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Cast 28 – Anaemia

$2^{1/2}$-year-old girl is referred to your ED with history of lethargy over the last 6 months. Born at 36 weeks, normal delivery and good APGAR, and is fully immunised. She is the Twin 2 and has been known to have delayed growth for past 1 year. Her sister Twin 1 is taller and 5 kg heavier. Otherwise, no other significant history.

On examination she is pale, but alert and active. She had normal observations.

The results are given below:
FBE

HB - 64g/L (115-150)
WCC - 8.1 x 10^9/L (5.0-15.0)
PLATELETS – 285 x 10^9/L (150-450)
RCC (Red Cell Count) – 5.12 x 10^12/L (3.90-5.30)
HCT (Haematocrit) – 0.25L/L (0.33-0.46)
MCV (Mean corpuscular volume) - 49 fL (75-90)
MCH (Mean corpuscular haemoglobin) - 12.4 pg (24.0-31.0)
MCHC (Mean Corpuscular Hemoglobin Concentration) - 256 g/L (310-355)
RDW (Red Cell Distribution Width) - 20.7 % (11.0-15.0)
MPV (mean platelet volume) - 8.3 fL (6.5-12.0)

NEUTROPHILS - 26.4 % - 2.10 x 10^9/L (1.50-8.00)
LYMPHOCYTES - 62.4 % - 5.00 x 10^9/L (1.50-7.00)
MONOCYTES - 6.6 % - 0.50 x 10^9/L (0.20-1.00)
EOSINOPHILS - 4.0 % - 0.30 x 10^9/L (0.00-1.00)
BASOPHILS - 0.6 % - 0.00 x 10^9/L (0.00-0.20)

IRON STUDIES (Serum/Plasma)
IRON - **<2** umol/L (7-30)
TRANSFERRIN - **5.0** g/L (2.0-3.6)
IRON BINDING CAPACITY - **124** umol/L (45-76)
IRON SATURATION - **<2** % (15-46)
FERRITIN - **3** ug/L (20-310)

Q 1 – List six (6) Red flags for anaemia in a child of this age group requiring admission? (6 marks)

- Hb <60g/L (including iron deficiency)
- Tachycardia, cardiac murmur or signs of cardiac failure
- Features of haemolysis eg dark urine, jaundice, scleral icterus
- Associated reticulocytopenia
- Presence of nucleated red blood cells on blood film
- Associated thrombocytopenia or neutropenia, may indicate malignancy or an infiltrative disorder
- Severe vitamin B12 or folate deficiency
- Need for red cell transfusion (where possible defer transfusion until a definitive diagnosis is made)

Q 2 – State the three (3) types of anaemia based on mean corpuscular volume (MCV)? (3 marks)

- Microcytic - **MCV<80 fl) (femtoliters)**
- Normocytic - **(MCV 80-100 fL)**
- Macrocytic - **(MCV>100 fL)**

Q 3 – List three (3) differentials for Microcytic Hypochromic Anaemia? (3 marks)

- **Iron Deficiency anaemia**
- **Beta or Alpha Thalassaemia Minor/trait**
- **Rare causes**
    - Chronic inflammation
    - Lead poisoning (high blood lead level)
    - Sideroblastic anaemia

Q 4 – List three (3) differentials for Normocytic normochromic Anaemia? (3 marks)

- **Haemolytic anaemia**
- **Sickle cell anaemia**
- **Hypoplastic/aplastic anaemia**
- **Chronic disease**
- **Blood loss**

Q 5 – List three (3) differentials you would consider for Macrocytosis with or without anaemia? (3 marks)

- **Vitamin B12 and folate deficiency**
- **Myelodysplasia**
- **Medications eg anticonvulsants, immunosuppressants and zidovudine**

Other possible answers below:

- **Liver disease**
- **Hypothyroidism**

Additional notes

	Iron	Transferrin/TIBC	Transferrin Saturation	Ferritin
Iron Deficiency	Low	High/Normal	Low	Low
Anaemia of Chronic inflammation	Low	Low/Normal	Low/Normal	High/Normal
Thalassaemia	High/Normal	Low/Normal	High/Normal	High/Normal

	Iron Depletion	Iron Deficiency	Iron Deficiency Anaemia	Iron Overload
Ferritin	Low	Low	Low	High
Iron	Normal	Low	Low	High
Transferrin	Normal	High	High	Low
Transferrin Saturation	Normal	Low	Low	High
Transferrin receptors	Normal	High	High	Normal
Mean Corpuscular volume	Normal	Normal	Low	Normal
Haemoglobin	Normal	Normal	Low	Normal

Reference:
https://www.rch.org.au/clinicalguide/guideline_index/Anaemia/
https://www.rch.org.au/clinicalguide/guideline_index/iron_deficiency/

Iron studies or serum iron should not be requested to diagnose iron deficiency. Serum iron reflects recent iron intake and does not provide a measure of the iron stores.

