

Chapter 7: Haematology and oncology

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Non-trauma bleeding

Definition

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

Risk factors/causes

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

Promotion prevention

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

Signs and Symptoms Thrombocytopenia

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

Coagulation disorders

- Deep seated haematomas
- Haemarthrosis

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- Renal bleeding
- Intracerebral bleeding

Differential Diagnosis

Decreased platelet production

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

Increased platelet destruction

- Immune thrombocytopenic purpura
- Infection
- Drugs
- Disseminated intravascular coagulation (DIC)
- Cavernous haemangioma

Ineffective thrombopoiesis

- Vitamin B 12 deficiency
- Folic acid deficiency

Platelet sequestration

- Hypersplenism

Assessment History

- Age
 - Neonatal: vitamin K, coagulation defects
- Sex
 - Male with swollen joints: haemophilia,
 - Adolescent females with menorrhagia: Von Willebrand's disease (VWD)
- Duration
 - Long duration: Factor deficiency, VWD
 - Short duration: ITP, Leukaemia
- Type:
 - Petechiae suggests platelet disorder
 - Haematoma suggests factor deficiency

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- Site:
 - Joint or muscle bleeding suggests Factor deficiency
 - Mucus membrane bleeding suggests low platelets or VWD
- History of jaundice: Vitamin K deficiency
- History of multiple blood transfusions: Bone marrow failure
- History of fever, anaemia, lethargy: Bone marrow failure
- Recent history of immunisation: Immune thrombocytopenic purpura (ITP).
- Recent history NSAIDS, methylphenidate: Thrombocytopenia
- Involvement of male siblings and maternal uncles: Factor deficiency

Examination

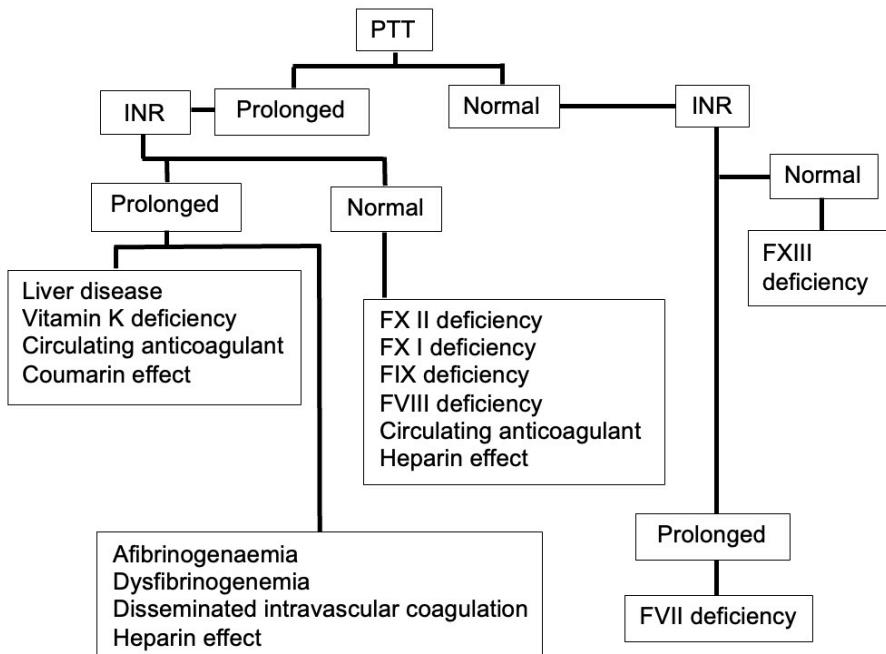
- Are there any dysmorphic features?
- Type and site of bleeding
- Severity of bleeding
- Signs of haemodynamic instability
- Evidence of jaundice
- Signs of systemic illness may suggest DIC
- Signs and severity of anaemia
- Presence of lymphadenopathy
- Presence hepatosplenomegaly
- Presence of limb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

Investigations

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

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Laboratory flow diagram



HAEMATOLOGY AND ONCOLOGY

Management

Primary level

- Manage according to ABCDE
- Refer

Secondary level

- As in primary but also:
 - Take blood samples for FBC, blood group, coagulation, factor levels
 - Transfuse whole blood 20ml/kg
- Refer

Tertiary level

- As in secondary but also:
 - Transfuse whole blood
 - Investigate for cause of bleeding
 - Factor deficiency must be corrected
 - Appropriate counselling
 - Sibling test

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- Provide follow up plan
- Multidisciplinary care may be done in factor deficiency

Follow up

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

Haemophilia

Definition

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

Note: mainly in male children

Causes of severe haemophilia in females

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

Severity

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

Prevention/promotion

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

Signs and symptoms

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

Laboratory

- APTT is prolonged
- Reduced levels of Factor VIII or Factor IX activity

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Management

Primary level

Stabilise patient then refer to tertiary

Secondary level

Stabilise patient then refer to tertiary

Tertiary level

- Stabilise patient
- Transfuse 20ml/kg of whole blood if indicated
- Factor VIII concentrate
 - The half-life is 8-12 hours
 - Treatment of choice for haemophilia A
 - Vials available in dosages ranging from 250 units to 3000 units
 - Consult haematologist for dosing
- Factor IX concentrate:
 - The half-life is approximately 18-24 hours
 - Used in treatment of haemophilia B
 - Consult haematologist for dosing
- Fresh frozen plasma 10ml/ kg IV over 1hour
- Cryoprecipitate
 - This is preferable to fresh frozen plasma in the treatment of haemophilia A
 - 5 – 10ml/kg IV
- Desmopressin (DDAVP)
 - Synthetic analogue of vasopressin that boosts plasma levels of FVIII and VWF
 - It does not affect factor IX levels and is of no value in haemophilia B
 - A single dose of 0.3 μ /kg intravenously or subcutaneously can be very effective
 - Rapid infusion may result in tachycardia, flushing, tremor and abdominal discomfort
- Tranexamic acid
 - 15 - 25mg/kg, given 3 to 4 times daily
- Emicizumab (consult haematologist before use)
 - Monoclonal antibody that binds Factor IX and X and activates Factor X
 - It is used in patients with haemophilia A
 - It is also used in patients with inhibitors to Factor VIII
 - Dose
 - Loading: 3mg/kg subcutaneous per week for 4 weeks
 - Maintenance: 1.5mg/kg subcutaneous per week

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- Consult haematologist

Follow up

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

Early warning signs of childhood cancer

Introduction

World-wide there are more than 400,000 new cases of childhood cancer and more than 70% of these will occur in the developing world. Despite this high incidence, childhood cancer is not a priority in the developing world, where other health needs are more immediate. In Malawi, the paediatric cancer registry recorded 500 new cases in 2022. The commonest malignancy recorded was Burkitt's Lymphoma followed by leukaemia, retinoblastoma and nephroblastoma. Survival from these tumours is often poor due to late presentation and late diagnosis.

Why do we need to make early diagnosis?

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

How do we make early diagnosis?

- High index of suspicion
 - Childhood cancer is rare, and unless you think of the diagnosis, it is going to be missed

Recognising the high-risk groups

- Patients with neurocutaneous syndromes
- Patients with chromosomal disorders e.g. Down syndromes
- Children with immunodeficiency states
- Children with previous history of malignancy or radiotherapy
- Children with congenital malformations e.g. Beckwith-Wiedemann syndrome

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

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

Pallor and bleeding

- Anaemia and bleeding in malignancy is due to bone marrow infiltration
- Malignancy associated with anaemia and bleeding include leukaemia, neuroblastoma and lymphoma.

