NEUROLOGICAL EMERGENCY

Management of cerebral infection

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Acute meningitis is the most common of the cerebral infection syndromes. Epidemiology, pathogenesis, and evolution are complex, and vary with geography and with age. Presentation occurs within hours, or at most a few days, of the onset of symptoms which, with the signs, are characteristic: headache, fever, photophobia, irritability, neck stiffness, and changed mental state. The causal agent is either a virus or a bacterium. Fungi and parasites cause acute meningitis only in exceptional circumstances. Viral meningitis is a much more benign illness than the bacterial form.

Viral meningitis

The term "acute aseptic meningitis" was coined by Wallgren in 1925¹ to describe acute meningeal irritation, benign and self-limiting, with complete recovery and sterile pleocytic CSF.

It has since become evident that at least 70% of such cases are caused by viruses. CNS viral infections are complications of systemic viral infections, and the virus gains access to the brain by the bloodstream or, less commonly, by travelling up peripheral nerves.² Viral meningitis is the result of haematogenous infection and, to enter the CNS, the virus must cross the endothelial cell junctions of the blood-brain barrier, the ability to do this being dependent upon surface adhesion molecules on the cells, surface charges and cellular receptors of the virus, and the property of entering infected cells.³ Certain viruses preferentially infect the meninges, choroid plexus, and ependyma rather than cerebral parenchyma, causing meningitis; others infect neurons and glia to cause encephalitis. There is, however, considerable overlap, and some viruses may cause meningoencephalitis, incorporating signs of both.

Most cases of viral meningitis occur in children and young adults worldwide. Infections occur throughout the year, with a preponderance in summer and autumn in temperate climates. The annual reported incidence varies from 11 to 27 cases per 100 000,^{4,5} and over 7000 cases are reported annually in the United States⁶: the actual number of infections is almost certainly several multiples higher, because of under-reporting. Over half are caused by enteroviruses—coxsackie-B or

echo, and less commonly by herpes simplex type 1, varicella zoster, mumps, lymphocytic choriomeningitis, and HIV.

The clinical onset is usually rapid over hours, with pyrexia, malaise, headache, neck stiffness, photophobia, lethargy, myalgia and irritability. Most cases do not progress further, and the subject can be roused easily and remains coherent. If the conscious level reduces, or focal signs or seizures occur, encephalitis is implied. Resolution begins within a few days and is complete within two weeks in most. A few will have persistent malaise and myalgia for some weeks. The pathogen is seldom identified clinically—parotitis and orchitis may point to mumps, arthralgia and lymphadenopathy to HIV, myalgia and myocarditis to coxsackie, and rashes to enteroviruses. The illness is not as severe and prolonged as bacterial meningitis, and the signs are not so marked.

DIFFERENTIAL DIAGNOSIS

Conditions from which viral meningitis must be differentiated are the early stages of bacterial meningitis, some cases of subarachnoid haemorrhage and other causes of aseptic meningitis, partially treated bacterial meningitis, meningitis caused by fastidious bacteria, fungi and parasites which do not readily grow in routine culture, parameningeal infection, inflammation or neoplasia, and collagen disease. To confirm the diagnosis, CSF examination is mandatory, but not before dangerously raised intracranial pressure (ICP) or a space-occupying lesion has been excluded by appropriate imaging. CSF pressure is normal or slightly raised, and the fluid is clear to the naked eye. Cell counts are in the range of up to 500–1000 white cells, mainly lymphocytes, although in some, polymorphs may predominate. In such cases it is prudent to re-examine CSF 12–24 hours later to identify a lymphocytosis and exclude a bacterial cause.⁷ CSF protein may be slightly raised, glucose is normal or only a little reduced. Numerous laboratory tests have been applied to CSF with the claim that they differentiate a bacterial from a viral aetiology, but none is sufficiently discriminating to be useful. These include lactate, lysozyme, C-reactive protein, and creatine kinase estimations. A similar lack of specificity applies to the occasional abnormalities that may be seen

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in blood counts, blood biochemistry, and the EEG.

In most cases it is not necessary to establish an exact aetiology for treatment purposes, as the disease is benign and self-limiting and, provided other similar treatable diseases have been excluded, symptomatic treatment with analgesics and anti-emetics is all that is required. Antibiotics should not be given.

To establish the aetiology, the virus may be isolated from CSF or by serological studies of acute and convalescent serum samples, identification of IgM antibody or viral antigen in CSF. The application of recently developed immunological and DNA probe amplification techniques, including polymerase chain reaction (PCR), to detect viral antigen, is promising.⁸ In the UK, their use at present is dictated more by local availability than by clinical need.

Viral encephalitis

Acute viral encephalitis is due to direct invasion of brain parenchyma, and the clinical manifestations are caused by cell dysfunction from this invasion and associated inflammatory change. At the bedside this may be indistinguishable from post-infectious encephalitis, the pathology of which is perivenous demyelination thought to be caused by allergic or immune reactions triggered after a latent period by viral infection.^{9,10} Viruses are far and away the commonest cause of encephalitis globally, but in certain locations and seasons other organisms such as malaria and other protozoans, rickettsiae and fungi may induce an encephalitic syndrome.

As with meningitis, so with encephalitis, the virus reaches the brain by the bloodstream. Entry may be through the skin following an insect bite, as with arbovirus infection, or via the respiratory or gastrointestinal route. Local replication ensues, the inoculum spills into blood and so to the reticuloendothelial system whence, following further replication, viraemia increases, and spread takes place to other sites including the CNS. Modification of this process by host immune responses may occur, and if these are compromised, disease progression may be fulminant. Most cases of encephalitis are caused in this way. The virus may also ascend neurons centripetally to lodge in brain cells, as with herpes simplex encephalitis and rabies. Fortunately, encephalitis is a rare complication of common viral infections, and most patients with systemic viral infections do not develop neurological signs.

Certain viruses exhibit tropism towards specific cell types—the limbic system in rabies, temporal lobes in herpes simplex encephalitis—and this may produce clinical signs that are diagnostically useful. In most cases of encephalitis, however, signs and symptoms are common to most pathogens, and diagnostic clues must be sought elsewhere: is there evidence of infection elsewhere, such as the characteristic rash of varicella or measles, or the parotitis of

mumps? Has there been travel to or from an area that harbours known vectors? Is there past or present evidence of an animal or insect bite? What is the season of the year? Diagnostic tests may help, yet in perhaps as many as a third of all cases, no specific aetiology can be established.

Viral encephalitis is not rare, and it occurs globally. In the UK and Europe, most cases are sporadic accompaniments of common infections such as mumps, measles, and herpes simplex. In the United States, sporadic and epidemic forms are caused by the arboviruses (*arthropod-borne*), and Japanese B encephalitis causes most epidemic infections elsewhere. As many as 20 000 cases per annum may occur in the United States.¹¹

Patients who develop viral encephalitis often have a prodrome lasting several days, which may include myalgia, fever, malaise, mild upper respiratory infection, rash, or parotitis. The development of headache, mental change, and drowsiness implies encephalitis, which is usually associated with meningitic features. As the disease progresses, disorientation and disturbance of behaviour and speech worsen, and drowsiness becomes coma. Epileptic seizures are common, and focal signs may appear appropriate to the area of the brain taking the brunt of the infection—hallucinations and memory upset from the temporal lobes, hemiparesis, spasticity, sensory loss and speech upset, and cerebellar deficits. There may also be signs of raised intracranial pressure. The very young, the very old, and those with compromised immune systems often have more severe disease. Signs should be sought in other organ systems, which may point to a particular virus. Some forms of encephalitis have specific features which are briefly discussed later.

DIFFERENTIAL DIAGNOSIS

The list of other diseases that may cause a similar clinical picture is large, and includes all forms of bacterial meningitis, malaria and other protozoal and fungal infestations, intracranial suppuration, septicaemia and endocarditis, metastatic disease and collagenoses, and drug abuse.

Faced with a patient with rapid onset of pyrexia and stupor or coma, the above potentially remediable conditions need to be excluded quickly. Blood counts and biochemical tests are not diagnostic but may be abnormal as a result of inadequate hydration or inappropriate secretion of antidiuretic hormone. Blood films should be examined for malaria parasites, and blood cultures set up.

As these results are awaited, the intracranial contents should be imaged to determine if there is space-occupation, cerebral oedema or focal areas of infarction such as may occur in the temporal lobes with herpes simplex encephalitis. Scans must be interpreted with close attention to their timing in the evolution of the disease: in the first two or three days no abnormality may be evident, and changes may not show for five or six days, so repeat

scanning may be necessary. The EEG is abnormal, most often showing non-specific diffuse slow-wave activity, perhaps with seizure activity. Temporal lobe focal abnormality with high-voltage spike and slow-wave complexes is highly suggestive of herpes simplex encephalitis. CSF should be examined as soon as possible when deemed safe; unfortunately cranial scanning does not convey an accurate picture of intracranial pressure, and judgement of the potential safety of lumbar puncture requires not a little luck. CSF is often under pressure and the cell count is raised, from 10 to as many as several thousand white cells per mm³, usually lymphocytes, but polymorphs may predominate in the early stages. Red cells may be found if there is a necrotising component, as in herpes simplex encephalitis. The glucose content is normal, protein is raised, and organisms are not seen.

