema. See management of heart failure in children.
- Monitor BP and other vital signs regularly
- If there is papilledema, altered mental status, seizures, or neurologic deficits on physical examination, request a CT scan or MRI if available
- Discuss the case with seniors/pediatrician/nephrologist/endocrinologist i.e. people with expertise in managing HTN in children

Follow up

- Follow up in PEN-Plus clinic in 1 month
- Conduct regular patient education on non-pharmacological management of hypertension in the clinic
- Perform regular blood test to assess for end organ damage
- Schedule regular fundoscopy to assess for end organ damage in the eyes
- Collaborate with allied medical departments needed for management of hypertension e.g. physiotherapy for stroke patient secondary to HTN, psychosocial support services if available, palliative care etc.

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CHAPTER 10. NEURODEVELOPMENTAL DISORDERS

Introduction

The neurodevelopmental disorders (NDD's) are a group of conditions with onset in the developmental period. The disorders typically manifest early in development, often before the child enters school, and are characterized by developmental deficits or differences in brain processes that produce impairments of personal, social, academic, or occupational functioning (DSM 5)

Affected children often have more than one NDD and have impairment in personal, social, academic, or occupational functioning. They are at increased risk of neglect, and abuse and may be unable to live an independent life even in adulthood. Accessing appropriate medical care is often challenging because children with NDD struggle to express their symptoms and therefore clinicians may miss a diagnosis and attribute the symptoms to another condition (diagnostic overshadowing). A good understanding of how such children present, their symptoms and effective communication with their guardians who know the child's baseline can improve clinical assessment.

Management of NDD's requires a multidisciplinary team involving teachers, social workers, occupational therapists, speech therapists, and health professionals with the child and their family at the centre of care.

These guidelines provide an overview of common NDD's and how they can be managed. Clinicians or any discipline of the profession must bear in mind that the management of children with NDD's is challenging and must always work with other professionals. Consultations with specialist centres will also help those working in primary and secondary levels of care to feel supported and avoid over-prescription of drugs which can be detrimental to the development of the affected child.

ATTENTION DEFICIT HYPERACTIVE DISORDER (ADHD)

Definition

Attention deficit hyperactivity disorder (ADHD) is a disorder that manifests in childhood with symptoms of hyperactivity, impulsivity, and/or inattention. The symptoms affect cognitive, academic, behavioral, emotional, and social functioning.

Risk factors

- Prenatal and perinatal factors: Low birth weight/prematurity, In-utero exposure to maternal stress, maternal obesity, hypertension, cigarette smoking, alcohol, drugs e.g., acetaminophen, valproate, and illicit substances, infections (cerebral malaria and encephalitis).
- Environmental toxins (in-utero or during early childhood): lead, organophosphate pesticides, and polychlorinated biphenyls.
- Nutritional deficiencies: zinc, magnesium, iron, omega-3 polyunsaturated fatty acids.
- Psychosocial factors: low income, family adversity, harsh or hostile parenting
- Genetic and physiological factors.

Prevention / Promotion

- Addressing some of the above risk factors may reduce the risk of developing ADHD.
- Increase awareness of the clinical condition to educators and health professionals

Diagnosis

A diagnosis of ADHD should only be made by a specialist psychiatrist, paediatrician, developmental paediatrician or another appropriately qualified healthcare professional with training and expertise in the diagnosis of ADHD.

If a diagnosis of ADHD is suspected, the child should be screened using the SNAP V tool [SNAP ADHD Rating Scale.pdf \(ohsu.edu\)](https://www.ohsu.edu/forefront/snap-adhd-rating-scale.pdf) (developed by Swanson, Nolan, and Pelham) or The NICHQ Vanderbilt Assessment Scale (<https://nichq.org/resource/nichq-vanderbilt-assessment-scales>).

The results should be forwarded to a person who can schedule the child for a review and full assessment and initiation of care.

A full clinical and psychosocial assessment should be carried out and should include;

- i. An understanding of behaviour and symptoms in different domains and settings of the child's everyday life;
- ii. A full developmental history
- iii. A full psychiatric history
- iv. Observer reports i. e. report from school describing the child's behaviour in class, academic performances etc.
- v. Clinical assessment of the person's mental state
- vi. Assessment of any medical conditions that might relate to the condition e.g. previous encephalitis, cerebral malaria, prematurity and ensuring no cardiac conditions or reasons for raised blood pressure exist.
- vii. Assessment for co-morbidities e.g. Autism spectrum disorder (ASD) and specific learning disorders.

According to DSM-5, Diagnostic Criteria for ADHD is as outlined in the table below

| | |
|---|--|
| <p>Symptoms and/or behaviors that have persisted ≥ 6 months in ≥ 2 settings (e.g., school, home, church). Symptoms have negatively impacted academic, social, and/or occupational functioning. In patients aged < 17 years, ≥ 6 symptoms are necessary; in those aged ≥ 17 years, ≥ 5 symptoms are necessary.</p> | |
| Inattentive Type Diagnosis Criteria | <ul style="list-style-type: none"> • Displays poor listening skills • Loses and/or misplaces items needed to complete activities or tasks • Sidetracked by external or unimportant stimuli • Forgets daily activities • Diminished attention span <p>Lacks ability to complete schoolwork and other assignments or to follow instructions</p> <ul style="list-style-type: none"> • Avoids or is disinclined to begin homework or activities requiring concentration • Fails to focus on details and/or makes thoughtless mistakes in schoolwork or assignments |
| Hyperactive/ Impulsive Type Diagnosis Criteria | <p><u>Hyperactive Symptoms:</u></p> <ul style="list-style-type: none"> • Squirms when seated or fidgets with feet/hands • Marked restlessness that is difficult to control • Appears to be driven by “a motor” or is often “on the go” • Lacks ability to play and engage in leisure activities in a quiet manner • Incapable of staying seated in class • Overly talkative <p><u>Impulsive Symptoms:</u></p> <ul style="list-style-type: none"> • Difficulty waiting turn • Interrupts or intrudes into conversations and activities of others • Impulsively blurts out answers before questions completed |
| Additional Requirements for Diagnosis | <ul style="list-style-type: none"> • Symptoms present prior to age 12 years <p>Symptoms not better accounted for by a different psychiatric disorder (e.g., mood disorder, anxiety disorder) and do not occur exclusively during a psychotic disorder (e.g., schizophrenia)</p> <ul style="list-style-type: none"> • Symptoms not exclusively a manifestation of oppositional behavior |

| | |
|-----------------------|--|
| Classification | <p>Combined Type: Patient meets both inattentive and hyperactive/impulsive criteria for the past 6 months</p> <p>Predominantly Inattentive Type: Patient meets inattentive criterion, but not hyperactive/impulse criterion, for the past 6 months</p> <p>Predominantly Hyperactive/Impulsive Type: Patient meets hyperactive/impulse criterion, but not inattentive criterion, for the past 6 months Symptoms may be classified as mild, moderate, or severe based on symptom severity</p> |
|-----------------------|--|

SOURCE- DSM-5 Diagnostic and Statistical Manual of Mental Disorders, 5th edition; ADHD: attention deficit hyperactivity disorder

Investigations

ADHD is a clinical diagnosis.

Differential diagnosis/ Comorbidity

Comorbid psychiatric disorders are common in children with ADHD and below are the most common ones;

- Oppositional Defiant Disorder (ODD)
- Conduct Disorder (CD),
- Intellectual Disability,
- Learning Disorders,
- Language Disorders,
- Sleep Disorders,
- Enuresis,
- Developmental Motor Coordination Disorders,
- Depressive and Anxiety Disorders,
- Tic Disorders, and Autism Spectrum Disorders.

Management

- Recognition of ADHD and other neurodevelopmental disorders should ideally be done by parents and teachers.

Primary Level

- Healthcare facilities should refer children with suspected ADHD to the secondary level of care.

Secondary Level

- Care facilities should screen suspected children and conduct a full assessment.
- If the clinical picture is suggestive of ADHD, secondary-level services should liaise with tertiary care services or specialist centers for assessment and confirmation of diagnosis.
- Once diagnosis has been made at Tertiary level, on going care and follow up can be provided at Secondary level.

Tertiary Level

- Medication should be started at tertiary level.
- Tertiary care services should provide diagnostic services and support more complex children and young people.
- Assess, diagnose and manage ADHD patients and support facilities in ongoing care of affected patients.

a. *Psychoeducation*

- Psychoeducation is the foundation of treatment because ADHD is a chronic condition.
- Clinicians should give information in a way that families can understand, using language, comparisons, and metaphors at the patient educational level and in a culturally sensitive manner.
- Diagnoses and treatment approaches should be outlined so that informed decisions can be made.
- The child requires support at all levels so with permission from parents, teachers should be informed so they can accommodate the child's needs.

b. *Behavioural and Psychosocial Treatment*

- In settings like Malawi where the availability of drugs is limited, behavioural and psychological treatments can help a lot of children with ADHD.
- Some psychological approaches used for treating ADHD include behaviour classroom interventions, social and organizational skills training, meditation-based therapy, and cognitive therapy which can be administered by appropriately skilled personnel.

c. *Medication*

- Medication for ADHD should only be initiated by a healthcare professional with training and expertise in diagnosing and managing ADHD.
- Healthcare professionals initiating medication for ADHD should:
 - be familiar with the pharmacokinetic profiles of all the short- and long-acting preparations available for ADHD
 - ensure that treatment is tailored effectively to the individual needs of the child, young person, or adult
 - take account of variations in bioavailability or pharmacokinetic profiles of different preparations to avoid reduced effect or excessive adverse effects

Baseline assessment BEFORE initiation of medication

Before starting medication for ADHD, people with ADHD should have a full clinical assessment, which should include:

1. a review to confirm they continue to meet the criteria for ADHD and need treatment
2. a review of mental health and social circumstances, including:
 - presence of coexisting mental health and neurodevelopmental conditions
 - current educational or employment circumstances
 - risk assessment for substance misuse and drug diversion
 - guardians need and support
3. a review of physical health, including:

- a medical history, taking into account conditions that may be contraindicated for specific medicines
 - current medication (always cross-check for drug-to-drug interaction)
 - height and weight (measured and recorded against the normal range for age, height, and sex) (stimulants cause growth retardation)
 - baseline pulse and blood pressure (measured with an appropriately sized cuff and compared with the normal range for age) (stimulants cause hypertension)
 - a cardiovascular risk assessment
 - an electrocardiogram (ECG) is required in those with cardiovascular risk factors or problems before starting medications for ADHD
4. Refer for a cardiology opinion before starting medication for ADHD if any of the following apply:
- history of congenital heart disease or previous cardiac surgery
 - history of sudden death in a first-degree relative under 40 years suggesting a cardiac disease
 - shortness of breath on exertion compared with peers
 - fainting on exertion or in response to fright or noise
 - palpitations that are rapid, regular, and start and stop suddenly (fleeting occasional bumps are usually ectopic and do not need investigation)
 - chest pain suggesting a cardiac origin
 - signs of heart failure
 - a murmur was heard on cardiac examination

Medication choice

- Offer methylphenidate (either short or long-acting as the first-line pharmacological treatment for children aged 5 years and over and young people with ADHD).
- Consider switching to lisdexamfetamine for children aged 5 years and over and young people who have had a 6-week trial of methylphenidate at an adequate dose and have not derived enough benefit in terms of reduced ADHD symptoms and associated impairment.
- Consider dexamfetamine for children aged 5 years and over and young people whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile.
- Offer atomoxetine or guanfacine to children aged 5 years and over and young people if they cannot tolerate methylphenidate or lisdexamfetamine or their symptoms have not responded to separate 6-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate doses.

NB: ***there is no evidence of risperidone in the treatment of ADHD. Prescription of risperidone should only be done if the benefits outweigh the risk and there should be an established comorbid behavioural difficulty of which psychological and behavioural interventions have failed.***

Follow up

- Follow up patients in general clinic/neurodevelopmental clinic at central level or secondary level PEN-Plus clinic that have availability of multidisciplinary team

AUTISM SPECTRUM DISORDER

Definition

Autism Spectrum Disorder (ASD) is a biologically based neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction, and restricted, repetitive patterns of behavior, interests, and activities.

- People with ASD have problems with establishing and maintaining meaningful interpersonal relationships.
- Symptoms start in early development but may be difficult to recognize until a child is older and the social demands exceed their capacity to function in normal society.

Risk factors / Causes

- The aetiology is unclear but risk factors include,
 - genetics e.g. down syndrome,
 - having a sibling with ASD,
 - advanced parental age
 - sodium valproate exposure during the prenatal period and other environmental toxins.

Prevention / promotion

- Early detection and support can improve functionality.
- Recognition of ASD should be done by parents and teachers who should then refer the child for assessment.

Clinical features

- ASD symptoms can be identified as early as 18 months of age.
- Signs and symptoms present early in childhood and red flags are outlined in the image below:



Fuentes J, Bakare M, Munir K, Aguayo P, Gaddour N, Öner Ö. Autism spectrum disorder. In Rey JM (ed), *IACAPAP e-Textbook of Child and Adolescent Mental Health*. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions 2014.

Diagnosis

- According to the DSM, Fifth Edition Text Revision (DSM-5-TR) criteria, a diagnosis of ASD requires all of the following:

Persistent deficits in social communication and social interaction in multiple settings; demonstrated by deficits in all three of the following (either currently or by history):

- Social-emotional reciprocity (eg, failure to produce mutually enjoyable and agreeable conversations or interactions because of a lack of mutual sharing of interests, lack of awareness or understanding of the thoughts or feelings of others)
- Nonverbal communicative behaviors used for social interaction (eg, difficulty coordinating verbal communication with its nonverbal aspects [eye contact, facial expressions, gestures, body language, and/or prosody/tone of voice])
- Developing, maintaining, and understanding relationships (eg, difficulty adjusting behaviour to social setting, lack of ability to show expected social behaviours, lack of interest in socializing, difficulty making friends even when interested in having friendships)

Restricted, repetitive patterns of behaviour, interests, or activities; demonstrated by ≥2 of the following (either currently or by history):

- Stereotyped or repetitive movements, use of objects, or speech (eg, stereotypies such as rocking, flapping, or spinning; echolalia [repeating parts of speech]; repeating scripts from movies or prior conversations; ordering toys into a line)
- Insistence on sameness, unwavering adherence to routines, or ritualized patterns of verbal or nonverbal behaviour (eg, difficulty with transitions, greeting rituals, need to eat the same food every day)
- Highly restricted, fixated interests that are abnormal in strength or focus (eg, preoccupation with certain objects [trains, vacuum cleaners, or parts of trains or vacuum cleaners]); perseverative interests (eg, excessive focus on a topic such as dinosaurs or natural disasters)
- Increased or decreased response to sensory input or unusual interest in sensory aspects of the environment (eg, adverse response to particular sounds; apparent indifference to temperature; excessive touching/smelling of objects)
- The symptoms must impair function (eg, social, academic, completing daily routines).
- The symptoms must be present in the early developmental period. However, they may become apparent only after social demands exceed limited capacity; in later life, symptoms may be masked by learned strategies.
- The symptoms are not better explained by intellectual disability or global developmental delay.

Investigations

- Every child with suspected ASD must have hearing and vision assessment as these may be the cause or be contributing to their symptoms
- Screening and diagnostic tools can be used to assess and identify children with suspected ASD such as the Childhood Autism Spectrum Test (CAST) ([Childhood Autism Spectrum Test \(CAST\) \(psychology-tools.com\)](https://www.psychology-tools.com/childhood-autism-spectrum-test-CAST/)) or Modified Check for

Autism in Toddlers (M-CHAT) (<https://www.mchatscreen.com/>) and Autism Diagnostic Observation Schedule (ADOS)

- A full assessment should include the child's behaviours in different context and settings e.g., home, school etc

Comorbidities

- Like most NDD, children and adolescents with autism spectrum disorder have a lot of comorbidities. Some of the common comorbidities include;

- Sleep disorders/disturbance
- ADHD
- Gastrointestinal disorders
- Feeding/eating challenges
- Obesity
- Bipolar disorder
- Intellectual Disability,
- Language disorders
- Sleep Disorders, Enuresis,
- Depressive and Anxiety Disorders,
- Epilepsy and epilepsy syndromes

Differential diagnosis

- Sensory deficit - such as hearing or visual impairment
- Intellectual disability
- Language and speech disorders
- Other neurodevelopmental disorders such as Rett syndrome
- Selective mutism
- Severe psychosocial deprivation
- Tic Disorder
- Language disorder

Management

- Identify and treat any comorbid disorders.
- There are no drugs for autism spectrum disorder.
- The treatment and management of ASD is complex and requires multidisciplinary approach with the child and family at the center of care.
- Referral to rehabilitation services (occupational therapy/speech therapy)
- The treatment approach should include parent and teacher training and support.
- Education support groups as early as possible, with special attention to social, communication, academic and behavioral development, are provided in the least restrictive environment by staff who have knowledge and understanding of both autism and the individual student.
- Accessible community support, in terms of appropriate, well-informed, multi-agency services that will help each individual to realize their potential and lifetime goals (either chosen by the individuals themselves or those who know, love, and legally represent them).
- Access to the full range of psychological and medical treatments (adapted as necessary to meet the needs of individuals with ASD) that are available to the general population.
- Access to social welfare services when available

Primary Level

- Healthcare facilities should refer children with suspected ASD to the secondary level of care.

Secondary Level

- Care facilities should screen suspected children and conduct a full assessment.
- If the clinical picture is suggestive of ASD, secondary-level services should liaise with tertiary care services or specialist centers for assessment and management.
- Once diagnosis has been made at Tertiary level, on going care and follow up can be provided at Secondary level.

Tertiary Level

- Assess, diagnose and manage ASD patients and support facilities in ongoing care of affected patients.

Follow up

- Follow up patients in general clinic/neurodevelopmental clinic at central level or secondary level PEN-Plus clinic that have availability of multidisciplinary team.

INTELLECTUAL DISABILITY (ID)

Definition

Intellectual disability (ID) is a neurodevelopmental disorder that begins in childhood and is characterized by limitations in both intelligence and adaptive skills, affecting at least one of three adaptive domains (conceptual, social, and practical), with varying severity. The extent of adaptive impairment is key to defining ID and its severity.

Risk factors

- Causes for ID are heterogeneous
- **Mild ID:** no specific cause in 40% of cases
 - Genetic causes, injury, infections, poor nutrition
- **Marked ID:** specific causes are found more often
 - Genetic: Trisomy 21, Fragile X, single gene disorder
 - Prenatal: fetal alcohol syndrome, maternal infection like HIV
 - Perinatal: placental dysfunction, birth trauma, septicaemia, jaundice
 - Postnatal: brain infection, head injury

Prevention / Promotion

- Antenatal screening and good obstetric care can prevent ID due to preventable etiological factors
- Early identification, and management of childhood illness can prevent ID e.g., hypothyroidism, inborn errors of metabolism.
- Screening in children with predisposing factors for ID should be done routinely to facilitate early detection of ID.
- Children can also be identified through schools and Early Child Development Centres
- Training teachers, parents, and medical professionals to identify those with learning difficulties will help early detection to improve functionality and outcome
- Prevention can be done at all levels of care:

Primary (preventing the occurrence of ID):

- Prenatal: (toxins, infections incl. HIV)
- Peri-natal: (delivery, neonatal screening)
- Post-natal: (immunization, treatment for infections, safe and enriching environment)

Secondary (halting disease progression):

- Identify ID early, and provide stimulation for optimal development

Tertiary (maximizing function):

- Support for families
- Stimulation, training, vocational opportunities (special schools)

Signs and symptoms

- Core symptoms
 - Low intellectual functioning IQ <70 (i.e., 2 SD below mean)
 - Impaired adaptive behavior
- The severity of intellectual disability can be categorised from mild to profound according to the level of adaptive impairment and the level of support needed, as summarized in the table below;

Typical adaptive needs and supports according to severity of intellectual disability

| Severity level | | Adaptive skill domains | | |
|------------------|------------------|--|---|---|
| DSM-5 categories | AAIDD categories | Conceptual | Social | Practical |
| Mild | Intermittent | Children require academic supports to learn skills expected for age. Adults may have difficulties with functional academic skills such as planning, reading, and money management. | Social skills and personal judgement are immature for age. The individual is at risk of being manipulated by others (gullibility). | Most individuals achieve independence in daily living and personal care activities; most are employable in jobs requiring simple skills and are often able to live independently. They typically need support for making decisions in health care, nutrition, shopping, finances, and raising a family. |
| Moderate | Limited | For children, conceptual and academic skills lag well behind those of peers. For adults, academic skills are typically attainable at an elementary level. Complex tasks such as money management need substantial support. | Successful friendships with family/friends are possible using simple spoken language, but the individual is limited by deficits in social and communicative skills. Social cues, social judgment, and social and life decisions regularly need support. | Most individuals are capable of personal care activities with sufficient teaching and support, and achieve independent self-care with moderate supports, such as is available in a group home. Adults may be employable in a supported environment. |
| Severe | Extensive | Individuals have little understanding of written language, or number, time, and money concepts. Caretakers provide extensive supports for problem-solving. | Individuals benefit from healthy supportive interactions with family/familiar people and may use very basic single words, phrases, or gestures pertinent to their direct experience. | Individuals are trainable in some basic activities of daily living with significant ongoing support and supervision. |
| Profound | Pervasive | Individuals may use objects in a goal-directed fashion for self-care and recreation. | Although understanding of symbolic communication is very limited, individuals may understand some gestures and emotional cues, and can express themselves nonverbally. | Individuals are typically dependent upon support for all activities of everyday living. Co-occurring sensory or physical limitations are common. |

This table provides examples of typical adaptive needs and supports according to the severity of ID. The severity of ID is defined by the level of adaptive impairment and the level of support needed. The American Psychiatric Association's DSM-5 categorizes adaptive impairment from mild to profound.^[1] The AAIDD uses categories of intermittent, limited, extensive, and pervasive.^[2] Supports are wide-ranging and aim to optimize the functioning, participation, and independence of the child in everyday environmental settings, including home, school, community. Profoundly impaired children usually require pervasive support.

ID: Intellectual disability; DSM-5: Diagnostic and Statistical Manual, 5th Edition; AAIDD: American Association on Intellectual and Developmental Disabilities.

Adapted from the following sources:

- American Psychiatric Association. *Intellectual Disability (Intellectual Developmental Disorder)*. In: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, American Psychiatric Association.
- American Association of Intellectual and Developmental Disabilities (AAIDD). *Definition of Intellectual Disability*. Available at: <http://aaidd.org/intellectual-disability/definition> (Accessed on July 17, 2018).

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- In the absence of these specific tools or expertise to do proper psychometric assessments for IQ, a rough estimate of the child's IQ can be done using the following formula;

$$\text{(Developmental age/chronological age)} \times 100 = \text{IQ}$$

- For example, a child who is 5 years of age (chronological age) is found to have the developmental abilities of a 2-year-old child (developmental age):

$$\text{IQ} = 2/5 \times 100 = 40$$

| Severity | Mild | Moderate | Severe | Profound |
|----------|-------|----------|--------|----------|
| IQ score | 50-69 | 35-49 | 20-34 | 0-20 |

Investigations

- To diagnose ID the following are required;
- IQ below 70
- Impairment in adaptive functioning
- Onset before age 18 years of age
- The following tools can be used to make the diagnosis:
- Interview: family medical history, pregnancy, development, the home environment.
- Physical examination
- Developmental assessment tools e.g., MDAT <https://mdat.org.uk/>
- Psychometric tests e.g., Kaufmann ABC if available
- Adaptive behavior: clinical judgment and scales
- Laboratory tests and genetic testing e.g. Thyroid function tests, iron levels, and lead levels where possible

Comorbidities

- Psychiatric co-morbidities are common (~50%)
 - Anxiety, ODD, autism
 - ADHD, depression, conduct problems
- Medical co-morbidity is also common
 - epilepsy, cerebral palsy, and sensory issues most common but are often undetected and under-treated.
 - Genetic conditions e.g., Down Syndrome (trisomy 21), Fragile X, Phenylketonuria (PKU), Congenital hypothyroidism, Fetal alcohol spectrum of disorders.

Differential diagnosis

- Exclude sensory (deafness, poor eyesight) problem
- Take good care to identify and manage underlying causes of ID, especially those that are reversible:
 - Infections (e.g. cerebral malaria)
 - Neurological disorders (e.g. epilepsy)
 - Endocrine disorders (e.g. hypothyroidism)
 - Severe under stimulation/abuse/neglect

- Specific developmental disorders (e.g. specific learning disorders)
- Autism (with or without ID)

NB!! Any sudden developmental *regression* (loss of skills that were once mastered) should be treated as a *medical* emergency and investigated.

Management

Concerns regarding ID should ideally be raised by parents and teachers.

Care for children with ID requires a multidisciplinary team to work with the child and guardians. The health professional should coordinate the care team which includes clinicians, nurses, teachers, social workers, occupational therapists, and speech therapists as they are usually the ones the family presents to.

Aims of treatment

- Identify and treat reversible causes of ID
- Engage occupational therapist to promote functionality, activities of daily living
- Education – enroll in special school or engage with the teacher in main stream school for additional support and extra classes.
- Engagement in vocational schools

Counselling of family to understand the diagnosis and provide support

Referral pathway

Primary Level

- Healthcare facilities should refer children with suspected ID to the secondary level of care.

Secondary Level

- Care facilities should screen suspected children and start management.
- If there are any uncertainties or lots of comorbidities, secondary-level services should liaise with tertiary care services or specialist centers for assessment and management.

Tertiary Level

- Assess, diagnose and manage ID patients and support facilities in ongoing care of affected patients.

Follow up

Follow up patients in general clinic/neurodevelopmental clinic at central level or secondary level that have availability of multidisciplinary team.

SPECIFIC LEARNING DISABILITY/DISORDERS

Definition

A specific learning disorder is a neurodevelopmental condition that is characterised by difficulties or delays in learning that are below what is expected for a child's cognitive ability.

- NB. These patients differ from those who have intellectual disability as they have normal IQ but struggle in a specific area of learning.

Risk Factors / Causes

- Personal factors
 - Family history – it has been shown that there is a genetic predisposition
 - Communication difficulties – receptive and expressive language difficulties
 - Other neurodevelopmental disorders – autism and severe learning disability
 - Visual impairment
- Environmental factors
 - Abusive or restrictive environment
 - Those with too much or too little stimulation
 - Changes in environment
 - Environment that demands more than is appropriate for the child's age.