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- Bleeding is usually from the nose or gum, gut or into the skin (petechiae)
- Bleeding is due to thrombocytopenia
- Intracranial bleeding may also occur

Bone and joint pain

- Common in primary and secondary bone tumours
- Bone pain usually wakes children at night
- 20-30% of patients with leukaemia will present with bone pain
- Other malignancies that present with bone pain include neuroblastoma, retinoblastoma, rhabdomyosarcoma and histiocytosis
- Backache in children must be taken seriously and may be due to spinal and vertebral tumours

Lymphadenopathy

- Considered enlarged if > 1 cm
- Most causes are benign and related to infection and inflammation
 - But may be a presenting sign and symptom of leukaemia, lymphoma, neuroblastoma or Kaposi's sarcoma
- Malignant nodes are firm, rubber and non-tender

Unexplained masses

- Mass in any area may be the first clinical sign or symptom of malignancy
- Masses may be a group of nodes or may arise from any organ in the body
- Masses in the abdomen may be renal (nephroblastoma, neuroblastoma) hepatic (hepatoblastoma, hepatocellular carcinoma), pelvic (germ cell tumour, rhabdomyosarcoma, lymphoma)
- Testicular masses are commonly due to leukaemia and rhabdomyosarcoma
- Head and neck masses are commonly due to neuroblastoma, rhabdomyosarcoma, leukaemia and lymphoma
- Mediastinal masses can be life threatening and often due to lymphoma, leukaemia and neuroblastoma

Headache

- Fairly common in children
- Rarely caused by intracranial tumours
- Headache associated with early morning vomiting or coordination difficulties needs to be evaluated urgently

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Changes in the orbit or eye

- Loss of vision and development of a squint are often indicative of a malignant process
- A squint in a child over 3 months may be due to retinoblastoma or neuroblastoma
- A white pupil may be suggestive of retinoblastoma or cataract
- Proptosis may be suggestive of neuroblastoma, lymphoma, leukaemia, rhabdomyosarcoma and extraocular retinoblastoma

Persistent fever and weight loss

- Fever is a common complaint in children and usually due to infection
- Fever that does not respond to routine treatment should arouse suspicion of malignancy
- Lymphoma is the classic malignancy that causes fever and weight loss
- TB and HIV should be considered in the differential diagnosis and be excluded

Who should you refer?

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

What should you do before referral?

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

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

Oncological emergencies

Definition

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

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

Febrile neutropenia

Definition

- Neutropenia is an absolute neutrophil count $< 1500/\text{mL}$
- Severe neutropenia is an absolute count of $< 500/\text{mL}$
- Fever is elevation of a single oral temperature $> 38^\circ$ for over 1 hour or 2 elevations $> 38\%$ degrees Celsius over 12-hour period

Risk Factors

- Advanced malignancy suppressing the bone marrow
- Radiotherapy
- Chemotherapy

Causes

- Bacteria: Streptococcus, Staphylococcus, E. coli, Pseudomonas, Enterobacter Species
- Viruses: Respiratory viruses, Herpes simplex, Varicella zoster
- Fungi: Candida species, Aspergillus, Cryptococcus
- Protozoa: *Pneumocystis jirovecii pneumonia*

Promotion/prevention

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

Signs and Symptoms

- Fever
- Cough
- Diarrhoea
- Mucositis

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Investigations

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

Management

Primary level

Stabilise patients and refer to tertiary

Secondary level

Stabilise patients and refer to tertiary

Tertiary level

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

Manage anaemia and thrombocytopenia

Follow up

- Follow up in haematology-oncology clinic at tertiary level

Tumour lysis syndrome (TLS)

Definition

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

Diagnosis of tumour lysis syndrome

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

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

Risk factors/causes

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

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

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

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	NHL, Neuroblastoma	
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Promotion/prevention

- Anticipate TLS
- Hyperhydration (Crystalloids 3L/m²/day)
- Urine alkalinization
- Diuresis to maintain urine output $\geq 100\text{ml/m}^2/\text{hour}$
- Intermediate to high risk of developing tumour lysis syndrome: prophylactic allopurinol

Signs and symptoms

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

Investigations

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

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Management

Primary level

Discuss with secondary level and refer patient to secondary level

Secondary level

- Identify patients at risk of tumour lysis syndrome
- Stabilise patient
- Start Potassium free IV maintenance fluids (normal saline)

Discuss patient with tertiary level and refer

Tertiary level

Treat hyperuricaemia

- Allopurinol 10mg/kg/day divided in 8 hourly doses PO
- Rasburicase 0.15-0.2mg/kg IV

Hyperhydration

- Potassium free IV fluid - Normal saline 3l/m²/day
- Monitor urine output, aim for urine output 100ml/m²/hour
- If not meeting urine output, give furosemide 1mg/kg to drive diuresis

Monitor and treat electrolyte imbalances

- Monitor electrolytes 4-6 hourly

Hyperkalaemia

- Avoid and stop all exogenous potassium
- Calcium gluconate 0.5ml/kg of 10% solution slow IV
- Nebulised salbutamol
- IV insulin and dextrose
- IV insulin and dextrose
- Kayexalate
- Dialysis

Hyperphosphatemia

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

Hypocalcaemia

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

Indications for renal replacement therapy

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

Follow up

All patients to be followed up in oncology clinic

Spinal cord compression

Definition

Mass compromising the spinal cord, conus medullaris or cauda equina

Risk factors/causes

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

Promotion/prevention

- Early detection of malignancy

Clinical Features

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

Investigations

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

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Management

Primary level

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

Secondary level

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

Tertiary level

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

Follow up

- All patients to be followed up in the oncology clinic

Superior vena cava compression syndrome

Definition

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

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

Risk factors/causes

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

Promotion/prevention

- Early detection and treatment of malignancy

Signs and symptoms

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

Investigations

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

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Management

Primary level

See the secondary-level guidance. Below

Secondary level

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

Tertiary level

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

Consult oncologist for chemotherapy and further management

Follow up

- All patients to be followed up in the oncology clinic

Hyperleukocytosis

Definition

White blood count > 50,000 or 100,000/ μ L

Risk factors/causes

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

Prevention/promotion

- Early detection of malignancy

Signs and symptoms

- Clinical features as a result of leukostasis

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

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Management

Primary level

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

Secondary level

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

Tertiary level

- Maintain airway, breathing, and circulation
- Continue IV normal saline with 5% dextrose at 2 times the patient's maintenance fluid rate
- Administer allopurinol at 10 mg/kg in 3 divided doses or rasburicase at 0.2 mg/kg
- Ensure urine output is between 1-2 ml/kg/hour
- Transfuse platelets at 10 units/kg if platelet count is less than 20,000/mL

Avoid transfusion of packed cells as they can increase blood viscosity

Follow up

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

Wilms tumour (WT)/Nephroblastoma

Definition

Wilms tumour or nephroblastoma is an embryonal tumour of the kidney

Risk factors/causes

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

WT1 related syndromes

- WAGR (Wilms' tumour aniridia genital urinary anomaly, mental retardation)
- Denys-Drash Syndrome

WT2 related syndrome

- Beckwith-Wiedemann syndrome

Other syndromes

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

Prevention/promotion

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

Signs and symptoms

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

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Investigations

- FBC
- Blood pressure measurement
- Urinalysis
- Chest radiography
- Ultrasound of the abdomen
- CT scan of the chest/abdomen
- Coagulation studies (Transient Von Willebrand like syndrome is recognized in 1% of the cases)

Staging

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

Differential diagnosis

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

Management

Primary level

- Appropriate counselling on suspected diagnosis
- Early referral

Secondary level

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

Tertiary level

- Ongoing counselling

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- Definitive treatment: Chemotherapy and surgery +/- radiotherapy

