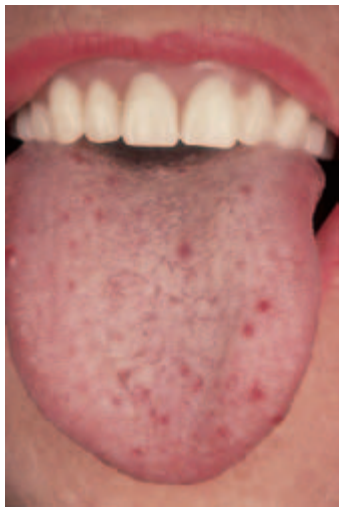
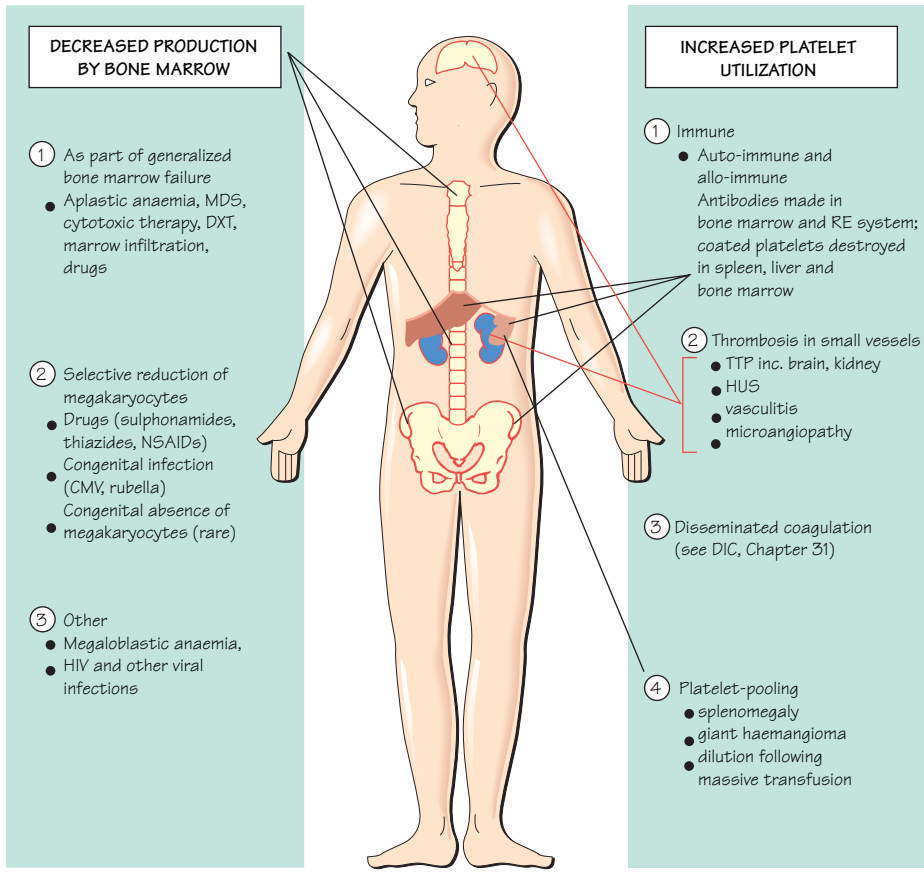
33 Disorders of haemostasis: vessel wall and platelets

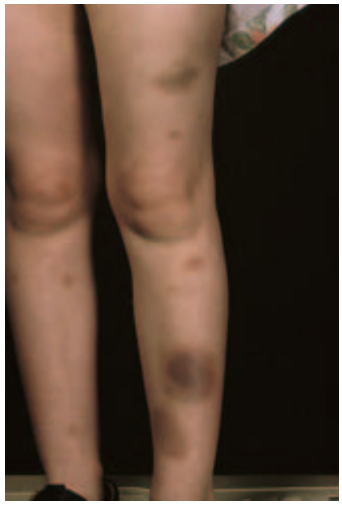
(a) Hereditary haemorrhagic telangiectasia: tongue showing multiple telangiectasia.



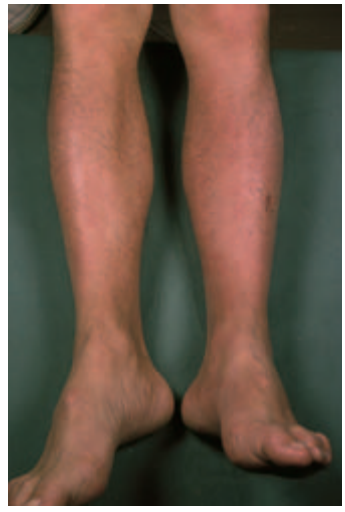
(b) Causes of thrombocytopenia.



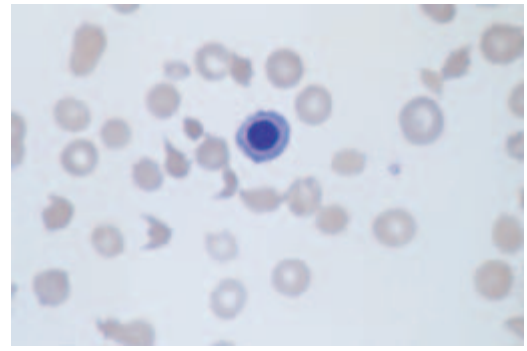
(c) Immune thrombocytopenia: multiple bruises, ecchymoses and purpura.