Promotion / Prevention

- Early recognition can improve overall academic performance and requires collaboration between teachers and psychologists.

Signs and symptoms

- The DSM-5 describes three groups of specific learning disorders with their characteristics as below:

With impairment in reading characterised by difficulties in:

- Word reading accuracy
- Reading rate or fluency
- Reading comprehension
- Note: Dyslexia is an alternative term used to refer to a pattern of learning difficulties characterized by problems with accurate or fluent word recognition, poor decoding, and poor spelling abilities.
- If dyslexia is used to specify this particular pattern of difficulty, it is important also to specify any additional difficulties that are present, such as difficulties with reading comprehension or math reasoning.

With impairment in written expression (also called dysgraphia):

- Spelling accuracy
- Grammar and punctuation accuracy
- Clarity or organization of written expression

With impairment in mathematics (also called dyscalculia):

- Number sense
- Memorization of arithmetic facts
- Accurate or fluent calculation

- Accurate math reasoning
- Note: Dyscalculia is an alternative term used to refer to a pattern of difficulties characterized by problems processing numerical information, learning arithmetic facts, and performing accurate or fluent calculations. If dyscalculia is used to specify this particular pattern of mathematic difficulties, it is important also to specify any additional difficulties that are present, such as difficulties with math reasoning or word reasoning accuracy.

Investigations /diagnosis

- A diagnosis requires an objective assessment using a child's history (developmental, medical, family, educational), school reports and psychological education assessment.
- DSM-5 gives the diagnostic criteria for specific learning disability as below; Difficulties learning and using academic skills, as indicated by the presence of at least one of the following symptoms that have persisted for at least 6 months, despite the provision of interventions that target those difficulties:
 1. Inaccurate or slow and effortful word reading (e.g., reads single words aloud incorrectly or slowly and hesitantly, frequently guesses words, has difficulty sounding out words).
 2. Difficulty understanding the meaning of what is read (e.g., may read text accurately but not understand the sequence, relationships, inferences, or deeper meanings of what is read).
 3. Difficulties with spelling (e.g., may add, omit, or substitute vowels or consonants).
 4. Difficulties with written expression (e.g., makes multiple grammatical or punctuation errors within sentences; employs poor paragraph organization; written expression of ideas lacks clarity).
 5. Difficulties mastering number sense, number facts, or calculation (e.g., has poor understanding of numbers, their magnitude, and relationships; counts on fingers to add single-digit numbers instead of recalling the math fact as peers do; gets lost in the midst of arithmetic computation and may switch procedures).
 6. Difficulties with mathematical reasoning (e.g., has severe difficulty applying mathematical concepts, facts, or procedures to solve quantitative problems)
- The affected academic skills are substantially and quantifiably below those expected for the individual's chronological age, and cause significant interference with academic or occupational performance, or with activities of daily living, as confirmed by individually administered standardized achievement measures and comprehensive clinical assessment.
- The learning difficulties begin during school-age years but may not become fully apparent until the demands for those affected academic skills exceed the individual's limited capacities (e.g., as in timed tests, reading or writing lengthy complex reports for a tight deadline, excessively heavy academic loads)
- The learning difficulties are not better accounted for by intellectual disabilities, uncorrected visual or auditory acuity, other mental or neurological disorders, psychosocial adversity, lack of proficiency in the language of academic instruction, or inadequate educational instruction.
- It is important to note that individuals demonstrate differences in degree of impairment and may not exhibit all the characteristics listed above.

- When summarising the areas affected this should be outlined based on which area the patient experiences impairment, impairment in reading, impairment in writing, or impairment in mathematics

Management of specific learning disorders

- Management will require a multidisciplinary team including; an educational psychologist, a clinical psychologist, psychologist, psychiatrist, behavioural analysts, nurses, social care staff, speech and language therapists, educational staff, occupational therapist, educational staff, occupational therapist, physiotherapist, physicians, paediatricians and pharmacists.

Primary / Secondary Level

- Children who are suspected to have specific learning disorders will need referral for appropriate assessment.

Tertiary Level

- These facilities will be critical in making the diagnosis but they will need to coordinate with other cadres and liaise with personnel at primary and secondary level facilities to substantiate the diagnosis.

Follow up

- Follow up patients in general clinic/neurodevelopmental clinic at central level or secondary level PEN-Plus clinic that have availability of multidisciplinary team.
- Engagement of special needs educators and psychologists is paramount in the follow up.

CHILD AND ADOLESCENT MENTAL HEALTH

STRESS, ANXIETY, AND OTHER EMOTIONAL DISTRESS

Definition - Anxiety/disorders

Anxiety disorders refers to conditions that share features of fear and anxiety. Fear being an emotional response to a real or perceived imminent threat and anxiety being the anticipation of future threat. Symptoms meet the criteria for a clinical anxiety disorder when the concerns are unexpected given the child's developmental level, persistent in the face of reassurance and support, and thus considered excessive.

It is easy to miss a diagnosis or misdiagnose children and adolescents presenting to a health facility with stress, anxiety, and other emotional distress

Some of the reasons include the following;

- presentation differs from the adult population (e.g., children and adolescents will present with irritability and multiple somatic symptoms when experiencing distress, and academic difficulties)
- children and adolescents struggle to express themselves (i.e. inability to name feelings and thoughts)
- assessing children and adolescents with these disorders is time consuming and requires the involvement of different cadres (school teachers, social workers, etc.).

Approximate Age of onset for various disorders may vary.

- Animal phobias – early childhood (around 6-7 years)
- Separation anxiety disorder – early to mid-childhood (around 7-8 years)
- Generalized anxiety disorder – late childhood (around 10-12 years)
- Social anxiety disorder – early adolescence (around 11-13 years)
- Obsessive-compulsive disorder – mid-adolescence (around 13-15 years)
- Panic disorder – early adulthood (around 22-24 years)

Risk factors / Causes

- Genetics: Anxiety runs in families. First-degree relatives of people with anxiety disorders are at significantly increased risk of also having anxiety and mood disorders
- Parenting characteristics: more common in parents who are overprotective, are intrusive and demonstrate negativity towards their child
- Life Events:
 - Increased negative life events
 - Bullying and teasing
 - Neglect and rejection by peers
 - Sexual abuse, physical abuse

Diagnosis

- PRAGMATIC APPROACH TO ASSESSING CHILDREN AND ADOLESCENTS
- The most important tool is the clinical assessment and collateral history including from school and other places where the child spends his/her time.
- Identify the presenting complaint (from the child, guardian, and any other cadres including school)

- Try to identify the triggers (keeping in mind that with children and adolescents, it might take several sessions to identify the triggers and clinicians should focus on building rapport rather than trying to make a diagnosis during the first session)
- Identify the functional consequences (i.e., behavioral difficulties, academic difficulties)
- Most importantly, try to involve as many cadres as possible. The child's functioning and psychological well-being are highly dependent on the family and school setting in which he or she is in so the child cannot be assessed in isolation.

Tools to aid in the assessment

The following tools are recommended in identifying specific anxieties in children;

1. Screen for Child Anxiety Related Disorders (SCARED) <https://www.ohsu.edu/sites/default/files/2019-06/SCARED-form-Parent-and-Child-version.pdf>
2. Feeling scale
3. Play and art (describing feelings and emotions using diagrams. This needs the assessor to be the child's friend and not a clinician)
4. Emotion diary
5. The patient can be assessed using the Generalised Anxiety Disorder GAD-7 tool (<https://www.ementalhealth.ca/index.php?m=survey&ID=3>).
6. If there are also concerns regarding depression Patient Health Questionnaire (PHQ-9) (<https://www.ementalhealth.ca/index.php?m=survey&ID=42>)
7. If there are concerns about both depression and anxiety, then the PHQ-4 can be used as screening tool for both anxiety and depression.

Management

- Management of stress and related disorders in kids requires a multidisciplinary approach.
- The aim of the treatment is to address the functional consequences of the presenting complaint and ensure that the child can achieve academically, and socially and be able to live an independent life.

Primary Level

- Assess the patient and refer all suspected cases to secondary level health facility.

Secondary / Tertiary Level

- Treatment involves skills-based programs which is the mainstay and medical management.
- Skills-based programs include the following:
 - Psychoeducation
 - Relaxation
 - Exposure therapy
 - Parent training
 - Cognitive restructuring
 - Social skills and assertiveness training
 - School programs
- Use of drugs should be the last option unless symptoms are very severe. If deemed necessary drugs should be initiated in liaison with a clinician who is very familiar with the principles of prescription and psychopharmacology in children.

Treatment approach:

- Start with skills-based therapy and review the patient every 2-4 weeks
- If they improve you may see them every three months
- If there is no response, consider starting medication with skills-based therapy
- Treatment should continue to 12 months to prevent relapse and drugs weaned slowly whilst monitoring for relapse
- NB. Always assess for **suicide risk** and refer such patients urgently.
- Monitor all patients on treatment especially SSRIs closely for any worsening including suicidal ideation and any change in behaviour. Advise family and close caregivers to monitor for the same.
- Refer such patients as required to a psychiatry unit/ mental health practitioner for assessment and treatment.

Follow up

See management section for frequency of follow up.

DEPRESSION

Definition

Depression is a mood disorder that is characterised by a persistent feeling of sadness accompanied with a loss of interest in things they previously engaged in.

Risk factors / Causes

- Biological vulnerabilities include genetic factors, prenatal factors, familial factors
- Environmental influences include children's family relationships, cognitive style, stressful life events, school and neighbourhood characteristics.

Promotion / Prevention

- Not all children who have risk factors for depression develop the disorder but there are some factors that have been shown to have a protective effect in adolescents at high risk for developing depression.
- Individual factors
 - Inherited resilience, high intelligence, emotional regulation capacity, coping mechanisms and thinking styles
- Familial factors
 - Good quality interpersonal relationships have been found to be protective and nurturing such relationship can be beneficial.
 - Children who have family relationships that are characterised by warmth, acceptance, low hostility and low parenteral control are protective in children who have a high risk for depression.
- Social factors
 - Strong peer support is protective.

Signs and symptoms

- The approach to depression in children and adolescents is not very different from anxiety disorders and there will almost always be comorbidity of the other disorder when one is present.
- Young people tend to present initially with behavioral or physical complaints which may obscure the typical depressive symptoms seen in adults.
- The following complaints should alert clinicians to the possibility of depression in children and adolescents;
 - Irritability or cranky mood
 - Chronic boredom or loss of interest in previously enjoyed leisure activities (for example, dropping out of sporting activities, or dance and music lessons)
 - Social withdrawal or no longer wanting to "hang out" with friends
 - Avoiding school
 - A decline in academic performance
 - Change in sleep-wake pattern (for example, sleeping in and refusing to go to school)
 - Frequent unexplained complaints of feeling sick, headaches, stomach-aches
 - Development of behavioural problems (such as becoming more defiant, running away from home, bullying others)
 - Abusing alcohol or other substances.
- Clinicians should ascertain if the current problems represent a change from the teenager's previous level of functioning or character. For example, depression may

account for the recent academic failure of a 15-year-old girl who had previously topped her class.

- ICD divides symptoms of depression into core and associated symptoms which are important for making the diagnosis.

Core symptoms of depression

- The core symptoms are sadness, unhappiness or irritability, and anhedonia. Irritability is the most ambiguous because it can be present in a wide range of psychiatric conditions (e.g., oppositional defiant disorder, obsessive-compulsive disorder, bipolar illness).
- To substantiate the diagnosis these symptoms must have the following characteristics
 - Pervasiveness - symptoms must be present every day, most of the day)
 - Duration - must be present for at least two weeks)
 - The symptoms must cause impairment in functioning or significant subjective distress, and
 - The symptoms are not the manifestation of the effects of a substance or another medical condition.

Associated symptoms

- These include:
 - Significant weight or appetite change (when not dieting)
 - Insomnia or hypersomnia
 - Psychomotor agitation or retardation
 - Fatigue or loss of energy
 - Feelings of worthlessness or excessive or inappropriate guilt
 - Diminished ability to think or concentrate or indecisiveness, and
 - Recurrent thoughts of death or suicide.
- A key aspect in the assessment of any depressed youth is the evaluation of risk, particularly of suicide and homicide. The outcome of the risk assessment will have an important bearing on management, for example in deciding the best setting (e.g., inpatient, outpatient) in which to treat the patient

Investigations / diagnosis

Screening for depression

- The Patient Health Questionnaire (PHQ)-2 is a simple questionnaire that is used as a screening tool for depression in adults and adolescents and has a high sensitivity and specificity for depression.
- It can be used as an initial assessment before referral at the primary or secondary level. If the patient screens positive for the PHQ-2, that is a score of $>/= 3$, this is suggestive of depression and a full assessment is required to adequately diagnose depression using PHQ-9 where the expertise exists.
- If there are concerns about both depression and anxiety, then the PHQ-4 can be used as screening tool for both anxiety and depression.
- Depending in the score and their distribution, the patient may be referred for further assessment using the Generalised Anxiety Disorder GAD-7 tool, PHQ-9 or both.
- Risk of suicide and how the adolescent functions at home and school should be assessed

Criteria for diagnosing depression

- Panel: Criteria for ICD-10 depressive episode
- Core symptoms (at least two must be present)
 - Depressed mood present for most of the day and almost every day
 - Loss of interest or pleasure in activities
 - Decreased energy or increased susceptibility to fatigue Associated symptoms
 - Loss of confidence or self-esteem
 - Unreasonable feelings of self-reproach or excessive inappropriate guilt
 - Recurrent thoughts of death or suicide, or any suicidal behaviour
 - Diminished ability to think or concentrate
 - Change in psychomotor activity, agitation, or retardation
 - Sleep disturbance
 - Change in appetite with corresponding change in weight

Severity of depression according to the International Classification of Diseases-10th Edition (ICD-10)

| Number of core symptoms* present | Severity of depression |
|---|-------------------------------|
| At least four | mild depressive episode |
| At least six | moderate depressive episode, |
| At least eight | severe depressive episode. |

*Symptoms must be present for at least 2 weeks

Differential diagnosis

- Adjustment disorder – is associated with a stressor and starts within 3 months of the stressor and does not extend more than 6 months of the stressor relates to Dysthymic disorder.
- Persistent low mood which is not severe enough to be depression and last for at least 2 years (1 year for children and adolescents)

Management

- The goal of management is to reduce symptoms and impairment, reduce the risk of relapses and shorten the duration of the current episodes.
- Many children will recover on their own within 4 weeks so watchful waiting is the best approach.
- In all cases of depression, an attempt must be made to identify and address any contributory factors such as abuse or bullying.
- Depression in paediatrics should be treated depending on severity:

Mild depression; psychosocial interventions (including group sessions, supportive psychotherapy, self-help guided therapy, Cognitive behavioral therapy, and behavioral activation). The friendship bench is a cognitive behaviour therapy intervention that can be used by lay persons and provides a forum to address common mental health problems including anxiety and depression.

Moderate to severe depression; antidepressants + psychosocial interventions.

- Antidepressants – selective serotonin reuptake inhibitors (fluoxetine), first line.

- Recommended start up dose 10mg. if 10mg tablets or capsules not available, give 20mg on alternate days. If no improvements after 4-6 weeks, refer/ liaise with tertiary services
- Mild to moderate depression can be managed at the primary and secondary level granted that the services are available and there is monitoring of patient progress.
- Severe depression is best managed at a tertiary facility and if in any doubt, patients should be discussed with a tertiary facility for guidance.

NB. Always assess for **suicide risk** and refer such patients urgently, use the P4 screener for suicide risk.

- SSRI may initially cause agitation especially in the first 2-4 weeks
- Monitor all patients on treatment especially SSRIs closely for any worsening symptoms including suicidal ideation and any change in behaviour. Advise family and close caregivers to monitor for the same.

Primary Level

- Facilities should screen for depression and refer to secondary facilities.

Secondary Level

- Facilities can assess, diagnose, and manage depression.
- If there is unavailability of trained staff or resources, the above interventions have failed or if the patient develops worsening symptoms or suicidal ideation always liaise with the tertiary-level team for referral for assessment and even admission depending on the severity and risk.

Tertiary Level

- Facilities can assess diagnose and manage complicated cases of depression.
- At risk patients should be assessed for inpatient management within appropriate psychiatric units.

Follow up

- Follow up patients in child psychiatry clinic at tertiary level or secondary level PEN-Plus clinic that have availability of multidisciplinary team.

SUICIDE/ SELF-HARM

Suicide is becoming an increasingly important cause of death amongst youth and adolescents. Worldwide it is the fourth leading cause of death in children aged 15-19 years old.

¹Definitions for suicide and self-harm terminology

Suicide, death by suicide, or suicide death: Death caused by injurious behaviour to the self with an intent to die

Suicide attempt, suicidal behavior: Non-fatal, potentially injurious behaviour to the self with an intent to die; might not result in injury

Suicidal ideation, suicidal thoughts: Thinking about, considering, or planning suicide

Self-injury, non-suicidal self-injury: Purposeful acts of physical harm to the self with the potential to damage body tissue but performed without the intent to die

Self-harm: Term used to describe any act of harm inflicted by the self; includes suicide attempt, self-injury, and non-suicidal self-injury

Risk factors / Causes

- *Personal* – history of depression and other mental health illnesses, previous suicide attempt, substance abuse, chronic disease or pain, adverse childhood experiences, sense of hopelessness
- *Environmental* – community violence, discrimination, suicide cluster in community, lack of access to healthcare
- *Societal Risk Factors* - stigma associated with help-seeking and mental illness, easy access to lethal means of suicide among people at risk, unsafe media portrayals of suicide
- *Relationship* – abusive environment, bullying, loss of a relationship, social isolation, history of suicide by a family member or loved one, violent relationships

Figure 1. P4 Screener for Assessing Suicide Risk^{a,b}

Have you had thoughts of actually hurting yourself?

NO YES

4 Screening Questions

1. Have you ever attempted to harm yourself in the past?
NO YES

2. Have you thought about how you might actually hurt yourself?
NO YES → [How? _____]

3. There's a big difference between having a thought and acting on a thought. How likely do you think it is that you will act on these thoughts about hurting yourself or ending your life some time over the next month?
 a. Not at all likely _____
 b. Somewhat likely _____
 c. Very likely _____

4. Is there anything that would prevent or keep you from harming yourself?
NO YES → [What? _____]

| Risk Category | Shaded ("Risk") Response | |
|---------------|---------------------------|---------------------------|
| | Items 1 and 2 | Items 3 and 4 |
| Minimal | Neither is shaded | Neither is shaded |
| Lower | At least 1 item is shaded | Neither is shaded |
| Higher | | At least 1 item is shaded |

^aP4 is a mnemonic for the 4 screening questions: *past* suicide attempt, *suicide plan*, *probability* of completing suicide, and *preventive* factors.
^bCopyright 2010 Kurt Kroenke, MD.

^bAny individual who responds “yes” to a question about thoughts of self-harm is asked 4 additional questions—the 4 P’s on past history, plan, probability, and preventive factors. Shaded responses are those that are more concerning for suicidal ideation.

Management

- General measures
- Screen for risk of harm to self as above
- Manage those with high risk of suicide as below:
 - Manage any injuries that may be present from previous attempts at self-harm
 - Do not leave person alone.
 - Admit
 - Remove access to means of self-harm/suicide (bleach, pesticides, firearms, medications) known to be toxic in overdose including paracetamol, amitriptyline, theophylline).
 - Maintain regular contact if possible – suggested weekly contact for the first 2 months.

Reduce immediate risk:

- Manage the patient who has attempted a medically serious act of self-harm: see Trauma and injuries.
- If medically stable, assess for imminent risk of self-harm/suicide: imminent risk of suicide is likely in a patient who is extremely agitated, violent, distressed or lacks communication with any the following:
 - Current thoughts or plan of self-harm/suicide or
 - History of thoughts or plan of self-harm in the past month or Act of self-harm.

Manage underlying factors:

- Ensure optimal treatment and support of other conditions like chronic pain and mental health conditions (depression, mood disorders, substance use disorders, psychosis, dementia)
- Identify psychosocial stressors like bereavement, intimate partner violence, bereavement, financial or relationship problems, bullying, divorce, separation.

Monitoring and follow-up:

- For all cases of medically serious acts of self-harm/suicide or where there is an imminent risk of self-harm/suicide:
 - Do not leave person alone. Place in a secure, supportive environment in health facility while awaiting referral.
 - Remove access to means of self-harm/suicide (bleach, pesticides, firearms, medications) known to be toxic in overdose including paracetamol, amitriptyline, theophylline).
 - Maintain regular contact if possible – suggested weekly contact for the first 2 months.
 - Follow-up for as long as the risk of self-harm/suicide persists. At every contact, reassess for suicidal thoughts and plans.
- Educate patient/carer:
 - If one has thoughts of self-harm/suicide, seek help from a trusted family member, friend or health worker.
 - Talking about suicide does not trigger the act of suicide, and may lower the risk of following through on suicidal plans.
- Refer to mental health services, if available or community resources like religious centres, crisis centres or support groups.
 - Try to locate family/friends to care for and support patient during this phase.
 - Encourage carers to find support for themselves as well.

POST TRAUMATIC STRESS DISORDER

Definition

This is a mental health disorder that comes about following experiencing or witnessing a negative event (e.g., physical, mental, sexual abuse, trauma) and is characterised by invasive thoughts about the event such as fear and anxiety leading to avoidance of similar situations and interferes in normal daily function or activity.

These symptoms should last for at least a month but can occur up to 6 months or more after the initial event. PTSD is may also be associated with depression, anxiety and substance abuse.

Risk factors

- Related to the event
 - The child's proximity to the event
 - The frequency of the event
 - Duration of the event
- Personal factors
 - Resilience – how easily or well a child recovers from negative events
 - Coping mechanisms
 - Underlying mental health disorder
- Environmental/social factors
 - The lack of family or community after the event
 - Lack of support system

Signs and symptoms

- The American Psychiatric Association characterizes the clinical presentation of PTSD by the presence of several symptom clusters that can be remembered by the mnemonic “**TRAUMA**”. This serves as quick way for people to remember the symptoms but is not a diagnostic test.
 - A **Traumatic** event occurred in which the person experienced, witnessed, or was confronted by actual or threatened serious injury, death, or threat to the physical integrity of self or other and, as a response to such trauma, the person experienced intense helplessness, fear, and horror
 - The person **Reexperiences** such traumatic events by intrusive thoughts, nightmares, flashbacks, or recollection of traumatic memories and images.
 - **Avoidance** and emotional numbing emerge, expressed as detachment from others; flattening of affect; loss of interest; lack of motivation; and persistent avoidance of activity, places, persons, or events associated with the traumatic experience
 - **Unable** to function – symptoms are distressing and cause significant impairment in social, occupational, and interpersonal functioning
 - These symptoms last more than **1 Month**
 - The person has increased **Arousal**, usually manifested by startle reaction, poor concentration, irritable mood, insomnia, and hypervigilance

Investigations / Diagnosis

- A patient who demonstrates these features should be referred to secondary level for further assessment using a diagnostic tool such as the DSM-5.

- DSM-5 criteria for diagnosis of PTSD for children 6 years and older:

A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:

1. Directly experiencing the traumatic event(s).
2. Witnessing, in person, the event(s) as it occurred to others.
3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains: police officers repeatedly exposed to details of child abuse).

B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.)
4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:

1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:

1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).
2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," "The world is completely dangerous," "My whole nervous system is permanently ruined").
3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.
4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).
5. Markedly diminished interest or participation in significant activities.
6. Feelings of detachment or estrangement from others.

7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
- E.** Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. Irritable behaviour and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects.
 2. Reckless or self-destructive behaviour.
 3. Hypervigilance.
 4. Exaggerated startle response.
 5. Problems with concentration.
 6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).
- F.** Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.
- G.** The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- H.** The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.

Criteria for diagnosis of PTSD for Children 6 Years and Younger (DSM-V)

- A.** In children 6 years and younger, exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:
1. Directly experiencing the traumatic event(s).
 2. Witnessing, in person, the event(s) as it occurred to others, especially primary caregivers. Note: Witnessing does not include events that are witnessed only in electronic media, television, movies, or pictures.
 3. Learning that the traumatic event(s) occurred to a parent or caregiving figure.
- B.** Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). Note: Spontaneous and intrusive memories may not necessarily appear distressing and may be expressed as play reenactment.
 2. Recurrent distressing dreams in which the content and/or effect of the dream are related to the traumatic event(s). Note: It may not be possible to ascertain that the frightening content is related to the traumatic event.
 3. Dissociative reactions (e.g., flashbacks) in which the child feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) Such trauma-specific reenactment may occur in play.
 4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
 5. Marked physiological reactions to reminders of the traumatic event(s).
- C.** One (or more) of the following symptoms, representing either persistent avoidance of stimuli associated with the traumatic event(s) or negative alterations in cognitions

and mood associated with the traumatic event(s), must be present, beginning after the event(s) or worsening after the event(s):

Persistent Avoidance of Stimuli

1. Avoidance of or efforts to avoid activities, places, or physical reminders that arouse recollections of the traumatic event(s).
2. Avoidance of or efforts to avoid people, conversations, or interpersonal situations that arouse recollections of the traumatic event(s). Negative Alterations in Cognitions
3. Substantially increased frequency of negative emotional states (e.g., fear, guilt, sadness, shame, confusion).
4. Markedly diminished interest or participation in significant activities, including constriction of play.
5. Socially withdrawn behaviour.
6. Persistent reduction in expression of positive emotions.

D. Alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:

1. Irritable behaviour and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects (including extreme temper tantrums).
2. Hypervigilance.
3. Exaggerated startle response.
4. Problems with concentration.
5. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).

E. The duration of the disturbance is more than 1 month.

F. The disturbance causes clinically significant distress or impairment in relationships with parents, siblings, peers, or other caregivers or with school behaviour.

G. The disturbance is not attributable to the physiological effects of a substance (e.g., medication or alcohol) or another medical condition.

