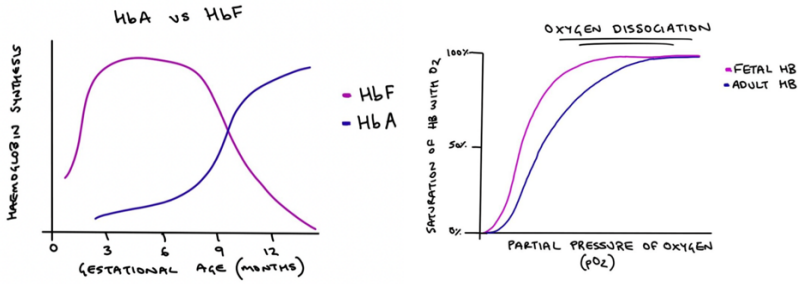
PAEDIATRIC HAEMATOLOGY

	Fetal haemoglobin (HbF)	Adult haemoglobin (HbA
Composition	2 alpha + 2 gamma units	2 alpha + 2 beta units
O2 affinity	Higher	Lower
Highest concentration	Embryo to 32 weeks	> 32-36 wks GA



Why is fetal Hb protective against sickle cell disease?

- Sickle cell disease – abnormal genetic coding of beta subunit
- Fetal Hb has NO beta subunits, hence has NO sickling or red blood cells
- Administer **hydroxycarbamide** to increase HbF production in sickle cell patients to prevent complications such as acute chest syndrome and sickle cell crisis

PAEDIATRIC ANAEMIA: *Refer to adult haematology section:*

Anaemia in infancy

Physiological anaemia:
- Main cause
- Normal Hb drop in 6-9 wks of age
- Due to high Hb at birth causing negative feedback – EPO production is suppressed leading to reduced Hb production by bone marrow

Other causes
- **Anaemia of prematurity**
  - **Reduced in-utero time to receive Fe from mother**
  - RBC production cannot maintain rapid growth in first few weeks
  - Reduced EPO levels
  - **Blood tests** remove circulating volume
- **Blood loss**
- **Haemolysis**
  - Heamolytic disease of newborn (ABO incomp., Rh disease)
  - Hereditary spherocytosis
  - G6PD def
- **Twin-twin transfusion**

Anaemia in older children

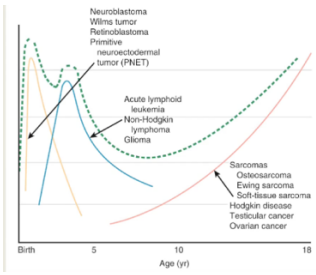
Microcytic causes:
- Thalessemia
- Anaemia of chronic disaes
- Iron def. anaemia
- Lead poisoning
- Sideroblastic anaemia

Normocytic anaemia (3 A's, 2 H's)
- Acute blood loss
- Anaemia of chronic disease
- Aplastic anaemia
- Haemolytic anaemia
- Hypothyroidism

Macrocytic anaemia
- B12 or folate def.
- Pernicious anaemia
- Alcohol
- Reticulocytosis
- Drugs (e.g azathioprine)
- Hypothyroidism
- Liver disease