TREATMENT

In the recent past, treatment of viral encephalitis was symptomatic, and no specific drug would influence the outcome. This has changed with the advent of acyclovir and other forms of antiviral chemotherapy, so it is now imperative to identify the organism as soon as possible, or at least to determine whether it is herpes simplex. Early reports of the application of PCR and other techniques to the rapid detection of viral antigen in CSF are encouraging.^{12,13} In my view, brain biopsy no longer has a place in the diagnosis of viral encephalitis, except to determine if a lesion demonstrated by scan is an abscess, granuloma, or tumour. The complication rate is over 3%, and there is no guarantee that the area biopsied will contain virus. It is safer to begin treatment with acyclovir if clinical suspicion is high.

With the exception of that caused by herpes simplex, the treatment of viral encephalitis is symptomatic, and requires the maintenance of adequate nutrition, hydration, and oxygenation. Seizures are controlled with anticonvulsants, and secondary infections are treated as necessary. Intracranial hypertension and cerebral oedema may be a problem, and there is no consensus on the correct treatment. Intubation and hyperventilation, glycerol, mannitol, and dexamethasone have all been used, and I continue to use dexamethasone in severely ill patients, despite theoretical objections.

SPECIFIC ENCEPHALITIDES

Herpes simplex

This is the most common cause of sporadic encephalitis in Europe and North America, with an incidence of up to 0.5 per 100 000 population each year—almost certainly an underestimate because milder cases go unrecognized. It occurs throughout the year, and almost all cases are caused by HSV-1. It is no more common in those with compromised immune systems, and it affects patients of any age. A third are below 20, and half

over 50.¹⁴ The clinical presentation is enormously variable. Onset is usually insidious, with a prodrome of 4–10 days, with malaise, pyrexia, and irritability, followed by frontal and temporal lobe disturbance of personality change, hallucinations, psychiatric upset, and increasing focal signs, seizures, and deteriorating conscious level. In perhaps as many as 87%, focal signs appear.¹⁵ In a few, the onset is cataclysmic, and the evolution is compressed into only a few days. Abscess, tumour, granuloma, vascular disease, and other forms of viral encephalitis are the other diagnoses that have been mistaken for herpes simplex encephalitis.¹⁶ Focal changes on CT, MRI, and EEG, as already described, are helpful but not pathognomonic.

Treatment must be given quickly with acyclovir, 10 mg/kg by i.v. infusion over one hour, every eight hours for 10 days. This has been shown to diminish mortality to 30%.¹⁷ Most people use dexamethasone despite objections that interferon synthesis may be inhibited.

VARICELLA ZOSTER

Encephalitis accounts for 90% of the neurological complications of varicella, which are in themselves rare, affecting 0.1% of cases.¹⁸ In half, the encephalitis is of cerebellar type, with ataxia, dysarthria, headache, and drowsiness coming on about a week after the rash begins,⁹ but the neurological onset may precede the rash. Convulsions are common,¹⁹ and progression to hemiplegia, cranial nerve palsies, aphasia, and coma may ensue. Patients with the cerebellar form usually recover completely, but 10% of those with the general form die.⁹ Encephalitis may rarely follow shingles. Management is symptomatic, as already described.

Cytomegalovirus

This is not an important cause of encephalitis except in neonates and in immunocompromised patients, recipients of organ transplants, and patients with AIDS. Treatment with antiviral agents has, to date, been nugatory.

Epstein-Barr virus

Meningoencephalitis has been described as a rare complication of Epstein-Barr virus infection.²⁰ There are no specific features, and the prognosis is excellent.

Measles

Acute encephalitis occurring in the course of measles infection is usually caused by a postinfectious, perivenous, demyelinating, allergic phenomenon, although in some there may be direct virus-induced cellular damage, and virus has been isolated.²¹ Clinically the manifestations are the same, and occur in up to one in 1000 cases above the age of two, the frequency increasing with age. Typically, as the exanthem begins to fade after seven or eight days, fever recurs and encephalitis develops rapidly, with convulsions, focal signs, myoclonus, and coma.^{22,23} There are no

specific features on investigation, and treatment is symptomatic. Mortality is high at 15%, and most are left with some disability.²³

Mumps encephalitis

This complication is rare, occurring in less than 1% of cases, and has no specific features; it follows up to two weeks after development of parotitis, though this may be absent in up to half.^{24 25} Treatment is symptomatic and prognosis is excellent.

EPIDEMIC ENCEPHALITIS

Arboviruses cause epidemic encephalitis in various parts of the world. They are not an important cause of encephalitis in Britain, but with the increasing ease and frequency of intercontinental travel, cases are now being recognised, and the likelihood is that the frequency will increase. It is imperative therefore that a full history of travel abroad be taken from anyone suspected of neurological infection, and arbovirus encephalitis should be suspected if there has been exposure to insect bites in countries known to harbour these viruses.

All of these arboviruses are perpetuated by zoonoses of insignificant infection in birds and smaller vertebrates. Transmission is by an arthropod vector, mosquito or tick. Replication and viraemia develop after being bitten. Most people suffer only a mild systemic illness, but some go on to develop encephalitis, the severity of which depends upon the strain of the virus. Clinical features are common to all, with some variation in incubation, progression, and severity, and they cannot be diagnosed on clinical grounds alone. There are no specific features to be found on imaging, on the EEG or in the CSF. Diagnosis is by demonstration of antibody rise in paired serum samples. Treatment is symptomatic.

Eastern equine encephalitis

Birds of the Atlantic and Gulf coasts of America are the reservoir of this rare condition. Epidemics may occur in horses. Cases occur at migration time, summer and autumn, and children are most affected, with an acute encephalitis which may be abrupt and virulent, with a mortality rate of 70%.²⁶

Western equine encephalitis

This is less severe, occurring in eastern, central and western United States, Canada, and eastern South America.

St Louis encephalitis

This disease shares the same clinical features in the same areas and in central America. West of the Mississippi it is endemic, and cases occur in epidemics or sporadically from July to October. Most cases are benign and of short duration.

California and La Crosse viruses

These viruses are similar and cause the same disease in central and midwest United States. The reservoir is small rodents and the vector

is an *Aedes* mosquito. Children are affected, with a peak in August and September. Clinical onset is sudden, and recovery takes place within 10 days.

Central European encephalitis

This encephalitis may be contracted from woodlands in Scandinavia through to northern Greece and the former Yugoslavia, and more cases are being reported from Austria. The virus is maintained in small woodland mammals and transmitted to people who enter the forest for recreation or work and are bitten by an *Ixodes* tick. There is a biphasic course with an initial flu-like illness, followed within two weeks by mild meningitis or encephalitis, perhaps with muscle weakness. Management is symptomatic and recovery is usually complete. Diagnosis is serological.

Russian spring-summer encephalitis

Russian spring-summer encephalitis is a similar, more severe, condition.

Japanese encephalitis

This is the most common arbovirus infection worldwide, and is endemic in southeast Asia, Japan, China, Philippines, Borneo, and large areas of the Indian subcontinent. Birds and domestic animals are the reservoir, mosquitos the vector. Encephalitis is seen most commonly in those under 15 and in the aged. After an incubation period of one to two weeks there is abrupt onset of encephalitis, often with myalgia. Extrapyramidal features have been noted.^{27 28} Convalescence may be prolonged and sequelae are common. Treatment is symptomatic and diagnosis is serological.²⁹

Rabies

In Britain, recognition of a case of clinical rabies is exceptionally rare and, numerically, barely merits inclusion in a description of neurological emergencies. However, rabies is endemic throughout the world except for the UK, Ireland, Antarctica, Australasia, Japan, and islands of the Caribbean, Mediterranean, and Scandinavia. Most of the cases now seen in the United States have been contracted abroad and, where countries have introduced programmes to control domestic rabies in cats and dogs, the incidence in humans has dropped.³⁰

DIAGNOSIS

Diagnosis is straightforward if an appropriate history can be obtained, but where that is lacking, the onset of hydrophobia provides the clue. Rabies should be considered in the differential diagnosis of all encephalitides contracted abroad, and it is important to remember that perhaps 15% of all cases present as a Guillain-Barré type of syndrome. Cranial imaging and EEG do not show specific features, and CSF may show a pleocytosis and raised protein. Rapid diagnosis can be reached by the demonstration of rabies antigen in neck skin-biopsy,³¹ which is said to be

more accurate than corneal smears. Virus may be isolated from saliva and other fluids.

TREATMENT

Treatment does not alter the inevitably fatal outcome but does relieve distress to patients and relatives. Sedation may be necessary in the "furious" stage, anticonvulsants may prevent seizures but it may be necessary to paralyse and ventilate the patient to prevent the severe generalised spasms of advanced hydrophobia. There is no evidence that steroids, immune suppression, antibiotics, or antiviral agents help. All secretions from the patient should be regarded as potentially hazardous, and any staff thought to have been inoculated by them should have a course of immunisation.