- Assessment should be done by a psychologist or someone trained and experienced in conducting such assessments

Differential diagnosis

- Acute stress disorder
- Adjustment disorder
- Disinhibited social engagement disorder
- Reactive attachment disorder

Management

- Not everyone who has PTSD requires medical attention but some will require treatment as the symptoms can be debilitating. Many people will work through it with social and family support and symptoms will resolve over time – watching and waiting.
- Treatment options when required include psychotherapy and in some cases medication is required.

Psychotherapy – cognitive behaviour therapy which includes group therapy and prolonged exposure therapy amongst others can be used

Medication – these can be used to control the symptoms of PTSD, can be used in combination with psychotherapy.

- Common medications that are used are SSRIs and SNRIs (Selective serotonin re-uptake inhibitors and serotonin-norepinephrine re-uptake inhibitors) with first generation antipsychotics such as aripiprazole or risperidone being the drugs of choice for children and adolescents.

Primary level

- Patients should be assessed and refer to secondary level facility

Secondary / Tertiary Level

- Facilities should assess and manage patients with PTSD if services are available there.

Ongoing treatment for stable patients may be continued at primary level facilities if the skills and services are available.

- **NB.** Always assess for **suicide risk** and refer such patients urgently. Monitor all patients on treatment especially SSRIs closely for any worsening including suicidal ideation and any change in behaviour. Advise family and close caregivers for monitor for the same. Refer such patients as required.

Follow up

- FOLLOW UP WITH COMPETENT QUALIFIED MENTAL HEALTH SERVICE PROVIDER.

PSYCHOSIS

Definition

Psychosis is defined as loss of contact with reality.

Psychosis in children and adolescents is very rare but has the worst prognosis if not identified and treated early. It is divided into early (>13 years) and very early onset (<13 years) psychosis

Risk factors / Causes

- Personal
 - Genetic predisposition
 - Older paternal age
 - Autoimmune disorders
 - Substance abuse
- Genetic syndromes
- Environmental
 - Poor social support
 - Abuse
 - Neglect

Promotion / Prevention

- Campaigns on the prevention of substance abuse especially in school going children

Signs and symptoms – according to DSM-5

- Early signs and symptoms may be difficult to detect but they will become overt over time. Psychosis is defined by the presence of symptoms from at least one of 5 domains:
 1. **Delusions** – these are fixed beliefs that are not amenable to change in light of conflicting evidence.
 2. **Hallucinations** – these are perception-like experiences that occur without an external stimulus. They are vivid and clear, with the full force and impact of normal perceptions, and not under voluntary control.
 3. **Disorganized thinking** (formal thought disorder) - this is typically inferred from the individual's speech. The individual may switch from one topic to another (derailment or loose associations). Answers to questions may be obliquely related or completely unrelated (tangentiality).
 4. **Grossly disorganized or abnormal motor behaviour** – this may manifest itself in a variety of ways, ranging from childlike "silliness" to unpredictable agitation. Problems may be noted in any form of goal-directed behaviour, leading to difficulties in performing activities of daily living. Catatonic behaviour is a marked decrease in reactivity to the environment.
 5. **Negative Symptoms** - Negative symptoms account for a substantial portion of the morbidity associated with schizophrenia but are less prominent in other psychotic disorders. Two negative symptoms are particularly prominent in schizophrenia: diminished emotional expression and avolition.

Investigations

- Get a full history and do a thorough physical examination
- Investigate for organic causes as is appropriate in view of the clinical findings e.g. lumbar puncture for encephalitis, HIV, levels of illicit drugs, electrolyte abnormalities, MRI/CT scan of the brain for brain tumours or history of trauma

Differential diagnosis

- Infections – encephalitis, rabies, neurosyphilis, HIV
- Drug intoxication
- Brain tumours
- Nutritional deficiencies eg. Vitamin B
- Autoimmune disorders – e.g., systemic lupus erythematosus (SLE)

Management

General measures:

- Ensure the safety of the patient and those caring for them.
- Minimise stress and stimulation (do not argue with psychotic thinking).
- Avoid confrontation or criticism, unless it is necessary to prevent harmful or disruptive behaviour.
- Start with antipsychotic drugs - second generation antipsychotics such as aripiprazole or risperidone being the drugs of choice for children and adolescents.

Acute psychosis with agitation:

- Oral diazepam may be used if the patient is willing to take the treatment
- If not cooperative, parenteral diazepam 0.25mg/kg IV stat, can be repeated once
- The patient will then be assessed and continue management depending on the clinical assessment

Primary / Secondary Level

- Facilities should screen for psychosis and refer all children with psychosis to tertiary facilities.

Tertiary Level

- Facilities should assess and initiate the acute management of psychosis.
- Organic causes should be ruled out once the diagnosis and treatment have been established, ongoing care may continue at secondary facility if services are available.

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CHAPTER 11. NEUROLOGY

ACUTE WEAKNESS

Definitions

- Acute onset weakness is typically caused by upper motor neuron lesions (UMNL) and lower motor neuron lesions (LMNL).
- Weakness in a child can be associated with either hypertonia or hypotonia
- Upper motor neuron weakness:
 - Results from lesions in the cerebral cortex and corticospinal tracts down to, but not including, the anterior horn cell in the ventral spinal cord.
 - Produces spastic paralysis- i.e. weak limbs with increased tone (hypertonia) and brisk reflexes. However, in the early stages, the affected limbs may be flaccid.
- Lower motor neuron weakness:
 - Results from lesions located in the anterior horn cell, nerve roots, peripheral nerve, neuromuscular junction, or muscle.
 - Produces flaccid paralysis- i.e. floppy, weak limbs, with reduced tone (hypotonia) and reduced reflexes or even areflexia.

Useful definitions and descriptions for weakness

Paraparesis: Partial paralysis or weakness of the lower limbs

Paraplegia: Complete paralysis of lower limbs;

Diplegia: weakness affecting all four limbs, but predominantly the lower

Quadriplegia: Significant paralysis of all four limbs

Hemiplegia: Paralysis affecting only one side of body (asymmetrical): upper and lower limbs

Truncal paresis: Paralysis affecting the muscles of the trunk

Causes of acute limb weakness due to LMNLs

| Lower motor neurone | Disease conditions |
|-------------------------------|---|
| Anterior Horn Cell | <ul style="list-style-type: none"> • Spinal muscular atrophy (SMA) • Polio |
| Nerve root | <ul style="list-style-type: none"> • Guillain Barre Syndrome • Paralytic rabies |
| Peripheral nerve | <ul style="list-style-type: none"> • Infections: Diphtheria, HIV • Drugs: Isoniazid, Vincristine • Toxins: mercury, helium, glue • Metabolic disorders: diabetes, uraemic neuropathy, vitamin B1 & B12 deficiency |
| Neuromuscular Junction | <ul style="list-style-type: none"> • Organophosphate poisoning • Botulism • Myasthenia gravis |
| Muscle | <ul style="list-style-type: none"> • Congenital myopathies |

| | |
|--|--|
| | <ul style="list-style-type: none"> • Muscular dystrophies – Duchenne Muscular Dystrophy |
|--|--|

Common Causes of Non - traumatic Paraplegia in Malawi

- Spinal Tuberculosis infection
- Epidural abscess
- Transverse Myelitis
- Schistosomiasis - often asymmetrical
- Non polio enteroviruses

| | | |
|---------------------------|--|--|
| UPPER MOTOR NEURON | <p>Cerebral Pathology</p> <ul style="list-style-type: none"> • Head Injury • Cerebrovascular Accidents: stroke, superior sagittal sinus thrombosis (hypernatremic dehydration) • Infections: HIV, meningitis • Tumours • Cerebral Palsy: 'new' neurological signs appear as child develops • Viral encephalitis • Congenital heart disease • Poliomyelitis • Non polio enterovirus • Acute demyelination syndromes: ADEM • Hydrocephalus | <p>Spinal cord compression syndromes</p> <ul style="list-style-type: none"> • Trauma • including HIV-related • Epidural abscess • Schistosomiasis • TB spine • Paravertebral tumours (e.g. Burkitt's lymphoma) • Spinal cord tumours • Spinal cord haemorrhage • Cysticercosis • Transverse Myelitis, |
| LOWER MOTOR NEURON | <p>Peripheral Neuropathies</p> <ul style="list-style-type: none"> • Guillain-Barre Syndrome (GBS) • HIV-related polyneuropathies: direct HIV-effect; or co-infections (e.g. CMV) • Rabies (flaccid form) • Diphtheria • Botulism • Tick Paralysis | <p>Muscle pathology</p> <ul style="list-style-type: none"> • Acute viral myositis • Muscular dystrophies (and other myopathies) • Myasthenia Gravis crisis |
| MISCELLANEOUS | <ul style="list-style-type: none"> • Organophosphate poisoning • Vitamin B deficiencies | |

Approach to a child with limb weakness

History

- Development of limb weakness
 - Speed of onset: acute, subacute or chronic
 - Progressive or static
 - Symmetry
 - Associated muscle tenderness
 - Paraesthesia of fingers and toes
 - Bowel and bladder function
 - Swallowing or speech difficulties
 - Respiratory difficulties
- Current associated symptoms
 - Fever
 - Confusion or deterioration of consciousness; seizures
 - Meningism (headache, photophobia, neck stiffness)
 - Symptoms of raised intracranial pressure (headache, vomiting, visual disturbance and in end stage bradycardia, high blood pressure and papillary edema)
 - Back pain or deformity
 - Seizures
 - Recent history of chicken pox
- Preceding health
 - Recent ‘viral’ illness; or history of meningitic symptoms
 - Past medical history (or episodes suggestive of) meningitis/ cerebral malaria/ sickle cell disease
 - Indicators of HIV infection or HIV treatment
 - Progressive weight loss, night sweats and TB exposure
 - Birth history, developmental milestones (developmental delay or regression), learning difficulties
 - Immunisation history

Examination

- Anthropometry
- Temperature, BP, heart rate to determine autonomic dysfunction.
- General examination: dysmorphology, Signs of HIV infection
- Full neurological assessment including fundoscopy
 - GCS and false lateralising signs due to cerebral edema
 - Full cardiac exam .
 - Cranial nerve exam including pupillary reaction and extraocular movements
 - Peripheral exam should comment on limb appearance, tone, power, reflex, sensation, gait of the patient is able to walk and cerebellar findings
 - Gower's sign, pseudohypertrophy of muscles (? Duchenne muscular dystrophy

- General exam
 - Cardiac examination including feeling all the pulses
 - Respiratory examination especially for hypoventilation/ associated pneumonia
 - Spinal gibbus or kyphoscoliosis
 - Muscle atrophy or tenderness
 - Spinal tufts or pits, and head circumference
 - Dactylitis, skull bossing (? sickle cell disease)
 - check for presence of all pulses
 - Evidence of valvular cardiac disease.

Promotion / prevention

- Immunisation e.g. polio, Haemophilus influenzae, BCG
- Promote good road safety practices e.g. use of helmets on motorcycles, use of car seat/ seat belts in motor vehicles.
- Use of Isoniazid preventative therapy in all children less than 6 years old who have a positive T.B contact

Investigations

- Infective causes:
Septic screen if febrile: FBC, LP if meningitic, reduced consciousness, or GBS.
Note: There is need to exclude features of raised intracranial pressure before an LP is done to avoid cranial herniation.
- Suspected TB: Mantoux test, Gene Xpert on induced sputum or gastric aspirate, CXR
- HIV testing
- Urine and stool for ova/ cysts/ parasite examination
- FBC: Fe deficiency; clotting profile including platelet count
- Sickle cell electrophoresis test
- Imaging:
 - USS head (infants)
 - cardiac echo
 - spinal Xray
 - CT/ MRI brain - discuss with seniors
- Muscle biopsy: may be useful if a myopathy suspected- discuss with specialist

Send stool specimen (and notification) to Ministry of Health in ALL cases of acute flaccid paralysis (please know your AFP focal person)

Management

Primary Level

- All children presenting with a new-onset neurological sign at a primary healthcare facility must be referred to a secondary healthcare facility for initial work-up and acute care
- If the child is at risk of respiratory compromise (such as in GBS, polio) consider referral directly to tertiary care level for airway

management/respiratory support

Secondary Level

- Specific treatments depend on cause identified or suspected.
- Meningitis: Broad-spectrum antibiotics, preferably after lumbar puncture (LP) (note: there are only very few absolute contraindications for LP). Contraindicated in a child with signs of raised intracranial pressure and suspected compressive myelopathy.
- Cerebral or spinal abscess: Ceftriaxone and seek surgical opinion.
- TB spine and tuberculoma: TB treatment and orthopaedic opinion.
- Schistosomiasis: Praziquantel, 40 mg/kg STAT (consider this whenever no other cause for paralysis found and in ALL cases of paraparesis). If very probable consider treating for three days with 60 mg/kg OD.
- Consider steroids for ALL spinal cord lesions, unless evidence of bacterial infection.

Tertiary Level

- Suspected GBS or polio with airway compromise will need airway assessment for possible intubation and respiratory support.
- Tumours: treat with surgery/ chemotherapy if appropriate. Palliative care.
- Organophosphate poisoning as per protocol.
- Thrombotic disease: prophylactic aspirin.

Follow-up

- Patient guided – Depending on cause identified, response to treatment, family wishes and social circumstances. Ideally the child will be stable/ improving on discharge. Therefore the family should have knowledge of the condition and its prognosis. The medical team and family can discuss how best they can assist the child.
- Early rehabilitation with physiotherapy – the intensity and duration of the rehabilitation will be guided by the severity of the neurological deficit.
- In children with progressive or terminal conditions, or those who are likely to have ongoing physical/ medical/ psychosocial needs, plans for follow up and community support should be made. Refer palliative care team.

STROKE

Definition

A neurological deficit attributed to an acute focal injury of a CNS vascular territory with neuro-radiological evidence of an ischemic or a haemorrhagic lesion

Risk factors / Causes

| ISCHAEMIC | HEMORRHAGIC |
|--|---|
| Vascular <u>Noninflammatory</u> <ul style="list-style-type: none"> Arterial dissection Hypertension Moyamoya Congenital heart disease <u>Inflammatory</u> <ul style="list-style-type: none"> Takayasu arteritis Giant cell arteritis Kawasaki disease Infectious/postinfectious vasculitis e.g HIV, Varicella, Syphilis, TB, Fungal | Vascular <ul style="list-style-type: none"> Hypertension Vascular malformations Arteriovenous malformations Cavernous malformations Aneurysms |
| Hematologic <ul style="list-style-type: none"> Sickle cell disease Iron deficiency anaemia <u>Inherited prothrombotic states</u> <ul style="list-style-type: none"> Protein C Protein S Factor V leiden Polycythaemia vera <u>Acquired prothrombotic states</u> <ul style="list-style-type: none"> Estrogen contraceptives Protein losing enteropathy Nephrotic syndrome Leukemia and other malignancies Pregnancy | Hematologic <ul style="list-style-type: none"> Thrombocytopenia Platelet dysfunction (ITP) Haemophilia Sickle cell disease |
| Cardiac <ul style="list-style-type: none"> Congenital heart disease, arrhythmia, cardiomyopathy, endocarditis, Rheumatic heart disease, myocarditis, cardiac surgery | Other <ul style="list-style-type: none"> Brain tumours |

Promotion / prevention

- Preventative measures depend on the etiology of stroke.
- As sickle cell anaemia is a common cause of stroke in our setting, chronic blood transfusion and the use of hydroxyurea play a role in preventing both primary and secondary strokes in these patients. (See the sickle cell section).
- Antenatal screening and treatment of syphilis; and treatment of congenital syphilis will prevent manifestations of tertiary syphilis.
- Children with stroke frequently present late to health facilities in our setting due to delayed self/ primary/ secondary health facility referral to tertiary level care.

Signs and symptoms

- Focal Manifestations
 - Hemiparesis and hemifacial weakness
 - Speech or language disturbance
 - Visual disturbance
 - Ataxia
 - Developing handedness before the age of 1 year
- Non localizing manifestations (usually pointing to haemorrhagic stroke)
 - Headache, neck pains
 - Altered mental status
 - Vomiting
 - Seizures

The signs and symptoms of stroke are frequently overlooked. The American Heart Association encourages the use of the acronym FAST standing for:

- **F** facial droop
- **A** arm weakness
- **S** speech difficulty
- **T** time to seek help.

This acronym can be used to help raise awareness amongst parents and health care workers at all levels of health care in so doing improving the early identification of strokes amongst children.

Investigations

Imaging:

- Urgent neuroimaging is vital to confirm the diagnosis of stroke and delineate the type of stroke guide appropriate targeted investigations
- If ischaemic, this facilitates the institution of hyper acute reperfusion therapies i.e within 4.5 hours from when the patient was last well for intravenous thrombolysis and mechanical thrombectomy within 24 hours from when they were last seen well
- Obtain a brain MRI and MRI Angiography as initial studies as these are more sensitive for the diagnosis of acute ischaemic stroke particularly on diffuse weighted imaging.
- If this is not available or cannot be obtained urgently, a CT scan of the brain with angiography can be done.
- It should be noted that children with haemorrhagic stroke are at risk of

subsequent ischaemic strokes due to compression of blood vessels as a result of mass effect from intracranial haemorrhage and vasospasm.

- It is possible to clinically localize strokes in children upon presentation even before confirmation with brain imaging. The table below can assist with stroke localization.

| | |
|--|---|
| Anterior cerebral artery (ACA) | Contralateral leg > arm and face weakness. |
| Right middle cerebral artery (MCA) | Left face & arm > leg weakness, left field cut, neglect |
| Left middle cerebral artery (MCA) | Right face & arm > leg weakness, right field cut, aphasia |
| Posterior cerebral artery (PCA) | Contralateral homonymous hemianopsia w/ central sparing |
| Internal Capsule (Deep MCA Branch) | Contralateral face=leg=arm weakness |
| Thalamus (MCA and PCA penetrators) | Can be very variable! Hemibody sensory loss, aphasia, field cuts all possible |
| Brainstem | Multiple cranial nerve anomalies |
| Lateral Medullary posterior inferior cerebellar artery (PICA) | Ipsilateral Horner's, ipsilateral ataxia, ipsilateral face pain/temp loss, contralateral body pain/temp loss, dysarthria/dysphasia. |
| Dystonia | Basal ganglia |

Laboratory Investigations:

- FBC
- Urea, Electrolytes and Creatinine
- Serum Glucose
- Clotting profile (PT, PTT, INR platelets)
- HB electrophoresis / Sickle cell rapid test
- VDRL
- LP: if infection suspected e.g. herpes, varicella encephalitis, TB. LP should only be done after brain imaging deems it safe.
- EEG if abnormal movements are suspected to be seizures and as an aid for making a diagnosis e.g. in herpes encephalitis.
- ECG, Cardiac Echo
- Consider a hypercoagulable state (prothrombotic work up: Protein C, S, antithrombin III)
- CRP, ESR and an ANA if suspicious of an inflammatory condition or unexplained etiology e.g. SLE, polyarteritis nodosa, adenosine deaminase 2 deficiency and primary angiitis of the CNS

Differential diagnosis

- Cerebral venous sinus thrombosis
- Todd's paralysis

- Migraine
- Bell's palsy
- Alternating hemiplegia of childhood
- Brain tumours
- CNS Infection: meningitis, encephalitis, abscess
- Posterior reversible encephalopathy syndrome (PRES)
- Acute disseminated encephalomyelitis (ADEM)
- Acute cerebellar ataxia

Management

Primary Level

- Manage ABCDE and neuroprotective care then urgent referral
- Keep the patient as cool as possible, high temperatures exacerbate ischemia
- Maintain normal glycaemia

Secondary / Tertiary level

- Manage the patient in a high care setting e.g HDU
- Patient should be placed on a monitor.
- Ascertain patient's ABC are stable
- Maintain normothermia treat any fever greater than 38oC.
- Maintain a euglycaemic state, avoid hyperglycaemia.
- Avoid hypotension.
- Monitor Fluid input and output.
- Treat seizures appropriately (see seizure management).
- Consider administration of hypertonic saline or mannitol
- Refer to neurosurgeon for CSF diversion: EVD or VP shunt if hydrocephalus

Ischaemic Stroke

- Discuss with your overseeing consultant if low dose aspirin 3-5mg/kg to a maximum of 300mg should be started depending on the absence of haemorrhagic transformation.

Haemorrhagic stroke

- If the cause of the stroke is hypertension and the blood pressure is elevated anti-hypertensives should be used cautiously with frequent BP monitoring.
- Do neurological observations and watch out for early signs of raised intracranial pressure i.e vomiting, worsening headache if awake, papilledema

Note: The development of cushings triad might be a late sign

- Discuss with neurosurgeons

Medical management of raised ICP

General neuroprotective measures include:

- Rapid treatment of hypoxia, hypercarbia, and hypotension

- Elevation of the head of the bed to at least 30 degrees
- Maintenance of the head and neck in the midline to facilitate venous drainage
- Aggressive treatment of fever with antipyretics
- Maintenance of adequate analgesia
- Control of shivering in intubated patients with muscle relaxants (eg, vecuronium, rocuronium)

Supportive and Rehabilitative management

- Maintained adequate Nutrition (May need feeding aids like NGT)
- Hourly turning to prevent pressure sores.
- Frequent changing of soiled/wet beddings/ nappies
- Urinary catheterization if necessary
- Initiate physiotherapy once the patient is haemodynamically stable.
- Psychosocial support should be offered to parent and child.

Long Term Management

- Follow up all patients in outpatient clinics
- Treat underlying cause to prevent recurrence of stroke
- Continued physiotherapy including mobility aids if necessary
- Some patients may need Speech therapy and occupational Therapy
- School needs assessment
- Family counselling
- Feeding and nutritional support
- Early rehabilitation through physiotherapy – the intensity of the rehabilitation will be guided by the severity of the neurological deficit.

Follow-up

- Patient guided – Depending on cause identified, response to treatment, family wishes and social circumstances. Ideally the child will be stable/ improving on discharge therefore the family should have knowledge of the condition and its prognosis. The medical team and family can discuss how best they can assist the child.
- In children with progressive or in terminal condition, or those who are likely to have ongoing physical/ medical/ psychosocial needs, plans for follow up and community support should be made. Involve palliative care team

HYDROCEPHALUS

Definition

A disorder characterized by ventricular dilatation and increased intracranial pressure resulting from the excessive accumulation of CSF within the cerebral ventricles and/or the sub arachnoid spaces which leads to raised intracranial pressure

Communicating hydrocephalus occurs as a result of impaired CSF absorption in the sub-arachnoid spaces. It may also result from an increased production of CSF.

Non communicating (Obstructive) hydrocephalus occurs as a result of excess accumulation of CSF due to structural obstruction of CSF flow within the ventricular system. The obstruction can occur at the level of the Foramen of Munroe, the aqueduct of Sylvius, the fourth ventricle or its outlets. Dilatation will occur proximal to the level of the obstruction.

Note: Many cases of hydrocephalus have a combination of obstructive and absorptive causes.

Risk Factors / Causes

| COMMUNICATING HYDROCEPHALUS | NON COMMUNICATING HYDROCEPHALUS |
|--|---|
| Congenital Causes <ul style="list-style-type: none"> • Infections (TORCH) • Intraventricular haemorrhage • Post infectious Aqueduct stenosis • Choroid plexus papilloma | Congenital Causes <ul style="list-style-type: none"> • Neuro tube defects (Myelomeningocele associated with Chiari 2 malformation, Encephalocele) • Aqueduct stenosis • X linked hydrocephalus • Dandy-Walker malformation • Vascular malformations. • Infections (TORCH) • Intraventricular haemorrhage • Post infectious Aqueduct stenosis • Choroid plexus papilloma |
| Acquired Causes <ul style="list-style-type: none"> • Post Haemorrhagic hydrocephalus • CNS infections • Dural venous sinus thrombosis | Acquired Causes <ul style="list-style-type: none"> • Post Haemorrhagic hydrocephalus • CNS tumours (medulloblastoma, astrocytoma, ependymoma) • CNS infections (bacterial and TB meningitis) |

Prevention / Promotion

- Immunisation
- Early diagnosis and adequate treatment of meningitis to prevent the complication of Hydrocephalus.
- Follow up patients with Meningitis after discharge and monitor head circumference.
- Maternal prenatal USS can assist in diagnosing fetal hydrocephalus due to structural malformations.
- Under five clinic nurses should be encouraged to measure infant head circumferences each time they come for their weight checks. Early detection and timely referral can change the outcome and the quality of lives of these children.
- Every preterm baby born less than 36 weeks should have cranial USS before discharge to look for features of intraventricular hemorrhage.
- Infants treated with bacterial meningitis should be flagged in the road to health books to have serial head circumference checks at their local clinic
- Early presentation to the hospital is critical in ensuring good long-term outcomes.
- Promote head circumference monitoring for all infants
- Folic acid before conception
- Avoid smoking, drinking alcohol and substance abuse during pregnancy

Signs and Symptoms

- Rapidly increasing head circumference (see image below on how to measure)
 - Measure and document at least weekly.
 - Compare to WHO head circumference charts for age and sex
- Bulging fontanelle
- Widening suture lines (if not closed yet)
- Distended scalp veins
- Sun setting eye sign
- Signs of raised intracranial pressure (early morning headache, vomiting, blurred vision, high BP, low PR, reduced conscious level, bradypnoea)
- Developmental delay or regression and/or ataxia
- Abnormal hypothalamic function in childhood
- Seizures

How to measure head circumference



Head circumference measurement

Measure the head circumference with a non-stretchable tape. Take three measurements until you get a consistent value. Use the same chart for the same child over time.

Investigations

- Cranial USS
- MRI or CT Scan of the brain
- CSF samples: for Cell counts and differential, Microscopy culture and sensitivity and Gene X-pert for T.B
- Consider ventricular tap if signs of infection / raised intracranial pressure (ICP) and prior to surgery.