	Thalessemia	Hereditary spherocytosis	G6PD deficiency
PP	➢ Genetic defect in protein chains of Hb ➢ Autosomal recessive	Spherically shaped RBC – makes them fragile and easily destroyed ➢ Autosomal dominant	Defect in G6PD enzyme ➢ X-linked recessive ➢ No cell protection from ROS causing haemolysis
RF	➢ Consanguineous parents	➢ Northern Europeans	➢ Males ➢ Triggers = infections, meds, fava beans, naphthalene
Sx	• XS damaged RBC → **Splenomegaly** • Bone marrow expansion to compensate → **pronounced forehead and malar eminences** • Anaemia Sx – pallor, fatigue, FTT	• **Pathological jaundice** • **Anaemia** • Gallstones • Splenomegaly	• **Pathological jaundice** • **Anaemia** • Gallstones ➢ Splenomegaly
Comp.	➢ Gallstones → Jaundice ➢ Fe overload (mimics haemochromatosis Sx)	• Haemolytic crisis (post-infection) • Aplastic crisis	➢
Ix	➢ FBC/MCV – microcytic anaemia ➢ HB electrophoresis ➢ Serum ferretin ➢ DNA testing	Clinical Dx – FHx and clinical features ➢ FBC + blood film ➢ MCHC – raised ➢ Haemolytic screen – raised reticulocytes	➢ FBC ➢ blood film (Heinz bodies – denatured Hb "inclusions") ➢ G6PD assay
Mx	Issue / Mx **a-thalassemia (Chr 16)**: • Monitor FBC & comp. • Blood transfusions • Splenectomy • BMT (Curative intent) **beta-thalassemia minor (Chr 11)** One abnormal + one normal gene: ➢ Microcytic anaemia ➢ NO active Rx **beta-thalassemia intermedia** (Chr 11) One defective + one delete gene OR both defective: ➢ Sig. Microcytic anaemia ➢ Blood transfusion ➢ +/- Fe chelation **beta-thalassemia major (Chr 11)** NO functional genes: ➢ Severe anaemia + FTT ➢ Splenomegaly ➢ Bone deformities ➢ Regular blood transfusions, Fe chelation, splenectomy ➢ BMT (curative intent)	➢ Folate supplementation ➢ Splenectomy **Manage complications** ➢ Cholecystectomy for gallstones ➢ Transfusions for aplastic or haemolytic crisis **WHAT IS APLASTIC CRISIS?** ➢ Normally bone marrow produces RBC in response to heamolysis (seen through raised reticulocytes) ➢ **Aplastic crisis** – NO reticulocytes in response to haemolysis – worsening heamolysis and jaundice	*Avoid triggers* ➢ *fava beans* ➢ *moth balls* ➢ *certain meds)* ○ ***primaquine*** *(antimalarial)* ○ ***ABx*** *(cipro, trimeth, nitro)* ○ ***Sulfur phased drugs*** *(sulfonylureas, sulfasalazine)*

