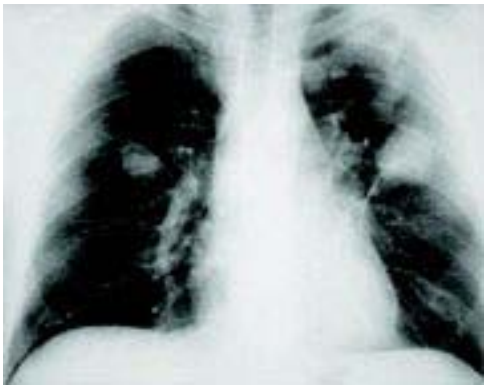
Case 7.1 Pneumocystis pneumonia complicating immunosuppressive therapy

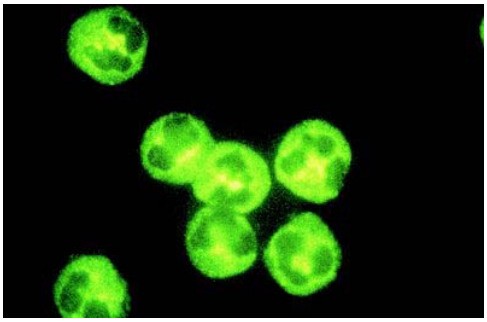
A 35-year-old man with granulomatosis with polyangiitis (GPA) (formerly Wegener's granulomatosis) was admitted to hospital with a 2-week history of fever and shortness of breath. The diagnosis of GPA had been made 18 months earlier when he presented with haemoptysis and glomerulonephritis. Disease remission was achieved with aggressive immunosuppressive therapy using a combination of pulse methylprednisolone and cyclophosphamide, enabling him to be maintained on his current tapering dose of steroids and azathioprine. The results of investigations on his current hospital admission were as follows:

- Chest X-ray: diffuse bilateral shadowing
- Serum C-reactive protein (CRP): 80 mg/l (NR < 10)
- Anti-neutrophil cytoplasmic antibody directed against proteinase 3: weakly positive at a titre of 1 : 40 (>1 : 640 at disease diagnosis)
- Serum creatinine: 102 μmol/l (NR 50–140)
- Urea: 4.5 mmol/l (NR 2.5–7.1)
- Urine microscopy: clear.

The differential diagnosis was between active GPA and infection complicating immunosuppressive therapy. It was crucial to distinguish between infection and active vasculitis in this situation, since an increase in immunosuppressive therapy in the face of sepsis could be potentially fatal. Further investigations, including bronchoalveolar lavage, revealed the presence of Pneumocystis carinii, a recognized lung pathogen in patients on long-term immunosuppressive therapy. He made a full clinical and radiological recovery following 2 weeks of co-trimoxazole therapy and was discharged home on his usual dose of maintenance immunosuppression.



Case Figure 7.1a Chest X-ray depicting bilateral lung nodules due to pulmonary vasculitis in Wegener's granulomatosis. In patients on immunosuppressive treatment, the possibility of opportunistic lung infection with Pneumocystis carinii should always be borne in mind.



Case Figure 7.1b Strongly positive cytoplasmic anti-neutrophil cytoplasmic antibody detected in blood using indirect immunofluorescence in a patient with Wegener's granulomatosis.

Essentials of Clinical Immunology, Sixth Edition. Helen Chapel, Mansel Haeney, Siraj Misbah, and Neil Snowden.

Case 7.2 Epstein–Barr virus-induced lymphoma in a transplant recipient

A 65-year-old insulin-dependent diabetic man underwent cadaveric renal transplantation for end-stage renal failure. The immediate post-operative course was complicated by acute rejection, which was successfully reversed by steroids and then anti-thymocyte globulin. He was discharged from hospital 2 weeks later on insulin, prednisolone, azathioprine and ciclosporin (to prevent further transplant rejection), co-trimoxazole (to prevent Pneumocystis infection), erythropoietin and ranitidine. Five months later, he developed progressive dyspnoea, fever and fatigue. Clinical examination revealed bilateral lung crackles and hepatosplenomegaly. Bilateral diffuse interstitial shadowing was noted on chest X-ray. The differential diagnosis is summarized in Box 7.2. His haemoglobin was 84 g/l and he was severely leucopenic at 1.0×10^9/l. Blood cultures were sterile and a bone marrow biopsy showed normal myeloid and erythroid maturation with no acid-fast bacilli or fungi evident on special stains. A transbronchial biopsy showed no histological abnormality; PCR for acid-fast bacilli, Pneumocystis and cytomegalovirus were negative. Open lung biopsy showed fibrinous pneumonia with obstructive bronchiolitis associated with a dense cellular infiltrate of highly atypical lymphoid cells containing pleomorphic nuclei. The lymphoid cells expressed B-cell markers (CD20, CD79) and stained positively for a number of EBV gene products (EBV nuclear antigens, EBV latent membrane proteins).

The lung biopsy results were diagnostic of a B-cell lymphoma secondary to EBV. Following the diagnosis, his immunosuppressive medication was stopped but the patient died 2 weeks later from progressive respiratory failure.