HOW TO PERFORM A VENTRICULAR TAP

Equipment

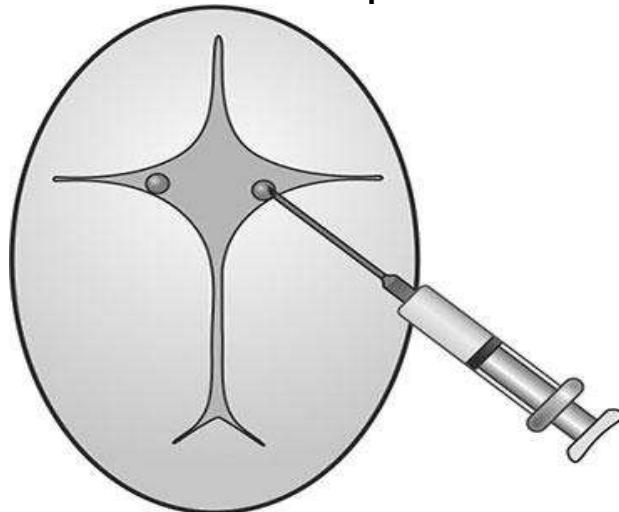
- Shave pack and Skin cleaning solution
- Sterile gloves
- Sterile drapes / Dressing pack
- Lumbar puncture needle (size 22G or 23G)
- Specimen bottles
- Plaster

Procedure

- 1) Shave the scalp overlying the lateral angle of the anterior fontanelle taking care not to injure the skin
- 2) Clean a wide area of the head with appropriate solution
- 3) Position the infant supine with the top of the infant's head facing toward the operator
- 4) With left hand index and thumb, move skin over point of entry such that when tap done and the needle is removed, the skin moves back to original position and the track of the needle is broken

- 5) Insert the spinal needle into the lateral angle of the fontanelle and advance it toward the inner angle of the ipsilateral eye. The needle should be inserted smoothly without change of direction to minimise trauma to the brain.

Position for ventricular tap



Kocher's point, is a traditional point for ventricular tap. Kocher's point is defined as a point 2-3 cm from the midline and 10-12 cm from the glabella or 1 cm anterior to the coronal suture.

- 6) Once the ventricle has been penetrated, the stylet is removed, and the CSF should drip out rather than be aspirated.
- 7) Once the required amount of CSF is obtained the needle should be removed and pressure applied to the area to prevent leakage of CSF.
- 8) Clean the area with 1% chlorhexidine and let dry.

Contraindications for Ventricular Tap

- Infection over the site of entry.
- Bleeding disorder due to coagulopathy.

Differential Diagnosis

- Tumours e.g
- Craniopharyngioma
- Pituitary Tumors
- Primary CNS Lymphoma
- NF1
- Sturge Weber
- Sotos
- Subdural Empyema
- Idiopathic Intracranial Hypertension
- Other causes of Macrocephaly e.g Familial macrocephaly, Sotos Syndrome

Management

Primary Level

- Manage ABCCCD and refer

Secondary / Tertiary level

- Treat infection if any (ventriculitis may require longer term parenteral treatment than meningitis).
- Therapeutic ventricular tap if signs of acute raised ICP.
- Medical reduction of CSF while awaiting surgery in communicating hydrocephalus- Acetazolamide or Furosemide
- Surgical/Neurosurgical referral for ventriculo-peritoneal (VP) shunt or endoscopic third ventriculostomy (ETV).

COMPLICATIONS OF VP SHUNTS

- Shunts can become infected or blocked and need to be treated urgently.
- Suspect infection or blockage in a child with VP shunt if any of the following:
 - Vomiting
 - Headache
 - Reduced level of consciousness
 - New onset or worsening seizures
 - Increasing head circumference
 - Ataxia
 - Cranial nerve palsy
 - Visual disturbance
 - Fever
 - Developmental regression
 - Ascites and peritonitis
 - Pain and/or inflammation along the shunt track

Investigations of possibly infected or blocked shunts

- FBC
- Blood culture if febrile
- Xray shunt series
- USS brain/ CT scan/ MRI if possible
- **Avoid LP as this can result in coning if shunt blocked!** If possible, perform a ventricular tap.

Management of Blocked Shunts

Primary Level

- Manage ABCCCD and refer

Secondary Level

- Assess patient and initiate treatment
 - Manage ABCD
 - Start iv antibiotics as for meningitis (Ceftriaxone 100mg/kg I.V daily)
- Urgent referral to Tertiary facility

Tertiary Level

- Manage the patient, including complications and comorbidities.
 - Manage ABCCCD
 - Start iv antibiotics as for meningitis (Ceftriaxone 100mg/kg I.V daily)
- Refer to neurosurgeons for possible urgent shunt removal if blocked or infected and subsequent revision / replacement at a later date.
- Coordinate efforts of the multidisciplinary team
 - Physiotherapy
 - Occupational therapy
 - Nutritional support
 - Hearing and Visual assessment
 - Hydrocephalus parental support groups

Follow up

- Follow up in a surgical or neurosurgical clinic every 3 months or more frequently if complications arise.
- Follow up can be done in tertiary facilities or secondary facilities where a multidisciplinary team is available.

CEREBRAL PALSY (CP)

Definition

It is a group of permanent disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain.

Risk Factors / Causes

Prenatal Factors:

- Maternal alcohol consumption, smoking, obesity
- Intrauterine infections; cytomegalovirus, syphilis, varicella virus, and toxoplasmosis
- Gestational hypertensive disorders
- Intrauterine growth restriction, antepartum hemorrhage, severe placental pathology, multiple pregnancy
- Genetic disorders
- Congenital abnormalities, particularly structural central nervous system abnormalities

Perinatal Factors:

- Perinatal hypoxia-ischemia
- Prematurity – due to periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and/or bronchopulmonary dysplasia (BPD)
- Kernicterus – typically resulting in choreoathetosis CP
- Perinatal stroke

Postnatal Factors in the older child (up to age 5 years):

- Infections e.g sepsis/meningitis, cerebral malaria
- Stroke; in congenital heart disease, prothrombotic disorder, sickle cell disease, vasculopathy, or metabolic disorder
- Traumatic brain injury
- Severe hypoxic events e.g near-drowning and uncontrolled seizures
- Metabolic disorders- hypoglycaemia, hypo and hyper natraemia, hypocalcemia
- Intracranial bleeding e.g trauma, coagulopathies, shaken baby syndromes

Promotion / Prevention

- Prevention is dependent on the causative insult.
- Focused antenatal and intrapartum care could reduce the risk for cerebral palsy.
- Parents and primary health care workers should be educated on early signs suggestive of CP.
- All children attending routine Under 5 clinic visits should be screened for these signs.

- Monitor at risk children for early detection and intervention.

Children presenting with these features should be referred early for evaluation:

- Abnormal eye/body movements
- Poor head control by 3 months
- Not sitting by 8 months
- Not walking by 18 months
- If a child is having developmental regression/ losing milestones, consider other causes.
- Refer to a tertiary facility for comprehensive assessment.

Signs and symptoms

- Specific CP syndromes recognized after five years of age, although suggestive signs and symptoms may be present in infancy.
 - Poor feeding, drooling, choking on feeds
 - Failure to thrive
 - Irritability, poor sleep, vomiting,
 - Leg scissoring
 - Difficult to handle and cuddle due to opisthotonic posturing
 - Poor visual attention
 - Hearing impairment
 - Delay disappearance of primitive reflexes
 - Seizures and abnormal movements
 - Motor tone in the extremities may be normal, decreased, or increased
 - Persistent or asymmetric fisting, abnormal oromotor patterns include tongue retraction and thrust, tonic bite, oral hypersensitivity, and grimacing.
 - Poor head control with excessive head lag. Not achieving motor milestones (e.g., six motor milestones - roll prone to supine, roll supine to prone, sit with support, sit without support, crawl, and cruise).
 - Constipation
 - Emotional and behavioral problems
- Perform full head to toe examination. Look out for features of dysmorphism, neurocutaneous lesions, malnutrition, neglect and pressure sores.

Classification of CP according to the Surveillance of Cerebral Palsy in Europe (SCPE)

1. **Spastic syndromes**: symmetric or asymmetric, involve one or more extremities, spastic hypertonia, and if very severe form may have rigidity in flexion or extension:

- ***Spastic Diplegia*** Lower limbs affected more than upper limbs. If mild, good hand function is preserved. In severely affected patients, upper limb function compromised, sensory loss, associated involuntary movements, and intellectual disability.
- ***Spastic Hemiplegia*** arm and leg on one side affected. The upper limb typically more affected than lower limb. Usually vascular origin
- ***Spastic Quadriplegia*** bilateral arms and legs equally affected with severe intellectual impairment and other comorbidities (severe intellectual disability, speech and language impairment and visual impairment, epilepsy, feeding difficulties)

2. **Dyskinetic syndromes**: involuntary movement:

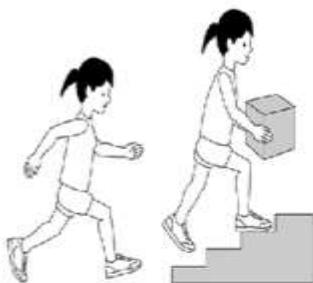
- ***Choreoathetosis***: rapid, irregular, unpredictable contractions of individual muscles or small muscle groups that involve the face, bulbar muscles, proximal extremities, and fingers and toes. Athetosis consists of slow, smooth, writhing movements that involve distal muscles. It should also be noted that some children with CP can have choreic and athetoid CP types in isolation.
- ***Dystonia***: pyramidal signs and anarthria. Sudden involuntary increase in tone that affects both flexor and extensor muscles. The limbs become stiff during attempted movement or with emotion

3. **Ataxic CP (rare)**: Motor milestones and language skills are delayed. Ataxia usually improves with time. Speech is slow, jerky, and explosive.

4. **Mixed CP**: mixture of all above motor disorders.

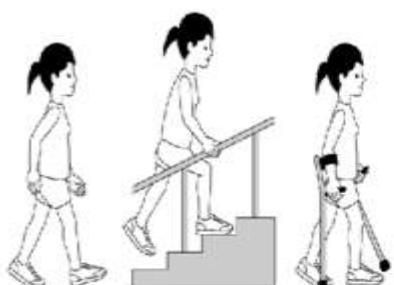
GROSS MOTOR FUNCTION CLASSIFICATION SYSTEM (GMFCS)

- The gross motor function of children and young people aged above 6 years of age with cerebral palsy can be categorized into 5 different levels using GMFCS tool.
- GMFCS looks at movements such as sitting, walking and use of mobility devices. It is helpful because it provides families and clinicians with:
 - A clear description of a child's current motor function
 - An idea of what equipment or mobility aids a child may need in the future, e.g. crutches, walking frames or wheelchairs.



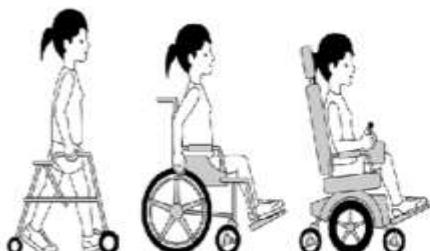
GMFCS Level I

Youth walk at home, school, outdoors and in the community. Youth are able to climb curbs and stairs without physical assistance or a railing. They perform gross motor skills such as running and jumping but speed, balance and coordination are limited.



GMFCS Level II

Youth walk in most settings but environmental factors and personal choice influence mobility choices. At school or work they may require a hand held mobility device for safety and climb stairs holding onto a railing. Outdoors and in the community youth may use wheeled mobility when traveling long distances.



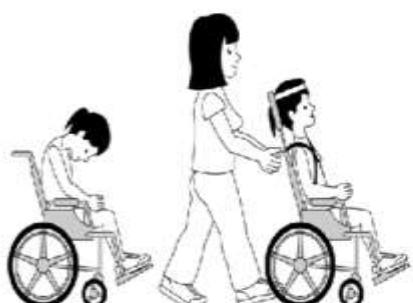
GMFCS Level III

Youth are capable of walking using a hand-held mobility device. Youth may climb stairs holding onto a railing with supervision or assistance. At school they may self-propel a manual wheelchair or use powered mobility. Outdoors and in the community youth are transported in a wheelchair or use powered mobility.



GMFCS Level IV

Youth use wheeled mobility in most settings. Physical assistance of 1-2 people is required for transfers. Indoors, youth may walk short distances with physical assistance, use wheeled mobility or a body support walker when positioned. They may operate a powered chair, otherwise are transported in a manual wheelchair.



GMFCS Level V

Youth are transported in a manual wheelchair in all settings. Youth are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements. Self-mobility is severely limited, even with the use of assistive technology.

Differential diagnosis

- HIV encephalopathy
- Leukodystrophy
- Congenital myopathy
- Muscular dystrophy
- spinal muscular atrophy
- Wilson's disease
- Huntington's Chorea
- Tethered cord syndrome
- Genetic syndromes (Angelman Syndrome)
- Hereditary Spastic paraplegia

Associated conditions/ comorbidities

- **Neurological disorders:** hearing impairment, visual impairment, pain, intellectual disability, speech-language disorders
- **Epilepsy:** onset of seizures during the first two years of life, usually partial seizures with secondary generalization. N.B seizure syndromes like infantile spasms may cause or worsen cerebral palsy.
- Behavior disorder, sleep disorder, self-injurious behavior, attention deficit
- **Urinary disorders:** (enuresis) bladder control problems
- **GI problems:** Chronic constipation, gastroesophageal reflux and/or vomiting, swallowing disorders,
- **Growth failure:** primarily due to poor nutrition. Other feeding issues include gastroesophageal reflux disease, pseudobulbar palsy with drooling, constipation,
- **Pulmonary disease:** recurrent aspiration, scoliosis, ineffective cough and clearance of pulmonary secretions
- **Orthopedic disorders:** subluxation, dislocation, and progressive dysplasia of the hip. Foot deformities, scoliosis, osteopenia, pathological fractures.
- **Skin:** pressure sores.

Investigations

- Should be guided by history, clinical examination and the presence of comorbidities.
- History and clinical examination will guide in identifying the timing of CP (prenatal, perinatal or postnatal)
- Consider imaging with brain ultrasound and/or CT scan/ MRI if organic cause suspected e.g. if there is developmental regression
- Investigate for any intercurrent problems e.g UTI, aspiration pneumonia.
- X- rays for dislocations and fractures

Management

- This requires a multidisciplinary approach. There is need for ongoing follow up care in a general/neurology clinic to address the evolving needs as the child ages.

Primary Level

- Education of child and guardians and community.
- Immunizations
- Nutrition: Needs ongoing assessment and rehabilitation. Look out for and manage undernutrition

- Screen all children attending routine Under 5 clinic visits for developmental delay. Children presenting with these features should be referred to the District Hospital for early evaluation.

Secondary

- Ophthalmology: Visual assessment
- Audiology: Hearing assessment and aids
- Physiotherapy: for limbs and chest. Physical mobility aid e.g wheel chair, feeding/sitting chair
- Speech therapy: sucking and swallowing assessment and therapy
- Antispasmodic Drugs: Diazepam 1-2.5mg po 4 to 6 hourly as initial dose to reduce spasticity. Can increase dose depending on response.
- Social and psychological support, palliative care.
- Adolescent sexual and reproductive health: discuss birth control.
- Explore education and occupational therapy based on the child's level of function
- Follow up children in General clinic and coordinate care with the different subspecialties as indicated above.
- Seizure management should be initiated in all children with epilepsy.
- Refer Children with poorly controlled epilepsy and those needing specialist care that is not available in the district hospital to the central hospital.

Tertiary Level

- Ophthalmology: Visual assessment
- Audiology: Hearing assessment and aids
- Physiotherapy: for limbs and chest. Physical mobility aid e.g wheel chair, feeding/sitting chair.
- Speech therapy: sucking and swallowing assessment and therapy
- Audiology: Hearing assessment and aids
- Drugs against spasticity and dystonia:
 - Baclofen: 1 - 2 mg/kg 8hrly. Side effects: confusion, sedation, hypotonia, ataxia, paresthesias, and nausea. Seizures if drug discontinued abruptly
 - Diazepam 1 - 2.5mg po 4 to 6 hourly as initial dose. Can increase dose depending on response.
- Antiepileptics – see seizures protocol
- Orthopedics: Contracture release, fracture care, acute hip disorders
- Social and psychological support, palliative care
- Adolescent sexual and reproductive health: discuss birth control
- Explore education and occupational therapy based on the child's level of function

Follow up

Follow up children in PEN-Plus clinic and coordinate care with the different members of the multidisciplinary team.

EPILEPSY

Definitions

A seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive neuronal activity in the brain. The onset of seizures can be focal, generalised, or unknown. Some focal seizures can evolve to bilateral tonic-clonic

Clinical definition of epilepsy, intended as a disease of the brain defined by any of the following conditions:

1. At least two unprovoked (or reflex) seizures occurring > 24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of epilepsy syndrome.

Risk Factors / Causes

- Idiopathic
- Infection: meningitis, abscess, encephalitis, neurocysticercosis, sepsis
- Metabolic and endocrine disorders: hyponatremia, hypocalcemia, hyperthyroidism
- Trauma: intracranial bleeding
- Perinatal complications: prematurity complications, perinatal asphyxia
- Drugs and alcohol (and its withdrawal)
- Tumors
- Syndromes and congenital disorders
- Vascular disease / Stroke: sickle cell, vasculitis, ischemia, brain malformations
- Neurocutaneous syndromes: Neurofibromatosis, Sturge Webber, Tuberous sclerosis
- Neurodegenerative or neurometabolic disease
- Epilepsy syndromes: Lennox Gestaut, Sturge Weber, benign familial, myoclonic epilepsy of the infant, Infantile spasms.
- Vitamin deficiency: vitamin B6 deficiency
- Note: In neonates and infancy most seizures are symptomatic of an identifiable etiology - HIE, metabolic disturbances metabolic: hypoglycaemia, hypocalcaemia, vit B6 deficiency, phenylketonuria, central nervous system or systemic infection.
- Note: In HIV/Aids consider CNS Toxoplasmosis, Cryptococcal meningitis, Herpes encephalitis, bacterial meningitis, CNS lymphoma, neurosyphilis

Prevention / Promotion

- Health education is needed to demystify epilepsy.
- Early diagnosis and optimal treatment can lead to improved long-term neuro developmental outcomes.
- Tools like epilepsy diaries should be rolled out to accurately monitor seizure frequency at home.
- Establish clinics within District and Central hospitals to follow up all patients regularly.
- Encourage the use of video on smart phones to document seizure episodes.
- Advise the patient to avoid sleep deprivation.
- Inform the school that the child has epilepsy.
- Educate the family on first aid for seizure episodes (see table below)

First Aid Measures during a Seizure (Advise for Parents / Teachers)

- Do not panic, remain calm. Note time of onset of the seizure
- Remove any harmful objects around them
- Loosen the child's clothing especially around the neck.
- Place the child in a left lateral position with the head lower than the body.
- Wipe any vomitus or secretions from the mouth.
- **Do not insert any object into the mouth even if the teeth are clenched.**
- Do not give any fluids or drugs orally.
- Stay near the child until the seizure is over and comfort the child as he/she is recovering.
- If the seizure lasts longer than 5 minutes seek medical attention.

Signs and symptoms

Focal seizures

- Originate from one hemisphere of the brain. They may be discretely localized or more widely distributed.
- A focal seizure may or may not be associated with impaired awareness.
 - Impaired awareness is defined as the inability to respond normally to external stimuli due to altered awareness and/or responsiveness.
 - When the patient is aware throughout the seizure, the seizure is described as a focal seizure without impairment of awareness (previously referred to as simple partial seizure).
 - Focal seizures without impairment of awareness may also manifest psychic symptoms including dysphasia, feelings of familiarity ("déjà vu"), distortions of time, affective changes (particularly fear), illusions, and formed hallucinations. Such seizures are often referred to as auras
 - Focal seizures with impaired awareness correspond to what have (previously called complex partial seizures).
 - During focal seizures with impairment of awareness, the patient may have a variety of repetitive semi purposeful movements that are referred to as motor automatisms. These can include chewing, swallowing, sucking, bicycling and kicking movements, flailing of the arms, and even running, jumping, and spinning.
- Focal seizures are further subdivided primarily based upon the clinical signs and symptoms and the EEG localization e.g.
 - Motor seizures may manifest as focal motor activity, sometimes with an anatomic spread or march of activity (Jacksonian), versive movement (turning of the eyes, head and/or trunk), vocalization, or arrest of speech
 - Sensory seizures: paresthesias, feelings of distortion of an extremity, vertigo, gustatory sensation, olfactory symptoms, auditory symptoms, and visual phenomena such as flashing lights
 - Autonomic seizures: may include an epigastric "rising" sensation (a common aura with medial temporal lobe epilepsy), sweating, piloerection, and pupillary changes.

Previously used terminology of "secondarily generalized seizure," could be confusing and is no longer recognized in the ILAE classification.

The preferred way to describe a seizure, that was known by EEG or by clinical symptoms to begin focally and later generalize is "focal seizure evolving to a bilateral tonic-clonic seizure."

Generalized seizures

- Originate within and rapidly engage both cerebral hemispheres.
- Awareness may be impaired, and this impairment may be the initial manifestation.
- Motor manifestations (if present) are bilateral.
- The ictal EEG patterns are bilateral from onset.
- Generalized seizures can be further divided into motor and non-motor types
- Motor types include:
 - tonic–clonic seizures:
 - myoclonic seizures: brief shock like contractions that can be generalised or confined to face, trunk or extremities.
 - Atonic: also known as drop attacks are characterised by loss of consciousness with loss of muscle tone.
 - epileptic spasms
- Non-motor types are absence seizures:
 - Absence seizures manifest as episodes of sudden, profound impairment of consciousness without loss of body tone. Patients may have low amplitude myoclonic movements as well as mild tonic involvement of the limbs and trunk and simple motor automatisms, similar to those seen in focal seizures with impairment of awareness
 - Typical: arrest of on-going activity and a blank stare of less than 20 seconds. Muscle tone is preserved, and the patient does not fall, usually with no recollection of the episode although some children will remember the episode
 - Atypical: longer absence seizure of more than 20 seconds. There is a much more pronounced change in tone and variability in consciousness level.
 - Myoclonic absence: absence seizures that are accompanied rhythmic myoclonic jerks of shoulders and arms with a tonic abduction that results in progressive lifting of arms during the seizure.
 - Absence with eyelid myoclonus: a triad of eyelid myoclonus that may be accompanied by absence seizures and eye deviation. EEG seizures and photosensitivity lasting less than 10 seconds.

Unknown onset

- With some types of epilepsy, the onset cannot be clearly determined as generalized or focal. Epileptic spasms are key example. Epileptic spasms, which include infantile spasms, are seizures that involve spasms of the muscles of the neck, trunk, and extremities.

| Generalized onset seizures | |
|--|---|
| Motor | Nonmotor (absence) |
| <ul style="list-style-type: none"> • Tonic-clonic • Clonic • Tonic • Myoclonic • Myoclonic-atonic • Atonic • Epileptic spasms | <ul style="list-style-type: none"> • Typical • Atypical • Myoclonic • Eyelid myoclonia |
| Focal onset seizures | |
| Motor onset | Nonmotor onset |
| <ul style="list-style-type: none"> • Aware • Impaired awareness • Unknown awareness | <ul style="list-style-type: none"> • Aware • Impaired awareness • Unknown awareness |
| <ul style="list-style-type: none"> • Automatisms • Atonic* • Clonic • Epileptic spasms* • Hyperkinetic • Myoclonic • Tonic | <ul style="list-style-type: none"> • Autonomic • Behavior arrest • Cognitive • Emotional • Sensory |
| <ul style="list-style-type: none"> • Focal to bilateral tonic-clonic | <ul style="list-style-type: none"> • Focal to bilateral tonic-clonic |
| Unknown onset seizures | |
| Motor | Nonmotor |
| <ul style="list-style-type: none"> • Tonic-clonic • Epileptic spasms | <ul style="list-style-type: none"> • Behavior arrest |
| Unclassified seizures[¶] | |

ILAE: International League Against Epilepsy.

* Degree of awareness usually is not specified.

¶ Due to inadequate information or inability to place in other categories.