Follow Up

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

Retinoblastoma

Definition

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

Risk factors

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

Prevention/promotion

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

Signs and symptoms

Early

- Leukocoria
- Strabismus (squint)

Late

- Proptosis
- Orbital mass
- Destruction of the eyeball
- Cervical lymphadenopathy
- Bone metastases
- Bone marrow failure
- Seizures due to intra-cerebral disease

Investigations

- FBC
- Urea and electrolytes
- Liver function tests (LFT)
- Bone marrow and cerebral spinal fluid examination (CSF)
- Biopsy of the lesion if feasible

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- Ocular ultrasound- B-scan
- Examination under anaesthesia
- CT or MRI brain
- Slit lamp exam

Note: Always check both eyes

Staging

The international classification of intraocular retinoblastoma grouping system

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

International Retinoblastoma Staging System

STAGE	DESCRIPTION
0	Conservative treatment, eye preserved
I	Eye enucleated, complete resection (See subclassification below)
II	Eye enucleated, microscopic residual (See subclassification below)
III	Regional extension <ul style="list-style-type: none">• Orbit• Preauricular or cervical lymph nodes

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IV	Metastatic disease <ul style="list-style-type: none">• Haematogenous metastasis (without CNS involvement)• CNS extension<ul style="list-style-type: none">• Pre-chiasmatic lesion• CNS mass• Leptomeningeal spread
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Sub-classification of stages I and II

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

Management

Primary level

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

Secondary level

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

Tertiary level

- Counselling on further investigations and treatment
- The primary goal of treatment is to preserve life
- Chemotherapy
- The following drugs are often used: vincristine, etoposide and carboplatin.
- The number of chemotherapy cycles depend on the stage of disease. Early staged disease may require 2-3 cycles. Extraocular disease requires six cycles;

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three are given preoperatively and the remaining three cycles are given postoperatively.

- Palliative chemotherapy may be offered in patients with metastatic disease
- Surgery
- Enucleation is the main surgery in advanced disease. It is done when there is no chance of preserving vision in the affected eye.
- Cryotherapy can be used for small primary anteriorly located tumours
- Photocoagulation can be used as primary therapy for posteriorly located tumours
- Exenteration is considered when the tumour has spread or reoccurred
- Radiotherapy
- External beam radiation therapy: this is considered in tumours with significant vitreous seeding, progression of disease during chemo-reduction and for tumours extending beyond cut margin of optic nerve.
- Radioactive plaques; Use of radioactive rods placed adjacent to the tumours has replaced external beam radiation therapy where it is available

Follow Up

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

Lymphoma

Definition

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

There are two types of lymphoma:

- Hodgkin lymphoma
- Non-Hodgkin lymphoma

Non-Hodgkin lymphoma (NHL)

Aggressive, high grade or rapidly proliferating malignancies originating from mature B or T cells. NHL occurring in childhood and adolescents falls into three categories

- Aggressive mature B cell NHL: Burkitt lymphoma, diffuse large B cell lymphoma and mediastinal B cell lymphoma
- Lymphoblastic lymphoma
- Anaplastic large cell lymphoma

Risk Factors

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

Prevention/promotion

Screening in at risk population

Signs and symptoms

- NHL is characterised by a short history of symptoms with a rapidly growing mass
 - Remember Burkitt lymphoma has doubling time of 24 hours
- Enlarged lymph nodes (>1cm)- (cervical, axillary, abdominal)

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- Jaw swelling
- Abdominal mass
- Paraplegia
- Mediastinal mass +/- pleural effusion
- Superior Vena Cava (SVC) syndrome
- Constitutional symptoms: fever, weight loss
- Signs of tumour lysis syndrome (refer to tumour lysis syndrome section)

St Jude Children's Research Hospital (Murphy) staging

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

Investigations

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

Differential diagnosis

- Tuberculosis
- Neuroblastoma

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- Rhabdomyosarcoma

Management

Primary level

Discuss patient and refer to secondary level

Secondary level

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

Tertiary level

- Treat medical emergencies
- **Mediastinal Masses**
 - Patients are at risk of tracheal compression, SVC syndrome, large pleural and pericardial effusions and right and left ventricular outflow compression.
 - They are at risk of cardiac and/or respiratory arrest if placed in supine position
 - Perform procedures while patient is on their side or prone e.g. Bone Marrow Aspiration and Trehpene biopsy (BMAT), CT scans,
 - Use the least invasive procedure to establish diagnosis e.g. Lymph node biopsy, thoracocentesis, BMAT
- **Treat and/or prevent tumour lysis syndrome**
 - Refer to tumour lysis section
 - Treat or prevent hyperuricaemia
 - Vigorous IV hydration with potassium free fluids
 - Monitor and treat electrolyte imbalances

Spinal cord compression

- Early identification is paramount
 - Dexamethasone 1-2mg/kg IV stat then 0.5mg/kg 6 hourly IV
 - Monitor neurology
 - Give chemotherapy if no improvement in neurology on steroids
-
- Initiate Chemotherapy as per facility protocol
 - Initial pre-phase of low dose chemotherapy
 - Multi agent high dose chemotherapy and CNS directed therapy

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Follow up

- All patients to be followed up in oncology clinic

Sickle cell disease (SCD)

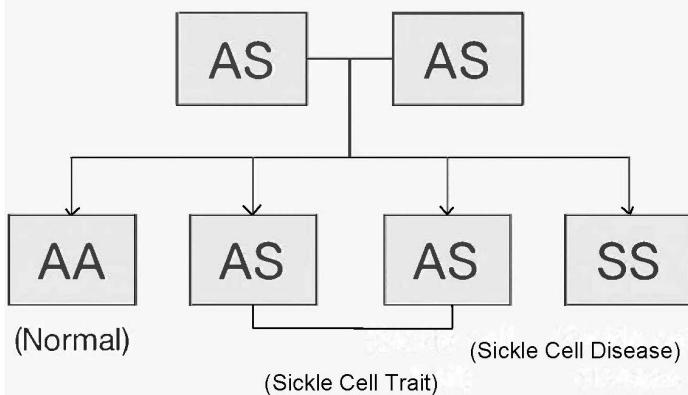
Definition

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

Risk factors

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

Inheritance pattern



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

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Prevention/promotion

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

Signs and symptoms

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

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

Investigations

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

Differential Diagnosis

- Leukaemia
- Thalassemia
- Juvenile arthritis
- Septic arthritis

Management

Sickle cell disease care pillars

- Use of hydroxyurea

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- Infection Prevention
- Folic Acid supplementation
- Blood Transfusions
- Management of acute crises in SCD
- Management of chronic crises in SCD

Primary level

- Manage pain crisis and treat any underlying infections
- Referral for secondary level review

