REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH

ZAMBIA PAEDIATRIC PROTOCOLS

First Edition | 2020

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Foreword

Acknowledgement

FLUID AND ELECTROLYTE REQUIREMENTS

FLUID AND ELECTROLYTES

The body loses fluids through urine, insensible loses (respiration, skin, stools) and intrinsic losses (by-product of metabolism).

FLUID AND ELECTROLYTE THERAPY-MAINTENANCE

The goal of maintenance therapy is to replace fluid and electrolyte needed by the average **child with normal renal function** over a 24-hour period.

Calculating maintenance fluids: Holliday-Segar method.

	Fluid per day	**Rate per hour**
1st 10kg	100 mL/kg/day	4 mL/kg/hr
Next 10kg	50 mL/kg/day	2 mL/kg/hr
For every additional kg	20 mL/kg/day	1 mL/kg/hr

Maintenance electrolyte requirements in children are:

- 2-3 mmol/kg/day of sodium,
- 1-2 mmol/kg/day of potassium
- 3-5 mmol/kg/day of chloride

HYPONATRAEMIA

Hyponatraemia is serum sodium (Na) concentration of less than **135 mmol/L.** Many patients presenting with acute neurological symptoms may have unrecognised hyponatraemia.

Causes

- Hypotonic fluid hydration
- Diarrhoea & vomiting
- Acute & chronic renal failure
- Hypothyroidism; adrenal insufficiency; SIADH
- Cirrhosis; congestive cardiac failure; nephrotic syndrome
- Ascites; effusions; pancreatitis
- Drugs - diuretics

Clinical features

Symptoms occur when serum Na levels fall ***below 125 mmol/L***. If the changes are chronic, the patient may be asymptomatic. These are:

- ◊ Early signs: anorexia, headache, nausea & vomiting
- ◊ Hypo/hypertension, muscle weakness & cramps,
- ◊ Bizarre behaviour, hallucinations, seizures, decorticate/decerebrate posture, coma

Investigations

- ◊ Serum Na+; serum osmolality; Urea & creatinine; Urine osmolality & Na+
- ◊ Aldosterone, cortisol, free T4 & TSH, ACTH & ADH levels
- ◊ Imaging studies for underlying cause – U/S & CT scans (head, abdomen)

Management

Correction of hyponatraemia should be slow, not exceeding 8 mmol/L/day.

- ◊ ***With neurologic symptoms***, raise the serum Na concentration by giving doses of 1-2 ml/Kg of 3% saline until symptoms resolve. Symptoms typically resolve with a rise in sodium of 3-7 mmol/L
- ◊ ***Hypovolaemic hyponatraemia*** - correct volume depletion with normal saline, then restriction of fluids to two-thirds (or less) of the volume needed for maintenance
- ◊ ***Normovoalemic hyponatraemia*** due to SIADH include fluid restriction to two-thirds (or less) of the volume needed for maintenance using normal saline; or the use of 3% NaCl, and IV administration of furosemide
- ◊ ***Hypervolemic hyponatraemia*** - restrict fluids and administer 3% NaCl to stop the symptoms
- ◊ Treat the underlying cause

NOTE: ***Osmotic Demyelination Syndrome****: Brain injury due to too-rapid correction of chronic hyponatremia is often associated*

with delayed neurological deterioration (onset of symptoms 1 to 4 days after serum Na is increased by > 12 mmol/L in less than 24 hours).

HYPERNATRAEMIA

Hypernatraemia is a serum sodium level greater than **145 mmol/L.**

Causes

Excessive Sodium	Water Deficit	Water and Sodium Deficit
Improperly mixed formula	Nephrogenic diabetes insipidus	Diarrhoea
Cow's milk (UHT, Fresh milk)	Central diabetes insipidus	Emesis
Excess sodium bicarbonate	Increased insensible losses	Burns
IV hypertonic saline	Inadequate intake	Chronic kidney disease
		Osmotic diuresis

Clinical Features

◊ Irritability
◊ Restlessness
◊ Lethargy
◊ High pitched cry
◊ Hyperpnoea
◊ Cerebral haemorrhage
◊ Seizures
◊ Coma
◊ Stroke

Complications

◊ Dural sinus thrombosis
◊ Peripheral thrombosis
◊ Renal vein thrombosis

Management

Priority is restoration of intravascular volume with isotonic fluid (slow infusion of normal saline).

Firstly, the water deficit is calculated as follows:

Water deficit (in Litres): = Body weight × 0.6 (1-145/ [current sodium])

Replacement fluid is then calculated as follows:

Replacement volume (in L)
= TBW deficit X [1 ÷ 1 - (Na concentration in replacement fluid in mmol/L ÷ 154 mmol/L)]

The volume calculated must be replaced slowly over 48-72 hours.

For example:

A 10kg child arrives with a history of dehydration. His labs reveal a Sodium 160 mmol/l.

Water Deficit: 10 x 0.6 x (1-145/160) = **0.6 litres**

Fluid available is ½ Strength Darrow's: Sodium content in Darrow's = 61 mmol/L.

Therefore:-

replacement volume: 0.6 litres x [1/1- (61/154)] =**1 litre**

This volume of fluid should be given over 48-72 hours in addition to the daily maintenance fluid requirement.

Please monitor sodium **six hourly.** Aim at not dropping sodium by more than 0.5 mmol/hour or a total of 12 mol in any 24 hour period.

Other measures

- ◊ Severe cases (>200 mmol/L) may require dialysis with a high glucose-low sodium dialysate.
- ◊ Hyperglycaemia resulting from hypernatremia is not usually treated with insulin as rapid lowering of glucose may precipitate cerebral oedema.
- ◊ The underlying cause should be treated whenever possible

◊ Central diabetes insipidus should be treated with desmopressin

HYPERKALAEMIA

Hyperkalaemia is defined as serum potassium (K) level of more than 5mmol/L or 6mmol/L in neonates.

Classification of Hyperkalaemia

Severe	Moderate	Mild
K+ >7.0 mmol/L or at risk of increasing and/or	K+ 6-7 mmol/L	K+ >5.5 mmol/L
Patient symptomatic and/or	Asymptomatic	Asymptomatic
ECG disturbance:	ECG may be normal	Normal ECG

Causes

Increased Intake	Decreased Excretion	Drugs
Intravenous or oral	Renal failure	Angiotensin converting enzyme inhibitors
Blood transfusions	Urinary tract obstruction	Angiotensin II blockers
	Renal transplant	Potassium sparing diuretics
	Renal tubular disease	Nonsteroidal anti-inflammatory drugs

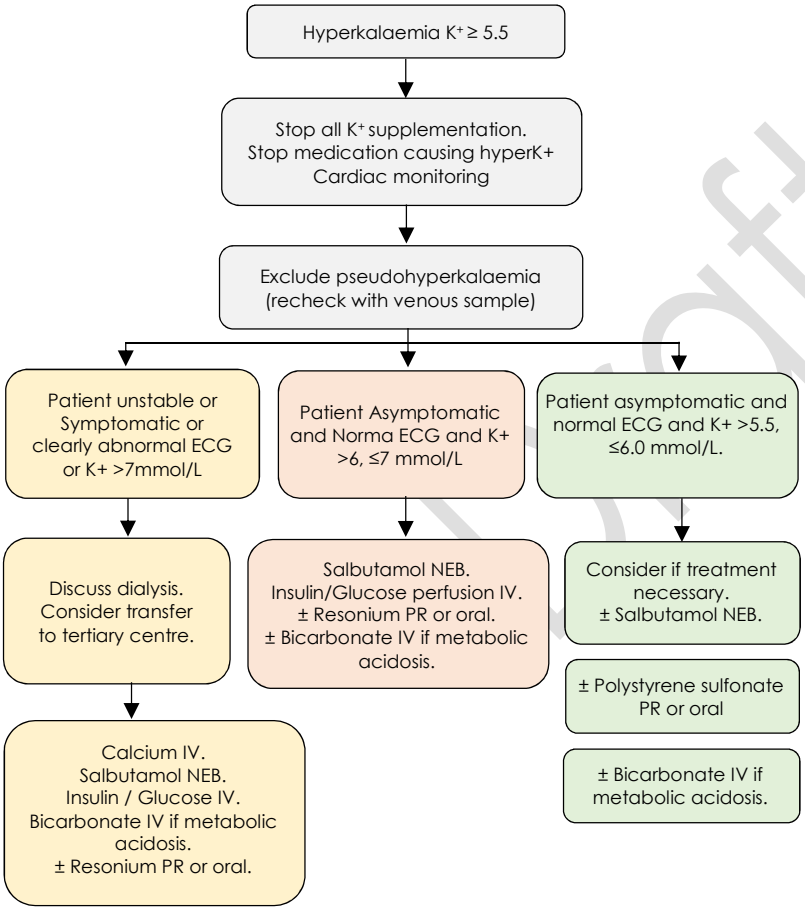
Clinical Features

◊ Paraesthesia
◊ Weakness
◊ Tingling
◊ ECG changes peaked T waves, wide P-R interval, flattening p wave, widening QRS complex
◊ Ventricular fibrillation
◊ Asystole

Management

Aims

- ◊ Stabilise the heart to prevent life threatening arrhythmias
- ◊ Remove potassium from the body
- ◊ The flow chart (figure xx) demonstrates the step by step approach



Drug	Dosage	Onset and Expected Actions	Mechanism	Considerations
Calcium 10% calcium gluconate (Approx. 225 micromol/mL) Calcium Chloride 10%	0.5mL/kg (0.11mmol/kg) in neonates and children <12 years. Max dose 4.5 mmol (20mL) of **10% calcium gluconate OR** 0.1-0.2 ml/kg slow IV injection (as above) (Max: 10ml) of **Calcium Chloride 10%**	**Onset of Action:** <3 minutes, should see normalisation of ECG. If not: repeat dose (twice) **Duration:** About 30 minutes	Stabilises the heart	**NOT** to be given simultaneously with bicarbonate **NOT** to be given if Digitalis toxicity
Soluble insulin/ Glucose	Average dosage: 0.3-0.6 IU/kg/hr in neonates, 0.05-0.2IU/kg/hr in children 1month and older; 5-10ml/Kg of D10% **If severe hyperkalaemia:** • Dextrose 10%: 5ml/kg IV bolus (if no hyponatremia) • Insulin short action: 0.1 U/kg IV bolus (Max 10 units) Then followed by infusion insulin/glucose (see below) **If moderate hyperkalaemia:** • Dextrose 10% IV at maintenance with 0.9% sodium chloride (normal saline) • Insulin short action infusion: 0.1 U/kg/h IV	**Onset of Action:** 15 min **Duration:** peak 60 minutes, 2-3hours	Shifts potassium into the cells	To be given at the same time. **Closely monitor glucose every 30-60 minutes**

Drug	Dosage	Onset and Expected Actions	Mechanism	Considerations
8.4% NaHCO3 (IV)	***Severe hyperkalaemia*** and ***metabolic acidosis*** Sodium Bicarbonate 8.4% 1mmol/ml: 1-3ml/kg IV over 5 minutes ***Mild to moderate hyperkalaemia*** and **metabolic acidosis:** Sodium Bicarbonate 8.4% 1mmol/ml: 1ml/kg in slow IV infusion over 30 minutes	**Onset of Action**: 30-60 minutes **Duration**: 2-3 hours	Shifts potassium into the cells	In metabolic acidosis, only.
Salbutamol (nebulised or IV)	< 25kg: 2.5 mg nebulised q 1-2h More than 25kg: 5mg nebulised (max 10-20mg) q 1-2h	**Onset of Action**: 30 minutes **Duration**: 2-3 hours	Shifts potassium into cells	Reduces intravascular K+ of 0.5-1.5mmol/L
Resonium	Mild effect, multiple doses necessary, may be used as long term agent Polystyrene sulfonate (Resonium) 0.3-1g/kg q 6h (Max 15-30g) Per Rectal (PR) or oral (with lactulose)	**Onset of Action:** 1-hour PR, 4-6hours oral, should reduce intravascular K+ of 0.5-1 mmol/L **Duration:** variable	Potassium excretion through gut	Mild effect, multiple doses necessary, may be used as long term agent. **NOT to be used** if ileus, recent abdominal surgery, perforation, hypernatremia
Dialysis	Transfer to tertiary care centre	Rapid- haemodialysis Slower- peritoneal	Removes potassium	Organise with local Paediatric renal or intensive care team.

Consider consultation with local paediatric team:

◊ Any child with moderate or severe hyperkalemia

◊ Underlying medical cause – e.g., renal abnormalities

When to consider transfer to tertiary centre:

◊ Any child with severe hyperkalemia

◊ Any child requiring dialysis

◊ Child requiring care beyond the comfort level of the hospital.

HYPOKALAEMIA

This a serum potassium level **< 3mmol/L.**

Causes

Decreased intake	Extra-renal losses	Renal losses	Drugs
Anorexia nervosa	Diarrhoea	Renal tubular acidosis	Amphotericin
	Laxative abuse	Diabetic ketoacidosis	Cisplatin
	Sweating	Interstitial nephritis	Aminoglycosides
		Uretero-sigmoidostomy	Loop and thiazide diuretics
		Cystic fibrosis	

Clinical features

◊ Muscle weakness and cramps

◊ Paralysis

◊ Heart block

◊ Paralytic ileus

◊ Polyuria

◊ Polydipsia

◊ ECG features: Flattened T waves, depressed ST segment, U wave

◊ Supraventricular tachycardia
◊ Ventricular tachycardia

Management

Oral Slow-K and Potassium chloride is preferred.

Intravenous potassium may be given at a dose of 0.5-1mmol/Kg usually given over one hour. Intravenous potassium should be used cautiously, with close monitoring of electrolytes, because of the risk of hyperkalaemia.

HYPOCALCEMIA

Hypocalcaemia is a total serum calcium concentration < 8.8 mg/dL (< 2.20 mmol/L) in the presence of normal plasma protein concentrations or a serum ionized calcium concentration < 4.7 mg/Dl (< 1.17 mmol/L).

Causes:

◊ Hypoparathyroidism
◊ Pseudohypoparathyroidism
◊ Vitamin D deficiency and dependency
◊ Renal disease
◊ Magnesium depletion
◊ Acute pancreatitis
◊ Hypoproteinaemia (asymptomatic)
◊ Persistent hypocalcaemia and hypophosphatemia correction of moderate to severe hyperparathyroidism
◊ Septic shock
◊ Hyperphosphatemia
◊ Drugs including anticonvulsants (e.g., phenytoin, phenobarbital) and rifampicin,
◊ Transfusion of > 10 units of citrate-anticoagulated blood

◊ Use of radiocontrast agents containing the divalent ion-chelating agent

◊ Infusion of gadolinium

Clinical features

Tetany characteristically results from severe hypocalcaemia but can result from reduction in the ionized fraction of serum calcium without marked hypocalcaemia, as occurs in severe alkalosis. It is characterized by the following:

◊ Sensory symptoms consisting of paraesthesia of the lips, tongue, fingers, and feet

◊ Carpopedal spasm, which may be prolonged and painful

◊ Generalized muscle aching

◊ Spasm of facial musculature

◊ Seizures

◊ Twitching

◊ Cramping

◊ Laryngospasm, a rare initial manifestation

Diagnosis

◊ Estimation or measurement of ionized calcium

◊ Measurement of serum magnesium, PTH, phosphate, alkaline phosphatase (ALP), and vitamin D concentrations

◊ Urine calcium, magnesium, and phosphate.

Treatment

◊ Oral calcium therapy (Calcium gluconate, Calcium carbonate) is preferred in asymptomatic patients and as follow-up treatment after intravenous (IV) calcium therapy

◊ IV calcium gluconate for tetany and patients having seizures, critically ill, and pre-operatives.

◊ Oral calcium for postoperative hypoparathyroidism

◊ Oral calcium and vitamin D for chronic hypercalcemia

◊ Ensure that the patient is well hydrated and passing urine

◊ Correction of hypomagnesemia is essential as hypocalcaemia does not respond until the low magnesium level is corrected.

Tetany

◊ ***IV Calcium gluconate*** should be given as follows:

- Give calcium gluconate 10 mL of 10% solution IV over 10 min; Calcium infusion drips should be started at 0.5 mg/kg/hr and increased to 2 mg/kg/hr as needed.
- Repeated boluses or a continuous infusion with 20 to 30 mL of 10% calcium gluconate in 1L of 5% D/W over the next 12 to 24 to may be needed.
- Give bolus of 0.5mL/kg (0.11mmol/kg) of 10% solution in neonates and children <12 years (Max dose 4.5 mmol i.e. 20mL of 10% solution). For IV infusion dilute to at least 45 micromol/mL with D5% or 0.9% sodium chloride.
- Oral supplements (Calcium gluconate) may precipitate NEC in neonates.

NOTE: (1) Infusions of calcium are hazardous in patients receiving digoxin and should be given slowly and with continuous ECG monitoring after checking for and correcting hypokalaemia. (2) When tetany is associated with hypomagnesemia, give a 10% magnesium sulphate solution (1 g/10 mL) IV, followed by oral magnesium salts (eg, magnesium gluconate 500 to 1000 mg po tid).

Transient hypoparathyroidism

Give supplemental oral calcium: 1 to 2 g of elemental calcium/day can give as calcium gluconate.

Chronic hypocalcaemia

Give oral calcium and/or vitamin D supplements: 1 to 2 g of elemental calcium/day as calcium gluconate or calcium carbonate.

In patients without renal failure, give vitamin D as a standard oral supplement (e.g., cholecalciferol 800 IU once/day) with adequate dietary or supplemental calcium and phosphate.

In patients with renal failure, give calcitriol or another $1,25(OH)_2D$.

In hypoparathyroidism, give calcitriol, 0.5 to 2 mcg po once/day.

In Pseudohypoparathyroidism give calcitriol requires 1 to 3 mcg/day.

Monitor Serum calcium concentration weekly at then at 1- to 3-mo intervals after calcium concentrations have stabilized as the maintenance dose of calcitriol or its analogy, dihydrocholecalciferol, usually decreases with time.

APPROACH TO INTERPRETATION OF ARTERIAL BLOOD GASES (ABGS)

ABG interpretation is especially important in critically ill patients.

6-step approach below, is essential during the interpretation:

***Step 1*:** Assess the internal consistency of the values using the Henderson-Hasselbalch equation:

$$[H+] = \frac{24(PaCO2)}{[HCO3-]}$$

If the pH and the [H+] are inconsistent, the ABG is probably not valid.

***Step 2*:** Is there alkalemia or acidaemia present?

pH < 7.35 acidaemia

pH > 7.45 alkalaemia

This is usually the primary disorder

Remember: an acidosis or alkalosis may be present even if the pH is in the normal range (7.35 – 7.45)

You will need to check the PaCO2, HCO3- and anion gap

Step 3: Is the disturbance respiratory or metabolic? What is the relationship between the direction of change in the pH and the direction of change in the PaCO2?

Acidosis	Respiratory	pH ↓	PaCO2 ↑

Acidosis	Metabolic&	pH ↓	PaCO2 ↓
Alkalosis	Respiratory	pH ↑	PaCO2 ↓
Alkalosis	Metabolic	pH ↑	PaCO2 ↑

***Step 4*:** Is there appropriate compensation for the primary disturbance? Usually, compensation does not return the pH to normal (7.35 – 7.45).

Disorder	Expected compensation	Correction factor
Metabolic acidosis	PaCO2 = (1.5 x [HCO3-]) +8	± 2
Acute respiratory acidosis	Increase in [HCO3-]= Δ PaCO2/10	± 3
Chronic respiratory acidosis (3-5 days)	Increase in [HCO3-] = 3.5(Δ PaCO2/10)	
Metabolic alkalosis	Increase in PaCO2 = 40 + 0.6(ΔHCO3-)	
Acute respiratory alkalosis	Decrease in [HCO3-]= 2(Δ PaCO2/10)	
Chronic respiratory alkalosis	Decrease in [HCO3-] = 5(Δ PaCO2/10) to 7(Δ PaCO2/10)	

Step 5: Calculate the anion gap (if a metabolic acidosis exists): AG= [Na+]-([Cl-] + [HCO3-])-12 ± 2

- ◊ A normal anion gap is approximately 12 mmol/L.
- ◊ In patients has hypoalbuminemia, the AG is about 2.5 mmol/L lower for each 1 g/dL decrease in the plasma albumin concentration (for example, a patient with a plasma albumin of 2.0 g/dL would have an AG of approximately 7mmol /L).
- ◊ If the anion gap is elevated, consider calculating the osmolal gap in compatible clinical situations.
    - o Elevation in AG is not explained by an obvious case (DKA, lactic acidosis, renal failure)
    - o Toxic ingestion is suspected
- ◊ OSM gap = measured OSM – (2[Na+] - glucose/18 – BUN/2.8
    - o The OSM gap should be < 10

Step 6: If an increased anion gap is present, assess the relationship between the increase in the anion gap and the decrease in [HCO3-].

Assess the ratio of the change in the anion gap (ΔAG) to the change in [HCO3-] (Δ[HCO3-]): ΔAG/Δ[HCO3-]

This ratio should be between 1.0 and 2.0 if an uncomplicated anion gap metabolic acidosis is present.

If this ratio falls outside of this range, then another metabolic disorder is present:

◊ If ΔAG/Δ[HCO3-] < 1.0, then a concurrent non-anion gap metabolic acidosis is likely to be present.

◊ If ΔAG/Δ[HCO3-] > 2.0, then a concurrent metabolic alkalosis is likely to be present.

Characteristics of acid-base disturbances

Disorder	pH	Primary problem	Compensation
Metabolic acidosis	↓	↓ in HCO3-	↓ in PaCO2
Metabolic alkalosis	↑	↑ in HCO3-	↑ in PaCO2
Respiratory acidosis	↓	↑ in PaCO2	↑ in [HCO3-]
Respiratory alkalosis	↑	↓ in PaCO2	↓ in [HCO3-]

Selected aetiologies of respiratory acidosis

◊ Airway obstruction

◊ CNS depression

◊ Sleep disordered breathing

◊ Neuromuscular impairment

◊ Ventilatory restriction

◊ Increased CO2 production: shivering, rigors, seizures, malignant hyperthermia, hypermetabolism, increased intake of carbohydrates

◊ Incorrect mechanical ventilation settings

Selected aetiologies of respiratory alkalosis

- ◊ CNS stimulation: fever, pain, fear, anxiety, CVA, cerebral oedema, brain trauma, brain tumour, CNS infection
- ◊ Hypoxemia or hypoxia: lung disease, profound anaemia, low FiO2
- ◊ Stimulation of chest receptors: pulmonary oedema, pleural effusion, pneumonia, pneumothorax, pulmonary embolus
- ◊ Drugs, hormones: salicylates, catecholamines, medroxyprogesterone, progestins
- ◊ Pregnancy, liver disease, sepsis, hyperthyroidism
- ◊ Incorrect mechanical ventilation settings

Selected causes of metabolic alkalosis

- ◊ Hypovolemia with Cl- depletion
  - GI loss of H+
    - Vomiting, gastric suction, villous adenoma, diarrhoea with chloride-rich fluid
  - Renal loss H+
    - Loop and thiazide diuretics, post-hypercapnia (especially after institution of mechanical ventilation)
- ◊ Hypervolemia, Cl- expansion
  - Renal loss of H+: oedematous states (heart failure, cirrhosis, nephrotic syndrome), hyperaldosteronism, hypercortisolism, excess ACTH, exogenous steroids, hyperreninemia, severe hypokalaemia, renal artery stenosis, bicarbonate administration

Selected aetiologies of metabolic acidosis

- ◊ Elevated anion gap:
  - Methanol intoxication
  - Uraemia
  - Ketoacidosis
  - Paraldehyde toxicity
  - Isoniazid
  - Lactic acidosis
  - Ethanol or ethylene glycol intoxication

- Salicylate intoxication

◊ Normal anion gap: will have increase in [Cl-]

- GI loss of HCO3- (Diarrhoea, ileostomy, proximal colostomy)
- Renal loss of HCO3- (proximal RTA, acetazolamide), Renal tubular disease (ATN, Chronic renal disease)

Selected mixed and complex acid-base disturbances

Disorder	Characteristics	Selected situations
Respiratory acidosis with metabolic acidosis	↓in pH ↓ in HCO3 ↑ in PaCO2	Cardiac arrest Intoxications Multi-organ failure
Respiratory alkalosis with metabolic alkalosis	↑in pH ↑ in HCO3- ↓ in PaCO2	Cirrhosis with diuretics Pregnancy with vomiting Over ventilation of COPD
Respiratory acidosis with metabolic alkalosis	pH in normal range ↑ in PaCO2, ↑ in HCO3-	COPD with diuretics, vomiting, NG suction Severe hypokalaemia
Respiratory alkalosis with metabolic acidosis	pH in normal range ↓ in PaCO2 ↓ in HCO3	Sepsis Salicylate toxicity Renal failure with CHF or pneumonia Advanced liver disease
Metabolic acidosis with metabolic alkalosis	pH in normal range HCO3- normal	Uraemia or ketoacidosis with vomiting, NG suction, diuretics, etc.

Treatment

Treatment is dependent on correctly identifying the acid-base disorder and, whenever possible, repairing the underlying causal process to maintain serum pH greater than 7.20.

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11. BNF for children 2014-15

MANAGEMENT OF SHOCK

Recognition of shock: Cold extremities *with* capillary refill time >3 second *and* weak and fast pulse.

Immediate goals [ABCDE]

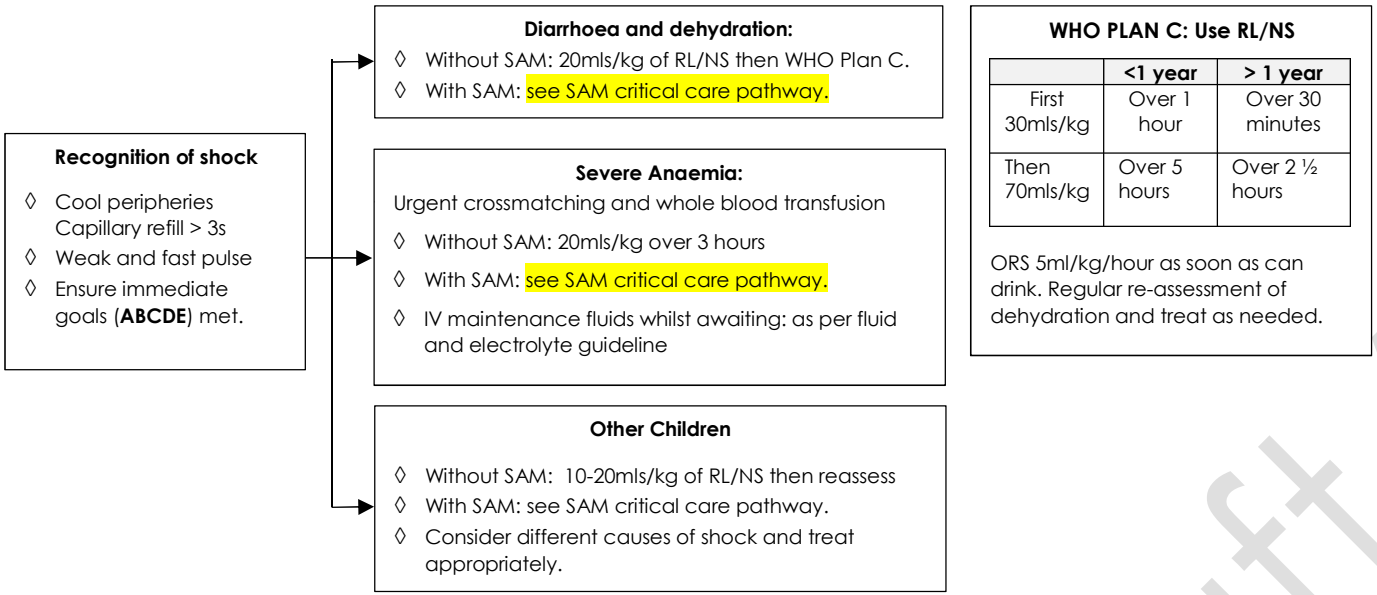
- **A:** Stabilize the airway, ensure patent using airway adjunct (e.g. airway positioning, chin tilt head lift, jaw thrust, guedel airway)
- **A:** If severe angioedema, consider severe anaphylaxis as cause
  - Treat as per WHO guidelines: Pocketbook of Hospital care of children page 108.
- **B**: Provide oxygen by mask (15L high flow) or nasal catheter if mask unavailable (2 litre/min).
- **C:** Establishment of vascular access
  - Two large bore peripheral intravenous catheters should be established.
  - If peripheral access is not readily available, intra-osseous access should be established.
- **C**: Assess for **malnutrition** (wasting, peripheral oedema, skin changes, z-score) and **severe anaemia** (pallor).
- **D:** Disability (AVPU – Alert/responsive to Voice/responsive to Pain/Unresponsive) and Do Not Forget Glucose (do RBS and treat appropriately).
- **E:** Exposure (body temperature, rash).

Weigh the child or estimate the child's weight using formulas below

- If <1 year old (kg) : (Age in months + 9) /2
- >1year old (kg) : (Age +4) x 2
- This does not substitute a child's true weight – the child must be weighed immediately once stable

See flow chart for management of shock on next page and table for different types of shock.

Fig. xx Management of Shock Flow Chart



SAM = Severe Acute Malnutrition, RL = Ringers Lactate, NS = 0.9% Normal Saline, ORS = Oral Rehydration Salts.

FURTHER MANAGEMENT

◊ Continually reassess with thorough history and clinical examination.

- **Start broad spectrum antibiotics within first hour (as per local protocol).**
- Maintain normothermia (temperature 36.5-37.5C): Keep warm / give antipyretics
- If blood sugar < 3.0 correct with 10% dextrose 5ml/kg and recheck after 15 minutes.
- Consider different types of shock (See next page) and treat appropriately.
- Liaise with senior doctors if not improving

◊ Refractory shock

- If no response to 20mls/kg fluid bolus, carefully administer second bolus of 20mls/kg.
- If no response to 40mls/kg fluid bolus, then assess for referral to ICU/higher level hospital, prepare for intubation and start inotropes with cardiac monitoring

◊ Unless the child is severely anaemic, whole blood transfusion is **not** recommended for circulatory shock. Prepare to use inotropes as a first line when not responding to fluid resuscitation.

TABLE XX. Types of shock

Type of shock	Signs and symptoms	Treatment
Hypovolaemic (reduced CO, increased SVR)	Increased HR, reduced pulses, delayed CRT, hyperpnoea, dry skin, sunken eyes, oliguria	- Repeat boluses of 20 ml/kg crystalloid as indicated up to 40 ml/kg in first hour. - Blood product as indicated for acute blood loss.
Septic (increased CO, increased SVR)	Increased HR, normal to reduced BP, reduced pulses, delayed capillary refill time, hyperpnoea, mental state changes, third spacing, oedema	-Repeat boluses of 20 ml/kg crystalloid; may need up to 40ml/kg in first hour. - Consider colloid if poor response to crystalloid. - Pharmacologic support of BP with dopamine or norepinephrine.
Distributive Anaphylaxis (increased CO, reduced SVR)	Angioedema, rapid third spacing of fluids, reduced BP, respiratory distress	- Repeat boluses of 20 ml/kg crystalloid as indicated. -Pharmacologic support of SVR with norepinephrine or phenylephrine.
Distributive Spinal cord injury (normal CO, reduced SVR)	Reduced BP with normal HR, paralysis with loss of vascular tone	-Pharmacologic support of SVR with norepenephrine or phenylephrine. -Fluid resuscitation as indicated by clinical status and associated injuries.
Cardiogenic (reduced CO, normal to increased SVR)	Normal to increased HR, reduced pulses, delayed CRT, oliguria, JVD, hepatomegaly BP normal until late in course	-Pharmacologic support of CO with dobutamine and dopamine. -Judicious fluid replacement as indicated clinically.

CO = cardiac output, SVR = systemic vascular resistance, HR = heart rate, BP = blood pressure, CRT = capillary refill time, MS = mental status, JVD = jugular venous distension

FORMULAE FOR ADMINISTRATION OF VASOACTIVE MEDICATIONS

Drug	Dose ranges	Infusion Preparation	Infusion rate
Dopamine Dobutamine	Dopamine (3 to 20 mcg/kg/min) Dobutamine (1 to 20 mcg/kg/min)	Body weight in kg x 6 = Amount of drug (mg) to be added to total volume of 100 ml IV fluid	1 ml/h = 1 mcg/kg per minute (Example: to deliver 10 mcg/kg per minute, run infusion at 10 ml/h)
Epinephrine Norepinephrine Milrinone	Epinephrine (0.01 to 1.0 mcg/kg/min) Norepinephrine (0.01 to 1.0 mcg/kg/min	Body weight in kg x 0.6 = Amount of drug (mg) to be added to total volume of 100 ml IV fluid	1 ml/h = 0.1 mcg/kg per minute (Example: to deliver 0.3 mcg/kg per minute, run infusion at 3ml/h)

NOTE: Dopamine and epinephrine can be given peripherally at a maximum dose of range of …. (need to check dose).

References

1. Christian A McKeirnan and Stephen A Leiberman. Circulatory shock in children: An overview. Pediatr. Rev 2005
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3. Updated Guideline: Paedaitric Emergency Triage, assessment and treatment. Geneva: World Health Organization; 2016.
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ANAPHYLAXIS REACTION PROTOCOL

Definition

Anaphylaxis is a severe allergic reaction that can be life threatening because of airway compromise and circulatory shock. Common causes include: Antibiotics, vaccines, blood transfusion and certain foods (e.g. nuts) and medications. There are associations with other allergic disorders e.g. asthma, eczema, family history.

Management

Manage via the ABCDE approach (see shock guideline), do not stop to take a detailed history – early treatment is lifesaving.

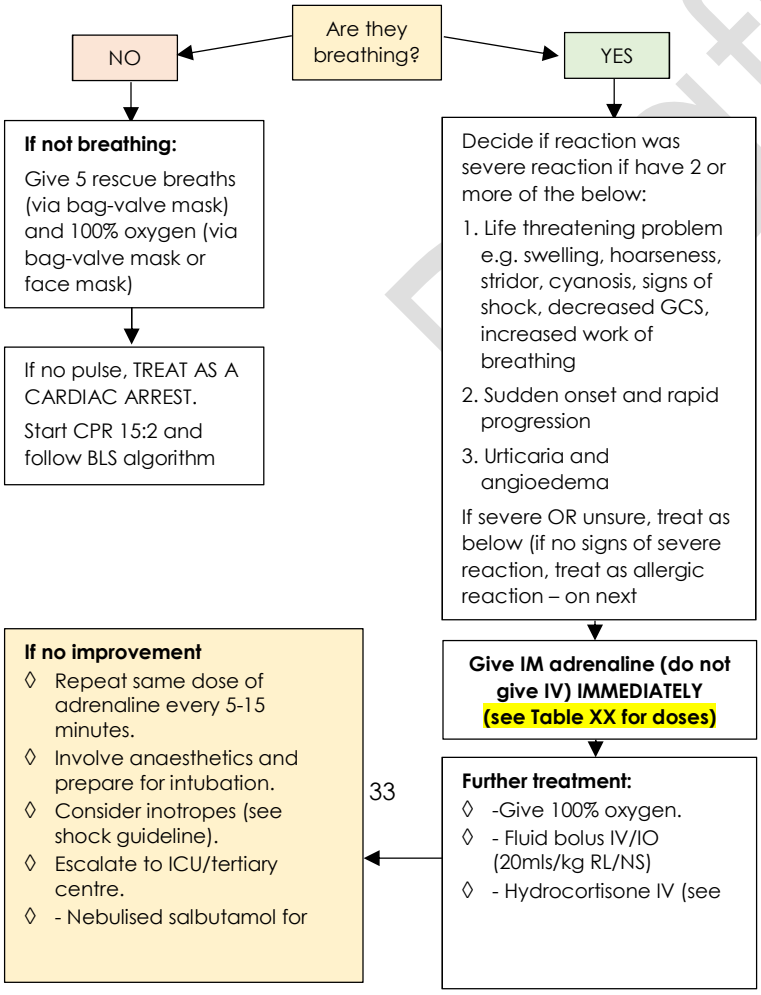

Table xx. Doses (improve title)

Drugs in anaphylaxis	< 6 Mo	6 Mo – 6 Yr	6 – 12 Yrs	>12 Yrs
Adrenaline/ epinephrine IM (Repeat every 5 -15 mins as needed)	150 µg (0.15mls of 1:1000)		300 µg (0.3 ml of 1:1000)	500 µg (0.5ml of 1:1000)
Hydrocortisone IV	25mg	50 mg	100 mg	200 mg
Chlorphenamine IM/IV (max 4 doses/day)	250 µg /kg max 2.5mg	2.5 mg	5 mg	10 mg

Mild and moderate allergic reactions

Not all allergic reactions cause anaphylaxis.
Symptoms and signs of mild and moderate allergic reactions are listed below:

Mild allergic reaction	Moderate allergic reaction
Mouth Itching, nausea, urticaria, conjunctivitis	***As mild;*** plus red throat, cough, mild wheeze, diarrhoea, sweating, tachycardia, pallor. ***If any life-threatening signs:***- treat as anaphylaxis urgently.

Management

- ◊ Remove the precipitating allergen if able
- ◊ Oral chlorphenamine for 24 hours.
  - < 2 years 1 mg BD
  - 2-5 years 1mg QID
  - 6-11 years 2mg QID
  - 12+ years 4mg QID
- ◊ Oral prednisolone for 3 days.
  - 1 mg/kg (max dose 40 mg) OD
- ◊ Observe for at least 4 hours after treatment before discharge home.

◊ Safety net advice for parents – warn regarding rebound allergic symptoms and urgent medical attention if signs of anaphylaxis.

References

1. APLS 6e. Advanced Life Support Group 2017.
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3. Joint Formulary Committee. British National Formulary for Children (Online) London. BMJ Group and Pharmaceutical Press 2019.

ASPIRIN

Aspirin is used as an analgesic, an antipyretic and an anti-inflammatory agent.

Clinical signs

- ◊ Tinnitus, rapid breathing, vomiting, dehydration, fever and double vision are early signs.
- ◊ Later signs include drowsiness, confusion, bizarre behaviour, unsteady walking and coma.
- ◊ Respiratory alkalosis and metabolic acidosis
- ◊ Rhabdomyolysis (dark urine), acute renal failure and respiratory failure may occur.

Management

- ◊ Plasma salicylate concentration should be measured in all patients with suspected toxicity where available.
- ◊ The acute toxic dose of salicylates is generally considered to be > 150 mg/kg
- ◊ Gastrointestinal decontamination: Activated charcoal, 1 g/kg (max: 50 g) within four hours of potential toxic ingestion
- ◊ Give IV sodium bicarbonate 8.4 % 1 mmol/kg over 4 hours to correct acidosis and raise urine pH to above 7.5
- ◊ Give maintenance IV fluids unless the child shows signs of dehydration
- ◊ Give supplemental potassium: 20-40 mEq/L to the maintenance fluids used
- ◊ Monitor blood glucose every 6 hours
- ◊ Where plasma salicylate concentration is available then treatment can be given according to Table xxx below:

Table xxx (Title)

Poisoning	Mild	Moderate	Severe
Plasma salicylate	< 350 mg/l	> 350 mg/l	> 700 mg/l
Fluids	Encourage oral fluids	Intravenous fluids [two thirds normal requirement]	Intravenous fluids [two thirds normal requirement]
Sodium bicarbonate 1 mEq/kg IV bolus then a continuous infusion of 100 -150 mEq in 1 L of 5% Dextrose to run at 2 times maintenance	No	Yes	Yes
Consider repeated doses of activated charcoal	No	Yes	Yes
Urgent referral for haemodialysis	No	No	Yes

References

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2. Pocket book of Hospital Care for Children: Guidelines for the Management of Common Illnesses With Limited Resources WHO 2005
3. Vree TB, Van Ewijk-Beneken Kolmer EW, Verwey-Van Wissen CP, Hekster YA. Effect of urinary pH on the pharmacokinetics of salicylic acid, with its glycine and glucuronide conjugates in human. Int J Clin Pharmacol Ther 1994; 32:550.

ORGANOPHOSPHATE POISONING

Source

Insecticides, rat poison, etc.

Clinical manifestations

Suspect in a patient with miosis, excessive salivation.

Muscarinic signs and symptoms:

Diaphoresis, emesis, urinary and faecal incontinence, excessive lacrimation, drooling, bronchorrhoea and bronchospasm, miosis, hypotension and bradycardia

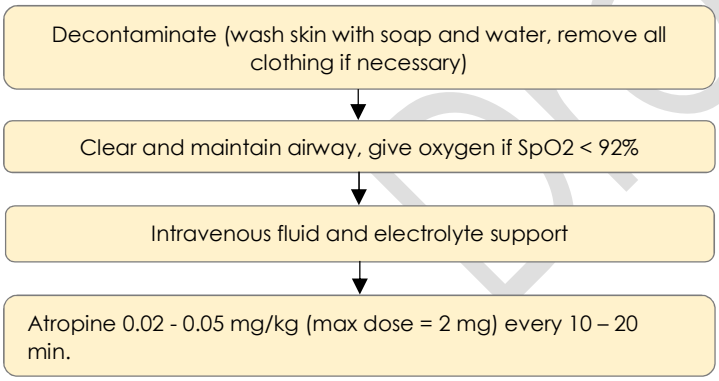
Nicotinic signs and symptoms:

Muscle weakness, fasciculations, tremors, hypoventilation, hypertension, tachycardia, and dysrythmias

CNS effects

Malaise, confusion, delirium, seizures and coma.

Management:



- ◊ Give atropine until heart rate and blood pressure are normal for age, chest is clear, sweating stops and pupils are dilated (Full atropinisation).
- ◊ Pralidoxime [in combination with atropine] at 20-50 mg/kg/dose. Repeat in 1-2 hours if muscle weakness has not been relieved, then 10 to 12 hours intervals if cholinergic signs recur.

◊ For management of seizures, (refer to seizure management).

HYDROCARBONS POISONING

Examples

Petrol, Kerosene, Lighter Fluid, Paraffin Oil, Diesel Fuel, Lubricating Oil, Furniture Polishes, Essential oils, Mineral Turpentine

Clinical signs

Transient mild CNS depression, aspiration is characterized by coughing. Respiratory symptoms may remain mild or may rapidly progress to respiratory failure. Fever occurs and may persist for as long as 10 days after aspiration.

Management

◊ Emesis is contraindicated because of the risk of aspiration.

◊ Gastric lavage is also contraindicated.

◊ If hydrocarbon-induced pneumonitis develops, respiratory treatment is supportive.

◊ Corticosteroids should be avoided, because they are not effective and may be harmful

◊ Do CXR after 24 hrs if signs of respiratory distress

IRON OVERDOSE

If Iron from overdosing of antenatal ferrous sulphate drugs (maternal), ensure to estimate amount of tablets taken….

Clinical features:

◊ Nausea, vomiting, abdominal pain and diarrhoea. The vomit and stools are often grey or black.

◊ In severe poisoning, there may be gastrointestinal bleeding, hypotension, drowsiness, convulsions and metabolic acidosis. Gastrointestinal features usually appear within the first 6 hr, and a child who has remained asymptomatic for this time probably does not require an antidote.

Management

◊ Consider a gastric lavage if potentially toxic amounts of iron were taken.

◊ **Do not** give activated charcoal

◊ Decide whether to give the antidote. As this can have side-effects, it should

◊ be given only if there is clinical evidence of poisoning (see above).

◊ Start fluid boluses of 20ml/kg of normal saline or ringer's lactate as children with iron overload are hypotensive.

