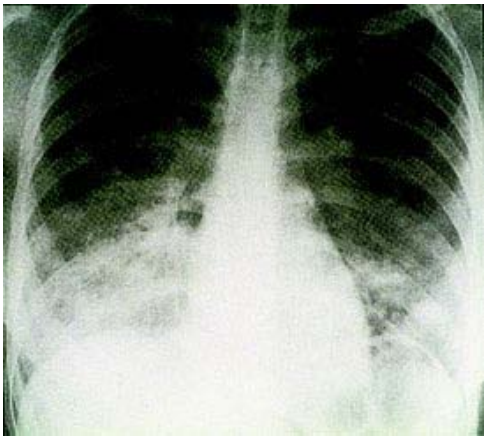
Case 13.1 Pneumonia and chronic lymphatic leukaemia [CLL]

A 65-year-old man was admitted with bilateral lower-lobe pneumonia. He had felt exhausted for 6 months, had lost 3 kg in weight and suffered 4 chest infections that responded to antibiotics. He did not smoke. He was clinically anaemic but had no finger clubbing, lymphadenopathy or splenomegaly. On investigation, he had a low haemoglobin (92 g/l) and a raised erythrocyte sedimentation rate (ESR) (84 mm/h). The white cell count was very high (98×10^9/l) and 95% of these were lymphocytes. The platelet count was normal. Serum immunoglobulins were all low: IgG 3.2 g/l (NR 7.2–18.0), IgA 0.6 g/l (NR 0.8–5.0) and IgM 0.3 g/l (NR 0.5–2.0); no paraprotein bands were seen.

A provisional diagnosis of pneumonia complicating chronic lymphatic leukaemia was made and CLL was confirmed by surface marker studies, which showed that 98% of peripheral lymphocytes were monoclonal B cells (Chapter 6).

Sputum cultures grew untypable Haemophilus influenzae. Treatment with amoxycillin resulted in rapid clearing of the pneumonia but, in view of his high lymphocyte count and mild anaemia, he was started on chlorambucil to control the lymphoproliferation. He lacked detectable serum antibodies and failed to make IgG antibodies to pneumococci on immunization; furthermore, all three major classes of serum immunoglobulins were low. Prophylactic IgG replacement therapy was started at a dose of 0.4 g/kg body weight per month, and he remained well for the next 5 years.

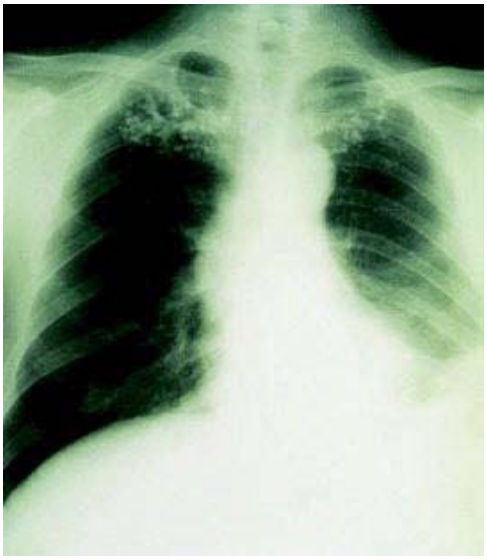


Case Figure 13.1a Chest X-ray showing consolidation at lung bases R & L.

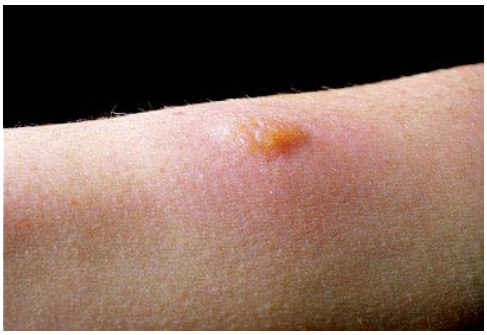
Essentials of Clinical Immunology, Sixth Edition. Helen Chapel, Mansel Haeney, Siraj Misbah, and Neil Snowden.