Febrile seizures

- Occur in association with a febrile illness (temperature of 38.3 °C) that is not caused by CNS infection or acute electrolyte imbalance in children that are aged between one month and less than 6 years that is otherwise normal.
- They can be simple and complex.
- Simple febrile seizures: generalized tonic-clonic in nature, lasting less than 15 minutes and do not recur within 24 hours.
- Complex febrile seizures: may be focal or last more than 10-15 minutes or reoccur within the 24 hours.
- There is always an identifiable cause to the febrile illness. An infective screen is mandatory. Acute seizure should be managed with acute anti-epileptic agents. However, EEG and long-term anti-epileptic medications are not indicated.
- Only 1 to 2% of children that present with first onset febrile seizure will develop epilepsy. The definite risk factors for developing epilepsy after a febrile seizure include:
 - a background of neurodevelopmental disability
 - complex febrile seizure
 - family history of epilepsy (genetics contribute significantly to febrile seizure epidemiology)
 - low grade fever at the time of the seizure

Important points in history

- Detailed description of the seizures, including duration and onset, bowel/ bladder incontinence, tongue bites, automatisms.
- Seizures in epilepsy are usually:
 - Stereotyped: each one is like the previous one
 - Random: occur at any time of the day or night
 - Rarely precipitated by specific environmental, psychological, or physiological events.
- Prior seizures
- Trauma
- Perinatal and birth history
- Family history of epilepsy
- Drugs: prescribed, recreational, local herbs.
- Other illness: diarrhoea (electrolyte imbalance), fever,

Electroencephalogram (EEG)

- EEG May help to confirm the diagnosis, however a normal EEG does not exclude the diagnosis.
- Criteria for EEG
 - Seizures that are difficult to control despite 2 appropriate AEM given at optimal doses
 - Suspected epilepsy syndrome
 - Suspected Infantile spasm

Criteria for Brain imaging (MRI/CT-scan):

- Abnormal neurological findings (particularly focal signs)
- Developmental regression
- Global development delay of unknown aetiology

Some Epileptic syndromes

| Epilepsy syndrome | Age group | Aetiology | Clinical features | EEG | Diagnosis | Management | Prognosis |
|-----------------------------------|--------------------------------------|---|---|---|---|--|--|
| Benign familial neonatal epilepsy | 2-3 days of life up to 1 week of age | Genetic | Hypertonia Apnea Autonomic features like chewing, vocalization | flattening with apnea and tonic activity. Spikes and waves discharges. | Family history of neonatal seizures Normal neuro exam | Phenobarbitone | Spontaneous Resolution by 6 months Good prognosis |
| Benign neonatal epilepsy | day 4 and 6 of life | No genetic predisposition | repetitive focal clonic seizures | normal | Clinical exam and no family history of neonatal seizures | None | Good |
| Ohtahara syndrome | 0-3 months | brain anomalies, metabolic disorders, genetic mutations in the ARX gene. | brief tonic spasms that occur in clusters (100-300 per day) profound developmental delay | burst suppression in both sleep and awake states. | Fitting risk factors, seizure pattern and EEG findings | Seizures are resistant to treatment. Benzodiazepines, phenobarbitone, levetiracetam | The prognosis is poor with high mortality rate. Seizures may evolve into West Syndrome |
| Early myoclonic encephalopathy | 0-7 days | Inborn errors of metabolism Family history | Triad: intractable myoclonic seizures, focal and tonic epileptic spasms. Encephalopathy Developmental regression | burst suppression and brain imaging may be normal initially then later cortical atrophy | Suspect in infants with erratic myoclonia and encephalopathy. | Trial of sodium benzoate for glycine encephalopathy; pyridoxine and pyridoxal deficiency disorders | 50% die in the first year of life. |
| West Syndrome | 3-12 months | Structural brain damage, Post-infectious, Metabolic disorders, Tuberous sclerosis | Triad: epileptic spasms, developmental regression and hypsarrhythmias on EEG of psychomotor development. | High amplitude hypsarrhythmia, asynchronous slow waves with multifocal spikes and polyspikes. MRI Brain needed to determine the cause. | Spasms as well as EEG findings will confirm the diagnosis. The absence of Hypsarrhythmia on EEG does not exclude the diagnosis | Epileptic spasms are a pediatric neurology emergency. Treat with prednisone(8mg/kg/day), max dose 60mg for 14 days then taper over another 14 days. Add Sodium Valproate or phenobarbitone concurrently. | Many of these children will evolve to have Lennox Gastaut Syndrome |

| | | | | | | | |
|---|---|--|--|---|---|---|--|
| Dravet Syndrome | infancy | onset recurrent complex febrile seizures or early onset afebrile hemi convulsions. | focal seizures, myoclonic seizures, absence, and atonic seizures and developmental delay ensues. | generalised spike waves with isolated bursts and poly spikes. Brain imaging is initially normal; however, later scans may show abnormalities due to seizures. | Clinically, the infant has developmental delay, limb spasticity and ataxia Plus the various seizure types including the myoclonic seizures | This is a pharmacoresistant epilepsy. Consider sodium valproate or topiramate as first line with clobazam, stiripentol or levetiracetam as adjunct therapy. | The prognosis is poor with Mortality rate As high as 18% Death is usually From Sudden Unexpected Death in Epilepsy (SUDEP) , Drowning or the Seizures themselves |
| Genetic epilepsy with Febrile seizures plus | Fabril e seizures beyond 6 years of age | Genetic cause, usually have a strong family history | Fabril e seizures beyond the age of 6 years and associated with other afebrile seizure types. | EEG findings are heterogenous and brain imaging is usually not indicated. | Clinical | Complex febrile seizures will require benzodiazepine rescue therapy for the parents to keep at home. For the afebrile seizure types, anti-epileptic agents should be tailored toward the seizure types that manifest. | Seizures will resolve by puberty and development remains normal. In some cases, children have grown to develop Doose or Dravet syndromes. |

Management

Primary level

- Treat the acute seizure, using ABCDE and seizure protocol.
- Child suspected to have epilepsy should be referred to their nearest district hospital for assessment and long term treatment initiation.
- Parents should be encouraged to take a video of the seizure episode if they have access to a phone with video.

Secondary Level

- Manage acute seizure using ABCDE and convulsion protocol
- A thorough evaluation of the patient must be undertaken to establish seizure type and the relevant patient characteristics and comorbidities
- Initiate long term anticonvulsant treatment if:
 - More than 2 afebrile seizure
 - 1 afebrile seizure in a child with neurological condition
- Select drug based on seizure type, epilepsy syndrome and patient characteristics (age, school going, behavioural issues)

SELECTING ANTI-SEIZURE MEDICATION ACCORDING TO SEIZURE TYPES

Focal Seizures

First Line: Carbamazepine, Valproate

Second Line: Lamotrigine, Levetiracetam, Phenytoin, Phenobarbitone

Generalised Seizures

Tonic-clonic / clonic only

First Line: Phenobarbitone, Valproate

Second Line: Lamotrigine, Levetiracetam, Carbamazepine, Phenytoin

Absence

First Line: Valproate, Ethosuximide

Second Line: Lamotrigine, Levetiracetam

Atonic, tonic

First Line: Valproate

Second Line: Lamotrigine, Phenytoin

Myoclonic

First Line: Valproate

Second Line: Levetiracetam,

- Aim for Monotherapy (single drug therapy)
- Start drug at minimum therapeutic dose and titrate upwards to maximum therapeutic dose.
- If the diagnosis is unclear or seizure control not attained after 3 months of optimal treatment, refer to tertiary level.

- Patients initiated on antiepileptics should be followed up at a designated clinic.
- Refer all complex cases including those with poor seizure control (recurrent seizures despite being on 2 antiseizure medications at their optimal therapeutic dose), those meeting criteria for EEG or further imaging

Tertiary level

- Perform relevant investigations to determine the cause of epilepsy.
- Attempt to classify the seizure syndrome if suspected.
- Coordinate referrals to multidisciplinary team if needed.
- All complex patients should be followed up at designated clinics.
- Monitor for drug side effects and drug interactions.
- Monotherapy:
 - If seizure control is not attained on a single drug, add another drug and optimize the dose slowly to therapeutic dose. Once therapeutic dose is attained, gradually wean off the first drug.
 - Alternatively, you can wean off the first drug while adding and optimizing the second drug.
- Rational combination therapy:
 - Combines drugs with different mechanism of action and consider their spectrum of efficacy, drug interactions adverse effects and availability.
 - Usually combines 2 or maximum 3 drugs.
- Avoid starting females of childbearing potential with sodium valproate because of risk of teratogenicity and neurodevelopmental impairment to the unborn child unless other treatments are ineffective or not tolerated.
- Withdrawal of medication:
 - Needs to be carefully planned and should only be attempted after the patient has been seizure free for 2 years,
 - Consider the likely prognosis and individual circumstances before attempting slow withdrawal of medication over 3-6 months (maybe longer if using clonazepam or phenobarbitone).
- Patients with known Epilepsy syndromes or structural defects must always be discussed with a paediatrician/ neurologist before discontinuation of drug.
- If seizures recur, the last dose reduction is reversed, and medical advice sought

The patients with “Intractable Epilepsy/ Supra refractory epilepsy

Please re-evaluate for the following possibilities:

- Is it a seizure or a non-epileptic event?
- Wrong classification of epilepsy syndrome, thus wrong choice of antiepileptic drug
- Antiepileptic drug dose not optimized
- Poor compliance to antiepileptic drug

- Antiepileptic drug aggravating seizures
- Lesional epilepsy, hence a potential epilepsy surgery candidate
- Progressive epilepsy or neurodegenerative disorder.
- Discuss with a paediatric neurologist for management options.

ORAL DOSING AND ADVERSE EFFECTS OF ANTI-SEIZURE MEDICATION

Carbamazepine*

Start at 2mg/kg 8 hourly,

Increase every 2 to 4 weeks to 5-10mg/kg 8 hourly

Drug class: Iminostilbene

Mechanism of action: Sodium channel modulator

Common side effects: Drowsiness, dizziness, ataxia, diplopia, rashes

Serious side effects: Steven-Johnson syndrome, agranulocytosis

*contraindicated in myoclonic epilepsy

Levetiracetam/ Keppra

Start at 7mg/kg 12 hourly

Increase every 2 to 4 weeks to a maximum of 30mg/kg 12 hourly

Drug class: Newer drug

Mechanism of action: Modulator of presynaptic machinery (SV2A)

Common side effects: Somnolence, asthenia, dizziness, irritability, behavioural change

Phenobarbitone

Start at 2mg/kg daily

Increase every 4 weeks to 5 to 8mg/kg once daily

Drug class: Barbiturate:

Mechanism of action: GABA enhancer

Common side effects: Behavioural disturbance, cognitive dysfunction, drowsiness, ataxia, rash

Phenytoin

2mg/kg 8 hourly or 12 hourly

Mechanism of action: GABA enhancer

Common side effects: Ataxia, diplopia, dizziness, sedation, gum hypertrophy, hirsutism, megaloblastic anemia

Sodium valproate

Start at 5mg/kg 12 hourly

Increase every 2-4 weeks to 20mg/kg 8-12 hourly

Mechanism of action: GABA enhancer, Sodium channel modulator

Common side effects: Nausea, epigastric pain, tremor, alopecia, weight gain, hair loss, thrombocytopaenia

Serious side effects: Hepatic toxicity, pancreatitis, encephalopathy

Vigabatrin

Start at 25mg/kg 12 hourly

Increase every 2-4 weeks to 75mg/kg 12 hourly

Common side effects: Drowsiness, dizziness, mood changes, weight gain

Serious side effects: Peripheral visual field constriction (tunnel vision)

Follow up

- Follow patients in PEN-Plus clinic regularly
- Monitor response to medication and optimise accordingly
- Monitor medication side-effects
- Monitor compliance and adherence to medication

STATUS EPILEPTICUS

Clinical definition

For clinical practice purposes status epilepticus (SE) is defined as either a single unremitting seizure lasting longer than five minutes or as frequent clinical seizures without an interictal return to the baseline clinical state. The five-minute window corresponds with the time at which urgent treatment should begin. If SE continues beyond 30 minutes, then long-term consequences including neuronal injury, alteration of neuronal networks, and neuronal death can occur.

Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected

| Type of SE | Operational dimension 1 Time (t_1), when a seizure is likely to be prolonged leading to continuous seizure activity | Operational dimension 2 Time (t_2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits) |
|---|--|--|
| Tonic-clonic SE | 5 min | 30 min |
| Focal SE with impaired consciousness | 10 min | >60 min |
| Absence status epilepticus | 10–15 min* | Unknown |

*Evidence for the time frame is currently limited and future data may lead to modifications.

Convulsive SE

This is defined as episodes of excessive abnormal muscle contractions, usually bilateral, which may be sustained, or interrupted. They may be generalized or focal.

Non-convulsive SE

This typically includes patients with 10 continuous minutes or >30 minutes of ictal activity on EEG in any given hour of recording (usually defined in patients on continuous EEG monitoring), with no or subtle evidence of clinical seizures, patients may present with confusion or coma.

Refractory SE

This is defined as persistent seizures despite appropriate use of two intravenous medications, one of which is a benzodiazepine. Can be seen in up to 40% of patients with SE.

Super-refractory SE

This is defined as SE that continues or recurs 24 hours or more after the onset of anaesthetic therapy, including those cases where status epilepticus recurs on the reduction or withdrawal of anaesthesia.

Classification

For classification/categorization of SE the following four axes are used (as far as possible):

1. Semiology – clinical presentation of seizures (generalized or focal)
2. Aetiology
 - a. Symptomatic – known cause
 - b. Idiopathic or genetic
 - c. Unknown
3. Electroencephalographic (EEG) correlates
4. Age

- a. Neonatal
- b. Infancy
- c. Childhood
- d. Adolescent

Causes / Risk Factors

- Central nervous system infections (cerebral malaria, acute bacterial meningitis, acute viral encephalitis)
- Acute hypoxic-ischemic insult
- Metabolic disease (e.g., hypoglycaemia, inborn error of metabolism)
- Electrolyte imbalance
- Traumatic brain injury
- Drugs, intoxication, poisoning
- Cerebrovascular event
- Epilepsy
- Undetermined

Clinical Presentation / Recognition of SE

The diagnosis of convulsive SE is clinical and is confirmed by verifying the presence of either an unremitting generalized seizure lasting longer than five minutes or frequent seizures without an interictal return to the baseline level of consciousness.

Management

The main goals of treatment are;

- Establish and maintain adequate airway, breathing, and circulation
- Identify and treat hypoglycaemia
- Stop the seizure as quickly as possible and thereby prevent brain injury
- Identify and treat life-threatening causes of SE such as trauma, sepsis, meningitis, encephalitis or structural brain lesion.
- SE is a medical emergency, please refer to the medications and algorithm below;

Medications for convulsive status epilepticus

Benzodiazepines

Diazepam 0.2 mg/kg IV/IO max 10 mg

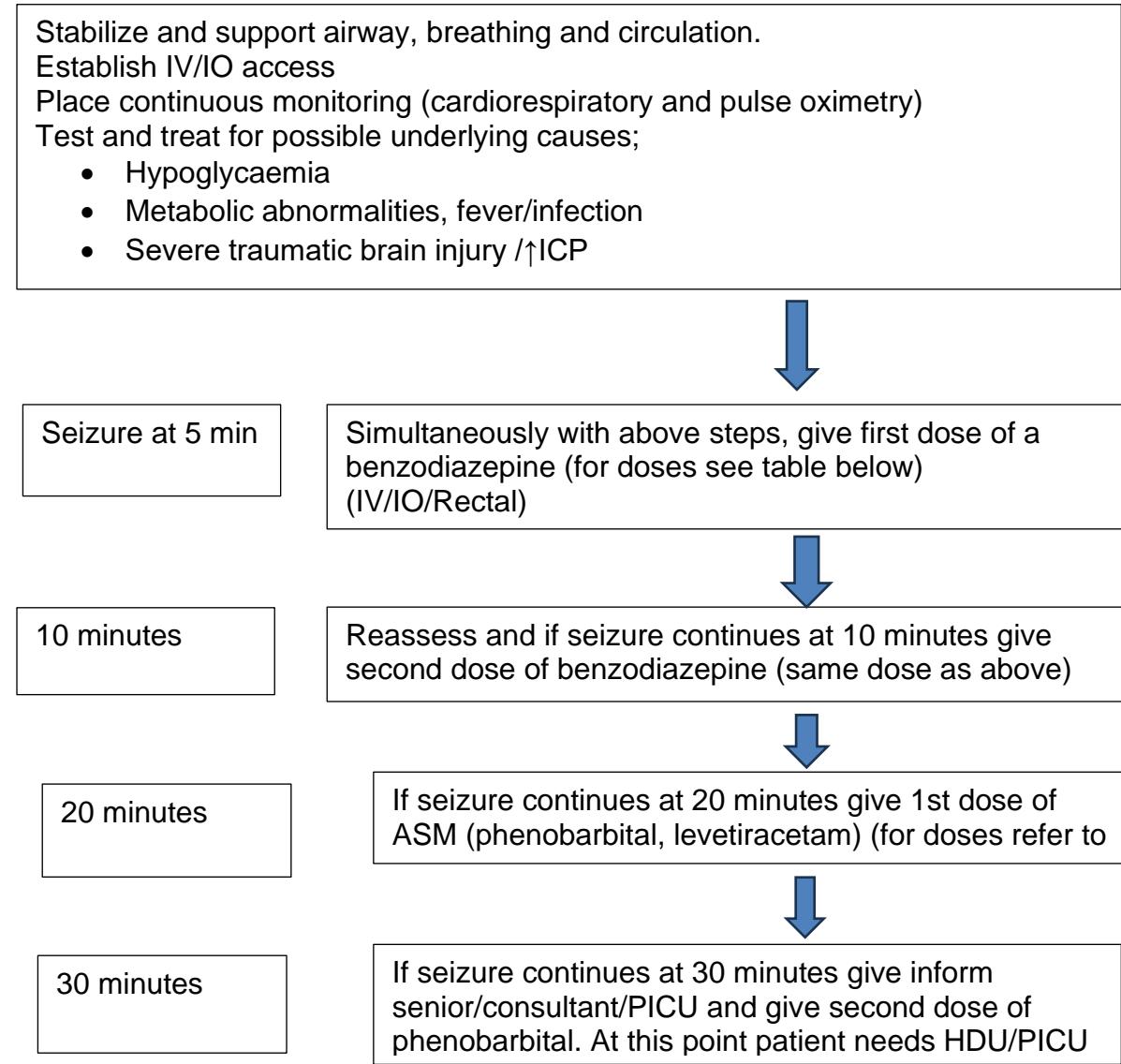
Rectal Diazepam 0.5 mg/kg max 20 mg

Antiseizure medications

Phenobarbital 20 mg/kg IV/IO (max 1000mg)

Levetiracetam 60 mg/kg IV/IO (max 4500 mg)

Algorithm for management of status epilepticus



Postictal recovery and further evaluation

- Prevent recurrent hypoglycaemia if at risk
- Further history and physical examination plus a detailed neurological evaluation to try and identify the cause
- Laboratory tests where indicated, e.g., CSF, blood culture, FBC, U&E's, blood gas, etc.
- Neuroimaging if indicated
- Remember to continue maintenance doses of antiseizure medications.
- The need for long-term ASM will depend on the underlying cause of SE.

NEURAL TUBE DEFECTS

Definition

A group of birth deformities of the central nervous systems resulting from defective neurulation or closure of the neural plate.

Risk Factors / Causes

- Maternal Folate deficiency
- Pre- gestational diabetes
- Genetic factors e.g previous child with NTD
- Maternal Obesity
- Maternal hyperthermia in the first trimester
- Amniotic band sequence
- Syndromes: trisomy 13 or 18, and triploidy.

Prevention / Promotion

- Women of childbearing age who are planning a family should be screened and treated for anaemia, micronutrient deficiencies and obesity.
- Prenatal supplements should be started on schedule and continued as per recommendation for both the general and at-risk population.
- For the general population
 - Supplemental folic acid is a safe and effective treatment for prevention of NTDs.
 - 0.4 mg taken once per day, beginning at least one to 3 months prior to attempting conception and continuing throughout pregnancy and for four to six weeks postpartum or until completion of breastfeeding.
- For women at risk of having a child with NTD
 - 4 mg dose folic acid supplementation.
 - This dose should be initiated one to three months prior to conception and maintained through the first 12 weeks of gestation, after which the dose is reduced to 0.4 mg and continued until four to six weeks postpartum or until completion of breastfeeding.

Signs and symptoms

- These vary and range from being asymptomatic in some closed NTD, lower limb weakness with a neuropathic bladder in the context of a tethered cord, ora fleshy pouch covered in either membrane or exposed notable at birth.
- The following associated complications occur with NTD depending on their severity:
 - Neuro developmental disorders e.g learning difficulties
 - Hydromyelia
 - Tethered cord
 - Seizures
 - Neurogenic bladder
 - Bowel dysfunction
 - Orthopedic problems (eg, scoliosis, hip dislocation and contractures, rotational abnormalities of the lower extremities)
 - Pressure ulcers
 - Infections (Meningitis, UTI)

Open neural tube defects: These are defects covered only by a membrane and make up 80% of all NTD. These include anencephaly, myelomeningocele, cranioraschisis, lipomyelomeningocele



Closed Neural Tube Defects: These are defects that are covered by skin. These include encephalocele, split cord malformation, spina bifida occulta, dermal sinus or dermal nevus



Anencephaly: cranial neuropore doesn't close during neural tube closure in the fourth week of embryogenesis. This leads to failure in the development of the brain and bony cranium and this is incompatible with life

Cranioraschisis: failure of the closure of the skull bones. Also incompatible with life

Myelomeningocele: failure of primary neurulation (ie, failure of the spinal neural tube to close normally by 28 days after conception)

Encephalocele: a sac containing brain / meninges / cerebrospinal fluid (CSF) forms outside the skull through a bone defect.

Split cord malformation: a split along the midline of the cord into 2 symmetric or assymmetric segments.

Investigations

- Prenatally: ultrasound scan and measurement of serum alpha feto-protein.
- Most NTD are diagnosed at birth.
- NTD is associated with VACTERL anomalies (Vertebral defects, Anal atresia, Cardiac defects, Tracheo-esophageal fistula, Renal anomalies, and Limb abnormalities)
 - Children with an NTD should therefore undergo routine scans to screen for abnormalities in the other organ systems i.e cardiac echo, ultrasound scan of kidneys, ureters and urinary bladder.

Differential diagnosis

- Tethered cord
- Spinal Cord Hemorrhage
- Spinal Cord Infarction
- Spinal Epidural Abscess
- Syringomyelia

Management

- Due to the complications associated with NTD their management requires a multidisciplinary approach

Primary Level

- Assess ABCDE, keep warm, then refer to secondary level.

Secondary Level:

- Assess ABCDE, keep warm.
- Nurse prone
- If leaking cover with vaseline gauze not dry gauze
- If leaking start on Cef and Metro. DO NOT GIVE AMINOGLYCOSIDES, ie no Gentamicin.
- If multidisciplinary team available, treatment can be given at secondary level. Refer to tertiary level if NTD severe and needs more extensive multidisciplinary team.
- Surgical review is required to assess for closure of MMC.
- Make sure the baby is passing urine and not in retention.
- Urological review is needed for training in continuous intermittent catheterization (CIC).
- Physiotherapy is required for passive physio required to prevent pressure ulcers.
- Bowel management given oral laxatives, suppositories, and enemas, singly or in combination as first line.
- Orthopedics are needed to correct associated deformities such as genu varus or valgus
- Psychosocial support
- Refer next day (need not travel at night) to tertiary level for corrective management

Tertiary Level

- Patient management requires a multidisciplinary approach often led by the surgical team.
- Management principles as in secondary above.
- Complications must be screened for and managed.
- Care can be stepped down care to a district hospital once treatment is established.

Follow up

- Patients should be booked to a Neurosurgical clinic for follow up at secondary or tertiary level.
- Follow up can initially every 3 months. Afterwards they need to be seen at least once a year for annual renal USS and urine dipstix due to a high lifetime risk of UTI and renal scarring.
- Parents and children receive lifelong support and education from CHILD HELP SBH and a parents' group: CHILD HELP SBH have contact persons at QECH, ZCH, KCH and Mzuzu CH. Parents training weeks happen regularly as well.

HEADACHE

Definition

Defined as pain located above the orbitomeatal line. It is one of the most common complaints in children and adolescents and the prevalence increases with age.

Primary headaches are most often recurrent, episodic and sporadic

Secondary headaches are headaches that are a symptom of an underlying illness. Once the underlying suspected cause is treated, the secondary headache should resolve.

Risk Factors / causes

Primary Headache:

- Migraine headaches, Tension-type headaches, Cluster headaches.

Secondary headache:

- Acute febrile illness (influenza, upper respiratory infection,)
- Recurrent rhinosinusitis (one of the most common misdiagnoses for headaches, with the majority actually being a primary headache and usually migraine)
- Posttraumatic headaches;
- Medications (headache is a potential side effect of multiple medications, frequent overuse of analgesic medication)
- Acute and severe systemic hypertension (may cause headache or be a response to increased intracranial pressure)
- Infections: Meningitis, encephalitis, malaria
- Brain tumor
- Idiopathic intracranial hypertension
- Hydrocephalus
- Intracranial hemorrhage (typically sudden severe unilateral headache)
- Visual refractive error

Promotion / Prevention

Please note that these suggestions are general recommendations, and it's important to consult with a healthcare professional for personalized advice and guidance if symptoms persist.

- *Ensure proper hydration:* Encourage your child to drink plenty of water throughout the day, as dehydration can contribute to headaches
- *Promote regular sleep patterns:* Establish a consistent sleep schedule for your child, ensuring they get enough sleep each night. Lack of sleep or irregular sleep patterns can trigger headaches
- *Encourage healthy eating habits:* Provide a well-balanced diet for your child, including fruits, vegetables, whole grains, and lean proteins. Avoid excessive consumption of sugary foods, processed snacks, and caffeine, as these can be headache triggers

- *Limit screen time:* Encourage breaks and outdoor activities to reduce screen time
- *Promote good posture:* Encourage your child to maintain proper posture, especially when sitting. Poor posture can strain the neck and contribute to tension headaches
- *Ensure a well-lit environment:* Provide adequate lighting in your child's study area and other spaces they spend time in. Poor lighting can strain the eyes and trigger headaches
- *Identify and avoid triggers:* Pay attention to any specific triggers that seem to cause headaches in your child, such as certain foods, strong odors, or environmental factors. Help your child avoid or minimize exposure to these triggers.

Signs and symptoms

- Are dependent on the cause of the headache. Primary headaches will have specific characteristics and/or patterns that can help distinguish them.

Migraine:

- Characterized by intermittent attacks of headache which are recurrent, typically moderate to severe in intensity, lasting 2 to 72 hours if not treated.
- Pain may be focal, throbbing, worsens with activity or causes avoidance of activity. It can be accompanied by nausea, vomiting, light sensitivity ("photophobia"), and sound sensitivity ("phonophobia")
- The duration of headache lengthens with age
- Pain is most often bilateral (bifrontal or bitemporal)
- Migraine remains the most common cause of occipital headaches however, they have an increased risk of a secondary cause and need to be investigated further.
- There may be a positive family history of migraine.
- Approximately 10 percent of children have associated auras that include visual, sensory, speech/language, motor, brainstem, or retinal symptoms, paresthesias, dysphasia, hemiplegia, weakness, ataxia, or confusion
- Chronic migraine is defined as headaches on 15 or more days per month, with at least eight having migraine features.

Tension-type headaches:

- Diffuse in location, non-throbbing, mild to moderate severity, and do not worsen with activity.
- The pain feels like there is a band squeezing their head
- They can last from 30 minutes to 7 days.
- May be associated with either photophobia or phonophobia but is not accompanied by nausea, vomiting, or aura.
- May have tenderness around the forehead.
- It is associated with stress, anxiety or depression.