◊ Do a chest x-ray in case of iron tablets as they may be seen

◊ If clinical signs are present give deferoxamine, preferably by slow IV infusion: initially 15 mg/kg/hour, reduced after 4–6 h so that the total dose does not exceed 80 mg/kg in

◊ 24 h. Maximum dose, 6 g/day.

◊ If deferoxamine is given IM: 50 mg/kg every 6 h. Maximum dose, 6 g/day.

◊ Stop infusion if patient is clinically stable. This is usually within 24 hours

References

1. Fiona Jepsen, Mary Ryan. Poisoning in children; Current Paediatrics, 2005; 15: 563-568.

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3. Kliegman, Berhman, Jenson and Stanton. Nelson Textbook of Pediatrics, 18th edition.

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PARAQUAT POISONING

Paraquat (1,1'-dimethyl-4,4'-dipyridylium) is a broad-spectrum liquid herbicide associated with both accidental and nonaccidental ingestion, leading to severe and often fatal toxicity. It is rapidly but incompletely absorbed and then largely eliminated unchanged in urine within 12–24 h.

Clinical Features

Clinical features are largely due to intracellular effects. Paraquat generates reactive oxygen species which cause cellular damage via lipid peroxidation, mitochondrial damage and apoptosis in many organs:

- ◊ Vomiting,
- ◊ Fever,
- ◊ Tachycardia
- ◊ Tachypnea,
- ◊ Occasional diarrhea.
- ◊ Drowsiness
- ◊ Paraquat is actively taken up against a concentration gradient into lung tissue leading to pneumonitis and lung fibrosis.
- ◊ It also causes pancreatic, renal and liver injury.

Investigations

- ◊ Electrolytes, renal and liver function tests, full blood count, should be done at least daily.
- ◊ A chest radiograph (if pneumomediastinum, pneumothorax or lung fibrosis is suspected).
- ◊ A CT scan of the chest (useful in detecting early lung fibrosis or assessing long-term damage in survivors).
- ◊ Amylase and lipase (acute pancreatitis suspected if patients develop abdominal pain and a raised blood sugar).
- ◊ Plasma paraquat concentrations
- ◊ Urine and plasma dithionite tests

Management

◊ Gastric lavage is helpful.

◊ Activated charcoal (1gm/kg of activated charcoal by gastric tube every 2 hours 3 to 4 doses) routinely given to minimize further absorption.

◊ **Supplemental oxygen should be withheld** because oxygen may contribute to the pulmonary damage, mediated through lipid peroxidation.

References

1. Buckley NA, Karalliedde L, Dawson A, Senanayake N, Eddleston M. Where is the evidence for treatments used in pesticide poisoning? Is clinical toxicology fiddling while the developing world burns? J Toxicol Clin Toxicol 2004;4: 113–6.

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3. Dawson AH, Eddleston M, Senarathna L, Mohamed F, Gawarammana I, Bowe SJ, Manuweera G, Buckley NA. Acute human lethal toxicity of agricultural pesticides: a prospective cohort study. PLoS Med 2010;7:e1000357.

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DIABETIC KETOACIDOSIS (DKA)

Definition

Diabetic ketoacidosis (DKA) is the state of uncontrolled catabolism associated with insulin deficiency, resulting in hyperglycaemia (RBS >11mmol/L), osmotic diuresis, and dehydration and ketonaemia (>3mmol/L) Acidaemia (blood pH <7.3), significant ketonuria (2+or more or standard urinalysis). It is the commonest endocrine emergency usually encountered in previously diagnosed diabetics.

Causes

It is caused by increased fatty acid metabolism and the accumulation of fatty acids due to reduced insulin activity or deficiency of insulin, an intercurrent illness or it could just be a new presentation.

Clinical features

- ◊ Dehydration
- ◊ Abdominal pain
- ◊ Ketone smell in the breath
- ◊ Acidosis
- ◊ Acidotic breathing/hyperventilation
- ◊ Unexplained coma
- ◊ Nausea
- ◊ Vomiting

In DKA, a child may die from hypokalaemia or cerebral oedema. Cerebral oedema is unpredictable, occurs more frequently in younger children and new diabetics, and has mortality of around 80%.

These guidelines are intended for the management of children who are more than 5% dehydrated and/or vomiting, drowsy or clinically acidotic.

Investigations

◊ Random glucose

◊ U/E, Creatinine, LFTs

◊ FBC

◊ Malaria parasite

◊ Urinalysis

◊ Urine m/c/s

◊ Arterial blood gases

Treatment

General resuscitation: A, B, C.

Airway: Ensure that airway is patent. If comatose, insert an airway. If comatose and has recently vomited, insert a NGT, aspirate and leave on open drainage.

Breathing: Give 100% oxygen ***where indicated***. Bag and mask ventilation if apnoeic.

Circulation: **Insert two large bore IV cannulae** and take blood samples.

If shocked (Tachycardia with poor capillary refill time or hypotension) give 20 ml/kg 0.9 saline as quickly as possible, and repeat if necessary up to a max of 60mls/kg.

Confirm the diagnosis:

◊ History: Polydypsia, polyuria

◊ Clinical: Acidotic respiration; dehydration; drowsiness; abdominal pain/vomiting

◊ Biochemical: High glucose, ketones or glycosuria, ketonuria

◊ Conscious Level

- GCS or BCS
- Cerebral oedema: Irritability, slow pulse, high BP. Fundal examination.

◊ Look for the focus of infection *and* ***treat accordingly.***

◊ Observation to be carried out:

- Strict fluid balance chart
- Hourly blood glucose
- Daily weights
- GCS or BCS
- ECG

Fluids

Requirement = maintenance + deficit

Deficit = % dehydration x body weight

Maintenance= 100mls/kg-1st 10kgs, 50mls/kg- next 10kgs, 20mls/kg for every kg thereafter.

Add deficit and maintenance and give over the next 36 – 48 hrs

Example:

For a 25kg diabetic patient, fluid is calculated as follows:

Deficit= 10% x 25 = 2.5L =2500mls, to be given over 48 hrs, therefore 1250mls to be given over 24hrs

Maintenance = 1000 mls + 500 mls +100mls = 1600mls/24hrs

Therefore, total amount of fluid to be given over 24hrs is 1600mls+1250mls =2850mls

This may be divided by 3 or 4 to be given at 950 mls 8 hourly or ~710 mls 6 hourly respectively.

Type of fluid is 0.9% normal saline. Change to DNS once RBS has fallen to around 12 mmol/l.

In the presence of hypernatraemia, then half normal saline must be used (***please consult***).

Potassium

Commence potassium immediately unless anuria is suspected or there are peaked T waves on ECG or the serum potassium is > 7 mmol/l.

Add 10 to 20 mmol KCl to every 500 ml intravenous fluids given for the first 24 hrs.

Insulin

Soluble insulin e.g. 0.1 IU/kg/hour continuous intravenous infusion.

Average rate of fall of blood glucose must not exceed 5mmol/l per hour. If the drop in blood sugar is more rapid (>5mmol/l per hour), dose may be reduced to 0.05 IU/Kg/hour to avoid cerebral oedema.

References

1. David Southall International Child HealthCare. A practical Manual for Hospitals Worldwide. First Edition, Book power 2003. Pages 213- 216. UK.
2. Richard E. Behrman, Nelson Textbook Of Paediatrics, 17th Edition, 2004. Pages 1954 – 1959. USA.
3. Sharma S, Kochar GS, Sankhyan N, Gulati S. Approach to the Child with Coma.
4. Department of Pediatrics, Child Neurology Division, All India Institute of Medical Sciences, New Delhi, 110029, India. Indian J Pediatric. 2010 Sep 10. [Epub ahead of print]

ADRENAL CRISIS

Definition

Severe adrenocortical insufficiency resulting in peripheral shutdown, cyanosis, tachycardia, tachypnoea, hypotension, drowsiness and coma. It can be fatal if not quickly recognised and urgently treated.

Causes

It may be due to several processes e.g.

◊ ***Congenital***

- Congenital adrenal hyperplasia
- Congenital adrenal hypoplasia
- Adrenoleukodystrophy

◊ ***Acquired***

- Acute haemorrhagic destruction of both adrenal glands in previously well children due to sepsis especially meningococcemia
- Rapid withdrawal of steroids
- Autoimmune process (Addison's disease)
- Tuberculosis
- Birth Asphyxia
- Hypopituitarism

Clinical Features

◊ Vomiting/diarrhoea

◊ Weight loss

◊ Nausea

◊ Dehydration
◊ Hypotension
◊ Signs of shock
◊ Acidosis
◊ Convulsions
◊ Meningococcaemia-high fever, rash (petechiae, ecchymoses, purpura, dermal gangrene, neck stiffness
◊ TB-weight loss, fever, cough,, night sweats, reduced appetite with positive history of TB contact

Investigations

◊ Random glucose (hypoglycaemia)
◊ Urinalysis (ketosis)
◊ ECG (Hyperkalaemia)
◊ Serum Cortisol - <3µg/dL in the morning (09.00) defines low cortisol
◊ ACTH- often high
◊ U/Es (Hyponatraemia, Hyperkalaemia), Creatinine – (GFR decreases)
◊ Aldosterone - levels are often normal
◊ Urinary Na and Cl increased, K is decreased
◊ Abdominal U/S, CT scan, MRI - size of adrenal glands
◊ CXR- miliary picture or opacities suggestive of TB
◊ Gene Xpert

Treatment

◊ Airway
◊ Breathing
◊ Circulation – correct shock with normal saline at 20 mls/kg, then correct dehydration
◊ Treat hypoglycaemia
◊ Normal saline to correct salt deficit.
◊ Hydrocortisone 8mg/kg start then

◊ Hydrocortisone 4mg/kg 6 hourly daily maintenance

◊ Treat underlying cause

Note: Dexamethasone has no mineralocorticoid activity and so should not be used to treat adrenal crisis

References

1. David Southall, International Child Health Care, A practical Manual for Hospitals worldwide. First edition, Book Power, Page 219. 2003, UK.
2. Behrman, Nelson Textbook of Paediatrics, 17th Edition, Page 1904, Saunders 2004. USA.
3. PJ Simm, CM McDonnell and MR Zacharin.16th April 2004
4. Department of Endocrinology and Diabetes, Royal Children's Hospital, Melbourne, Victoria, Australia .Review of Primary Adrenal insufficiency In Childhood And Adolescence. Advances In Diagnosis and Management.

CONGESTIVE CARDIAC FAILURE (CCF)

Definition

CCF is a clinical syndrome in which the heart:

- ◊ Is unable to pump enough blood to the body to meet its needs,
- ◊ Is unable to dispose of venous return adequately,
- ◊ **OR** a combination of the two.

Diagnosis of CCF relies mainly on clinical findings and no single test is specific.

Aetiology

CCF may result from congenital or acquired heart diseases with volume and/ pressure overload or from myocardial insufficiency.

Table XX

Cause	Example/s
1. Cardiac	
A. Congenital	◊ Ventricular Septal Defect (VSD) ◊ Atrial Septal Defect (ASD) ◊ Patent Ductus Arteriosus (PDA) ◊ Arrhythmias
B. Acquired	◊ Endocardial/Valvular disease e.g. Rheumatic Heart Disease (RHD) ◊ Myocardial diseases e.g. Viral myocarditis, Dilated cardiomyopathies, hypertrophic cardiomyopathy ◊ Pericardial diseases e.g. TB pericarditis
2. Extracardiac	

- ◊ Anaemia
- ◊ Pulmonary diseases e.g. Pulmonary hypertension,
- ◊ Severe pneumonia especially in neonate
- ◊ Systemic hypertension
- ◊ Metabolic disorders e.g. Electrolyte imbalances, hypoglycaemia
- ◊ Endocrine e.g. Thyroid disease
- ◊ Drugs e.g. antineoplastic

Diagnosis

The diagnosis is based on:

- ◊ ***History***: Poor feeding, FTT, Difficulties in breathing, poor weight gain, easy fatiguability in older children.
- ◊ ***Examination***: tachypnoea, tachycardia, hepatomegaly, +/- Cardiac murmurs, oedema in older children.
- ◊ ***Investigations***: FBC, U&Es, Serum Creatinine, Echocardiography, Chest x-ray and ECG.

Aims of treatment

- ◊ To relieve symptoms
- ◊ Elimination of the underlying/precipitating cause
- ◊ Improve survival

General measures

- ◊ Propped up position
- ◊ Oxygen
- ◊ Salt and fluid restriction
- ◊ Daily weight in hospitalised patients

Drug therapy

The cornerstones of management are:

- ◊ Preload reduction: Diuretics e.g. Frusemide
- ◊ Afterload reduction: ACEIs (Captopril, Enalapril),
- ◊ Inotropes: digoxin (stable patient), Dobutamine/dopamine (Severe CCF)
- ◊ β-blockers e.g. Carvedilol (used in chronic heart failure state typically in dilated cardiomyopathies)

Dosages Table XX

Drug	Route	Dosage
Frusemide	IV Oral	1mg/kg/dose, 2-3 times a day 1-2mg/kg/dose, 1-3 times a day
Spironolactone	Oral	1-2mg/kg/dose, 1-2 times a day
Hydrochlorothiazide	Oral	2-4 mg/kg/day in 2 – 3 divided
Digoxin	Oral	0.02 - 0.05 mg/kg OD PO
Captopril	Oral	0.1-0.5mg/kg Divided 8hourly, max. dose 0.6mg/Kg
Enalapril	Oral	0.1mg/Kg divided OD or BD, Max. dose 0.5mg/kg/day
Carvedilol	Oral	0.08 mg/kg 12 hourly, if tolerated increase by 0.08 mg/kg every 1-2 weeks to a maximum 0.50mg/kg 12 hourly.

NOTE: If in cardiogenic shock and requiring Dopamine, Dobutamine or Milrinone, refer to the shock protocol.

Diagnosis

Diagnostic criteria for rheumatic fever is done according to the modified 2015 Jones criteria. Has defined high risk population recognizing variability in clinical presentation and had included Echocardiography as a tool to diagnose cardiac involvement (for subclinical carditis). (Zambia is in a high-risk category).

Modified 2015 Jones' criteria

Major	**Minor**
Carditis (clinical or subclinical)	Monoarthralgia
Arthritis – monoarthritis or polyarthritis	Fever (≥ 38.0°C)
Polyarthralgia	ESR ≥ 30 mm/hour and/or CRP ≥ 3.0 mg/dl
Chorea	Prolonged PR interval (after considering the differences related to age; if there is no carditis as a major criterion)
Erythema marginatum	
Subcutaneous nodules	

ESR – erythrocyte sedimentation rate; CRP – C-reactive protein (Adapted from ref 13). All patients with ARF should have an Echocardiography done even in the absence of clinical suspicion of valvular done.

Revised Jones Criteria

WHO guidelines set the international standard for diagnosis of ARF:

Two major manifestations ***plus*** evidence of preceding streptococcal infection **OR one major** and **two minor** manifestations **plus** evidence of preceding streptococcal infection.

Management

Treat the illness

1. Benzathine penicillin injection stat or oral penicillin for ten days
2. Relieve symptoms
    - Bed rest
    - Relief of arthritis, pain and fever
    - Treat chorea (if severe)
    - Anti- heart failure medication (see table 2 above)

Recommended Anti-inflammatory Agents

	Arthritis	Carditis
Prednisolone	Nil	2 – 4 weeks
Aspirin	1 – 2 weeks	Until symptoms subside
*Ibuprofen	Until symptoms subside	Until symptoms subside

Dosages: Prednisolone 2 mg/kg/day in four divided doses

Aspirin 50 to 60 mg/kg/day in four to six divided doses

*Ibuprofen can be given at 30 mg/kg/day in 3 divided doses, where Aspirin not tolerated.

The dose of prednisolone should be 2 mg/kg/day (max 60 mg); then taper by 20–25% per week. Aspirin can be reduced to 25 to 30 mg/kg/day when symptoms improve. The dose of prednisolone should be tapered, and aspirin started during the final week.

Management of Sydenham's chorea

1. Reduce physical and emotional stress and use protective measures as indicated
2. Benzathine penicillin IM stat (Eradicate GAS), then every 28 days for secondary prophylaxis.
3. Anti-inflammatory agents not indicated
4. For severe chorea, any of the following drugs may be used:

- Carbamazepine 7–20 mg/kg/day (7–10 mg/kg day usually sufficient) given TDS PO until chorea is controlled for at least 2 weeks, then trial off medication
- Valproic acid Usually 15–20 mg/kg/day (can increase to 30 mg/kg/day) given TDS PO until chorea is controlled for at least 2 weeks, then trial off medication.
- Phenobarbitone, Haloperidol and Chlorpromazine can be used when above not available.

Further management plan

◊ Baseline echocardiography (ECHO)
◊ ARF register (cardiac clinic), issue ARF prophylaxis card
◊ Education of patient and family
◊ Dental examination
◊ Long term secondary prophylaxis plan

Secondary prophylaxis to prevent recurrent ARF is a long term, regular administration of antibiotics to:

◊ Prevent group A β-Haemolytic Streptococcal (GAS) pharyngitis
◊ Prevent repeated development of ARF
◊ Prevent development of rheumatic heart disease (RHD)
◊ Reduce severity of RHD
◊ Help reduce the risk of death from severe RHD

Antibiotic regimens for secondary prophylaxis (*Adapted from ref 14*)

Antibiotic	Dose	Route	Frequency
First line			
Benzathine Penicillin G	1,200,000 U (900 mg) ≥ 30 Kg 600,000 U (450 mg) ≤30 Kg	Deep IM Injection	4-weekly
***Second line* (If IM route is not possible or refused, adherence should be carefully monitored)**			

Phenoxymethylpenicillin (Pen V)	250mg	Oral	Once daily
Following documented penicillin allergy			
Erythromycin	250mg	Oral	Twice daily

NOTE: Duration of prophylaxis in all persons with ARF is for a minimum of 10 years after the most recent episode of ARF or until age 21 years (whichever is longer). For RHD, the duration of prophylaxis is for life.

RHEUMATIC HEART DISEASE

Rheumatic hear disease (RHD) is includes a spectrum of lesions from pericarditis, myocarditis, and valvulitis during ARF, to chronic valvular lesions that evolve over years following one or more episodes of ARF.

The common valvular lesions in RHD

- ◊ Mitral regurgitation/stenosis
- ◊ Aortic regurgitation/stenosis
- ◊ Tricuspid regurgitation/stenosis

Best practice for RHD requires:

- ◊ Access to echocardiography (for diagnosis)
- ◊ Secondary prevention with penicillin prophylaxis (see above on ARF)
- ◊ Access to oral healthcare
- ◊ Access to a specialist physician, paediatrician and/ or cardiologist
- ◊ Adequate monitoring of anticoagulation therapy in patients with atrial fibrillations (AF) and/or mechanical prosthetic valves (where possible)
- ◊ Access to cardiothoracic and interventional cardiology services (where possible).

RHD patients may present with:

- ◊ Heart failure (as a result of valvular insufficiency or stenosis) and/or
- ◊ Complications such as atrial arrhythmias, pulmonary oedema, recurrent pulmonary emboli, infective endocarditis, intracardiac thrombus formation, and systemic embolism.

Treatment of RHD

- ◊ ***Medical:***
    - o Prevent ARF (Elimination GAS pharyngitis as above)
    - o Supportive treatment for CCF (as above)
    - o Prevent recurrent ARF in children with RHD (see secondary prophylaxis above)

- Monitoring for the complications and sequelae of chronic RHD.

◊ ***Surgery:***

- Indicated in patients with persistent CCF **OR**
- Worsening after aggressive medical therapy for RHD to decrease valve insufficiency/regurgitation.

INFECTIVE ENDOCARDITIS

Infective endocarditis (IE) is defined as an infection of the endocardial surface of the heart (heart valves and mural endocardium) by microorganisms (mainly bacteria) hence also called bacterial endocarditis.

Risk factors

- ◊ Congenital heart disease especially Cyanotic CHD
- ◊ Rheumatic heart disease
- ◊ Prosthetic heart valve
- ◊ History of endocarditis
- ◊ IV drug use or chronic IV access
- ◊ Immunocompromised (HIV, diabetes)

Classification

1. ***Acute infective endocarditis***

   Caused by virulent organisms, like *S. aureus, enterococci and streptococcus,* which are harmful even on healthy endocardium. Onset of disease is stormy with high grade fever and causes destructive lesions on the endocardium like ulcerations, perforation, regurgitation and ring abscesses especially around prosthetic valves.

2. ***Subacute infective endocarditis***

   Caused by relatively low virulent organisms e.g S.*viridans* and HACEK group (Haemophilus, Aggregatibacter, Corynebacterium, Eikanella, Kingelle). It runs a more insidious course:

   - o low grade fever, anorexia, weight loss, influenza like syndromes, myalgia, pleuritic pain
   - o No specific heart pathological features. Characterised by slowly growing chronic inflammation, fibrosis and with tightly held endocardial vegetations. Chronicity of this type of IE causes chronic antigenemia which in turn is prone to immune complex formation.

Diagnosis

A fever with new/or changing murmur is IE until proven otherwise.

Dukes criteria for the diagnosis of IE

Major criteria	Minor criteria
Positive blood culture Typical microorganism consistent with IE from ≥2 blood cultures, Microorganisms consistent with IE from persistently positive blood cultures, defined as: ≥2 Positive cultures of blood samples drawn >12 h apart or All of 3 or a majority of ≥4 blood cultures, irrespective of the timing 1 Positive blood culture for Coxiella burnetii or antiphase-I immunoglobulin G antibody titre >1:800 Evidence of endocardial involvement Positive echocardiogram, defined as: Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation or Abscess **OR** New partial dehiscence of prosthetic valve **OR** New valvular regurgitation (worsening or changing of pre-existing murmur not enough)	Predisposition: predisposing heart condition or IV drug use Fever: temperature ≥38.0°C Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway lesions Immunologic phenomena: glomerulonephritis, Osler nodes, Roth's spots, and rheumatoid factor Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE

Diagnosis is made when there are 2 major criteria or 1 major plus 3 minor or 5 minor criteria. Adapted from ref 15

Treatment

	Drugs	Dosage	Duration	Remarks
1st Line	Crystalline Penicillin (X Pen)	50-100,000 IU/kg in 4 divided doses/day And, Gentamicin 3-5mg/kg/day in 2-3 divided doses/day	4 weeks	Then, Ciprofloxacin 15mg/kg/day in 2 divided doses for 2 weeks
	Ceftriaxone	80-100mg/kg/day 1-2 times daily/day And, Gentamicin 3-5mg/kg/day 2-3 divided doses/day	4 weeks	Then, Ciprofloxacin 15mg/kg/day in 2 divided doses for 2 weeks
2nd Line	Vancomycin	30-40mg/kg/day in 4 divided doses And, Gentamicin 3-5mg/kg/day in 2-3 divided doses	4 weeks	Then, Ciprofloxacin 15mg/kg/day in 2 divided doses for 2 weeks

SYSTEMIC HYPERTENSION

Definitions

- **Hypertension:** Systolic and/or diastolic pressure levels greater than the 95th percentile for age and gender on at least three occasions. **BP readings of 5mmHg or more above the 99th centile values are considered as severe hypertension.**
- **Pre-hypertension:** average systolic or diastolic blood pressure between the 90th and 95th percentiles for age and gender.

To insert table for normal values

Aetiology ///Are we going to stick with cause or aetiology?/

- Essential or primary hypertension, in which a specific aetiology cannot be identified
- **Secondary hypertension in which a cause can be identified** (commonest in paediatric population)

More than 90% of the cases of secondary hypertension are caused by chronic renal disease, renovascular disease and coarctation of the aorta.

Commonest causes of secondary hypertension in children

	Examples of lesions/pathology
Renal	Acute and chronic Glomerulonephritis Acute and chronic Pyelonephritis Congenital anomalies [polycystic or dysplastic kidneys] Obstructive uropathies [hydronephrosis] Haemolytic-uremic syndrome Renal damage from nephrotoxic medications, trauma or radiation
Renovascular	Renal artery disorders (e.g. stenosis, polyarteritis, thrombosis) Renal vein thrombosis

Cardiovascular	Coarctation of the aorta Conditions with large stroke volume [PDA, aortic insufficiency, system A-V fistula, complete heart block]. These conditions cause only systolic hypertension
Endocrine	Hyperthyroidism (systolic hypertension) Excessive catecholamine levels (Pheochromocytoma, Neuroblastoma) Adrenal dysfunction Cushing's syndrome Hyperaldosteronism
Neurogenic	Increased intracranial pressure
Drugs and chemicals	Steroids Sympathomimetic drugs [cough medications] Heavy metal poisoning [mercury, lead] CNS stimulants: Cocaine [acute or chronic use]

Most common causes of hypertension by age groups

Age	Causes
Newborns	Renal artery stenosis, renal artery thrombosis, congenital renal malformation coarctation of the aorta, bronchopulmonary dysplasia
< 6 years	Renal parenchymal disease, Coarctation of the aorta, Renal artery stenosis
6 -10 years	Renal artery stenosis, renal parenchymal disease, primary hypertension
>10 years	Primary hypertension, renal parenchymal disease

Diagnosis and work-up

- ◊ Mild hypertension is usually asymptomatic and may only be picked up incidentally
- ◊ Severe hypertension may be symptomatic (headache, dizziness, nausea and vomiting, irritability, personality changes) occasionally presenting with neurological manifestation, CCF, renal dysfunction, and stroke.
- ◊ History, physical findings and laboratory tests usually point to the cause of hypertension.

Routine and special laboratory tests and their significance

Routine Laboratory Tests	Significance of Abnormal Results
Urinalysis, urine culture, urea Creatinine, uric acid	Renal parenchymal disease
Serum electrolyte (hypokalaemia)	Hyperaldosteronism 1° or 2°, Adrenogenital syndrome, renin producing tumours
ECG, CXR, ECHO	Cardiac causes e.g. coarctation of the aorta
Specialised tests	
IVU, US KIDNEY, CT scan	Renal parenchymal disease, renovascular disease, tumours (neuroblastoma, Wilms)
Plasma renin activity	High-renin hypertension Renovascular disease Renin-producing tumours Some Cushing's syndrome Some essential hypertension Low-renin hypertension Adrenogenital syndrome Primary hyperaldosteronism
24-hr urine collection for 17-ketosteroids and 17-hydroxycorticosteroids	Cushing's syndrome, adrenogenital syndrome
24-hr urine collection for catecholamine levels and VMA	Pheochromocytoma, neuroblastoma
Aldosterone	Hyperaldosteronism, primary or secondary renovascular disease, renin-production tumours
Renal vein plasma renin activity	Unilateral renal parenchymal disease, renovascular hypertension
Abdominal aortogram	Renovascular hypertension, abdominal CoA, unilateral renal parenchymal disease, pheochromocytoma.

Management

As most of the causes of hypertension in children are secondary, the ultimate aim of treatment, in addition to general measures and pharmacological therapy should be to remove the cause of hypertension whenever possible: e.g coarctation repair or renal artery balloon angioplasty or surgery for renovascular disease.

Non-pharmacologic/General measures:

- ◊ Encourage weight reduction if indicated
- ◊ low salt foods/diet
- ◊ avoidance of smoking
- ◊ Regular exercise and restriction of sedentary lifestyle

Pharmacologic measures:

Whom to treat

- ◊ Symptomatic hypertension and severe hypertension
- ◊ Prehypertension in presence of comorbid conditions, such as chronic kidney disease or diabetes mellitus
- ◊ Hypertensive children with diabetes mellitus or other risk CVD factors, such as dyslipidaemia
- ◊ Hypertensive target-organ damage, most often left ventricular hypertrophy (LVH)
- ◊ For essential hypertension (without any evidence of target-organ damage) that persists despite a trial of four to six months of nonpharmacologic therapy.

Antihypertensive drugs

Secondary hypertension is the commonest cause of hypertension in children and the treatment of the underlying medical conditions influences the choice of specific class of antihypertensive drugs.

- ◊ In children with chronic kidney disease, we suggest that ACE inhibitors be used as the initial antihypertensive agent. In patients who cannot tolerate ACE inhibitors, angiotensin-receptor blockers (ARBs) are a reasonable alternative.
- ◊ In adolescents with primary HTN without target-organ damage, we suggest that low-dose thiazide diuretic therapy be used as the first antihypertensive agent

- ◊ In children with either type 1 or type 2 diabetes mellitus, we suggest that ACE inhibitors be used as the initial antihypertensive agent. In patients who cannot tolerate ACE inhibitors, angiotensin-receptor blockers (ARBs) are a reasonable alternative.
- ◊ Diuretics are the cornerstone of antihypertensive drug therapy in essential hypertension and are not used in patients with renal failure. Their action is related to a decrease in extracellular and plasma volume.
- ◊ ACE inhibitors are contraindicated in obstructive lesions like bilateral renal artery stenosis, aortic stenosis and coarctation of the aorta.

The stepped-care approach, using three classes of drugs: diuretics, B-blockers, and vasodilators, is popular.

Step 1

Initiate with a small dose of a single antihypertensive drug (thiazide diuretic or adrenergic inhibitor), adjust upwards as necessary

Step 2

If the first drug is not effective, a second drug may be added to, or substituted for, the first drug, starting with a small dose and proceeding to full dose.

Step 3

If the blood pressure remains elevated, a third drug, such as a vasodilator, may be added to the regimen. At this point, the possibility of secondary hypertension should be reconsidered.

Recommended oral dosage of selected antihypertensive drugs for children

Drugs	Dose	Times/day
***Calcium channel blockers* (CCB)**		
◊ Nifedipine	◊ 0.1 -1 mg/kg/day	◊ 1-2 times a day
◊ Amlodipine (≥ 6 yrs old)	◊ 2.5-5mg/day	◊ Once a day
β-Blockers		

◊ Propranolol ◊ Atenolol	◊ 1-3mg/kg/day ◊ 1-2mg/kg/day	◊ 2-3 times per daily ◊ Once daily
ACE inhibitors		
◊ Captopril ◊ Enalapril ◊ Lisinopril	◊ 0.3-0.5mg/kg/dose (max 6mg/Kg/day) ◊ 0.08-0.6mg/kg/day ◊ 0.07-0.6mg/kg/day	◊ 3 times per day ◊ 1-2 times per day ◊ Once daily
ARB		
◊ Losartan	◊ 0.7-1.4mg/kg/day	◊ Once daily
Diuretics		
◊ Hydrochlorothiazide ◊ Furosemide [lasix] ◊ Spironolactone [aldactone]	◊ 1-2mg/kg/day ◊ 0.5- 2mg/kg/dose ◊ 1-3mg/kg/day	◊ Once daily ◊ 1-2 times per day ◊ 1-2 times per day

Hypertensive crisis

A hypertensive emergency is defined as any of the following features:

- ◊ The patient has severe hypertension [>180 mm Hg systolic or 110 mm Hg diastolic] or rapidly increasing blood pressure.
- ◊ The patient has neurologic signs [hypertensive encephalopathy] with severe headache, vomiting, irritability, apathy, papilloedema, retinal haemorrhage, or exudates.
- ◊ The patient has CHF or pulmonary oedema.

Aggressive administration of antihypertensive drugs is indicated to lower blood pressure – no more than 25% reduction of systolic BP in the first 8hours; gradually attain normal BP over 24-48 hours:

Drug	Dose	Comment
Nifedipine	0.2 - 0.5 mg/kg, every 4 to 6 hours, 12 to 24 hourly if retard Nifedipine is used ***maximum 10mg per dose**	If patient is conscious
Hydralazine	0.15 mg/kg IV slow infusion over 20 minutes	The dose may be repeated at 4 to 6 hours interval.

		The dose may be repeated at 4-6 to 6-hours interval.
Nitroprusside	1-3µg/kg per min as IV drip	
Labetalol	0.2-2mg/kg/hour IV drip	Alpha and beta blocker
Diazoxide	3-5mg/kg as IV bolus	
Furosemide	1mg/kg IV bolus	To initiate diuresis

(*Fluid balance must be controlled carefully, so intake is limited to urine output plus insensible loss. Seizures may be treated with slow intravenous infusion of diazepam [Valium], 0.2 mg/kg or another anticonvulsant medication. When a hypertensive crisis is under control, oral medications replace the parenteral medications.)

CYANOTIC SPELL

Definition

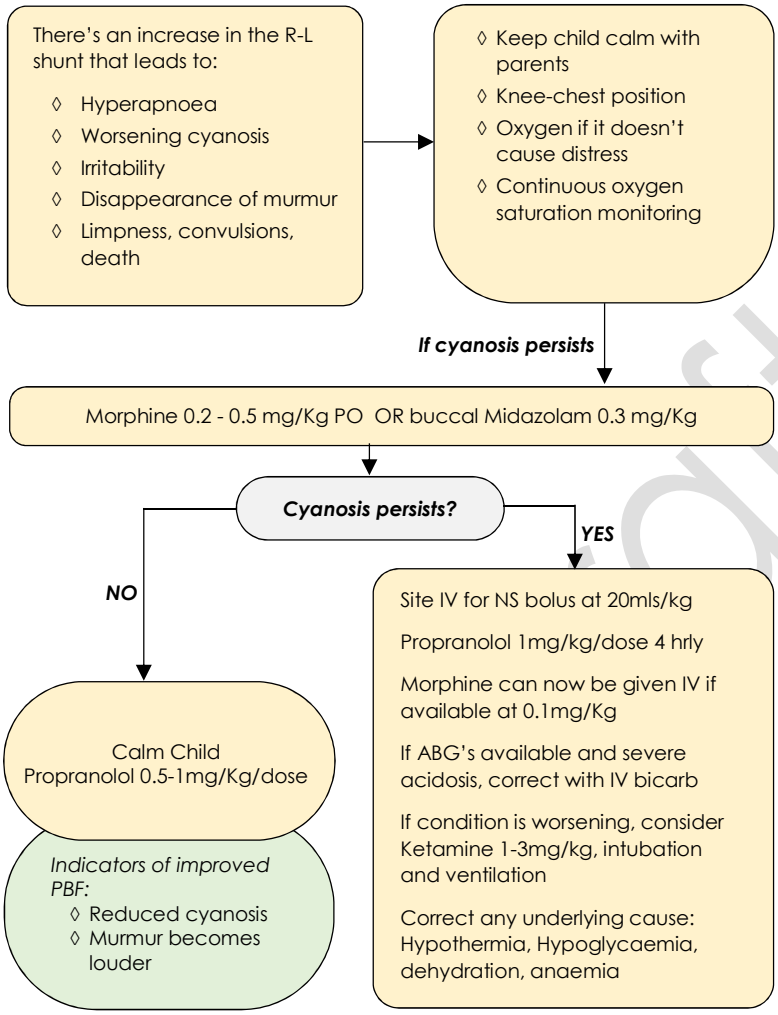
Also called hypoxic spell or "tet" spell occurs in young infants with Tetralogy of Fallot (TOF). It consists of hyperpnoea (i.e. rapid and deep respiration) worsening cyanosis and the disappearance of the heart murmur.

This occasionally, if not treated, results in complication of the central nervous system and even death.

Place the infant who has a hypercyanotic spell in the knee-chest position. This position increases systemic vascular resistance in the lower extremities.

Adapted from Child Health Nursing: Partnering with Children and Families, 2006.

Step by step approach to a hypercyanotic spell



Treatment

- ◊ Using the knee-chest position and holding the baby traps systemic venous blood in the leg thereby decreasing the systemic venous return and helping to calm the baby. The knee-chest position may also increase SVR by reducing arterial blood flow through the femoral arteries.
- ◊ Morphine sulphate, at 0.2 mg/kg administered SC, IM or IV suppresses the respiratory centre and abolishes hyperpnoea.
- ◊ Sodium bicarbonate (NaHCO3) at 1 mmol/l IV. Corrects acidosis and eliminates the respiratory centre–stimulating effect of acidosis. The same dose can be repeated in 10 to 15 minutes
- ◊ Administration of oxygen may improve arterial oxygen saturation a little.
- ◊ Vasoconstrictors such as phenylephrine at 0.02 mg/kg IV raise SVR.
- ◊ Ketamine at 1 to 3 mg/kg given over 1 minute is a good drug to use since it simultaneously increases the SVR and sedates the patient. Both effects are known to terminate the spell.
- ◊ Propranolol at 0.01 to 0.25 mg IV slowly has been used successfully in some cases both acute or chronic. Its mechanism of action is not entirely clear. When administered for acute cases propranolol may reduce the spam of the RV outflow tract and slow the heart rate. The successful use of propranolol in the prevention of hypoxic spell is more likely the result of the drugs peripheral action. It may stabilize vascular reactivity of the systemic arteries thereby preventing a sudden decrease in the SVR.
- ◊ Oral propranolol therapy at 2 to 6 mg/kg/day in three to four divided doses may be used to prevent recurrence of hypoxic spell and delay corrective surgical procedures in high risk patients.

- Physicians should recognize and treat hypoxic spells. It is important to educate parents to recognize the spell and what to do.
- Maintenance of good dental hygiene and antibiotic prophylaxis against SBE are important
- Relative iron-deficiency anemia should be detected and treated. Anaemic children are more susceptible to CVA. Normal Hb or HCT or decreased RBC indices indicate iron- deficiency anaemia in cyanotic patients.

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CHILD WITH STRIDOR

Definition

Stridor is a harsh noise during inspiration, which is due to narrowing of the airway from the oropharynx, glottis and the trachea. It usually occurs in inspiration but may occur in expiration.

The commonest causes of stridor in children are viral croup, foreign body, epiglottitis and congenital anomalies especially in neonates. Others include anaphylaxis burns and retropharyngeal abscesses. A good history helps to establish the possible cause.

VIRAL CROUP (LARYNGOTRACHEOBRONCHITIS)

Introduction

- Croup (laryngotracheobronchitis) is a common cause of upper airway obstruction in toddlers (1-3 years old)
- It is characterised by varying degrees of inspiratory stridor, barking cough, and hoarseness due to inflammation in the laryngeal region

Clinical Presentation

- Low grade fever and coryzal symptoms are followed over 12–24 h by a harsh, barking cough
- Stridor is most evident when the child is upset or agitated
- Respiratory distress of varying degrees
- Usually, resolves spontaneously over a 3-4 day period

Diagnosis

- Croup is a clinical diagnosis
- Neck x-rays are unnecessary unless the diagnosis is in doubt
- Important differential diagnoses
    - Acute epiglottitis
    - Bacterial tracheitis
    - Foreign body inhalation

- Anaphylaxis
- Retropharyngeal abscess

Table XXX. Assessment of severity

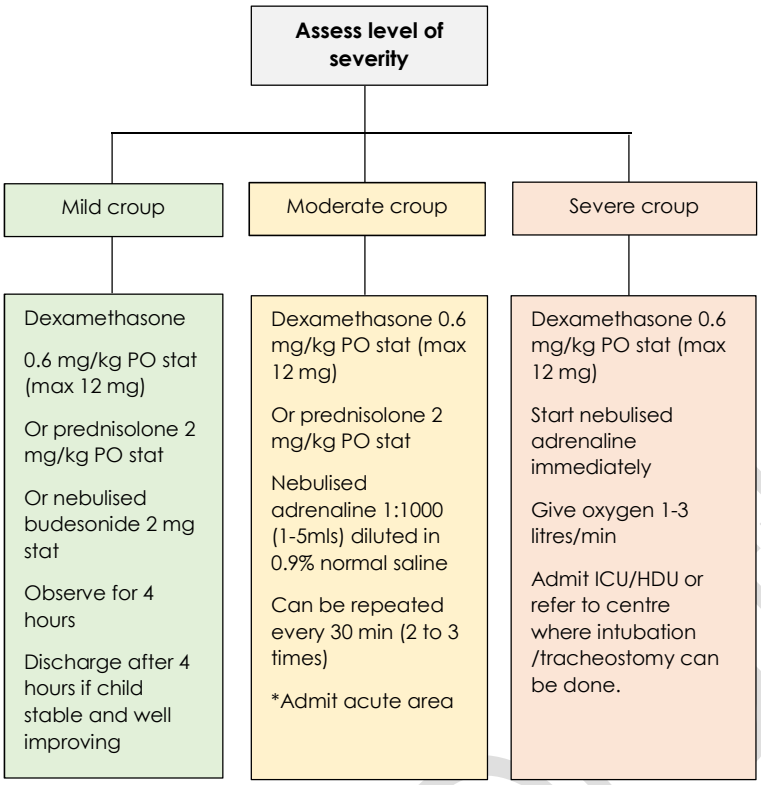
Sign	Mild croup	Moderate croup	Severe croup
Stridor	Only when agitated	At rest	Severe, biphasic
Recession	Mild subcostal	Moderate tracheal tug	Use of accessory muscles
Level of consciousness	Restless when disturbed	Anxious, agitated	Lethargic, drowsy

Management

◊ Keep the child on the mother's lap and handle gently

◊ **Do not** attempt to *forcefully* examine the oropharynx

◊ See flow chart below:



* As airway obstruction can occur suddenly, ensure that facilities for an emergency intubation and/or tracheostomy are immediately available if required.

Caution

◊ Avoid using oxygen unless there is impending airway obstruction. Nasal prongs or a nasal or nasopharyngeal catheter can upset the child and precipitate obstruction of the airway.

◊ Do not use antibiotics or bronchodilators unless diagnosis is in doubt

◊ Do not give adrenaline nebulisations if baseline heart rate >200/min

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ACUTE EPIGLOTTITIS

Epiglottitis is inflammation of the epiglottis. The epiglottis closes the airway during swallowing. Epiglottitis is a medical emergency that may result in death if not treated quickly due to rapid airway obstruction.

The incidence of epiglottitis due to Haemophilus influenza has reduced due to Hib vaccine in the Extended program on immunisation.

Signs and Symptoms

- ◊ sore throat with difficulty in speaking
- ◊ difficulty in breathing
- ◊ stridor
- ◊ fever
- ◊ drooling of saliva difficulty in swallowing or inability to drink.

Management

Treatment of patients with epiglottitis is directed to relieving the airway obstruction and eradicating the infectious agent.

- ◊ Keep the child calm in a seated or leaning forward position, and provide humidified blow-by oxygen, with close monitoring. Avoid laying the child in supine position.
- ◊ Avoid examining the throat if the signs are typical, to avoid precipitating obstruction.
- ◊ Elective intubation is the best treatment if there is severe obstruction but may be very difficult due to severe swelling; consider the need for surgical intervention to ensure airway patency.
- ◊ Give IV antibiotics when the airway is safe: ceftriaxone at 80 mg/kg once daily for 5 days.
- ◊ Give Paracetamol 15mg/kg qid or Ibuprofen 10mg/kg tds when airway is secure.

FOREIGN BODY INHALATION

Children are usually at high risk due to the tendency of inhaling small objects. The foreign body usually lodges in a bronchus (more often in the right) and can cause collapse or cause consolidation of the portion of lung distal to the site of blockage.

Choking is a frequent initial symptom. Objects such as fish bones can lodge in the larynx, causing stridor or wheeze. Sometimes the chocking may be followed by a symptom-free interval of days or weeks before the child presents with persistent wheeze, chronic cough or pneumonia, which fails to respond to treatment.

A large object lodged in the larynx can cause death from asphyxia, unless it can be dislodged, or an emergency tracheostomy be done.

Diagnosis

Inhalation of a foreign body should be considered in a child with the following:

- ◊ sudden onset of choking, coughing or wheezing; or
- ◊ segmental or lobar pneumonia that fails to respond to antibiotic therapy.
- ◊ Examine the child for:
  - o unilateral wheeze
  - o an area of decreased breath sounds that is either dull or hyper-resonant on percussion
  - o deviation of the trachea or apex beat.
- ◊ Obtain a chest X-ray at full expiration to detect an area of hyperinflation or collapse, mediastinal shift (away from the affected side) or a foreign body if it is radiopaque.