Case 13.2 Pulmonary tuberculosis

A 23-year-old man presented with a 4-week history of coughing, breathlessness and malaise. He had lost 4 kg in weight, but had no history of night sweats or haemoptysis. He had returned from holiday in Pakistan 2 months earlier. On examination, he was mildly pyrexial (37.8°C) but had no evidence of anaemia or clubbing. Crepitations were audible over the lung apices; there were no other physical signs. His haemoglobin and white cell count were normal but the C-reactive protein (CRP) was 231 mg/l. The chest X-ray showed bilateral upper- and middle-lobe shadowing but no hilar enlargement. Sputum was found to contain acid-fast bacilli and Mycobacterium tuberculosis was confirmed by PCR and subsequently cultured. A diagnosis of pulmonary tuberculosis was made. The patient was treated with isoniazid and rifampicin for 6 months, together with pyrazinamide for the first 2 months. He was allowed home on chemotherapy when his sputum became negative on direct smear. The chest X-ray is now much improved.



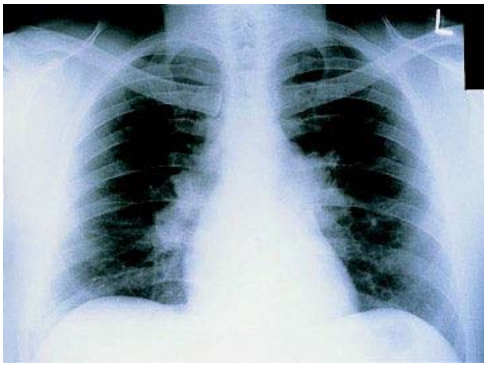
Case Figure 13.2a Chest X-ray shows lesions at both apices plus shadowing on L.



Case Figure 13.2b Strongly positive Mantoux test in a patient with active tuberculosis. Intradermal injection of M. tuberculosis antigen has induced a florid type IV hypersensitivity reaction with some blistering.

Case 13.3 Sarcoidosis

A 36-year-old man complained of breathlessness on exercise for 6 months. He also had mild chest tightness and stiff joints but no skin or eye problems. There was no family history of chest disease and he had never been abroad. He had been immunized with BCG as a schoolboy. On examination, he had no clubbing and no abnormal chest signs. Investigations showed a normal haemoglobin (143 g/l), white cell count (4.4×10^9/l) and differential (27% lymphocytes, 70% neutrophils), a mildly raised CRP (23 mg/l) and increased serum levels of angiotensin-converting enzyme (ACE). A serum biochemical profile, including serum calcium, was otherwise normal. A chest X-ray showed fine, diffuse radiological shadows, predominantly in the mid zones, and bilateral hilar lymphadenopathy. Lung function tests were normal and a Mantoux test was negative. A clinical diagnosis of sarcoidosis was made. Since he had pulmonary infiltration on X-ray, he was treated with corticosteroids to good effect.



Case Figure 13.3 Bilateral hilar lymphadenopathy in sarcoidosis. Intestinal changes are not easily seen on this chest X-ray but were strongly suggested by the results of pulmonary function tests which showed a restrictive defect with reduced gas transfer.

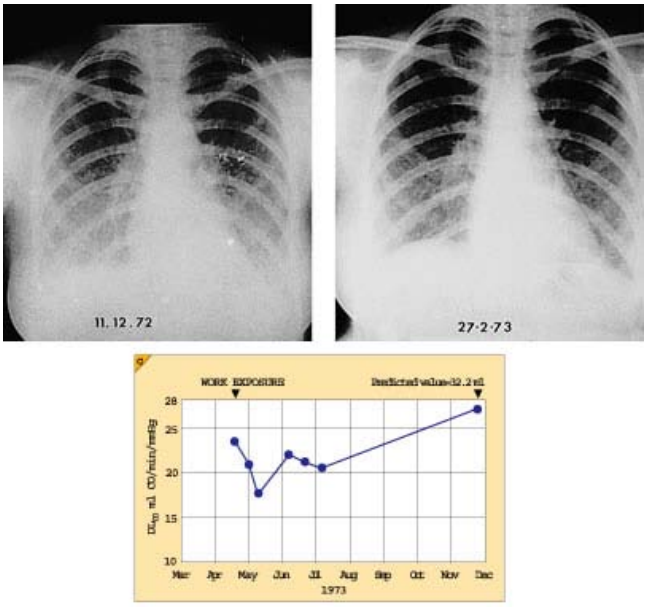
Case 13.4 Allergic bronchopulmonary aspergillosis