HIV

Cerebral infection is a frequent accompaniment of HIV infection. The virus itself affects the brain, and the systemic immune suppression which accompanies AIDS renders the sufferer liable to superadded and opportunistic infection which frequently attacks the brain. The manifestations of HIV infection of the brain coexist with opportunistic infection, and may result in a complex and confused syndrome constellation. Many of the features are chronic in evolution and some are acute. In practice, any change in neurological status in a patient with AIDS usually presents as an emergency because of the danger of opportunistic infection. Conversely, the finding of an unusual cerebral infection in a patient not known to be immune suppressed should raise the suspicion that he or she may have HIV infection. Many excellent accounts of the epidemiology and classification of the natural progression of HIV infection are available, and are not discussed further here.³²⁻³⁴

AIDS DEMENTIA COMPLEX

AIDS dementia complex occurs during established AIDS and, with more subtle neuropsychological and neurophysiological techniques, it is possible to demonstrate mild cognitive defects in early infection.³⁵ It is now recognised that 90% of AIDS patients will develop this complex before death. The usual course is for the subject to become withdrawn, apathetic, and mentally slow, and progress inexorably to become increasingly demented.³⁶ The course may, however, be interrupted by acute relapses with confusion and psychosis, when the patient may present as a neurological emergency, and it is necessary to exclude other CNS infections, neoplasia, and systemic illness as a cause.

OPPORTUNISTIC INFECTIONS

Infection and lymphoma can complicate and alter the progression of AIDS and precipitate a neurological emergency. Toxoplasma, cytomegalovirus, herpes simplex, herpes zoster, cryptococcus, histoplasma and other

fungi appropriate to geography, tuberculosis and syphilis are all frequent pathogens. Progressive multifocal leukoencephalopathy may also complicate AIDS and, unfortunately, more than one syndrome may be present at any given time, so the clinical picture can be confused.

All patients with AIDS should be checked for syphilis with a specific antitreponemal test. A negative tuberculin skin test is likely in these patients even if they have tuberculosis.³⁷ If a focal lesion is seen on CT or MRI, it may be toxoplasmosis,^{38,39} tuberculoma, lymphoma, or brain abscess. Lymphoma usually shows solid, multicentric lesions, but can show ring enhancement. Single or multiple ring-enhancing, hyperdense or hypodense lesions may be caused by any of these pathologies: no appearance is specific. Because 10–40% of patients with AIDS will develop toxoplasmosis during the course of their illness, and serological tests are not sufficiently specific to confirm that toxoplasmosis is the cause of the lesion, biopsy must be considered. In such circumstances accepted practice (which I adopt) is to treat for toxoplasmosis with pyrimethamine and sulphadiazine, and with dexamethasone to reduce brain swelling. If the lesion is due to toxoplasmosis, improvement occurs within 10–14 days and can be monitored by serial scanning.⁴⁰

If improvement does not occur, if there is clinical deterioration, or if diagnostic doubt remains, biopsy should take place, and treatment given as appropriate. Tuberculosis is an increasing problem due both to *Mycobacterium tuberculosis* and to *M. avium* complex disease, and the author's threshold for deciding to perform a biopsy is diminishing, in order to make this diagnosis early: treatment of *M. avium* complex disease responds better to regimens that incorporate clofazimine and amikacin.⁴¹ At present there is no satisfactory regimen for the treatment of established HIV infection, but appropriate and prompt treatment of these infective complications can lead to prolonged remission.

Bacterial meningitis

Any bacterium is capable of causing meningitis, given favourable circumstances. Meningitis may come about as part of a generalised illness or as a complication of disease elsewhere. In practice, most cases are caused by organisms with properties of virulence which allow access to the CNS. With the exception of the neonatal period, *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae* account for 70% of all cases. Neonatal meningitis may be caused by any organism, and the most frequently encountered pathogens are Gram-negative bacilli, particularly *E. coli* K1, other enteric bacilli, *Pseudomonas* and group B streptococci. Neonatal meningitis is not discussed further here.

The epidemiology of meningitis is complex, and varies with the age of the patient

and geography. About 70% of cases are seen in children. *H influenzae* and *N meningitidis* are the main causes in this group; in adults, *S pneumoniae* and *N meningitidis* predominate, and there is an increasing number of cases caused by Gram-negative bacilli and *Listeria*, particularly in the elderly. Streptococci and staphylococci also cause sporadic cases—the meningococcus remains the only significant cause of epidemics. *H influenzae* is a more common pathogen in the United States than in the UK (48% *v* 29%) where the meningococcus and pneumococcus predominate (45% *v* 33%).⁴²⁻⁴³ Gram-negative bacilli tend to occur in association with head injuries, following neurosurgery, in patients who have compromised immune systems, and in the elderly. One disturbing factor is the increase in the number of cases nosocomially acquired.⁴⁴ The streptococcus infects puerperal women, the elderly and those with immunosuppression, as does *Listeria*. Staphylococcal infection may complicate neurosurgical procedures and head trauma, and also affect those immunosuppression or endocarditis. Anaerobic organisms cause less than 1% of cases. Infection with more than one organism also occurs in 1%, and in similar circumstances—paranasal sinus and ear infections, skull fractures, neurosurgery, and immunosuppression.⁴⁵⁻⁴⁶ Tuberculosis remains a significant cause of meningitis in the UK and the United States. Many other organisms may also cause meningitis, commonly of a more chronic nature, which may rapidly develop into an acute emergency in patients with compromised immune systems.

PROGRESS IN DIAGNOSIS AND TREATMENT

Advances in the investigation and management of bacterial meningitis over the past 40 years or so, including the continuing development of antibiotics, the introduction of CT and MRI imaging, the application of improved techniques of bacterial culture, and now the widespread use of molecular methods incorporating PCR,⁴⁷ have permitted treatment to be given on a more rational basis to a wider range of patients. It is disappointing therefore that mortality and morbidity from the main forms of bacterial meningitis have failed to diminish to any substantial degree over the same length of time. Fortunately, in recent years, new understanding of the pathophysiology of the changes that occur in bacterial meningitis has become available,⁴⁸⁻⁵⁰ from which it will be possible to develop new strategies for treatment.

One of the major features of meningitis is a CSF neutrophil response. The exact mechanism by which white blood cells cross the blood-brain barrier is not yet known. The release of some bacterial cell wall components into the CSF stimulates the release of inflammatory cytokines, including interleukins 1 and 6, tumour necrosis factor, and prostaglandins into CSF, and there is strong evidence that their presence induces inflammation and disruption of the blood-brain barrier. By a complex series of interactions, as

yet ill understood, cerebral blood flow increases, inducing vasogenic cerebral oedema and raised intracranial pressure. With the progression of inflammation, cytotoxic oedema develops, cerebral blood flow falls, vasculitis progresses and intracranial pressure rises further. Interstitial oedema results from obstruction of CSF flow from subarachnoid space to blood. Cerebrovascular autoregulation is disrupted⁵¹ and the brain becomes at risk from either hyper- or hypoperfusion. Evidence is accumulating that many of these changes occur early in the course of meningitis, and treatment regimens that reduce intracranial pressure while maintaining cerebral perfusion and blood flow may be useful.⁵⁰

DIAGNOSIS

The clinical features of a typical case of meningitis are easy to recognise—fever, malaise, headache, neck stiffness, irritability, and confusion. Usually these features appear over the space of a day or two but in some fulminant cases the signs may develop within hours. In as many as 20% of cases these typical features may be lacking: this is particularly so with the very young, the very old, the very ill, and those with compromised immune systems. The possibility of meningitis should be entertained in every child or adult in the above groups who has lethargy, altered mental status, drowsiness, or pyrexia, especially if neck stiffness is present. It is important to recognise that neck stiffness may *not* be present, and the physician must include meningitis in the differential diagnosis of a very wide range of diseases.

Epileptic convulsions occur with meningitis in any age group, are particularly common in young children, affecting up to 40% of cases, and may be the presenting feature.⁵² Convulsions associated with pyrexia—“febrile convulsions”—commonly occur in the very young age group; each such patient may have meningitis, which poses the question, does each require lumbar puncture? Evidence suggests that the answer is no. In one study,⁵³ four out of 328, and 15 of 304 in another,⁵⁴ had signs of meningitis on lumbar puncture. If the convulsion is brief and not associated with continuing neurological deficit or focal feature, if the child rapidly regains consciousness, and there are no other signs of meningitis, it is reasonable to observe the child closely for some hours rather than perform a lumbar puncture straight away.

Skin rashes are evident in about a third of patients, and their presence should be sought, for in some they may be sparse. A diffuse maculopapular eruption which progresses to include petechiae or frank purpura accompanies 50–60% of cases of meningococcal meningitis. Other bacteria—*Listeria*, staphylococci, pneumococci, *Haemophilus*, and viruses, particularly echo 9, may also cause rashes. Rarely, a rash may be due to a reaction to an antibiotic or other drug, but this seldom occurs early in the course of the disease. Shock may accompany any fulminant or

overwhelming meningitis, and often complicates meningococcal infection. Focal neurological signs complicate meningitis in at least 15% of cases.⁵⁵ Hemiparesis implies arteritis or phlebitis and resulting infarction, or an evolving brain abscess. Cranial nerve palsies, commonly of the sixth and third nerves, are caused by basal exudation and inflammation. Sixth-nerve palsies may indicate that intracranial pressure is rising dangerously. The level of consciousness must be closely observed and documented, for it correlates best of all with the likely clinical outcome. Mortality rises dramatically as consciousness decreases,^{56 57} and approaches 55% for adults in coma. Cerebellar signs may be noted in some cases, and have no aetiological significance.