Treatment

Emergency first aid for the choking child: Attempt to dislodge and expel the foreign body. The management depends on the age of the child.

***For infants*:**

a) Lay the infant in a head-down position on one of your arms or on your thigh.

b) Strike the middle of the infant's back five times with the heel of your hand.

c) If the obstruction persists, turn the infant over and give five firm chest thrusts with two fingers on the lower half of the sternum.

d) If the obstruction persists, check the infant's mouth for any obstruction that can be removed

e) If necessary, repeat this sequence with back slaps.

Adapted from WHO pocketbook of care for children in hospital, 2nd ed, 2013

***For older children*:**

While the child is sitting, kneeling or lying, strike the child's back five times with the heel of the hand.

If the obstruction persists, go behind the child and pass your arms around the child's body; form a first with one hand immediately below the sternum; place the other hand over the fist and thrust sharply upwards into the abdomen. *Repeat this up to five times.*

Heimlich manoeuvre for a chocking older child

◊ Then check the child's mouth for any obstruction that can be removed.

◊ If necessary, repeat the sequence with back slaps.

Once this has been done, it is important to check the patency of the airway by:

◊ looking for chest movements

◊ listening for breath sounds and

◊ feeling for breath.

If further management of the airways is required after the obstruction is removed, keep the child's airways open and prevent the tongue from falling back to obstruct the pharynx while the child recovers.

Later treatment of suspected foreign body aspiration

◊ If a foreign body is suspected but cannot be confirmed, refer the child to a hospital where diagnosis is possible, and the object can be removed after bronchoscopy.

◊ If there is evidence of pneumonia, begin treatment with ampicillin (or benzylpenicillin) and gentamicin, as for severe pneumonia (see above), before attempting to remove the foreign body.

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THE WHEEZING CHILD

Introduction

Wheezing is a common presentation in young children. Diagnosis and treatment of these children can be challenging, as arriving at a final diagnosis often requires a process of exclusion

Without a clear diagnosis, a correct treatment approach is not possible, and a diagnosis may become more certain depending on the treatment response.

The algorithm shown in Fig xxx below considers the most common primary presentations with wheeze and gives one possible approach to this problem. A brief summary of the major wheezing conditions is provided in *Table* xxx

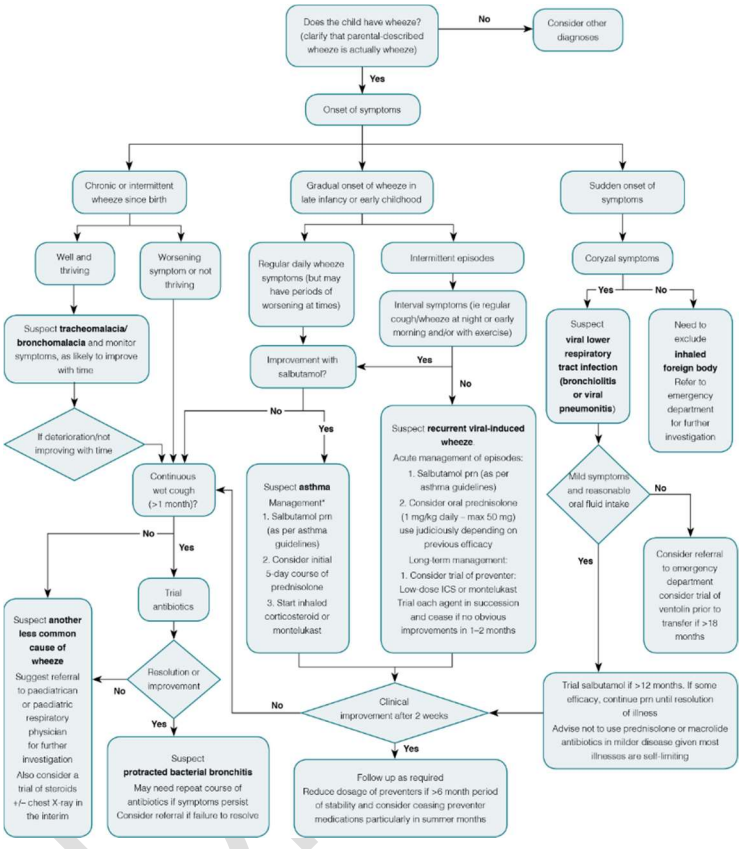

Figure x. Algorithmic approach to young children presenting with wheeze. *Therapeutic benefit from asthma medications is poor for those 1-2 years of age and usually absent in the first year; ICS, inhaled corticosteroids

Table xx Summary of the most common wheezing conditions in young children (continues on next page)

Condition	Estimated incidence in children	Clinical signs	Investigation	Expected clinical course	Management
Viral wheezing (these include a spectrum of viral LRTIs that are not always clearly separated e.g. viral LRTI/recurrent viral-induced wheeze/bronchiolitis – management of episodes is identical and the distinction is sometimes arbitrary)	Very common, especially in the first 2 years of life 50% of children will have at least one wheezing episode	Wheeze associated with respiratory tract infections May be singular or recurrent Bronchiolitis (usually in children <2 years) manifests with fine crackles +/– wheeze on auscultation	No specific investigations Nasal samples sent for virology usually do not change clinical management but isolation of RSV in infants is highly suggestive of bronchiolitis	60% will outgrow wheeze by 6 years A further 15% acquire wheezing after 6 years After 7–8 years, only 1 in 5 will outgrow it	Trial salbutamol if >1 year of age and continue only if effective Supportive care involving monitoring adequate fluid intake (>50% of usual intake) and for signs of increasing respiratory distress
Asthma	15–20 % of the paediatric population	Wheeze on a regular basis Some will have persistent/interval symptoms between episodes of viral wheeze (cough and/or	Spirometry with bronchodilator response may be possible in children ≥5 years of age in experienced laboratories	Usually expected to be lifelong but clinical courses can vary widely between individuals	Exacerbations: Regular salbutamol (as per asthma guidelines) and consider oral prednisolone for up to 5 days Regular preventer usually indicated

		wheeze at night or with exercise)			

Table xx Summary of the most common wheezing conditions in young children (continued)

Condition	Estimated incidence in children	Clinical signs	Investigation	Expected clinical course	Management
Airway malacia (airways floppiness): either tracheomalacia or bronchomalacia	1 in 2100	Usually present soon after the neonatal period with wheeze, stridor, cough and rattling; children are usually well and often labelled as 'happy wheezers'	Bronchoscopy usually diagnostic but not necessary in most cases	Majority outgrow it by age 2 years Secondary PBB can occur, presumably from poor cough clearance	Treatment rarely required If there are worsening symptoms or failure to thrive, specialist referral is indicated

Protracted bacterial bronchitis (PBB)	Probably common, but exact incidence unknown	Chronic wet cough (typically >4 weeks). Concurrent wheeze and/or rattly breathing is common	Bronchoscopy may assist diagnosis, but usually unnecessary Radiological findings usually normal or non-specific	Majority resolve with 1–2 courses of antibiotics	2–6 week course of antibiotics: commonly amoxicillin/clavulanic acid (approximately 20 mg/kg/dose twice daily)

Is it asthma or viral wheeze? Which children outgrow this phenomenon?

Key points

- ◊ Determining the cause of wheeze in young children can be difficult and sometimes is determined only following a trial of treatment.
- ◊ Parents' description of wheeze can be inaccurate and often needs elaboration or confirmation with impersonation or video recordings.
- ◊ Asthma is very common but other causes are also common and worth considering in the event of poor efficacy of asthma treatment.
- ◊ A diagnosis of protracted bacterial bronchitis should be considered for children with >4 weeks of continuous wet cough.

BRONCHIOLITIS

Introduction

Bronchiolitis is a clinical diagnosis, based on history and examination. It typically begins with an acute upper respiratory tract infection followed by onset of respiratory distress and fever. Illness usually resolves without intervention in 7 – 10 days, with peak severity two to three days post onset.

Diagnosis

History

History should include:

- recent respiratory symptoms
- feeding including:
  - duration of feeds (feeding more difficult with more severe illness)
  - breast feeding refusal
- underlying medical conditions including chronic lung disease, congenital heart disease and chronic neurological conditions
- chromosomal abnormalities including Trisomy 21
- prematurity
- post-natal exposure to cigarette smoke

Symptoms and signs

- cough
- tachypnoea
- retractions
- diffuse crackles or wheeze on auscultation

Table xx. Examination

Assessment of severity of acute bronchiolitis			
	Mild	**Moderate**	**Severe**
Behaviour	Normal	Some/intermitten t irritability	Increasing irritability and/or lethargy, fatigue
Respiratory rate	Normal – mild tachypnoea	Increased	Marked increase or decrease
Use of accessory muscles	Nil to mild chest wall retraction	Moderate chest wall retractions Tracheal tug Nasal flaring	Marked chest wall retractions Marked tracheal tug Marked nasal flaring
Oxygen saturations in room air	SpO2 >92%	SpO2 90-92%	SpO2 <90% May not be corrected by O2
Apnoeic episodes	None	May have brief apnoea	May have increasingly frequent or prolonged apnoea
Feeding	Normal	May have difficulty with feeding or reduced feeding	Reluctant or unable to feed

When to admit

When assessing a child in a secondary care setting, admit them to hospital if they have any of the following:

- ◊ apnoea (observed or reported)
- ◊ persistent oxygen saturation of less than 92% when breathing air
- ◊ inadequate oral fluid intake (50–75% of usual volume, taking account of risk factors (and using clinical judgement)
- ◊ persisting severe respiratory distress, for example grunting, marked chest recession, or a respiratory rate of over 70 breaths/minute.

When deciding whether to admit a child with bronchiolitis, take account of any known risk factors for more severe bronchiolitis such as:

- ◊ chronic lung disease (including bronchopulmonary dysplasia) haemodynamically significant congenital heart disease
- ◊ age in young infants (under 3 months)
- ◊ premature birth, particularly under 32 weeks
- ◊ neuromuscular disorders
- ◊ immunodeficiency.

When deciding whether to admit a child, take into account factors that might affect a carer's ability to look after a child with bronchiolitis, for example:

- ◊ social circumstances
- ◊ the skill and confidence of the carer in looking after a child with bronchiolitis at home. Confidence in being able to spot red flag symptoms
- ◊ distance to healthcare in case of deterioration.

Consider seeking senior emergency/paediatric advice for infant with moderate disease

Seek senior advice or refer for a child with severe bronchiolitis.

Risk factors for severe disease

- ◊ gestational age less than 37 weeks
- ◊ chronological age at presentation less than 10 weeks
- ◊ chronic lung disease
- ◊ congenital heart disease
- ◊ chronic neurological conditions
- ◊ failure to thrive
- ◊ Trisomy 21
- ◊ post-natal exposure to cigarette smoke
- ◊ breast fed for less than 2 months

Differential diagnoses

Whilst bronchiolitis is the most common cause of respiratory distress in infants, less common diagnoses, or dual diagnoses must be considered in all children.

Table 3. Differential diagnoses

Less common causes of respiratory distress in infants	
Respiratory	◊ bacterial pneumonia, including pertussis ◊ aspiration of milk/formula or foreign body ◊ tracheo/bronchomalacia
Other	◊ congestive cardiac failure ◊ sepsis ◊ intrathoracic mass ◊ allergic reaction

Caution

Consider cardiac disease presenting with congestive cardiac failure in infants with no precipitating viral illness, hypoxia out of proportion to severity of respiratory disease and/or presence of abnormal or unequal peripheral pulses, cardiac murmur or hepatomegaly.

Investigations

Investigations are not routinely recommended. Chest X-rays may lead to unnecessary antibiotic treatment. The primary treatment of bronchiolitis is supportive. This involves ensuring appropriate oxygenation and maintenance of hydration.

Seek urgent paediatric critical care advice for infants with any of the following:

- ◊ significant or recurrent apnoea
- ◊ persistent desaturations
- ◊ severe disease who are failing to improve with initial treatment

Management

Treatment

Children are often more settled if comfort oral feeds are continued.

Table xx. Initial management (continues on next page)

INITIAL MANAGEMENT The main treatment of bronchiolitis is supportive. This involves ensuring appropriate oxygenation and fluid intake, and minimal handling			
	Mild	Moderate	Severe
Likelihood of admission	Suitable for discharge Consider risk factors	Likely admission, may be able to be discharged after a period of observation Management should be discussed with a local senior physician	Requires admission and consider need for transfer to an appropriate children's facility/PICU Threshold for referral is determined by local capacity but should be early
Observations Vital signs (respiratory rate, heart rate, O2 saturations, temperature)	Adequate assessment in ED prior to discharge (minimum of two recorded measurements or every four hours)	One to two Hourly (not continuous) Once improving and not requiring oxygen for 2 hours discontinue oxygen saturation monitoring	Hourly with continuous cardiorespiratory (including oximetry) monitoring and close nursing observation

Table xx. Initial management (continued)

	Mild	Moderate	Severe
Hydration/nutrition	Small frequent feeds	If not feeding adequately (less than 50% over 12 hours), administer NG hydration	If not feeding adequately (less than 50% over 12 hours), or unable to feed, administer NG hydration
Oxygen saturation/oxygen requirement	Nil requirement	Administer O2 to maintain saturations greater than or equal to 90% Once improving and not requiring oxygen for 2 hours discontinue oxygen saturation monitoring	Administer O2 to maintain saturations greater than or equal to 90%
Respiratory support		Begin with NPO2 HFNC to be used only if NPO2 has failed	Consider HFNC or CPAP

Table xx. Initial management (continued)

	Mild	Moderate	Severe
Disposition/ escalation	Consider further medical review if early in the illness and any risk factors are present or if child develops increasing severity after discharge	Decision to admit should be supported by clinical assessment (including risk factors), social and geographical factors, and phase of illness	Consider escalation if severity does not improve. Consider ICU review/ admission or transfer to local centre with paediatric HDU/ICU capacity if: ◊ Severity does not improve ◊ Persistent desaturations ◊ Significant or recurrent apnoea associated with desaturations ◊ Has risk factors
Parental education	Provide advice on the expected course of illness and when to return (worsening symptoms and inability to feed adequately)	Provide advice on the expected course of illness and when to return (worsening symptoms and inability to feed adequately)	Provide advice on the expected course of illness

Oxygen and respiratory support

Administer oxygen for children with saturations persistently below the target oxygen saturations (SpO2) ≥92%

Table xx. Low flow oxygen

Low flow oxygen for infants with bronchiolitis by method of delivery	
Nasal prongs	**Hudson mask**
Maximum flow rate of 2 L/min	Commence at a minimum flow rate of 4 L/min to ensure adequate delivery if oxygen requirement is greater than 2 L/min

High flow nasal cannula oxygen (HFNC) Therapy

Consider HFNC therapy in infants with bronchiolitis who are hypoxic (SpO2 <92%) with moderate to severe work of breathing. HFNC therapy is **not** recommend for infants without hypoxia.

Continuous positive airways pressure (CPAP)

Nasal CPAP therapy for infants with bronchiolitis can also used.

Monitoring

Continuous pulse oximetry is recommended for hypoxic infants or unstable infants receiving oxygen.

Hydration/nutrition

- ◊ Give small frequent feeds for infants with mild bronchiolitis
- ◊ Consider nasal saline drops prior to the time of feeding
- ◊ Suction of the nares may assist feeding in infants with moderate distress

  Caution – Deep suctioning of the nasopharynx is not recommended as may cause oedema and irritation of the upper airway resulting in increased length of illness.

- ◊ NGT insertion is highly recommended for infants on HFNC. Advantages include:
  - o gastric decompression
  - o ability to feed without interrupting HFNC

- avoid potential for worsening of respiratory symptoms during feeding

◊ NG or IV hydration is recommended for infants with moderate -severe bronchiolitis who are feeding inadequately (less than 50% over 12 hours)

◊ if using IV route, isotonic IV fluids (0.9% sodium chloride with glucose, or similar) are recommended

◊ the volume of fluids required to maintain hydration is unclear

Treatments NOT recommended

◊ beta 2 agonists (e.g. Salbutamol) regardless of a personal/family history of atopy

◊ corticosteroids

◊ adrenaline (nebulised, IM, or IV) except in peri-arrest or arrest situation

◊ hypertonic saline

◊ antibiotics

◊ antivirals

◊ deep nasal suction

◊ chest physiotherapy

When to refer

Immediately refer children with bronchiolitis for emergency hospital care if they have any of the following:

◊ apnoea (observed or reported)

◊ child looks seriously unwell

◊ severe respiratory distress, for example grunting, marked chest recession, or a respiratory rate of over 70 breaths/minute

◊ central cyanosis

◊ persistent oxygen saturation of less than 92% when breathing air.

◊ difficulty with breastfeeding or inadequate oral fluid intake (50–75% of usual volume, taking account of risk factors and using clinical judgement)

◊ clinical dehydration.

When to discharge

Consider discharge for the following infants:

- ◊ is clinically stable
- ◊ has maintained oxygen saturation over 92% in air for 4 hours, including a period of sleep.
- ◊ feeding adequately
- ◊ parent/caregiver can safely manage the infant at home (consider time of day, parent/carer comprehension and compliance, access to transport and distance to the local clinic).

Key safety information for looking after a child at home

Provide key safety information for parents and carers to take away for reference for children who will be looked after at home. This should cover how to recognise developing *'red flag'* symptoms:

- ◊ Worsening work of breathing (for example grunting, nasal flaring, marked chest recession)
- ◊ Fluid intake is 50–75% of normal or no wet nappy for 12 hours
- ◊ Apnoea or cyanosis
- ◊ Exhaustion (for example, not responding normally to social cues, wakes only with prolonged stimulation).
- ◊ That people should not smoke in the child's home because it increases the risk of more severe symptoms in bronchiolitis
- ◊ How to get immediate help from an appropriate professional if any red flag symptoms develop
- ◊ Arrangements for follow-up if necessary.

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ACUTE EXACERBATION OF ASTHMA

Definition and clinical presentation

Asthma is a chronic inflammatory disorder of the airways, associated with airway hyperresponsiveness leading to recurrent wheezy episodes, breathlessness, chest tightness and persistent cough.

Diagnostic criteria

- ◊ Episodes of breathlessness
- ◊ Chest tightness
- ◊ Wheezing
- ◊ Persistent cough
- ◊ Airflow obstruction, variability and reversibility by peak flow measurement or spirometry

Table Assessment of Asthma Severity

Sign	Mild to Moderate exacerbation	Severe exacerbation	Life-threatening exacerbation
$Sa0_2$	92-95%	< 92%	< 90%
RR 2-5 years > 5 years	< 50/min < 30/min	> 50/ min > 30/ min	Variable
HR	100-120/min	> 120/min	Variable
Effort of breathing	Normal	Use of accessory neck muscles	Poor respiratory effort
Wheeze	Expiratory	Expiratory and inspiratory	Silent chest
Speech	Normal	Speaking with difficulty	Unable to speak
Level of consciousness	Fully conscious	Agitated	Confused

If no pulse oxymeter is available, check for cyanosis.

Table XX. Management

Mild to Moderate exacerbation	Severe exacerbation	Life-threatening asthma
Salbutamol 4-10 puffs via MDI and spacer every 20 minutes for one hour then every 30 minutes to 4 hourly, **OR** Salbutamol nebulisations 2.5 mg < 2 years 5 mg > 2 years ↓ Start prednisolone early 2 mg/kg (Max 40 mg) PO OD for 3 days ↓ Discharge if improving ↓ Otherwise admit and continue with regular salbutamol	High flow Oxygen 5-10 L/min. Salbutamol as for mild to moderate exacerbation ↓ Add ipratropium bromide via spacer or nebuliser: 125 mcg < 1 year 250 mcg if 1-5 years 500 mcg >5 years 4-6 hourly ↓ Give prednisolone PO If not improving or vomiting ↓ IV hydrocortisone 4 mg/kg 6 hourly ↓ IV aminophylline 5 mg/kg stat over 20 min, then infusion at 1 mg/kg/hour ↓ ◊ Admit to PICU ◊ Regular reviews ◊ Footnote on aminophylline and adrenaline	Admit to PICU and treat as for severe exacerbation ↓ In addition: Do FBC, ESR, U&Es blood culture, ABG if available ↓ IV 50% magnesium sulphate 40 mg/kg over 20 min (Max 2 grams) Diluted 1:5 in 0.9% Saline ↓ SC adrenaline 1:1000 0.01 mg/kg (Max 0.5 mg) ↓ If not improving, Prepare for intubation and mechanical ventilation

NOTE. Aminophylline and adrenaline should never be used as first line treatment for acute exacerbation of asthma, except in situations where no better alternative is available.

Discharge plan

- ◊ Patient can be discharged when stable on 4 hourly salbutamol inhalations.
- ◊ To complete 3 days course of prednisolone.
- ◊ Patient/parent education to be done on the ward.
- ◊ Patients with mild exacerbation of asthma can be reviewed at the local clinic.
- ◊ Those with moderate, severe or life-threatening exacerbations should be booked for review in the asthma clinic.
- ◊ **Reliever**: as-needed rather than routinely
- ◊ **Controller**: Higher dose for short term (1-2 weeks) or long term (3 months) depending on the background of the exacerbation.
- ◊ **Risk factors**: Check and correct modifiable risk factors including inhaler technique.
- ◊ Written **action plan.**

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PNEUMONIA

Pneumonia is an important cause of morbidity and mortality in developing countries

Both bacteria and viruses are important causes of pneumonia

Bacteria are the most common cause of pneumonia in HIV-infected children

Community-acquired pneumonia

- ◊ Pneumonia acquired outside the hospital settings
- ◊ In younger children, viral organisms are the common causative agents
- ◊ Streptococcal pneumoniae is the most likely cause in older children
- ◊ Mycoplasma pneumoniae should be considered in school going children and adolescents

Clinical presentation

- ◊ Fever >38.5^0 C
- ◊ Tachypnoea, tachycardia
- ◊ Subcostal and intercostal recession
- ◊ Crackles
- ◊ Abdominal pain (referred pleural pain)

Age	Cut-offs for fast breathing
< 2 months	60 breaths/min or more
2 – 12 months	50 breaths/min or more
12 Months - 5 Years	40 breaths/min or more

Indications for admission

◊ Cyanosis, Sp O_2 < 92%
◊ Increased respiratory rate
◊ Subcostal recession
◊ Intermittent apnoea, grunting (infants)
◊ Poor feeding
◊ Convulsions
◊ Restlessness or agitation
◊ Signs of dehydration
◊ Unconscious or lethargic
◊ Capillary refill time >3 seconds

Investigations

◊ Chest x-ray
◊ FBC, ESR
◊ Urea, electrolytes (may have hyponatremia owing to possible SIADH), and creatinine
◊ Blood culture
◊ If able to produce good sputum (send for gene xpert)
◊ Nasopharyngeal aspirates (send for gene xpert)
◊ Arterial blood gases (if available)

Management

◊ ***General measures***
  - Oxygen by nasal cannula or mask
  - IV fluids if required should be < 2/3 of requirements (risk of SIADH in hypoxic children)
  - Antipyretic and analgesia as indicated
  - Monitor vital signs

◊ ***Antibiotics therapy***
  - **0-3 months**
    - Benzyl penicillin 50,000 IU/kg/dose every 6 hours and gentamicin 7.5 mg OD or BD (in divided doses)

- **More than 3 months**
  - Benzyl penicillin 50,000 IU/kg/dose every 6 hours
- Ceftriaxone (50-80 mg/kg/dose OD) or cefotaxime (50 mg/kg QDS) should be considered if no improvement within 48 hours
- In infants with HIV infection or exposure, PCP therapy with high dose IV/PO cotrimoxazole (20 mg/kg/day of trimethoprim) should be included
- In suspected staphylococcus pneumonia, add IV Cloxacillin
- Macrolides should be considered in school-going children and adolescents who do not improve on 1st line treatment
  - ***Erythromycin***

    1 month – 2 years: 125 mg QID
    2 – 8 years: 250 mg QID
    8 – 18 years: 250-500 mg QID
  - ***Azithromycin***

    6 months-2years: 10 mg/kg OD
    3 – 7 years: 200 mg
    8 – 11 Years: 300 mg
    12 – 14 years: 400 mg
    >14 years: 500 mg

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COMA

Definition

A state of deep unarousable unconsciousness with total loss of awareness of self and environment. Consciousness is awareness of oneself and surroundings in a state of wakefulness, altered by disease, poisoning or trauma.

Causes

Coma with fever	Coma without fever
◊ Meningitis/sepsis ◊ Cerebral malaria ◊ Viral meningo-encephalitis	◊ Metabolic disorder ◊ Hypertensive encephalopathy ◊ Post-ictal state ◊ Non-Convulsive status epilepticus ◊ Stroke ◊ Poisoning/intoxications ◊ Mass brain lesions with raised ICP

Focused clinical history

◊ Child's health and activity in the last 5 days (preceding viral illness)

◊ Any history of fever

◊ Any chronic condition (DM, SCA, epilepsy)

◊ Time of last meal

◊ Pre-existing neurological disability

◊ Recent trauma

General physical examination

- ◊ Check vital signs- for signs of increased intracranial pressure(bradycardia, hypertension, respiratory rate/pattern (Cheyne stokes breathing)- Cushing triad
- ◊ Head – Full AF
- ◊ Eyes – Pupillary size and reaction to light and position (CN III,IV and VI palsies)
- ◊ Neck – Rigidity
- ◊ Odour – Metabolic disorders, poisoning
- ◊ Abdomen – Enlarged liver associated with hypoglycaemia
- ◊ Skin – Rash, trauma, haemorrhage

Primary assessment/resuscitation

A	Airway
B	Effort of breathing: Recessions, RR, grunting, flaring, use of accessory muscles. Effect of breathing: HR, skin colour, mental state, cyanosis Pattern of b breathing: Cheyne- stokes
C	Circulation: Pulse volume, pulse rate, capillary refill time, BP
D	Disability: **A** Alert **V** Verbal **P** Pain **U** Unresponsive Degree of coma (see below), posture (decorticate, decerebrate, hemiparesis), pupils, seizures
E	Exposure: Temperature, rash, evidence of poison

Degree of coma

This can be measured using:

Glasgow Coma Scale

	> 1 Year		< 1 year	Score
EYE OPENING	Spontaneously		Spontaneously	4
	To verbal command		To shout	3
	To pain		To pain	2
	No response		No response	1
MOTOR RESPONSE	Obeys		Spontaneous	6
	Localises pain		Localises pain	5
	Flexion withdrawal		Flexion withdrawal	4
	Flexion-abnormal (decorticate rigidity)		Flexion-abnormal (decorticate rigidity)	3
	Extension (decerebrate rigidity)		Extension (decerebrate rigidity)	2
	No response		No response	1
	> 5 years	**2 – 5 years**	**0 – 23 Months**	
VERBAL RESPONSE	Oriented	Appropriate words / phrases	Smiles/ cools appropriately	5
	Disoriented/confused	Inappropriate words	Cries and is consolable	4
	Inappropriate words	Persistent cries and screams	Persistent inappropriate crying and/or screaming	3
	Incomprehensible sounds	Grunts	Grunts, agitated, and restless	2
	No response	No response	No response	1
			TOTAL PAEDIATRIC GLASGOW COMA SCALE (3 – 15):	

Investigations

- ◊ Blood glucose
- ◊ Malaria parasite slide/RDT
- ◊ FBC, Renal function tests, Electrolytes (calcium, phosphate, Mg), blood culture,
- ◊ LFTs
- ◊ Blood/
- ◊ Urine toxicology
- ◊ CSF studies (if not contraindicated)
- ◊ EEG
- ◊ Imaging studies
    - o X-rays in order to localise infection (e.g. Chest x-ray to r/o disseminated TB)
    - o Neuro-imaging based on clinical findings and judgement .

Management

- ◊ Pay meticulous attention to Airway, Breathing, Circulation and Disability
- ◊ Check RBS (if not available, give 5mls/kg of 10% dextrose IV)
- ◊ Treat for raised ICP, if present- See next chapter
- ◊ Nursing care (skin care, oral hygiene, eye care, feeds, fluid balance)
- ◊ Further treatment depends on the provisional diagnosis

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INTRACRANIAL PRESSURE

Definition

◊ Intracranial pressure (ICP) is the pressure within the cranium and is measured in mm Hg. Normal values are 5-15 mmHg.

◊ Intracranial hypertension (or raised ICP) is defined as sustained ICP levels above 20mmHg.

Causes

◊ Traumatic Brain Injury, with mass effect

◊ Large vessel ischemic stroke (Carotid or MCA occlusion)

◊ Cytotoxic cerebral oedema with mass effect.

◊ Intracranial haemorrhage with mass effect.

◊ Hydrocephalus

◊ Diffuse cerebral oedema(hepatic failure, cerebritis/encephalitis/meningitis)

◊ Jugular venous obstruction or elevated right sided cardiac venous pressure

◊ Brain neoplasms causing mass effect or vasogenic oedema

◊ Idiopathic oedema

Focused history

◊ Pain/vomiting with valsalva manoeuvres

◊ Headache

◊ Nausea

◊ Vomiting

Examination

◊ Papilledema in awake patients(may proceed to stupor and coma over time)

◊ Bradycardia, hypertension and cheyne stokes breathing in comatose patients.

◊ Papillary dilation, extensor or flexor posturing and Cheyne stokes breathing, as a result of acute stupor or coma

◊ Nuchal rigidity

◊ Retinal haemorrhages

◊ Bulging fontanel and sun-setting eyes in infants

◊ CN III (often ipsilateral anisocoria), IV, or VI palsies (VI very common!)

Management

CLINICAL SIGNS OF RAISED ICP PRESENT
This is a medical emergency

Document findings; start continuous cardiopulmonary monitoring and alert intensive care/senior doctor to attend urgently.

CT imaging and liaison with Neurosurgical / Anaesthetic team if available

MAXIMAL MEDICAL THERAPY

1. ABCDE assessment and stabilisation: REMINDERS:-
   - If head/neck injury is suspected, protect and stabilise the C-spine as a priority
   - If the airway is at risk if GCS <8. Use airway control with airway manoeuvres, adjuncts as appropriate
   - Breathing – ventilate as required, give oxygen
   - Circulation – maintain mean arterial pressure with vasopressors if required
2. Elevate head of bed by 15 – 30 degrees.
3. Maintain normothermia (36.5°C – 37.5°C).
4. Consider hyperventilation if available, with close monitoring (note – effects only lasts for minutes).
5. Give 20% mannitol if available, with close monitoring.
6. Give 3% saline if available, with close monitoring.
7. If no signs of improvement, discuss with senior staff to advise on further management (e.g. sedation, intubation, ventilation).

Dose for mannitol 20% (APLS 2018)
250 – 500 mg/kg single dose, IV infusion over 30 min (1.25 – 2.5 ml/kg of 20% solution)

Dose for 3% saline (APLS 2018)
3 – 5 ml/kg IV over 15 minutes

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First unprovoked seizure

Definitions (ILAE)

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain

Epilepsy is defined as a chronic disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure. The definition of epilepsy is usually practically applied as:

- ◊ Having two unprovoked seizures >24 h apart.
- ◊ A patient with a first unprovoked seizure after a remote brain insults (such as a stroke, CNS infection, trauma) with a recurrence risk of further seizures comparable to the general recurrence (greater than 60%) risk for further seizures after two unprovoked seizures over the next ten years.
- ◊ A diagnosis of an Epilepsy syndrome

First unprovoked seizure: A focal or generalized seizure, including multiple seizures within 24 hours with full recovery of consciousness between seizures, without a clear provoking factor such as head trauma immediately preceding the seizure, CNS infection, or other known acute cause. Also to be excluded are neonatal seizures (in children <28 days old), status epilepticus, and febrile seizures.

Careful history and Examination

Specifically evaluate for risk factors of epilepsy including:

- ◊ Prior seizures
- ◊ Family history of epilepsy
- ◊ Any concerning historical factors for provoked seizures- including dehydration, vomiting, diarrhoea, toxicology exposure

◊ abnormality on neurologic exam

◊ concern for other neurologic disorders

Investigations

◊ Laboratory testing should be performed based upon individual clinical circumstances.

◊ Serum glucose, sodium, calcium and magnesium in particular should be considered if concern for electrolyte abnormalities per history

◊ Toxicology screening should be considered in any paediatric patient if any question of drug exposure or substance abuse

◊ EEG should be considered in cases of first time seizure to assess for underlying epileptiform abnormalities and determine risk of future seizures (e.g. diagnosis of epilepsy) **when the study is feasible** to obtain and clinical management is in question. Findings should be interpreted with the clinical history to make a determination if the child has epilepsy. **A normal study does not exclude epilepsy.** EEG testing is **not necessary** to diagnose epilepsy or initiate antiepileptic medication.

◊ Emergent neuro-imaging should be obtained in any child with

- persistent unresponsiveness
- Lack of return to baseline within a few hours
- Persistent Todd's paresis (transient weakness or paralysis of part or all of the body after a focal-onset seizure) that is not resolving within a few hours.

As timing is essential, the recommended study would be CT unless MRI is feasible within hours.

If the child is back to baseline, a non-urgent MRI/CTI (depending on availability and clinical suspicion- e.g. CT should be performed to rule out neuro-cystercercosis) should be considered for any child who has

◊ A focal seizure

◊ Focal EEG findings

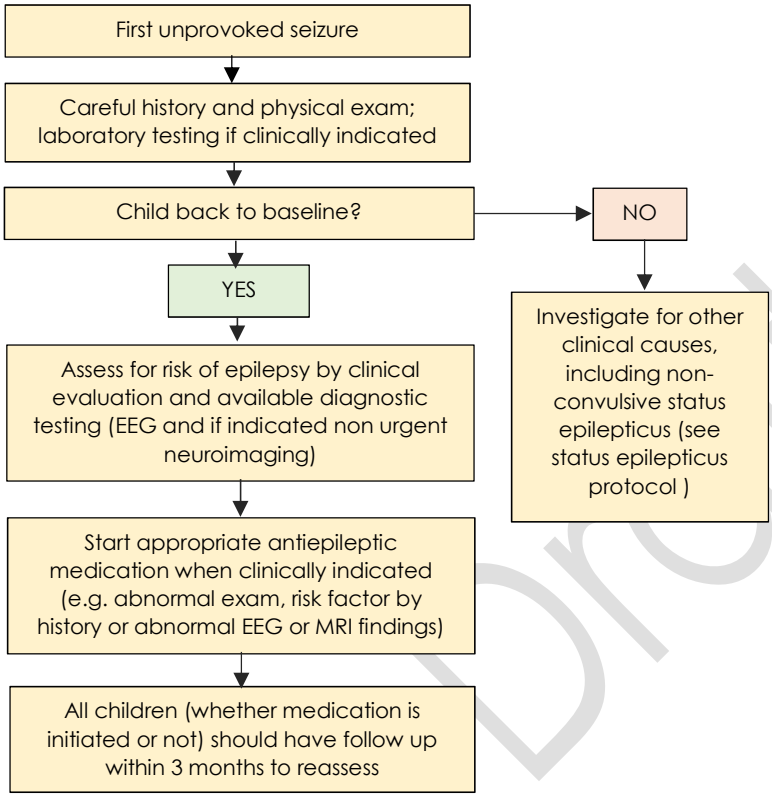
- ◊ Significant cognitive or motor impairment without known aetiology
- ◊ Other unexplained abnormality on neurological exam particularly if unresponsiveness to AED treatment or progressively worsening development is noted.

A diagnosis of epilepsy should be made if:

- ◊ A child with 1 unprovoked seizure presents with
  - o an abnormal EEG
  - o structural abnormality on neuro-imaging
  - o clear neurologic abnormality on examination suggestive of an underlying neurologic abnormality as the risk of seizure recurrence within a 10 year period is estimated as being higher than 60%.
- ◊ A child has 2 or more unprovoked seizures greater than 24 hours apart.

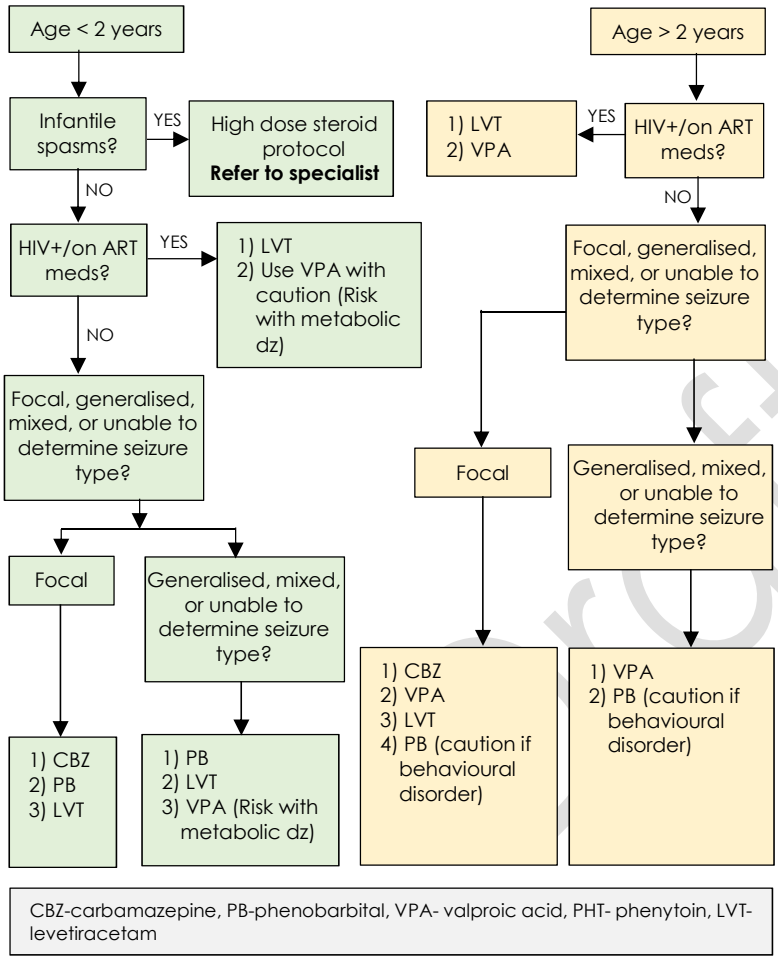
If epilepsy is diagnosed, consideration for antiepileptic treatment should be made based upon the clinical circumstances,

All children should be followed up after the first unprovoked seizure to see if there have been any recurrent events and reassess for risk of epilepsy, even if EEG and other evaluations were normal.


First unprovoked seizure
Careful history and physical exam; laboratory testing if clinically indicated
Child back to baseline?
NO
YES
Investigate for other clinical causes, including non-convulsive status epilepticus (see status epilepticus protocol)
Assess for risk of epilepsy by clinical evaluation and available diagnostic testing (EEG and if indicated non urgent neuroimaging)
Start appropriate antiepileptic medication when clinically indicated (e.g. abnormal exam, risk factor by history or abnormal EEG or MRI findings)
All children (whether medication is initiated or not) should have follow up within 3 months to reassess

Treatment

Guidelines for first line anti-epileptic drug choice



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STATUS EPILEPTICUS

Conceptual definition (ILAE 2015)

Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t1 - 5min) and can have long-term consequences (after time point t2 – 30min), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.

Classical Definition:

Continuous convulsion lasting longer than 20 to 30 mins or the occurrence of serial convulsions between which there is no return of consciousness.

Operational Definition

Seizure lasting more than 5 min or recurrence of two or more seizures, between which there is incomplete recovery of consciousness

Every child who presents for clinical care while having a seizure must be treated as status epilepticus.

Causes

- ◊ Febrile seizures
- ◊ Known epileptic who is non-compliant to treatment, is on erratic supply of drugs, had sudden withdrawal of anticonvulsants, is sleep deprived or has an inter-current infection
- ◊ Initial presentation of epilepsy
- ◊ CNS infections
- ◊ Congenital malformations of the brain (lissencephaly, shizencephaly)
- ◊ IEMs especially in neonates
- ◊ Electrolyte abnormalities – hypocalcaemia, hypoglycaemia
- ◊ Drug intoxication – amphetamines, cocaine, phenothiazines, theophylline, TCAs

◊ Others – Reye's syndrome, lead intoxication, extreme hyperpyrexia, brain tumour.

Investigations

◊ FBC and DC
◊ Random Blood Sugar
◊ Electrolytes & creatinine
◊ LFTs
◊ Calcium, magnesium, phosphate
◊ Gas analysis
◊ Lactate
◊ CSF studies (after brain CT)

Treatment

There are 4 goals of therapy:

◊ Ensure adequate vital signs, systemic and cerebral oxygenation
◊ Terminate seizure activity
◊ Prevent seizure recurrence
◊ Establish the diagnosis and treat the underlying cause if possible

1. First steps in management include stabilizing the child- ensure airway is open and circulation is stable. Administer oxygen. Place an IV line if possible.

    16. Immediately treat first with diazepam (or if available, Lorazepam).

        - If IV access is available, use 0.2-0.3mg/kg of diazepam IV (or 0.1mg/kg of Lorazepam) and there after give glucose (5ml/kg of 10% dextrose)
        - If no IV access, administer diazepam 0.5mg/kg rectally. **Diazepam should NOT be administered intramuscularly.**

17. 5 minutes:

- Administer a 2nd dose of diazepam. **DO NOT EXCEED 2 DOSES.**
- Alternatively, after the 1st dose of diazepam is administered, and there are limited resources for respiratory support, consider proceeding to step 4

18. 10 minutes

- If the seizures do not stop and Phenytoin is available, administer 20mg/kg IV x 1 (max 1gm), ***(dilute in normal saline- 100mg in 50ml)*** given over 20minutes.
- **This must be administered in a new IV (not in dextrose) using a G22 cannula. Cardiorespiratory monitoring is also indicated due to risk for arrhythmias and hypotension.**
- An additional 10mg/kg can be administered if seizures continue 15 minutes after the first dose

19. If phenytoin is not available:

- Stable respiratory status: administer 15-20mg/kg over 20 minutes (maximum dose 1gm) of **phenobarbital** with caution, very closely monitoring respiratory status.
- If respiratory status is not stable, provide available respiratory support. If there is an option for mechanical ventilation, emergently prepare to intubate the child if needed as you administer phenobarbital. If there is no mechanical ventilation available, choose one of the following based upon medication availability:
  - Levetiracetam 40mg/kg (max dose 1gm) IV (preferred) or NGT
  - Sodium valproate 20mg/kg (max dose 1gm) (only in children over 2 years) IV if no other option consider administer via NGT
  - OR Phenobarbital 10mg/kg IV or IM x 1 and repeat the dose as you monitor respiratory status closely.

