## Case 17.1 Haemophilus influenzae type b meningitis

Alice was a normal, full-term baby who was breast-fed and gained weight appropriately in the first 6 weeks of life. At 7 weeks she became acutely miserable, stopped feeding and her mother felt that she was very warm; when she took her temperature, it was 40°C. In the surgery, the doctor found that she had neck stiffness and Alice then vomited all over the couch. There was no rash or bruising but the left eardrum was inflamed. Meningitis was suspected; the doctor gave Alice an intramuscular injection of penicillin and instructed her mother to take her straight to the hospital where the on-call paediatrician was waiting. The clinical diagnosis of meningitis was confirmed and blood and cerebrospinal fluid (CSF) samples were taken immediately and intravenous antibiotics started. The CSF showed increased numbers of neutrophil leucocytes ($131 \times 10^6$/l) and a few Gram-negative coccobacilli despite the initial dose of penicillin. Three days later these were shown to be Haemophilus influenzae and serotyping showed them to be Haemophilus influenzae type b. The full blood count showed a circulating neutrophilia ($29 \times 10^9$/l), the C-reactive protein level was 230 mg/L. Alice made a rapid recovery with intravenous and subsequently oral antibiotics, with supportive management to ensure adequate ventilation and fluids. There were no long-term sequelae and she was immunised with childhood vaccines (including Hib) once she was fully recovered at 6 months (4 months later than healthy children).

## Case 17.2 Multiple sclerosis

A 38-year-old woman presented with tingling, numbness and clumsiness of both hands for 1 week, with a band of numbness from the umbilicus to the axillae. Six months earlier, following an upper respiratory tract infection, she had experienced a short episode of blurred vision that she put down to tiredness. She was now anxious because her maternal grandmother had suffered from multiple sclerosis (MS).

On neurological examination, she had absent abdominal reflexes with brisk tendon jerks and bilateral extensor plantar responses. Blood investigations were normal, including a full blood count, C-reactive protein, vitamin $B_{12}$ and folate levels and syphilis serology. A lumbar puncture was carried out. The cerebrospinal fluid (CSF) investigation results are shown in Table 17.2. Oligoclonal IgG bands (see Fig. 19.8) are not found in normal CSF, but are found in 90% of patients with MS; in the absence of clinical signs of infection, this test is almost diagnostic of MS (see Box 17.2).

The clinical diagnosis was multiple sclerosis; other possible diagnoses, such as neurosyphilis or subacute combined degeneration of the cord, were excluded by investigation. MRI showed some silent lesions; she asked to be followed carefully without specific therapy at this stage in view of her mild symptoms.

**Table 17.2** Cerebrospinal fluid investigations in Case 17.2, multiple sclerosis

| | |
|---|---|
| Protein concentration | 0.4 g/L (NR 0–0.4 g/L) |
| Red blood cells | None |
| Lymphocytes | $3 \times 10^6$/L (NR $< 5 \times 10^6$/L) |
| IgG/albumin ratio | 26% (NR 4–22%) |
| Isoelectric focusing | Oligoclonal bands present |

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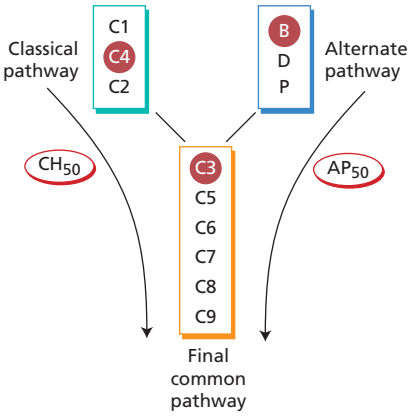
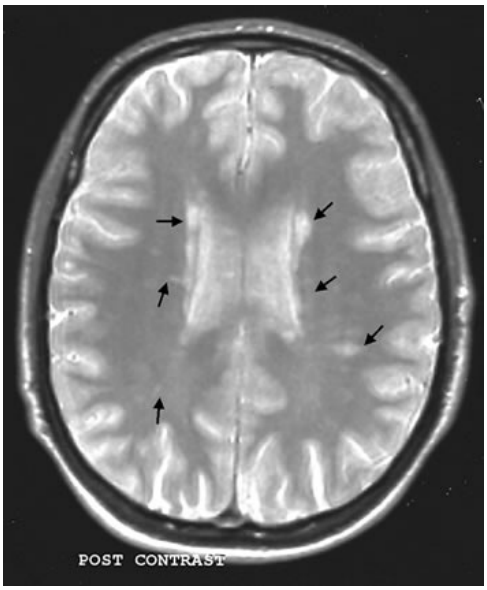



**Fig. 19.8** Complement components distributed into three groups (see text). Ringed components are those measured as representatives of the groups. Functional integrity of the classical and alternate pathways is measured by $CH_{50}$ and $AP_{50}$ assays (see text).