When assessing a case of meningitis, diligent search must be made for a non-neurological locus of infection, and cultures made from it, or for a pre-existing or contemporaneous illness that enables organisms to become more rapidly pathogenic.

There is some correlation between organism and condition. Pneumococcal meningitis is associated with otitis media, skull fractures, alcoholism, and sickle cell disease, and up to 50% will have pneumonia. *Haemophilus* meningitis is uncommon after early childhood and its occurrence raises the possibility of a parameningeal focus of infection, including ear, nose, and basal skull fracture. Staphylococcal infection complicates the implantation of neurosurgical devices such as shunts. In those with immunosuppression, including AIDS, simultaneous infection with more than one organism can occur. Tuberculosis meningitis may rarely be complicated by superadded infection. In the author's experience, diabetic patients are dangerously liable to misdiagnosis because their symptoms may be misinterpreted as being due to hypoglycaemia or to uncontrolled diabetes, and meningitis can exacerbate diabetes. If there is a history of meningitis in the past, there is probably a dural fistula from previous head injury or, much more rarely, the patient suffers from an inherited immunodeficiency state. In all cases, blood cultures should be taken before antibiotics are given.⁵⁵

Once the possibility of meningitis is entertained the diagnosis must be confirmed straight away. Next to the conscious level on admission, the factor that has the most deleterious effect on prognosis is delay in beginning treatment. CSF examination is the only sure way to confirm the diagnosis, and this is almost always done by lumbar puncture. It may, in circumstances such as the existence of hydrocephalus, be necessary to puncture the ventricle to obtain a specimen. In established meningitis there is usually no difficulty in reaching a diagnosis. Very early in the evolution of the disease, however, or if antibiotics have already been administered, or if the organism is fastidious in its requirements for laboratory culture, it may not be possible to identify the causal bacterium. Discussion of

the problem with the microbiological laboratory before taking CSF usually more than recoups the time spent, in order to ensure that appropriate culture media are available, and precautions taken to look for anaerobic organisms.

Lumbar puncture

Bacterial meningitis raises intracranial pressure. In most cases physiological mechanisms cope, and no long-term, untoward effects result. It is now becoming recognised that the intracranial pressure can rise to potentially lethal levels, with cerebral oedema and brain herniation. In such circumstances, to do a lumbar puncture can lead to rapid deterioration and death. To reconcile this with the necessity of reaching an early diagnosis is, in some cases, difficult; the correct decision depends on experience and a degree of luck. In my view, CT should be undertaken immediately if there is evidence of focal neurology on examination or historically, if the conscious level is reduced or the patient is confused, if headache is severe, or if there are frequent seizures. A recent report⁵⁷ suggested that CT had little influence on the management of bacterial meningitis in children, but did not address the problem of recognition of raised intracranial pressure and lumbar puncture. Cerebral herniation and death do occur as a result of injudicious CSF examination in cases of suspected meningitis,⁵⁸⁻⁶⁰ and a normal CT scan does not always mean that it is safe to proceed to lumbar puncture: until better procedures to monitor intracranial pressure become routine, this decision must be left to clinical experience, reassured by brain imaging to exclude space occupation and cerebral oedema.

If there is a bleeding diathesis or coagulation defect, these should be corrected before lumbar puncture. If it is decided that lumbar puncture is too dangerous, or there will be a delay before scanning can be done, immediate treatment with antibiotics should be given, after blood cultures have been taken. The antibiotic regimen chosen will be a "best guess", based on the age, medical background, geographical location, and clinical findings of the patient. CSF may be examined later when it is considered to be safe, and evidence of bacterial infection can be found by demonstration of antigen with newer techniques.^{61 62} Anxiety that infection may be introduced to CSF by lumbar puncture in patients with bacteraemia is largely unfounded.⁶³

CSF findings are of a raised cell count with polymorphs predominating, at least 60%. There is no agreed value for the absolute count but usually this falls within the hundreds or more. The protein content is increased, and the glucose is reduced. A sample of blood should be taken at the time of lumbar puncture for comparison: a ratio of CSF:blood glucose of less than 0.3 is abnormal and is found in about three-quarters of patients.⁶⁴ Unfortunately this is not specific and may be found in other chronic forms of meningitis.

Identification of the causal organism under the microscope or on culture should be possible in up to 80% of patients. A plethora of tests has been devised over the years to differentiate bacterial from other forms of meningitis: unfortunately they all suffer from lack of specificity or sensitivity,⁶⁵ and are being superseded by newer, molecular techniques.⁶¹

CT and MRI scans need to be interpreted with due consideration given to the timing of the scan in relation to the evolution of meningitis: early in the disease the scan may be normal, but such a finding does not exclude meningitis. There may be meningeal and ventricular ependymal enhancement, basal purulent exudate, small ventricles with cerebral oedema, or large ventricles from CSF flow obstruction in the aqueduct or basal cisterns. Later in the disease, areas of infarction from vasculitis, and subdural collections may be seen, particularly in children with *Haemophilus* infection.^{66,67} Brain imaging also permits exclusion of other conditions that may present like meningitis—subarachnoid and intracerebral haemorrhage, infarction, tumour, and brain abscess. MRI is better at demonstrating more subtle changes than CT, but it is technically much more difficult to carry out MRI on a confused and uncooperative patient, or on one who requires artificial ventilation, than it is to perform CT.

A full blood count and sedimentation rate should be carried out. These are frequently abnormal but unfortunately do not point to a specific pathogen. Blood gases, electrolytes and serum osmolality must be monitored carefully, especially in children. Inappropriate secretion of antidiuretic hormone can lead to a rapid fall in sodium, particularly but not exclusively with *Haemophilus* infection.⁶⁸ Other tests should be carried out according to clinical need.

TREATMENT

Once the diagnosis of bacterial meningitis has been made, treatment must be begun immediately. Precedence is given to maintaining cardiorespiratory function, adequate oxygenation, and tissue perfusion while the causal organism is being identified and the appropriate antibiotic regimen determined. If no organism can be found, antibiotic treatment is given on a "best guess" basis.

As mentioned earlier, the release of bacterial cell wall products into CSF stimulates inflammation, mediated in part by cytokines. Studies to determine the efficacy of the anti-inflammatory action of corticosteroids in reducing this inflammation have produced encouraging results in children, and trials are proceeding with adults. There is now good evidence that dexamethasone in a dose of 15 mg/kg body weight every six hours for four days reduces the incidence of neurological sequelae,⁶⁹⁻⁷² and this should be begun just before antibiotics are given. I believe the evidence is sufficiently good to justify the adoption of a similar policy in adult bacterial meningitis until further trial results are available. Dexamethasone also helps to reduce

raised intracranial pressure and, given for a short time, any side effects are minimal.

Other anti-inflammatory agents which act at different stages are currently undergoing trials. These include non-steroidal, anti-inflammatory drugs, pentoxifylline and monoclonal antibodies targeted specifically against human β_2 integrin.^{48,73} There is a complex inter-relationship between cerebral blood flow, cerebral blood volume, cerebral perfusion pressure, cerebral oedema, and intracranial pressure which becomes disturbed in bacterial meningitis. Decreased cerebral blood flow,⁷⁴ cerebral oedema,⁵⁸ and reduced cerebral perfusion pressure⁷⁵ all adversely affect the outcome. Intracranial pressure is raised maximally within the first 48 hours,^{76,77} and it should be possible to anticipate this and ameliorate the effects. Patients whose conscious level deteriorates should be considered for intracranial pressure monitoring; if the level rises above 15 mmHg, treatment to lower the pressure should be given. The head of the bed should be raised, hyperventilation induced, and dexamethasone and mannitol administered.⁷⁸

CHOICE OF ANTIBIOTIC

To treat meningitis effectively, it is necessary to achieve adequate bactericidal levels of antibiotic in CSF 10–20 times higher than the minimal bactericidal concentration *in vitro* for the particular organism. Ideally the antibiotic should be lipid soluble to facilitate transfer across the blood-brain barrier but this is not usually a problem in practice because meningeal inflammation disrupts the barrier and allows sufficient penetration. The rate at which it is metabolised and cleared from CSF determines the frequency and amount which must be given, and it should be active within purulent and acidic CSF. The choice of antibiotic will be determined by the organism found on microscopy, culture or antigen detection, and modified by knowledge of local and nosocomial drug resistance patterns.

As important as the choice of antibiotic, is the identification and eradication of any parameningeal focus of suppuration.