Case 7.3 Kawasaki's disease treated with intravenous immunoglobulin

A 2-year-old boy was admitted to hospital with a 7-day history of high fever, lymphadenopathy, conjunctivitis and an erythematous exfoliative rash affecting his trunk and extremities (see Fig. 7.5). On the basis of the characteristic clinical picture, a clinical diagnosis of Kawasaki's disease (also known as acute mucocutaneous lymph node syndrome), an acute vasculitic disorder of infants affecting small and medium-sized blood vessels, was made. Other infective causes of a similar clinical presentation were excluded on the basis of negative blood and urine cultures. The results of initial investigations were as follows:

- Hb 110 g/l (NR 120–150)
- White cell count 14×10^9 (NR 4–11)
- Platelets 550×10^9 (NR 250–400)
- C-reactive protein 80 mg/l (NR < 10)

Since untreated or delayed treatment of Kawasaki's disease is associated with the development of coronary artery aneurysms, urgent treatment with high-dose IVIG (total dose 2 g/kg) was given in conjunction with anti-inflammatory doses of aspirin. This led to rapid resolution of fever and normalization of CRP (within 48 h). While IVIG is undoubtedly effective in Kawasaki's disease, the mechanism of action is unclear. For maximum benefit, treatment should be administered within 10 days of onset of fever.

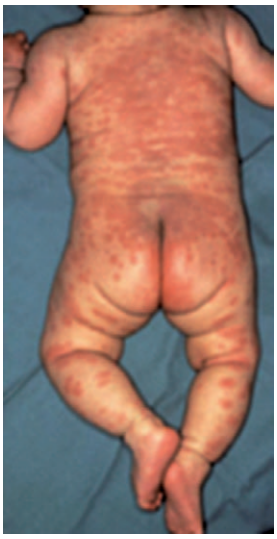
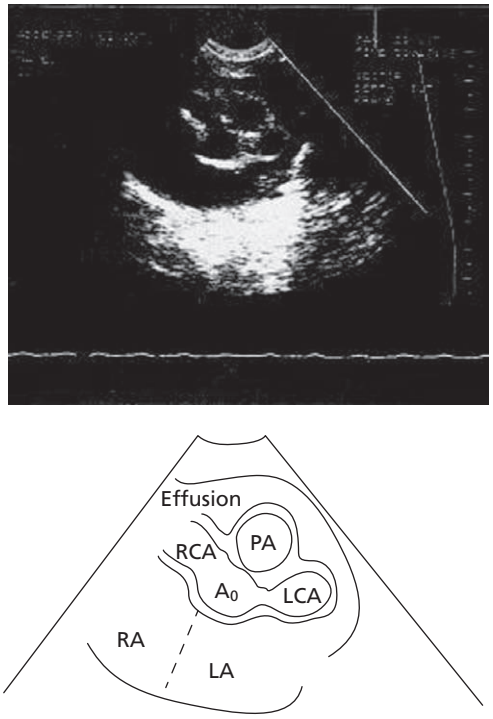


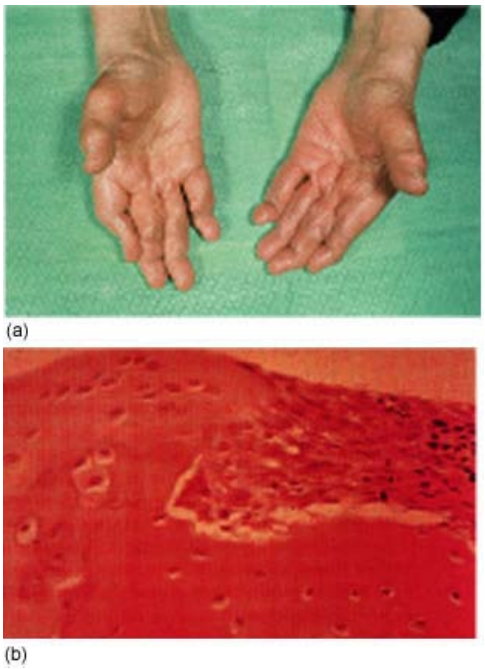
Fig. 7.5 Infant with Kawasaki's disease with an erythematous, predominantly truncal rash. With permission from Alexander F.Freeman and Stanford T. Shulman.



Case Figure 7.3 Echocardiogram depicting R and L Coronary artery dilatation in a child with Kawasaki disease; reproduced with kind permission of E J Tizard, Current Paediatrics 1999;9:97-101
RCA-Right Coronary Artery, LCA-Left Coronary Artery, PA-Pulmonary Artery, Ao-Aorta, RA-Right Atrium, LA-Left Atrium.

Case 7.4 Severe rheumatoid arthritis treated with anti-tumour necrosis factor-α monoclonal antibodies

A 55-year-old woman with active RA, previously unresponsive to multiple disease-modifying agents, was treated with a humanized mouse monoclonal antibody to TNF-α (anti-TNF-α) as part of a clinical trial. Following her first uneventful infusion of anti-TNF-α, a significant reduction (60–70%) in clinical indices of inflammation (number of swollen and tender joints, duration of morning stiffness and pain score) and serum CRP was noted within 3 days. Clinical and laboratory improvement was sustained for 6 weeks following the first infusion.



Case Figure 7.4 (a) Hands in RA. (b) Histology of Pannus. Roitt & Rabson 2000.

Case 7.5 Fatal pneumococcal sepsis 8 years following splenectomy

A 35-year-old man felt non-specifically unwell for 24 h before being found collapsed at home. Despite intensive attempts at resuscitation by ambulance staff he was pronounced dead on arrival in hospital. Post-mortem examination revealed acute bacterial pneumonia and meningitis due to Streptococcus pneumoniae. His previous medical history was unremarkable except for a ruptured spleen following a road traffic accident, necessitating emergency splenectomy, 8 years previously. It transpired that immunization with 'Pneumovax' (23 valent pneumococcal polysaccharide) had been overlooked at the time and the patient's compliance with subsequent antibiotic prophylaxis had been erratic.