Secondary level

- Use of hydroxyurea

Starting hydroxyurea

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

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

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49-51kg	14	56	168
<ul style="list-style-type: none"> Consider withholding hydroxyurea when: <ul style="list-style-type: none"> HGB <4.0 g/dL ANC < 1.0 x 10⁹/L PLT < 80 x 10⁹ /L Recheck counts every 2 weeks: If, recovery within 2 weeks, start same dose If >2 weeks to recover or history of previous toxicity at same dose, then decrease dose by 5mg/kg Refer to tertiary centre if persistent toxicity to hydroxyurea Hydroxyurea dose escalation <ul style="list-style-type: none"> Firstly, before considering dose escalation check adherence to hydroxyurea A pill count may reveal some adherence issues in addition to a clinical history Secondly, prior to dose escalation do an FBC to ensure that the MCV is $\geq 100\text{fl}$ Dose escalation is indicated in children on HU fixed dose with: <ul style="list-style-type: none"> Cerebral vascular accident (stroke) Any acute chest syndrome (ACS) event in the preceding 24 months More than one previous pain crisis requiring hospital care & admission in the previous 24 months. High conditional ($> 170 \text{ cm/sec}$) or abnormal ($> 200 \text{ cm/sec}$) velocities on transcranial Doppler (TCD) Refer to tertiary centre for hydroxyurea dose escalation Infection prevention Daily Penicillin V is recommended for all children less than 5 years. 			
<p>Alternatives if Penicillin V not available: Amoxicillin - 10 mg/kg/dose BD (max 250 mg BD); Azithromycin - 5 mg/kg once daily (max 250 mg)</p> <ul style="list-style-type: none"> Malaria Prophylaxis: SP monthly for all children and use Chloroquine for those with Sulphur allergy If a SCD patient is noted to have repeated infections, refer to tertiary level Patients to receive all vaccines as per Malawi National EPI schedule. Ideally should also get PCV13 (PCV23 where available), Influenza, Meningococcal, and COVID vaccines Pneumococcal (PCV13) Recommendations: <ul style="list-style-type: none"> Age 2 – 5 years: < 3 PCV doses: Give 2 doses of PCV (8 weeks after the most recent dose and administered 8 weeks apart) Only 3 PCV doses: Give 1 dose of PCV at least 8 weeks after last dose Age 6 -18 years: No history of PCV13: Give 1 dose of PCV13 			

SP dosing table

Weight (kg)	No. of tablets/ month
<10kg	0.5
10 - <20	1
20 -<30	1.5
30 - 45	2
> 45	3

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Penicillin V Dosing Table

Age	Dose
< 3 years old	125mg BD Daily
3-5 years old	250mg BD Daily

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- Nutritional supplementation
- Folic acid: 2.5mg OD
- Iron: Avoid iron therapy unless iron deficiency is documented
- Blood transfusion in sickle cell disease
 - Indications for blood transfusion: Haemoglobin <6g/dL in all patients
 - Haemoglobin 6-8g/dL and/or >2 points below patient's baseline Hb (check health passport) and if the patient has the following:
 - Laboured breathing or impaired consciousness
 - Stroke - aim for Hb of ~10g/dL
 - Note: If stroke and Hb >8g/dL, then perform red cell manual exchange transfusion
 - Acute Chest Syndrome (ACS) with laboured breathing and/or requiring oxygen
 - Aim for a Hb of ~10g/dL
 - Note: If ACS and Hb >8g/dL with laboured breathing, poor oxygenation (O₂ saturation <95%) despite oxygen therapy, and/or escalating oxygen/respiratory support, then perform red cell manual exchange transfusion
 - Acute splenic or hepatic sequestration - aim for Hb of ~8g/dL
 - Before surgery requiring general anaesthesia that is expected to last more than 30-60 minutes - aim for Hb of ~10g/dL
 - Severe complicated malaria
 - Organ failure present (e.g. lungs, liver, kidney, brain, heart)

Safety measures while blood transfusion is running:

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

Pain Crisis

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

Management

- Collect lab samples for FBC & group and crossmatch. Place IV cannula
- Hydration: The aim is to have the patient on 100% maintenance fluids orally and wean IV fluids as able
- If dehydrated, correct appropriately

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Note: hyperhydration can lead to pulmonary compromise

- Give pain medicine as per Faces Score grading for pain
- If in mild to moderate pain, give paracetamol 15mg/kg/dose PO 4-6 hourly or ibuprofen 10mg/kg/ dose PO 6 hourly

If in severe pain, in addition to the paracetamol and ibuprofen, you can give morphine 0.1mg – 0.2mg/kg/dose orally 4 hourly and escalate cautiously.

This is as per WHO analgesic ladder

- Constipation is a common adverse effect of morphine. Stool softeners (liquid paraffin) should be prescribed. The patient should be assessed daily for stooling and constipation regimen escalated as necessary
- Blood transfusion is indicated if Hb is = <6g/dL or 2 points below the patient's normal baseline Hb
- (check in health passport)
- If febrile (defined as >38.5o), see fever guidelines section

Fever

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

Management

Antibiotics

- Treat with antibiotics ceftriaxone 50mg/kg IV every 24 hours
- If very sick treat for 7 to 10 days with antibiotics
- If not improving at 48 hours re-examine patient and refer to tertiary level
- Inpatient hospital admission:
 - Indications:
 - Age less than 6 months or not up to date with immunizations
 - Family lives far from a health facility

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- Temperature > 40°C
- Patient is tachycardic, tachypnoeic, hypotensive, poorly perfused, or drowsy
- WBC >30,000 or <5,000 or if significantly different from patient's baseline
- Hb < 6g/dL or Hb which is 2 g/dL lower than patient's baseline (Check previous Hbs in the health passport or file)
- Previous history of sepsis
- Any concerning signs or symptoms
- Monitor closely as such patients can deteriorate quickly
- Continue ceftriaxone 50mg/kg IV every 24 hours. Malaria treatment if malaria tests positive as per national guidelines
- If in septic shock, needs a minimum of every 30 min observations (heart rate, pulse rate, O₂ saturation, blood pressure, GCS) until the patient stabilises.
- Give IV fluid bolus of 10ml/kg and re-evaluate in 15 min, repeat x 2 (total of 30ml/kg) within 1 hour or until BP/HR stabilise
- If vital signs are stable on admission, then check vital signs (heart rate, pulse rate, O₂ saturation, blood pressure) 1 hour after the first dose of antibiotics given, and every 6 hours for the first 48 hours
- Start O₂ therapy if increasing RR or O₂ saturation <92% (see Acute Chest section)
- Hydration: The aim is to have the patient on 100% maintenance fluids; orally and wean IV fluids as able. If dehydrated, correct appropriately. Pre-hydration can lead to pulmonary compromise.
- Blood transfusion is indicated if Hb is = <6g/dL or 2 points below baseline the patient's normal baseline Hb (check-in health passport)

Management

- If requiring oxygen or increased work of breathing, admit patient as it is life threatening and patients can decompensate quickly. Place on a monitor.
- Collect samples for FBC, malaria test (if febrile), creatinine, group and crossmatch
- Obtain chest X-ray
- Continuous monitoring of vital signs- heart rate, respiratory rate and oxygen saturations
 - If O₂ saturations <95% on room air, administer supplemental O₂ and consider blood transfusion (see below)
 - Aim for oxygen saturations > 95%. If low oxygenation, then refer
- Simple blood transfusion if Hb <=6g/dL in all patients with ACS. If laboured breathing is present or the patient is requiring oxygen then give a simple blood transfusion for Hb <=8g/dL, with goal of 10g/dL.

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- If Hb is >8g/dL and persistent respiratory insufficiency despite oxygen therapy. Refer to tertiary level
- Initiate antibiotics with ceftriaxone IV 50mg/kg every 24 hours PLUS an oral macrolide such as azithromycin (10mg/kg OD on day 1 followed by 5mg/kg on days 2-5 days; or 10mg/kg OD for 3 days)
- Pain relief as appropriate (See Pain section)
- Hydration with caution: The aim is to have the patient on 75% maintenance (oral + IV fluids). If tolerating oral fluids can give all fluids orally.
 - If one needs to support with IV fluids consider adding 5% dextrose if limited oral intake. Use of an infusion pump is preferred when giving IV fluids
 - Encourage oral fluid intake and wean IV fluids as able
 - If dehydrated, correct appropriately in discussion with a senior colleague
 - Note that hyperhydration can be detrimental in SCD and can lead to pulmonary oedema and respiratory decompensation
 - Give furosemide if signs/symptoms for fluid overload and/or pulmonary oedema
- Start chest physiotherapy.