For *H. influenzae* type B infections, ampicillin and chloramphenicol have been the mainstay of treatment, but an increasing number of β -lactamase-producing strains are resistant to ampicillin, and a smaller number of chloramphenicol acetyltransferase-producing organisms are resistant to chloramphenicol.⁷⁹ Third-generation cephalosporins are to be preferred, and cefotaxime or ceftriaxone have been most widely used and demonstrated to be effective.^{80,81} For meningococcal meningitis, penicillin remains the preferred drug. There have been reports of meningococci resistant to penicillin,⁸² but to date this does not appear to cause problems if large doses are given. Chloramphenicol or a third-generation cephalosporin may be used in people with adverse reactions to penicillin. Pneumococcal meningitis is best treated with penicillin. Penicillin-resistant strains are being

recognised,⁷⁹ and in these circumstances, a third-generation cephalosporin or vancomycin should be used. Cephalosporins have been shown to be more effective than aminoglycosides for the treatment of Gram-negative bacillary meningitis,⁸³ and third-generation antibiotics should now be used.

Group B streptococcal infection should be treated with penicillin or a combination of penicillin and ampicillin, which is said to be synergistic, and ampicillin covers those rare cases where the organism is penicillin-resistant. Listerial infection responds to ampicillin, and for those with penicillin allergies, trimethoprim-sulfamethoxazole is effective. Nafcillin, flucloxacillin or oxacillin in high dose is the recommended treatment for *S aureus* meningitis, with vancomycin for those who cannot have penicillin.⁸⁴

Shunt infections are commonly caused by coagulase-negative staphylococci, and vancomycin—perhaps with added rifampicin—is effective. In most cases it is necessary to remove the device to eradicate the infection completely. The combination of penicillin and chloramphenicol with metronidazole is recommended for anaerobic infections.

In cases where an organism cannot be identified, children should be treated with a combination of ampicillin and chloramphenicol, or a third-generation cephalosporin alone⁸⁵; adults with penicillin or a third-generation cephalosporin; and the elderly with a third-generation cephalosporin and ampicillin. For empirical treatment of those with immunosuppression, the type of immunological abnormality governs the choice of antibiotic.⁸⁶ If the defect is of cell-mediated immunity, ampicillin should be included to treat *Listeria*; if humoral immunity is depressed, penicillin and a third-generation cephalosporin are recommended; and for the patient with neutropenia, a third-generation cephalosporin, with ceftazidime and an aminoglycoside, if *Pseudomonas* infection is likely.⁴⁹

Parenteral treatment for all forms of bacterial meningitis is recommended, and dosage schedules and a description of the adverse effects of these drugs may be found in pharmacological texts. The author's policy is to discuss the treatment of any case which is at all complicated with a specialist in infectious diseases. The length of time for which treatment is given must be tailored to each case and should be at least 10 days. Failure to respond prompts a review of the diagnosis and treatment, search for a continuing source of infection, and repeat brain imaging to demonstrate abscess or subdural fluid accumulation. Repeat CSF examination should be considered in most cases where no explanation can be found.

SPECIFIC BACTERIAL MENINGITIDES

Tuberculous meningitis

Tuberculous meningitis does not commonly present as a neurological emergency. The time course over which the clinical syndrome

evolves is longer than purulent meningitis, up to three weeks in children and rather longer in adults. In some cases, however, the onset may be acute and exactly similar to purulent meningitis, so tuberculosis must be considered in each case.

Details of treatment regimens may be found in references 87, 88 and 89. Chemotherapy is given for between six months and a year, dependent upon the severity of disease and the response to treatment. Steroids are not given routinely. Dexamethasone in high dose for a short time is useful to reduce cerebral oedema. Hydrocephalus commonly develops, sometimes acutely, and should be treated early by surgical drainage.

Lyme disease

Lyme disease, caused by the spirochaete *Borrelia burgdorferi*, can present as meningitis, in most cases of chronic type but sometimes in an acute fulminant manner.

Meningitis may occur as part of the second stage of the disease, one to six months after being bitten by the vector, an *Ixodes* tick, and because the original bite and the skin lesion of erythema chronicum migrans were not noticed or had been forgotten, presentation may rarely be with acute meningitis.⁹⁰⁻⁹²

Treatment should be given with parenteral third-generation cephalosporins⁹² for a minimum of two weeks. Intravenous penicillin in high dose is also effective,⁹³ but may induce temporary worsening of symptoms akin to the Jarisch-Herxheimer reaction, which occurs when treating neurosyphilis; so it would be prudent to cover the first doses with steroids.

Syphilitic meningitis

Another spirochaete, *Treponema pallidum*, may also cause acute meningitis. Admittedly rare, such cases are occurring more frequently in association with HIV infection and clinical AIDS.^{94,95} It occurs within two years of infection, and presents acutely with headache, vomiting, pyrexia and neck stiffness. Cranial nerve palsies are not infrequent, nor are epileptic seizures.⁹⁶ CT scan appearances are of non-specific meningeal enhancement, and CSF contains a predominantly mononuclear pleocytosis, raised protein, and normal sugar. The diagnosis is made by finding a positive CSF or serum VDRL test, and confirming it with the FTA-ABS test. The results of PCR tests for treponemal DNA are awaited with interest, in the hope that it may be possible to differentiate active syphilis from an acute neurological syndrome occurring in a patient who has had yaws in the past.

Acute syphilitic meningitis is managed by the parenteral application of large doses of penicillin for 10 days, with steroids for the first 24 hours to diminish the possibility of inducing a Jarisch-Herxheimer reaction. It is necessary to follow up all cases closely to ensure that serological changes and CSF revert to normal, and to treat any re-infection rapidly.

Rickettsial meningitis

As a consequence of the proliferation of inter-continental travel by air, the person arriving from abroad may harbour an infection not usually seen in the UK and, as the incubation period of some of these infections may be two to three weeks, symptoms may not appear until some time has been spent in the country. It is therefore of the first importance to obtain a full history of recent travel, places visited, including stop-overs, and activities undertaken, from any patient who presents with an acute meningoencephalitis. Such an illness may be caused by Rickettsial diseases, which are transmitted to man by the bites of ticks or mites, and are prevalent in every continent except Antarctica. Rocky Mountain spotted fever caused by *R. rickettsii* may be contracted in the Americas; Mediterranean spotted fever (*R. conorii*) in Africa, Asia and the Mediterranean basin; scrub typhus (*R. tsutsugamushi*) in Asia, the Pacific and Australia; typhus (*R. prowazekii*) and Q fever (*Coxiella burnetii*) are ubiquitous. Rickettsiae invade small blood vessels throughout the body, multiply, causing endothelial wall proliferation, thrombosis, and perivascular inflammation, and when this affects the brain, meningoencephalitis results.

The incubation period, clinical features, and progression of the illness vary between organisms, but all share the triad of high fever, skin rash, and headache, with meningoencephalitis developing during the second week of the illness in a significant proportion of cases. Rocky Mountain spotted fever may occur without a rash; Q fever is not usually accompanied by a rash; and Mediterranean spotted fever is characterised by a distinctive eschar at the site of the bite.

Neurological features are typically non-focal, with headache, neck stiffness, photophobia, and, in more severe cases, confusion and reduction in conscious level.^{97 98} Convulsions may occur. CSF examination reveals no specific features: there may be a slight pleocytosis, the protein content may be raised, and glucose is normal. Diagnosis is confirmed by serological tests, but treatment must be started on the basis of clinical suspicion, and not delayed for test results to become available. Direct immunofluorescence of skin biopsies taken from a rash of Rocky Mountain spotted fever offered hope as a rapid method of diagnosis. Unfortunately it is not very specific, and is not widely available. The treatment of choice is tetracycline 500 mg four times per day for 10 days in adults. Chloramphenicol may also be used but it is thought that tetracycline is better and less likely to result in relapse.⁹⁹

Malaria

Malaria is the most important parasitic disease in the world, affects as many as 300 million people, and is being imported to the UK more often—12 patients died of malaria in 1991, 10 in 1992.¹⁰⁰ Involvement of the brain occurs in patients infected with *Plasmodium*

falciparum and results in cerebral malaria. For practical purposes, *P. vivax*, *P. ovale* and *P. malariae* do not cause cerebral malaria. Malaria is found in large parts of Asia, sub-Saharan Africa, parts of Greece, Turkey, and the Middle East, and Central and South America. People who live in endemic areas may acquire a degree of immunity which diminishes with time. Those most at risk of developing severe malaria are the traveller who has no immunity and is being exposed for the first time, the emigrant returning home from a long spell abroad, whose immunity has lapsed, pregnant women and those who have immunosuppression.

Cerebral malaria is an acute diffuse encephalopathy with fever, which will kill within 72 hours if not recognised and treated, and even then carries a mortality rate of 25–50%.¹⁰¹ Delay in making the diagnosis and initiating treatment is a major factor contributing to this.