(d) Thrombocytopenia: petechial rash.



(e) Haemolytic uraemic syndrome (HUS): blood film showing red cell fragmentation with a circulating nucleated red blood cell and low platelet count.



Defective haemostasis with abnormal bleeding may be caused by:
- abnormalities of the vessel wall;
- thrombocytopenia;
- disordered platelet function;
- defective blood coagulation (see Chapters 34 and 35).

Vessel wall abnormalities

These are associated with easy bruising, purpura and ecchymosis and spontaneous bleeding from mucosal surfaces. The bleeding time, prothrombin time (PT), activated partial thromboplastin time (APTT) and platelet count are all normal.

Inherited

- Hereditary haemorrhagic telangiectasia. This is autosomal dominant with multiple dilated microvascular swellings, typically in oropharynx (Fig. 33a) and gastrointestinal tract, which bleed spontaneously or following minor trauma. Local treatment (e.g. nasal packing) may control bleeding; tranexamic acid helps to reduce bleeding. Chronic iron deficiency is frequent.
- Ehlers–Danlos syndrome, Marfan's syndrome and other rare connective tissue disorders.

Acquired

Causes include vitamin C deficiency (scurvy), steroid therapy, normal ageing (senile purpura), amyloid in blood vessels, cryoglobulinanaemia and immune complex deposition (e.g. purpura fulminans in septicaemia). Henoch–Schönlein purpura is an allergic vasculitis which follows an acute infection, usually in childhood, and may be associated with arthropathy, haematuria and gastrointestinal symptoms.

Platelets

Excessive bleeding caused by thrombocytopenia or disordered platelet function is mucosal (e.g. epistaxis, gastrointestinal bleeding or menorrhagia) or affects the skin (purpura, petechiae and ecchymoses). Symptoms usually occur when the platelet count is $<10 \times 10^9$/L but this may be higher when there is impaired platelet function.

Thrombocytopenia (platelets $<140 \times 10^9$/L) (Fig. 33b)

Congenital

This is rare: causes include congenital aplastic anaemia, thrombocytopenia with absent radii (TAR) syndrome or Wiskott–Aldrich syndrome (thrombocytopenia with eczema and hypogammaglobulinaemia). Congenital infection (e.g. rubella, cytomegalovirus) frequently leads to thrombocytopenia.

Acquired

This is a result of deficient platelet production or accelerated platelet destruction.

Autoimmune thrombocytopenia

The platelets are coated with autoantibody (immunoglobulin) and are removed by the macrophages of the reticuloendothelial system. Their lifespan is therefore reduced from 7–10 days to a few hours.

Acute

- Usually presents in childhood (2–7 years).
- Often follows a viral infection.
- Purpuric rash or epistaxis frequent (Figs 33c, d).
- Typically resolves spontaneously. A minority develop mucosal bleeding and should be treated with prednisolone or intravenous immunoglobulin. Up to 20% develop chronic immune thrombocytopenia.

Chronic

Immune thrombocytopenia in adults is less likely to resolve without therapy and is usually chronic. It is more common in females (M/F ratio 1 : 4). Autoantibody is present on the platelet surface and may also be present as free antibody in serum.

Laboratory findings

- Normal haemoglobin and white cell count; platelets low, often $<20 \times 10^9$/L.
- Bone marrow is normal or there are increased numbers of megakaryocytes.
- PT and APTT are normal, fibrinogen is normal.

Immune thrombocytopenia also occurs in association with some malignancies (e.g. chronic lymphocytic leukaemia, non-Hodgkin lymphoma, myelodysplasia), infections (e.g. Epstein–Barr virus, HIV, malaria) and connective tissue disease (e.g. systemic lupus erythematosus). Patients should be tested for ANF and anticardiolipin antibodies.

Treatment

Treatment, if necessary, is with the following:
- Prednisolone (1 mg/kg/day, reducing over 4–6 weeks).
- Intravenous immunoglobulin is valuable for obtaining a temporary rise in platelet count.
- Splenectomy is required for non-responders with continuing symptoms and/or very low platelet counts.
- Additional immunosuppressive therapy (e.g. azathioprine, cyclophosphamide, cyclosporin A, rhesus anti-D, vincristine) or combination chemotherapy have been used. Rituximab (anti-CD20) and danazol are also of value in some cases.

Alloimmune thrombocytopenia

Transplacental passage of maternal antibody in immune thrombocytopenia can lead to neonatal thrombocytopenia, which typically resolves spontaneously over a few weeks. Mothers who have been sensitized (e.g. by blood transfusion or previous pregnancy) to platelet antigens may develop antibodies which cross the placenta and coat fetal and neonatal platelets, which are then removed in the reticuloendothelial system (RES). Individuals with such platelet alloantibodies can also become thrombocytopenic after blood transfusion (post-transfusion purpura). The antibody is then directed against the HPA1-a antigen on platelets.

Other causes of thrombocytopenia

Drugs

Drugs cause thrombocytopenia by inhibiting marrow production or by an immune mechanism. The most common immune mechanism (e.g. quinine, heparin) is when the drug forms an antigen with a