Splenic Sequestration

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

Management

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

Refer to tertiary level as soon as patient has been stabilised

Stroke

Stroke in children with SCD is defined as the occurrence of any new neurological

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symptoms in a patient with SCD. It could also be the presentation of a new diagnosis of SCD.

Management

- Stabilise Airway Breathing Circulation Coma Convulsions (ABCCC) approach.
- Blood sample for labs: rapid bedside glucose. FBC, U&Es including creatinine, LFTs, group and cross-match.
- If fever, obtain blood culture (and malaria test and initiate ceftriaxone 50mg/kg IV (Refer to Fever section).

Refer to tertiary level once stabilised

- Oxygen therapy should be initiated to ensure oxygen saturations of >95% (If hypoxia present, refer to Acute Chest Syndrome Section).
- The treatment for stroke in SCD is a simple whole blood transfusion of 20ml/kg, if haemoglobin = <8 g/dL or manual red cell exchange transfusion if Hb >8 g/dL.
 - This should be performed as soon as possible and preferably within 6 hours of recognition of acute neurological symptoms.
 - Simple transfusion should be performed with a goal of an Hb of 10 g/dL.
- Hydration with caution: The aim is to have the patient on 75% maintenance oral + IV fluids.
 - This can be all orally if tolerated or as IV fluids 0.9% normal saline (consider adding 5% dextrose if limited oral intake) if necessary.
 - Encourage oral fluid intake and wean IV fluids as able.
 - If dehydrated, correct appropriately.
 - Note that hyperhydration can be detrimental in SCD and can lead to cerebral oedema.
 - Use of an infusion pump is preferred when giving IV fluids.

For long term management of stroke, priapism and transient red cell aplasia refer to tertiary level for continued management.

Management of chronic complications and end-organ damage of SCD - Refer to tertiary level.

Tertiary level

Use of hydroxyurea

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

Infection prevention- Refer to secondary level

Nutritional supplementation- Refer to secondary level

Blood transfusions- Refer to secondary level

Management of acute complications

Pain Crisis

- Refer to secondary level guidelines
- If localised pain not improving after 48-72 hours of analgesics and there is a concern for osteomyelitis, consider imaging of affected limb

Note that x-ray changes associated with osteomyelitis may take 10-14 days to appear)

- If persistent localised signs and symptoms raising concern for osteomyelitis or septic arthritis, obtain a blood culture, start ceftriaxone (per fever protocol), and add cloxacillin or clindamycin
- **A painful crisis without fever does not require antibiotics.**

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- Blood transfusion is not indicated in the management of uncomplicated pain episodes. It is indicated if Hb is = <6g/dL or 2 below baseline the patient's normal baseline Hb (check in health passport).
- All patients should be encouraged to mobilise and to do incentive spirometry to prevent the development of acute chest syndrome. Ensure the head of the bed is elevated at all times. Where possible involve the physiotherapy team in the management of all SCD patients.
- At discharge ensure that the patient receives counselling on avoiding the triggers of vaso-occlusive crisis such as keeping warm, and continuing to have good oral intake so as to ensure good hydration. Additionally, supply the patient with 48 – 72 hours supply of pain medication. Always consult the paediatric oncology team prior to discharge and organise follow up

Fever

- Refer to secondary level guidelines

Acute chest syndrome

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

Splenic sequestration

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

Signs and symptoms

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

Immediate action

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

Management

- If febrile, obtain blood culture and Malaria test. Give broad spectrum antibiotics with ceftriaxone 50mg/kg IV every 24 hours (Refer to fever section).
- **Immediate** blood transfusion with packed red cells 10cc/kg or whole blood 20cc/kg to be given over 3-4 hours to a goal Hb of 8 g/dL.
 - Care must be given not to over-transfuse as subsequent release of pooled blood from spleen to the circulation can lead to hyper viscosity
 - Check Hb 4-6 hours after transfusion. Repeat transfusion as appropriate.
- Monitor spleen size for the first 12-24 hours until it is seen to be reducing in size
- Give supportive oxygen therapy if O₂ saturation <95%
- At discharge ensure that the patient receives counselling. Always consult the oncology team prior to discharge and organise follow up

Stroke

- Admit patient to **high dependency unit/ resuscitation**. Airway Breathing Circulation Coma Convulsions (ABC₃C) approach. Call the on-call consultant and haematologist consultant.
- Blood Sample for labs: Rapid bedside glucose, FBC, U&Es including creatinine, LFTs, group and cross-match
- If fever, obtain blood culture (obtain prior to first dose of antibiotics, but do not delay initiation of antibiotics >30 min) and malaria test and initiate ceftriaxone 50mg/kg IV (Refer to Fever section).
- **Oxygen therapy** should be initiated to ensure oxygen saturations of >95% (If hypoxia present, refer to Acute Chest Syndrome Section).
- The treatment for stroke in SCD is a simple whole blood transfusion of 20ml/kg, if haemoglobin = <8 g/dL or manual red cell exchange transfusion if Hb >8 g/dL. This should be

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

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to 35mg/kg/day as per the guidelines of dose escalation of hydroxyurea)

- Annual TCD screening to assess for risk of recurrence

Priapism

- Priapism is a prolonged and painful penile erection, often not associated with sexual stimulation. Male children, especially adolescents, with SCD should be made aware of this and advised to inform parents/doctors as it can lead to impotence if left untreated. It can also be triggered by sexual activity or a full bladder

Signs and symptoms

- Assessment: Clinically assess whether the patient has urinary retention and whether or not the glans penis is soft or turgid. This determines treatment

Management

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

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phenylephrine, and washout might be necessary. If these procedures fail to relieve the priapism, a shunting procedure will be necessary by urology

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

Follow up

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

Anaemia

Definition

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

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

Normal values of the red series according to age and gender (various sources)				
Age		Hb (g/dl)	Hct (%)	MCV (fl)
1-3 days		19.5 (14.5-23.5)	58 (45-72)	98-118
7 days		17.5 (14-22)	55 (43-67)	88-126
14 days		16.5 (13-20)	50 (42-66)	86-119
1 month		14 (10-18)	43 (31-51)	85-123
2 months		11.5 (9-14)	35 (28-42)	77-118
3-12 months		11.5 (9.5-13.5)	35 (29-41)	74-108
12-24 months		12.5 (11-14)	37 (32-42)	71-89
2-3 years		12.6 (11-14.2)	37 (33-41)	74-89
4-6 years		12.9 (11.7-14.1)	38 (34-42)	77-91
7-10 years		13.5 (12-15)	40 (35-45)	78-91
11-14 years	Female	13.7 (12.3-15.1)	40 (36-44)	80-94
	Male	14.3 (12.6-16)	46 (40-52)	80-94
15-18 years	Female	13.7 (11.5-15.9)	40 (34-46)	81-96

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	Male	15.4 (13.7-17.1)	46 (40-52)	81-96
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- Anaemia can be an isolated abnormality or be a part of multiple cell line abnormalities (red cells, white cells, and platelets). Abnormalities of two- or three-cell lines may indicate one of the following:
 - Bone marrow involvement (e.g. infections, aplastic anaemia, leukaemia, toxicity from medications)
 - Autoimmune disorders (e.g. connective tissue disease, evans syndrome)
 - Sequestration (e.g. hypersplenism) or intravascular trapping and destruction (e.g. thrombotic microangiopathy)