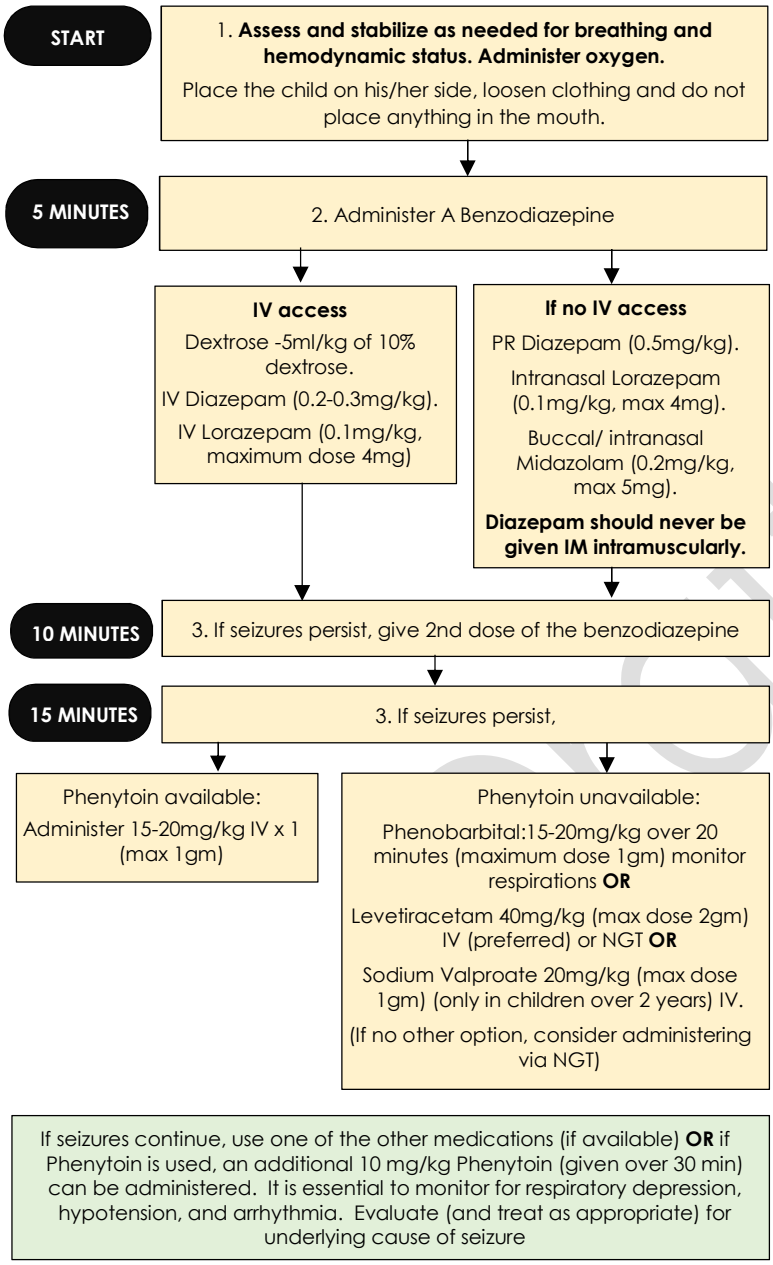
20. If the seizures continue, use any of the other medication options listed. **Alternatively, if no other options are available and there is no clear infection,** consider a trial

of high dose steroids of 30mg/kg daily Methylprednisolone (max 1gm) x 3 days, followed by a one-week oral prednisolone taper.

- If available, other treatment options for refractory status epilepticus include midazolam infusion, ketamine, propofol, pentobarbital coma, thiopental and other inhaled anesthetics.

21. Evaluate (and treat as appropriate) for underlying cause of seizure:
    - Consider head CT, and request urgent EEG (if feasible) if there is any concern for non-convulsive status epilepticus.
    - Review medication compliance, dose and formulation for all children with prior Epilepsy diagnosis and re-dose home medication if indicated
22. If the child has high risk of seizure recurrence (e.g. CNS infection), maintain on antiepileptic medication until child can be seen in follow up (within 3 months)
23. If no provoking factor for SE can be identified, and the child does not have known epilepsy, proceed with investigations as noted in first unprovoked seizure guidelines
24. Children with known epilepsy and on medication who present in status epilepticus should have re-evaluation of treatment plan and adjustment of medication prior to discharge
25. All children who present in status epilepticus should be given a rescue medication (e.g. rectal diazepam) and instructions on seizure first aid.

See appendix X/next page


START
1. Assess and stabilize as needed for breathing and hemodynamic status. Administer oxygen.
Place the child on his/her side, loosen clothing and do not place anything in the mouth.
5 MINUTES
2. Administer A Benzodiazepine
IV access
Dextrose -5ml/kg of 10% dextrose.
IV Diazepam (0.2-0.3mg/kg).
IV Lorazepam (0.1mg/kg, maximum dose 4mg)
If no IV access
PR Diazepam (0.5mg/kg).
Intranasal Lorazepam (0.1mg/kg, max 4mg).
Buccal/ intranasal Midazolam (0.2mg/kg, max 5mg).
Diazepam should never be given IM intramuscularly.
10 MINUTES
3. If seizures persist, give 2nd dose of the benzodiazepine
15 MINUTES
3. If seizures persist,
Phenytoin available:
Administer 15-20mg/kg IV x 1 (max 1gm)
Phenytoin unavailable:
Phenobarbital:15-20mg/kg over 20 minutes (maximum dose 1gm) monitor respirations OR
Levetiracetam 40mg/kg (max dose 2gm) IV (preferred) or NGT OR
Sodium Valproate 20mg/kg (max dose 1gm) (only in children over 2 years) IV.
(If no other option, consider administering via NGT)
If seizures continue, use one of the other medications (if available) OR if Phenytoin is used, an additional 10 mg/kg Phenytoin (given over 30 min) can be administered. It is essential to monitor for respiratory depression, hypotension, and arrhythmia. Evaluate (and treat as appropriate) for underlying cause of seizure

References

1. World Health Organization Updated Guideline on Paediatric Emergency Triage, Assessment and Treatment Care of Critically Ill Children. Geneva, World Health Organization, 2016.
2. WHO, Department of Mental Health and Substance Abuse. Mental Health Gap Action Programme (mhGAP) Intervention Guide version 2.0. October 2016.
3. Trinka, E. et al. A definition and classification of status epilepticus--Report of the ILAE Task Force on Classification of Status Epilepticus. *Epilepsia*. 2015.
4. Trinka, E et al. *Pharmacotherapy for Status epilepticus.* Drugs (2015) 75:1499–1521
5. Birbeck et al, A clinical trial of enteral Levetiracetam for acute seizures in pediatric cerebral malaria BMC Pediatrics, (2019) 19:399

FEBRILE SEIZURES

Definition

Febrile seizures are seizures that occur in **febrile** children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizures or significant neurological impairment. Fever may not be detected before the seizure, but it must be present at least in the immediate post-acute period and may be the only symptom of presenting illness.

- ◊ Simple febrile seizure
  - o Usually generalized tonic-clonic
  - o Lasting for a maximum of 15 min
  - o not recurrent within a 24-hour period.
- ◊ Complex febrile seizure
  - o More prolonged (>15 min)
  - o Maybe focal
  - o With/without associated post-ictal palsy (Todds paresis)
  - o And/or recurs within 24 hours
- ◊ Febrile seizures frequently occur in the contest of:
  - o Viral URTIs
  - o HHV6 infection
  - o Acute otitis media
  - o Malaria
  - o Genetic predisposition, e.g. autosomal inheritance pattern in some families

Clinical features

- ◊ Core temperature to ≥ 38^0c
- ◊ Generalized tonic- clonic, lasting up to 15 min
- ◊ Occurs once in 24 hrs (usually on first day of fever)
- ◊ For complex type – see above
- ◊ Recurrence is possible
- ◊ The vast majority are harmless, prognosis is good

Complete general and neurological examination

- ◊ Stabilize the child
- ◊ If the child arrives seizing to the facility, treat as status epilepticus (see status epilepticus protocol)
- ◊ Check for focus of infections
- ◊ Check for possible signs and symptoms of meningitis (see protocol for meningitis).
- ◊ **NB:** Lumbar puncture is not required in simple febrile seizures. It should be considered in the following scenarios:
    - o Children under 18 months of age (other signs and symptoms of meningitis might not be present or be very subtle).
    - o Complex febrile seizures (should only be considered after excluding need for neuro-imaging)
    - o Children who have received antimicrobials prior to assessment
    - o Children not immunised against Haemophilius and Pneumococcal species

Investigations

- ◊ Investigation should be done on individual basis to determine the cause of fever - MPS, FBC, nasopharyngeal swab, urine m/c/s, if no obvious focus is found.
- ◊ EEG and Neuroimaging are not routinely required for febrile seizures
- ◊ The work-up of children with complex febrile seizures needs to be individualized. This can include EEG and neuro-imaging where there is a clear focality concerning for possible CNS lesion.

Treatment

- ◊ Abort seizure - Diazepam IV 0.2 – 0.5 mg/kg slowly (can also be given rectally 0.5 mg/kg) if duration more than 3-5 min.

- ◊ Supportive therapy – tepid sponging, nurse in semi-prone position, ensure adequate airway.
- ◊ Assess for the cause of fever and treat appropriately - Coartem, amoxyl...
- ◊ Antiepileptic medications are not indicated.
- ◊ Antipyretic should be used at the same dose and intervals used for lowering fever during a febrile illness at optimal dosing:
    - o Paracetamol at 10 to 15 mg/ kg/dose every 4-6 hours (max 5 doses/day)
    - o Ibuprofen: 20-30 mg/kg/day in 3 doses.
- ◊ Families should be provided counselling on risk or recurrence of febrile seizures (25-40%), risk of epilepsy (10% if complex febrile seizures, similar to general population if simple febrile seizures), and seizure first aid.

References

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3. Oxford Handbook of Paediatrics; Oxford University Press; First ed; 2008.
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5. R.S. Fisher at al. Epilepsia. 2005;46:470-2)
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8. World Health Organization Updated Guideline on Paediatric Emergency Triage, Assessment and Treatment Care of Critically Ill Children. Geneva, World Health Organization, 2016.

9. WHO, Department of Mental Health and Substance Abuse. Mental Health Gap Action Programme (mhGAP) Intervention Guide version 2.0. October 2016.

PAEDIATRIC STROKE

Definition

A focal neurological deficit with an underlying vascular pathology is defined as:

Stroke	lasting > 24h
Transient ischaemic attack (TIA)	lasting < 24h
Reversible ischaemic neurological deficit (RIND)	lasting> 24 h but with full recovery
"Stroke-like episode"	Focal neurological deficit lasting >24 hr with no obvious vascular pathology, e.g. Brain tumour, brain abscess. Rare in childhood (1-3 / 100,000 per year)

Paediatric stroke can be **ischaemic** (vessel spasm, stenosis, dissection or vessel occlusion by thrombosis or embolism) or **haemorrhagic** and occur at any age;

- ◊ Neonatal stroke:28 weeks gestation- 28 days post natal life
- ◊ Childhood stroke: Greater than 28 days -18 years

Note: SCD is the most common cause of stroke in Zambian children.

Ischaemia (Arterial or Venous)

Embolism	Cyanotic CHD, Endocarditis
Large vessel stenosis	SCD, Varicella, HIV, Homocystinuria
Vessel spasm	CNS infections
Thrombosis	SCD, Severe dehydration (cerebro-venous-sinus thrombosis), Malignancies (Leukemia) Thrombocytosis, CNS infections, hyper coagulable states i.e Protein S or C deficiency, Antithrombin III deficiency, Lupus antibodies, Factor V Laiden, Renal disorders i.e Nephrotic syndrome
Vessel dissection	Trauma, Congenital Heart Disease
Cerebral Arteropathy	Moya Moya, Focal/transient arteriopathy, Post varicella
Drugs	i.e Aspiraginase
Syndromes	Williams syndrome, Downs syndrome

Haemorrhage

Low platelets	Idiopathic thrombocytopaenic purpura
Bleeding disorder	Coagulation factor deficiencies i.e Hemophilia
Vessel disorder	A-V malformation, A-V fistulas, cerebral aneurysm, Carvenous malformations
Trauma	

Clinical features

- ◊ Hemiparesis
- ◊ Hemi-sensory signs
- ◊ Visual field defects
- ◊ Seizures (common in neonates)
- ◊ Deterioration in level of consciousness (seen in progression of bleed)
- ◊ Headache

◊ Nausea and vomiting

Investigations

◊ FBC, differential count, ESR, random blood sugar, sickling test, clotting defects (e.g. protein C & S deficiencies, Antithrombin III deficiency)

◊ Clotting profile

◊ Electrolytes initially, then daily until stable

◊ Blood, urine and CSF cultures if febrile (remember to withhold LP if evidence of ↑ICP)

◊ After stabilization , Neuro-imaging (preferably MRI) and angiography

MRI brain scan	Outline area affected (thrombosis, bleed, abscess, tumour, etc.
CT scan	If MRI unavailable (to exclude haemorrhage)
MRA /MRV	Vascular outline to R/O Arteriopathy, Vessel anomalies and Venous thrombosis
ECG and ECHO	cardiac anomaly or arrhythmia

Investigate for a possible thrombophilia even with an obvious cause like trauma as these two conditions may co-exist.

Management

Ischemic Stroke

◊ Initial attention to ABCDE

◊ Consider admission to PICU for 1st 24 hours or until stable

◊ Monitor vital signs (BP, Pulse, Respiratory rate), input & output, level of consciousness

◊ Allow permissive hypertension- Recommended BP goal between the 50th-95th percentile for age and height, **with permissive hypertension** up to 20% above the 95th percentile

- Persistent, significant hypertension should be treated with caution to lower blood pressure by approximately 25% over 24 hours.

◊ Nurse head flat for 24 hours (unless signs of raised ICP)

- ◊ Fluid management- isotonic IVF for at least 24 hours
- ◊ Keep nil by mouth
- ◊ Maintain normoglycaemia
- ◊ Control fever-Maintain normothermia
- ◊ O_2 to by face mask if indicated (keep SpO2 greater than 92%)
- ◊ Treat acute seizures (no role for AED's for seizure prophylaxis)
- ◊ Manage ↑ICP if present (see management of ICP protocol)
- ◊ Control systemic hypertension
- ◊ If high index of suspicion for CNS infection give Antibiotics (Cefotaxime 100 mg/kg q 6 hr or Ceftriaxone 100 mg/kg per day)
- ◊ Other management is dependent on cause, e.g. exchange transfusion/ blood transfusion in SCD, anticoagulants in prothrombotic coagulopathy
- ◊ Anti viral treatment with Acyclovir has been recommended for varicella zoster virus vasculopathy with **virologic confirmation of active central nervous system VZV infection**

In neonates, treatment for prevention of a 2nd stroke is often not required because the risk of recurrence is low. In children however, the recurrence risk is higher and long term therapy with low dose aspirin is often needed (1-5mg/kg/day not). Aspirin is recommended for a minimum of two years.

Hyper transfusion therapy and hydroxyurea in patients with SCD for secondary prevention of Stroke

Refer to specialist for immunosuppressant therapy for vasculitis.

Haemorrhagic stroke

- ◊ Stabilize patient ABCDE
- ◊ Admit in the PICU
- ◊ Monitor for new or worsening neurological symptoms- extension of haematoma, herniation, hydrocephalous
- ◊ Isotonic IVF for at least 24 hours
- ◊ Maintain normothemia and normoglycemia
- ◊ Maintain normal blood pressure

◊ Manage raised ICP, if present

◊ Manage acute seizures

◊ Manage the cause

- Replace clotting factors, platelet transfusion for thrombocytopenia
- MRI/MRA to look for vascular malformation if possible
- Neurosurgery sometimes can embolize/resect malformation to prevent future strokes

Rehabilitation

A plan for rehabilitation should be discussed with the parents. Speech, occupational and physical therapies, psychological services, special education should be offered.

High risk of future Epilepsy.

References

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2. Kliegman, Behrman, Jenson, Stanton, Nelson Textbook of Paediatrics, 18th Edition
3. Robert C Tasker, Robert J McClure, Carlo Acerini, Oxford Handbook of Paediatrics
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URINARY TRACT INFECTION

Definition

UTIs are usually caused when bacteria invade and ascend up the urinary tract from the urethra and into the bladder. Cystitis, a lower UTI, occurs when the infection and inflammatory response are localised to the bladder. Pyelonephritis is an upper UTI in which the bacteria and subsequent inflammatory response further ascend to the ureters and kidneys.

Causes

Colonic bacteria are typically the culprits: coliforms Escherichia coli is the most common bacteria that causes UTIs in all ages, accounting for 54% to 67% of UTIs in children. Klebsiella (6%-7%), Proteus (5%-12%), Enterococcus (3%-(%) and Pseudomonas (2%-6%) are other common causative organisms.

Clinical features

Infants generally present late in the course of infection because of initial nonspecific signs, such as fever, and the inability to express symptoms or localize pain.

Older children can usually localise early symptoms of UTI, such as dysuria or abdominal pain, and therefore present earlier in the clinical course.

◊ Fever, Dysuria, Urinary frequency, Suprapubic discomfort, Flank pain, Costovertebral pain, Abdominal pain.

Urine sampling

◊ Obtaining urine samples from children who are not toilet trained involves urethral catheterization, suprapubic

aspiration(SPA), urine collection bag or leaving the child to void and obtaining a clean catch urine.

◊ For toilet trained children, a midstream urine sample should be collected.

Investigations

◊ Urinalysis

- A positive nitrite test makes UTI very likely, but the test maybe falsely negative.
- The leukocyte esterase test is an indirect measure of pyuria.

◊ Urine microscopy

- A microscopic urinalysis finding of 10 white blood cell per microliter in uncentrifuged urine specimen is reported to be a more sensitive indicator.

◊ Urine culture

- For children who are not toilet trained, only urethral catheterisation and SPA are considered to be reliable methods for specimen collection for the purpose of culture.
- A negative bag culture rules out a UTI but a positive result is not useful.

Minimum colony counts that are indicative of a urinary tract infection			
	CFU/ml	**CFU/L**	**Comments**
Clean catch(midstream)	$\geq 10^5$	$\geq 10^8$	Mixed growth is usually indicative of contamination. Sitting a girl backward on the toilet is a good way to spread the labia when collecting midstream urine
In and out catheter specimen	$\geq 5x10^4$	$\geq 5x10^7$	Mixed growth is usually indicative of contamination. Specimens from indwelling catheters are less reliable
Suprapubic aspiration	Any growth	Any growth	

Treatment

- ◊ Start empiric treatment with Quinolones but depends on local susceptible patterns then change according to culture results.
- ◊ Oral antibiotics 10 to 14 days or
- ◊ IV antibiotics for 3 days ,then 10 days oral antibiotics

Reference

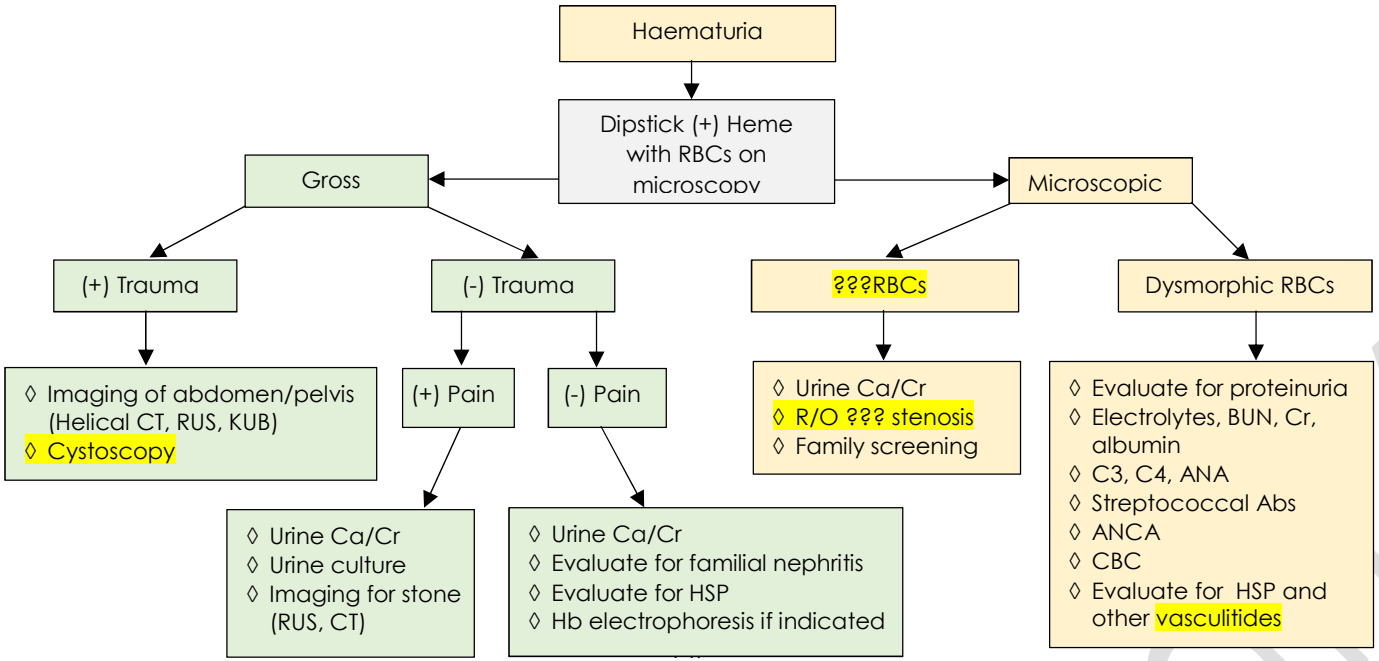
Eric Balighian, Micheal Burke: Paediatics in review January 2018,39(1)3-12

HAEMATURIA

Haematuria is defined as the presence of five or more RBCs per high-power (40x) field in three consecutive fresh, centrifuged specimens obtained over the span of several weeks. Confirmation of haematuria is critical. A positive urine dipstick test may result from myoglobinuria or hemoglobinuria, in which the urine often is discoloured, but no RBCs are noted on microscopic evaluation.

Glomerular Versus Extraglomerular Hematuria		
Factor	**Glomerular**	**Extraglomerular**
Color	Smoky, tea-or cola-colored, red	Red or pink
RBC Morphology	Dysmorphic	Normal
Casts	RBC,WBC	None
Clots	Absent	Present (+/-)
Proteinuria	≥2+	

Algorithm for the evaluation of haematuria (adapted from Paediatrics in Review???)



History	Possible Diagnosis
Lower tract symptoms(dysuria,urgency,frequency, suprapubic pain)	UTI
Recent illness(pharyngitis,impetigo,viral illness)	Postinfectious glomerulonephritis
Abdominal pain	UTI,HSP,Crystalluria/stone
Arthralgias	HSP,SLE
Diarrhea(±bloody)	HUS
Cough ,hemoptysis	Vasculitis
Sickle cell disease	Glomerulonephritis,papillary necrosis
Swimming in streams	Schistosomiasis
Physical findings	Possible diagnosis
Suprapubic pain	UTI
Flank Pain	IgAN,stones,renal vein thrombosis,pyelonephritis
Edema	Glomerulonephritis,nephritic syndrome
Abdominal mass	Wills tumour,hydronephrosis,cystic kidney disease
Meatal stenosis	Infection,trauma
Family History	Possible Diagnosis
Sickle cell disease or trait	

Diagnostic evaluation

The first step involves measurement of blood pressure

- A dipstick urinalysis evaluates for pyuria, proteinuria, heme positivity, and urinary concentrating defects;
- Microscopy evaluates for white blood cells and clumps, RBC morphology, crystals and casts.
- Crystalluria can be caused by calcium oxalate, calcium phosphate, uric acid, or cystine crystals. Hypercalciuria is by far, the most common cause of crytalluria

◊ Urine culture should be done for suspected UTI.

◊ Radiographic studies if indictated.

The second stage of evaluation involves a more thorough search for underlying renal disease, particularly when edema, hypertension, alterations in urine output, or systemic symptoms are present.

◊ Evaluation for sickle cell disease or trait by solubility test and electrophoresis were available.

◊ Suspicion of acute PIAGN should prompt ordering of ASO and other streptococcal antibody titres and a C3 measurement.

◊ Secondary causes of renal disease warrant checking for antibodies, complement levels(C3,C4), hepatitis serologies, or HIV serology.

◊ A complete blood count is helpful in the setting of petechiae, bruising, fatigue, abdominal masses, or suspicion of chronic disease.

◊ Renal ultrasonography can identify structural abnormality.

◊ Abdominal radiographs may identify radiopaque stones .

When to refer

◊ If cause of gross haematuria is unclear refer to next level

◊ Refer early if patient experiencing symptomatic microscopic haematuria.

◊ The patient who has asymptomatic haematuria needs periodic evaluation every 1 to 2 years to reavaluate for coexisting symptoms or protienuria and to revisit the family history with respect to other family members having haematuria or hearing deficits.

◊ The child who has persistent asymptomatic haematuria and concomitant proteinuria needs additional evaluation, often including a renal biopsy, refer to next level.

References

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NEPHROTIC SYNDROME

Nephrotic syndrome is characterised by:

- ◊ Heavy proteinuria > 40 mg/m²/hr or urine protein 3+ or greater on a dipstick test
- ◊ Hypoalbuminaemia (serum albumin < 25g/L)
- ◊ Hyperlipidaemia
- ◊ Oedema

Causes

- ◊ Idiopathic (primary) nephrotic syndrome
- ◊ Secondary nephrotic syndrome (secondary to a known cause e.g. Hepatitis B, malaria syphylis, SLE etc).
- ◊ Congenital nephrotic syndrome- occurring in a child less than three months- it may be primary or secondary.

Clinical features

- ◊ Oedema with or without ascites, pleural effusions, and genital oedema.
- ◊ Hypertension and haematuria maybe present.

Investigations

- ◊ **Blood**: FBC/ESR; U&Es; Creatinine; LFTs including serum albumin ; C3/C4 ; ANA, ASOT, anti- Dnase B, RPR, HCV antibodies, HbSAg, Triglycerides and cholesterol levels.
- ◊ **Urine**: Dipstick urinalysis. Morning urine protein/creatinine ratio ≥ 200mg/mmol or 0.2g/ mmol (morning so as to avoid orthostatic proteinuria).
- ◊ CXR, KUB ultrasound
- ◊ If available: Varicella zoster IgG blood levels, tuberculin skin test.

◊ Renal biopsy only if atypical features at presentation: macroscopic hematuria, less. than 12 months or older than 12 years, low C3, vasculitic rash, suspected vasculitis.

Treatment

Symptomatic treatment

◊ No added salt diet

◊ Diuretics- usually Lasix 1mg/kg BD initially- ensure that patient does not have intravascular volume contraction before commencing- best to discuss with nephrology first.

◊ 20% albumin 1g/kg given over 4-6 hours with frusemide only if patient does not respond to Lasix alone. Ensure that patient does not have renal failure as under these circumstances albumin can cause pulmonary oedema. Also watch out for hypertension with this treatment. **Further albumin infusions must only be given on week days and during regular working hours so that the MO is available to react to any potential complications.**

◊ Prophylactic antibiotic cover (pen v) as long as patient has gross oedema including ascites. In penicillin sensitive use erythromycin

◊ Daily weight and daily urinalysis

◊ By and large children with nephrotic syndrome do not need to be fluid restricted because they have intravascular volume depletion.

◊ If antihypertensives are required ensure that the patient has a normal creatinine and serum potassium before using ACE-inhibitors. For initial treatment calcium channel blockers such as amlodipine or nifedipine are ideal- discuss with Nephrology.

Specific treatment

Dose of prednisolone in m^2

60mg/m^2 [2mg/kg] in the first 4 weeks and then reduced to 40mg/m^2 [1.5 mg/kg] given on alternate days for 4 weeks then tapered off slowly over another 4-6 weeks.

Definitions

Remission	Urine albumin nil or trace (or proteinuria <40 mg/m^2 /h) for 3 consecutive days
Relapse	Urine albumin 2 + or more for 3 consecutive days, having been in remission previously
Frequent relapses	Two or more relapses in six months of initial response, or more than four relapses in any twelve months
Steroid dependence	Children who relapse whilst on steroids therapy or within 14 days of discontinuation of steroid therapy
Steroid resistance	Absence of remission following at least 28 days of steroid therapy at a dose of 2 mg/kg per day

Complications

- ◊ Increased susceptibility to bacterial infections.
- ◊ Spontaneous bacterial peritonitis.
- ◊ Hypovolaemia and thromboembolism.
- ◊ Complications related to chronic steroid administration include hypertension, obesity, and linear growth retardation.

Steroid resistant nephrotic syndrome and steroid dependant nephrotic syndrome:

- ◊ These patients will require a renal biopsy and introduction of steroid sparing agents.
- ◊ Ideally these patients should be discussed with nephrology and referred if possible.

References:

1. KDIGO glomerulonephritis guidelines
2. Rees L, Brogan P, Bockenhaeur D, Webb N, "oxford sub-specialist handbooks in paediatrics: paediatric nephrology" 2nd edition, Oxford University Press, 2012
3. Avner [editor], Paediatric Nephrology

ACUTE GLOMERULONEPHRITIS

Definition

Results from inflammation in the glomerulous. It is a clinical syndrome that is said to be present when a constellation of four features are present in a patient.

◊ Oedema
◊ Hypertension
◊ Hematuria
◊ Renal dysfunction

Causes

Causes of acute glomerulonephritis include post-infectious, renal, and systemic aetiologies.

Post-infectious aetiologies

◊ Bacterial: *Streptococcus* species (i.e. group A beta-haemolytic), the commonest cause. syphilis, TB, salmonella, *E.coli.*
◊ Viral: Hepatitis B and C, HIV.
◊ Parasitic: Malaria.

Systemic causes

◊ Collagen vascular diseases (e.g. SLE)
◊ Vasculitis- IgA nephropathy, HSP, ANCA associated vasculitis
◊ Drug-induced (i.e. gold, penicillamine)
◊ HUS,TTP
◊ Ventriculo-atrial shunts

Clinical Features

History

◊ Sudden development of puffiness of the eyelids and facial oedema in the setting of a post-streptococcal infection.
◊ The urine may be dark and scanty.

◊ Non-specific symptoms include weakness, fever, abdominal pain, and malaise.

Physical examination

◊ Most frequently patients present with a combination of oedema, hypertension, haematuria and oliguria.

◊ Look for signs of scabies or furuncles on skin: common in post-strep

◊ Other signs depend on the underlying cause e.g. malar rash and other vasculitic rashes.

Investigations

◊ Urine microscopy – RBC's, RBC casts (dysmorphic red blood cells), proteinuria, leukocytes

◊ Blood – FBC, U/E and creatinine, ESR

◊ Cultures – throat swab

◊ Other (as indicated) - CXR, U/S-renal, ECHO, ASOT, antinuclear antibody, anti-DNA antibodies.

◊ Complement levels (C3, C4),ANA, ANCA

◊ CXR, KUB ultrasound

◊ +/- renal biopsy

Treatment

◊ Antibiotic, i.e. penicillin if thought to be post-strep

◊ Antihypertensive, i.e. diuretics, calcium channel blockers, beta-blockers.

Important note: Please avoid ACE-inhibitors in this group of patients as initial antihypertensive choice until blood results for serum creatinine and potassium are known. And even if normal cautious use of ACE-I is advised unless one can easily monitor renal function of the patient.

◊ Sodium restriction.

◊ Renally adjust all drug doses based on estimated GFR. This can be calculated using the scwartz formula in children= 40 X height[cm]/ serum creatinine (in micromoles/l).

◊ Fluid restriction may be necessary depending on extent of renal dysfunction.

◊ Treat underlying cause.

◊ If patient progresses to acute renal failure, refer to acute renal failure protocol.

◊ As some patients may end up with rapidly progressive glomerulonephritis early nephrology consultation is highly encouraged.

◊ Admit patient initially for investigation.

Post-strep glomerulonephritis

◊ Commonest cause in our environment.

◊ Often associated with skin bacterial infection by group A beta haemolytic streptococcus. Bacterial infection may also be facilitated by infestation with sarcoptes scabies.

◊ Usually benign in over 90% of patients but has the potential to complicate into rapidly progressive glomerulonephritis.

◊ Expected to have normal C3 by 8 weeks post onset. If not then patient requires a biopsy.

◊ If significant proteinuria present after 6 months patient will need a renal biopsy.

◊ Patient may continue to have microscopic hematuria for upto 2 years after initial onset.

◊ Residual hypertension can occur and so patient will need continued monitoring of blood pressure.

References

1. KDIGO glomerulonephritis guidelines
2. Rees L, Brogan P, Bockenhaeur D, Webb N, "oxford sub-specialist handbooks in paediatrics: paediatric nephrology" 2nd edition, Oxford University Press, 2012

3. Avner [editor], Paediatric Nephrology

ACUTE KIDNEY INJURY

Definition

An acute, potentially reversible, deterioration in kidney function resulting in failure to maintain normal physiological homeostasis, characterized by an increase in blood urea and serum creatinine values, often accompanied by hyperkalaemia, metabolic acidosis, and hypertension. It may be accompanied by a urine output < 0.5ml/kg/hour or < 1.0 ml/kg/hour in the neonate. Note however that some forms of AKI are accompanied by polyuria e.g. aminoglycoside toxicity.

Paediatric RIFLE [pRIFLE] classification of AKI

- ◊ R- risk of renal dysfunction (serum creatininie x 1.5 of baseline).
- ◊ I- injury to the kidney (serum creatinine x 2 of baseline).
- ◊ F-failure of kidney function (serum creatinine x 3 of baseline).
- ◊ L- loss of kidney function.
- ◊ E-end-stage renal disease.

Causes

- ◊ **Pre-renal -** Prerenal failure refers to causes resulting from reduced blood pressure or reduced effective intravascular volume thus resulting in hypoperfusion of the kidneys. This can be due to dehydration, haemorrhage, sepsis, cardiac failure, hypoalbuminaemia (nephrotic syndrome, liver disease).
- ◊ **Renal (intrinsic)** – Renal parenchymal damage, e.g. Acute glomerulonephritis, Intrarenal vascular disease (Haemolytic-uremic syndrome, Vasculiditis), Acute interstitial nephritis, Acute tubular necrosis, Nephrotoxins.
- ◊ **Post-renal**
    - o ***Congenital*** - posterior urethral valves, pelvi-ureteric junction if bilateral, vesico-ureteric junction obstruction if bilateral, ureterocoeles, prune belly syndrome, bladder outlet obstruction, neurogenuc bladder.
    - o ***Acquired (rare)*** – Urolithiasis, Clots, Tumours if both kidneys involved or if these result in bladder outlet obstruction.

Clinical features

These will reflect the cause and the consequent abnormalities.

- ◊ Signs of ARF include signs of fluid overload (hypertension, oedema) and signs of congestive cardiac failure (CCF), such as hepatomegaly, gallop rhythm, and pulmonary oedema.
- ◊ Signs of intravascular volume depletion include tachycardia, hypotension, decreased skin turgor, dry mucous membranes, and changes in sensorium.
- ◊ Although oliguria is a criterion used to diagnose and stage acute renal failure (ARF), ARF can be present without oliguria, especially in patients with nephrotoxic kidney injury, interstitial nephritis, or perinatal asphyxia. Oliguria may be defined as urine output less than 0.5 ml/kg/h in children and < 1mlkg/hr in neonates.
- ◊ Rash and arthritis(e.g. SLE and Henoch-Schonlein purpura nephritis), flank masses (renal vein thrombosis, tumours, cystic diseases, urinary tract obstruction)

Investigations

- ◊ **Dipstick urinalysis:** leucocytes (UTI), Proteinuria & Haematuria (Glomerulonephritis, nephrotic/nephritic syndrome), specific gravity.
- ◊ **Urine microscopy:** red blood cell casts (dysmorphic red blood cells), granular casts, and red blood cells, findings seen in glomerulonephritis.
- ◊ **Urine:** sodium and urine osmolality.
- ◊ **Serum bicarbonate: if not done by lab routinely can be obtained from blood gas strip.**
- ◊ **Electrolytes:** K^+, Na^+, Ca^{++}, Phosphate, Uric acid and urea, creatinine.
- ◊ **Full blood count:** peripheral smear as indicated.
- ◊ Other blood tests as dictated by underlying cause.
- ◊ **CXR:** pulmonary congestion (fluid overload).
- ◊ **KUB ultrasound** (urinary tract obstruction).

◊ **KUB x-ray**

◊ **+/-Renal biopsy:** ultimately if cause unclear or suspected rapidly progressive glomerulonephritis.

Treatment

◊ **Pass urinary catheter** e.g. in neonates with suspected posterior valves, or for urine output monitoring in non-ambulatory children/adolescents during ARF. If size 6 Fr foley catheter is unavailable one can easily use a size 6 Fr feeding tube [NGT] to catheterise the bladder. This can be held in place by strapping to the thigh of the infant so that it does not fall out.

◊ ***NOTE:*** in cases of PUV please note that the patient may develop post-obstruction polyuria once a urinary catheter is inserted. If not properly managed the infant may become severely fluid depleted and develop a pre-renal AKI or even go into shock and die. Thus monitor urine output and 6 hourly weight changes meticulosly. Ideally use hypotonic solutions such as half strength darrows in older infants and quarter strength darrows in the newborn. This is because the post-obstructive kidney often has a poor concentrating ability.

◊ **Fluids –** if hypovolaemic will require volume expansion with isotonic saline at 20 ml/kg over 30 min. This may be repeated one or two more times at most depending on the response.

◊ Those with relatively normal intravascular volume – give insensible losses at 400 ml/m^2/day (30ml/kg/day) plus urine output for the previous 24 hours & extra renal losses as appropriate.

◊ Daily monitor urine & stool output, fluid intake, body weight, blood chemistries.

◊ Renally adjust all drug doses. Use the Schwartz formula to calculate the estimated GFR

◊ Involve your nearest paediatric nephrology unit earlier rather later in the management of all paediatric AKI patients as per KDIGO AKI guidelines

Complications

◊ *Hyperkalaemia* > 6 mmol/l (indicated by the following ECG changes: peaked T-waves, widening QRS complex, ST segment depression, ventricular arrhythmias and cardiac arrest).

◊ Eliminate exogenous potassium (IVF, diet) including drugs sources, oral or enema K^+-binding resin (Na polystyrene sulfonate [kayexalate]) at 1g/kg single dose.

◊ If K^+ >7 mmol/l, + ECG changes, give the following:

◊ Nebulised salbutamol 2.5 mg if weight < 25kg or 5 mg if weight >25 kg or IV salbutamol 4µg/kg in 10 ml of water over 10 min

◊ 10% calcium gluconate (cardio-protective) at 0.5ml/kg IV over 10 min

◊ 8.4% sodium bicarbonate 1-2 mmol/kg IV over 5-10 min

◊ Regular insulin 0.1 u/kg with 50% glucose 1 ml/kg over 1hr

◊ Lasix at 1mg/kg BD may also be used to drive out potassium

◊ **The above are only temporizing measures. Please discuss with nephrology for arrangement of dialysis ASAP.**

Hypocalcaemia

Calcium carbonate orally 45 to 65 mg/kg per day. If tetany, IV 10% calcium gluconate 0.5 to1 ml/kg (up to 10 ml) if patient is symptomatic, with low phosphorus diet or phosphorus binders (calcium carbonate given with meals).

Hyponatraemia (dilutional usually***)***

Treat if < 120 mmol/l or symptomatic (seizures, lethargy). Correct to 125 mmol/l using the following formula:

Required NaCl (mmol) = 0.6×weight×deficit (125 mmol/l – serum Na) given over 4-6 hours

◊ One would need to use 3% hypertonic saline if not available discuss with pharmacist how NaCl tablets or table salt can be given orally in-lieu of hypertonic saline

Metabolic acidosis

Mild acidosis is common and requires not treatment. However, severe acidosis (pH = 7.15, serum bicarbonate < 8 mmol/l) should be corrected partially with IV sodium bicarbonate to pH = 7.20, serum HCO_3^- = 12 mmol/l, then the remainder corrected by oral sodium bicarbonate. *Rapid metabolic acidosis correction with IV $NaHCO_3$ may reduce ionised serum calcium leading to tetany!*

Preferably correct metabolic acidosis by instituting dialysis

Hypertension and Anaemia treat as per appropriate protocol.

Nutrition

Nutritional requirements should be addressed accordingly in consultation with the dietician.

Renal replacement therapy

Dialysis (peritoneal dialysis or haemodialysis)

Dialysis indications:

- ◊ Fluid overload/hypertension
- ◊ Severe acidosis not responding to medical management
- ◊ Persistent hyperkalaemia or other above uncontrollable electrolyte imbalance (iv). Symptomatic uraemia or urea > 35.7 - 53.6 mmol/l
- ◊ Dialyzable toxin
- ◊ Established anuria

References

1. KDIGO AKI guidelines
2. Rees L, Brogan P, Bockenhaeur D, Webb N, "oxford sub-specialist handbooks in paediatrics: paediatric nephrology" 2nd edition, Oxford University Press, 2012
3. Avner [editor], Paediatric Nephrology

ACUTE DIARRHOEAL DISEASE

Definition

Passage of three or more loose/watery stool or one voluminous loose/watery stool per day.

Causes

◊ ***Infectious***

- Bacterial infections: Commonly, Vibrio cholerae, Salmonella species, Shigella, and Escherichia coli (E. coli), Campylobacter pylori
- Viral infections: rotavirus, novovirus, adenovirus, Norwalk virus, astrovirus
- Parasites: Giardia lamblia, Entamoeba histolytica, Cryptosporidium

  N.B. Diarrhoea may be watery or bloody (dysentery)
- ***Systemic infections*** associated with diarrhoea include:
  - influenza, measles, fever, HIV, malaria, pneumonia, urinary tract infection, meningitis, and sepsis.

◊ ***Non-infectious causes***

- Food poisoning
- Drugs: Antibiotics, anti-hypertensive, cancer drugs, and antacids containing magnesium
- Intestinal diseases: Inflammatory bowel disease and coeliac disease
- Food intolerance: Lactose
- Food allergy: Cow's milk, Soya

NOTE: Some of the above causes may lead to persistent/chronic diarrhoea

Clinical features:

◊ Watery or loose stools ± bloody stools

◊ Abdominal cramps

◊ Tenesmus
◊ Urgency
◊ Abdominal pain
◊ May be associated with vomiting and fever, poor appetite
◊ Dehydration

Clinical assessment

Divided into four components to guide clinical management:

◊ Classification of the type of diarrhoeal illness
◊ Assessment of hydration status
◊ Assessment of nutritional status
◊ Assessment of co-morbid conditions

Signs of dehydration

◊ Dry mucous membranes
◊ Rapid thready pulse, low blood pressure, capillary refill > 2sec
◊ No tears when crying
◊ No wet diapers for 3 hours or more
◊ Sunken eyes/anterior fontanelle
◊ High /low temperature
◊ Listlessness or irritability
◊ Reduced skin turgor

Classification of levels of dehydration; **using a combination of two to three physical signs reliably predict dehydration.**

	No dehydration	**Some dehydration**	**Severe dehydration**
General condition	Well, alert	Restless, irritable	Lethargic or unconscious
Eyes	Normal	Sunken	Very sunken
Thirst	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, or not able to drink at all
Skin pinch	Goes back quickly	Goes back slowly (< 2sec)	Goes back very slowly (>2sec)
Treatment	**PLAN A**	**PLAN B**	**PLAN C**

Investigations

- ◊ FBC, ESR
- ◊ Stool m/c/s for bloody and PDD
- ◊ U&E, Creatinine
- ◊ Abdominal x-ray
- ◊ Barium enema/meal

  NOTE: Other investigations will depend on the underlying/systemic conditions identified such as RDT/MPS,

Principles of management

- ◊ Fluid replacement
- ◊ Zinc supplements
- ◊ Continued feeding
- ◊ Antibiotics

Fluid management

Intravenous fluids are required in the following cases (in all others, ORS should be preferred):

- ◊ Resuscitation from shock
- ◊ Dehydration with severe acidosis and prolonged capillary refill time
- ◊ Severe abdominal distension and ileus
- ◊ An altered level of consciousness
- ◊ Resistant vomiting despite appropriate oral fluid administration
- ◊ Deterioration or lack of improvement after 4 hours of adequate oral fluids:
  - o Check vital signs
  - o Assess and grade hydration status
  - o **If in shock, refer to protocol on shock**
  - o Depending on level dehydration, give fluids as outlined below

PLAN C– Severe dehydration:

Rapid intravenous rehydration, Give 100 ml/kg RL or ½ strength Darrow's with 5-10% dextrose:

Age	First give 30 ml/kg in	Then give 70 ml/kg in
Infants	1 hour *	5 hours
Older children	30 min *	2½ hours

Reassess patient every 1-2 hours. If hydration is not improving, give the **IV drip more rapidly.**

◊ After completion of IV fluids, reassess the patient and choose the appropriate treatment Plan (A, B or C).