PATHOGENESIS

The clinical manifestations of cerebral malaria are the end result of a complex, and not fully understood, series of interactions within the cerebrovascular tree mediated by humoral, vascular, and haematological factors. There is evidence of an immune-mediated inflammatory reaction that releases vasoactive products which produce endothelial damage.^{102 103} The presence of trophozoites within erythrocytes induces changes as they mature, which renders them capable of adhering to vascular endothelium, and these red cells packed with mature trophozoites are to be found sequestered in small cerebral venules, resulting in microvascular congestion and tissue hypoxia.^{104 105}

Other organ systems are vulnerable to similar changes. Acute tubular necrosis and the adult respiratory distress syndrome may need simultaneous treatment. Disseminated intravascular coagulation occurs in severe cases, but seems to be a complication and does not affect most patients. Whether cerebral oedema contributes significantly to the pathophysiology of cerebral malaria is debatable. It has been observed in pathological specimens and it is claimed that this may be an agonal event. CT studies do not support the presence of cerebral oedema,¹⁰⁶ yet CSF pressure has been found to be high at the time of lumbar puncture in a group of African children.¹⁰⁷ Routine administration of dexamethasone does not improve the outcome.¹⁰⁸

Hypoglycaemia is an important and frequent complication of cerebral malaria and undoubtedly contributes to depression of consciousness and the appearance of neurological signs. It results from a complex series of interactions which include malabsorption of glucose from the gut, hyperinsulinaemia which may be induced by treatment using intravenous quinine, the metabolic demands of infection, and increased metabolism of available glucose by a large biomass of parasites.^{109 110} Pregnant women are particularly susceptible.

DIAGNOSIS

Definitions of the clinical criteria required to justify a diagnosis of cerebral malaria have been drawn up to standardise parameters for research.¹⁰⁸ For the purposes of this discussion, any person from an endemic area, with cerebral symptoms or signs should be suspected of suffering from cerebral malaria, and demands immediate monitoring, investigation, and treatment. Such a patient will usually have been ill for days and have a temperature. Exceptions occur: the onset of neurological symptoms may be abrupt, and very ill patients can be hypothermic. Commonly there are convulsions, more so in the young and in 45% of adults; coma follows the convulsion. Young children have febrile convulsions associated with many varieties of infection, and with these, consciousness is rapidly regained. Coma lasting more than an hour or two in such circumstances should raise the suspicion of cerebral malaria.

Symptoms before the onset of the cerebral state are diverse and non-specific, and the most common misdiagnosis is of flu. The level of consciousness is invariably impaired, and there is evidence of an organic brain syndrome which manifests as confusion, hallucinations, delirium, and psychosis; in some, complicated by motor signs and movement disorders. Meningism and opisthotonus may be found, and it is important to remember that bacterial and other forms of meningitis may coexist with malaria. Furthermore, severely ill patients are susceptible to Gram-negative septicaemia. There may be signs of damage to other organ systems—anaemia is common and may be severe, jaundice complicates severe infection in adults, hepatosplenomegaly of mild to moderate degree is frequent, and haemorrhages may be found in the retina. Prolonged coma and frequent convulsions should trigger a search for hypoglycaemia and pyogenic meningitis.

TREATMENT

Confirmation of the diagnosis of a case of suspected cerebral malaria must be obtained forthwith, but if this cannot be done, and suspicion is high, treatment should be given straight away. The best way to confirm the diagnosis is to have thick and thin smears of blood examined by an experienced microscopist after appropriate staining. Should no parasites be seen, and the diagnosis seems likely, treatment should be given and the blood re-examined every six to eight hours for the next 48 hours. Blood sugar should be estimated and monitored frequently, and hypoglycaemia corrected if found. A full blood count, urea, electrolytes, and blood gases must be checked and monitored as treatment progresses. It is necessary to examine the CSF to exclude pyogenic or other forms of meningitis as a cause of coma: CSF examination is not otherwise helpful in the diagnosis of malaria. In the UK it should be possible to obtain an urgent CT brain scan, to give some estimate of intracranial pressure

before lumbar puncture and, if the brain looks swollen, it may be better to treat for meningitis empirically, with cover for Gram-negative organisms, and to consider giving mannitol. Blood cultures should be taken. All such patients should be nursed in intensive care.

Because of widespread resistance of *P. falciparum* to chloroquine, this should not be used: quinine is the drug of choice. In the United States quinine is not available, and quinidine gluconate is used instead.^{111 112} Quinine is given by slow, intravenous infusion after an initial loading dose (provided none has been given in the preceding two days). Dosage schedules vary but approximate to 5 mg/kg by intravenous infusion over two hours every 8–12 hours. In patients from southeast Asia, it may be necessary to double the loading dose. Quinine should not be given by bolus injection. When the patient regains consciousness, oral treatment can be given. Plasma concentrations should be monitored, as should the ECG. It is recommended that an antifolate metabolite, either pyrimethamine-sulfadoxine (3 tablets) or doxycycline, be given during the course of quinine. If the parasite load is very high and the patient is very ill, exchange transfusion is useful. Anticonvulsants are given to counter any tendency to seizures. Intravenous glucose is given for hypoglycaemia, anaemia is corrected by blood transfusion, and renal failure by dialysis. Mechanical ventilation is necessary for the adult respiratory distress syndrome. Gram-negative septicaemia causing septic shock can be a life-threatening complication which should be anticipated and treated. Chloroquine is just as effective as quinine provided that the organism is not resistant.

Features that adversely affect the outcome are failure to make the diagnosis, delay in starting treatment, not recognising concurrent infection, deep and prolonged coma, and continuing seizures.

Primary amoebic meningoencephalitis

This condition is caused by free living amoebae of the species *Naegleria fowleri*. *Acanthamoeba* tends to cause a subacute granulomatous meningoencephalitis. They live in moist soil, and most cases have been reported in children who have been swimming or playing in stagnant water.¹¹³ Amoebae enter the nasal cavity, cross the nasal epithelium and ascend to the brain along olfactory nerves and blood vessels to frontal and basal meninges, and spread, causing a florid necrotising inflammation.

Clinically the presentation is of sudden onset, with a severe meningitis indistinguishable from bacterial meningitis—the clue to diagnosis is the history of exposure to warm, stagnant water. CSF examination reveals pleocytosis in which polymorphs predominate, raised protein and reduced glucose. No organisms are seen on the Gram stain, and special examination of fresh, warm specimens

of CSF will show motile trophozoites. Most patients die rapidly despite treatment, but survival following therapy with amphotericin B has been described,¹¹⁴ and this should be given in the highest tolerated dose parenterally, reinforced by intracisternal injection, and by rifampicin and tetracycline, which have some activity against *Naegleriae*.

Brain abscess

Parenchymal brain abscess remains a diagnostic and therapeutic challenge to the physician and surgeon, notwithstanding the considerable advances that have taken place in the last decades in imaging techniques, neurosurgical practice, bacteriological isolation of causal organisms, and the introduction of more potent antibiotics. Patterns of infection are changing but the number of cases seen is not diminishing, and the result of treatment is little better than it was years ago. Brain abscesses frequently present as emergencies, and as with other forms of cerebral infection, delay in diagnosis and implementation of treatment, and inappropriate investigation, adversely affect the end result.

The incidence of brain abscess has remained at one in 10 000 of general hospital admissions, approximating to a prevalence of 4–5 per million population,¹¹⁵ which is almost certainly an underestimate.

PATHOGENESIS

Bacteria reach brain parenchyma via the bloodstream, by direct extension from an adjacent focus of infection or by implantation through wounds as a result of trauma or neurosurgery. In as many as 20% of cases the source of infection cannot be identified. Experimental data indicate that bacteria cannot set up a nidus of infection in normal, undamaged brain, and it may be that thrombophlebitis spreads from contiguous infection, or microinfarction occurs from emboli or hypoxaemia to produce a microscopic area of necrosis where infection can become established. Thereafter the evolution of an abscess passes through four main stages, which have been documented experimentally and correlate well with both clinical and CT findings.

The first stage is of cerebritis, with surrounding oedema of white matter; next the centre of cerebritis becomes necrotic, enlarges, capsule formation begins with the appearance of fibroblasts and neovascular change at the periphery, reactive astrogliosis, and surrounding oedema. The third stage is of capsular development; and the fourth is of capsular maturity as it thickens and reactive astrogliosis increases.^{116 117} The time course is variable and probably related to the virulence of the organism and to the immune status of the host, and may be as short as three weeks to encapsulation and fibrosis, and the capsule may thicken by 1 mm per month.

The range of primary foci from which bacteria spread to produce an abscess is large. There is a relationship between the primary

focus and the bacterial composition of the abscess. Orogenic infection from otitis media or a cholesteatoma spawns abscesses in the temporal lobe or cerebellum. Paranasal sinusitis leads to abscess formation in the frontal lobes and the deeper parts of the temporal lobes. Metastatic abscesses, borne by blood, have a predilection for grey-white matter junctions where the blood supply is relatively reduced, and they are often multiple. The primary source may be lung, heart, or teeth, but a source of infection such as osteomyelitis may be implicated. Chronic pulmonary sepsis, congenital heart disease, particularly cyanotic, and pulmonary arteriovenous fistulae are all fruitful sources, as are dental sepsis and dental manipulation. Those abscesses that are caused by direct implantation occur in proximity to the site of injury or surgery, commonly a depressed fracture or gunshot wound. Bacterial meningitis may be complicated by brain abscess but it is difficult to know how often this happens.

Depression of the immune system from drugs or a disease such as AIDS renders the neuraxis vulnerable to attack by a wide range of organisms, including those that would not normally be pathogenic. The relative frequency with which these predisposing factors occur changes with time, age of the patient, population studied, and geographical location. In any single patient, all potential sources should be considered and excluded in turn by appropriate investigation.

