Haematological problems in pregnancy
Anaemia

A normochromic, normocytic anaemia may occur from the 7–8th week of gestation, due to the physiological increase in plasma volume that is relatively greater than the increase in red cell mass. However, the haemoglobin (Hb) should not fall to $<11 \text{ g/dl in the first, or } <10 \text{ g/dl}$ in the second and third trimesters [1,2]. More marked anemia may be due to iron, folate, or more rarely, vitamin B12 deficiency or haemoglobinopathy.
Haematology

• Maternal haemoglobin levels are decreased because of the discrepancy between the 1000 to 1500 mL increases in plasma volume and the increase in erythrocyte mass, which is around 280 mL.
• Transfer of iron stores to the fetus contributes further to this physiological anaemia. The mean haemoglobin concentration falls from 13.3 g/dL in the non-pregnant state to 10.9 g/dL at the 36th week of normal pregnancy.
• Pregnant women require increased amounts of iron, and absorption of dietary iron from the gut is increased as a result. Suggesting that pregnancy without iron supplementation leads to depletion of iron stores.
• Renal clearance of folic acid increases substantially during normal pregnancy and plasma folate concentrations fall.
• Folate supplementation for haematinic purposes in women eating an adequate diet and carrying a single fetus is therefore not routinely indicated.
• maternal platelet count usually remains stable throughout pregnancy
Haematinic requirements

Pregnancy requires an iron intake of around 2.5 mg/day throughout, with perhaps 3.0–7.5 mg/day required in the third trimester. Folate requirements increase to around 400 μg/day during pregnancy. Folate deficiency is more common in multiple pregnancy, frequent child birth, and adolescent mothers. The body stores around 3 mg of B12, with a daily dietary requirement of 3μg/day. The only B12 source is animal foodstuffs; thus, vegetarians and vegans are most at risk of dietary deficiency.
The effects of deficiency

The signs and symptoms of early deficiencies are nonspecific, including tiredness and features of any underlying cause. Aside from anaemia, folate and B12 deficiency are linked to neural tube defect.

The effect of iron deficiency mild deficiency is linked to increased delivery bleeding, poor fetal iron stores and an increased placenta:fetus weight ratio.

Severe maternal iron deficiency is associated with premature delivery and low birthweight [ }
Diagnosis of deficiency

Serum iron, Total Iron Binding Capacity (TIBC), ferritin, serum transferrin receptor levels and red cell-derived protoporphyrin can be used to diagnose iron deficiency. Markedly reduced serum ferritin (<12 ug/l) remains diagnostic. Megaloblastic anaemia from B12 or folate deficiency is suggested by an MCV >100 fl, with right-shifted neutrophils on the blood film. Megaloblastic erythropoiesis can be demonstrated by bone marrow examination.
Treatment

• The treatment of established iron deficiency is with 200 mg/day of elemental iron.
• Iron absorption is maximized when combined with ascorbic acid such as taking the iron supplements with fresh orange juice or a vitamin C preparation.
• Parenteral therapy is useful in malabsorption and failed compliance, but otherwise does not produce a faster response than oral iron and side effects are common.
• Proven folate deficiency anaemia should be treated with folic acid (5 mg/day).
• In B12 deficiency, a single dose of 1000 μg of intramuscular B12 should lead to a reticulocyte response within 3–7 days. Weekly injections should be employed until anaemia resolves and lifelong replacement is often required.
Clinically significant variants of haemoglobin:
- Sickle cell trait (Hb AS)
- Sickle cell disease (Hb SS)
- Sickle cell/haemoglobin C disease (Hb SC)
- Sickle cell/beta thalassaemia

**Sickle cell anaemia**
Sickle cell disease (SCD) is an autosomally inherited genetic condition, where abnormal haemoglobin (HbS) contains beta-globin chains with an amino acid substitution that results in it precipitating when in its reduced state.
The red blood cells become sickle shaped and occlude small blood vessels.
There is severe anaemia, chronic hyperbilirubinaemia, apredisposition to infection, vaso-occlusive complications including the acute chest syndrome, and chronic kidney disease. Pulmonary hypertension is found in 30 per cent of patients and is associated with a high mortality rate.
management