Risk factors

- Worldwide the most common cause of anaemia is iron deficiency
- Causes of anaemia in children vary based upon age at presentation and sex
- Age

Birth to three months

- The most common cause of anaemia in young infants is "physiologic anaemia," which occurs at approximately six to nine weeks of age
- Pathologic anaemia in newborns and young infants is distinguished from physiological anaemia by any of the following:
 - Anaemia (Hb <13.5 g/dL) within the first month of life
 - Anaemia with lower Hgb level that is typically seen with physiological anaemia (e.g. <9 g/dL)
 - Signs of haemolysis (e.g. jaundice, scleral icterus, or dark urine) or symptoms of anaemia (e.g. irritability or poor feeding) to immature liver function
 - Prematurity

Infants: three to six months

- Anaemia detected at three to six months of age suggests a haemoglobinopathy.
- Nutritional iron deficiency is an unlikely cause of anaemia before the age of six months in term infants

Toddlers, children and adolescents

- In toddlers, older children and adolescents, acquired causes of anaemia are more likely, particularly iron deficiency anaemia
- Sex:

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- Some inherited causes of anaemia are X-linked (e.g. G6PD deficiency and X-linked sideroblastic anaemia) and occur most commonly in males
- In postmenarchal girls, excessive menstrual bleeding is an important cause of anaemia, and clinicians should suspect and evaluate for an underlying bleeding disorder

Prevention/promotion

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

Signs and symptoms

- Symptoms attributable to anaemia – common symptoms of anaemia include:
 - Lethargy
 - Tachycardia
 - Pallor
 - Infants may present with irritability and poor oral intake
- However, because of the body's compensatory abilities, patients with chronic anaemia may have few or no symptoms compared with those with acute anaemia at comparable haemoglobin (Hb) levels
- Symptoms of haemolysis – Changes in urine colour, scleral icterus, or jaundice may indicate the presence of a haemolytic disorder
- Bloody stools, haematemesis, severe epistaxis, or severe menstrual bleeding suggest anaemia from blood loss and/or iron deficiency
- Pica – The presence of pica, the intense craving for non-food items, should be assessed given its strong association with iron deficiency
- Infectious symptoms (e.g. fevers, cough) suggest an infectious aetiology of anaemia
- Prior episodes of anaemia suggest an inherited disorder
- Anaemia in a patient with previously documented normal FBC suggests an acquired aetiology
- Hyperbilirubinemia in the new-born period suggests a haemolytic aetiology; microcytosis at birth suggests chronic intrauterine blood loss or thalassaemia
- Underlying renal disease, malignancy, or inflammatory/autoimmune disorders may be associated with anaemia
- Anaemia following exposure to oxidant drugs or fava beans suggests G6PD

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deficiency

- Exposure to paint, home renovations, or use of imported or glazed ceramics suggest lead toxicity
- Family members with jaundice, gallstones, or splenomegaly suggests an inherited haemolytic anaemia
- In infants and young children, iron deficiency is suggested by the following:
 - Use of low iron formula
 - Introduction of unmodified cow's milk before the age of 1 year
 - Excessive milk intake (>24 ounces per day)
 - Poor intake of iron-rich foods (meats or fortified infant cereal)
- Developmental delay is associated with iron deficiency, vitamin B12/folic acid deficiency and Fanconi anaemia
- Hyperpigmentation
- Petechiae, purpura
- Jaundice
- Ulcers on lower extremities
- Frontal bossing, prominence of the malar and maxillary bones
- Glossitis
- Angular stomatitis
- Splenomegaly

Investigations

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

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Diagnosis

Anaemia classification according to MCV and reticulocytosis		
	Regenerative (RPI \geq 3)	Aregenerative (RPI < 2)
Microcytic*	<ul style="list-style-type: none">Iron deficiency anaemia under treatmentCongenital or corpuscular haemolytic anaemias (spherocytosis, thalassemia, sickle cell disease)	<ul style="list-style-type: none">Iron deficiency anaemiaChronic infection / inflammationLead poisoning
Normocytic *	<ul style="list-style-type: none">Extra corpuscular haemolytic anaemia (hypersplenism, microangiopathy, drugs, infections)Corpuscular haemolytic anaemiaAcute bleeding	<ul style="list-style-type: none">Medullary aplasiaSpinal infiltrationAplastic crisis or transient erythroblastopenia in corpuscular haemolytic anaemiaInfectious anaemiaChronic kidney disease
Macrocytic*	<ul style="list-style-type: none">Haemolytic crisis in AIHA with marked reticulocytosis	<ul style="list-style-type: none">Folic acid or vitamin B12 deficiencyFanconi anaemiaDiamond–Blackfan anaemiaLiver diseaseMyelodysplastic syndromeSideroblastic anaemiaHypothyroidism

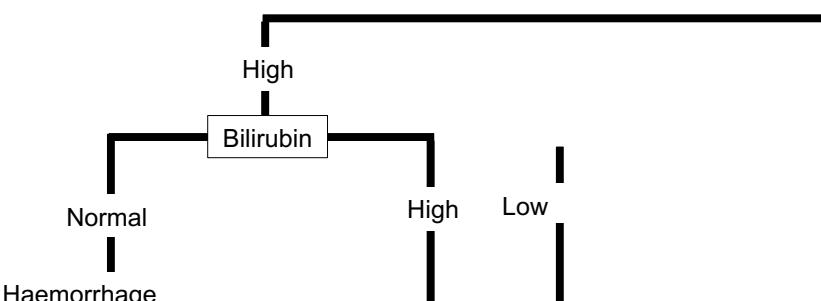
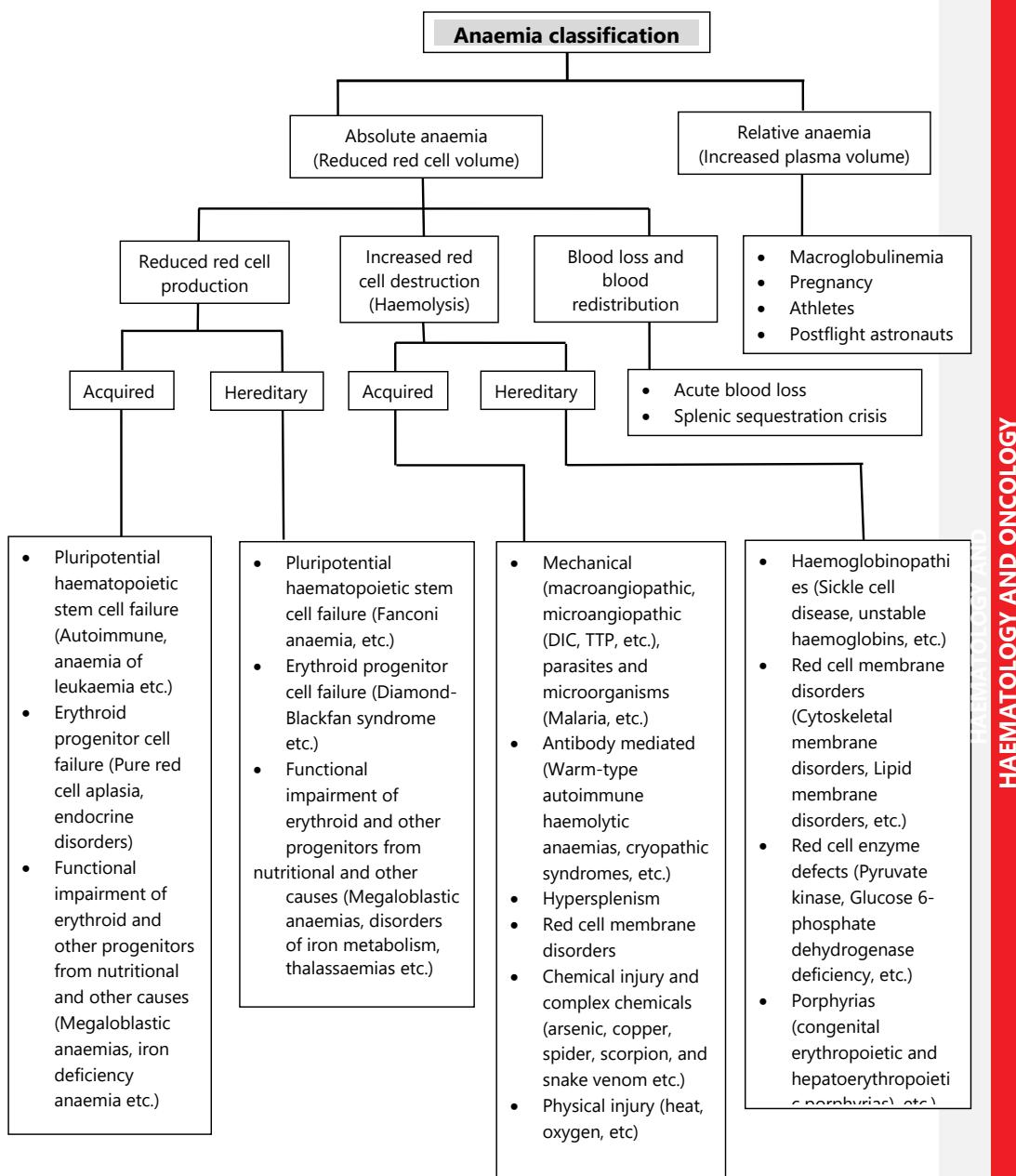
*Always adjust MCV according to age and sex for each patient.