A 54-year-old woman presented with a 5-year history of a cough productive of mucopurulent sputum. On several occasions she had coughed up plugs of mucus. Courses of antibiotics had proved ineffectual. She had suffered from asthma for over 20 years and had a daughter with asthma. On examination, a few crepitations were audible in the left axillary region but the chest X-ray was apparently normal. She had a blood eosinophilia (1.05×10^9/l; normal $< 0.4 \times 10^9$/l). The total serum IgE was 325 IU/ml (normal < 125 IU/ml). Skin tests showed immediate (type I) hypersensitivity to cat fur, grass pollen and Aspergillus fumigatus. Her serum also contained strong precipitating antibodies ('precipitins') to this mould. At bronchoscopy, the left lingular bronchus was plugged with golden, tenacious mucus. This was aspirated and sent for culture; Aspergillus fumigatus was subsequently grown. Her allergic bronchopulmonary aspergillosis was treated with Itraconazole and a 10-day course of oral corticosteroids. She has subsequently remained symptom-free on a low-dose steroid inhaler and the antifungal agent in the spore season (September–December).

Case 13.5 Extrinsic allergic alveolitis: Farmers' lung

A 36-year-old farmer was admitted as an emergency with headache, fever, shortness of breath, a non-productive cough and myalgia. These symptoms came on suddenly. He had no features of upper respiratory tract infection, although he had had similar symptoms 3 weeks previously and had been treated with antibiotics. On examination, he had a tachycardia of 120/min, a temperature of 38 °C and bilateral widespread crepitations. His chest X-ray showed faint mottling in the middle and lower zones of both lung fields, but no hilar enlargement. He had a high white cell count (15×10^9/l). A Mantoux test was negative. Lung function studies showed a restrictive defect.

His serum contained precipitating antibodies (see Chapter 19) to Micropolyspora faeni and Aspergillus fumigatus. The probable diagnosis was farmers' lung, a variety of extrinsic allergic alveolitis caused by hypersensitivity to antigens found in mouldy hay. In retrospect, his earlier bronchial 'infection' was almost certainly a similar episode. His symptoms and X-ray changes gradually improved, although he continued to have exertional dyspnoea for 3 weeks. This man depended on his farm for his livelihood and was therefore reluctant to consider changing his job. He was strongly advised to dry his hay before storage or to let someone else handle the hay! Six weeks after discharge, he returned with acute symptoms after feeding hay to his cattle. He had had no immediate shortness of breath, but 5 h later had again experienced acute fever, malaise, shortness of breath, a cough and myalgia. This episode convinced him that there was a relationship between hay and his illness; his wife has fed the animals and handled the hay for the last 6 years and the patient (and his wife!) have remained well.



Case Figure 13.5 Extrinsic allergic alveolitis due to rat serum proteins. Roitt & Rabson.

Case 13.6 Extrinsic allergic alveolitis: Bird fanciers' lung

A 41-year-old woman presented with gradual weight loss, lethargy and breathlessness on exertion of 4 months' duration, with intermittent mild wheezing and a cough. She was a non-smoker who bred budgerigars as a hobby. On examination, there were scattered crepitations throughout both lung fields but finger clubbing was absent. On investigation, she had a normal haemoglobin, white cell count and CRP. A chest X-ray showed a diffuse, generalized haziness in both lower zones but pulmonary function tests were normal. A Mantoux test was negative. Precipitating antibodies to budgerigar antigens were present in her serum.