Cluster headaches:

- Most common trigeminal autonomic cephalgias characterized by trigeminal location and association with autonomic features
- Typically, unilateral and frontal-periorbital in location

- The pain is severe and lasts less than three hours, but multiple headaches occur in a very short period of time (hence "cluster")
- Usually associated with ipsilateral autonomic findings, including lacrimation, conjunctival injection, nasal congestion and/or rhinorrhea, facial and forehead sweating, eyelid edema, and miosis and/or ptosis
- Usually occur between the ages of 10 and 20 years, but may occur in younger children

| Symptom | Migraine | Tension type headache | Trigeminal autonomic cephalgias (eg, cluster headache) |
|----------------------------|--|---|--|
| Location | Young children; commonly bilateral. Adolescents and young adults; commonly unilateral, global in 30% | Bilateral | Always unilateral, usually begins around the eye or temple |
| Characteristic | Gradual in onset, crescendo pattern; pulsating; moderate or severe intensity; aggravated by routine physical activity | Pressure or tightness that waxes and wanes | Pain begins quickly, reaches a crescendo within minutes; pain is deep, continuous, excruciating, and explosive in quality |
| Patient appearance | Patient prefers to rest in a dark, quiet room | Patient may remain active or may need to rest | Patient remains active |
| Duration | 2 to 72 hours | Variable | 30 minutes to 3 hours |
| Associated symptoms | Nausea, vomiting, photophobia*, phonophobia*; may have aura (usually visual, but can involve other senses or cause speech or motor deficits) | None | Ipsilateral lacrimation and redness of the eye; stuffy nose; rhinorrhea; pallor; sweating; Horner syndrome; focal neurologic symptoms rare; sensitivity to alcohol |

| Clinical feature | Possible significance |
|--|---|
| General appearance | Altered mental status (meningitis, encephalitis, intracranial hemorrhage, elevated intracranial pressure, hypertensive encephalopathy). |
| Vital signs | Hypertension may cause headache or be a response to increased intracranial pressure Fever suggests infection |
| Head circumference | Macrocephaly may indicate slowly progressive increases in intracranial pressure. |
| Height and weight trajectories | Abnormal or altered trajectories may indicate intracranial pathology. |
| Auscultation of the neck, eyes, and head for bruit | Bruit may indicate arteriovenous malformation. |
| Palpation of the head and neck | Localized scalp tenderness may occur in migraine and tension-type headaches Scalp swelling may indicate head trauma Sinus tenderness may indicate sinusitis Temporomandibular joint (TMJ) and/or masseter tenderness suggests TMJ dysfunction Nuchal rigidity may indicate meningitis Posterior neck pain may indicate an anatomic abnormality (eg, Chiari malformation) Thyromegaly may indicate thyroid dysfunction |
| Visual fields | Visual field abnormalities may indicate increased intracranial pressure and/or a space-occupying lesion. |
| Fundoscopy | Papilledema may indicate increased intracranial pressure Fundoscopic examination is normal in primary headache |
| Otoscopy | May demonstrate otitis media; hemotympanum may indicate trauma. |
| Oropharynx | Signs of pharyngitis? Dental decay or abscess? |
| Neurologic examination | Abnormal examination may indicate intracranial pathology but also may occur with migraine headache. |
| Skin examination | Trauma, neurocutaneous disorders (eg, neurofibromatosis, tuberous sclerosis complex), |
| Spine | Occult spinal dysraphism may be associated with structural abnormalities (eg, Chiari malformation). |

Investigations

- FBC with differential and ESR
- Serum or urine toxicology screens (if acute or chronic intoxication is suspected)
- Thyroid function tests (if thyroid dysfunction is suspected)
- LP if suspected intracranial infection, subarachnoid hemorrhage, or idiopathic intracranial hypertension.
- Brain MRI: Indicated in children with any of the following features:
 - Abnormal neurologic examination
 - Younger than six years old
 - Who have features worrisome for a pathologic intracranial process.

Differential diagnosis

Refer to causes of secondary headaches.

Management

Primary / Secondary / Tertiary level

Treat underlying conditions

Some common management principles when managing recurrent headaches include:

- A diary in which the quality, location, severity, timing, precipitating and relieving factors, and associated features of the headache are recorded is useful.
- Providing realistic expectations (i.e. the frequency and severity of the headaches may decrease over weeks to months of therapy, but the headaches may continue to occur).
- Return to school for children who have been absent; if necessary, they can go to the school nurse or office once daily for 15 minutes when headache pain peaks.
- Avoidance of headache triggers (e.g. dietary triggers, caffeine, lack of sleep, inadequate hydration, overuse of electronic devices).
- Daily exercise for 20 to 30 minutes.
- Addressing comorbid sleep problems (e.g. delayed sleep onset, frequent night waking)
- Avoid overuse of headache medication as this can worsen headache.
- Educating and enabling patients to manage their disease to enhance personal control.
- Reduction of headache-related distress and psychologic symptoms.

MIGRAINE HEADACHE

Primary level: Relieve headache as quickly as possible with return to normal function. Can use NSAIDS

Secondary level: Relieve headache as quickly as possible with return to normal function. This mainly includes 2 groups of medications: nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans

Tertiary Level: Consult neurologist for persistent headaches

TENSION TYPE HEADACHE

Primary Level: Simple analgesics (ibuprofen or paracetamol) can be effective for acute treatment.

Secondary level: amitriptyline can be effective for prevention of tension type headache.

Tertiary level: Bio-behavioral therapy and copings skills training may also be beneficial if stress is suspected as an underlying cause. Consult neurologist for persistent headaches

Referral

Primary level: Manage ABCD. If no underlying cause of headache found, refer to secondary level.

Secondary level: Manage ABCD. Screen for underlying causes of headache. Initiate treatment. Refer all patients with persistent headaches and complex causes of secondary headaches to tertiary facility.

Tertiary Level: Discuss and manage all patients with persistent headaches and complex causes of secondary headaches with a paediatric neurologist.

Follow up

Patients with headache should be scheduled for follow up in general/neurology clinic at secondary or tertiary level.

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CHAPTER 12. PULMONOLOGY

ASTHMA

Definition

- Chronic airway inflammatory disease characterized by increased airway responsiveness, reversible airway obstruction and episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or early morning.
- Diagnostic criteria for asthma in children 6-11 years and adolescents
 1. History of variable respiratory symptoms
 - wheeze, shortness of breath, chest tightness, cough
 - often worse at night or on waking
 - triggered by exercise / allergens / cold air / laughter
 - worse with viral infections
 2. Confirmed variable expiratory airflow limitation
 - Documented expiratory airflow limitation
 - reduced Forced Expiratory Volume to Forced Vital Capacity ratio in 1 second (FEV₁/FVC) ratio
 - Documented excessive variability in lung function
 - positive bronchodilator reversibility test
 - significant increase in lung function after 4 weeks of anti-inflammatory treatment
 - positive exercise challenge test
 - excessive variation in lung function between visits
 - excessive variability in twice daily Peak Expiratory Flow (PEF) over 2 weeks
- Diagnostic criteria in children 5 years and under
 - Recurrent wheezing occurs in a large proportion of children 5 years and younger, typically with viral upper respiratory tract infections. Deciding whether this is an initial presentation of asthma is difficult.
 - A diagnosis of asthma in young children with a history of wheezing is more likely if they have:
 1. Recurrent or persistent non-productive cough that may be worse at night or accompanied by wheezing or breathing difficulties.
 2. Wheezing or coughing that occurs with exercise, laughing or crying, or exposure to tobacco smoke in the absence of an apparent respiratory infection.
 3. Reduced activity - not running, playing or laughing at the same intensity as other children; tires easily during walks.
 4. A history of other allergic disease (eczema or allergic rhinitis), allergen sensitisation or asthma in first degree relatives.
 5. Clinical improvement during 2-3 months of controller (medication that prevent asthmatic attacks) treatment and worsening after cessation.

Health Promotion/Prevention

- Every child with a diagnosis of asthma should have appropriate reliever medication such as a salbutamol inhaler
- Every child using an inhaler MUST USE A SPACER
- Education on potential triggers and avoidance of the same
- Increased awareness in community
- Advocacy for availability of appropriate medications in health facilities
- Educate on importance of not discriminating / stigmatizing children with asthma
- Addressing myths and misconceptions about asthma. (asthma medication do not kill)

Risk factors

- Genetics: positive family history of asthma / eczema / allergic rhinitis
- Viral infections at a young age: recurrent viral infections e.g., viral induced wheeze or bronchiolitis
- Allergies: Family history of allergies
- Other environmental exposures e.g., tobacco smoke, dust mites, cold, pets, cockroaches, molds, damp houses

Signs and symptoms

- Common symptoms
 - Dyspnoea
 - Increased coughing
- Vital signs and general appearance
 - Tachypnoea
 - Tachycardia
 - Pulsus paradoxus
 - Hypoxaemia
 - Low mental status
- Signs of bronchoconstriction
 - prolonged expiratory phase
 - expiratory wheezing
 - silent chest
 - hyperresonance on percussion
 - inferior displacement and poor movement of the diaphragm
- Signs of increased work of breathing
 - Use of accessory muscles

Classification of severity of acute exacerbations

| | MILD | MODERATE | SEVERE | LIFE THREATENING |
|-----------------------|---------------|--|--------------------------------------|----------------------------|
| Breathlessness | While walking | While at rest (infant—softer, shorter cry, difficulty feeding) | While at rest (infant—stops feeding) | Extreme dyspnea Anxiety |

| | | | | |
|---|-------------------------------------|-------------------------------|---|---|
| Posture | Can lie down | Prefers sitting | Sits upright | Upright, leaning forward |
| Talks in... | Sentences | Phrases | Words | Unable to talk |
| Alertness | May be agitated | Usually agitated | Usually agitated | Drowsy or confused |
| Respiratory rate [†] | Increased | Increased | >30 breaths/min in > 5years old > 50 in <5yrs olds | >30 / min in > 5years old > 50 / min in <5yrs olds |
| Use of accessory muscles; suprasternal retractions | Usually not | Commonly | Usually | Paradoxical thoracoabdominal movement |
| Wheeze | Moderate; often only end-expiratory | Loud; throughout exhalation | Usually loud; throughout inhalation and exhalation | Absence of wheeze |
| Pulse rate (beats/min) [‡] | <100 | 100-120 | >120 | Bradycardia |
| Oxygen saturation | > 92% | > 92% | <92% | <92% |
| PEFR | > 80% | 60-80% | <60% | <60% |
| Pulsus paradoxus | Absent <10 mm Hg | May be present 10-25 mm Hg | Often present >25 mm Hg (adult) 20-40 mm Hg (child) | Absence suggests respiratory muscle fatigue |

Differential Diagnosis

- Pneumonia
- Inhaled foreign body.
- Bronchiolitis (especially infants) or viral induced wheeze (especially toddlers)
- Cardiac disease
- Allergy/ Anaphylaxis
- Loeffler's syndrome

A: ACUTE MANAGEMENT OF ASTHMA

Primary Level

Mild Asthma

- Salbutamol inhaler via spacer (and facemask if <3 years)
 - 100 -200 micrograms (1 - 2 puffs) every 20 minutes for 1 hour
OR
 - Nebulised Salbutamol 2.5mg every 15 minutes for 3 times
- Target oxygen saturation 94 -98%
- Discharge with advice:
 - Check good inhaler and spacer technique
 - Avoid allergens.
 - Return if worsens
 - Add in daily inhaled steroid inhaler via spacer if frequent episodes
- For primary health facility, refer all cases with moderate asthma to be managed at secondary or tertiary level

Secondary Level

Moderate Asthma

- Salbutamol inhaler via spacer (and facemask if <3years)
 - <4yrs - 500mcg (5 puffs) every 20 mins x3
 - >4 yrs - 1mg (10 puffs) every 20 mins x3
- Prednisolone:
 - < 5 years - 20mg PO OD 3/7
 - > 5years - 30mg PO OD x 3/7
- Clinician to review child after three treatments.
 - Admit if there is no improvement.
 - Look carefully for life-threatening features
 - Continue 2-4 hourly salbutamol via spacer
- Add in daily inhaled steroid inhaler via spacer if frequent episodes

Severe / Life-threatening asthma

- Oxygen
 - 5l/min via face mask
- Salbutamol Nebulisers (3 back-to-back to start with)
 - < 4 years: 2.5 mg
 - > 4 years: 5 mg
- Steroids
 - < 5 years - 20mg PO OD 3/7
 - > 5years - 30mg PO OD x 3/7
OR
 - Oral or IV Dexamethasone 0.6 mg/kg STAT - (max. 10 mg)
OR
 - Hydrocortisone IV (<5 yrs: 50mg; >5 yrs: 100mg IV STAT)
- 2/3 maintenance IV fluids plus 20 mmol KCl per litre of fluid

- Monitor for deterioration or improvement. If there is no improvement or if there is worsening refer to tertiary level on oxygen.

Tertiary Level

Mild / Moderate Asthma

Manage as in secondary level above.

Severe / Life Threatening Asthma

- Oxygen
 - 5l/min via face mask
- Give salbutamol nebuliser 3 times back to back then reassess.
 - If good response, stretch the nebs to hourly.
- Steroids
 - Oral or IV Dexamethasone 0.6 mg/kg STAT - (max. 10 mg)
OR
 - Hydrocortisone IV (<5 yrs: 50mg; >5 yrs: 100mg IV STAT)
OR
 - Prednisolone 2 mg / kg (max 40 mg / dose)
- 2/3 maintenance IV fluids plus 20 mmol KCl per litre of fluid
 - IV Magnesium-sulphate
 - 40 mg/kg maximum 2g (**diluted to at least 10 %**)
 - If you have a 50% ampule, dilute 4mls of the 50% Magnesium Sulphate with 16ml 0.9% saline (**Not Ringers lactate**) to make a 10% concentration.
 - **Give 0.4ml/kg of this 10% solution IV slowly over 20 min**
 - Monitor BP (hypotension)
 - Consider IV Aminophylline
 - Consult Paediatrician
 - Loading dose = 5mg/kg (max. 300 mg) diluted with Normal Saline (maximum concentration 25mg/mL) and administered over 20 mins
- Watch for tachycardia (pulse rate of >180/min), headache or convulsion, vomiting, flushing
- Intensive care unit admission if a patient has signs of impending respiratory failure.

Discharge Plan / Follow - up

- Prescribe salbutamol via spacer 200 - 400 mcg (2 -4 puffs) 4 hourly for 2-3 days, then as required
- Complete 3 days of prednisolone **or** give a second dose of dexamethasone (24 hours after the first one) before discharge
- Consider rethinking pre-existent background therapy, may need additional 'controller' medication.
- Advise when to seek help (i.e. breathlessness not controlled by inhalers, sudden increase in the need for 'relievers')
- Identifying and avoiding possible triggers

- Follow up in PEN-Plus clinic after 2 weeks then according to need thereafter.
- Teach inhaler and spacer technique (ensure you observe).

Steps for use inhaler with spacer

1. Shake inhaler
2. Insert inhaler into the hole in the bottle
3. Teach the child to form a tight seal around the mouthpiece of the bottle
4. Apply a puff from the inhaler into the bottle
5. Count for 10 seconds whilst the child breathes in and out (10 breaths)
6. Take inhaler out of bottle and shake to mix
7. Repeat steps 1-6 to give the number of puffs needed.

For children under 3 years

Attach a face mask to the mouthpiece of the bottle. If the mask has holes in it, put tape over these. Then follow above steps. This requires 2 people.

B: CHRONIC MANAGEMENT OF ASTHMA

- Children with asthma need thorough evaluation and on-going care to improve quality of life and reduce complications.
- On each visit, the patient needs to be evaluated as outlined in the table below:

Assessment of asthma in children > 5 years

| Asthma symptom control | |
|--|--|
| Day symptoms | How often does the child have cough, wheeze, dyspnoea or heavy breathing (number of times per week/day)? What triggers the symptoms? How are they handled? |
| Night symptoms | Cough, awakenings, tiredness during the day? |
| Reliever (Short Acting B-agonists (SABA)) use | How often is reliever medication used? (Distinguish between pre-exercise use and use for relief of symptoms) |
| Level of activity | What sports/hobbies/interests does the child have? How does the child's level of activity compare with their peers or siblings? How many days is the child absent from school? |
| Risk Factors for adverse outcomes | |
| Exacerbations | How do viral infections affect the child's asthma? What are other exacerbating factors (URTI, exercise, exposure to pollen or dust, heating system in the house, second-hand smoke). Do symptoms interfere with school or sports? How long do the symptoms last? How many episodes have occurred since their last medical review? Any urgent doctor/emergency department visits? Any hospitalizations and what interventions were done during hospital stay? What was the duration of stay if admitted? Does the child have a written action plan? |
| Lung Function Tests | Plot FEV ₁ and FEV ₁ /FVC ratio. Plot the values to see trends over time. Check technique of lung function tests. |
| Side-effects | Yearly height checks and plot growth velocity. Ask about frequency and dose of inhaled corticosteroids. |
| Treatment factors | |
| Inhaler technique | Ask the child to show how they use the inhaler and spacer. |
| Adherence | Is there any controller medication in the home at present? On how many days does the child use their controller weekly? Is it easier to remember to use it in the morning or evening? Where is the inhaler kept? Check expiry date of inhaler. |
| Goals / concerns | Does the child or their parent have any concerns about their asthma? What are the child/parent/carer's goals for treatment? |
| Comorbidities | |
| Allergic rhinitis | Any itching/sneezing/nasal obstruction? Can the child breathe through their nose? What medications are being taken for nasal symptoms? |
| Eczema | Sleep disturbance, use of topical corticosteroids? |
| Food allergy | Is the child allergic to any foods? |
| Obesity | Check age-adjusted BMI. Ask about diet and physical activity. |
| Other investigations (if needed) | |
| 2-week diary | If no clear assessment can be made based on the above questions, ask the child or parent/carer to keep a daily diary of asthma symptoms, reliever use and peak expiratory flow rate (best of 3) for 2 weeks. |

- After taking the history, classify the child's symptoms into the appropriate category of severity classification. Asthma can be classified as intermittent or persistent

Classification of asthma severity in children > 5 years

| Components of severity | Classification of Severity | | | |
|--|---|--|---|---|
| | <i>Intermittent</i> | <i>Persistent</i> | | |
| | | <i>Mild</i> | <i>Moderate</i> | <i>Severe</i> |
| Symptoms | 2 days / week | > 2 days / week but not daily | Daily | Throughout the day |
| Night-time awakenings | 2 times / month | 3-4 times / month | > 1 time per week but not nightly | Often 7 times / week |
| SABA use for symptom control | 2 days / week | > 2 days / week but not daily | Daily | Throughout the day |
| Lung Function | Normal FEV ₁ between exacerbations FEV ₁ > 80% FEV ₁ /FVC >85% | FEV ₁ > 80% FEV ₁ /FVC >85% | FEV ₁ 60 - 80% FEV ₁ /FVC 75 - 80% | FEV ₁ <60% FEV ₁ /FVC <75% |
| Exacerbations requiring oral systemic corticosteroids | 0 – 1 / year | > 2 / year | | |

- Chronic management of asthma should follow a stepwise approach depending on the severity level (Table above)

Starting Asthma treatment in children > 5 years

| | RELIEVER | PREFERRED CONTROLLER | OTHER CONTROLLER OPTIONS |
|--|--|---|--|
| Step 1 (Intermittent) Symptoms less than twice a month | | Low dose Inhaled Corticosteroids (ICS ¹) taken whenever SABA ² taken. | Consider daily low dose ICS |
| Step 2 (Mild persistent) Symptoms twice a month or more, but less than daily | As needed short acting beta-2 agonist (SABA) | Daily low dose ICS + SABA when having acute symptoms | Daily leukotriene receptor agonist (LTRA ³) OR Low dose ICS taken whenever SABA taken |
| Step 3 (Moderate / severe persistent) Symptoms most days, or waking with asthma once a week or more | OR Low dose Inhaled corticosteroid (ICS)-formoterol maintenance and reliever (MART) | Low dose ICS or Long Acting Beta Agonist (LABA ⁴) OR Very low dose ICS-Formoterol MART | Low dose ICS + LTRA |
| Step 4 (Severe persistent) Symptoms most days, or waking with asthma once a weeks or more, and low lung function | | Medium dose ICS-LABA ⁵ OR Low dose ICS-formoterol MART Refer for expert advice. | Add tiotropium or add LTRA Short course oral corticosteroid may also be needed for patients presenting with severely uncontrolled asthma |
| Step 5 (Severe persistent) | | Refer for phenotypic assessment +/- higher dose ICS-LABA or add on therapy e.g. IgE | Add on anti-IL5 or add-on low dose OCS, but consider side effects |

¹ ICS - Beclomethasone (<2yrs 100mcg BD, 2-12yrs 200mcg BD, 12-18 years 200-400mcg BD)

² SABA - Salbutamol, Albuterol, Levoalbuterol

³ LTRA - Monteleukast and zafirlukast

⁴ LABA - Formoterol, Salmeterol, Indacaterol

⁵ ICS-LABA - Budesonide-formoterol

LARYNGOMALACIA

Definition

Congenital abnormality of laryngeal tissues that leads to supraglottic collapse during inspiration leading to airway obstruction.

- Commonest congenital cause of stridor in children
- Symptoms begin within first 2 months of life

Risk factors / Causes

- Neurological abnormalities
- laryngeal anatomical abnormalities
- genetic syndromic disorders
- male sex

Signs and Symptoms

- Inspiratory stridor worse in supine position, when upset, crying, during feeding, and when they have a respiratory tract infection.
- Failure to thrive in severe cases

Investigations

- Flexible or direct laryngoscopy with infant breathing spontaneously (gold standard)
- Visualization of an omega-shaped epiglottis and/or collapse of supraglottic structures over the glottis during inspiration.

Differential diagnoses

- Vocal cord paralysis
- Subglottic stenosis
- Laryngeal papillomatosis
- Foreign body aspiration
- Subglottic haemangioma
- Laryngeal web

Management

Primary / Secondary Level

- Refer all cases

Tertiary Level

- Consult Ear, Nose and Throat (ENT) team or pediatric surgeons
 - Supraglottoplasty- Only severe and persistent cases
- For confirmed patients
 - Reassure the parents -90% resolve by 2 years of age
 - Swallowing therapy (nursing upright after feeds, smaller frequent feeds, and feed thickeners) and acid suppression therapy (Proton pump inhibitors like Omeprazole or histamine receptor blockers e.g., famotidine) for associated gastroesophageal reflux disease.

Follow up

- Close follow up is required especially for those being managed conservatively
- Monitor weight gain during routine under-5 visits

OBSTRUCTIVE SLEEP APNEA

Definition

Episodes of partial or complete upper airway obstruction occurring during sleep leading to interrupted breathing

Causes / Risk Factors

- Male
- Obesity
- Adenotonsillar hypertrophy
- Craniofacial abnormalities e.g., retrognathia, micrognathia, midfacial hypoplasia,
- Allergic rhinitis
- Nasal polyps
- Endocrinopathies e.g., hypothyroidism, acromegaly
- Neuromuscular conditions e.g., muscular dystrophies, cerebral palsy
- Metabolic disorders e.g., mucopolysaccharidoses
- Genetic syndromes e.g., Prader-Willi syndrome, Down syndrome

Promotion / Prevention

- Weight loss
- Sleeping on the sides

Signs and Symptoms

- Snoring (stertor) during sleep
- Restless sleep with waking, gasping or choking.
- Morning headaches: older children
- Excessive daytime sleepiness and aggressiveness
- Hyperactivity: especially younger children as a sign of sleepiness
- Poor suckling
- failure to thrive in infants
- Enuresis
- Nocturnal sweating
- Night terrors

Investigations

- In-laboratory Polysomnography: Gold standard
- Continuous overnight pulse oximetry
- Charting of overnight severity of stertor, apnoea and any stimulation/intervention needed

Differential diagnosis

- Gastroesophageal reflux disease
- Central sleep apnea
- Hypoventilation disorders
- Narcolepsy

Management

Primary Level

- Refer all cases

Secondary / Tertiary Level

Management depends on cause:

- Adenotonsillar hypertrophy can be treated by surgery
- Consult maxillofacial surgeons for structural facial problems
- Positive airway pressure (CPAP) mask when sleeping or other upper airway modification appliances
- Lifestyle modification in children with obesity
- Positional therapy. Patients should sleep in lateral position instead of supine

Follow up

- Growth and development and to assess for any complications

BRONCHIECTASIS

Definition

Irreversible abnormal dilatation and anatomic distortion of the bronchial tree. Results from cyclic bronchial inflammation, infections, and progressive airway destruction.