- Pre-pregnancy optimization of maternal health and education about the risks in pregnancy.
- High-dose folate supplements (5 mg daily) are recommended. managed from early pregnancy on low-dose aspirin (75 mg daily).
- Crises in pregnancy may be precipitated by hypoxia, stress, infection and haemorrhage. Mothers are also at increased risk of miscarriage, pre-eclampsia, fetal growth restriction (FGR) and premature labour, with three times the risk of eclampsia compared to women without SCD. Thromboembolic events including cerebral vein thrombosis and deep venous thrombosis are implicated in the higher rates of maternal deaths reported in SCD.
- Sickle cell carriers have a 1:4 risk of having a baby with SCD if their partner also has sickle cell trait.
Management of sickle cell crisis in pregnancy

- Prompt treatment
- Adequate hydration
- Oxygen
- Analgesia
- Screen for infection (urinary, respiratory)
- Antibiotics
- Blood transfusion (leukocyte depleted and phenotype specific)
- Exchange transfusion
- Prophylaxis against thrombosis (heparin)
- Fetal monitoring
Thalassaemia

The thalassaemia syndromes are the commonest genetic blood disorders. The defect is a reduced production of normal haemoglobin and the syndromes are divided into alpha and beta types, depending on which globin chain is affected.

In alpha-thalassaemia minor, there is a deletion of one of the two normal alpha genes required for haemoglobin production. There is a 1:4 chance of the fetus having alpha-thalassaemia major, which is lethal.

The beta-thalassaemias result from defects in the normal production of the beta chains. However, if both partners have beta-thalassaemia minor, there is a 1:4 chance that the fetus could have beta-thalassaemia major, which is associated with profound anaemia in post-natal life.
Thrombocytopenia is defined as a platelet count 150 109/L. Incidental or gestational thrombocytopenia is common and is found in 7–8 per cent of pregnant women. Bleeding is rarely a complication unless the count is 50 109/L. The diagnosis of gestational thrombocytopenia is a diagnosis of exclusion and can only be made when autoimmune and other causes have been excluded. It usually occurs in late pregnancy, with no prior history of thrombocytopenia outside pregnancy and a normal platelet count recorded at the start of pregnancy. No intervention is required other than monitoring of the platelet count during and after pregnancy.
Autoimmune thrombocytopenia

In immune thrombocytopenic purpura (ITP), autoantibodies are produced against platelet surface antigens, leading to platelet destruction by the reticuloendothelial system. The incidence in pregnancy is around 1 in 5000. The maternal platelet count may fall at any stage of pregnancy and can reach levels of 50 109/L.

Maternal haemorrhage at delivery is very unlikely if the platelet count is 50 109/L, and spontaneous bleeding during pregnancy very unlikely if the platelet count is 20 109/L. There is a 5–10 per cent chance of associated fetal thrombocytopenia (50 109/L), which cannot be predicted using maternal counts or antibody tests.
Management in pregnancy should include serial monitoring of platelet counts and, provided the count remains above 80 \times 10^9/L, no complications are likely. If the count falls below 50 \times 10^9/L approaching term, treatment should be considered. Corticosteroids act by suppressing platelet autoantibodies; however, high doses are often required to improve the platelet count.

The use of intravenous immunoglobulin G (IgG) has been a major advance in the treatment of autoimmune thrombocytopenia. If the duration of treatment is likely to be prolonged, or if unacceptably high maintenance doses of prednisolone are required.
Vaginal delivery should be facilitated. Regional anaesthesia avoided.
If the platelet count is 80 109/L. Fetal blood sampling in labour and instrumental delivery by ventouse are best avoided because of the risk of fetal thrombocytopenia. A cord blood sample must be collected for platelet counting, but the nadir of the neonatal platelet count occurs 2–5 days after delivery.
Causes of thrombocytopenia in pregnancy
• Idiopathic
• Increased consumption or destruction
• autoimmune (ITP)
• antiphospholipid syndrome
• pre-eclampsia
• HELLP syndrome (haemolysis, elevation of liver enzymes and low platelets)
• disseminated intravascular coagulation
• thrombotic thrombocytopenic purpura
• hypersplenism
• Decreased production
• sepsis
• HIV infection
• malignant marrow infiltration