**Case Figure 17.2** Periventricular white matter lesions in MS.

## Case 17.3 Myasthenia gravis

A 67-year-old man, complaining of double vision, was found to have bilateral ptosis, covering most of the pupil on the right side and partially obscuring that on the left. The ptosis was worse in the evening and almost absent in the morning. He admitted to tiredness in the arms and legs on exercise, which recovered with resting. A clinical diagnosis of ocular myasthenia gravis was made. A Tensilon test, involving intravenous injection of edrophonium, a short-acting cholinesterase inhibitor to abolish the symptoms, was positive but electromyography was inconclusive.

His serum contained antibodies to thyroid microsomes and to acetylcholine receptors (see section 19.7). The patient improved on treatment with pyridostigmine, which prolongs the action of acetylcholine by inhibiting the breakdown.

This case is not typical of myasthenia gravis but demonstrates that myasthenia may affect mainly ocular muscles (although only 60% have detectable antibodies to acetylcholine receptors). Myasthenia gravis is more commonly a disease of young women, who present with increasing systemic muscle fatigue (see Case 5.2 in Chapter 5, Autoimmunity).

## Case 17.4 Guillain–Barré syndrome

A 14-year-old boy awoke one morning 2 weeks after an episode of influenza with a mild weakness in his legs; his sceptical parents wondered if this was a ploy to avoid school but during the day he developed pain in his back and 'pins and needles' in his feet. He was considerably worse the next day and complained of weakness in his arms as well, and he was admitted to hospital that evening with suspected acute idiopathic inflammatory polyneuropathy. Lumbar puncture showed no cells but a slightly raised protein level in the CSF. Peripheral nerve conduction studies the next day revealed demyelination, confirming a diagnosis of Guillain–Barré syndrome. Antibodies to ganglioside GD1 were present in his blood. His condition was by now stable and so he was not treated with high-dose intravenous immunoglobulin but monitored carefully; he made a complete recovery in 8 days.

## Case 17.5 Multifocal motor neuropathy

A 48-year-old man presented with gradually increasing weakness in his arms. Leg weakness followed after 2 weeks and he experienced steady but slow downhill progression over 4 weeks. He had no consistent sensory symptoms. On examination, he was found to have a motor tetraparesis, most marked in the arms. Sensation was normal. Nerve conduction studies showed a demyelinating motor neuropathy in upper and lower limbs, with motor conduction velocities of 26 m/s. Antibodies to GM1 ganglioside were present in the serum, confirming the diagnosis of chronic multifocal motor neuropathy. He was treated initially with prednisolone but this provoked further deterioration.

IVIG (2 g/kg body weight) was initially instituted every 8 weeks, with an initial excellent response after 5 days that gradually deteriorated after 4 weeks, returning to pretreatment levels by 8 weeks, in keeping with the half-life of IgG in the serum. This response to therapy was confirmed by a further infusion, after which changing the interval between infusions to 3 weeks and infusing IVIG (at a dose of 0.8 g/kg) resulted in sustained improvement. This condition is unusual in young children.

## Case 17.6 Systemic lupus erythematosus

A 45-year-old woman presented with acute disorientation so severe that she was unable to dress herself. On neurological examination, there were no abnormal findings, and routine laboratory investigations, including examination of the urine, were normal. Nuclear MRI showed three frontal lobe lesions with the characteristic appearances of vasculitis, so a detailed search for a cause was undertaken.

A laboratory diagnosis of systemic lupus erythematosus (SLE) was made (Table 17.7). Prednisolone was given with a dramatic improvement in the patient's mental state; within a week she was able to dress herself, and 10 days after admission she was able to go home. Serological tests 9 months later showed only a weakly positive ANA at 1/160, a normal C3 level of 0.77 g/L, a low C4 level of 0.14 g/L, and persistent elevated DNA binding (68%).

**Table 17.7** Investigations for Case 17.6, cerebral SLE

| | |
|---|---|
| Antinuclear antibody (ANA) | Positive: 1/80 |
| Antineutrophil cytoplasmic antibodies | Negative |
| dsDNA binding | High, 91% (normal <30%) |
| DNA antibodies (IgG) | Positive on Crithidia luciliae (titre 1/120) |
| Serum IgG | 16.5 g/L (NR 6.0–12.0) |
| C3 | 0.54 g/L (NR 0.65–1.25) |
| C4 | 0.03 g/L (NR 0.2–0.5) |