◊ Repeat Plan C once if no improvement.

◊ If IV therapy is not available, then ORS by nasogastric tube or orally at 20 ml/kg/hour for 6 hours (total of 120ml/kg) should be given. If abdomen becomes distended or the child vomits repeatedly, then ORS should be given more slowly.

NOTE: Dehydration may be hypotonic, isotonic or hypertonic. Hypertonic dehydration is common in infants fed on cow's milk.

PLAN B – Some dehydration:

75mls of ORS x patient's weight (kg) to be given in 4 hours

The approximate amount of ORS required (in ml) can be calculated by multiplying the child's weight (in kg) by 75, to be given in 4 hours.

◊ After 4 hours, reassess the child and decide what treatment to be given next as per level of dehydration.

◊ Children who continue to have some dehydration even after 4 hours should receive ORS by nasogastric tube or ½ strength Darrow's intravenously (75 ml/kg in 4 hours).

◊ In case of Resistant vomiting despite appropriate oral fluid administration, IV fluids may be used.
    - **Avoid Promethazine (Phenergan)**
    - Ondansetron may be used up to two doses
◊ If abdominal distension occurs, oral rehydration should be withheld and only IV rehydration should be given.

PLAN A – No dehydration:

Amount of ORS to be given per loose stool dependent on specific age as listed below:

Age (years)	<2	2-5	Older children
ORS (mls)	50-100	100-200	As much as they want

Zinc supplementation

Give zinc supplement for 10 to 14 days

◊ Infants below 6months of age 10mg daily
◊ Children 6months and above 20mg daily

Continued feeding

Nutritional Status:

◊ Children presenting with diarrhoea should be assessed for malnutrition according to WHO standards.
◊ Children with acute diarrhoea and malnutrition are at increased risk for developing fluid overload and heart failure during rehydration.
◊ The risk of serious bacterial infection is also increased.
◊ Such children require an individualized approach to rehydration and nutritional care.

NOTE: Diarrhoea is a major risk factor for malnutrition which is associated with high mortality and deficits in physical and cognitive development.

Give appropriate feeds. Avoid juices and carbonated drinks

Drugs

- ◊ Antibiotics are not indicated for most children with acute watery diarrhoea; dysentery and suspected cholera are important exceptions.
- ◊ Children with acute diarrhoea should NOT receive antimotility agents or antiemetics.

  NOTE: Antimotility agents (loperamide, diphenoxylate-atropine, and tincture of opium) prolong some bacterial infections and may cause fatal paralytic ileus in children

References

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2. K Reddy; M E Patrick - Management of acute diarrhoeal disease at Edendale Hospital, in: S. Afr. j. child health vol.10 n.4;10(3):215-220. Cape Town Dec. 2016
3. WHO-Hospital care for children, 2013 edition.
4. Ryan ET, Dhar U, Khan WA, et al. Am J Trop Med Hyg 2000;

PERSISTENT DIARRHOEA (PD)

Passage of 3 or more watery stools within 24hrs lasting for more than 14 days.

- ◊ Though PD accounts for 2-20% of total diarrhoea cases, it accounts for 23-62% of all diarrhoea related deaths.
- ◊ Dehydration, malnutrition and infections are major contributors to PD morbidity.
- ◊ The many causes of PD can be divided into four principle pathophysiologic mechanisms: osmotic, secretory, dysmotility associated, and inflammatory.

Clinical features

- ◊ Liquid stools often passed after eating, may be explosive
- ◊ Occasionally stool may contain visible blood
- ◊ Weight loss often evident and signs of malnutrition often present
- ◊ Signs of dehydrations
- ◊ Features of Extra-intestinal infections: e.g. Pneumonia, UTI

Causes

Cause	Major Clinical Features (In addition to PD)	Laboratory and Imaging Findings
Infectious (e.g. E. *coli*, Cryptosporidium. Giardia, Salmonella, E. *histolytica*)	Possible blood and/or mucus in stool Possible fever and/or abdominal pain	Positive stool culture, ova and parasite examination,
Lactose malabsorption	Abdominal discomfort, bloating, flatulence	Elevated breath hydrogen concentration after lactose ingestion
Immunodeficiency state (various diseases)	Recurrent infections Young age, typically in infancy	Abnormal immunoglobulins (eg, low IgG, low IgA, high IgM) Lymphopenia Low antigen titers to previous immunizations
Food Allergy	Most commonly in response to cow or soy milk	May have hypoalbuminemia and anemia

		Electrolyte abnormalities from diarrhea/ vomiting Serum IgE may be elevated
Hirschsprung disease	Delayed passage of meconium Abnormal barium enema Distended abdomen Explosive stool with rectal examination	Abnormal barium enema Absent ganglion cells on rectal biopsy
Toddlers diarrhoea	Usually thriving toddler. Sweetened juices usually the cause	Normal laboratory and imaging results
IBS	Alternating constipation with diarrhea Abdominal pain relieved by defecation Typically diagnosed in adolescence or later	Normal laboratory and imaging results
Celiac disease	FTT, abdominal distention, vomiting Typically 9-24mo of age	Elevated anti-TTG IgA, antiendomysial IgA Antibodies
IBD	Bloody stool Stooling urgency, abdominal pain, Fatigue. Weight loss. Arthritis	Elevated ESR & fecal calprotectin thrombocytosis Iron-deficiency anemia Hypoalbuminemia

Treatment Objectives

Treatment of PD consists of:

- ◊ Appropriate fluids to prevent and treat dehydration (refer to table xxx)
- ◊ A nutritious diet to promote weight gain. BEWARE of foods worsen diarrhea
- ◊ If SAM is present, treat according to SAM protocol (refer to section on SAM)
- ◊ Supplementary vitamins and minerals, including zinc for 10-14 days
- ◊ Antimicrobials to treat diagnosed infections

Reference

1. B. Umamaheswari, Niranjan Biswal, B. Adhisivam, S.C. Parija1 and S. Srinivasan. Persistent Diarrhea: Risk Factors and Outcome. *Indian J Pediatr*. 2010; 77 (8): 885-888.
2. Zella G, Israel EJ. Chronic diarrhea in children. Pediatrics in Review. 2012: vol 33 no 5

ACUTE UPPER GI BLEEDING (OLD)

Definition

Upper gastrointestinal (GI) bleeding refers to haemorrhage from any level above the ligament of Treitz.

Causes:

Age Group	Cause
Neonates	◊ Haemorrhagic disease of the newborn ◊ Swallowed maternal blood ◊ Stress ulceration ◊ Coagulopathy
Infants (1 month – 1 year)	◊ Oesophagitis ◊ Gastric ulceration
Infants (1 -2 years)	◊ Peptic ulcer disease ◊ Gastritis
Children older than 2 years	◊ Oesophageal varices ◊ Gastric varices
Adolescents	◊ Duodenal ulcers

Clinical features

Presentation of bleeding depends on the amount and location of haemorrhage.

◊ Haematemesis
◊ Coffee ground vomiting
◊ Melaena
◊ Haematochezia- if the haemorrhage is severe
◊ May also present with complications of anaemia/shock

Investigations

◊ FBC, ESR
◊ U/E's, Creatinine, LFTs
◊ Barium swallow/meal

◊ Clotting profile

◊ Endoscopy

Treatment

◊ ABCDE

◊ Brief history as to possible cause of the bleeding

◊ Consider gastric wash out

◊ Consider antidote for bleeding due to poisoning

- Iron – Desferrioxamine
- Warfarin – Vitamin K

◊ Monitor vital signs

◊ Replacement of volume with intravenous solutions and blood products if required

◊ Endoscopy (electrocautery, clipping or banding)

◊ Pharmacotherapy including the following:

- Proton pump inhibitors (PPIs) – Omeprazole IV
- H_2 receptor inhibitors - Cimetidine/ranitidine IV
- Octreotide is a somatostatin analog believed to shunt blood away from the splanchnic circulation
- Terlipressin is a vasopressin analog used for variceal upper GI haemorrhage
- Propranolol

References

1. Kliegman R, Berhman R et al; Nelson Textbook of Pediatrics; Saunders Elsevier; 18th ed, 2007

2. McIntosh N, Helms J. P, Smyth L. R, Logan S. Forfar & Arneil's textbook of paediatrics, *7th edition, Edinburgh, Churchill Livingstone, 2008*

FUNCTIONAL CONSTIPATION

This is amongst the commonest conditions associated with **chronic** or **recurrent abdominal pain** in children. Usually during weaning, toilet training and beginning of schooling as well as during stressful events. History and examination is usually sufficient to make a diagnosis. A plain abdominal X-ray may help make a diagnosis.

Features last 2 weeks or more and may include:

- ◊ Non-specific chronic/recurrent abdominal pain.
- ◊ ≤2 defecations per week.
- ◊ At least one episode/week of incontinence after the acquisition of toileting skills
- ◊ History of retentive posturing or excessive stool retention
- ◊ History of painful or hard bowel movements
- ◊ Soiling of underwear
- ◊ History of large diameter stools

Accompanying symptoms may include:

- o irritability,
- o decreased appetite, and/or
- o early satiety.

NOTE: Accompanying symptoms disappear immediately following passage of a large stool.

Review feeding practices (formula, fibre/water intake).

Red Flags

The presence of the following signs warrants further investigation or referral.

- ◊ Fever
- ◊ Blood in stool
- ◊ Weight loss
- ◊ Vomiting
- ◊ Anemia

Differential diagnosis

◊ UTI

◊ PUD

◊ Hypothyroidism

◊ Rarely: IBS and IBD

NOTES: Neonates/Infants: Obtain good history to rule out congenital causes of constipation (Hirshsprung's disease, spine abnormalities, metabolic/endocrine, etc).

Treatment

◊ Parental/patient education and behaviour interventions are paramount (toilet training coupled with a reward system).

◊ Diet modification (increase fluids, fibre and fruits).

◊ Disimpaction with either polyethelene glycol (PEG) or lactulose +/- enema.

◊ Maintenance therapy with either polyethelene glycol, lactulose or liquid

◊ paraffin. Others include Magnesium hydroxide, magnesium citrate, senna and sorbitol.

◊ Counsel parents on need for prolonged treatment duration (usually months) to avoid recurrence and overcome fear of pain during defecation in the child.

References

1. Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders.2006
2. Borowitz SM, Windle ML, Cuffari C. Liacouras CA. Pediatric constipation. *Medscape*. Updated May, 2019.
3. Nurko S and Zimmerman LA. Evaluation and treatment of constipation in children and adolescents. American Academy of Family Physicians. 2014;90(2):80-90

ACUTE HEPATIC FAILURE (OLD)

Definition

Fulminant hepatic failure (FHF) is usually defined as the severe impairment of hepatic functions in the absence of preexisting liver disease.

Causes

- ◊ Infective
- ◊ Viral - Hepatitis A, B, C and D, HIV, Parvovirus, Herpesvirus, Enterovirus, Adenovirus, Varicella, Echovirus, CMV
- ◊ Drugs - Paracetamol, antituberculous drugs, carbamazepine, sodium valproate, halothane
- ◊ Toxins - Mushroom, particularly amanita phalloides, herbs and traditional medicines
- ◊ Infiltrative - Leukaemias, lymphomas
- ◊ Metabolic - Wilson's, galactosemia, tyrosinaemia

Clinical Features

The child may present within hours or weeks with

- ◊ Protracted vomiting
- ◊ Jaundice
- ◊ Tender hepatomegaly
- ◊ Coagulopathy (bruising, petechiae, bleeding)
- ◊ Hypoglycaemia
- ◊ Electrolyte disturbance
- ◊ Encephalopathy (early signs of encephalopathy include alternate periods of irritability, confusion and drowsiness. Older children may be aggressive or show unusual behaviour)

Investigations

- ◊ Liver Function tests:
    - o Prothrombin time (PT) or International normalised ratio (INR)
    - o Serum albumin

- Transaminases
- Bilirubin total and direct
- Alkaline Phosphatase

◊ Blood Glucose levels

◊ Full Blood Count

◊ Urea, creatinine and electrolytes

◊ CRP/ESR

◊ Imaging

◊ Investigate for underlying cause

Treatment

◊ ABCDE

◊ Oxygen by nasal cannulae or face mask

◊ Vitamin K, stat dose IV or IM (300 micrograms/kg for age 1 month to 12 years and 10 mg if >12 years to attempt correction of prolonged clotting time

◊ If frank bleeding (GI or other), fresh frozen plasma at 10 ml/kg IV

◊ Maintain blood glucose between 4 and 9 mmol/litre using 2/3 of maintenance fluid volume consisting of 10% dextrose IV or orally

◊ Strictly monitor urine output and fluid balance, aim for a urine output of not less than 0.5 ml/kg/hr

◊ Correct hypokalaemia if present as it can worsen encephalopathy

◊ Broad spectrum antibiotics for example cephalosporin to treat sepsis

◊ Systemic fungal infection may require IV amphotericin or oral fluconazole

◊ Maintain normothermia by environmental measures, **do not give paracetamol**

◊ Lactulose 5-10 mls 2-3 times daily to produce two to four soft and acid stools per day, to be omitted if diarrhoea occurs

◊ Neomycin 20-30 mg/kg/day 6 hrly orally, maximum dose 2 gm/day

References

1. Kliegman R, Berhman R et al; Nelson Textbook of Pediatrics; Saunders Elsevier; 18th ed, 2007
2. McIntosh N, Helms J. P, Smyth L. R, Logan S. Forfar & Arneil's textbook of paediatrics, *7th edition, Edinburgh, Churchill Livingstone, 2008*

INTESTINAL OBSTRUCTION

This is the most common condition requiring emergency surgery in infants and children. Most causes result from complications of congenital anomalies or from inflammatory conditions that affect the bowel.

Causes

A. Small bowel obstruction

- Duodenal stenosis or atresia– One third of patients with Down's syndrome and it is also associated with other congenital malformations
- Atresia or stenosis of the jejunum or ileum
- Malrotation with volvulus
- Meconium ileus
- Meconium plug

B. Large bowel obstruction

- Mainly caused by peristaltic dysfunction as in Hirschsprung's disease and congenital anomalies (rectal atresia).

C. Mixed (small or large bowel)

- Inflammatory lesions like tuberculosis and Crohn's disease
- Worm infestation

D. Extrinsic causes

- Incarcerated hernia
- Vascular bands
- Intussusception.

Symptoms and Signs

◊ Vomiting which progresses to become bowel stained

◊ Cramping abdominal pain with anorexia

◊ Constipation

◊ Abdominal distension which is greater the more distal the obstruction
◊ Tachycardia and signs of dehydration
◊ Abdominal tenderness
◊ Hyperactive or absent bowel sounds

Investigations

◊ Full blood count
◊ Urea, creatinine and electrolytes
◊ Group and save
◊ Abdominal x-rays, supine and erect
◊ Chest x-ray
◊ Barium meal is needed for bilious vomiting and for incomplete obstruction
◊ Barium enema may be required for distal obstruction

Treatment

The goal of treatment is to relieve the obstruction before ischemic bowel injury occurs. The patient should be resuscitated in the following way:

◊ Keep NPO
◊ Give Oxygen if saturations ≤ 92 %
◊ IV access and collect blood for investigations
◊ Rehydrate according to the level of dehydration
◊ Give maintenance fluids if patient is not dehydrated
◊ If patient is hypokalaemic, add potassium chloride to fluids
◊ Nasogastric tube for gastric decompression
◊ Give IV 10% dextrose if patient is hypoglycemic
◊ Fluid input and Output balance chart
◊ Broad spectrum antibiotics: Triple antibiotic therapy:
    - Crystalline Penicillin, 50 000IU/kg/dose QID IV
    - Gentamycin, 7.5mg/kg/day OD IV
    - Metronidazole, 7,5mg/kg/dose TDS IV
◊ Give adequate analgesia

Once the patient is adequately resuscitated and fluid and electrolyte imbalances corrected, laparotomy is performed and the cause treated.

References.

1. Kliegman R, Stanton B et al; Nelson Textbook of Paediatrics 20th Edition, Elsevier, 2016
2. McIntosh N, Helms J. P, Smyth L. R, Logan S. Forfar & Arneil's textbook of paediatrics, *7th edition, Edinburgh, Churchill Livingstone, 2008*

INTUSSUSCEPTION

Definition

Intussusception refers to the invagination (telescoping) of a part of the intestine into itself. It is the most common abdominal emergency in early childhood, particularly in children younger than two years of age. Ileocolic intussusception accounts for 90% of all cases.

Clinical Manifestations

- ◊ Typically presents between 6 and 36 months
- ◊ Intermittent, severe, crampy, progressive abdominal pain of sudden onset
- ◊ Inconsolable crying and drawing up of legs to the abdomen
- ◊ Relative calm between paroxysms of pain
- ◊ Vomiting, non-bilious initially but later bilious as condition progresses
- ◊ Stool with red blood and mucus, currant jelly stool
- ◊ Palpable sausage shaped mass in the right upper quadrant
- ◊ Progressive weakness and lethargy
- ◊ Shock like state with fever and peritonitis may develop

Diagnosis

- ◊ Ultrasonography which shows the classic "target sign"
- ◊ Plain abdominal X-ray to rule our perforation

Treatment

- ◊ Refer to intestinal obstruction for notes on how to stabilize the patient.
- ◊ Reduction of an acute intussusception is an emergency procedure and should be performed immediately after diagnosis in preparation for possible surgery.
- ◊ Non-operative reduction in patients with no evidence of bowel perforation by hydrostatic or pneumatic pressure.
- ◊ Surgical intervention in patients who are acutely ill or have evidence of perforation and where radiographic facilities and

expertise to perform non-operative reduction are not readily available.

References

1. Kliegman R, Stanton B et al; Nelson Textbook of Paediatrics 20th Edition, Elsevier, 2016
2. Nghia, JV. Thomas TS. Intussusception in Children. In: UpToDate, Jonathan/Singer (Ed), UpToDate, Waltham MA, 2019

INFANTILE COLIC

It is a behavioural syndrome in neonates and infants that is characterized by excessive, paroxysmal crying. For clinical purposes it is defined broadly as crying for no apparent reason that lasts for ≥3 hours per day and occurs on ≥3 days per week in an otherwise healthy infant <3 months of age.

It is a poorly understood phenomenon with no difference in incidence between males and females, breastfed and formula-fed or full term and preterm infants

Clinical Manifestations

- ◊ It is paroxysmal and occurs mostly in evening hours
- ◊ The crying is louder, higher and more variable in pitch and more turbulent than non- colicky crying
- ◊ Associated tensing of the abdomen with drawing up of the legs
- ◊ Clenching of the fingers and stiffening of the arms
- ◊ Arching of the back
- ◊ Difficult to console with relief at times after passage of flatus or stool

Diagnosis

- ◊ The diagnosis is confirmed in retrospect after it has run its characteristic course
- ◊ Other causes of prolonged crying need to be excluded:
    - o Hunger/Inadequate feeding
    - o Diaper pin poking the skin/Diaper rash
    - o Trauma (abusive/non-abusive)
    - o Corneal abrasion or foreign body
    - o Otitis media
    - o Oral candidiasis
    - o UTI
    - o Meningitis

Treatment

- The goal of management is to help parents cope with the child's symptoms and prevent long term sequelae in the parent-child relationship
- **Drug treatment generally has no place in the management of colic**
- Parental support is the mainstay of management
- Parental education and support should include:
    - Reassurance that it is common and usually resolves spontaneously by three to four months of age
    - Reassurance that the infant is not sick.
    - Education that colic is not caused by something they are doing or not doing
    - Providing tips and techniques to soothe baby
    - Reassurance that the infant is difficult to soothe. This prevents the parents feeling like they have failed
    - Encourage parents to access additional caretakers when they are overly tired or stressed
- Parents should experiment with several soothing techniques and continue with those that are helpful. Some techniques include:
    - Using a pacifier
    - Rocking the infant
    - Changing the scenery
    - Providing a warm bath
    - Rubbing the infant's abdomen

References

1. Deshpande, GP. (2017). Colic. Medscape
2. Turner TL, Palamountain S. Infantile Colic: Management and Outcome. In: UpToDate, Augustyn M (Ed), UpToDate, Waltham MA, 2014.
3. Gail M Cohen, Laurie W Albertine. In Brief. Pediatrics in Review July 2012, 33 (7) 332-333

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Gastroesophageal reflux disease (GERD) is a condition that develops when reflux of stomach contents causes troublesome symptoms and/or complications.

Diagnosis

Can be based on Signs and Symptoms

Infants	Older Children and Adolescents
Feeding resistance	Abdominal pain
Recurrent vomiting	Heartburn
Failure to thrive	Recurrent vomiting
Fussiness/irritability	Dysphagia
Apnea/choking episodes	Chronic cough/wheezing
Opisthotonic posturing Poor weight gain Excessive crying Disturbed sleep	Hoarseness

Diagnostic Evaluation of Pediatric GERD

- ◊ History and physical examination
- ◊ Upper gastrointestinal series
- ◊ Esophageal pH monitoring
- ◊ Esophagoscopy with biopsy (Rule out Eosinophilic esophagitis)

Goals for treatment of GERD are to:

- ◊ Relieve symptoms
- ◊ Heal esophagitis if present
- ◊ Maintain remission of symptoms, and
- ◊ Manage or prevent complications.

Treatment options to achieve these goals include dietary or behavioral modifications, pharmacologic intervention, and surgical therapy.

Lifestyle Changes in the Management of Pediatric GERD should be the initial form of management before medical.

Infants	Older Children and Adolescents
Thickened feedings	Weight reduction if overweight
Smaller, more frequent feedings	Dietary modification
Anti-reflux positioning after feedings	Smoking cessation
Avoid passive tobacco smoke exposure	

Drug treatment

Three classes of drugs can be used in infants and children who do not respond to feeding modification and positioning:

- ◊ Histamine-2 (H2) blockers
- ◊ Proton pump inhibitors (PPI)
- ◊ Promotility drugs

Typically, treatment is begun with an H2 blocker such as ranitidine. If the infant responds, the drug is continued for several months and then tapered and stopped (if possible). If infants fail to respond to H2 blockers, a PPI such as Omeprazole can be considered. PPIs are more effective at suppressing gastric acid than are H2 blockers. For infants with GERD and an acute symptom such as irritability, a liquid antacid can be used.

Infants who have gastroparesis may benefit from a promotility drug in addition to acid-suppressive therapy. Erythromycin is one of the most commonly used promotility drugs for this situation.

Medication	Dose	Frequency
H2RAs		
Cimetidine	40 mg/kg/day	Thrice daily or 4 times daily
Famotidine	1 mg/kg/day	Twice daily
Ranitidine	5–10 mg/kg/day	Twice daily or thrice daily
PPIs		

Medication	Dose	Frequency
Lansoprazole	0.4–2.8 mg/kg/day	Once daily
Omeprazole	0.7–3.3 mg/kg/day	Once daily
PROMOTILITY DRUGS		
Erythromycin	0.15mg/kg	Four times daily
Metoclopromide	– 0.2mg/kg (max 10mg/dose)	Four times daily
Domperidone	– 0.2mg/kg (max 10mg/dose)	Four times daily

Surgery:

Patients with severe or life-threatening complications of reflux that are unresponsive to medical therapy can be considered for surgical therapy. The main type of antireflux surgery is fundoplication

References

1. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during infancy: a pediatric practice-based survey. Pediatric Practice Research Group. Arch Pediatr Adolesc Med. 1997; 151: 569-572.
2. Nelson's Textbook of Pediatrics, 20th Edition

PROLONGED JAUNDICE

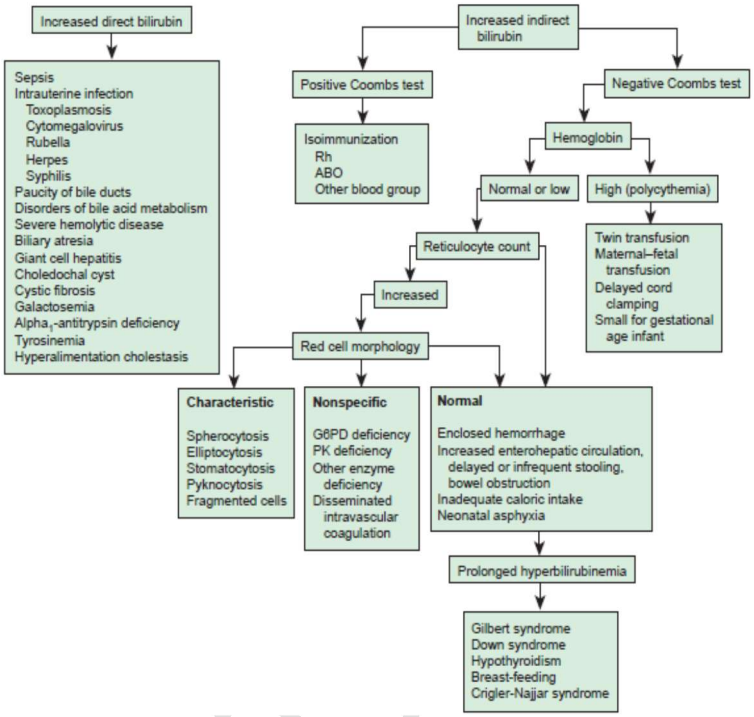
Definition

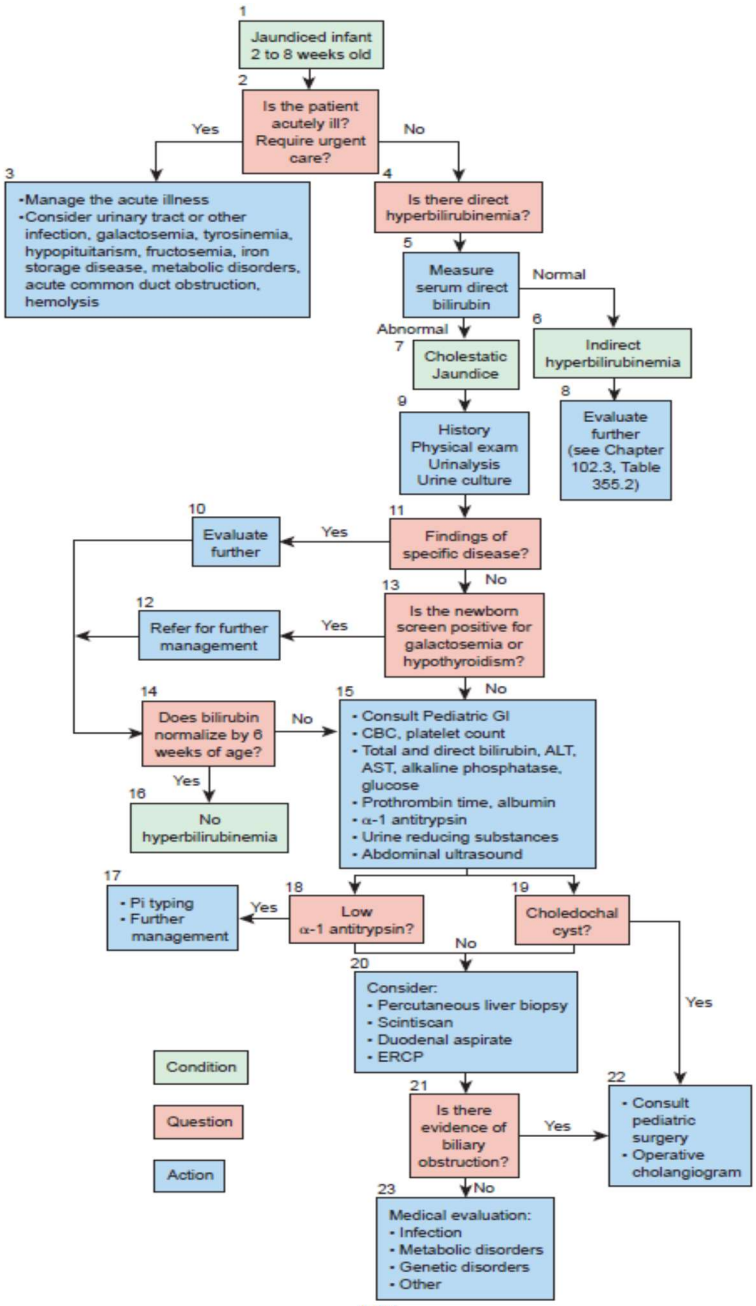
Prolonged neonatal jaundice is defined as a jaundice lasting more than 14 days of life in the full-term infants. Etiologically it is helpful to distinguish jaundice related to unconjugated (indirect) or conjugated (direct) hyperbilirubinemia.

Causes

A prolonged unconjugated hyperbilirubinemia may be related to breastfeeding or to some pathological conditions as hemolytic diseases (due to Rh or AB0 incompatibility, or G6PD deficiency), congenital hypothyroidism, urinary infection, Crigler-Najjar or Gilbert syndromes.

Conjugated hyperbilirubinemia (cholestasis jaundice) is never physiologic. It affects 1/2500 live births and it should be suspected in all jaundiced infants with light stools and dark urine.


Increased direct bilirubin
Sepsis
Intrauterine infection
Toxoplasmosis
Cytomegalovirus
Rubella
Herpes
Syphilis
Paucity of bile ducts
Disorders of bile acid metabolism
Severe hemolytic disease
Biliary atresia
Giant cell hepatitis
Choledochal cyst
Cystic fibrosis
Galactosemia
Alpha1-antitrypsin deficiency
Tyrosinemia
Hyperalimentation cholestasis
Increased indirect bilirubin
Positive Coombs test
Isoimmunization
Rh
ABO
Other blood group
Negative Coombs test
Hemoglobin
Normal or low
High (polycythemia)
Twin transfusion
Maternal–fetal transfusion
Delayed cord clamping
Small for gestational age infant
Reticulocyte count
Increased
Red cell morphology
Characteristic
Spherocytosis
Elliptocytosis
Stomatocytosis
Pyknocytosis
Fragmented cells
Nonspecific
G6PD deficiency
PK deficiency
Other enzyme deficiency
Disseminated intravascular coagulation
Normal
Enclosed hemorrhage
Increased enterohepatic circulation, delayed or infrequent stooling, bowel obstruction
Inadequate caloric intake
Neonatal asphyxia
Prolonged hyperbilirubinemia
Gilbert syndrome
Down syndrome
Hypothyroidism
Breast-feeding
Crigler-Najjar syndrome


1
Jaundiced infant 2 to 8 weeks old
2
Is the patient acutely ill? Require urgent care?
Yes
No
3
•Manage the acute illness
•Consider urinary tract or other infection, galactosemia, tyrosinemia, hypopituitarism, fructosemia, iron storage disease, metabolic disorders, acute common duct obstruction, hemolysis
4
Is there direct hyperbilirubinemia?
5
Measure serum direct bilirubin
Normal
Abnormal
6
Indirect hyperbilirubinemia
7
Cholestatic Jaundice
8
Evaluate further (see Chapter 102.3, Table 355.2)
9
History
Physical exam
Urinalysis
Urine culture
10
Evaluate further
Yes
11
Findings of specific disease?
No
12
Refer for further management
Yes
13
Is the newborn screen positive for galactosemia or hypothyroidism?
No
14
Does bilirubin normalize by 6 weeks of age?
No
Yes
15
• Consult Pediatric GI
• CBC, platelet count
• Total and direct bilirubin, ALT, AST, alkaline phosphatase, glucose
• Prothrombin time, albumin
• α-1 antitrypsin
• Urine reducing substances
• Abdominal ultrasound
16
No hyperbilirubinemia
17
• Pi typing
• Further management
Yes
18
Low α-1 antitrypsin?
19
Choledochal cyst?
No
Yes
20
Consider:
• Percutaneous liver biopsy
• Scintiscan
• Duodenal aspirate
• ERCP
21
Is there evidence of biliary obstruction?
Yes
22
• Consult pediatric surgery
• Operative cholangiogram
No
23
Medical evaluation:
• Infection
• Metabolic disorders
• Genetic disorders
• Other
Condition
Question
Action

References

1. Nelson' Textbook of Pediatrics 20th edition
2. American Academy of Pediatrics in Review

PEPTIC ULCER DISEASE

Definition

Peptic ulcer disease (PUD), the end result of inflammation caused by an imbalance between cytoprotective and cytotoxic factors in the stomach and duodenum, manifests with varying degrees of gastritis or frank ulceration.

The pathogenesis of peptic ulcer disease is multifactorial, but the final common pathway for the development of ulcers is the action of acid and pepsin-laden contents of the stomach on the gastric and duodenal mucosa and the inability of mucosal defense mechanisms to allay those effects.

Gastric ulcers are generally located on the lesser curvature of the stomach, and 90% of duodenal ulcers are found in the duodenal bulb.

The common causes of peptic ulcers include *H pylori*, medication use, and stress-related gastric injury. Less common causes include ingestion of corrosive substances, hypersecretory states (Zollinger-Ellison syndrome), IBD, systemic mastocytosis, chronic renal failure, and hyperparathyroidism.

Symptoms and signs

Vary with the age of the patient.

- ◊ Hematemesis or melena is reported in up to half of the patients with peptic ulcer disease.
- ◊ Epigastric pain and nausea, especially in school going children.
- ◊ Dyspepsia, epigastric abdominal pain or fullness, is seen in older children.
- ◊ Infants and younger children usually present with feeding difficulty, vomiting, crying episodes, hematemesis, or melena.
- ◊ In the neonatal period, gastric perforation can be the initial presentation.

Examination

Includes weight-for-height and/or BMI should be calculated, oropharynx for caries and eroded enamel, Pale conjunctiva,

tachycardia, or flow murmur, Halitosis, wheezing, areas of tenderness on abdomen

Diagnosis

- ◊ Esophagogastroduodenoscopy is the method of choice.
- ◊ Safely performed in all ages by experienced pediatric gastroenterologists. Endoscopy allows the direct visualization of esophagus, stomach, and duodenum.
- ◊ Biopsy specimens may be obtained from the stomach for histopathology, culture or rapid urease testing for H. *pylori*.
- ◊ Endoscopy also provides the opportunity for hemostatic therapy including injection and the use of a heater probe or electrocoagulation if necessary.
- ◊ Other investigations include **faecal**-H. *pylori* antigen test and urea breath test.
- ◊ ***Blood**-H. *pylori* antigen test and abdominal ultrasound are less informative hence a diagnosis should not be based solely on these.

Treatment

PUD treatment includes eradication of H. *pylori* and gastric acid suppression using triple therapy comprising of 2 antibiotics and a proton pump inhibitor (PPI). Examples of triple therapy regimens are shown in the table xx

Medication	Dosage	Duration
Omeprazole	1mg/Kg/day in 2 divided doses	1 month
Amoxillin	50mg/Kg/day in 2 divided doses	14 days
Clarithromycin	15mg/Kg/day in 2 divided doses	14 days
Omeprazole	1mg/Kg/day in 2 divided doses	1 month
Tinidazole	50mg/Kg/day (max 2g)	14 days
Clarithromycin	15mg/Kg/day in 2 divided doses	14 days
Omeprazole	1mg/Kg/day in 2 divided doses	1 month
Metronidazole	20mg/Kg/day in 2 divided doses	14 days
Clarithromycin	15mg/Kg/day in 2 divided doses	14 days

VOMITING

Vomiting and nausea are common sequelae of a multitude of disorders.

◊ Can range from mild, self-limited illnesses to severe, life-threatening conditions.

◊ Vomiting and nausea may or may not occur together, or may be perceived at the same level of intensity.

Definitions

◊ **Vomiting:** a forceful oral expulsion of gastric contents associated with contraction of the abdominal and chest wall musculature.

◊ **Nausea**: The unpleasant sensation of the imminent need to vomit,

- usually referred to the throat or epigastrium;
- a sensation that may or may not ultimately lead to the act of vomiting.

◊ **Regurgitation**: The act by which food is brought back into the mouth without the abdominal and diaphragmatic muscular activity that characterizes vomiting.

◊ **Retching**: Spasmodic respiratory movements against a closed glottis with contractions of the abdominal musculature without expulsion of any gastric contents. This is referred to as **"dry heaves."**

◊ **Rumination**: Chewing and swallowing of regurgitated food that has come back into the mouth through a voluntary increase in abdominal pressure within minutes of eating or during eating.

Differential Diagnosis of Vomiting

Vomiting is a symptom with a wide differential diagnosis, ranging from lesions of the GI tract to systemic illnesses.

A detailed history, including dietary history, review of systems, family history, medication history, medical history and surgical history is important in the initial evaluation to identify a cause.

- ◊ Acute onset of vomiting with severe abdominal pain may suggest a surgical origin; common associated symptoms include localized or generalized abdominal tenderness, signs of peritonitis, and absent or hyperactive bowel sounds.
- ◊ Vomiting is often characterized as **non-bilious, bilious, or bloody** based on the content. Vomitus from the esophagus, stomach, and first part of the duodenum usually consists of ingested food and is clear or yellow.
- ◊ Bilious vomiting denotes the presence of bile and appears light green to dark **green.** Bilious vomiting suggests obstruction of the intestine beyond the ampulla of Vater until proven otherwise.
- ◊ Hematemesis is the presence of blood in the vomitus. The presence of bright red blood in emesis or gastric lavage indicates active upper GI tract bleeding that may require immediate attention.
    - o The presence of coffee-ground material in the vomitus indicates that blood has been acted on by gastric acid.
    - o The presence of blood in vomitus in relationship to other symptoms is also important.
    - o Blood that develops after initial episodes of retching or emesis may be suggestive of a Mallory-Weiss tear

Vomiting is often described as projectile or non-projectile. Projectile vomiting is commonly seen in gastric outlet obstruction, such as pyloric stenosis, and in conditions that result in raised intracranial pressure.

Management of the acutely vomiting child

It is vital to assess the degree of dehydration and manage accordingly.

Most children can be rehydrated with oral or nasogastric feeds unless they have severe dehydration, in which case intravenous resuscitation is essential.

◊ The child with vomiting should continue to be fed, (including breastfeeding as appropriate) unless severely dehydrated.

◊ Specific treatment should be directed toward the underlying etiology.

◊ The etiology should be sought, taking into account the child's age, and whether the nausea and vomiting is acute, chronic, or episodic.

◊ The consequences or complications of nausea and vomiting (eg, fluid depletion, hypokalemia, and metabolic alkalosis) should be identified and corrected.

◊ **Antiemetics** are ***typically are not recommended for vomiting of unknown etiology***, only useful for selected causes of persistent vomiting, to avoid electrolyte abnormalities or nutritional sequelae. **They are not appropriate for treatment of vomiting** caused by anatomic abnormalities or surgical abdomen; they are also contraindicated in infants.

◊ However, antiemetic drugs can be used **cautiously in children > 2 yr.** Useful drugs include:

- **Ondansetron**: 0.15 mg/kg (maximum 8 mg) IV q 8 h or, if the oral form is used, for children 2 - 4 yrs. 2 mg q 8 h; for those 4 to 11 yr, 4 mg q 8 h; for those ≥ 12 yr, 8 mg q 8 h
  - **Ondansetron** is a selective serotonin (5-HT_3) receptor blocker that inhibits the initiation of the vomiting reflex in the periphery.
  - A single dose of ondansetron is safe and effective in children who have acute gastroenteritis and do not respond to oral rehydration therapy (ORT).
  - By facilitating ORT, this drug may prevent the need for IV fluids or, in children given IV fluids, may help prevent hospitalization.
  - Typically, only a single dose is used because repeated doses can cause persistent diarrhea.

References

1. Deborah M. Consolini, MD, Sidney Kimmel Medical College of Thomas Jefferson University -Nausea and Vomiting in Infants and Children, MSD MANUALS, 2019

2. T. Matthew Shields, Jenifer R. Lightdale, MPH - Vomiting in Children in: Pediatrics in Review, July 2018, 39 (7) 342-358;

3. Carlo Di Lorenzo, MD, Approach to the infant or child with nausea and vomiting, 2019 UpToDate, B UK Li, MD (ED)

HYPERTROPHIC PYLORIC STENOSIS

Hypertrophic Pyloric Stenosis (HPS) is a condition that is caused as a result of pylorus wall hypertrophy and hyperplasia, and incomplete mechanical obstruction.

It is a common cause of gastric outlet obstruction in infants.

The cardinal features of HPS are non-bilious projectile vomiting and visible peristalsis in the left upper abdominal quadrant.

◊ Bilious vomiting in this condition is rarely reported and may create confusions in diagnosis

◊ Hypertrophic Pyloric Stenosis occurs in 2 to 3 infants per 1000 live births.
  - It occurs much more commonly in males, with a male-female ratio of 4:1 to 6:1.
  - Up to one-third of cases of pyloric stenosis are seen in first-born infants.

◊ Genetic factors play a role in pyloric stenosis;
  - maternal history of pyloric stenosis is a risk factor
  - Use of erythromycin in infants, especially within the first weeks of life
  - Maternal use of macrolide antibiotics during late pregnancy and during breastfeeding

◊ The typical presentation is a 3- to 6-week-old infant with progressive or intermittent vomiting after feeding.
  - frequent vomiting, usually 10 to 30 min after feeding,
  - The infant is hungry after vomiting.
  - Infants with continued vomiting develop hypochloraemic, hypokalaemic contraction alkalosis and aciduria.

On physical examination

◊ Infant may be dehydrated

◊ Visible gastric peristalsis, from left to right across the hypogastrium may be seen after a feed, just before the baby vomits

◊ A pyloric mass, an **olive-like mass** may be felt below the liver edge just lateral to the edge of the right rectus abdomens muscle. It is best felt when the stomach is empty, just after a vomit.

Investigations

◊ Bloods - FBC, RBS, venous blood gas (VBG),
  - VBG shows a metabolic alkalosis (hypochloraemic, hypokalaemic alkalosis) in those with metabolic derangement
  - Urea, creatinine and electrolytes

◊ Abdominal ultrasound will usually confirm the diagnosis.
  - pyloric thickness of 4 mm (from 3 to 5 mm).
  - pyloric length of 14 to 20mm, and
  - pyloric diameter of 10 to 14 mm.

◊ Where U/S is not readily available plain abdominal films may show the **'single bubble'** of gastric dilatation (with little or no air beyond the pylorus).

◊ Upper GI tract radiocontrast series can also be used to make the diagnosis and have the added advantage of excluding other obstructive lesions, such as antral web or malrotation with volvulus.
  - delayed gastric emptying
  - peristaltic waves (***caterpillar sign***)
  - elongated pylorus with a narrow lumen (***string sign***) which may appear duplicated due to puckering of the mucosa (***double-track sign***)
  - the pylorus indents the contrast-filled antrum (shoulder sign) and (tit sign) or base of the duodenal bulb (***mushroom sign***)
  - the entrance to the pylorus may be beak-shaped (***beak sign***)

Differential diagnosis

- ◊ Feeding problem or milk intolerance.
- ◊ Gastro-oesophageal reflux.
- ◊ Gastroenteritis.
- ◊ Duodenal atresia, oesophageal atresia or other bowel obstruction in the newborn.
- ◊ Intestinal malrotation/acute midgut volvulus.

Initial management

Vomiting of gastric contents leads to depletion of sodium, potassium, and hydrochloric acid, which results in hypokalemic, hypochloremic metabolic alkalosis.

- ◊ Infants with HPS require hospitalization and intravenous fluid replacement therapy
- ◊ Nil by mouth
- ◊ A nasogastric tube is inserted all gastric losses via the NGT are replaced with Hartmann's solution or 0.9% saline via a second infusion
- ◊ Insert intravenous cannula (and take bloods)
- ◊ Assess degree of dehydration
- ◊ Commence **intravenous fluids**
    - o Fluid rate = maintenance plus calculated deficit over 24 hours
    - o usually consisting of 5% dextrose in 0.45% saline (DNS) at 1.5 times maintenance rate.
- ◊ Surgical referral.