Causes/Risk factors

- Post infectious: e.g., tuberculosis, severe pneumonia, measles, pertussis
- Aspiration syndromes
- Airway obstruction: tumors, vascular ring
- Missed foreign body aspiration
- Genetic disorders e.g., Cystic fibrosis, Primary ciliary dyskinesia, Alpha 1 antitrypsin deficiency
- Immune deficiency e.g., Allergic broncho-pulmonary aspergillosis, Immunoglobulin A and G deficiencies
- Congenital bronchiectasis

Promotion / Prevention

- Childhood vaccination for pertussis, pneumococcus, measles, and haemophilus influenzae type B, Respiratory Syncytial Virus (RSV)
- Screening for Tuberculosis in immunosuppressed and early treatment

Signs and symptoms

- Chronic productive cough
- shortness of breath
- hemoptysis
- finger clubbing
- crackles, wheeze – on auscultation
- May also have a barrel chest
- Failure to thrive

Investigations

- FBC, HIV test
- Chest Xray
- Sputum/ gastric aspirate for culture, sensitivity and geneXpert
- Lung function tests
- Sweat chloride or genetic testing- Cystic fibrosis
- Chest x-ray
- High resolution CT chest- gold standard
- Milk scan and upper GI contrast- aspiration syndromes
- Bronchoscopy- missed foreign body

Differential diagnosis

- Bronchiolitis obliterans
- Childhood interstitial lung disease
- Infections: e.g., Tuberculosis

Management

Primary

- Refer all cases

Secondary / Tertiary Level

Acute exacerbation

- Oxygen therapy if necessary
- Empirically start antibiotics while awaiting sputum results
- Chest physiotherapy and optimize airway clearance techniques
- Mucolytic therapy/ hypertonic saline nebulisers

Long term goals and therapy

- Chest physiotherapy
- Prevent infections and exacerbations:
 - Ensure all vaccines are up to date
 - Avoid triggers
 - Regular sputum cultures
 - Prophylactic antibiotics in immunosuppressed: cotrimoxazole
- Growth and development
 - Adequate nutrition
 - Micronutrient supplementation
 - Pancreatic enzyme replacement therapy- Cystic fibrosis
- Prevent further lung damage and complications
 - Immune modulator therapy- Azithromycin 10mg/kg 3x a week- (for 3 months; then long term if good response; stop if no response after 3 months)
 - Inhaled corticosteroids if has wheezing

Follow up

- Review in general medical clinic monthly initially, 3-6 months if stable
- During every visit
 - Do sputum culture
 - Spirometry if available
 - Anthropometry
- If poorly controlled localized disease- consider lobectomy

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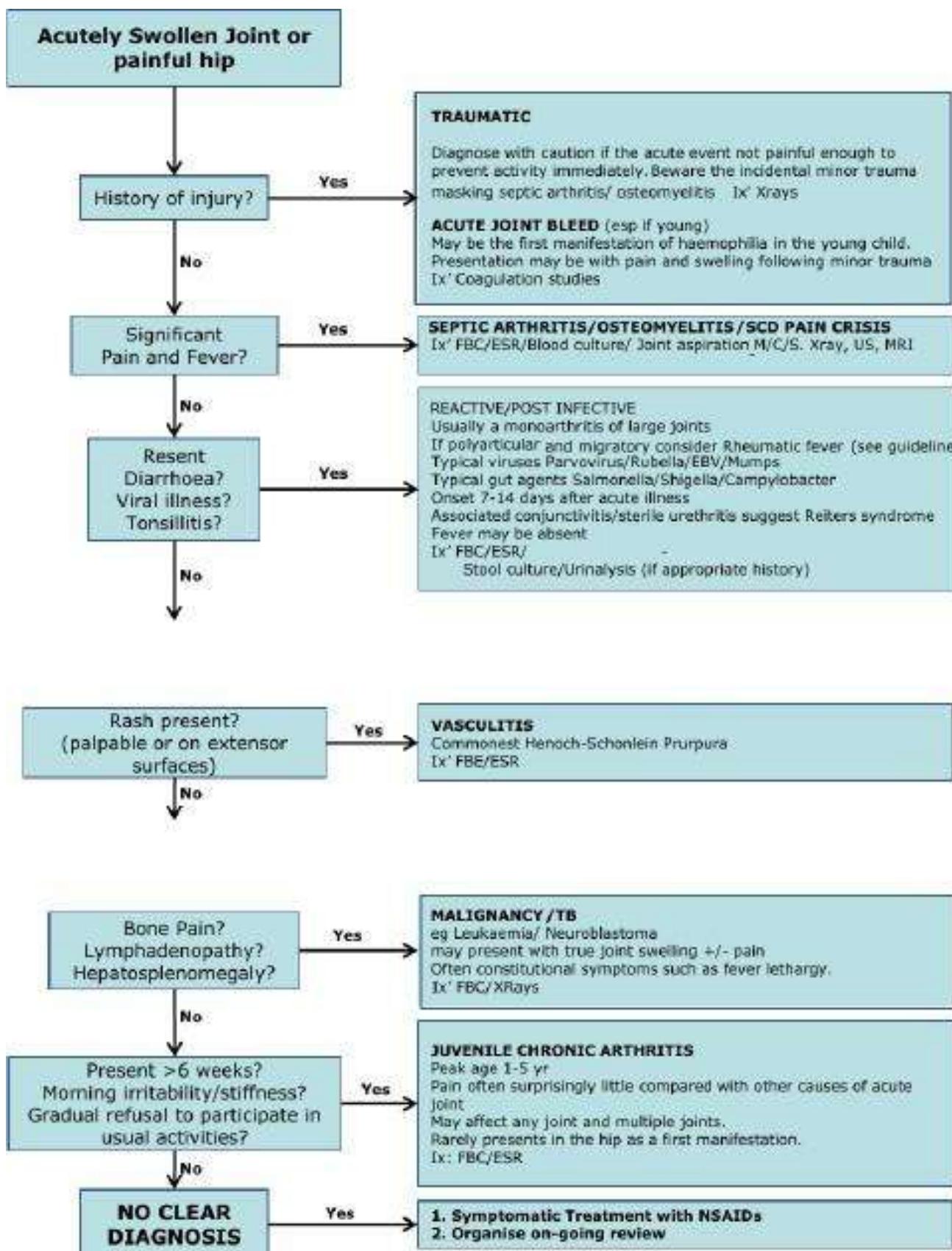
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CHAPTER 13. RHEUMATOLGY

Acronyms

| | |
|------------|---|
| ANA | Antinuclear antibodies |
| CRP | C-Reactive Protein |
| CXR | Chest X-ray |
| DCMO | Dilated Cardiomyopathy |
| DIC | Disseminated Intravascular Coagulopathy |
| DMARDs | Disease Modifying Antirheumatic Drugs |
| ECHO | Echocardiogram |
| ESR | Erythrocyte Sedimentation Rate |
| EULAR/ACR | European League Against Rheumatism/American College of Rheumatology |
| FB | Foreign Body |
| FBC | Full blood count |
| HSP | Henon-Schonlein Purpura |
| JDM | Juvenile Dermatomyositis |
| JIA | Juvenile Idiopathic Arthritis |
| KD | Kawasaki Disease |
| MAS | Macrophage Activation Syndrome |
| MCS | Microscopy, culture and sensitivity |
| MCP joints | Metacarpophalangeal joints |
| MRI | Magnetic Resonance Imaging |
| NAI | Non accidental injury |
| NSAID | Non-Steroidal Anti-Inflammatory Drugs |
| Ortho | Orthopaedics |
| pGALS | Paediatric Gait Arms Legs and Spine |
| SCD | Sickle cell Disease |
| SLE | Systemic Lupus Erythematosus |
| SO-JIA | Systemic Onset Juvenile Idiopathic Arthritis |
| US | Ultrasound |
| VDRL | Venereal Disease Research Laboratory Test |

THE SWOLLEN JOINT



Important points in history

- Length of history of swelling
- Any trauma or injury. N.B. Beware the incidental minor trauma masking septic arthritis/ osteomyelitis
- Was the onset sudden or insidious
- Recent history of viral illness e.g. gastroenteritis, sore throat etc
- History of migratory arthritis
- Fever
- Rash
- Maternal infection e.g. syphilis
- Any other joints involved or have been involved
- Decreased movement of the joint and pain
- Are symptoms worse in the morning or later in the day
- Past history of sickle cell disease, asplenia, or frequent malaria infections
- Previous admissions for same problem
- Family history of sickle cell disease, haemophilia or arthritis

Important points on examination

- Is the child 'toxic' i.e., looks unwell, listless
- Is the child in pain
- Is there fever
- Is the affected joint
 - swollen (if so is there an effusion present)
 - warm
 - red
 - painful
- Can the joint be moved by patient or observer?
- Any rashes or skin changes (including psoriasis, rheumatic nodules, or purpura)
- Are any other joints abnormal, and if so what is their distribution e.g. symmetrical/asymmetrical, large joint/ small joint?
- Is there a cardiac murmur?
- Are there enlarged LNs or hepatosplenomegaly (consider leukaemia or systemic Juvenile Idiopathic Arthritis)

Relevant investigations

- Blood culture if febrile, FBC and diff
- X ray of affected area (look for effusion, for bony changes or double periosteum in syphilis)
- Ultrasound, useful in hip involvement to demonstrate an effusion
- Inform ortho team if septic arthritis or osteomyelitis
- Consider MRI if uncertain diagnosis
- Maternal VDRL in infant

Indications for admission

- Unless obvious history of sprain or minor trauma admit for investigation and observation.

SEPTIC ARTHRITIS

Definition

Intra-articular infection with bacteria or rarely, fungi.

- Medical emergency (surgical emergency if hip or shoulder involved)
- Peak age 2 yrs, unwell febrile child & reduced range of movement of joint. Child may refuse to weight bear on the joint

Risk factors

- Trauma
- Young age
- Immune deficiency
- Poor wound care / treatment

Causes

- *Staphylococcus aureus* and non-Group A β Streptococcus are most common overall
- *Streptococcus pneumoniae* is common in children younger than 2 years
- *Neisseria gonorrhoeae* in sexually active adolescents
- *Salmonella* is commonly associated with sickle cell disease
- *Mycobacterium tuberculosis* is an unusual cause of septic monarthritis in childhood
- *Kingella kingae* is emerging as an important pathogen in children with septic arthritis and may also account for a significant portion of culture negative cases
- *Haemophilus influenzae* less likely due to immunizations

Prevention

- Early presentation to hospital

Promotion

- Early presentation to hospital
- Antibiotic treatment to be started early and should be a long course (only start after culture from blood and bone are done)
- Proper wound care

Signs and symptoms

- Systemic signs of illness (e.g., fever, vomiting, headache)
- May be a component of a more generalized infection that may include meningitis, cellulitis, osteomyelitis, or pharyngitis
- Joint pain is usually severe
- Infected joint and periarticular tissues are swollen, hot, and sometimes erythematous
- Joints of lower extremity are most commonly the sites of infection:
 - Knees,
 - Hips,
 - Ankles, and
 - Elbows

Investigation

- Joint aspirate prior to antibiotics/ Synovial fluid culture
 - Characteristics of synovial fluid: Cloudy, very high WBC count (50,000-300,000, > 75% neutrophils) Gram stain positive
- FBC, elevated WBC with neutrophilia.

- CRP and ESR
- Culture from subperiosteal space
- Blood culture
- Plain radiographs
- MRI/CT (MRI superior to CT in delineation of soft tissue structures and MRI changes may be seen as soon as 24 hours following infection; synovial enhancement detected in virtually all patients)

Management

Primary / Secondary Level

- Manage ABCDE
- Refer all cases to tertiary level

Tertiary Level

- Analgesia – paracetamol, non-steroidal anti-inflammatory drugs (if available), and opiates may be required
- Rest the joint – sling for arm, bed rest for lower leg.
- Intravenous antibiotics followed by high dose oral antibiotics (total antibiotic course of 2 weeks)
 - **NOTE:** Choice of antibiotics depends on presence of predisposing factors, age of child, suspected organism or positive culture and local resistance patterns
 - **Neonates:** flucloxacillin & gentamicin IV until fever settles then oral treatment for 4 weeks depending on bacterial susceptibilities
 - **Older children:** Ceftriaxone 50mg/kg IV OD
 - Treat until fever is settled then oral ciprofloxacin for a maximum of 2 weeks if improving
- Surgical debridement and joint aspiration and injection of sterile fluid until its clear performed by orthopedic surgery

Complications

- Stiff immovable joint – is a late presentation of septic arthritis as articular surface may have been destroyed.
- There may be a coexistent osteomyelitis in ~15% cases.

Follow up

- Patients to be follow up in orthopedics and PEN-Plus clinic

OSTEOMYELITIS

Definition

Intraosseous infection with bacteria or rarely, fungi. Classified as acute, subacute, or chronic.

Acute osteomyelitis:

- Is of recent onset and short duration. Most often hematogenous in origin but may result from trauma such as a compound fracture or puncture wound.
- Can be metaphyseal, epiphyseal, or diaphyseal in location.

Subacute osteomyelitis:

- Is of longer duration and is usually caused by less virulent organisms

Chronic osteomyelitis:

- Results from ineffective treatment of acute osteomyelitis and is characterized by necrosis and sequestration of bone

Risk factors

- Young age
- Immunodeficiency
- Open fracture
- Sickle cell
- Untreated/under treated septic arthritis

Causes

- *Staphylococcus aureus*
- *Salmonella Typhimurium*
- *Salmonella* spp (sickle cell disease)
- Group B Streptococci (neonate)
- Coliforms (neonate - esp. preterm)
- *Neisseria meningitidis*
- Tuberculosis (note the following regarding tuberculosis):
 - Can cause osteomyelitis and septic arthritis
 - Signs are less marked than other bone infections, history more chronic
 - Signs of systemic TB are sometimes apparent
 - Spinal TB can cause paraplegia and deformity (Pott's disease)
 - Treatment is anti TB medications and surgery. (D/W orthopaedic surgeons)

Prevention / Promotion

- Early presentation to hospital
- Antibiotic treatment to be started early and should be a long course (only start after culture from blood and bone are done)
- Proper wound care

Signs and symptoms

- Fever
- Severe bone pain and tenderness with or without local swelling should suggest the possibility of acute osteomyelitis
- Unique features:

- Neonates may present with pseudoparalysis or sepsis; fever is common; organisms frequently cross the physis and cause growth arrest
- Patients with hemoglobinopathy frequently have Salmonella and other gram-negative organisms

Investigations

- Elevated WBC, ESR, CRP are non-specific
- Blood cultures
- Bone cultures (sensitivity 80%)
- Imaging:
 - X-rays important for exclusion of other diagnoses (X-ray signs include soft-tissue swelling, soft tissue edema, subperiosteal changes and bone destruction (diagnostic findings may not be clear until days 10 to 21)
 - Bone scan
 - MRI

Management

Primary / Secondary Level

- Manage ABCDE
- Refer all cases to tertiary level

Tertiary Level

- Analgesia – paracetamol, non-steroidal anti-inflammatory drugs (if available), and opiates may be required
- Rest the joint – sling for arm, bed rest for lower leg.
- Intravenous antibiotics followed by high dose oral antibiotics (total antibiotic course of 2 weeks)
 - **NOTE:** Choice of antibiotics depends on presence of predisposing factors, age of child, suspected organism or positive culture and local resistance patterns
 - **Neonates:** flucloxacillin & gentamicin IV until fever settles then oral treatment for 4 weeks depending on bacterial susceptibilities
 - **Older children:** Ceftriaxone 50mg/kg IV OD
 - Treat until fever is settled then oral ciprofloxacin for a maximum of 4 weeks if improving.
- Osteomyelitis abscess drainage required. Discuss with orthopaedic surgeons.
- Post surgery: need physiotherapy and early mobilization to prevent stiffness and to preserve function when pain free.

Treatment of Congenital Syphilis

- 10 days IM/IV benzylpenicillin and treat both parents.

Complications

- Chronic osteomyelitis - If acute osteomyelitis goes untreated pus escapes the intramedullary space to form a sequestrum (avascular cortical bone) by spreading proximally and distally removing periosteum and making the cortex ischaemic. New bone is formed by the periosteum (involucrum). Management is difficult – consult orthopaedic surgeons and refer.

Follow up

- All patient to be follow up in orthopedic and PEN-Plus clinic

THE LIMPING CHILD

Definition

Abnormal gait

Risk factors (Indications for urgent assessment of a limping child)

- The very young (under 3 years of age)
- The ill and febrile
- The non-weight bearing
- Children with painful restricted hip movements
- The child who is immunosuppressed - when septic arthritis, osteomyelitis, malignancy is suspected, fractures
- When non-accidental injury, SUFE (Slipped Upper Femoral Epiphysis) and malignancy are suspected

Causes of Limp by age

| | 0-3 years | 4-10 years | 11-16 years |
|--|---|---|--|
| Most common | <ul style="list-style-type: none"> • Trauma (including toddler's fracture) • Injury/FB/splinter to sole of foot | <ul style="list-style-type: none"> • Trauma • Transient synovitis • Perthes' disease | <ul style="list-style-type: none"> • Trauma • Osgood-Schlatter disease |
| Conditions requiring urgent intervention | <ul style="list-style-type: none"> • Osteomyelitis • Septic arthritis • Non accidental injury (NAI) • Malignancy (e.g. neuroblastoma) • Testicular torsion • Inguinal hernia | <ul style="list-style-type: none"> • Osteomyelitis • Septic arthritis • NAI • Malignant disease (e.g. ALL) • Testicular torsion • Appendicitis • Inguinal hernia | <ul style="list-style-type: none"> • Osteomyelitis • Septic arthritis • Slipped upper femoral epiphysis (SUFE) • Malignancy (e.g. bone tumours) • Testicular torsion • Appendicitis • Inguinal hernia |
| Other important conditions to consider | <ul style="list-style-type: none"> • Developmental dysplasia of the hip • Juvenile Idiopathic Arthritis | <ul style="list-style-type: none"> • Juvenile Idiopathic Arthritis | <ul style="list-style-type: none"> • Juvenile Idiopathic Arthritis |
| | <ul style="list-style-type: none"> • Metabolic (e.g. rickets) • Haematological disease (e.g. sickle cell disease) • Reactive arthritis • HSP • Multisystem diseases (e.g. Juvenile Systemic Lupus Erythematosus, Juvenile Dermatomyositis) | | |

Differential diagnoses

- Septic arthritis: unilateral swollen joint, pain and fever needs urgent orthopaedic consultation.
- Malignancy (e.g. bone tumours, leukaemia). Perform diagnostic work up if any
- Suspicion
- Acute Rheumatic fever
- HIV arthropathy
- Tuberculosis
- Joint bleeds e.g. in haemophilia
- Other autoimmune conditions and vasculitides eg Henoch Schonlein Purpura (HSP), Systemic Lupus Erythematosus (SLE), dermatomyositis

Investigations

- Will depend on the suspected cause of the limp.
- Discuss management with seniors (either consultant paediatrician or rheumatologist if available) and the orthopaedic team.
- In patients without red flag features who have symptoms for > 6 weeks and are presumed to have JIA
 - HIV test
 - Malignancy/ TB work up if suspicion
 - FBC (often normal in oligoarticular JIA. In systemic onset, polyarticular JIA it may reveal normo/microcytic anaemia, leucocytosis and/or thrombocytosis)
 - ESR
 - CXR/ECHO if suspicion of alternative diagnosis or pleuritis/pericarditis
 - X rays may reveal deformities, erosions, joint space narrowing, but can be normal in early disease
 - Ultrasound of joints useful if expertise exists to show joint effusions

Examination

- Joints:
 - **LOOK** (swelling, deformity, colour changes),
 - **FEEL** (heat, tenderness),
 - **MOVE** (passive and active) every joint.
 - Don't forget spine and temperomandibular joints.
 - **pGALS** is a good screening tool (see Musculoskeletal assessment: pGALS questions and examination [versusarthritis.org] for details),
- Systemic: look for lymphadenopathy, hepatosplenomegaly, pleural/pericardial effusions (can all be seen in SO -JIA), features of psoriasis, rashes,

Alert Box

- Red flags to look out for in case of infection, malignancy or Non-Accidental Injury
- Fever, malaise, reduced appetite, weight loss, night sweats
 - Bone or joint pain with fever
 - Refractory or unremitting pain, persistent night waking
 - Unclear history and presentation with regards to pattern of physical findings plus previous history of neglect

General Joint screening

pGALS (paediatric gait, arms, legs, spine) screen-validated for use in school aged children

Screening questions

- Do you have any pain or difficulty in moving your arms, legs, neck or back?
- When you get dressed, are you able to do this yourself without any help?

Then an examination (if all is normal it makes musculoskeletal pathology very unlikely)

- Observe the child from the back front and side
- Observe the patient walking.
- 'Walk on your heels.'
- 'Walk on your tip-toes.'
- 'Put your hands out in front of you.'
- 'Turn your hand over and make a fist.'
- 'Touch the tips of your fingers.'
- Squeeze MCP joints.
- 'Put your hands and wrists together.'
- 'Put your hands back to back.'
- 3 fingers vertically inside
- 'Reach up as far as you can.'
- 'Look at the ceiling.'
- 'Put your hands behind your neck.'
- 'Place your ear on your shoulder.'
- 'Open your mouth wide and place 3 fingers inside.'
- Feel for effusion at the knee.
- 'Bring your ankle up to your bottom.'
- Passive movement of hip and knee including rotation of hip.
- Observe curvature of spine from the side and behind. 'Bend forwards.'

Treatment

Depends on the underlying cause.

Referral

Refer to secondary or tertiary level depending on cause and treatment needed.

Follow up

Follow up will depend on cause and treatment needed.

JUVENILE DERMATOMYOSITIS

Definition

Juvenile dermatomyositis is a rare systemic, autoimmune myopathy and vasculopathy in childhood. The skin and skeletal muscles are primary areas of involvement.

Causes / Risk factors

- Possible link to genetic susceptibility

Prevention / Promotion

- There is no primary prevention for JDM
- Secondary and tertiary prevention should focus on controlling underlying myositis (to be discussed under management) and control of complications of the disease (contractures and calcinosis) and treatment (long term Steroid use or immunosuppressive agents- to avoid acquisition of opportunistic infections like TB)
- Ambulatory support, if not able to walk. (physiotherapy)
- School support- provide a letter of support for the teacher to consider child physical limitations.
- Once diagnosis is made and a care plan instituted by a specialist- establish a mechanism for follow up at the nearest facility.
- Adherence counseling and therapeutic monitoring and support
- Patient and family support group

Signs and symptoms

Diagnostic criteria according to Bohan and Peter criteria, 1975:

- Presence of pathognomonic rash (Gottron papules, Heliotrope rash) plus 3 or 4 of the following features for a “definite diagnosis”**
 - Symmetrical proximal muscle weakness (Gower sign positive)
 - Elevated serum levels of muscle enzymes (CK,AST, LDH, aldolase)
 - Electromyographic changes of chronic inflammatory myositis
 - Muscle biopsy (Histopathological changes of inflammatory myositis)
 - Nailfold capillary microscopy abnormalities
- Probable diagnosis: would require presence of typical rash plus 2 of the above features
- Note:** Typical muscle findings on MRI and USS (MRI has become more important diagnostic tool for muscle inflammation)
- Other signs and symptoms include:
 - Calcinosis cutis,
 - Arthritis,
 - constitutional symptoms (fever, weight lose, fatigue)
- It is important to assess for 3D's – dysphagia, dysphonia and dyspnea – that indicate severe disease.
- Nasal voice, difficulty swallowing and choking on foods (18-44%) may indicate weakness of the palate and cricopharyngeal muscles.
- Other organ systems may also be involved:
 - Arthritis (23-58%)
 - GI tract symptoms (22-37%), including dysphagia, GI ulceration, perforation
 - Lungs (interstitial lung disease)
 - Heart (cardiomyopathy) – very rare

- **JDM can also present with cardiopulmonary (conduction defects, myocarditis, DCMO) and gastrointestinal involvement.**
- Muscle biopsy has limited role in JDM diagnosis (consult rheumatologist if considered)

Investigations

- Laboratory tests
 - Full Blood count
 - Urea and Electrolytes
 - Inflammatory markers (ESR, CRP)
 - Muscle enzymes (creatine kinase, lactate dehydrogenase, aspartate aminotransferase and aldolase). These may be normal at times
 - Lupus profile (ANA, extractable nuclear antigens[ENA])
 - myositis-specific antibody assays (e.g Anti MJ/ Anti MDA5, Anti NXP2, Anti TIF1)
 - Antinuclear antibodies – ANA
- Imaging studies
 - Nailfold capillary microscopy
 - Muscle ultrasound scan (may be normal)
 - MRI
 - Electromyography

Differential diagnosis

- Consider other myopathies (noninflammatory myopathies like muscular dystrophies, metabolic myopathies: Inflammatory myopathies like viral myositis, pyomyositis)

Management

- Goal: treat myositis, prevent mortality prevent calcinosis and long term morbidity
- All patients should be managed at a tertiary facility level with the supervision of a specialist (rheumatologist/ neurologist)

Primary / Secondary Level

Tertiary Level

First line: (mild to moderate disease)

Pharmacological

- Corticosteroids (dose, route and duration dependent on disease characteristics).
 - Methylprednisolone pulse 10-30mg/kg/day for 3 days (given over 1-4 hours in 100mls of Normal Saline and to measure BP during administration at 30 minutes intervals)
 - Prednisolone 1-2mg/kg slow weaning dose over the next 18 months
- Methotrexate 15mg/m² subcutaneous preferably
- Calcium and Vitamin D supplementation
- TB INH Prophylaxis and folic acid for those on methotrexate
- Hydroxychloroquine at 3-6mg/day

Non-Pharmacological:

- Photoprotective measures
- Physio and occupational therapy

Second line: refer to rheumatologist

Pharmacological

- IV immunoglobulins
- Ciclosporin
- Azathioprine

Third Line: refer to rheumatologist

Pharmacological

- Cyclophosphamide
- MMF (mycophenolate mofetil)
- Tacrolimus
- Rituximab
- Anti-TNF α agents

Referral should be urgent to paediatrician / paediatric rheumatologist

- if suspected to have cardiopulmonary or gastrointestinal manifestations.
- All patients requiring DMARD.
- Adverse reaction to NSAID.
- Severe JDM or suspected JDM not responding to first line therapy

Follow up and treatment monitoring

- Muscle enzymes should return to normal
- Inflammatory markers should return to normal
- Increase muscle strength subjectively and objectively using the Childhood Myositis Assessment Scale
- Resolution of skin rash
- Improvement in capillary nail fold changes

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Definition

Multi-system inflammatory disease characterized by autoantibody and immune-complex mediated inflammation of blood vessels and connective tissues. It can lead to a spectrum of disease ranging from mild to life-threatening illness.

