Anaemia

Defined as [$Hb_{sea\ level}$] <125-130g/L (M) or <110-120g/L (F). It may be due to a low red cell mass (e.g. ↓production or loss of RBC), or ↑plasma volume (e.g. in pregnancy) and has many causes.

Presentation

History

Fatigue, dyspnoea, syncope, palpitations, headache, worsening IHD/CCF/COPD if pre-existing. Symptoms suggestive of underlying cause.

Examination

Pallor (look at conjunctivae, skin creases), hyperdynamic circulation (e.g. tachycardia, murmurs and cardiac enlargement±HF), Signs of underlying cause e.g. dysphagia due to oesophageal web with chronic iron deficiency (=Plummer-Vinson Syndrome – has association with oesophageal Ca). Koilonychia/angular cheilitis (Fe-def), glossitis (Vit B12 def)

Classification

One classification is based on MCV:

Microcytic (MCV<80fl)

- Iron-deficiency anaemia (most common cause).
- Thalassaemia (may have disproportionately low MCV for Hb, normal RDW & ↑RCC,)
- Congenital sideroblastic anaemia (very rare).
- Lead poisoning
- Multiple myeloma
- Chronic systemic illness

Normocytic (MCV 80-100fl)

- Chronic disease (chronic inflammation, infection, connective tissue disease, cancer, etc.)
- Renal failure
- Hypothyroidism (or macrocytic)
- Bone marrow failure
- Haemolysis (or macrocytic)
- Pregnancy
- Congenital (Fanconi's, Diamond-Blackfan)
- Early stages of most anaemias

Macrocytic (MCV>100fl)

- B12 or folate deficiency (esp if MCV>115fl)
- Chronic EtOH
- Liver disease
- Hypothyroidism
- Myelodysplastic syndromes
- Marrow infiltration /Aplastic anaemia
- Reticulocytosis (>2% e.g. haemolysis)
- Antifolate drugs (e.g. phenytoin)
- Cytotoxics (e.g. hydroxyurea)
- Congenital cyanotic heart disease

Management

Depends on underlying cause (see below). Transfusion may be considered if symptomatic and Hb<7, or Hb<10 and IHD or risk of haemorrhage ± **frusemide** 10-40mg PO/IV if CCF.

↓MCV Iron Deficiency Anaemia

Ave. adult diet = 15mg/d, abs. ~10%. Losses M 1mg/d, F 1.5mg/d. Common. Often asymptomatic.

Causes

- Blood loss – GIT (NSAID, GORD, PUD, Ca, Angiodysplasia, haemorrhoids, varices), GUT (menstruation), chronic haemolysis, excessive donation
- Malabsorption – Drugs (tetracyclines), IBD, coeliac, post-gastrectomy.
- Pregnancy (↑demand)
- Dietary - childhood (often milk-related), vegetarians with poor diet, high phytate diet (cereals, nuts, seeds & legumes – impairs Fe absorption), calcium.

Management

Investigate for underlying cause:

- **Urine:** U/A for RBC.
- **Blood:** FBC, iron studies (Ferritin low, serum iron low), film (anisocytosis [variation in RBC size] and poikilocytosis [abnormally shaped RBC]), coeliac screen.
- **Other:** Gastro-/colonoscopy, stool

Iron replacement:

Ferrous sulphate 325mg od (child Ferro-liquid 0.5ml/kg od) (**SE:** Constipation/diarrhoea, black stools, heartburn, nausea, abdo pain), diet advice. Rpt FBC in 1/12 cont Rx until Hb ok for 3 /12.

↓↑MCV Sideroblastic Anaemia

Abnormal ringed RBC precursors (sideroblasts) + non-haem Fe granules in bone marrow aspirate.

Causes:

- Congenital (rare, X-linked)
- Acquired
  - Myelodysplastic syndromes
  - 2° to myeloproliferative disorders (myeloma, Polycythaemia ruba vera, leukaemias)
  - Drugs & toxins – lead, alcohol, chloramphenicol, isoniazid, linezolid, pyrazinamide
  - Other 2° causes: SLE, RA, myxoedema, pregnancy
  - Idiopathic

Management

Investigate for underlying cause:

- **Blood:** FBC (↓MCV in cong, may ↑in aquired), iron studies (serum iron high & ferritin high)
- **Other:** BMA (sideroblasts)

Treatment:

- Supportive. Transfusion if symptomatic (may need iron chelation if multiple).
- Drugs:
  - **Erythropoietin ± GCSF** or **Cyclosporin A** in myelodysplastic syndrome
  - Hereditary sideroblastic anaemia may respond to pyridoxine
- Stem cell transplantation

↓MCV Thalassaemia

See Haemoglobinopathies

↑MCV

Vitamin B_{12} Deficiency

Liver stores 3/12 supply. B_{12} binds gastric intrinsic factor & complex absorbed in terminal ileum.