References

1. The Royal Children's Hospital Clinical Practice Guidelines - Pyloric stenosis, July 2019
2. Kalyan Ray Parashette, MD, Joseph Croffie, MD, MPH; Vomiting -Pediatrics in Review Vol.34 No.7 July 2013

ANAEMIA

Definition

Haemoglobin (**Hb**) concentration or haematocrit two or more standard deviations below the mean value for age and sex. See table below:

Table xx Age-Specific Normative Red Blood Cell Values

Age	*Haemoglobin (g per dL)*		*Haematocrit (%)*		*Mean corpuscular volume (fL)*	
	Mean	***2 SDs below mean***	***Mean***	***2 SDs below mean***	***Mean***	***2 SDs below mean***
26 to 30 weeks' gestation	13.4	11.0	41.5	34.9	118.2	106.7
28 weeks' gestation	14.5	NA	45	NA	120	NA
32 weeks' gestation	15.0	NA	47	NA	118	NA
Full term (cord sample)	16.5	13.5	51	42	108	98
1 to 3 days	18.5	14.5	56	45	108	95
2 weeks	16.6	13.4	53	41	105	88
1 month	13.9	10.7	44	33	101	91
2 months	11.2	9.4	35	28	95	84
6 months	12.6	11.1	36	31	76	68
6 months to 2 years	12.0	10.5	36	33	78	70
2 to 6 years	12.5	11.5	37	34	81	75
6 to 12 years	13.5	11.5	40	35	86	77
12 to 18 yrs (male)	14.5	13.0	43	36	88	78
12 to 18 yrs (female)	14.0	12.0	41	37	90	78
Adult (male)	15.5	13.5	47	41	90	80
Adult (female)	14.0	12.0	41	36	90	80
NA = not available; SD = standard deviation.						

Adapted from Robertson J, Shilkofski N, eds. The Harriet Lane Handbook. *17th ed. Philadelphia, Pa.: Mosby; 2005:337.*

Causes

Decreased red cell production

◊ Deficiency of haematopoietic precursors (Iron, Folate, vitamin B12)

◊ Bone marrow failure (Malignant infiltration, Aplastic, Congenital defects)

Increased red cell destruction

◊ Haemolytic disease

- Extracorpuscular defects (immune mediated)
- Intracorpuscular defects (Enzyme defect, membrane defect, Globin defects)

Blood loss

◊ Acute

◊ Chronic

Clinical features

Symptoms associated with anaemia include

◊ Fever

◊ Poor weight gain or weight loss

◊ jaundice

◊ Pica

◊ Headache

◊ Poor concentration

◊ Palpitations

◊ Easy fatigability

◊ Bruising episodes

◊ Bleeding episodes

Signs associated with anaemia include:

◊ Pallor

◊ Fever

◊ Wasting

◊ Tachycardia

◊ Oedema

◊ Hepatosplenomegaly
◊ Lymphadenopathy
◊ Petechiae
◊ Purpura

Investigations

◊ Full blood count
◊ Peripheral blood smear
◊ Reticulocyte count
◊ Total and direct serum bilirubin levels

NOTE: These above first four tests are key in the characterisation of the type of anaemia and possible cause

Other tests

◊ ESR – (erythrocyte sedimentation rate)
◊ Coombs – direct and indirect - tests
◊ Sickling test
◊ Bone marrow aspiration and bone marrow biopsy
◊ Coagulation studies (APTT, PT/ INR, D-dimers, FDPs)
◊ Stool for occult blood and parasites and ova
◊ Urinalysis – dipstick, microscopy

Principles of management

◊ Treat the underlying pathology
◊ If the anaemia reoccurs, without establishing the underlying cause, refer to the next level of care.
◊ Replace the appropriate blood product deficiency
◊ Include component of Rx for mild anaemia with haematinics. This raise the Hb by 1g/dl in a month.
◊ Do not routinely give iron in sickle cell disease unless there is documented iron deficiency.

Blood replacement formulae when a transfusion is indicated:

◊ Packed red blood cells in mL = body weight x **deficit Hb** x **4**

◊ Whole blood in mL = Body weight x **deficit Hb** x **6**

◊ **Do not exceed a maximum 20ml/kg/day.**

◊ **Indicate amount of blood to be transfused on the drug chart**

References

1. Nelson Textbook of Pediatrics, 18th edition, 2007
2. Blueprints Pediatrics, 4th edition, 2007
3. WHO/ UNICEF. Anaemia statement. 2004
4. Essential Revision Notes in Paediatrics, 2nd edition, 2006

SICKLE CELL DISESASE – CVA

Stroke is one of the major complications of sickle cell disease (SCD). Brain dysfunction occurs when oxygen supply to the brain falls below a critical level based on need.

The approach to management depends on the specific brain manifestations and the age of the patient. Symptoms of brain ischemia include:

◊ Hemiparesis
◊ Facial weakness
◊ Severe headache
◊ Visual and language disturbances
◊ Seizures (especially focal seizures)
◊ Altered sensation

Differentials

Differentials include CNS infections (Meningitis/Encephalitis), cerebral malaria, trauma with consequent subdural hematoma, or intoxication, particularly if focal signs are not prominent.

Investigations

◊ Full blood count with differential & reticulocyte count
◊ Group and cross match
◊ Quantitative D- dimer if available
◊ Emergent CT or MRI/MRA (where available). Note that contrast may exacerbate sickling. Discuss using contrast with paediatric haematologist.
◊ Malaria parasite slide
◊ Blood culture
◊ Kidney and liver functions tests
◊ EEG (where indicated)

Management

◊ Admit patient to Intensive care Unit
◊ Adequate hydration at least two third of requirements to guard against cerebral oedema.

◊ Immediate transfusion with packed cells within four hours and repeat on day 4 or exchange transfusion.

◊ Hourly Glasgow Coma Scale monitoring

◊ Empirical antibiotics

◊ Anti-Epileptic drugs if seizures are present (Diazepam is usually used at 0.2mg/kg).

◊ Start hyper transfusion protocol (See Appendix I).

◊ Commence hydroxyurea. The initial dose is 15/kg/day given as a single daily dose. Dose escalation by 5mg/kg every 4- 6 weeks.

◊ Commence iron chelation therapy, deferasirox 10- 30mg//kg once daily PO for 6 months.

Exchange transfusion

Definition

◊ Full exchange transfusion (30ml/kg)

◊ Partial exchange (15ml/kg)

Indications

◊ Severe sickle cell chest syndrome or Girdle syndrome

◊ A new CVA

◊ Multi- organ failure, e.g. Associated with systemic fat embolism.

◊ Fulminant priapism (> 4 hours) unresponsive to pharmacological therapy.

Aim

◊ To reduce the HbS% level to < 30% over 2- 3 days if acutely ill, when more rapid exchange may be appropriate.

◊ To keep Hb < 10 g/dL initially and by the end of the procedure (or at steady state level in those with higher baseline Hb, e.g HbSC patients of 11- 12g/dL

◊ To maintain a steady blood volume and Hb throughout the exchange.

◊ There are two types of exchange transfusions. These are manual and automated methods.

- A simple early method consists of removal of 500 mL blood followed by infusion of 2 units of donor cells which aims to achieve a 30% exchange in 90 minutes. More recent techniques generally use 2 intravenous lines with simultaneous or sequential withdrawal of SS blood and is replaced by donor AA cells. However, although manual procedures are effective in conducting exchange, they are tedious and time-consuming.
- Machines performing centrifugal separation of red blood cells provide a rapid and efficient method of performing partial exchange transfusion. Two types of machines are in common use, the discontinuous- and continuous-flow models.
- Discontinuous-flow separators are small, mobile, simple to operate, relatively cheap, and require only 1 intravenous line. Discontinuous-flow cell separators act as batch processors, pumping blood from the patient's arm, centrifuging it to separate red cells from the plasma, discarding the red cells, and returning the plasma to the patient along with donor cells.
- Continuous-flow separators are more complex and expensive, and more efficient but require 2 intravenous lines with large needles or catheters capable of carrying the large flows. Continuous-flow separators use 2 intravenous lines, one extracting blood and the other returning the processed blood to the patient. Controlling rates of inflow and outflow ensures that the patient's blood volume does not vary during the procedure. Supplies for both cell separator techniques are considerably more expensive than manual methods but require less professional time.

Preliminary investigations

◊ Full Blood Count

◊ Hb electrophoresis (not urgent at first exchange)

◊ Group and Cross match

◊ Urea, electrolytes, Creatinine, liver function tests, Serum calcium.

◊ Arterial blood gases in those with symptoms suggestive of Acute Chest Syndrome or girdle syndrome.

◊ Hepatitis B and C and HIV.

Hydroxyurea

Mechanism: Hydroxyurea is an antineoplastic that may cause inhibition of DNA synthesis by acting as a ribonucleotide reductase inhibitor. It increases fetal haemoglobin, reduces neutrophils, and alters adhesion of red blood cells to endothelium, increasing water content of red blood cells and increases deformability of sickled cells.

Indications: All children above nine months of age with SCD should be on hydroxyurea.

Exclusions: acute liver disease, history of severe hydroxyurea toxicity or hypersensitivity, pregnancy or sexually active and unwillingness to use contraception.

Baseline investigations:

◊ FBC with Differential count.

◊ Hb electrophoresis with quantitative Hb F %.

◊ Chemistry profile.

◊ Liver function tests (AST, ALT).

◊ Renal function tests (BUN, creatinine)

Consult with paediatric haematologist for appropriate work- up before initiating a patient on hydroxyurea.

Dosing:

◊ Initial dose 15/kg/day given as a single daily dose.

◊ Dose escalation by 5mg/kg every 4- 6 weeks.

◊ Increase dose until ANC 2, 000- 3, 000 achieved or 35mg/kg/day dose achieved or evidence of haematological toxicity.

◊ Liquid formulation can be prepared by compounding pharmacy using published guideline.

Transcranial Doppler Ultrasound

A transcranial Doppler (TCD) ultrasound examination is a nonivasive technique that assesses blood flow within the circle of Willis and the vertebrobasilar system.

It can identify children with SCD who are at high risk for stroke by documenting abnormal high blood flow velocity.

In children with SCD, screen annually with TCD according to methods employed in the STOP studies, beginning at age 2 years and continuing until at least age 16. In children with conditional (170- 199cm/sec) or elevated (>200cm/sec) TCD results need to be commenced on chronic transfusion therapy aimed at preventing stroke.'

References

1. Evidence- based Management of Sickle Cell Disease, Expert Panel Report, 2014. http://nhlbi.gov/guidelines
2. Adams R.J. et al Prevention of a first stroke by transfusions in children with sickle cell anaemia and abnormal results on transcranial Doppler
3. Anderson R, Cassell M, Mullinax GL, Chaplin H Jr. Effect of normal cells on viscosity of sickle-cell blood: in vitro studies and reports of six years' experience with a prophylactic program of "partial exchange transfusion". *Arch Intern Med*. 1963; 111:286–294.
4. Janes SL, Pocock M, Bishop E, Bevan DH. Automated red cell exchange in sickle cell disease. *Br J Haematol*. 1997; 97(2):256–258.

HAEMOPHILIA

Haemophilia is a congenital bleeding disorder affecting 1 in every 10,000 males caused by deficiency of factor VIII (haemophilia A) or factor IX (haemophilia B) or rarely factor XI (haemophilia C). Haemophilia A and B are X-linked, whereas haemophilia C is autosomal recessive. Haemophilia A is the most common.

Diagnostic Testing

◊ Prolonged APTT with normal PT and normal platelet count is suggestive.

◊ Confirm with Factor VIII or Factor IX assay.

Severity	Factor Level
Severe	< 1%
Moderate	4%
Mild	5- 30%

NOTE: Normal factor level ranges from 50- 200%.

Prophylaxis

All patients should receive prophylaxis using the low dose protocol at 15-20 iu/kg once weekly subcutaneously.

Inhibitor Screening

Where available, screening for inhibitors should be performed. Mixing study is a qualitative inhibitor screen. Bethesda assay is the gold standard.

Treatment of bleeding

Patients with haemophilia can have spontaneous bleeding and/ or excessive bleeding with trauma. It's imperative to treat haemophilia patients with factor **within 30 minutes of presentation** first and then consider diagnostic testing.

◊ Factor VIII deficiency (Haemophilia A)

- 1 unit/kg increases Factor VIII activity by 2%
- Give 30 units/kg of Factor VIII for an acute mild bleed.
- Give 50 units/kg of Factor VIII for an acute major bleed.

- Half-life of Factor VIII is 8- 12 hours. Major bleeds require 8- 12 hour dosing.
- Discuss treatment plan with paediatric Haematologist.

◊ Factor IX deficiency (Haemophilia B)

- 1 unit/kg increases Factor IX activity by 1%.
- Give 50 units/kg of Factor IX activity for an acute minor bleed.
- Give 100 units/kg of Factor IX for an acute major bleed.
- Half- life of Factor IX is 18- 24hours. Major bleeds require at 24 hour dosing.

  NOTE: It's important to round up both Factor VIII and Factor IX to a unit vial dose whenever possible to avoid wastage. E.g. if unit vial is 500 units and patient's dose is 400 units, order 500 units Factor VIII.

◊ Where Factor VIII or Factor IX is unavailable, or not immediately available in emergency situations give plasma (Fresh Frozen Plasma- FFP) at 10- 20mL/kg IV to run over 1 hour.

Supportive care

◊ Ice for 20 minutes to both haemoarthosis and soft tissue bleeds.

◊ Immobiliastion for mucosal bleeding and dental extraction may also add tranexamic acid 10mg/kg/dose every 8 hours for 2- 8 days.

◊ Head trauma should have an emergent CT scan after the first dose of factor given even if there are no neurologic signs.

Immunisations

Haemophilia patients, young and old, can and should receive recommended immunisations for their age group. Subcutaneous vaccines are generally safer and more acceptable. Were necessary, intramuscular vaccines should be given using a small needle such as 24 gauge needles (or smaller) in a larger muscle.

◊ It might be necessary to administer factor before immunizing a known Haemophilia patient. The best method is to schedule vaccination at or around the same time as the factor dose for patients on prophylactic factor therapy.

◊ After immunization, apply gentle pressure and treat with ice to reduce bleeding.

◊ Always warn about the risk of hematoma.

◊ Provide pain relief; Acetaminophen is the drug of choice.

Emicizumab

Emicizumab is a novel bispecific monoclonal antibody which mimics coagulation factor VIII and therefore, is capable of promoting the activation of FX by FIXa, resulting in downstream haemostasis at the site of bleeding in patients with haemophilia A who have decreased or no circulating levels of FVIII.

Indications

Emicizumab is indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A with factor VIII inhibitors.

Emicizumab is effective in prophylactic treatment among adult and paediatric patients, with or without inhibitors. The priority for emicizumab and the WFH in Zambia is as follows:

A. Children under 12 years of age, diagnosed with inhibitors.
B. Patients with haemophilia 12 years and above diagnosed with inhibitors.
C. Children under 12 years of age, without inhibitors based on bleeding patterns.

Dosage

The recommended dose is 3 mg/kg once weekly for the first 4 weeks (loading dose), followed by 6 mg/kg once monthly (maintenance dose), administered as a subcutaneous injection.

Administration of Emicizumab will only be done at the University Teaching Hospital- Children's Hospital Haemophilia Treatment Centre (HTC) in Lusaka at the moment.

Storage

Opened vials:

◊ Single use

◊ Discard any unused solution remaining after administering dose.

Unopened vials:

- ◊ Storage in refrigerator at 2- 8°C in original carton to protect from direct light
- ◊ Do not freeze
- ◊ Do not shake
- ◊ If necessary, unopened vials may be stored at room temperature and then returned to refrigeration; temperature should not exceed 30° C for up to 7 days.

References

1. Guidelines for the management of haemophilia, World Federation of Hemophilia (WFH) second edition 2012. www.wfh.org
2. Johnny N Mahlangu and Anne Gilham, 2008. Guidelines for the treatment of Haemophilia in South Africa, SAMJ, Vol 99, No. 2.

IMMUNE THROMBOCYTOPENIA (ITP)

Introduction

Immune thrombocytopenia (ITP) is a syndrome in which platelets become coated with autoantibodies to platelet membrane antigens, resulting in splenic sequestration and phagocytosis by mononuclear macrophages. The resulting shortened life span of platelets in the circulation, together with incomplete compensation by increased platelet production by bone marrow megakaryocytes, results in a decreased number of circulating platelets (thrombocytopenia).

Etiology

In children, most cases of immune thrombocytopenia (ITP) are acute, manifesting a few weeks after a viral illness. In adults, most cases of ITP are chronic, manifesting with an insidious onset, and occur in middle-aged women. These clinical presentations suggest that the triggering events may be different. However, in both children and adults, the cause of thrombocytopenia (destruction of antibody-coated platelets by mononuclear macrophages) appears to be similar and involve.

◊ Autoantibody stimulation
◊ Autoantibody specificity
◊ Role of the spleen
◊ Platelet destruction

Signs and Symptoms

ITP manifests as a bleeding tendency, easy bruising (purpura), or extravasation of blood from capillaries into skin and mucous membranes (petechiae). Although most cases of acute ITP, particularly in children, are mild and self-limited, intracranial hemorrhage may occur when the platelet count drops below 10×10^9/L ($< 10 \times 10^3$/μL); this occurs in 0.5-1% of children, and half of these cases are fatal.

ITP is a primary illness occurring in an otherwise healthy person. Signs of chronic disease, infection, wasting, or poor nutrition

indicate that the patient has another illness. Splenomegaly excludes the diagnosis of ITP.

An initial impression of the severity of ITP is formed by examining the skin and mucous membranes, as follows:

- ◊ Widespread petechiae and ecchymoses, oozing from a venipuncture site, gingival bleeding, and hemorrhagic bullae indicate that the patient is at risk for a serious bleeding complication.
- ◊ If the patient's blood pressure was taken recently, petechiae may be observed under and distal to the area where the cuff was placed and inflated.
- ◊ Suction-type electrocardiograph (ECG) leads may induce petechiae.
- ◊ Petechiae over the ankles in ambulatory patients or on the back in bedridden ones suggest mild thrombocytopenia and a relatively low risk for a serious bleeding complication.

Findings suggestive of intracranial hemorrhage include the following:

- ◊ Headache, blurred vision, somnolence, or loss of consciousness.
- ◊ Hypertension and bradycardia, which may be signs of increased intracranial pressure.
- ◊ On neurologic examination, any asymmetrical finding of recent onset.
- ◊ On fundoscopic examination, blurring of the optic disc margins or retinal hemorrhage.

Diagnosis

On complete blood cell count, isolated thrombocytopenia is the hallmark of ITP. Anemia and/or neutropenia may indicate other diseases. Findings on peripheral blood smear are as follows:

- ◊ The morphology of red blood cells (RBCs) and leukocytes is normal.
- ◊ The morphology of platelets is typically normal, with varying numbers of large platelets.

◊ If most of the platelets are large, approximating the diameter of red blood cells, or if they lack granules or have an abnormal color, consider an inherited platelet disorder.

Many children with acute ITP have an increased number of normal or atypical lymphocytes on the peripheral smear, reflecting a recent viral illness. Clumps of platelets on a peripheral smear prepared from ethylenediaminetetraacetic acid (EDTA)–anticoagulated blood are evidence of pseudothrombocytopenia. This diagnosis is established if the platelet count is normal when repeated on a sample from heparin-anticoagulated or citrate-anticoagulated blood.

No single laboratory result or clinical finding establishes a diagnosis of ITP; it is a diagnosis of exclusion. The differential diagnosis includes such other causes of thrombocytopenia as leukemia, myelophthisic marrow infiltration, myelodysplasia, aplastic anemia, and adverse drug reactions. Pseudothrombocytopenia due to platelet clumping is also a diagnostic consideration.

Aspects of bone marrow aspiration and biopsy are as follows:

◊ The value of bone marrow evaluation for a diagnosis of ITP is unresolved.

◊ Biopsy in patients with ITP shows a normal-to-increased number of megakaryocytes in the absence of other significant abnormalities.

◊ In children, bone marrow examination is not required except in patients with atypical hematologic findings, such as immature cells on the peripheral smear or persistent neutropenia.

◊ In adults older than 60 years, biopsy is used to exclude myelodysplastic syndrome or leukemia.

◊ In adults whose treatment includes corticosteroids, a baseline pretreatment biopsy may prove useful for future reference, as corticosteroids can change marrow morphology.

◊ Biopsy is performed before splenectomy to evaluate for possible hypoplasia or fibrosis.

◊ Unresponsiveness to standard treatment after 6 months is an indication for bone marrow aspiration.

Management

ITP has no cure, and relapses may occur years after seemingly successful medical or surgical management. Most children with acute ITP do not require treatment, and the condition resolves spontaneously.

Treatment is as follows:

- ◊ Corticosteroids remain the drugs of choice for the initial management of acute ITP.
- ◊ Oral prednisone, IV methylprednisolone, or high-dose dexamethasone may be used.
- ◊ IV immunoglobulin (IVIG) has been the drug of second choice for many years ·
- ◊ For Rh(D)-positive patients with intact spleens, IV Rho immunoglobulin (RhIG) offers comparable efficacy, less toxicity, greater ease of administration, and a lower cost than IVIG.
- ◊ RhIG can induce immune hemolysis (immune hemolytic anemia) in Rh(D)-positive persons and should not be used when the hemoglobin concentration is less than 8 g/dL.
- ◊ Sporadic cases of massive intravascular hemolysis, disseminated intravascular coagulation (particularly in elderly individuals), and renal failure have been reported with RhIG.
- ◊ Rituximab is third-line therapy.
- ◊ Platelet transfusions may be required to control clinically significant bleeding but are not recommended for prophylaxis.
- ◊ If 6 months of medical management fails to increase the platelet count to a safe range (about 30,000/µL), splenectomy becomes an option.
- ◊ Thrombopoietin receptor agonists (ie, eltrombopag, romiplostim) may maintain platelet counts at safe levels in adults with chronic ITP refractory to conventional medical management or splenectomy.

Pregnant adolescents require special consideration for delivery, as follows:

- ◊ If the platelet count is greater than 50 × 10^9/L (>50 × 10^3/μL), the risk of serious hemorrhage is low, but beginning oral prednisone a week before delivery is a reasonable precaution.
- ◊ If the platelet count is less than 50 × 10^9/L (50 × 10^3/μL) before delivery, treatment with oral prednisone and IVIG is recommended.
- ◊ Avoiding the use of IV RhIG in this situation until safety data are available is advisable.
- ◊ Rarely, splenectomy may be required to manage acute hemorrhage.

APLASTIC ANEMIA

Introduction

Aplastic anemia is a syndrome of bone marrow failure characterized by peripheral pancytopenia and marrow hypoplasia (see the image below). Although the anemia is often normocytic, mild macrocytosis can also be observed in association with stress erythropoiesis and elevated fetal hemoglobin levels.

Signs and symptoms

The clinical presentation of patients with aplastic anemia includes symptoms related to the decrease in bone marrow production of hematopoietic cells. The onset is insidious, and the initial symptom is frequently related to anemia or bleeding, although fever or infections may be noted at presentation.

Signs and symptoms of aplastic anemia may include the following:

- ◊ Pallor
- ◊ Headache
- ◊ Palpitations, dyspnea
- ◊ Fatigue
- ◊ Foot swelling
- ◊ Gingival bleeding, petechial rashes
- ◊ Overt and/or recurrent infections
- ◊ Oropharyngeal ulcerations

Etiology

The theoretical basis for marrow failure includes primary defects in or damage to the stem cell or the marrow microenvironment. The distinction between acquired and inherited disease may present a clinical challenge, but more than 80% of cases are acquired. Clinical and laboratory observations suggest that acquired aplastic anemia is an autoimmune disease.

Congenital or inherited causes

Congenital or inherited causes of aplastic anemia are responsible for at least 25% of children with this condition and for perhaps up to 10% of adults. Patients may have dysmorphic features or physical stigmata, but marrow failure may be the initial presenting feature.

Fanconi anemia

Fanconi anemia is characterized by the following:

◊ Multiple congenital anomalies (60-75%): Short stature, abnormal skin pigmentation, malformations of the thumbs with or without dysplastic or absent radii, as well as microphthalmos and malformations of the heart, kidneys, intestines, and ears.

◊ Bone marrow failure: Thrombocytopenia, leucopenia, or aplastic anemia; most patients with Fanconi anemia have bone marrow failure by adulthood.

Dyskeratosis congenita

Dyskeratosis congenita is characterized by the diagnostic physical triad of dysplastic nails, lacy reticular pigmentation of the upper torso, and oral leukoplakia. However, over the past decade, it has been increasingly recognized that patients may have dyskeratosis congenita without the triad.

Familial aplastic anemia

This is an isolated aplastic anemia.

Cartilage-hair hypoplasia

Cartilage-hair hypoplasia, characterized by the following:

◊ Short stature with short and bowed limbs

◊ Sparse, lightly pigmented hair

◊ Variably severe immune deficiency

◊ Anemia during childhood

◊ Hematopoietic malignancies, as well as malignancies of the skin, eyes, and liver

◊ Gastrointestinal malformations and malabsorption

Pearson syndrome

Pearson syndrome causes sideroblastic anemia and exocrine pancreatic dysfunction.

Thrombocytopenia-absent radius syndrome

Thrombocytopenia-absent radius (TAR) syndrome is characterized by bilateral absence of the radii with presence of the thumbs, as well as thrombocytopenia. Other congenital anomalies can also occur (e.g. cardiac disease, skeletal anomalies, urogenital anomalies).

Shwachman-Diamond syndrome

Shwachman-Diamond syndrome is inherited in an autosomal recessive manner. This disease is characterized by dysfunction of the exocrine pancreas with malabsorption and growth failure, as well as cytopenias of single or multiple lineage. Patients with Shwachman-Diamond syndrome also have an increased risk of MDS and AML.

Dubowitz syndrome

Dubowitz syndrome is characterized by intrauterine growth retardation, extremely short stature, and wizened facial appearance. Patients also have microcephaly and mild developmental delay. Dubowitz syndrome is also associated with eczema, immune deficiency, and aplastic anemia. Malignancy is more common with this disorder, particularly lymphoma and neuroblastoma.

Diamond-Blackfan anemia

Diamond-Blackfan anemia (DBA) is characterized by a normochromic macrocytic anemia that can be isolated, or it can be associated with growth retardation or congenital malformation in the upper limbs, heart, and genitourinary systems. In a small minority of patients, DBA can progress to aplastic anemia. Approximately 50% of cases are inherited from a parent and about 50% result from de novo mutations.

Acquired causes

Acquired causes of aplastic anemia (80%) include the following:

◊ Idiopathic factors

- ◊ Infectious causes, such as hepatitis viruses, Epstein-Barr virus (EBV), human immunodeficiency virus (HIV), parvovirus, and mycobacteria.
- ◊ Exposure to ionizing radiation.
- ◊ Exposure to toxic chemicals, such as benzene or pesticides.
- ◊ Transfusional graft versus host disease (GVHD)
- ◊ Orthotopic liver transplantation for fulminant hepatitis.
- ◊ Pregnancy
- ◊ Eosinophilic fasciitis
- ◊ Anorexia
- ◊ Severe nutritional deficiencies (B12, folate)
- ◊ Paroxysmal nocturnal hemoglobinuria (PNH)
- ◊ MDS
- ◊ Acute lymphoblastic leukemia (ALL) rarely.
- ◊ Drugs and elements (e.g., chloramphenicol, phenylbutazone, gold) may cause aplasia of the marrow.

Diagnosis

Laboratory testing for suspected aplastic anemia includes the following:

- ◊ Complete blood count
- ◊ Peripheral blood smears
- ◊ Hemoglobin electrophoresis and blood-group testing
- ◊ Biochemical profile
- ◊ Serology for hepatitis and other viral entities
- ◊ Autoimmune-disease evaluation for evidence of collagen-vascular disease.
- ◊ Kidney function studies
- ◊ Liver function studies
- ◊ Transaminase, bilirubin, and lactate dehydrogenase levels.

Procedures

Bone marrow biopsy is performed in addition to aspiration to assess cellularity qualitatively and quantitatively. Bone marrow culture may be useful in diagnosing mycobacterial and viral infections; however, the yield is generally low.

Management

Severe or very severe aplastic anemia is a hematologic emergency, and care should be instituted promptly. Clinicians must stress the need for patient compliance with therapy. The specific medications administered depend on the choice of therapy and whether it is supportive care only, immunosuppressive therapy, or hematopoietic cell transplantation.

Pharmacotherapy

The following medications are used in patients with aplastic anemia:

- Immunosuppressive agents (e.g. cyclosporine, methylprednisolone, equine antithymocyte globulin, rabbit antithymocyte globulin, cyclophosphamide, alemtuzumab).
- Hematopoietic growth factors (eg, eltrombopag , sargramostim, filgrastim).
- Antimetabolite (purine) antineoplastic agents (eg, fludarabine).
- Chelating agents (eg, deferoxamine, deferasirox).

Nonpharmacotherapy

Nonpharmacologic management of aplastic anemia includes the following:

- Supportive care
- Blood transfusions with blood products that have undergone leukocyte reduction and irradiation.
- Hematopoietic cell transplantation

APPROACH TO DIAGNOSIS AND INVESTIGATION OF COMMON MALIGNANCIES

Causes of malignancy

Risk factors for cancer can be broadly classified as:

◊ Genetic causes

◊ Environmental causes

Clinical features

In the first two years of life, embryonic tumours tend to be common. Examples include Nephroblastoma, Retinoblastoma, Neuroblastoma, Teratoma, Rhabdomyosarcoma, Medulloblastoma.

From 2-5 years of age, the embryonic tumours combine with Acute Lymphoblastic Leukaemia, Non-Hodgkin's Lymphoma, and Glioma.

In adolescents Hodgkin's disease, Bone, Gonadal and Connective tissue tumours predominate

Common signs and symptoms of cancer in children

◊ Abdominal mass

◊ Persistent generalized lymphadenopathy

◊ More than one abnormal hematopoietic lineage

◊ Specific neurologic deficit

◊ Increased intracranial pressure

◊ Proptosis

◊ White pupillary reflex

◊ Vaginal bleeding or mass

◊ Joint or bone swelling or pain

Uncommon symptoms and signs of cancer in children

◊ Superior vena cava syndrome

◊ Subcutaneous nodules

◊ Chronic diarrhoea

◊ Failure to thrive

◊ Skin lesions

History

General: a single symptom might cause patient to seek medical Attention (e.g. Pain, mass, Bleeding, recurrent fevers, weakness)

Specific: symptoms to look for in the history

CNS	R/S	MSS
Headache	Cough	Swelling
Fits	Difficulties breathing	Wasting
Blindness	Haemoptysis	Bone/joint pain
Vomiting	Neck	Non healing ulcer
Stiff neck	Swelling	Skin lesion
Confusion	Engorgement	Bleeding spots

GIT	GUT	OTHERS
Abdominal mass	Pelvic/suprapubic mass	Malaise
Diarrhoea	Dysuria	Anorexia
Easy satiety	Haematuria	Nights sweats
Dysphagia	Urinary retention	Fever
Poor appetite		
Melaena		

PHYSICAL EXAMINATION		
CNS	**R/S**	**MSS**
Mentation	Tachypnoea	Skin lesion
Cranial palsy	Reduced breath sounds	Wasting
Paraplegia/Paraparesis	Stridor	Oedema
Meningismus	Haemoptysis	
Vomiting		
Confusion		
GIT	**GUT**	**NECK**

Abdominal mass Hepatomegaly/splenomegaly Visible distension of vessels	Proteinuria Haematuria	Lymphadenopathy Engorged vessels

Common cancers on the Haematology-Oncology Unit

- ◊ Nephroblastoma
- ◊ Retinoblastoma
- ◊ Leukaemia
- ◊ Hodgkin's lymphoma

Investigations

Blood Tests

- ◊ Complete Blood count
- ◊ Peripheral Smear
- ◊ Erythrocyte sedimentation rate
- ◊ Liver and Kidney Test
- ◊ Retroviral test

Imaging Studies

- ◊ **Chest radiography**: Postero-anterior and lateral views to
  - o Assess mediastinal masses
  - o Evaluate the airway
  - o Exclude pulmonary parenchymal lesions
- ◊ **Ultrasonography**: Abdomen, Pelvis, Eye, Cranial to identify site and disease extent
- ◊ **Computed tomography**
  - o CT scans of the chest, abdomen, and pelvis can be used to stage lesions

- Chest CT scan is indicated to assess for the degree of tracheal compression
- Head CT scans assist in excluding mass lesions and possible meningeal involvement among individuals with CNS disease.

◊ **Bone scanning and skeletal surveys**

- When additional symptoms are present, these tests help in identifying additional sites of disease.

◊ **Echocardiography**

◊ can be obtained as baseline findings before patients are given chemotherapy with anthracyclines, which can cause cardiomyopathy.

Procedures

Bone marrow aspiration/biopsy

◊ Biopsy is necessary to assess for evidence of bone marrow involvement in patients with lymphomas. Sites for BMA include the anterior iliac crest, posterior iliac crest, sternum and tibia (in infants).

Biopsy

◊ For patients with a mass, tissue is generally available from resection or intra-operative biopsy.

◊ As an alternative, a diagnosis may be made by using pleural fluid or ascetic fluid.

Lumbar puncture

◊ To determine the CSF cell count and differential: This test is done to assess CNS involvement, the presence of which alters therapy.

Management

Once diagnosis is made either histologically of clinically, stage the patient according to the staging used for that particular tumour. Consult the protocol to determine treatment modality which could be either one or a combination of two or all three:

◊ Surgery
◊ Chemotherapy
◊ Radiation

Treatment should aim at either:

◊ Cure, or
◊ Palliation

MANAGEMENT OF PAINFUL CRISIS

Pain is a common, underreported and under- diagnosed problem for hospitalised children wide, especially for infants and mentally challenged children.

Assess the intensity of the pain by using: "face pain" intensity scale or visual analogy scale (See appendix), multi- dimensional scale, clinical acumen.

WHO analgesic ladder advocates for a step- wise approach to treating pain. At every step of the analgesic ladder non- opioid analgesics form the basis of the pain management. Paracetamol and NSAIDs (if not contraindicated) should always therefore be prescribed with opioid analgesia.

Treat pain aggressively and promptly. Begin analgesic management within 15 minutes of triage or within 30 minutes of registration.

Severity	Management
Mild	Reassurance, warm packs, reposition, massage, distraction (stories, play) ***Child:*** Paracetamol 15mg/kg QID ***Adult:*** Paracetamol 1g QID
Moderate	As for mild pain, PLUS ***Child:*** Ibuprofen 5mg/kg TDS OR Diclofenac 1mg/kg TDS ***Adult:*** Ibuprofen 400mg TDS OR Diclofenac 100mg TDS
Severe	As for moderate pain PLUS ***Child:*** Oral morphine 0.2- 0.3mg/kg 4 hourly as needed ***Adult:*** Oral morphine 5- 10mg 4 hourly as needed

Step I:

Establish Intravenous (IV) access.

Begin with hydration to facilitate circulation of blood: use 5% Dextrose normal saline IVF (1.5 x maintenance or 2,250 ml/ square metre/day) if no cardiopulmonary compromise.

Step II:

Assess for cause of pain and complications. Use pain assessment tool (See appendix). Ask the patient to rate the pain as mild/moderate/severe. Ask about site, severity and duration of pain (usually bones/spine/abdomen). Conduct a complete systemic examination to look for complications.

Step III:

- ◊ Give analgesia as per guidelines (Table above).
- ◊ If febrile, commence IV antibiotics.
- ◊ Monitor pulse, respiratory rate and oxygen saturations.
- ◊ Look out for side effects of morphine- nausea/vomiting, pruritis, drowsiness and constipation. Always prescribe laxatives (stool softener + stimulant) when starting opioids.

Step IV

- ◊ Stop IV fluids when the patient is stable, and pain controlled
- ◊ Weigh the child daily
- ◊ Avoid fluid overload

MALARIA

Malaria is one of the top five diseases causing morbidity and mortality in Zambian children. Malaria is a febrile illness caused by infection with the *plasmodium falciparum* parasite which is transmitted from person to person by mosquitoes. Malaria is diagnosed by examining a patient's stained blood slide through a microscope (MPS). A rapid malaria diagnostic test (RDT) for malaria antigen can be done in the examination room and results are available within 15 minutes. It is also important to also do a full blood count (FBC). Left untreated, Malaria can be fatal

Uncomplicated malaria symptoms and signs are as follows:

- ◊ Fever
- ◊ Headache
- ◊ Abdominal pain
- ◊ Nausea
- ◊ Diarrhoea and Vomiting
- ◊ General body pains
- ◊ Weakness

Simple malaria is treated with Artemether 20 mg and Lumefantrine 120 mg) given with food as follows:

- ◊ stat,
- ◊ after 8 hrs,
- ◊ then 12 hourly doses on day 2 and day 3.

If the drug is spat out or vomited within 30 minutes, the dose should be repeated. If more than two consecutive episodes of vomiting occur, parenteral Artesunate should be administered.

WEIGHT (Kg)	AGE (approx. in yrs.)	DOSE (number of tabs of AL, Artemether 20, Lumefantrine 120 mg)
5-<15	2months - 3yrs	1 tab
15-25	3-8yrs	2 tab
25-35	9-12yrs	3 tab

>35	>12yrs	4 tab

Severe Malaria

Severe forms of malaria, may involve the

◊ Brain (cerebral malaria),
◊ Kidney (black water fever, acute kidney injury),
◊ Lungs (pulmonary oedema) ,
◊ Blood (severe anaemia)
◊ Cardiovascular system (shock).

The symptoms and signs of severe malaria include

◊ Convulsions
◊ Changes in behaviour
◊ Reduced level of consciousness
◊ Coma
◊ Severe pallor
◊ Respiratory distress
◊ Jaundice
◊ Shock
◊ Coca Cola coloured urine
◊ Reduced urine output
◊ Bleeding tendency
◊ Generalized weakness

If a blood slide or RDT is negative then only children with severe disease or those with severe anaemia should get presumptive treatment immediately then to send a sample to the National Malaria Elimination Centre for further analysis.

Investigations for severe malaria

◊ Thick and thin malaria parasite smear or RDT
◊ FBC
◊ Dextrostix
◊ U&Es and Creatinine
◊ LFTs

◊ Blood gases

◊ CXR

◊ Urinalysis

◊ Do LP to exclude meningitis if indicated and if no signs of ICP

Severe malaria = fever + any of the following

◊ Impaired level of consciousness (AVPU= V, P, U or low GCS <11,Blantyre Coma Scale <3).

◊ Unable to drink/feed.

◊ Respiratory distress with acidotic breathing.

◊ Severe anaemia Hb < 5 g/dl.

◊ Hypoglycaemia blood glucose < 3 mmol/L.

◊ 2 or more convulsions within 24 hours or a single episode of status epilepticus.

◊ Plasma bicarbonate of < 15mmol/l 0r PH<7.35.

◊ Serum creatinine >3 times from baseline for age.

◊ Bleeding tendency- recurrent or prolonged bleeding from the nose, gums, melaena, haematemesis, venepuncture sites.

◊ Shock – impaired perfusion (Capillary refill time of >3 seconds, cool peripheries).

If yes, those >20kg should be given Artesunate 2.4mg/kg of body weight IV or IM given on admission (time=0), then at 12hrs and 24hrs, then re-assess the patient and repeat MPS.

For patients with weight <20kg give Artesunate at 3mg/kg IV or IM

After initial parenteral treatment for a minimum of 24hrs, once the patient regains consciousness and can take medications orally, and repeat MPS is negative, discontinue parenteral therapy and commence full course of Artemether Lumefantrine

After initial parenteral treatment for a minimum of 24 hrs, and the patient has not regained consciousness or cannot take medications orally, and repeat MPS is positive continue parenteral therapy once a day for a maximum of 6 days and commence full course of Artemether Lumefantrine .

Repeat the blood slide every 24 hours until there is zero parasitaemia.

If MPS remains positive despite full course of treatment, to consult the National Malaria Elimination centres and to send DBS on filter paper for further analysis.

There should be an interval of at least 8hrs between the last dose of artesunate and the first dose of artemether lumefantrine.

In the absence of IV Artesunate, artemether may be used at 3.2mg/kg IM loading dose, then maintain with 1.6mg/kg OD for 5days

OR Alternative 2nd line drug for severe malaria is **QUININE IV**

- ◊ Loading dose of 20mg/kg body weight diluted in 10ml/kg of 5% or 10% dextrose by IV infusion over 4 hours. After eight hours hours, give a maintenance dose at 10mg/kg body weight over 4 hours, and repeat every eight hours until patient can swallow.
- ◊ Then use oral quinine at 10mg/kg body weight every eight hours to complete a seven-day course of treatment
- ◊ Treat hypoglycaemia with 5 ml/kg 10% dextrose IV, followed by a continuous infusion of either 5% or 10% dextrose
- ◊ Maintenance fluids/feeds and supportive oxygen by mask
- ◊ If weak pulse and CRT > 3 sec, give 20 mls/kg normal saline, up to 40mls/kg/day. Use blood for resuscitation, if Hb < 5g/dl at 20 ml/kg whole blood).
- ◊ Use inotropes when there`s poor response to fluid boluses
- ◊ Treat convulsions as indicated in the algorithm for treatment of convulsions.

References

1. Guidelines for the diagnosis and treatment of Malaria in Zambia, Fourth edition, 2014
2. Artesunate versus quinine for treating severe Malaria (review). The Cochrane Collaboration. Published by John Wiley &Sons, Ltd.

3. Guidelines for the diagnosis and treatment of Malaria in Zambia, Fifth edition, 2017

TYPHOID (ENTERIC FEVER) - DR MULENGA

Causes

Salmonella typhi, Salmonella paratyphi

Clinical features

High grade fever, coated tongue, anorexia, vomiting, hepatomegaly, diarrhoea, toxicity, abdominal pain, pallor, splenomegaly, constipation, headache, jaundice, obtundation, ileus, intestinal perforation.

Diagnosis

◊ ***Blood culture***

- Ideally 1st week of symptoms - Blood culture
- 2nd week of symptoms - Urine culture
- 3rd week of symptoms - Stool culture

NOTE: As most patients present late, all three cultures should be taken on admission.

◊ ***Widal test***

- A single Widal test may be positive in only 50% cases in endemic areas
- Serial tests may be required

◊ ***Mainstay of diagnosis remains clinical***

- Any high fever of >72 hours duration (with aforementioned features), especially with no localizing upper respiratory signs or signs of meningitis or malaria must be suspected of typhoid and managed accordingly.

◊ ***Full Blood count (White cell count)***

- Leucopoenia (WCC < 4 x10^9/litre) with a left shift in neutrophils may be seen in a third of children; young infants may also commonly present with leukocytosis.

◊ ***Other serological tests (expensive)***

- Dot-Elisa
- Coagglutination
- Tubex^R

Management

◊ Early diagnosis and instituting appropriate supportive measures and specific antibiotic therapy is the key to appropriate management

◊ Adequate rest, hydration, correction of fluid-electrolytes and nutrition

◊ Anti-pyretic therapy (paracetamol) as required if fever > 39^{o}C

◊ Antibiotic therapy

- 1st line therapy- **ciprofloxacin** (while awaiting culture results). Alternative → Azithromycin
- 2nd line (drug resistant) – **imipenem**

◊ Monitor vital signs to recognise **surgical emergencies**

Intestinal haemorrhage (<1%) and perforation (0.5-1%)

Pain- sudden increase in abdominal pain

- Pulse Rate -a sudden rise in pulse rate,
- BP- hypotension,
- Temperature
- Respiratory rate
- Plain –X-ray abdomen should be done

Intestinal perforation and peritonitis may be accompanied by:

◊ a sudden rise in pulse rate,

◊ hypotension,

◊ marked abdominal tenderness and guarding, and

◊ subsequent abdominal rigidity.