Causative organisms

A very wide spectrum of organisms has been isolated from brain abscesses, and is set to widen further as immune suppression and AIDS spread. The ability to identify an organism from pus is dependent on several factors: have antibiotics already been administered? Has there been a delay between collection and culture? Is the organism fastidious, and have the correct methods of culture been used? When proper attention has been given to those details it has become evident that anaerobic bacteria play a larger role in brain abscess than had been appreciated, and the yield of positive cultures can be significantly increased.¹¹⁸

Orogenic brain abscesses commonly have a mixed flora, which include Enterobacteriaceae, streptococci and *Bacillus fragilis*. Those caused by sinus infection grow *Streptococcus milleri* and *Bacteroides*. Dental sepsis causes mixed infection with streptococci, *Bacteroides* and *Fusobacterium*; pulmonary disease results in a very mixed bag including *Fusobacterium*, other anaerobes, streptococci and actinomycetes. Patients with congenital heart disease are likely to have *S. viridans*, anaerobic and microaerophilic streptococci. Staphylococci are found with penetrating head trauma, as are streptococci and *Clostridium*. In patients who are immune compromised, *Nocardia* and a wide range of fungi may be implicated.

Published reports abound of single cases of abscesses from which unusual organisms have

been grown. It therefore behoves the attending physician to alert the bacteriological laboratory to the relevant circumstances of the case under investigation so that appropriate techniques can be employed to identify the causal organism.

DIAGNOSIS

The clinical features of brain abscess are many and varied. Typically there is a combination of raised intracranial pressure, focal neurological signs, signs of infection—either focal or systemic—and rapid progression. Unfortunately such a combination exists in only half of all patients, with the result that many other disease states may be mimicked: “Any neurologist or neurosurgeon who can claim never to have made an error in the clinical diagnosis of a brain abscess either has a conveniently short memory span or has not been in practice long enough.”¹¹⁹

Headache is common and may be diffuse, localised and intermittent.

Emergency presentation may be with focal signs pointing to the site of the lesion, with convulsions, which are usually generalised but may be focal, with raised intracranial pressure even to the point of coning, and with neck stiffness to suggest meningitis. There may be a pyrexia in 50% of patients and, in some, symptoms relating to the source of infection, such as otitis, may predominate.^{120–124} In young children, the presentation may be even more confusing—an enlarging head associated with vomiting and seizures can be mistaken for tumour or congenital anomaly. Cerebral abscess therefore must be included in the differential diagnosis of those who present acutely with raised intracranial pressure, epileptic seizures, strokes, meningitis and encephalitis, and primary and secondary intracranial malignancy.

Faced with a patient in whom intracranial abscess is a possible diagnosis, the priority is to confirm the diagnosis, identify the source of infection and the responsible organism or organisms, once vital functions have been stabilised. A full examination should be made for a locus of infection, such as otitis media or pelvic sepsis, and if found, cultures should be made and steps taken to eradicate the source. Blood cultures should be set up. Baseline haematological and biochemical parameters should be established: they are seldom useful for diagnosis but may change rapidly in the course of the disease. CT of the head should be done as soon as possible. In addition to visualising the intracranial contents, note should be made of the state of the paranasal sinuses and the mastoid air cells. Skull fractures and cranial defects should be looked for.

Interpretation of the CT scan should always be made with reference to timing in the evolution of the abscess. In the earliest stages of cerebritis, a low-density area may be evident, perhaps with surrounding oedema, and no enhancement after contrast injection. Later there may be patchy enhancement which, with maturity, adopts a “ring” appear-

ance as encapsulation takes place. Later still this becomes more evident and the centre of the lesion or lesions becomes increasingly hypodense. Adjacent white matter is swollen with cerebral oedema. Location and multiplicity of abscesses, hydrocephalus, and cerebral mass effect are readily identified.^{125 126} Unfortunately such appearances are not specific and may be seen with brain tumours, granulomas, necrotising encephalitis, and infarction. If ventriculitis is demonstrated by ependymal enhancement, then infection is likely.

MRI is likely to prove more sensitive than CT in demonstrating early cerebritis, cerebral oedema, and the contents of abscess cavities.^{127 128} As an emergency investigation it is not widely available in the UK, however, and there are problems accommodating severely ill patients within the machine. Lumbar puncture should *never* be carried out on patients suspected of harbouring a brain abscess. If the urgency of the patient's condition allows, a chest radiograph should be carried out.

TREATMENT

When the diagnosis of brain abscess is confirmed, the therapeutic strategy will be influenced by several factors, and there is no overall agreement on when surgery should be undertaken, and if it is, which technique should be used. Indications for surgery are relief of space occupation, confirmation of the diagnosis, and obtaining specimens of pus for culture. If the abscess is a consequence of head trauma, then surgery is mandatory for appropriate toilet, debridement, removal of fragments, and closure of dural defects. If lesions are multiple or deeply situated, it is best to treat with antibiotics on the basis of organism identification from other sources, or if that is not possible, on a “best guess” principle governed by the likely source of infection. Close monitoring of the lesions with serial CT or MRI is necessary; if they do not diminish in size, aspiration should be undertaken. In people with immunosuppression, including those with AIDS, the threshold for aspiration of pus to identify the offending organism is substantially lowered. It is seldom necessary to resort to complete surgical excision of an abscess: simple aspiration of the contents of an abscess is the most frequently advocated technique—when carried out under CT stereotactic control, diagnostic material may be obtained in as many as 95% of cases.^{129–131} There is an increasing trend towards treating multiple abscesses, or those that are deeply situated, with antibiotics alone.^{124 132 133} Results seem to justify this course of action.

Choice of antibiotics

The choice of antibiotic to be used is influenced by its capacity to penetrate not only into CSF but through the capsule wall and into the pus, and to be active in the presence of pus. Little information is available on the penetration of newer antibiotics into brain.

Currently the favoured regimen for empirical treatment, while awaiting the results of culture studies, is a combination of penicillin 24 mega units per day intravenously, chloramphenicol 1 g intravenously every six hours, and metronidazole. If staphylococci are suspected, nafcillin or flucoxacin, vancomycin, or fusidic acid should be used. The length of time for which treatment should be given must be determined for each case by clinical response and improvement of CT scan appearances, and is usually no less than six weeks, often longer. In patients with AIDS, toxoplasmosis is the likeliest cause of a focal brain lesion, particularly if multiple. The range of possible pathogens is very wide, however, and biopsy should be considered for every patient who has a negative toxoplasma serology test or in whom CT scans are atypical. In others, treatment should be given with pyrimethamine and sulfadiazine, and progress monitored. Clinical and CT improvement should take place within 14 days.

Dexamethasone is commonly used to treat cerebral oedema, and in practice the benefit obtained in reducing intracranial pressure outweighs the potential hazard of diminishing the host inflammatory response. Mannitol and hyperventilation may be necessary in addition. The risk of developing epileptic seizures is not insubstantial, and prophylactic anticonvulsants are recommended.

Subdural empyema

This potentially lethal infection of the space between the dura and arachnoid mater is most often due to spread of infection from ear or nose,^{134 135} and less commonly osteomyelitis. Rarely it may be caused by haematogenous spread from a distant focus, and it may follow penetrating head trauma. In children, subdural effusions that complicate meningitis become infected.¹³⁶ Because the subdural space is extensive, pus can readily track over the brain surface from one side to another, and may accumulate along the falx, or it may remain localised and become encapsulated in proximity to the primary focus. The organisms that are found reflect the underlying cause. In adults organisms from otitis and sinusitis predominate—aerobic and anaerobic streptococci, staphylococci and Gram-negative organisms including *Proteus* and *Pseudomonas*. In infants and young children *H influenzae*, Gram-negative bacteria and pneumococci are common. In as many as a quarter of all cases no organism can be cultured from pus.¹³⁴

DIAGNOSIS

Subdural empyema affects the young—more than half of all cases are aged less than 20, and it is more common in boys. Presentation is frequently acute, as an emergency with rapid deterioration. There is usually evidence of general infection: fever, tachycardia, malaise and rigors, and there may be signs of local infection: face ache, and tenderness over the sinuses or over the mastoid process.

Headache and signs of meningeal irritation are common, vomiting, papilloedema, and diminution of conscious level imply raised intracranial pressure. Focal signs of hemiparesis, dysphasia and, less frequently, cerebellar disturbance may occur. Epileptic seizures are very common and are often focal.¹³⁷ A parafalcine collection may herald its presence with signs of a paraparesis, sphincter disturbance, or weakness of one leg.¹³⁸ The diagnosis should be considered in any patient who presents acutely with neurological dysfunction on a background of infection, especially if there are focal seizures and if there is evidence of infection in the ear or paranasal sinuses.

To confirm the diagnosis, CT of the head with contrast enhancement should be undertaken as an emergency. MRI may be more sensitive,¹³⁹ but the same strictures apply as for brain abscess. CT appearances may be subtle in the early stages of development. The classical appearance is of an extracerebral collection of lower density than brain over the surface of the hemispheres and in the parafalcine region. A rim of enhancement follows contrast injection. If large enough, adjacent structures will be displaced, but bilateral effusions may not cause evident shift. There may be adjacent infarction and brain oedema.¹⁴⁰ Pus or fluid may be seen in the paranasal sinuses or in the ear, and there may be evidence of osteomyelitis. A blood count should be taken: it often shows a polymorphonuclear leucocytosis and raised ESR. Lumbar puncture should *not* be carried out even if meningitis is suspected.