Causes:

- IF deficiency – Pernicious anaemia (Abs to IF, 2% pop., assoc with autoimmune diseases), post-gastrectomy.
- Malabsoption – bacterial overgrowth syndrome, ileal disease, IBD
- Pancreatic disease
- Dietary deficiency (vegans)
- Nitrous oxide – prolonged exposure destroys endogenous cobalamin

Complications:

Peripheral neuropathy, dementia, psychosis, subacute degen of spinal cord, heart failure

Management:

Investigations:

- **Blood:** FBC, film (macrocytes, hyperseg. neutrophils & Howell-Jolly bodies), B_{12} level & folate level (red cell better than serum), IF & gastric parietal-cell antibodies.
- **The Schilling Test:** Differentiates PA & malabsorption. Low urinary excretion of B12 than can be increased by giving IF suggests PA.
- **Bone-marrow aspiration:** esp if myelodysplasia, aplastic anaemia, myeloma, or other marrow disorders are suspected. In B12 and folate deficiency, megaloblasts and giant metamyelocytes (early granulocyte precursors) are seen.
- **Gastroscopy:** to confirm gastric atrophy and exclude gastric cancer and polyps.

Treatment

- No neurological involvement: 6 x hydroxocobalamin 1 mg IM over 6 weeks. Then 3monthly
- Neurological involvement: hydroxocobalamin 1 mg alt days until stable. Then 2monthly.
- Don't give folic acid before B12 if B12 deprived as may → fulminant neurologic deficit.

↑MCV

Folate Deficiency

Red cell folate level reflects body stores.

Causes

- Dieatary deficiency – EtOHlics
- Malabsorption
- Increased demand – pregnancy, malignancy. Psoriasis
- DHF reductase inhibitors – methotrexate, trimethoprim, pyramethamine
- Other drugs – phenytoin, salazopyrine

Management

- Vitamin B12 if concomitant deficiency suspected - prevents subacute cord degeneration
- 5mg folate PO od for 4mo
- Folinic acid 10-100mg/kg/m2 IV/IM q3-6h for 72hr if DHF reductase inhibitor toxicity

Anaemia of Chronic Disease

↔MCV

Most common cause in ED. Serum iron↓. Transferrin sat^{n}↓. Transferrin↓ or ↔. Ferritin↑ or ↔.

Causes

- ↓Erythropoietin production – e.g. renal failure
- Bone marrow suppression
- Iron distribution disturbances – ↑RES uptake, or cytokine-mediated
- Decreased RBC life span

Management

- Transfusion
- Consider Fe therapy
- Erythropoietin – Response: CRF (95%), myeloma (80%), myeloplastic syndromes (25%)

Haemolytic Anaemia

↔MCV

Classification

RBC defects

- Membrane – HS, HE
- Haemoglobinopathies – Thalassaemia, HbS
- Enzyme defects – G6PD, pyruvate kinase, paroxysmal nocturnal haemaglobinuria (PNH)

Others

- Autoimmune –transfusion/ABO reaction, SLE, RA, drugs (penicillin, methyldopa), UC, hepatitis, EBV, mycoplasma, lymphoma, CLL
- Mechanical trauma – long-distance runners, prosthetic heart valves

These can be reclassified as:

Intravascular

- Microangiopathic – DIC, HUS, TTP, malig HT, PET, vasculitis, malignancy, heart valves
- March haemoglobinuria
- Chronic cold agglutinin disease
- PNH

Extravascular (in RES)

- Autoimmune
- Rh incompatibility
- Chronic haemolytic disorders

Investigations

Blood: ↑retics (may ↑MCV), Heinz bodies, ↑Bil, ↑LDH, ↓haptoglobin, methaemalbumin (if sev.)

Management

Treat underlying cause. Avoid precipitants. May require splenectomy. Cx pigment gallstones.

↔MCV

Aplastic Anaemia

Rare. Caused by stem cell losses. Anaemia, low retics/plts/WCC. If severe 10% 1yr survival.

Causes

- Idiopathic - >50% of cases
- Fanconi's syndrome – AR disorder. Dysmorphic, hyperpigmentation, ↓plts.
- Chemical/physical agents (↑risk in Sickle Cell)
    - Dose related - radiation, alkylating agents, antimetabolites
    - Idiosyncratic – chloramphenicol, sulphur, gold, phenylbutazone
    - Others – viruses, SLE, pregnancy, GVHD, other immune mediated

Management

- Supportive
- Transfusions
- G-CSF
- Immunosuppression
- BMT/stell cell transplant

Anaemia Algorithm