A laboratory diagnosis of extrinsic allergic alveolitis due to hypersensitivity to budgerigar serum proteins (bird fanciers' lung) was made. The patient gave away her birds, and her symptoms regressed over a few months. Eight years later, her serum still contains antibodies to budgerigar serum proteins but she is asymptomatic – and birdless.

Case 13.7 Idiopathic pulmonary fibrosis

A 57-year-old man complained of malaise, anorexia and increasing exertional breathlessness for 4 months. When pressed, he admitted that the dyspnoea had been present for 2 years but he had attributed this to smoking 30 cigarettes a day. He had been treated for two episodes of 'bronchitis' in the preceding winter. On examination, he had finger clubbing and widespread crepitations in his chest but no arthropathy, cyanosis or skin lesions. Investigations showed a normal haemoglobin, CRP and white cell count but a raised ESR (80 mm/h).

All serum immunoglobulin levels were raised; IgG was 24 g/l (NR 6.8–19.0), IgA 9.7 g/l (NR 0.8–5.0) and IgM 12.0 g/l (NR 0.5–2.0). No paraprotein was detected. His serum contained antinuclear antibodies (titre 1/160) and rheumatoid factor (titre 1/64). A chest X-ray showed diffuse fine shadowing throughout both lung fields, especially in the lower zones, consistent with diffuse pulmonary fibrosis. A high-resolution computed tomography (HRCT) scan showed extensive established fibrosis with no evidence of ground-glass shadowing (Fig. 13.9). This was supported by results of lung function tests. A video-assisted thorascopic lung biopsy showed extensive non-uniform fibrosis and minimal inflammation. Since no other cause was found, a diagnosis of idiopathic pulmonary fibrosis was made. The histology, CT findings and the rapid clinical progression suggested a poor prognosis. A trial of oral corticosteroids, ciclosporin and azathioprine had no beneficial effect. He was referred for lung transplantation but died from respiratory failure before a suitable organ became available.

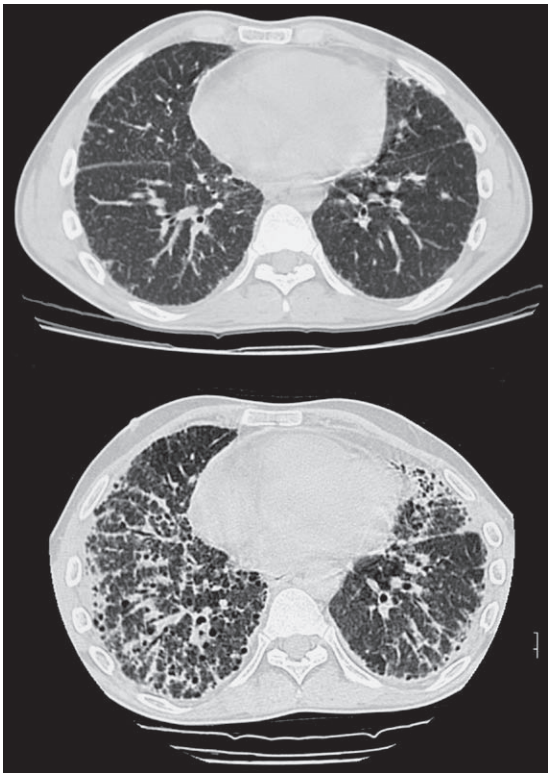
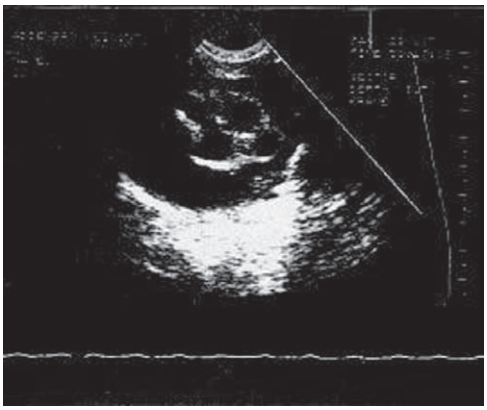
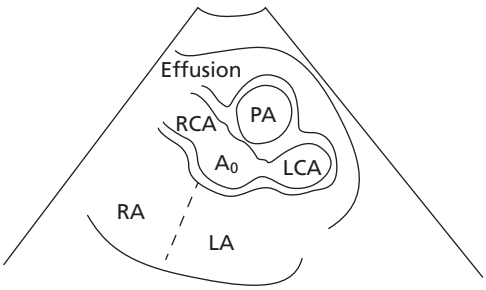