- Common organs/systems involved: Skin, Joints, Kidneys, Blood cells and Nervous system

Risk factors

- Childhood onset average age is 12 years
- Affects more females than males
- Race- more common in blacks and Hispanics
- Sun exposure
- Viral infections ?
- Genetic predisposition

Causes

- Aetiology unknown

Prevention / Promotion

- Primary prevention to focus on disease progression reduction strategies for those not fulfilling SLE diagnosis criteria: (reduced sun exposure, vitamin D and calcium supplementation, hydroxychloroquine and close monitoring of biomarkers)
- Secondary and tertiary prevention to consider: physiotherapy for joint involvement, prevention of drug toxicities (steroids), and infections.
- Patient education of medication adherence.
- Improve access to care : development of care plan at tertiary facility inclusive of ongoing care and nearest primary care (follow up primary care could include physiotherapy, BP monitoring, Urine dipsticks)
- Patient and family support groups

Signs and symptoms

- Malar rash
- Photosensitive rash
- Ulcers/Mucocutaneous involvement
- Kidneys: Proteinuria, urinary cellular casts, hypertension, renal failure
- Seizures
- Thrombocytopaenia
- Haemolytic anaemia
- Fever
- Lymphadenopathy
- Pruritis
- Hepatosplenomegaly
- Other clinical features of SLE not included in above classification criteria:
- Constitutional symptoms – fevers, fatigue, weight loss, anorexia
- Other rashes (e.g. annular erythema, maculopapular or linear (nonspecific) rash, bullous lupus (rare), palmar/plantar/periungual erythema, livedo reticularis, or vasculitic rash)

- Alopecia classically in the frontal area, but can be diffuse
- Polyarthralgia, myalgia, and/ or myositis
- Raynaud phenomenon (see Section 5A) o Lymphadenopathy
- Hypertension
- Decreased concentration and cognitive dysfunction
- Stroke
- Mood disorder
- Headache
- Pneumonitis
- Pulmonary hemorrhage
- Myocarditis
- Libman-Sacks endocarditis

EULAR/ACR Criteria for Classification of SLE: Entry criteria:

ANA positive (titres ≥1:80)

| Clinical domain | points |
|--|------------------|
| Constitutional <ul style="list-style-type: none"> • Fever • Weight loss • Fatigue | 2 |
| Cutaneous <ul style="list-style-type: none"> • Non-scarring alopecia • Oral Ulcers • Subcutaneous/discoid lupus • Acute cutaneous lupus (malar rash) | 2 2 4 6 |
| Arthritis <ul style="list-style-type: none"> • Synovitis or tenderness in at least 2 joints | 6 |
| Neurologic <ul style="list-style-type: none"> • Delirium • Psychosis • Seizure | 2 3 5 |
| Serositis <ul style="list-style-type: none"> • Pleural or pericardial effusion • Acute Pericarditis | 5 6 |
| Haematology <ul style="list-style-type: none"> • Leucopaenia • Thrombocytopenia • Autoimmune haemolysis | 3 4 4 |
| Renal Proteinuria >0.5g/24hr Class II or V Lupus Nephritis Class III or IV Lupus Nephritis | 4 8 10 |

| | |
|---|--------|
| Immunologic antiphospholipid antibody • anticardiolipin IgG>40GPL • or anti-β2GP1 IgG>40 units • or lupus anticoagulant | 2 |
| Complement protein Low C3 or Low C4 Low C3 and Low C4 | 3 4 |
| Highly specific antibodies • Anti-dsDNA antibody • Anti-Sm antibody | 6 6 |

Important points to note:

- Patients must have ≥ 10 points to be classified as SLE
- Items counted only if no other likely cause suspected
- Count the highest criterion in the domain
- Points from at least 1 clinical domain required for classification
- Rare complication- MAS

Investigations

Laboratory tests:

- FBC with differentials
- Urea and Electrolytes
- Urinalysis with microscopy
- Inflammatory markers (CRP, ESR)
- Complement levels
- Liver function tests
- Creatinine kinase assay
- Spot protein/Spot creatinine ratio
- Autoantibodies (ENA, ANA, antiphospholipid antibodies)
- Thyroid function test
- Coombs

Imaging studies:

- Joint radiography
- Chest Xray
- Echocardiography
- Abdominal USS
- Brain MRI (contrast)

Procedures and other tests (depending on presentation):

- Lumbar puncture to rule out CNS infection in someone presenting with CNS symptoms
- Arthrocentesis
- Kidney biopsy (refer to American College of Rheumatology (ACR) guidelines for indications)
- Pleural or ascitic tap (send samples for chemistry, microbiology and cytology)

- Ophthalmology assessment
- Lung function test

Differential diagnosis

- Other connective tissues diseases (JDM, JIA, scleroderma)
- Autoinflammatory diseases (interferonopathy, monogenic autoinflammatory diseases)

Management and follow up (refer all patients to rheumatologist)

- **Goal:** prevent mortality, and improve function and long term morbidity (organ damage)
- To be managed at a tertiary facility
- To be done in consultation with a paediatric rheumatologist and requires a multidisciplinary team
- To keep in mind disease and treatment complications (eg atherosclerosis, osteoporosis, neurocognitive impairment, renal complications)
- UV light protection

Primary / Secondary Level

- Refer all cases

Tertiary Level

- Vitamin D and Calcium supplementation
- All patients should be on Hydrochloroquine 200mg OD
- Corticosteroids
 - IV methylprednisolone followed by oral prednisolone
- Disease modifying drugs
 - Azathioprine
 - Mycophenolate mofetil (MMF)
 - Cyclophosphamide
 - Methotrexate
- Biological therapies
 - Rituximab
- Monitor inflammatory markers and renal functions

JUVENILE IDIOPATHIC ARTHRITIS

Definition

Juvenile idiopathic arthritis is arthritis of unknown etiology that begins before the **16th birthday** and persists for at **least 6 weeks** and in which other known causes of arthritis are excluded.

- Arthritis is diagnosed in the presence of joint effusion OR two or more of the following: **limited range of movement with joint line tenderness or painful range of movement.**

Risk factors

- Girls more than boys (particularly oligoarticular)
- Other autoimmune diseases
- Trauma

Causes (inclusive of differential diagnosis)

- Consider other causes of arthritis (see approach to swollen joint section)
- For systemic arthritis rule out- Kawasaki's disease, scarlet fever, acute rheumatic fever
- Other autoimmune conditions or vasculitides (HSP, SLE,)

Prevention / Promotion

- Early diagnosis and treatment
- Secondary prevention of complication e.g., infection, deformity, reduced function
- Patient and family education about the disease and its management
- Provide emphasis of medication adherence and clinic follow ups
- Promote exercise to improve joint mobility and function (physiotherapy)
- Encourage regular eye examination
- Emotional support for patients and guardians through professional counselling and support groups

Signs and symptoms

- Arthritis is diagnosed in the presence of joint effusion OR two or more of the following:

- limited range of movement with joint line tenderness
- painful range of movement

(See general description above (limping child / the swollen joint))

The current classification system by the International League of Associations for Rheumatology (ILAR) recognizes 7 distinct subtypes of JIA, based on their presentation within the first **6 months**:

| No | Class | Description |
|----|---|--|
| 1 | Oligoarthritis | <ul style="list-style-type: none"> • Involve 1-4 joints during the first 6 months • Has two subtypes: <ul style="list-style-type: none"> ○ persistent (≤ 4 joints throughout the disease) ○ Extended (> 4 joints after 6 months) • Consider TB if only one joint is involved • Has high risk of anterior uveitis (all need screening) • Most common in young girls with positive ANA (around 5 years old) • Frequent joints to be involved are knees, ankles, wrists, or elbows • Good prognosis unless extended |
| 2 | Polyarthritis (Rheumatoid factor negative) | <ul style="list-style-type: none"> • Affects $>=5$ joints in first 6 months • Negative rheumatoid factor • Joint involvement is frequently symmetrical, affecting large and small joints alike • Children with RF negative polyarthritis are frequently younger and have a better prognosis |
| 3 | Polyarthritis (Rheumatoid factor positive) | <ul style="list-style-type: none"> • Affects $>=5$ joints in the first 6 months • Positive rheumatoid factor on 2 occasions at least 3 months apart during first 6 months of disease • Share many characteristics with adults with rheumatoid arthritis (RA). • Affects mostly adolescent girls • Clinical symptoms are similar to the adult disease with symmetrical polyarthritis especially involving the PIP joints and MCP joints |
| 4 | Systemic Arthritis | <ul style="list-style-type: none"> • Arthritis in 1 or more joints (initially can lack arthritis) • 2 weeks of fever documented as daily quartan fever at least 3 days • Accompanied by 1 or more of: <ul style="list-style-type: none"> ○ Erythematous macular rash (salmon rash) ○ Serositis (pericarditis, and pleuritis) ○ Hepatosplenomegaly ○ Generalised lymphadenopathy • Strongly associated with macrophage activation syndrome |
| 5 | Enthesitis related arthritis | <ul style="list-style-type: none"> • Arthritis and enthesitis OR • Arthritis or Enthesitis and 2 of the following |

| | | |
|---|-----------------------------------|---|
| | | <ul style="list-style-type: none"> ○ Sacroiliac joint tenderness and/or inflammatory back pain ○ HLA-B27 positive ○ One 1^o or 2^o relatives with HLA-B27 related disease ○ Arthritis in a boy after 6 years ○ Acute (symptomatic) anterior uveitis, pain, redness or photophobia ○ History of ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflammatory bowel disease, or acute anterior uveitis in a first-degree relative |
| 6 | Psoriatic arthritis | <ul style="list-style-type: none"> ● Arthritis plus psoriasis in a child, OR ● Arthritis and 2 of the following <ul style="list-style-type: none"> ○ Dactylitis ○ Nail pitting ○ Psoriasis in 1^o relatives ● Arthritis is typically asymmetric, and involves both large and small joints. |
| 7 | Undifferentiated arthritis | <ul style="list-style-type: none"> ● Arthritis not fitting any of the above or more than one group |

Alert box (important points to note)

- see above under the limping child and the swollen joint

Investigations (primary secondary and tertiary level)

- see above under the limping child and the swollen joint

Differential Diagnosis

- see above under the limping child and the swollen joint

Management

Treatment goals:

- Eliminate inflammation with goal to achieve clinical remission (rapid escalation of therapy may be required to achieve this goal)
- Prevent joint damage
- Promote normal growth and development
- Maintain normal function and optimize quality of life
- Minimize medication toxicity

Treatment in general:

- Multidisciplinary approach is part of comprehensive JIA management
- Occupational and physical therapists play an important role in treating JIA
- Psychosocial aspects of disease must be recognized and addressed

- Initial therapy with an NSAID may be started by a patient's primary care physician; however, a referral should be made to a pediatric rheumatologist as quickly as possible

Primary / Secondary Level

- Pharmacotherapy, initial therapy:

Oligoarticular JIA / Polyarticular JIA

- NSAID and/or intraarticular steroids
 - eg Ibuprofen 10mg/kg/dose 6-8 hourly for 1-2 months if no joint contractures and low disease activity
- Refer all patients to tertiary level of care

SJIA, psoriatic, enthesitis, non-specific

- Refer to tertiary level

Tertiary Level

- To be managed in consultation with paediatric rheumatologist

Oligoarticular; if no improvement after initial therapy

- Intra articular injections for all active joints
 - Methylprednisolone or Triamcinolone hexacetonide 1mg/kg with 1% lignocaine, 0.5ml
 - Repeat after 2 months if no response or response but not in remission
- If disease still active after 3 months
 - Methotrexate 10-15mg/m²/week (Max-25mg/week) stat on empty stomach.
 - Increase dose at 1mg/kg/week until response and maintain same dose
- Note: screen for uveitis**
- Add folic acid 5mg po weekly during treatment with MTX
- Monitor FBC, LFT, 3 monthly and creatinine 6 monthly**
- If no improvement, start biologic. TNF inhibitor (consult rheumatologist)

Polyarticular JIA

- If no improvement after a month of initial therapy
 - Consider MTX as above
 - Intra articular steroids can be used together with methotrexate
 - For rapid symptom relief: Prednisolone 1mg/kg/day starting dose and reduce to 5mg-7.5mg/day if good response.

SJIA

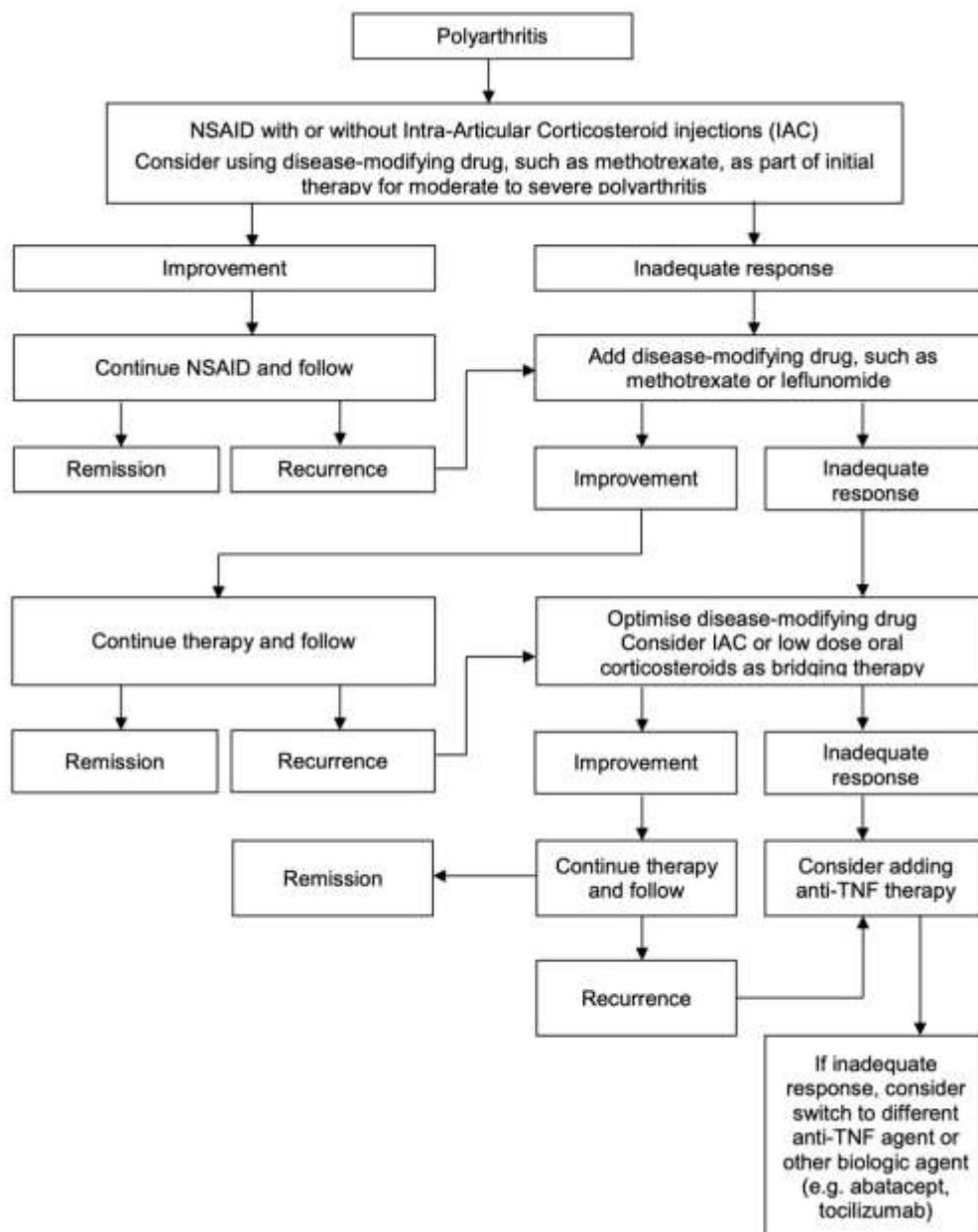
- Mild disease
 - Prednisolone 2mg/kg PO daily- tapper if remission achieved
- Critically ill patients with serositis
 - Methylprednisolone 30mg/kg/day IV for 3 days
 - Followed by prednisolone 2mg/kg/day until disease controlled
 - Start biologic (IL-1/IL-6 inhibitor) change be initiated at diagnosis
- Note:** Monitor for development of Macrophage Activation Syndrome.
- If possible start with IL-1 inhibitor without prior steroids

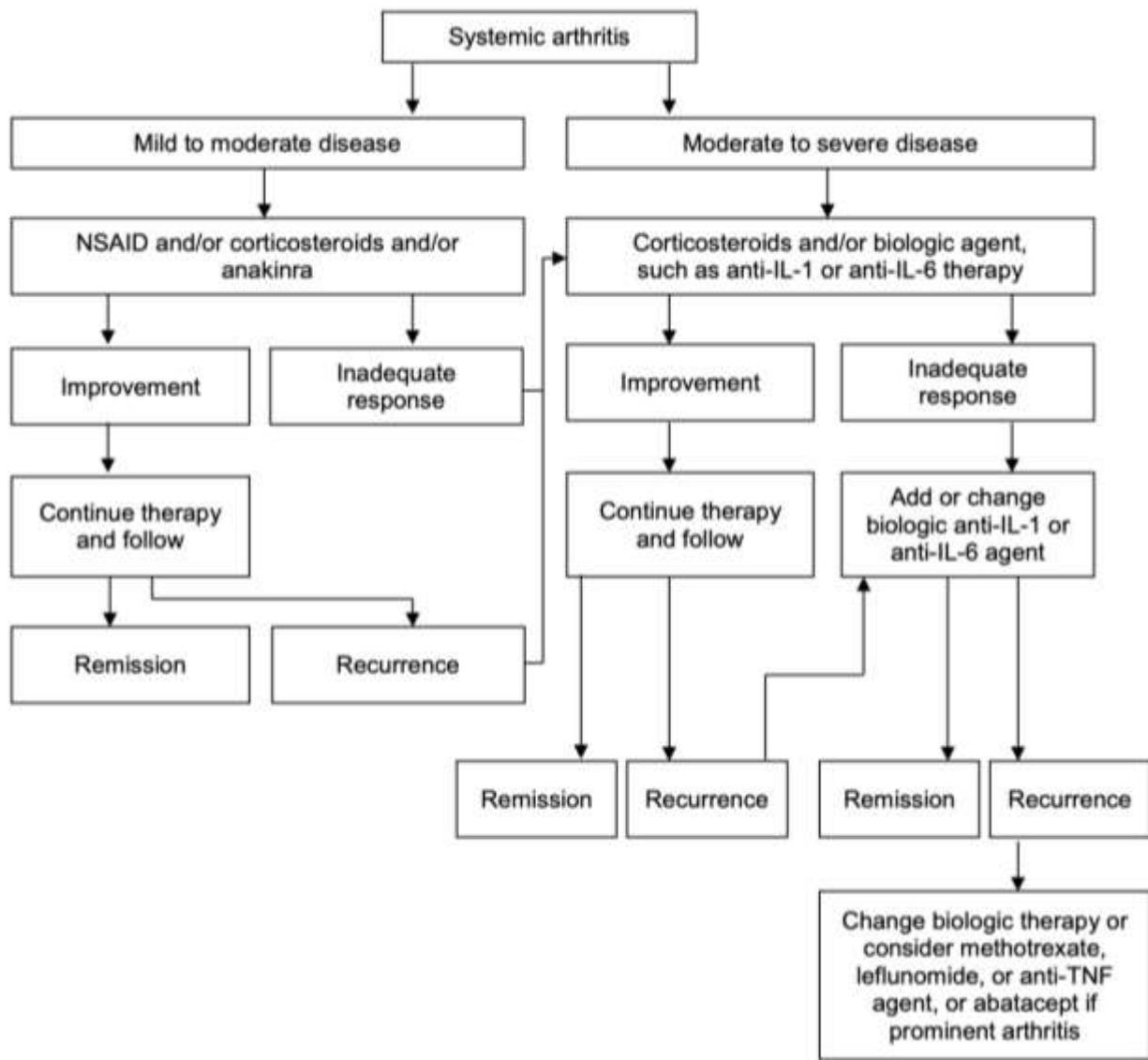
Psoriatic JIA

- NSAIDs eg Ibuprofen 10mg/kg/dose 6-8 hourly for 1-2 months if no joint contractures and low disease activity
- Treat like oligoarticular arthritis above.
- If no improvement, start biology- anti-IL-17 Secukinumab

Enthesitis related arthritis

- Primary treatment as in primary level with NSAIDs
- In severe disease
 - Prednisolone 2mg/kg/day oral
 - Consult paediatric rheumatologist





Follow up

- New patients need a monthly follow up
- Stable patients need 3 monthly follow up

KAWASAKI DISEASE

Definition

- A medium vessel vasculitis of unknown etiology characterized by fever, rash, conjunctival injection, oral mucositis, extremity changes, cervical lymphadenopathy and in a proportion of cases, dilation or aneurysms of the coronary arteries.
- The commonest Vasculitides in children < 5 years of age

Risk factors

- Males
- Prolonged fever
- Infants >1 year or <5 years of age
- Asian or Hispanic ethnicity
- Familial risk is uncertain

Causes (inclusive of ddx)

- Aetiology is unknown
- May be an immunologic response,
- Infectious trigger (viral and /or bacterial)
- Genetic susceptibility are some of the suggested factors in the pathophysiological process.

Prevention / Promotion

- No primary prevention of the disease.
- Secondary prevention should consider early diagnosis and treatment of children suspected to have the disease.
- Patient support.
- Educating patients about the disease and its complications.

Signs and symptoms

- Diagnostic criteria for Kawasaki Disease

| Diagnostic Criteria for Kawasaki Disease | |
|---|--|
| Fever lasting at least 5 days. | |
| At least 4 out of 5 of the following: | <ul style="list-style-type: none"> • Bilateral non-purulent conjunctivitis. • Mucosal changes of the oropharynx (injected pharynx, red lips, dry fissured lips, strawberry tongue). • Changes in extremities (oedema and/or erythema of the hands or feet, desquamation, beginning periungually). • Rash (usually truncal), polymorphous but non vesicular. • Cervical lymphadenopathy. |
| Illness not explained by other disease process. | |

Important points to note:

- In presence of fever and coronary artery involvement on echo, <4/5 criteria sufficient
- Incomplete KD if ≥ 5 days of fever with 2 or 3 features (common in infants who are at higher risk of coronary artery involvement)
- Atypical KD of KD with unusual manifestation (e.g renal failure)

Other clinical manifestations:

- Relatively common - irritability (aseptic meningitis), skin peeling in groin, arthritis, sterile pyuria (urethritis), gastroenteritis (abdominal pain, vomiting, diarrhea), uveitis
- Uncommon – gallbladder hydrops, GI ischemia, jaundice
- Cardiac – myocarditis, pericarditis, cardiac failure, valvular regurgitation
- Maybe be complicated with macrophage activation syndrome (MAS), DIC
- Periungual desquamation in weeks 2 or 3

Coronary artery disease in KD:

- Major concern is the development of coronary artery aneurysms, which most commonly occurs at 6-8 weeks after the acute illness (can occur earlier)

Investigations

- Full blood count - anaemia, leukocytosis with left shift, thrombocytosis.
- ESR and CRP (usually elevated)
- Serum albumin $< 3\text{g} / \text{dl}$; Raised transaminases
- Urine $> 10 \text{ wbc} / \text{hpf}$
- Chest X-ray, ECG
- Echocardiogram in the acute phase; Repeat at 6-8 wks/earlier if indicated

Differential diagnosis

- COVID MIS-C
- Meningitis
- Viral infections (adenovirus)
- Polyarteritis nodosa (systemic, cutaneous)
- SJS (Steven Johnson Syndrome)
- IgA vasculitis (once known as HSP)

Management**Primary / Secondary Level**

- Refer all suspected cases to tertiary level.

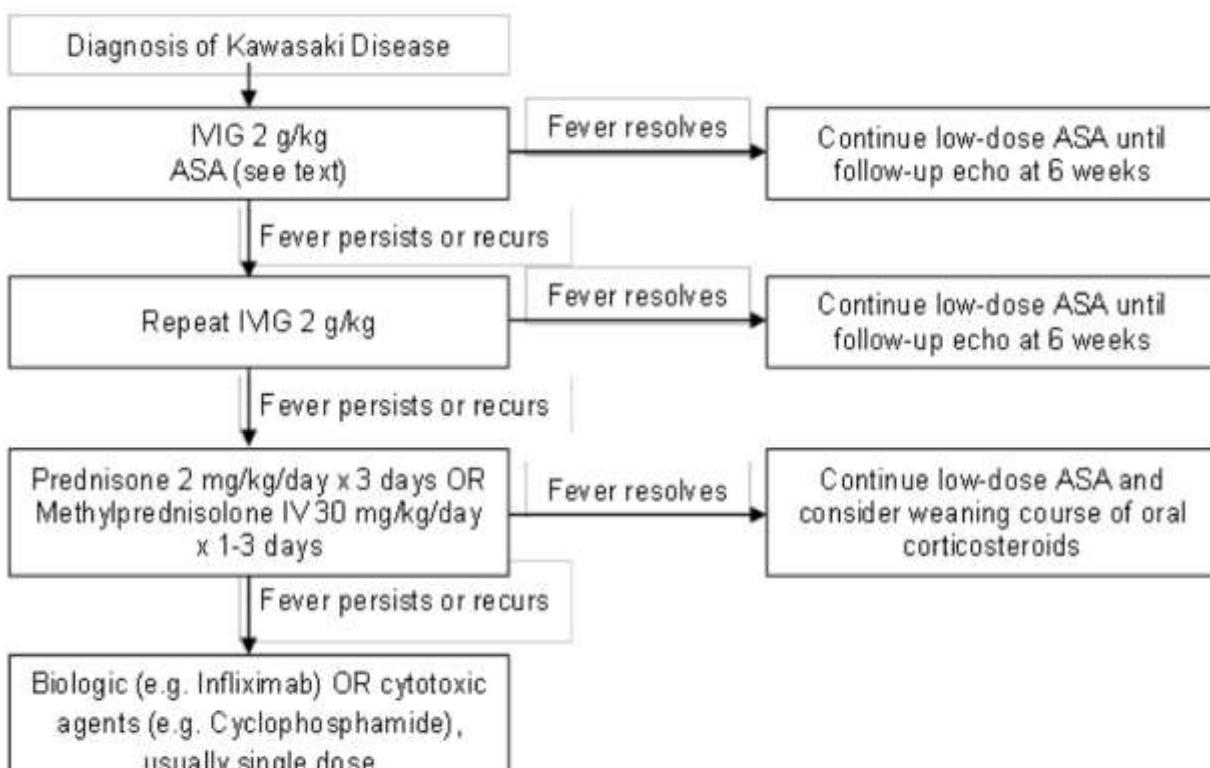
Tertiary Level

- IV Immunoglobulins 2 g/kg infusion over 10 - 12 hours.
 - Therapy < 10 days of onset effective in preventing coronary vascular damage.
- Oral aspirin (anti-inflammatory dose) 30-50mg/kg/day in 3 divided doses till day 14 of illness or until patient is afebrile for 2-3 days. (view algorithm below)

Maintenance:

- Oral aspirin 3-5 mg/kg daily (anti-platelet dose) for 6 - 8 weeks or until ESR and platelet count normalise.
- If coronary aneurysm present, then continue aspirin until resolves.
- **Note:** Kawasaki Disease not responding to primary treatment is defined as persistent or recrudescent fever \geq 36hrs after completion of initial dose of IV Immunoglobulins.
 - Repeat IV immunoglobulins 2 Gm/kg infusion over 10 - 12 hours

An algorithm for treatment of Kawasaki disease



Adapted from: Luca NJC, Yeung RSM. Epidemiology and management of Kawasaki disease. *Drugs* 2012; 72(8):1029-1038.

Alert Box

- Routine echocardiography [Note in-hospital mortality is 0.17% (all cardiac-related)]
- ~ 2% risk of recurrent KD
- Without treatment, coronary artery aneurysms occur in ~25% of patients → reduced to ~4% if IVIG treatment within 10 days
- If coronary artery aneurysm → risk for thrombosis, obstruction and stenosis at inlet/outlet of aneurysm, ventricular dysfunction/arrhythmia, early atherosclerosis, myocardial infarction (highest risk if aneurysm \geq 8 mm)

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