Other features on the blood film appearance that prompt further investigation.

Film features	Cause	Investigation
Target cells	Iron deficiency anaemia Haemoglobinopathies	Ferritin Haemoglobinopathy testing (HPLC/Hb Electrophoresis)
Elliptocytes or pencil cells	Iron deficiency anaemia Haemoglobinopathies	Ferritin Haemoglobinopathy testing (HPLC/Hb Electrophoresis)
Spherocytes	Hereditary spherocytosis Autoimmune haemolysis	Direct antiglobulin test (DAT)(Coombs test) Blood group and antibody screening (BGAB Eosin 5 maleimide (E5M)
Fragmented red cells	Haemolysis	Platelet count Bilirubin, Reticulocyte count Urea + Creatinine Coagulation profile
Bite and blister cells	G6PD deficiency	G6PD assay
Nucleated red blood cells	Bone marrow infiltration Haemolysis	Consider bone marrow examination Thalassaemia testing (HPLC/Hb Electropho
Sickle cells	Sickle cell anaemia	Haemoglobinopathy testing (HPLC/Hb Electrophoresis)
Tear drop cells	Bone marrow infiltration Vitamin B12 deficiency	May need bone marrow examination Active vitamin B12

Normocytic Normochromic Anaemia

Haemolytic anaemia

- Acute haemolysis in childhood can be a life-threatening illness and all cases should be discussed with a haematologist
- Admit children with haemolytic anaemia for observation. Frequent heart rate monitoring is required to identify tachycardia which may indicate a further drop in Hb
- Repeat FBC within 6-12 hours to detect ongoing haemolysis
- Monitor reticulocyte count and bilirubin
- Additional investigations will be guided by blood film findings eg Coombs test (direct antiglobulin test), blood group and antibody screening (BGAB), G6PD assay and Eosin-5 maleimide red cell staining (diagnosis of hereditary spherocytosis)

Sickle cell anaemia

Hypoplastic/aplastic anaemia

- Causes
- Acute leukaemia, aplastic anaemia, infiltrative disorders
- Drugs (eg cytotoxics, chloramphenicol, sulfonamides)
- Viral infection
- Severe nutritional deficiencies (vitamin B12 or folate deficiency), however usually children present with macrocytic red cells
- Reticulocyte count is usually low
- Differential diagnosis based on FBC results
- Consider bone marrow infiltration if neutrophils and/or platelets also decreased
- If isolated anaemia with low reticulocyte count with normal platelet and neutrophil counts, consider transient erythroblastopenia of childhood (TEC) or congenital forms (eg Diamond-Blackfan anaemia)
- Bone marrow aspirate is usually required for diagnosis

Chronic disease

- Normochromic normocytic anaemia can be seen with chronic inflammation and chronic disease such as renal disease

- Reticulocyte count may be low
- Platelet count may be elevated
- Further investigation (eg UEC, LFT and ESR) may be indicated depending on clinical features

Blood loss

- Normochromic normocytic anaemia can be seen with acute blood loss
- Reticulocyte count may be normal or elevated
- Correlate with any bleeding symptoms

Macrocytic Anaemia

Vitamin B12 and folate deficiency

- Can be associated with failure to thrive or neurodevelopmental problems (regression, seizures, irritability, poor feeding)
- Vitamin B12 deficiency may be seen in exclusively breast-fed infants of mothers with vitamin B12 deficiency, children with a vegan or vegetarian diet, pernicious anaemia and metabolic disorders
- Characteristic blood film findings include teardrop red cells and hypersegmented neutrophils and often neutropenia or thrombocytopenia
- Requires urgent investigation with red cell folate and active vitamin B12
- If low active vitamin B12 suggest serum homocysteine and urine methylmalonic acid
- Treatment must be commenced urgently, particularly if neurological symptoms or regression

Other causes of red cell macrocytosis with or without anaemia

- **Myelodysplasia**
- **Medications eg anticonvulsants, immunosuppressants and zidovudine**
- **Liver disease**
- **Hypothyroidism**