Fig. 13.9 High-resolution computed tomography scan showing (top) established fibrosis at diagnosis with relentless progression over 1 year despite aggressive immunosuppressive therapy (bottom).

Case 13.8 Kawasaki's disease

A 2-year-old girl became unwell and feverish. She was seen by her GP who felt she had a chest infection and prescribed a broad-spectrum antibiotic. She remained persistently unwell over the next 2 days and was admitted to hospital. On admission she was febrile (38.2 °C), looked ill and had enlarged lymph nodes in her neck and a blotchy red rash on her limbs. Her chest was clear and ear drums normal. Systemic infection was suspected. Investigations showed a raised white cell count (24×10^9/l, 90% neutrophils), a platelet count of 600×10^9/l and a CRP of 143 mg/l; however, a chest X-ray was clear, urine and cerebrospinal fluid (CSF) contained no cells on microscopy and subsequent blood, urine and CSF cultures were sterile. She remained unwell over the next 4 days and over this time developed marked swelling and redness of the hands and feet. Kawasaki's disease was suspected and this diagnosis was confirmed by an echocardiogram which demonstrated aneurysms of the right and left anterior descending coronary arteries. She was treated with high-dose (2 g/kg) intravenous immunoglobulin (IVIG) and oral aspirin and her fever subsided over the next 48 h. Over the next 2 weeks she developed striking peeling of the skin over the hands and feet. A repeat echocardiogram showed that the coronary arteries had improved but localized dilation was still apparent. The best results of IVIG treatment are seen when given early in the course of disease, before aneurysms have developed. She remains under long-term cardiological follow-up.





Case Figure 13.8 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 13.9 Takayasu's arteritis

A 23-year-old typist was referred to a rheumatologist with a 3-month history of cramp-like discomfort, which occurred reproducibly with any task involving the left arm. She was otherwise well, smoked five cigarettes per day and her only medication was a combined oral contraceptive. Examination revealed no abnormality in the neck or arm. A provisional diagnosis of tendonitis was made and she was treated with physiotherapy without benefit. Her ESR was found to be mildly elevated at 30 mm/h (normal < 10) but no cause was identified for this.

Two months later she was admitted to hospital following an episode of right-sided weakness associated with speech disturbance. She had a very mild right hemiparesis (which resolved over the next 6 h), a left-sided carotid bruit and a mild fever (37.7 °C). Her blood pressure was 165/90, taken from the right arm. Investigations included a CRP of 31 mg/l, normal creatinine, cholesterol 4.8 mmol/l (normal < 5.7), negative ANA, ANCA, cardiolipin antibodies, lupus anticoagulant and normal immunoglobulins. An ECG and echocardiogram were also normal. Three days after admission she asked why the nurses had such great difficulty measuring her blood pressure in the left arm, and used the right instead. Further assessment revealed that the radial and brachial pulses were almost impalpable on the left. Doppler ultrasound studies indicated an arterial systolic pressure of 80 mmHg in the left arm. An aortogram showed long, tapering tight stenoses of the left common carotid and subclavian arteries, with less severe lesions in the left renal artery. A diagnosis of Takayasu's arteritis was made and she was treated with high-dose corticosteroids. Her ESR returned to normal and subsequent ultrasound studies showed partial resolution of the carotid and subclavian stenoses.