AIHA: Autoimmune haemolytic anaemia

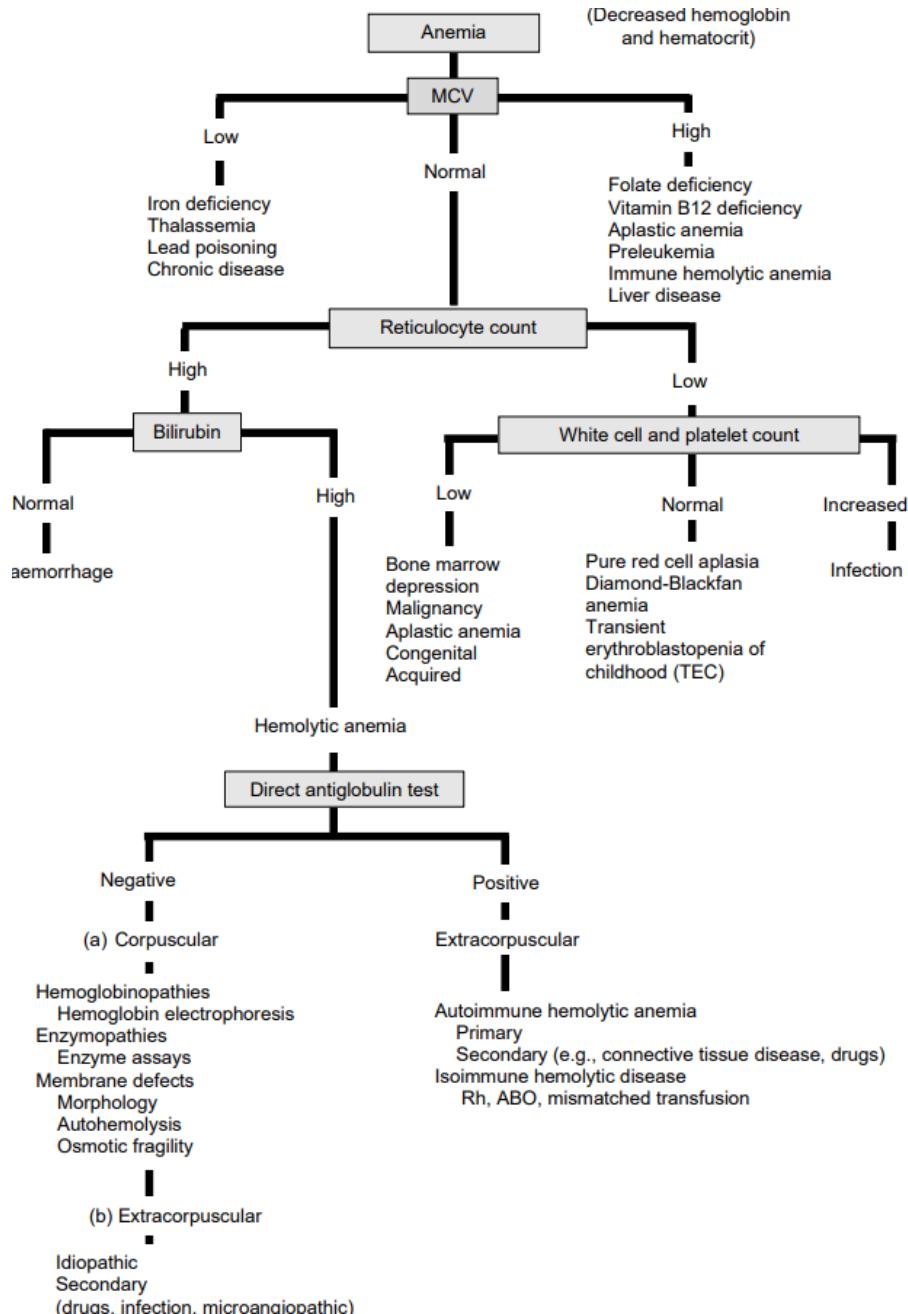
Adapted from: *San Roman S, Mozo Y, 2017*

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Pathologic Classification of Anaemia



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Management

Primary level

- Supportive management
- Treat any underlying infections or parasites
- Referral for secondary level review

Secondary level

Non-severe anaemia

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

Severe anaemia

- Give a blood transfusion as soon as possible (see below) to:
- All children with an Hct of \leq 12% or Hb of \leq 4 g/dl
- Less severely anaemic children (Hct, 13–18%; Hb, 4–6 g/dl) with any of the following clinical features:
 - Clinically detectable dehydration
 - Shock
 - Impaired consciousness
 - Heart failure
 - Deep, laboured breathing
 - Very high malaria parasitaemia (> 10% of red cells with parasites).
- If packed cells are available, give 10 ml/kg over 3–4 hour in preference to whole blood. If not available, give fresh whole blood (20 ml/kg) over 3–4 h.
- Check the respiratory rate and pulse rate every 15 min. If either rises or there is other evidence of heart failure, such as basal lung crepitations, enlarged liver or raised jugular venous pressure, transfuse more slowly. If there is any evidence of fluid overload due to the blood transfusion, give IV furosemide at

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- 1–2 mg/kg, up to a maximum total of 20 mg.
- After the transfusion, if the Hb remains as low as before, repeat the transfusion.
 - In children with severe acute malnutrition, fluid overload is a common and serious complication. Give packed cells when available or whole blood at 10 ml/kg (rather than 20 ml/kg), and do not repeat transfusion based on the Hb level, or within 4 days of transfusion
 - If the cause is unknown, do a PBF for microscopy
 - Treat the cause!