◊ A rising white blood cell count with a left shift and free air on abdominal radiographs may be seen in such cases.

References

1. Southall D, Coulter B, Ronald C, International Child Health Care, A practical manual for hospitals worldwide pg 426-428
2. Kliegman, Behrman, Jenson, Stanton, Nelson Textbook of Paediatrics, 19th Edition, 2007

SCHISTOSOMIASIS

Definition

Schistosomiasis is an acute and chronic parasitic disease caused by blood flukes (trematode worms) of the genus *Schistosoma*.

Causes

◊ People become infected when larval forms of the parasite released by freshwater snails penetrate the skin during contact with infested water

◊ There are 2 major forms of schistosomiasis that are caused by 5 main species of blood fluke:

I. Intestinal

- Schistosoma mansoni,
- Schistosoma japonicum
- Schistosoma mekongi (uncommon)
- Schistosoma intercalatum (uncommon)

II. Urogenital

- Schistosoma haematobium

Clinical Features

In the acute infection, mild, maculopapular skin lesions may develop within hours after exposure. Depending on which species is responsible for the infection, the clinical features will be distinguished between intestinal, urogenital or both:

◊ **Intestinal schistosomiasis**

- ***Acute:*** Abdominal pain, diarrhoea, blood in the stool, fatigue.
- ***Chronic:*** hepatomegaly, splenomegaly ascites, portal and pulmonary hypertension.

◊ **Urogenital Schistosomiasis**

- ***Acute:*** Haematuria, dysuria, urinary frequency.
- ***Chronic:*** Fibrosis of the bladder and ureter, kidney dysfunction, bladder cancer (later stages).
- ***Adolescent girls:*** genital lesions, vaginal bleeding, pain during sexual intercourse, nodules in the vulva.
- ***Adolescent boys:*** pathology of the seminal vesicles, prostate and other organs.

Investigations

◊ Stool/Urine M/C/S for blood (including occult) and Schistosoma ova.

◊ FBC, DC (usually shows eosinophilia).

◊ Urea, Electrolytes, LFTs.

◊ Chest x-ray

◊ Plain abdominal x rays

◊ Abdominal ultrasound

◊ Blood culture (if possible concomitant disease i.e. salmonellosis).

◊ Rectal Snip

Treatment

◊ Praziquantal is the treatment of choice for all forms of Schistosomiasis (children >2 years and adults: 40mg/kg as a single dose). Consider steroid therapy if very severe disease.

◊ Adverse effects of praziquantel include dizziness, headache, nausea, vomiting, diarrhea, abdominal discomfort, bloody stool, urticaria, and fever following initiation of treatment. These are usually mild and last about 24 hours.

Prevention

Praziquantel 40/mg/kg as a single dose.

References

1. Medicins sans frontieres, Clinical Guidelines
2. WHO, Fact sheet, Schistosomiasis, 2019
3. Shadab Hussain Ahmed, Schistosomiasis (Bilharzia), 2018, Medscape
4. Nelson's Textbook of Pediatrics, 19th edition

TUBERCULOSIS IN CHILDREN

TB in children is an indicator of recent and ongoing transmission of M. tuberculosis in the community, as majority of children will develop tuberculosis disease within 1 year after infection. (Unlike tuberculosis in adults who may develop TB disease when their immunity goes down).

Pulmonary TB is the commonest type of TB in children but extrapulmonary disease is also common estimated to be around 30-40% of cases.

Most immunocompetent children with TB disease present with nonspecific symptoms of a chronic disease. In infants the presentation may be more acute and can present as acute severe, recurrent or persistent pneumonia. TB should be suspected when there is a poor response to appropriate conventional antibiotics.

Key risk factors for TB in children

- ◊ Household contact with a newly diagnosed smear positive case.
- ◊ Age < 5 years
- ◊ HIV infection
- ◊ Severe malnutrition

Symptoms of tuberculosis

TB should be suspected in children presenting with following symptoms especially if they persist for more than 2 weeks or show no response to (appropriate) treatment for the initial diagnoses.

- ◊ Cough
- ◊ Fever
- ◊ Loss of appetite
- ◊ Weight loss or failure to thrive
- ◊ Decreased activity.

Other symptoms will depend on the anatomical site of tuberculosis disease.

Clinical signs suggestive of pulmonary TB.

There are no specific features on clinical examination that can confirm that the presenting illness is due to pulmonary TB.

Clinical signs suggestive of extrapulmonary TB.

- ◊ Gibbus- Spinal TB, especially of recent onset.
- ◊ Non-painful enlarged cervical lymphadenopathy, with or without fistula formation- TB of lymphnodes.
- ◊ Pleural effusion
- ◊ Pericardial effusion
- ◊ Distended abdomen with ascites- TB abdomen.
- ◊ Non painful enlarged joints- Osteoarticular TB.
- ◊ Meningitis not responding to antibiotic treatment - TB meningitis.

Guidance on approach to diagnosis of TB in children

- ◊ Careful history (including history of TB contact and symptoms consistent with TB).
- ◊ Clinical examination (including growth assessment).
- ◊ Bacteriological confirmation with Xpert MTB/RIF or culture or smear microscopy).
- ◊ Chest X-ray
- ◊ Tuberculin skin testing
- ◊ Urinary lateral flow lipoarabinomannan (LAM) for HIV infected children or presumed severe TB disease.
- ◊ Investigations relevant for suspected extra-pulmonary TB.
- ◊ HIV testing

Appropriate specimens should be obtained for Xpert MTB/RIF testing, staining and microscopy, culture (and histopathological examination in extrapulmonary TB).

For pulmonary tuberculosis

Samples for Xpert MTB/RIF or culture testing should be obtained using any the following methods depending on the age of the child;

- ◊ Gastric lavage

◊ Sputum induction

◊ Nasopharyngeal aspiration

◊ Expectorated sputum

For extrapulmonary TB

◊ Pleural fluid: Xpert MTB/RIF, biochemistry, cell count and culture.

◊ Pericardial fluid: Xpert MTB/RIF, biochemistry, cell count and culture.

◊ Lymph node biopsy or Fine-needle aspiration of enlarged lymph glands: Xpert MTB/RIF, ZN staining, culture and histology.

◊ CSF: Biochemistry, cell count, Xpert MTB/RIF.

◊ In addition, appropriate imaging studies such as abdominal ultrasound, Echocardiogram, CT and MRI should be used depending of the site of disease of extrapulmonary disease.

Recommended TB treatment regimens in children

TB disease category	Recommended regimen	
	Intensive phase	Continuation phase
All non-severe forms of PTB and EPTB	2 (HRZE)	4 (HR)
Severe forms - TB meningitis, Osteo-articular TB, Spinal TB, Miliary TB, other severe forms of TB	2 (HRZE)	10 (HR)

TB drug dosing table

Weight bands	Number of Tablets		
	Intensive Phase		Continuation Phase
	RHZ (75/ 50/150 mg)	E* (100 mg)	RH (75/50 mg)
4-7 kg	1	1	1
8-11kg	2	2	2
12 – 15 kg	3	3	3

16- 24 kg	4	4	4
25 and above			

Rifampicin (R) – 15 mg/kg (range 10 – 20 mg/kg); maximum dose 600 mg/kg, Isoniazid (H) –10 mg/kg (range 7 – 15 mg/kg); maximum dose 300 mg/kg, Pyrazinamide (Z) – 35 mg/kg (30 – 40 mg/kg) and Ethambutol (E) – 20 mg/kg (15 – 25 mg/kg)

Use of corticosteroids

Corticosteroids are indicated in the management of some complicated forms of TB such as:

- ◊ TB meningitis.
- ◊ Complications of airway obstruction by TB lymph glands.
- ◊ Pericardial TB.

Prednisolone is recommended at a dose of 2mg/kg daily, increased to 4 mg/kg daily in the case of the most seriously ill children, with a maximum dosage of 60 mg/day for 4 weeks. The dose should then be gradually tapered over 1–2 weeks before stopping.

Pyridoxine supplementation.

Isoniazid may cause symptomatic pyridoxine deficiency, which presents as neuropathy, particularly in severely malnourished children and HIV-positive children on antiretroviral therapy (ART). Supplemental pyridoxine (5–10 mg/day) is recommended in HIV-positive or malnourished children being treated for TB.

Drug resistant tuberculosis in children

Drug-resistant TB (DR TB) should be suspected under the following conditions:

- ◊ Close contact with a person known to have DR-TB including household and other contacts.
- ◊ Close contact with patient that died from TB, failed or is not adherent to TB treatment.
- ◊ History of previous TB treatment (in the past 6-12 months).
- ◊ Not improving after 2-3 months of first line TB treatment, including persistence of positive smear or culture, persistence

of symptoms and failure to gain weight (radiological improvement is frequently delayed).

◊ A child who develops active TB while on Isoniazid (INH) prophylaxis.

Appropriate samples should be obtained in any suspected case of DR-TB. These should include the following:

◊ Xpert MTB-RIF

◊ Mycobacterial culture

◊ drug susceptibility testing (DST)

◊ line-probe assays (LPA)

Indications to initiate MDR TB regimen in children;

◊ Confirmed MDR TB by DST or LPA.

◊ RR on Xpert MTB/RIF.

◊ Smear positive case with confirmed MDR contact.

◊ Child with TB and unconfirmed DST resulting who is not responding to standard TB therapy and is a known contact of an MDR TB case.

For treatment of DR TB refer to the Guidelines for the Programmatic Management of Drug Resistant Tuberculosis.

Indications for Tuberculosis preventive therapy (TBT) in children

TB preventive therapy is recommended for the following at risk groups of children

◊ Asymptomatic HIV negative children aged <5 years who are household contacts of bacteriologically confirmed tuberculosis in whom active TB disease has been excluded.

◊ All HIV infected children aged, regardless of TB contact status, in who are considered unlikely to have active TB disease. For HIV infected infants preventive therapy is provided only when child has established TB contact.

Recommended and dosing options for TBT in children

Drug regimen	Dose per kg body weight	Maximum dose
Isoniazid daily for 6 – 9 months	H 10 mg (range, 7 – 15 mg)	300 mg

isoniazid plus rifampicin daily for 3 – 4 months	H 10 mg (range, 7 – 15 mg) R 15 mg (range, 10 – 20 mg)	H – 300 mg R – 600 mg
Rifapentine plus isoniazid Weekly for 3 months (12 doses)	H: Age ≥ 12 years: 15 mg/kg, H: Age 2 – 11 years: H 25 mg/kg Rifapentine 10.0 – 14.0 kg = 300 mg 14.1 – 25.0 kg = 450 mg 25.1 – 32.0 kg = 600 mg 32.1 – 49.9 kg = 750 mg ≥ 50.0 kg = 900mg	H 900 mg Rifapentine, 900 mg

References

1. Desk guide for the management of tuberculosis in children-Africa. 3rd Edition. International Union Against TB and Lung Disease. 2016.
2. National Tuberculosis and Leprosy Programme-Guidelines for the management of tuberculosis in children. 1st Edition. 2016.
3. National Tuberculosis and Leprosy Programme-TB Manual. 5th Edition. 2017 Guidance for national tuberculosis programmes on the management of tuberculosis in children. WHO 2014.
4. Guidelines for the programmatic management of drug-resistant tuberculosis in Zambia. 3rd Edition. 2018.
5. Guidelines for the management of latent tuberculosis infection. 2nd edition. 2019.

POST EXPOSURE PROPHYLAXIS - OCCUPATIONAL HIV EXPOSURE

Post exposure prophylaxis is the use of ART to prevent HIV transmission, in adults exposure occurs commonly from occupational injuries.

The risk of infection after occupational exposure to HIV infected blood is low and estimated at:

- 1: 300 in percutaneous exposure
- 1: 1000 in mucocutaneous exposure

There is no risk of transmission if the skin is intact but there are factors that can increase the risk of infection e.g.

- Deep injury
- Visible blood on device caused injury
- Injury with a large bore needle
- Non-suppressed viral load in source patient

Other body fluids that can lead to HIV transmission include: amniotic fluid, CSF, breast milk, pericardial, pleural, peritoneal fluids, synovial fluid, unfixed human tissue, vaginal secretions, semen, any other visibly blood stained fluid, fluid from burns or skin lesions.

Management of occupational exposure

Immediately after exposure to infectious .

- Clean site: wash skin injuries with soap and running water, do not squeeze, allow wound to freely bleed.
- If the exposed area is eye or mucous membrane, rinse with copious amount of clean water.
- Contact the person responsible for PEP/ Medical staff on duty.
- Person in charge of PEP should assess need for PEP and benefits of taking ART prophylaxis.

PEP Treatment Regimen

Risk Category	ART prophylaxis	Duration
Skin intact	No PEP	
Medium Risk- invasive injury, no visible blood on needle/device	Preferred: TDF +XFTC + DTG Alternative: TDF + XTC + ATV/r Children below 10 yrs: AZT +3TC+ LPV/r	28 days
High Risk-large volume of blood/fluid, deep extensive injury, known HIV infected patient, large bore needle		

ELIMINATION OF MOTHER TO CHILD HIV TRANSMISSION - EMTCT

Four (4) Pillars of EMTCT

3. **Primary prevention of HIV infection in women of child bearing age-** IEC-STIs , HIV, provision of condoms, PrEP for discordant couples, ART for positive partners.
4. **Prevention of unwanted pregnancies among women living with HIV:** Counselling and provision of Family planning services.
5. **Prevention of HIV transmission in a woman living with HIV to her infant:** Testing and ART initiation in all HIV positive pregnant and breastfeeding mothers.
6. **Provision of appropriate treatment, care and support to women and children with HIV and their families.** Treatment and adherence support for HIV positive women and infected infants, ART prophylaxis for their uninfected infants.

Management of HIV exposed uninfected infants (HEU)

Situation	Management of mother at delivery and Postnatal care	Infant prophylaxis, and Tests
High Risk HIV exposed Infant		

HIV +Mother less 12 weeks on ART HIV + mother, viral load > 1000copies within 4 weeks before delivery	Start or continue ART	Start ART prophylaxis - AZT +3TC+NVP for 12 weeks
HIV + ve mother not on ART HIV +ve mother who refuses ART	Start ART or continue ART Counselling for mother to start ART	Start ART prophylaxis AZT+3TC+NVP - ,continue untill confirmed HIV negative after cessation of breastfeeding
Low Risk HIV exposed infants		
HIV +ve mother, on ART for > 12 weeks	Continue ART	Start ART- AZT+3TC+NVP for 6 weeks
HIV -ve woman with an HIV+ve partner	NAT, if negative- put woman on PrEP, repeat HIV test every 3 months	if mother's NAT test is +ve, NAT on infant,

NOTE: *All HIV positive pregnant women should have viral load testing within 4 weeks before delivery.*

Dosing table for the EMTCT ART Prophylaxis

	Age of Infant		
	Dose from Birth to 6 weeks		**6 weeks to 12 weeks**
Weight	2000gm-2499gm	2500gm-2999gm	3000gm-5990gms
AZT+ 3TC Suspension	10mg/5mg twice daily *1ml twice daily	15/7.5mg twice daily 1.5 mls twice daily	60/30 mg tablet 1 tab twice daily
NVP	10mg once daily 1ml syrup once daily	15mg once daily 1,5 mls syrup	20mg once daily Or 1/2 tablet of 100mg tablet once daily

AZT +3TC is a tablet containing 60mg AZT and 30mg 3TC

- ◊ Dissolve 1 tablet of AZT+3TC in 6mlf of water, 1ml of suspension has 10mg of AZT and 5mg of 3TC
- ◊ The suspension made should be kept in a cool place and used as soon as possible. Daly reconstitution is recommended.

Follow up of HEU infant, breastfeeding, non breastfeeding

In an HEU infant who is breastfed

NAT at birth/first week of life or first contact with health staff, at 6 weeks, at 9 months and 6weeks after cessation of breast feeding.

DISORDER OF SEXUAL DIFFERENTIATION (DSD)

Definition

◊ DSDs include anomalies of sex chromosomes, gonads, reproductive ducts and the genital.

◊ Usually presents in the neonatal period and during adolescence

◊ Neonates usually present with atypical genitalia while adolescents present with atypical sexual development during puberty

Causes

1. 46 XY DSD
    - 46XY gonadal dysgenesis (partial or complete)
    - 46XX/46XY (chimeric, ovotesticular DSD)
    - Testicular regression syndrome
2. 46XX DSD
    - 46 XX gonadal dysgenesis
    - 46XX ovotesticular DSD
    - 46 XX testicular syndrome
3. Disorders in sex development due to androgen excess (CAH)
    - 21 hydroxylase deficiency
    - 11B hydroxylase deficiency
    - 3b HSD deficiency
4. Disorders of sexual development due defective hormone synthesis or action
    - Androgen insensitivity syndrome (AIS)—can be partial (PAIS) or complete (CAIS
    - 5-alpha reductase deficiency (5-AR deficiency)
    - LH receptor defect
5. Others
    - Maternal hyper-androgen exposure

- Placental aromatase deficiency

Clinical features

- ◊ Ambiguous genitalia
- ◊ Bilateral cryptorchidism
- ◊ Hypospadias
- ◊ Micropenis
- ◊ Delayed puberty
- ◊ Atypical puberty

Diagnostic approach to a patient with DSD

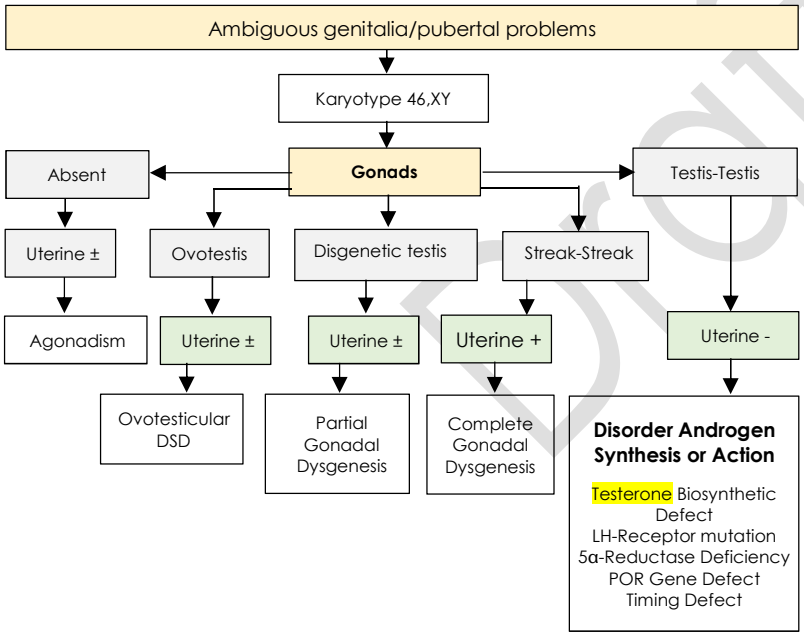


Figure XXXa. Diagnostic Algorithm of 46,XY DSD for new classification.
DSD. Disorders of sexual development

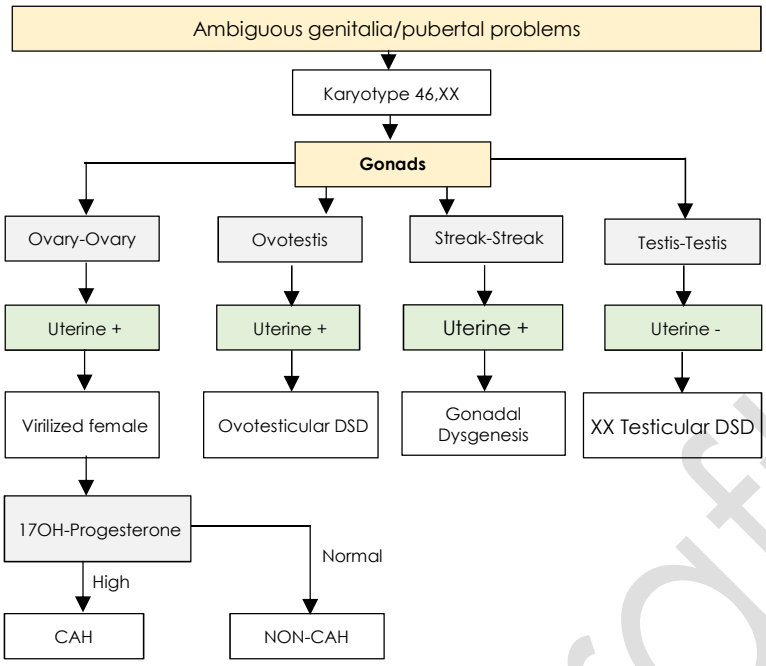


Figure XXXb. Diagnostic Algorithm of 46,XY DSD for new classification.
DSD. Disorders of sexual development

Treatment

Treatment of a patient with DSD aims to;

- ◊ Confirm the diagnosis
- ◊ Promptly rule out life threatening emergency (CAH or hypopituitarism)
- ◊ Sex assignment

Management of a patient with DSD should be family/patient centered with a multi-disciplinary approach:

◊ Rule out CAH in every child with genital ambiguity (if patient in adrenal crisis treat the shock, glucocorticoids and mineralcortocoids)

◊ Sex assignment is a multi-step process and should be done by a multidisciplinary team with the involvement of the patient

◊ A multi-disciplinary team should comprise of paediatrician, paediatric endocrinologist, paediatric surgeon, urologist, psychologist and social worker

◊ Continuous counselling and psychological care should be offered to the family through out the process of care.

Important notes:

◊ **DO NOT** assign sex at birth to a child with atypical genitalia. If the child has to be named advise the parents to assign a sex neutral name and DO NOT call the child, he or she until gender is appropriately assigned

◊ The parents should be reassured in an empathetic manner that the child's sex shall be determined collectively after appropriate investigations are conducted

◊ A child with atypical genitalia must be referred to a centre with a paediatrician for appropriate management

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RICKETS

Definition

Rickets is a disease due to defective mineralization at growth plates in growing bones.

Aetiological classification

Calcipenic rickets; inadequate vitamin D, defective utilization of vitamin D or inadequate calcium	Nutritional vitamin D deficiency Calcium deficiency Distal renal tubular acidosis
Phosphopenic rickets; is not common but occurs in special situations	Low phosphorus intake Renal phosphate wasting Prematurity/ total parenteral nutrition

Symptoms and signs

Age category	Signs and symptoms
During infancy	◊ Delayed milestones ◊ Delayed dentition ◊ Craniotabes ◊ Irritability ◊ Sweating ◊ Delayed closure of anterior fontanelle ◊ Bossing of the skull
Older children	◊ Waddling gait, ◊ Harrison sulcus, ◊ Rachitic rosary, ◊ Genu valgum, ◊ Genu varum (intercondylar distance more than 5cm) or windswept deformity are known to occur
Adolescents	◊ Seizures and bone pain are the major features ◊ Short stature may be a feature in hypophosphataemic rickets.

Investigations

Biochemical investigations

- ◊ U&Es, Creatinine
- ◊ FBC
- ◊ Bone profile (Ca, Mg, phosphate, alkaline phosphatase)
- ◊ 25-OH Vitamin D levels (combined vitamin D2 and D3)
- ◊ Additional testing may be required depending on context

Radiological investigation

- ◊ X- rays of wrist and knee

Classification for serum 25(OH)D;

- ◊ Sufficiency: >50 nmol/L (>20 ng/mL);
- ◊ Insufficiency: 30–50 nmol/L (12–20 ng/mL);
- ◊ Deficiency: <30 nmol/L (<12 ng/mL).

Definite rickets	◊ Rachitic changes on radiographs (cupping and fraying of metaphysis, widening of epiphyseal plate) ◊ High blood alkaline phosphatase ◊ Hypophosphataemia or hypocalcaemia ◊ ***Clinical signs:*** bone deformities such as genu varum and valgum, abnormal spinal curvature, craniotabes, open fontanelles, rachitic rosary, joint swelling
Possible rickets	◊ Rachitic changes on radiographs (cupping and fraying of metaphysis, widening of epiphyseal plate) ◊ High blood alkaline phosphatase ◊ Hypophosphataemia hypocalcaemia

Treatment

Age	Vit D daily dose for 12 weeks	Vit D single dose	Vit D maintenance dose (IU)	Calcium dose mg/day
<3 mo	2000 IU/day	N/A	400	500
3 -12 mo	2000 IU/day	50,000	400	500

>12 mo – 12 yr	3000–6000 IU/day	150,000	600	1000
>12 yr	6000 IU/day	300,000	600	1000

Important Notes

- ◊ Maintenance dose to be given until resolution of symptoms
- ◊ Patients require monitoring of nutritional rickets after the onset of treatment until resolution of symptoms
- ◊ Patients with non-nutritional rickets should be managed at a tertiary centre
- ◊ In children with tetany or convulsions, treat with intravenous calcium gluconate at a rate of 10–20 mg/kg in 5–10 minutes, repeated as needed. (for calcium treatment in severe hypocalcaemia refer to hypocalcaemia protocol)

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PRECOCIOUS PUBERTY (PP)

Introduction

Puberty is the period of physical, hormonal and psychological transition from childhood to adulthood, with accelerated linear growth and achievement of reproductive function. Puberty starts at age 8 in females and 9 in males.

Definition

Precocious puberty is defined as onset of puberty before age 8 in girls and before age 9 in boys.

Classification of Precocious puberty

Precocious puberty is classified according to the underlying physiopathologic mechanisms as;

- ◊ Variants of normal pubertal development; isolated forms of thelarche, pubarche and vaginal bleeding which may or may not be of hormonal aetiology
- ◊ Central precocious puberty (CPP); gonadotropin dependent-precocious puberty also called true precocious puberty. Due to early maturation of the HPG axis
- ◊ Peripheral precocious puberty; gonadotropin-independent precocious puberty also called pseudo-precocious puberty

Aetiology

- ◊ ***Central precocious puberty(CPP);*** causes include; idiopathic, genetic (e.g. activating mutation of KISS1R and KISS1 gene), hypothalamic hamartomas, tumours (e.g. craniopharyngioma, astrocytoma, ependymoma, neurofibroma e.t.c.), cerebral malformations (e.g. hydrocephalus, spina bifida, meningomyelocele, septo-optic dysplasia, vascular malformations), acquired disease such as meningitis, sarcoidosis, tuberculous meningitis, radiation
- ◊ ***Peripheral precocious puberty;*** McCune Albright Syndrome (MAS), ovarian cyst, oestrogen secreting ovarian tumours, oestrogen secreting adrenal tumours, exogenous oestrogen exposure, CAH, Leydig cell tumours, exogenous exposure to testosterone

Symptoms and signs

The clinical manifestation of puberty include the following;

- ◊ Girls; breast development (thelarche), pubic hair (pubarche), axillary hair, apocrine ador, menarche, eostrogenization of vaginal epithelium
- ◊ Boys; testicular enlargement, penile enlargement, pubic hair development, axillary hair, breaking of voice
- ◊ Accelerated growth in both sexes

Evaluation of the patient with precocious puberty

- ◊ Onset and progression of symptoms
- ◊ Presence of neurological symptoms
- ◊ Current and previous therapies (e.g. radiation therapy)
- ◊ Height, weight, BMI (plotted on growth charts)
- ◊ Height velocity
- ◊ Target height

Diagnostic testing

- ◊ Height, weight, BMI plotted on appropriate growth charts
- ◊ Height velocity
- ◊ X-ray of left wrist and hand for bone age determination
- ◊ Pelvic ultrasound
- ◊ Additional testing may include; CT scan or MRI, testing for underlying condition as guided by history and physical examination
- ◊ Hormonal tests (LH, FSH, oestrogen, testosterone, GnRH stimulation test)

Treatment

Treatment of precocious puberty depends on the type and cause.

Isolated benign variant of puberty;

◊ Premature thelarche, vaginal bleeding, premature pubarche, lipomastia without any other sign of puberty usually just requires surveillance every three to six months

◊ Parents need adequate counselling to alley anxiety

Peripheral precocious puberty

◊ Treatment is based on the cause (e.g. MAS, exogenous steroids, gonadal tumours etc)

Central precocious puberty

◊ The goal of therapy is preservation of adult height potential and manage psychological difficulties that come with early puberty

◊ The main stay of treatment is GnRHa e.g. leuprolide acetate.

◊ Administered every 4 weeks

◊ Monitor height velocity, breast and testicular size

◊ Dosage is age dependant

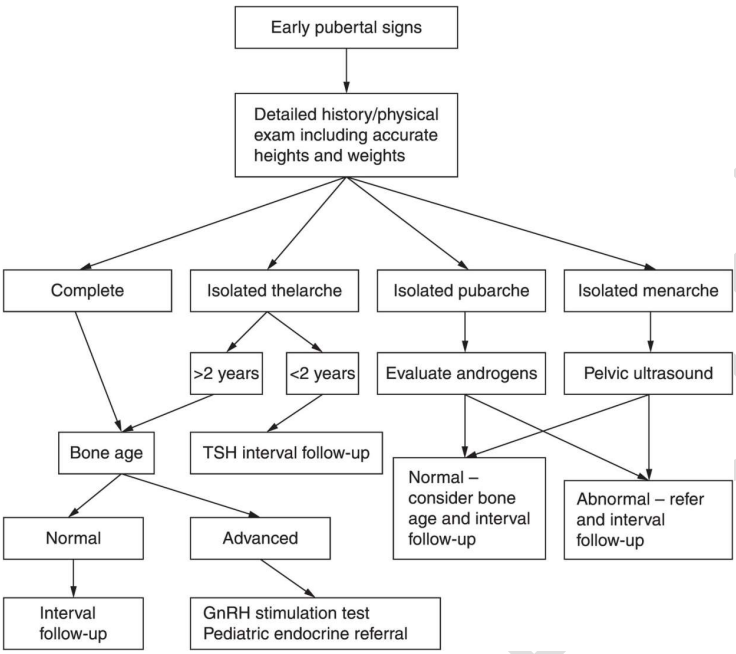
Body Weight	Recommended Dose
≤ 25 kg	7.5 mg
> 25-37.5 kg	11.25 mg
> 37.5 kg	15 mg

Referral criteria for a patient with PP

◊ Every patient with suspicion of PP should be referred to a second or third level hospital with a presence of a paediatrician

◊ Patients with PP should be managed by a paediatrician or paediatric endocrinologist

Precocious Puberty evaluation flow chart



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HYPOGLYCAEMIA IN CHILDREN AND ADOLESCENTS

Definition

Hypoglycaemia is defined as plasma glucose of less than 2.6 mmol/l. However, of note is that in preterm neonates in the 1st three days of life, glucose maybe as low as 1.1 mmol/l without any underlying abnormality. In term neonates, it may be as low as 1.7 mmol/L in the first three days and 2.2 mmol/l in the remainder of the week. Thereafter, a glucose of 2.6 mmol/L or lower requires investigations.

Causes

- ◊ Intrauterine growth retardation and prematurity
- ◊ Perinatal asphyxia
- ◊ Infant of a diabetic mother
- ◊ Intrauterine infections and sepsis
- ◊ Rhesus incompatibility
- ◊ Inborn errors of metabolism
    - o Amino acids and organic acids
    - o Disorders of carbohydrate metabolism e.g. glycogen storage disease, fructose intolerance, lactosaemia
    - o Fatty acid oxidation defects
    - o Urea cycle defects
- ◊ Endocrine causes
    - o Hypopituitarism
    - o Growth hormone or adrenal insufficiency
    - o Persistent hyperinsulinaemic hypoglycaemia of infancy
    - o Beckwith-wiedemann syndrome
    - o Insulinoma
- ◊ Ketotic hypoglycaemia
- ◊ Drugs including alcohol, aspirin, beta blockers
- ◊ Sepsis especially due to gram negative organisms

Signs and symptoms

Hypoglycaemia is often accompanied by signs and symptoms of autonomic (adrenergic) activation and/ or neurological dysfunction (neuroglycopenia)

- ◊ Autonomic signs and symptoms
  - o Tremors
  - o Pounding heart
  - o Cold sweatiness
  - o Pallor
- ◊ Neuroglycopenic signs and symptoms
  - o Difficulty concentrating
  - o Blurred vision
  - o Disturbed colour vision
  - o Difficulty hearing
  - o Slurred speech
  - o Poor judgment and confusion
- ◊ Problems with short-term memory
- ◊ Dizziness and unsteady gait
- ◊ Loss of consciousness
- ◊ Seizure
- ◊ Death
- ◊ Behavioral signs and symptoms
  - o Irritability
  - o Erratic behavior
  - o Nightmares
  - o Inconsolable crying
- ◊ Non-specific symptoms (associated with low, high or normal blood glucose)
  - o Hunger
  - o Headache
  - o Nausea

- Tiredness

Investigation of hypoglycaemia

Blood taken for a diagnostic screen is only useful if taken when the patient is hypoglycaemic (glucose < 2.6 mmol) and should include the following:

- ◊ Glucose
- ◊ Insulin
- ◊ Cortisol
- ◊ Growth hormone
- ◊ Lactate
- ◊ Free fatty acids
- ◊ Amino acids
- ◊ Ketone bodies (hydroxyl butyrate and acetoacetate)
- ◊ Urine
- ◊ Organic acids

NOTE: In hypoglycaemic states and in the absence of ketones, it is important to look at free fatty acids (FFA). Normal FFA suggests hyperinsulinism and raised FFA suggests a fatty acid oxidation defect. Hypoglycaemia in the presence of urinary ketones suggests either a counter regulatory hormone deficiency or an enzyme defect in the glycogenolysis or gluconeogenesis pathways.

Treatment

Hypoglycaemia should be treated promptly after obtaining the critical intravenous samples by intravenous infusion of 5 ml/kg of 10% dextrose followed by adequate glucose infusion to maintain euglycaemia.

Severe hypoglycemia can be reversed by the injection of glucagon: glucagon 0.5 mg < 12yr, 1.0 mg for ages >12yr or 10-30 mcg/kg body weight. Glucagon is given intramuscularly or subcutaneously.

Treatment should also be aimed at the underlying cause of hypoglycaemia. Fig XX shows flow chart for the emergency management of hypoglycaemia

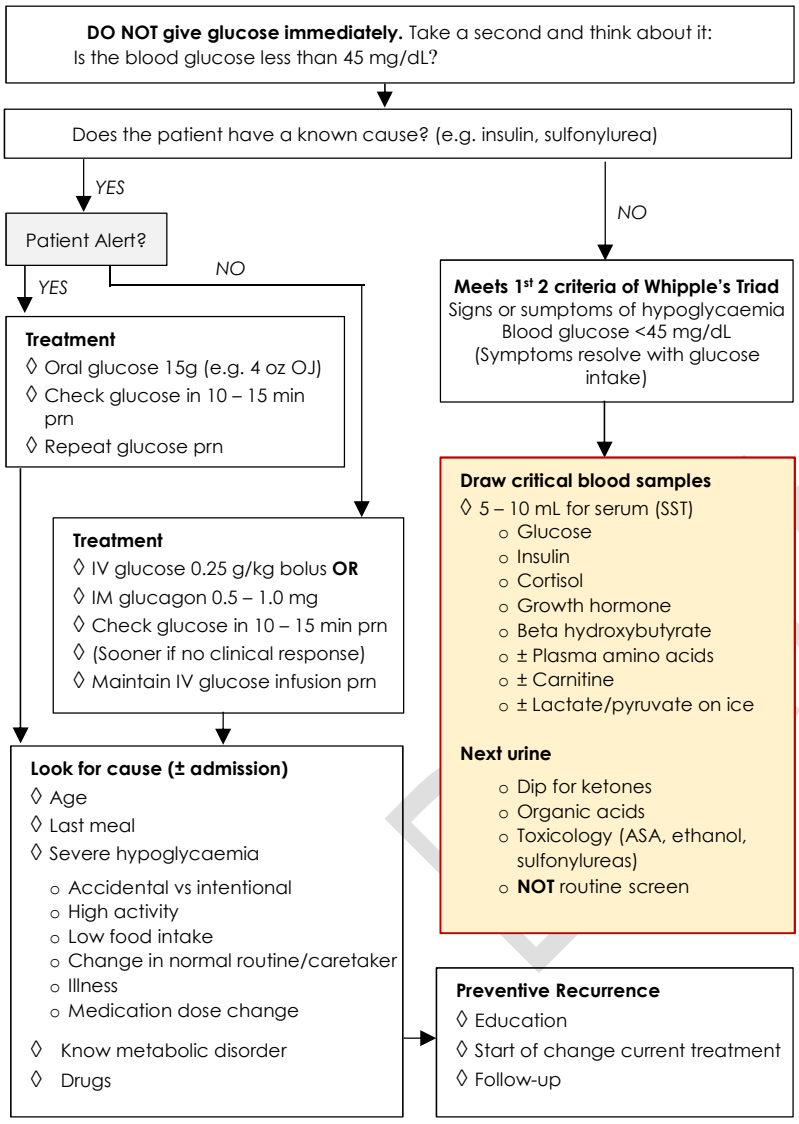

Figure X Emergency management of hypoglycaemia

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GRAVE'S DISEASE (GD)

Introduction

Graves disease is the most common form of hyperthyroidism in children, due to an autoimmune induced overproduction of thyroid hormones. In Graves disease the immune system produces antibodies called thyroid stimulating immunoglobulins (TSIs) that bind to thyroid receptors and activate production of thyroid hormones outside of the negative feedback mechanism that occurs with normal thyroid function. GD may be associated with other autoimmune diseases such as type 1 diabetes mellitus, vitiligo, rheumatoid arthritis etc.

Symptoms and signs

Common Symptoms of GD include:

- ◊ Heat intolerance, sweating
- ◊ Palpitation
- ◊ Exophthalmos
- ◊ Nervousness
- ◊ Irritability
- ◊ Emotional instability
- ◊ Tremor
- ◊ Weight loss in spite of increased appetite,
- ◊ Deterioration of attention,
- ◊ Restless sleep,
- ◊ Fatigue
- ◊ Nocturia, frequent micturition,
- ◊ Irregular menstrual periods

Signs

- ◊ Tachycardia, atrial fibrillation
- ◊ Goiter
- ◊ Ophthalmopathy
- ◊ Diffuse goiter
- ◊ Wide pulse pressure,

◊ Uncoordinated movements,
◊ Pretibial myxedema
◊ Anxiety
◊ Muscle wasting
◊ Signs of heart failure

Laboratory test Investigations

Type of test	Values
TSH	0 – 1uU/ml in severe disease (1 -3 uU/ml in mild disease
FT4	
FT3	

Thyroid ultrasound scan; is useful to confirm or exclude the presence of a nodule particularly if a colour doppler if performed

Antithyroid antibodies; the presence of antibodies provide supporting evidence for Graves disease.

◊ More than 95% of patients with GD are positive for TPO (thyroperoxidase antibody)
◊ About 50% have positive anti-thyroglobulin antibody titres
◊ Thyroid stimulating-thyrotropin receptor antibodies (TRab, TSI) present in about 90%

Radioisotope scan is of little value in the diagnosis of graves disease

Treatment

Antithyroid drug therapy

◊ Carbimazole 0.5-1 mg/kg
◊ Propylthiouracil (PTU) 5-10 mg/kg

Iodine-131 therapy

◊ Radioiodine ablation of the thyroid gland is quick, easy, moderatly expensive, avoids surgery, and is without significant risk in adults and probably teenagers.

Surgery

◊ Thyroidectomy was the main therapy, has been to a large extent replaced by 131-I treatment.

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HYPOTHYROIDISM

Introduction

Neonatal hypothyroidism results from decreased T4 production in a newborn. It is the most preventable cause of potential intellectual disability.

Childhood hypothyroidism also known as acquired hypothyroidism usually occurs after 6 months of age. The hypothyroidism is caused by failure of the hypothalamic-pituitary-thyroid axis, which results in decreased production of thyroid hormones. The hypothyroidism may be primary (at the level of thyroid gland), secondary (at the level of pituitary gland), or tertiary (at the level of hypothalamus).

Symptoms and Signs

Congenital

- ◊ More than 95% of newborns who have congenital hypothyroidism have little if any symptoms or signs at birth.
- ◊ Some maternal T4 crosses the placenta, so infants who cannot make any thyroid hormone still have serum T4 concentrations that are 25% to 50% of normal.
- ◊ Birth length and weight are within the normal range, but head circumference may be increased.
- ◊ An open posterior fontanelle in a term baby may signal congenital hypothyroidism.
- ◊ Lethargy
- ◊ Hypotonia
- ◊ Hoarse cry
- ◊ Feeding problems
- ◊ Constipation
- ◊ Macroglossia
- ◊ Umbilical hernia
- ◊ Dry skin
- ◊ Hypothermia, and prolonged jaundice
- ◊ Goiter is uncommon

◊ Newborns who have congenital thyroid dyshormonogenesis may have a palpable goiter, but the goiter typically develops later in untreated patients.

Acquired

◊ Decline in linear growth
◊ Fatigue
◊ Constipation
◊ Cold intolerance
◊ Poor school performance
◊ Weight gain
◊ Irregular menstrual periods, and somnolence
◊ Children afflicted with Hashimoto thyroiditis also may have other autoimmune disorders and a family history of thyroid and other autoimmune disorders to support the diagnosis.
◊ Other clinical features of acquired hypothyroidism include bradycardia
◊ Short stature
◊ Increased weight for height
◊ Dry skin
◊ Increased body hair
◊ Pallor
◊ Myxedema of the face
◊ An enlarged thyroid gland
◊ Proximal muscle weakness
◊ Delayed relaxation phase of the ankle reflex, and
◊ Delayed puberty
◊ Occasionally, acquired childhood hypothyroidism presents with precocious puberty.
◊ The enlarged thyroid gland usually is diffuse and non tender; Sometimes the gland may be firm.
◊ The onset of acquired childhood hypothyroidism often is very subtle; in retrospect, it may be evident that signs and symptoms were present for a longer time, sometimes for 2 to 3

or more years. If previous height measurements are available, a decline in linear growth from the onset of hypothyroidism will be evident.

Laboratory Tests

For new-born screening:

- ◊ Initial T4 testing with follow-up TSH testing
- ◊ Between 1 and 4 days of age, the normal range for serum total T4 concentrations is 10 to 22 mcg/dL (128.7 to 283.2 nmol/L).
- ◊ Between 1 and 4 weeks of age, the normal range for serum total T4 concentrations is 7 to 16 mcg/dL (90.1 to 205.9 nmol/L).
- ◊ Subclinical hypothyroidism is defined as a normal serum total or free T4 concentration and a high serum TSH concentration.
- ◊ Infants who have subclinical hypothyroidism should be treated during the first 3 years after birth due to the critical dependence of the myelinizing CNS on thyroid hormone.

Management

Congenital

- ◊ The overall goals of treatment are normal growth and good cognitive outcome.
- ◊ Serum T4 concentrations should be restored rapidly to the normal range, followed by continued maintenance of euthyroidism.
- ◊ The aim of treatment is to keep the serum T4 or free T4 concentration in the upper half of the normal range adjusted for age.
- ◊ Of note, many commercial laboratories do not provide age-adjusted normal ranges in their reports.
- ◊ In the first postnatal year, serum T4 should be 10 to 16 mcg/dL and serum freeT4 should be1.4 to 2.3ng/dL.
- ◊ The serum TSH concentration should be less than 5 mU/L.
- ◊ Oral T4 (levothyroxine) is the treatment of choice.
- ◊ Initial dose of 10 to 15 mcg/kg per day, usually 50 mcg/day.