PAEDIATRIC RARE DISEASES

	Leukemia	ITP	Sickle cell anaemia	Childhood tumours
PP	➢ Unregulated proliferation of specific cell line (myeloid or lymphoid) Main types include: ➢ **ALL > AML > CML** [Alphabetical order] ➢ **ALL -** 2-3 years old ➢ **AML -** < 2 years old	• Idiopathic thrombocytopenia causing non-blanching purpuric rash • Type 2 hypersensitivity reaction - IgG autoantibodies taret plts	➢ **Autosomal recessive** [abnormal gene for B-globin in chr 11] ➢ **Sickle shaped RBC** – more vulnerable to haemolysis	• Mainly primary CNS tumours • **Most cancers** = primary • **Inherited** = NF1, li-fraumelli (p53), turcot syndrome (APC)
RF	**AML - Radiation exposure during pregnancy** **Genetic syndromes:** ➢ Down's – **AML/ALL** ➢ Klinefelter's ➢ Noonan syndrome ➢ Fanconi's anaemia	**Primary ITP** ➢ Idiopathic (post-viral) **Secondary ITP** ➢ SLE, lymphoma, HIV, HCV	➢ Consanguineous parents ➢ Africans (evolutionary trait)	 CNS brain tumours (gliomas) ➢ **Signs of Raised ICP** (headache, N/V, vision, changes, ➢ **Cushing's triad** (widened PP, irregular RR and bradycardia) Retinoblastoma ➢ Dx on newborn check (loss of red eye reflex) ➢ < 5yo = RB1 mutant (poor survival rate) ➢ Strabismus and impaired vision ➢ **Rx: radiotherapy** Sarcomas (CT tumour) ➢ **Osteosarcoma** = "sun-burst" appearance in areas of max growth (prox. Humerus and bone) ➢ **Ewing sarcoma** = "onion" on axial skeleton ➢ **Rx: induction chemo +/- curative surgery** Neuroblastoma ➢ **Tumour of neural crest cells** (SNS chain and adrenal) ➢ 18/12 old ➢ Fixed firm abdo mass ➢ **Rx: neoadjuvant chemo + surgery** Nephroblastoma (Wilm's tumour) ➢ **Most common RENAL malignancy** ➢ Assoc. w/ beckwith, Sotos, WAGR ➢ 2-3 yo ➢ Asymptomatic firm abdo mass ➢ **Rx: Nephrectomy and chemo (90% cure rate)**
Sx	**Systemic Sx** ➢ Unexplained Fever, UWL, NS ➢ Generalised LN ➢ FTT **Anaemia Sx** • Persistent Fatigue • SOB • Palpitations **Thrombocytopenia sx** • Easy bruising / bleeding • petechiae **Leucopenia Sx** • Recurrent infection	Within 24-48 hrs • Unexplained bleeding (epistaxis, gum bleeds, menorrhagia) • Bruising • Petechial or purpuric rash **DDx:** ➢ TTP ➢ HIT	**Asymptomatic** ➢ If carriers (i.e. sickle cell trait) **Protective against malaria** ➢ Having single copy of mutant gene – less likely to infect sickle shaped RBC	
Comp.	Death w/o treatment **Complications of chemotherapy** ➢ Failure to cure ➢ Tumour lysis syndrome → febrile neutropenia ➢ Stunted growth and development ➢ Secondary malignancy ➢ Neurotoxicity ➢ Infertility ➢ Cardiotoxicity	• Chronic ITP • Anaemia • ICH – SAH • GI bleeding (melaena or PR bleed)	➢ **Anaemia** ➢ Increased infection risk ➢ Stroke ➢ **Avascular necrosis (**large joints e.g hip) ➢ **PHTN** ➢ **Priapism –** painful, persistent penile erection (**vaso-occlusive crisis)** ➢ **CKD** ➢ **Sickle cell crisis** ➢ **Acute chest syndrome**	
Ix	➢ FBC – cell line affected? ➢ Blood film - ?blasts ➢ EUC, LFT, CRP, Urate – **lysis screen** ➢ Bone marrow biopsy For staging ➢ CXR ➢ CT ➢ LP ➢ Gnetic analysis and immunophenotyping of abnormal cells	➢ **FBC – check plts** ➢ **Baseline EUC, LFT** ➢ CRP	➢ **Newborn blood spot test** ➢ **FBC** o **Raised HCT – Vaso-occlusive crisis** ➢ **Blood film**	
Mx	MDT approach ➢ Paediatric oncologist Main stay of Rx (curative intent) ➢ Chemotherapy ➢ RT ➢ Bone marrow transplant ➢ Surgery – remove secondary mets **CHEMO DRUG REGIME** ➢ ALL = vincrtisine, MTX, glucocorticoids, mercaptopurine ➢ AML = anthracyclines, cytarabine **GOALS OF THERAPY** 1. Induction – sig. reduce tumour cell number 2. Consolidation – destroy remaining tumour cells 3. Maintenance – maintain remission with low dose regime	**Conservative** ➢ Avoid contact sports ➢ Avoid IM injections ➢ Avoid blood thinners (e.g. NSAID, aspirin) ➢ Manage nosebleeds conservatively ➢ 70% go into remission without treatment **Active Rx if active bleeding or severe thrombocytopenia (plt < 10)** ➢ Prednisolone ➢ IVIg ➢ Blood or plt transfusions if needed	***Conservative*** ➢ *Avoid dehydration* ➢ *Ensure IUTD* ***Medical*** ➢ *ABx prophylaxis (e.g. penicillin V – phenoxymethylpenicillin)* ➢ *Blood transfusions (if hypovol. Shock – **splenic sequestration crisis*** ➢ *BMT – curative intent* ***How to deal with sickle cell crisis?*** ➢ *Spectrum of acute crisis (mild to life-threatening)* ➢ *Triggered by infection, dehydration, extreme cold* ***Conservative Mx*** ➢ *Hydrate, keep cool* ➢ *Low threshold for admission* ➢ *Simple analgesia* ***Specific Mx*** ➢ ***Vaso-occlusive (painful) crisis*** *– sickle RBC clog up capillaries– aspiration blood from penis (priapsism)* ➢ ***Splenic sequestration due to splenic infarct*** *→ fluid resus + blood transfusion* ➢ ***Aplastic (Parvovirus B19)*** *→ supportive +/- blood transfusions* ➢ ***Acute chest syndrome*** → high mortality rate o *ABx / antiviral = for infection* o *Blood transfusion = anaemia* o *PEEP or I+V*	