Iron deficiency anaemia

- If female and menorrhagia identified, refer for gynae evaluation
- If occult bleeding identified, refer for GI evaluation
- Following diagnosis, treat with oral iron supplementation - ferrous sulphate, ferrous gluconate or liquid iron preparations.
- Refer to tertiary centre if there is intolerant response or sub-optimal response to oral iron after 6-8 weeks

Sickle Cell Disease- see SCD guidelines

Refer to tertiary level if:

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

Sickle Cell Disease- see SCD guidelines

Refer to tertiary level if:

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

Tertiary level

Non-severe anaemia

- Young children (aged < 6 years) are anaemic if their Hb is < 9.3 g/dl (approximately equivalent to an Hct of < 27%).

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- If anaemia is present, begin treatment, unless the child has severe acute malnutrition
 - Give (home) treatment with iron (daily iron-folate tablet or dose of iron syrup) for 14 days.
 - Ask the parent to return with the child in 14 days. Treat for 3 months, when possible, as it takes 2–4 weeks to correct anaemia and 1–3 months to build up iron stores.
 - If the child is \geq 1 year and has not received mebendazole in the previous 6 months, give one dose of mebendazole (500 mg) for possible hookworm or whipworm infestation.
 - Advise the mother about good feeding practice.

Severe anaemia

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

Iron deficiency anaemia

- If female and menorrhagia identified, refer for Gyn evaluation
- If occult bleeding identified, refer for GI evaluation
- Following diagnosis, treat with oral iron supplementation - ferrous sulphate, ferrous gluconate or liquid iron preparations

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- Refer to tertiary centre if there is intolerant response or sub-optimal response to oral iron after 6-8 weeks

Sickle Cell Disease - see SC guidelines Neonatal anaemia

Haemorrhage: acute or chronic:

- Blood loss may occur during the prenatal, intrapartum, or postnatal periods
- Prenatal blood loss may be transplacental, intraplacental, or retroplacental or may be due
 - to a twin-to-twin transfusion.
- The clinical and laboratory manifestations of haemorrhage depend on the volume of the haemorrhage and the rapidity with which it occurs.
- Clinical Findings
 - Anaemia—pallor, tachycardia, and hypotension (if severe, e.g. 20 mL/kg blood loss). Nonimmune hydrops can occur in severe anaemia
 - Liver and spleen not enlarged (except in chronic transplacental bleed)
 - Jaundice absent (except after several days in entrapped haemorrhage)

Laboratory findings:

- Reduced haemoglobin (as low as 2 g/dl)
- Increased reticulocyte count
- Polychromatophilia,
- Nucleated RBCs are raised
- Foetal cells in maternal blood (in foetomaternal bleed), and direct antiglobulin test (DAT) negative

Treatment

- Severely affected
 - Transfusion of packed Red Blood Cells
 - Crossmatch blood with the mother. If unavailable, use group O Rh-negative blood or intravenous fluids, temporarily for shock, while awaiting available blood
- Mild anaemia due to chronic blood loss
 - Ferrous sulphate (4-6 mg elemental iron/kg body weight per day) for 3 months
 - Haemolysis:
 - Congenital haemolytic anaemias or due to immune haemolytic anaemias
 - Refer to neonatologist and hematologist

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Hypoplasia:

- Failure of red cell production in inherited bone marrow failure syndromes, for example, Diamond–Blackfan anaemia (pure red cell aplasia) (see bone marrow failure syndromes below)

Congenital infections:

- Refer to neonatologist
- Test for syphilis in mother and child

Aplastic anaemia

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

Inherited bone marrow failure syndromes

- The key shared clinical manifestations of IBMFs are as follows:
 - Bone marrow failure
 - Congenital anomalies
 - Cancer predisposition
- Refer to haematologist

Other Haemolytic Anaemias

Refer to Haematologist

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Follow up

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

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Blood transfusion

Storage of blood

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

Problems in blood transfusion

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

Indications for blood transfusion

There are five general indications for blood transfusion:

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

Giving a blood transfusion

Before transfusion, check that:

- The blood is the correct group, and the patient's name and number are on both the label and the form (in an emergency, reduce the risk for incompatibility or transfusion reactions by cross-matching group-specific blood or giving O-negative blood if available)
- The blood transfusion bag has no leaks
- The blood pack has not been out of the refrigerator for more than 2 hours, the plasma is not pink nor has large clots, and the red cells do not look purple or black
- The child has no signs of heart failure. If present, give 1 mg/kg of furosemide
- IV at the start of the transfusion to children whose circulating blood volume

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- Is normal. Do not inject into the blood pack
- Make baseline recordings of the child's temperature, respiratory rate and pulse rate
- The volume of whole blood transfused should initially be 20 ml/kg, given over 3–4 hours

During transfusion, check that:

- If available, use an infusion device to control the rate of transfusion
- Check that the blood is flowing at the correct speed
- Look for signs of a transfusion reaction (see below), particularly carefully in the first 15 min of transfusion
- Record the child's general appearance, temperature, pulse and respiratory rate every 30 minutes
- Record the times the transfusion was started and ended, the volume of blood transfused and any reactions

After transfusion, check that:

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

Transfusion reactions

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

Management of transfusion reactions according to severity level of signs and symptoms

	Sign and symptoms	Management
Mild reaction	<ul style="list-style-type: none"> • Itchy rash 	<ul style="list-style-type: none"> • Slow the transfusion • Give chlorphenamine at 0.1 mg/kg IM, if available • Continue the transfusion at the normal rate if there is no progression of symptoms after 30 minutes • If the symptoms persist, treat as a moderately severe reaction (see below) • Moderately severe reaction (due to

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		moderate hypersensitivity, non-haemolytic reactions, pyrogens or bacterial contamination)
Moderate reaction	<ul style="list-style-type: none"> Severe itchy rash (urticaria) Flushing Fever $> 38^{\circ}\text{C}$ ($> 100.4^{\circ}\text{F}$) (Note: fever may have been present before the transfusion.) Rigor Restlessness Raised heart rate 	<ul style="list-style-type: none"> Stop the transfusion, remove the IV line but not the cannula. Set up a new infusion with normal saline. Give 200 mg hydrocortisone IV or 0.25 mg/kg and chlorphenamine IM, if available. Give a bronchodilator if wheezing (see respiratory section) Send the following to the blood bank: the blood-giving set that was used, a blood sample from another body site and urine samples collected over 24 h. If there is improvement, restart the transfusion slowly with new blood and observe carefully. If there is no improvement in 15 min, treat as a life-threatening reaction (see below), and report to the senior doctor in charge and to the blood bank Life-threatening reaction (due to haemolysis, bacterial contamination and septic shock, fluid overload or anaphylaxis)
Severe reaction	<ul style="list-style-type: none"> Fever $> 38^{\circ}\text{C}$ ($> 100.4^{\circ}\text{F}$) (Note: Fever may have been present before the transfusion.) Rigour Restlessness Raised heart rate Fast breathing Black or dark-red urine (haemoglobinuria) Unexplained 	<ul style="list-style-type: none"> Stop the transfusion, take out the IV line, but keep in the cannula. Set up an IV infusion with normal saline. Maintain airway and give oxygen (see emergency section). Give adrenaline 0.15 ml of 1:1000 solution IM. Treat shock (see GIT section). Give 200 mg hydrocortisone IV or chlorphenamine 0.1 mg/kg IM, if available. Give a bronchodilator, if there is wheezing. Report to the senior doctor in charge and

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	<p>bleeding</p> <ul style="list-style-type: none">• Confusion• Collapse• Note that in an unconscious child, uncontrolled bleeding or shock may be the only signs of a life-threatening reaction.	<p>to the blood laboratory as soon as possible.</p> <ul style="list-style-type: none">• Maintain renal blood flow with IV furosemide at 1 mg/kg.• Give antibiotics as for septicaemia
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Chapter 12: Pulmonology

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