- In preterm and other low-birthweight infants, the thyroid replacement dose should be calculated by using10 to15mcg/kg per day, with the higher end administered to babies who have low T4 concentrations.
- **Only T4 tablets should be used because thyroid suspensions prepared by individual pharmacists may result in unreliable dosing.**
- Parents should be instructed to crush the T4 tablet and mix It with a small volume of human milk, formula, or water. **Soy formulas or any preparation containing concentrated iron or calcium should not be used because they reduce the absorption of T4**.
- The more rapidly T4 concentrations are corrected, the better the neurologic outcome. Aim to normalise the T4 concentrations within two weeks

Patient follow up

The recommended follow up schedule is as follows;

- At 2 and 4 weeks after the initiation of T4 treatment
- Every1to2monthsduringthefirst6postnatalmonths
- Every3to4monthsbetween6monthsand3yearsofage
- Every 6 to12months thereafter until growth is complete
- 2 weeks after any change in dose
- At more frequent intervals when compliance is questioned or abnormal results are obtained

Acquired

- Childhood hypothyroidism is treated with levothyroxine. (refer to table below for dosage)
- Treatment should be individualized because the absorption of T4 and metabolism vary among individuals.
- Serum freeT4 and TSH concentrations should be monitored periodically, preferably at 3-to 6-month intervals.
- The goal is to keep the serum free T4 concentration at the mid-normal range and the TSH concentration in the normal range.

◊ Once the patient is euthyroid, many of the symptoms disappear.

Dosage of levothyroxine				
Age band	6 to 12 months	1 to 3 years	3 to 10 years	10 to 18 years
Dosage	5 to 8 mcg/kg	4 to 6 mcg/kg	3 to 5 mcg/kg	2 to 4 mcg/kg

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HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

Definition

HIE is an acquired syndrome of acute brain injury characterized by Neonatal Encephalopathy (NE) and evidence of intrapartum hypoxia.

NE is characterized by an abnormal level of consciousness, abnormal tone and abnormal primitive reflexes. Abnormal breathing and seizures may also occur.

Intrapartum hypoxia may be suggested by the presence of one or more of the following features:

- ◊ An acute intrapartum event
- ◊ Fetal bradycardia or reduced variability on CTG
- ◊ Meconium stained liquor
- ◊ Prolonged second stage
- ◊ Need for resuscitation at birth for 10 minutes or longer
- ◊ a 5-minute Apgar score < 7
- ◊ Acidosis on cord or neonatal blood in the first hour of life (defined as pH < 7 or Base Excess < - 10).

NOTE: The presence of features that suggest intrapartum hypoxia does not exclude other causes of encephalopathy.

Immediate management on admission

- ◊ Manage A- airway, B- breathing and C- circulation
- ◊ Check glucose, give glucose at 3mls/kg if < 2.6 mmol/L
- ◊ Document congenital anomalies
- ◊ Document the Thompson HIE score
- ◊ If there are signs of encephalopathy:
    - ◊ Keep nil by mouth
    - ◊ Commence IV fluids at 40 ml/kg/day
    - ◊ Apply the aEEG as soon as possible if available

If there are clinical or aEEG signs of moderate-severe HIE, refer to the cooling protocol in the *National Neonatal Guidelines* – discuss all cases with a senior clinician.

Initial investigations of infants with moderate – severe HIE should include:

- ◊ Blood gas
- ◊ FBC, CRP, blood culture
- ◊ Electrolytes; Sodium, Potassium, Calcium, Magnesium
- ◊ Urea, creatinine

NOTE: If history/signs suggest sepsis, perform a septic screen that includes a lumbar puncture and commence antibiotics

Initial investigations of infants with moderate – severe HIE

Cerebral function monitor, aEEG

- ◊ If available, apply aEEG to all infants with signs of HIE as soon as possible
- ◊ Monitor for at least 6 hours if not cooled (preferably 24h). If cooled, continue until rewarm is complete
- ◊ A severely suppressed background persisting for 6 hours predicts a poor outcome in over 80% and if this persists beyond 48 hours, despite cooling, the prognosis is almost invariably poor
- ◊ A normal voltage pattern at 48 hours in cooled infants associated with a good outcome in most infants

Cranial ultrasound

- ◊ Performed at least on Day 1 and again at Day 7-14
- ◊ Cranial US shows gross anatomy, established damage at birth and evolving focal or global injury.

MRI

- ◊ MRI is the most reliable guide to prognosis and diagnosis available. It is best done at 7-14 days for optimal prognostic information.

Clinical management of infants with moderate – severe HIE

Temperature and Cooling

- ◊ Avoid overheating infants at any stage
- ◊ Maintain normothermia
- ◊ Refer to separate cooling protocol for details of eligibility and refer to a facility that is able to cool (Discuss with a senior clinician).
- ◊ It is not necessary to obtain the aEEG result before cooling if infants have obvious moderate-severe encephalopathy on clinical grounds

Ventilation

- ◊ Aim for normal PaCO2 and oxygen saturation (Targets: PaCO2 35-45mmHg; Preductal Sats 90-95%)
- ◊ If oxygen is needed and respiratory effort is good, nasal CPAP or nasal cannulae are often adequate
- ◊ Ventilate if apnoea or respiratory acidosis with pH < 7.25 and inform senior clinician
- ◊ If ventilated do blood gases 8 hourly or more often if abnormal

Blood pressure

- ◊ Monitor blood pressure and keep it in the normal range (Mean arterial pressure [MAP] = 40-55)
- ◊ Avoid fluid boluses unless hypovolaemia is suspected. Give fluid bolus of normal saline at 10mls/kg if suspected hypovolemia
- ◊ Metabolic acidosis alone, is not an indication for a fluid bolus
- ◊ Treat normovolaemic hypotension with inotropes. Use central access via UVC or other central line
- ◊ An echocardiogram to assess cardiac function can inform fluid and inotrope management

Haemoglobin

- ◊ Transfuse if significant anaemia
- ◊ Transfusion thresholds:
  - o Hb < 10g/dL if on CPAP
  - o Hb < 11g/dL if FiO2 < 0.3; < 12 if FiO2 > 0.3 in neonates on assisted ventilation

Coagulation management

- ◊ Check INR/PTT/Fibrinogen in severely anaemic or bleeding infants (e.g. subaponeurotic haemorrhage)
- ◊ Treat active bleeding with vitamin K (1-2mg/kg IV) and FFP (15mls/Kg over 30 minutes) – consider cryoprecipitate if poor response or low fibrinogen

Fluid balance, acidosis and metabolic management

Intrinsic renal injury and SIADH commonly occur

- ◊ Initially fluid restrict to 40 ml/kg/24 hours
- ◊ Initially use 10% dextrose solution
- ◊ Potassium-containing fluid should only be used if urine output and serum potassium are normal
- ◊ Monitor urine output, electrolyte, blood glucose and blood gases
- ◊ Catheterise if urine retention or oliguric (<1 ml/kg/hr)
- ◊ Hypocalcaemia and hypomagnesemia should be anticipated and treated
- ◊ Treat Hyponatraemia< 130 mmol/l with fluid restriction if oliguric – if not oliguric, consider increasing fluids and using 0.9% saline in maintenance fluids
- ◊ There is no proven benefit of Sodium Bicarbonate to treat lactic acidosis
- ◊ Monitor plasma glucose
- ◊ Increase IV glucose concentration if plasma glucose remains < 2.6 mmol/l use 12.5% or 15% glucose as an infusion solution rather than increase volume

Feeding

◊ Beware of necrotizing enterocolitis

◊ Introduce feeds slowly, preferably breast milk (assess suck reflex)

◊ Keep nil by mouth on admission then commence 3-hourly feeds after 12-24 hours:

◊ Increment by 12-24mls/kg/day during the first 3 days and by up to 30ml/kg/day thereafter if abdomen exam normal

◊ Infants with mild encephalopathy who are not cooled can be fed with higher volumes

Sepsis

◊ Treat with first line antibiotics as per hospital protocol.

◊ Discontinue antibiotics at 36 hours if sepsis excluded with normal CRP at 36-48 hours or follow hospital antibiotic policy.

Seizures

Refer to seizure management guideline

Communication with Parents

◊ Explain the clinical condition and the potential for other causes

◊ Explain the management

◊ Document the parent's version of events

◊ Prepare them for a potential poor outcome if investigations and signs are suggestive

Clinical neurological assessment

Clinical signs vary with time. There are three stages of encephalopathy:

◊ Stage 1(mild): Irritability, increased tone, poor sucking and exaggerated moro reflex

◊ Stage 2 (moderate): Lethargy, decreased tone and primitive reflexes. Often with seizures

◊ Stage 3 (severe): Stupor or Coma, flaccid tone and seizures often clinically less apparent Moderately or severely affected

infants typically develop increasingly obvious signs during the first 48-72 hours. Seizures are often clinically silent.

The Thompson HIE score

The Thompson HIE score should be performed on admission, before age 5 hours, and daily until normal or age 7 days (up to 10 days if cooled). The maximum score, based on the clinical signs in the previous 24 hours, is recorded in each category and then totalled for the day. A score of < 5 in the first 5 hours of life is associated with a normal aEEG at 6 and 24 hours.

If infants are not cooled:

A peak score of 10 or less during the first 6 days with a score of 0 by day 7 predicts a normal outcome, a score of 11-15 at any time or a score above 0 on day 7 predicts an abnormal outcome in 65% and a score of above 15 predicts an abnormal outcome in 92%.

When to stop resuscitation or offer withdrawal/redirection of care

- ◊ Stop resuscitation after 10 minutes of asystole
- ◊ Consider stopping resuscitation if no spontaneous respiration after 20 minutes – first ensure that infant is not hypocarbic and has not been exposed to maternal opiates/benzodiazepines
- ◊ Discuss with senior clinician before stopping resuscitation

Withdrawal of intensive care or ventilation

Should be discussed with the senior clinician and should be considered (withdrawal may be mandatory if resources are limited), in the following circumstances:

- ◊ Infants who initially met resuscitation discontinuation criteria but ventilation was continued and there is persisting isoelectric aEEG and/or coma and persistent apnoea in the absence of sedative drugs

◊ Infants with severely abnormal aEEG (upper and lower margins below 10mcV or burst suppression) persisting beyond 24 hours if not cooled or 48 hours if cooled.

NOTE: high dose midazolam or opiates can affect the clinical and electrical data

◊ Additional factors such as cranial ultrasound and MRI findings and multiorgan failure should also be considered.

Follow-up

◊ Arrange neurodevelopmental follow up at 20 (18-22) weeks (to follow up with local hospital guidelines)

◊ Document head circumference and neurological exam at birth and at discharge

◊ Document maximum HIE grade and Thompson score

◊ Plan and discuss the need for long-term anticonvulsant management (refer to neonatal seizures section).

◊ Limited consensus exists concerning the duration of long-term AED therapy and controlling seizures

◊ Normal examination, in particular a normal nutritive suck at age 7 days carry a good prognosis.

◊ An infant who can feed well and visually fix and follow by age 10-14 days can still have significant focal basal ganglia lesions that may lead to an athetoid type of CP with good preservation of intellect and head growth

◊ Infants with adequate feeding by 2-3 week but often slightly slow visual attention may have significant white matter injury that will lead to relative microcephaly and some slowness in learning without a major motor problem.

NOTE: If MRI is done after discharge, ensure that a developmental appointment is made soon after to discuss results.

Reference

Zambia Neonatal Protocols and Drug Doses 2016

PREMATURITY

Delivery of an infant born before 37 completed weeks of gestation. It is categorized by gestation age or birthweight.

Gestation age

Late preterm infant - infant born between 34 and 36 weeks gestation

Moderately preterm infant - infant born between 32 and 34 completed weeks of gestation

Very preterm infant - infant born between 28 and 32 completed weeks of gestation

Extreme Preterm infant - born before 28 weeks

Birth weight

◊ Low birthweight (LBW) - 1500g-< 2500g

◊ Very low birthweight (VLBW) - 1000g- <1500g

◊ Extremely low birthweight (ELBW) - <1000g

Diagnosis

By assessing the gestational age at birth by using Ballard scoring system or foot length (Refer to the Zambia Neonatal Protocols and Drug Doses).

Management

Routine care

◊ Airway, breathing, cord and eye care

Thermal protection

◊ Maintain a set environmental temperature of 25°C

◊ All infants should be received into a clean, dry pre-warmed towel

◊ Infants less than 30 weeks gestation age or 1200g birth weight should be placed into a plastic bag up to neck. Cover the head but not the face. DO NOT DRY THESE INFANTS

◊ Continue to resuscitate with the infant in the plastic bag. Cut holes in bag for limb or umbilical vascular access if needed

◊ Weigh the infant inside plastic bag

◊ Keep infant in bag during transfer to neonatal unit

◊ Remove plastic bag once stabilized in the NICU in an incubator

◊ Use KMC for the stable preterm infant (Refer to National KMC Guidelines)

◊ Document temperature on arrival in NICU and after 1 hour

Fluid requirements

The expected early postnatal weight loss is higher in preterm infants and they may lose up to 15% of their body weight.

Give 10% dextrose in the first 36 – 48 hours, 5% dextrose is suitable for ELBW infant because it has a low solute load which can easily be handled by the immature kidneys. After 36 - 48 hours change to either ¼ strength Darrow's solution in 10% dextrose or 10% Neonatalyte.

Initiate fluids as below:

Birth Weight(g)	Fluids	Day 1 (ml/kg/day)	Glucose (mg/kg/min)
<1000	5% Dextrose	90	3.2
1000 – 1199	10% Dextrose	80	5.6
1200 – 1499	10% Dextrose	70	4.2
>1500	10% Dextrose	60	4.2

◊ Maintain glucose between 2.6 – 7mmol/l

◊ Increase total fluid intake daily in increments of 10 – 20 ml/kg/day, dependent on urine output, weight and serum sodium

Enteral feeding

◊ Breast milk feeding must be encouraged for all infants.

◊ Donor breast milk is preferable to formula for preterm infants unable to access mother's own breast milk.

◊ Fluid and enteral intake prescriptions should be individualized for sick infants and infants with risk factors or feed intolerance.

≥ 1 500 G OR ≥ 32 Weeks

- In the absence of mother's own milk, consider preterm formula
- Start on bolus feeds 2 -3 hourly at 60ml/kg on day 1
- Increase to 75, 100, 125, 150ml/kg/d from D2-D5 as feeds are tolerated

< 1 500 G OR 32 Weeks

- Start with bolus tube feeds (expressed breast milk (EBM))
- Orogastric tubes are preferable to nasogastric tube
- Start milk on D1 at 12-24 ml/kg/d
- Increase feeds daily by 24 ml/kg/day
- Consider continuous feeds if prolonged significant feeding intolerance – discuss with senior clinician.
- Syringes should be changed every 4 hours for all feeds given via a syringe driver
- Continue until a rate of 10ml/hr or weight of 1 200 g is achieved before challenging with 2-hourly bolus feeds
- Stop supplemental IV fluids when an enteral intake of 150 ml/kg/day is achieved (consider individual baby tolerance)
- Increase enteral volume incrementally to 180-200 ml/kg/day
- Add supplements and breast milk fortifier according to guidelines
- The feeding tube must be changed weekly, and the administration set three times a week
- Initiate TPN for confirmed prolonged feeding intolerance > 3 days and for confirmed cases of NEC (See TPN Protocol in the Zambia Neonatal Protocols)

Preterm Supplements

Preterm infants on full feeds or feeds at 150ml/kg should be given the following supplements for 6 months:

◊ ***1500g – 2500g***

- Multivit 0.6ml PO daily
- Iron syrup or drops 0.6ml PO from day 28 of life

◊ ***< 1500g***

- Introduce Multivit 0.3ml PO daily 48 hours after establishing full feeds
- Iron syrup or drops 0.2ml PO from day 28 of life
- Add human milk fortifier to breastmilk 24 hours after establishing full feeds

Infection

Treatment and /or prevention (See section on sepsis in neonates)

RESPIRATORY DISTRESS SYNDROME

- ◊ RDS is a problem often seen in premature babies
- ◊ The condition makes it hard for the baby to breathe
- ◊ Occurs in infants whose lungs have not yet fully developed due to a lack of surfactant which helps the lungs fill with air and keeps the air sacs from deflating.

Clinical Features

Appear within minutes of birth, however, they may not be seen for several hours. These may include:

- ◊ Cyanosis
- ◊ Apnea
- ◊ Nasal flaring
- ◊ Rapid breathing
- ◊ Shallow breathing
- ◊ Grunting

Investigations

- ◊ Blood gas analysis shows low oxygen and excess acid in the body fluids
- ◊ Chest x-ray shows a "ground glass" appearance to the lungs that is typical of the disease. This often develops 6 to 12 hours after birth.
- ◊ Lab tests help to rule out infection as a cause of breathing problems

Treatment

- ◊ Give warm, moist oxygen
- ◊ Monitor carefully to avoid side effects from too much oxygen
- ◊ Give surfactant intra-tracheal
- ◊ Start CPAP or HFNC
- ◊ Intubate and ventilate for preterm infants who are not coping on CPAP or remain apnoeic

NECROTISING ENTEROCOLITIS (NEC)

- ◊ NEC is a life-threatening condition that affects the bowel of infants, the majority of whom are preterm
- ◊ Patients are severity ill, with an acute abdomen
- ◊ NEC should be considered in any preterm infant with abdominal distention
- ◊ Etiology is multifactorial; prematurity is the biggest independent risk factor but infection, hypoxia, feeding regimens and type of feed (hyperosmolar formula), polycythemia, PDA, indomethacin may play a role
- ◊ The use of breast milk is associated with a lower incidence of NEC.

Clinical features

- ◊ NEC can occur in the first few days of life in term patients, but more commonly from the second week onward in preterm infants.
- ◊ Onset can be insidious but patients with a rapid onset deteriorate quickly
- ◊ Lethargy, abdominal distension, absent bowel sounds, bloody stools, vomiting and discolored abdominal wall are the cardinal signs
- ◊ Other signs of illness are tachycardia, respiratory distress and poor perfusion may be present.

Modified Bell's staging

Stage 1. Suspected NEC: clinically ill.

Abdominal X-ray: normal to mild distension of bowel loops

Stage 2. Definite NEC: mild or moderate systemic illness, absent bowel sounds, abdominal tenderness, metabolic acidosis, low platelets.

Abdominal X-ray: pneumatosis intestinalis or portal venous gas.

Stage 3. Advanced NEC: severely ill, marked distension, signs of peritonitis, hypotension metabolic and respiratory acidosis, DIC.

Abdominal X-ray: pneumatosis intestinalis, portal venous gas or pneumoperitoneum

Management

- ◊ Resuscitate: Support breathing and intubate if required.
- ◊ Assess circulatory status; apply fluid and inotropic support judiciously
- ◊ Stop enteral feeds immediately. Insert naso-/orogastric tube, leave on free drainage, monitor gastric output
- ◊ Strict input-output monitoring
- ◊ Investigations: Abdominal X-ray, FBC, CRP, blood culture. Consider U&E, ABG and INR/PIT.
- ◊ Start broad-spectrum antibiotics including adequate gram-negative cover
- ◊ Serial abdominal examination is important

Stage 1

- ◊ Reassess abdomen in 24-48 hours. Restart small volume feeds cautiously if examination is normal

Stage 2 and 3

- ◊ Keep NPO for 5-10 days. Start total parental nutrition preferably via a deep percutaneous venous line by 48 hours NPO.
- ◊ Patients with advanced disease may require repeat FBC, and clotting profile. Blood products (i.e. packed RBC, platelets or FFP) should be transfused if anaemic and/or DIC present (Refer to transfusion protocol in Zambia Neonatal Protocols).
- ◊ Surgery: operative intervention may be indicated if: pneumoperitoneum, fixed bowel loop, abdominal mass palpable or persistent metabolic acidosis. Paediatric surgeons should be consulted after initial stabilization.
- ◊ DO NOT GIVE INDOMETHACIN TO AN INFANT with suspected or definite NEC
- ◊ Peritoneal drainage can be used in patients who are too unstable for surgery or in whom ventilation is difficulty due to

abdominal fluid. Consult with Paediatric surgeon present. Restart feeds slowly (20-30ml/kg/day)

◊ Continue antibiotics until septic markers are normalized

Preventive measures

◊ Start small volume feeds early to stimulate GIT mucosal development

◊ Cautious advancement of feeds in small premature infants

◊ Do not increase feeds if infant has gastric residual of 50% or more

◊ Breast milk appears protective

High risk patients

In the presence of the following risk factors, feeds should be initiated more cautiously in discussion with a senior clinician:

◊ Neonatal encephalopathy

◊ Preterm and metabolic acidosis at birth

◊ Cardiorespiratory instability

Other complications associated with prematurity are discussed in the Zambia Neonatal Protocols and Drug doses:

◊ Apnoea of Prematurity

◊ IVH

◊ BPD

◊ ROP

◊ PDA

Reference:

Zambia Neonatal Protocols and Drug Doses 2016

SEPSIS IN NEONATES

Definition

Neonates are particularly susceptible to bacterial sepsis. The highest incidence being in the very low birth weight infants.

Early-onset sepsis

◊ < 72 hours after birth

◊ Results from vertical exposure to bacteria before and during birth

Late-onset sepsis

◊ > 72 hours after birth

◊ Mostly from organisms acquired by nosocomial transmission

◊ May also be caused by community acquired organisms

Risk factors

Early-onset sepsis

◊ Preterm infant

◊ Prolonged rupture of membranes > 18 hours

◊ Maternal fever in labour (>38 C)

◊ Chorioamnionitis

◊ Maternal colonization with Group B Streptococcus

Late-onset sepsis

◊ Preterm infant

◊ Indwelling catheters or tracheal tube

◊ Prolonged antibiotics

◊ Damage to skin

Clinical features

◊ Usually non-specific

◊ Altered behaviour or responsiveness

◊ Apnoea and bradycardia

◊ Respiratory distress - increase in oxygen requirement/respiratory support
◊ Poor feeding, poor suck, vomiting, abdominal distension
◊ Hypoglycaemia or hyperglycaemia
◊ Fever, hypothermia or temperature instability
◊ Cyanosis or poor colour
◊ Poor perfusion (CRT>3sec; mottling)
◊ Hypotension
◊ Tachycardia
◊ Circulatory collapse or shock
◊ Irritability, inactivity, lethargy
◊ Seizures
◊ Hypotonia
◊ Jaundice
◊ Rash

Meningitis

◊ Tense or bulging fontanelle
◊ Head retraction (Opisthotonus)

Investigations

◊ Full Blood count
◊ C-reactive protein
◊ Blood culture
◊ Lumbar puncture – if blood culture positive or clinical features of meningitis
◊ CXR – if indicated
◊ Tracheal aspirate
◊ Coagulation screen
◊ Blood gas
◊ Placental tissue culture and histopathology

Interpretation of laboratory investigations

Features suggestive of sepsis:

◊ Neutropenia or neutrophilia
◊ Increased ratio of immature(bands): total neutrophils
◊ Thrombocytopaenia
◊ Positive blood culture
◊ Raised CRP (>10 mg/L)

Treatment

◊ Supportive care
◊ Start antibiotics – antibiotic choice depends on local incidence and practice

Duration of antibiotics

◊ Blood culture negative, CRP remains normal and no clinical signs of infection – Stop antibiotics at 36-48 hours
◊ Blood culture negative but CRP raised – treat as infected
◊ Blood culture positive – treat until clinical improvement and CRP has returned to normal (7-10 days)
◊ Meningitis – 14-21 days

NOTE: In the absence of proven sepsis there is no role for a course of antibiotics

Antibiotic policy for suspected sepsis

Antibiotics policy is determined by considering the organism known to have caused infection in the neonatal unit/nursery in the last 6 months. This policy should be regularly reviewed and revised as necessary. A disciplined and consistent approach to antibiotic usage is necessary to provide optimal broad-spectrum cover in suspected sepsis and to limit the emergence of resistant organisms in areas of high usage.

Proposed antibiotics

Decide according to unit cultures and sensitivities

Early onset sepsis (< 72hrs of age): Penicillin G and gentamicin

Late onset sepsis (> 72hrs of age):

◊ First line Penicillin/Cloxacillin and gentamicin/ amikacin

◊ Second line antibiotics: Cefotaxime and cloxacillin

◊ Third line: Ciprofloxacin/Meropenem

◊ Meropenem should be used if meningitis or NEC is suspected

◊ Vancomycin only if the patient has central lines in place and is at risk of Staphylococcus aureus sepsis.

Once started, the duration of treatment should be tailored to clinical circumstances. If cultures come back normal, laboratory indices are normal and the patient no longer shows signs of sepsis, stop antibiotics after 36 – 48 hours. In the absence of proven sepsis, there is no place for "a course" of antibiotics.

Criteria for commencing antibiotics in a baby with risk of having an early onset infection

1. ***Absolute indication for empiric antibiotic treatment***
   - Maternal invasive bacterial infection requiring antibiotics (eg: septicaemia) – suspected or confirmed (NB: Not prophylaxis)
   - Confirmed or suspected infection in twin
   - Respiratory distress starting more than 4 hrs after birth
   - Mechanical ventilation in a term baby
   - Seizures
   - Signs of shock
   - Home delivery

2. ***Start antibiotics if two or more are present of:***

   Antenatal
   - Preterm birth following spontaneous labour <37 weeks or Prelabour ROM
   - ROM ≥18 hours
   - Maternal fever ≥ 38°C or chorioamnionitis

   Postnatal
   - Altered behavior/tone/responsiveness

- Feeding difficulties (eg. Poor feeding in a term baby) or intolerance
- Respiratory distress
- Apnoea
- Abnormal heart rate (bradycardia or tachycardia)
- Altered glucose homeostasis (hypo/hyperglycaemia)
- Metabolic acidosis
- Temperature abnormality >38° or < 36° not explained by environmental factors

NOTE: If only one risk factor is present, consider observation for 24 hrs

Reference

Zambia Neonatal Protocols and Drug Doses 2016

NEONATAL SEIZURES

Definition

An abnormal synchronous electrical discharge of a group of neurons in the central nervous system.

Status epilepticus: continuous seizures lasting 30 minutes or recurrent seizures occupying 50% of the EEG recording for at least 60 minutes.

Clinical manifestations

Clinical manifestation may be:

- ◊ Absent
- ◊ Subtle: eye deviation, eyelid fluttering, bucco-lingual movement or pedaling of arms and legs
- ◊ Focal: tonic or clonic
- ◊ Generalised: multifocal rhythmic jerking, generalized posturing or myoclonic

Important causes

Brain damage:	Hypoxia – ischaemia, bleeding, infarction, oedema
Brain malformations	
Meningitis or encephalitis:	*Acute*: (bacterial or viral) or *Chronic*: (viral, syphilis)
Bilirubin encephalopathy	
Biochemical:	Hypoglycaemia, hypomagnesaemia Hypernatraemia, hyponatraemia Hyperammonaemia, pyridoxine dependency, other
Inborn errors of metabolism	
Drug withdrawal	Maternal opiate or cocaine abuse
Iatrogenic:	Air embolism
Familial:	Fifth day fits (benign)

Diagnosis

- ◊ History: family, pregnancy, birth, clinical course
- ◊ Confirm seizure and monitor response to treatment using aEEG if available
- ◊ Measure serum glucose, magnesium, calcium and sodium

◊ Do a lumbar puncture if sepsis is suspected

◊ Head ultrasound may be diagnostic if intracranial bleed, structural abnormality or ventriculitis is present

◊ Consider inborn errors or metabolism if other causes are not obvious

◊ Measure serum lactate, ammonia and amino acid and urine organic acids. Discuss with the consultant need for CSF lactate and glycine levels. Note serum and CSF glycine levels have to be done simultaneously.

◊ Discuss and arrange with the laboratory before taking any samples.

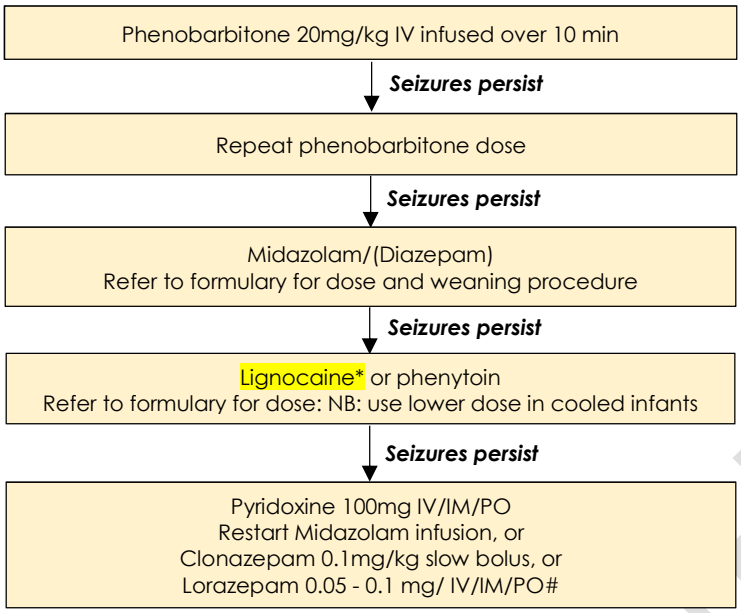
Treatment

◊ Treat electrolyte and glucose abnormalities and sepsis

◊ Ensure adequate ventilation and perfusion. Commence CFM/Brain monitor

◊ Treat seizures (clinical and/or electrical) with anticonvulsants if they are recurrent or last more than 3 minutes.

Anticonvulsant treatment algorithm for term infants



- ◊ If IV Phenobarbitone is not available, use midazolam, clonazepam or Lorazepam as first line. In addition, consider treating with oral phenobarbitone as crushed tablets.
- ◊ If Lignocaine is not available, use Phenytoin as second line.
- ◊ Do not use Lignocaine and Phenytoin in the same patient within 72 hours of each other.
- ◊ #Lorazepam: IV use, dilute to 0.1mg/ml. IM use (emergency) dilute to 1mg/ml. Use sugar free suspension for oral use.

NOTE: Ensure the lignocaine vial is suitable for IV use. Lignocaine infusions must be checked by 2 senior staff before commencement

In preterm infants follow the same algorithm but use phenytoin as second line instead of lignocaine

Treatment considerations

1. When the seizures are controlled, keep the newborn in Phenobarbitone maintenance at 3-5 mg/Kg/day.

   NOTE: In case of excessive sedation do not discontinue Phenobarbitone (probably the drowsiness is secondary to the underlying condition) and evaluate reduction of Phenobarbitone at lower maintenance dose with close clinical monitoring.

2. In case of acute symptomatic seizures resolved by correction of the underlying etiology and not associated with increased risk of brain injury, AEDs can be discontinued gradually.
3. If the infant is taking medication and seizures recur, increase the dose back to levels at which no seizures occurred and ask for neurological evaluation.
4. Generally, patients who had neonatal seizures that required recommencement of anticonvulsants/continued AEDs; should be discharged on maintenance phenobarbital and followed up monthly at least until 3 months of age. The choice to tapper down Phenobarbitone after 1 month should be evaluated case by case considering risk factors for recurrence of seizures.
5. Paediatric neurology evaluation and EEG at 1- 3 month for infant at increase risk of epilepsy should be requested where available.

NEONATAL JAUNDICE

Definition

- ◊ Between 50-60% of normal newborns become clinically jaundiced in the first week of life
- ◊ Jaundice may be physiological or pathological

Physiological jaundice is due to:

- ◊ Increased production of bilirubin (large erythrocyte mass with shortened life span)
- ◊ Decreased hepatic excretion of bilirubin (low hepatocyte ligandin level, low glucoronyl transferee activity)
- ◊ Increased entero-hepatic circulation of bilirubin (high intestinal B-glucoronidase levels decreased intestinal motility)
- ◊ Breast feeding jaundice is thought to be due to feeding problem, which lead to a decreased intake of milk, increased entero-hepatic circulation and sometimes dehydration
- ◊ Breast milk jaundice is diagnosed in clinically well breastfed infant who remains jaundiced for several weeks following physiological jaundice. The mechanism is unknown. It is thought that breast milk glucoronidase leads to increased absorption of unconjugated bilirubin via increased entero-hepatic circulation. Diagnosis is by exclusion. Breastfeeding may be continued.

Pathological jaundice

may result from an increased unconjugated or conjugated fraction or both.

Red flags (features of pathological jaundice plus)

- ◊ Mother Rh negative
- ◊ Mother blood group O. If known check total serum bilirubin (TSB) at 6 hours post-delivery
- ◊ Baby Coombs positive
- ◊ Anaemia
- ◊ Evidence of haemolysis
- ◊ Preterm

◊ Acidosis, hypoglycaemia, hypoxaemia, hypothermia

◊ Features of kernicterus

◊ Bilirubin levels not decreasing despite effective phototherapy, (i.e. 17 – 34 µmol/l within 4 – 6 hours)

◊ Family history of pathological jaundice

Features	Physiological jaundice	Pathological jaundice
Clinical onset of jaundice (after birth)	> 36 hours	≤ 24 hours
Duration of jaundice	Term <10days Preterm <21 days	Term >Day 10-14 Preterm > Day 21
Peak TSB (days after birth)	Term Day 3 Preterm Day 5 – 7	Early or late
Peak TSB	< 275 µmol/l	> 272µmol/l
Rise in TSB per 6 hours		>50 µmol/l
Conjugated serum bilirubin	Only unconjugated fraction increased	>34 µmol/l
Evidence for haemolysis	No	Yes/No
Underlying illness	No	Yes/No
Hepatomegaly	No	Yes/No
Pale stool/dark urine	No	Yes/No

Management

Early onset jaundice (within 24 hours) – caused by haemolytic disease of new born (HDN) (ABO or rhesus):

◊ Check mother's blood group

◊ If the mother's blood group is O, ABO likely. Do following investigations:

- Infants blood group and Coombs

- FBC and peripheral smear
- Check TSB 3 hourly
- Start phototherapy
- In rare cases look for other causes for haemolysis

Jaundice after 24 hours

◊ Exclude blood incompatibility
◊ Exclude obvious infection or extravasated blood/bruising
◊ Check feeding and infant's weight to exclude breastfeeding jaundice
◊ Exclude polycythaemia
◊ Often a cause will not be found; in term infants thought to be an exaggeration of physiological hyperbilirubinaemia and in preterm infants due to the immaturity of the conjugation mechanism
◊ Treatment will depend on the level of the TSB which should be checked daily

Other modes of assessment

Transcutaneous bilirubin (TCB) screening

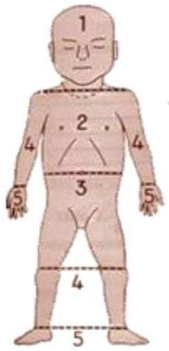
◊ TCB is a **screening tool** to select infants who require formal total serum bilirubin (TSB)levels
◊ TCB screening decreases the number of heel pricks and readmissions for phototherapy
◊ **Do not rely on TCB monitoring in severe hyperbilirubinaemia**
◊ TCB should not be used within 24 hours of phototherapy or an exchange transfusion
◊ Localised oedema and decreased tissue perfusion affects accuracy of TCB measurements
◊ **Technique:**
  - Ensure all staff are properly trained on the TCB device
  - Calibrate the TCB device daily in accordance with the manufacturer's specification
  - Preferred sites are inter-scapular (for infants < 35 weeks), forehead or sternum

- Measurements should not be made over bruised skin, areas covered by hair or birthmarks
- Measure TCB by gently pressing the tip of the device over the examination site then press the trigger button until the device indicates the measurement is complete
- Take 3 - 5 measurements (device dependent) from the examination site, ensuring consistent placement of the tip and amount of pressure applied
- If the TCB reading is within 20 µmol/L of the phototherapy line do TSB

Kramer's rule

In a resource limited country like Zambia, laboratory diagnostics may not be available in a timely manner. Clinical examination (e.g Kramers rule) can be used in making the decision to start phototherapy *(It should be known that clinic estimation of jaundice is very unreliable, especially in dark skinned infants)*

Kramer's rule entails visual inspection in natural light. Depth of jaundice progresses from head to toe as the level of bilirubin rises a follows:

Zone	Baby's body area	Approximate bilirubin level	Diagram
1	Head and neck	6 mg/dl (100 µmol/L)	
2	Upper body (chest)	9 mg/dl (150 µmol/L)	
3	Lower body, below the belly button and upper thighs and arms	12 mg/dl (200 µmol/L)	
4	Lower legs and forearms	15 mg/dl (250 µmol/L)	
5	Hands and feet	>15 mg/dl (>250 µmol/L)	

If you can assess the level of jaundice, any jaundice from the chest and below, you must initiate phototherapy. (Initiate phototherapy for any jaundice from the chest and below)

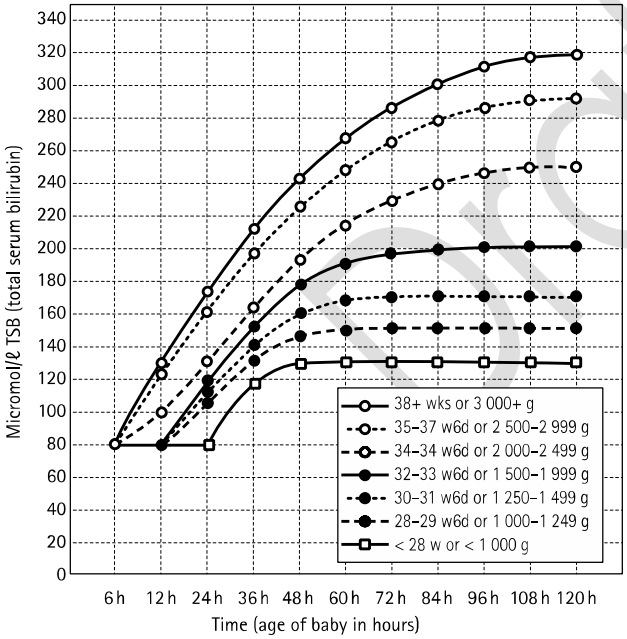
PHOTOTHERAPY

WESTERN CAPE 2006 CONSENSUS GUIDELINES

In presence of risk factors use one line lower (the gestation below) until < 1 000 g
If gestational age is accurate, rather use gestational age (weeks) instead of body weight

Infants > 12 hours old with TSB level below threshold, repeat TSB levels as follows:
1–20 µmol/ℓ below line: repeat TSB in 6 hrs or start phototherapy and repeat TSB in 12–24 hrs
21–50 µmol/ℓ below line; repeat TSB in 12–24 hrs
> 50 µmol/ℓ below line: repeat TSB until it is falling and/or until jaundice is clinically resolving

Infants under phototherapy:
Check the TSB 12–24 hourly but if TSB > 30 µmol/ℓ above the line, check TSB 4–6 hourly.
STOP phototherapy:
If TSB > 50 µmol/ℓ below the line. Recheck TSB in 12–24 hrs.



Start intensive phototherapy when the TSB is ≥ the line according to gestation or weight

Treatment

Phototherapy

High intensity phototherapy (PT) reduces total serum bilirubin (TSB) and decreases exchange transfusions.

Indications

- ◊ See phototherapy guideline charts
- ◊ Indicated for unconjugated hyperbilirubinaemia
- ◊ In the absence of TCB to help in decision making, DO NOT wait for TSB results before starting phototherapy (Kramer classification can be used if possible)
- ◊ A low threshold to start phototherapy in high risk infants (e.g. with sepsis, HIE etc)

Contraindications

- ◊ Congenital porphyria or a family history of porphyria
- ◊ Concurrent therapy with metalloporphyrin haem oxygenase inhibitors
- ◊ Concurrent use of drugs or agents that are photosensitisers

Technique

- ◊ Intensive PT is defined as light wavelengths between 430-490nm, delivered spectral irradiance of 30μW/cm^{2}/nm or higher to the greatest exposed body surface
- ◊ Position the PT unit approximately 40cm from the infant
- ◊ Measure the irradiance of phototherapy units periodically with the use of a photoradiometer

◊ PT units require adequate ventilation. Do not cover with blankets

Care of the infant receiving phototherapy

◊ Monitor temp and ensure adequate fluid intake

◊ Cover the eyes with gauze pads and place infant naked under lights (nappy un tied)

◊ Remove the eye pads during feeds and observe for conjunctivitis

◊ Turn infant every 2-3 hours

◊ In severe jaundice check the TSB 3 hourly

◊ Visual assessment of jaundice is unreliable once the infant is under phototherapy

Efficacy of PT

◊ Successful PT should produce a decline in TSB of 17-34 µmol/L within 4-6 hours and TSB should continue to fall

◊ Stop PT if TSB ≥ 50µmol/L below the PT line

Complications

Rashes, "bronzing", loose stools, dehydration, hypothermia, hyperthermia and separation for mother

PROLONGED NEONATAL JAUNDICE

Defined as jaundice lasting >14 days in term infant >21 days in a preterm infant

Determine whether it is unconjugated or conjugated hyperbilirubinaemia.

Unconjugated hyperbilirubinaemia

- ◊ Determine whether or not the baby is breastfed
- ◊ Collect urine for MCS and reducing substances to exclude galactosaemia
- ◊ Check liver enzymes
- ◊ Exclude hypothyroidism
- ◊ Exclude haemolysis, check reticulocytes and Hb
- ◊ Hereditary enzyme defects such as Gilbert's and Crigler – Najjar syndromes are rare

Conjugated hyperbilirubinaemia

- ◊ History and examination
- ◊ Liver function tests and cholesterol
- ◊ Examine stools daily. Acholic (white) stools require urgent referral to exclude biliary atresia
- ◊ Exclude infective causes
- ◊ Exclude metabolic causes
- ◊ Exclude genetic conditions

Causes of conjugated hyperbilirubinaemia

Causes	
Infective	***Viral:*** Hepatitis A, B, CMV, HIV, rubella, herpes simplex
	Bacterial: Syphillis, septicaemia, UTI
	Protozoal: Toxoplasmosis gondii
Biliary	Biliary atresia, choledochal cyst, Alagille's syndrome, bile plugs, cystic fibrosis
Metabolic/ genetic	Alpha 1-antitrypsin, tyrosinaemia type 1, galactosaemia, wilson's disease, hypothyroidism, hypopituitarism, familial intrahepatic cholestasis, rotor and Dubin-Johnson syndrome
Drug/toxins	TPN
Autoimmune	Autoimmune hepatitis, sclerosing cholangitis

Diagnostic workup for conjugated hyperbilirubinaemia

Investigation	Test	Date Taken	Results
Haemotology	FBC		Hb, WCC, platelets, reticulocytes
	Coagulation		INR, PTT, fibrinogen
	Blood group		
	Coombs		
Biochemistry	U&E		Na, K,urea, Creatinine
	TSB, conjugated bilirubin		TSB, conjugated bilirubin
	Liver functions		AST/ALT, ALP, GGT
	CMP		Ca, Mg, PO_4, Albumin
	Cholesterol*		
	Glucose		
Microbiology	Blood culture		
	Urine culture		
Virology	IgM		Rubella, HSV
	Urine CMV		
	Hepatitis A, B, C		
	HIV		
Metabolic	Urine reducing substances		
	GAL-1-PUT*		
	alpha 1-antitrypsin*		
	Plasma amino acids*		
	Urine amino acids*		
	Urine organic acids*		
	Sweat test*		
Endocrine	Thyroid functions		
Radiology	Abdominal U/S		
	CXR/spinal X-ray*		
	Radio-isotope scan*		
Histology	Liver biopsy*		
Other	Stool		
	Ophthalmology*		

*Second line investigations, discuss with senior clinician