TREATMENT

Most authorities agree that once the diagnosis is established, treatment should be started immediately with a combination of systemic chemotherapy together with surgical exploration and removal of pus, and the eradication of the primary source of infection. Unless culture sensitivities indicate otherwise, a combination of penicillin, chloramphenicol, and metronidazole is given, as for brain abscess. Prophylactic anticonvulsants should be prescribed and measures taken to combat raised intracranial pressure.

There are considerable differences of opinion concerning the relative merits of burrhole aspiration and craniotomy in the treatment of subdural empyema, and which method is employed depends upon the prejudices and experience of the neurosurgeon on call. Whichever technique is used it is important to ensure that all loculi of pus are removed. Working in an institution where there are vociferous proponents of each method, I consider that craniotomy produces better results.

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The introductory chapter by R J Douglas sets out the view that the various properties of the visual world such as form, orientation, colour and movement are processed by separate cortical regions with the primary visual cortex acting as an elementary detection and relay station. However there are differing views on how these regions are arranged. In the hierarchical model, based mainly on morphological studies of neural connexions, visual stimuli are analysed for the various properties of form, colour and orientation by successive relay to specific regions at increasing distance from the calcarine cortex. A second view proposes two major pathways one concerned with what a visual object is and the other where it is. The 'what' task is performed by the ventrally situated inferior temporal cortex and the 'where' task by the dorsally situated occipito-parietal cortex. This view is derived from behaviour experiments in animals and on the effects of brain lesions in man. A third view based on physiological recording from various points on the visual pathway proposes that visual information is divided from the retina onwards into two streams, a P (parvocellular) system thought to convey high resolution visual images at high contrast and an M (magnocellular) system conveying low acuity visual information concerned with motion and depth perception. The first chapter discusses these theories and also describes the precise oculomotor mechanisms necessary to maintain high quality retinal images of moving objects. There follow a series of chapters on various visual disorders in man including visual illusions and hallucinations, colour vision, prosopagnosia, Balint's syndrome, object agnosia and residual vision and blindsight. The chapter by Milders and Perrett on facial recognition and by Ruddock on acquired disorders of colour vision are particularly informative and comprehensive.

Considering the scope of the book and the different backgrounds and nationalities of the contributors the style is remarkably even. Illustrations are used sparingly, perhaps too sparingly, and the book compares unfavourably in this respect with the superbly illustrated accounts of visual physiology and psychology aimed at the general reader. References are comprehensive and up to date. Altogether this is a scholarly and stimulating book for neurologists interested in how the brain analyses the visual world (and that should include all of us).

R ROSS RUSSELL

An Introduction to Clinical Neurology (Essentials of Clinical Practice). By ALAN GUBERMAN. (Pp 610; Price: £36.95). 1993. A Little, Brown Medical title distrib. in Europe by Churchill Livingstone, Edinburgh. ISBN 0-316-33073-6.

Contemporary medical books may have two purposes. Either they can provide fundamental instruction about the principles and practice of clinical medicine, or they may assemble and order factual knowledge for reference purposes. The huge growth in factual detail has meant that fewer and fewer books combine these roles. Dr Guberman's book is one of a dying breed which tries to serve both functions. I think it is predominantly intended as a textbook, being titled 'An Introduction.....' and the preface states that it is intended for 'medical

students, postgraduate trainees, non-neurologists, paramedicals and basic neuroscientists'. I would be pleasantly surprised if American students, let alone British, would read a book of this size as a basic text. Basic neuroscientists usually require highly detailed information from reference books when considering the clinical context of their own specific research endeavour. Dr Guberman's book might provide a suitable neurology reference text for paramedicals, but surely the book's main niche must be those training in general internal medicine, such as MRCP candidates in the UK. Here it already faces competition from established books such as "Brain and Bannister's Clinical Neurology" and from the neurology chapters of general medicine textbooks.

Dr Guberman is to be congratulated on the exhaustive breadth of his subject coverage making him one of the most generally knowledgeable neurologists around. The disease coverage is comprehensive, well-laid out, with extensive referencing to core papers. There is a most useful compendium of the neurological side-effects of therapeutic drugs. Inevitably reviewers can have minor quibbles. Colour fundus photographs would have been more helpful. Unfortunately, the illustrations include too many CT scans and myelograms, sometimes reproduced with mediocre quality, in an era where MRI now reigns supreme. I personally don't believe that you can see fibrillations, rather than fasciculations, in the tongue. How often is it necessary to 'extend' the legs to measure the spinal fluid pressure when relaxed breathing and only slight unbunching from the foetal position generally seem to be sufficient?

The extensive sections on clinical method include topics such as probability, Baye's theorem and decision trees. I am never sure about the decision tree model for the diagnostic process. Most neurologists of my acquaintance seem to arrive at the right diagnosis intuitively, only resorting to the decision tree approach in desperation when otherwise baffled. Dr Guberman's advice about testing hypotheses during history taking is sound enough in principle, but his example is somewhat abstruse. When faced with a subacutely weak patient, how many neurologists, let alone students, are sufficiently blessed with knowledge or time enough to enquire about 'making lead glass as a hobby or whether he has ever had wine-coloured urine'? The advice about the clinical methodology or neurology lacks sufficient encouragement to focus the history on the problem in hand, and to develop the technique of performing a selective, five-minute examination pertinent to this problem. Yet Dr Guberman's account of how to perform all the myriad components of neurological examination is lucid and could be used profitably by students wishing to learn "how to do it all".

Dr Guberman has undertaken the difficult task of writing a comprehensive textbook of general neurology by writing 26 out of the 29 chapters himself. I wonder how many more detailed neurological treatises of this quality, written by a single author, we will see in the future.

MICHAEL DONAGHY

Stereotactic Radiosurgery. Edited by E ALEXANDER III, J S LOEFFLER and L D LUNSFORD. (Pp 254, Illustrated; Price:

£75.00). Oxford, Blackwell Scientific Publications Ltd. ISBN 0-07-001020-X.

Stereotactic Radiosurgery has had an unexpectedly large influence on neurosurgical practice as Charles Wilson points out in his foreword to this excellent book on this subject. As Radiosurgery in its various forms is used in many centres by doctors of widely differing experiences and training it becomes more and more crucial that its use is securely based on sound principles of radiobiology and physics as well as of stereotaxy and neurosurgical practice. Its distinguished panel of authors are respected exponents of the technique and well placed to give this volume authoritative accounts of the different characteristics of Gamma Knife, Linac, and Heavy Particle therapy, the principles involved as well as the results that can be achieved and pitfalls to be avoided. The range of conditions that have been treated by radiosurgery is wide but it is no panacea and its proper application requires careful selection and disciplined execution. This book offers a valuable survey of the present situation as well as some provocative thoughts about what the future may hold for the method.

D M C FORSTER

The Surgical Management of Epilepsy. Edited by A R WYLER AND B P HERMANN. Publisher: Butterworth-Heinemann, Oxford 1994. (Pp 277; £60.00). ISBN 0-7506-9416-5.

This is another book targeted at the growing market of clinical groups seeking education in the surgical treatment of epilepsy.

It is a multi-author book divided into four sections. The first deals with prognosis and is a helpful contribution; especially the chapter devoted to epileptic syndromes. The next section deals with preoperative evaluation and is reasonably comprehensive, although the separation of the chapters on basic neuropsychology and the Wada test by a chapter on preoperative psychiatric evaluation is bizarre. Unfortunately the chapter on surgical procedures is weak. Ten pages on cortical resections including temporal lobe resections is quite inadequate. The chapters on outcome are reasonable, although the one on reoperation presents only the editors' own series.

Much of the material in this book is from the editors' own writings, or those of their colleagues, and although much of it is valuable, it does not constitute a good overview. As an introduction to the topic it is excellent, well produced and at a reasonable price, and as such would be a good introduction for trainees in the appropriate neurosciences disciplines, and nursing and paramedical staff who wish to have a detailed account of these matters.

CE POLKEY

CORRECTION

Anderson, Milne. Management of cerebral infection. *J Neurol Neurosurg Psychiatry* 1993;56:1243-58 (Neurological emergency). The dosage of dexamethasone should be 0.15 mg/kg body weight every six hours for four days.

This correction was wrongly attributed to the editorial in the May issue.

Who will read this review? Probably not paediatric neurologists/epileptologists. They will already have the first edition of the book and will not need me to tell them how good the second edition is. Probably not paediatricians (not likely to take the journal)—however any paediatrician who has wandered into view should make sure that the local library has a copy. I hope adult neurologists and their colleagues will read this review and will be persuaded to put the book on their own shelves. They will then understand why paediatricians have such a difficult (but interesting!) time.

CHRIS VERITY

Mitochondrial Disorders in Neurology.

Edited by A H V SCHAPIRA AND S DIMAURO. Published by Butterworth Heinemann, Oxford 1994. Pp 254 £45.00 ISBN 0-7506-0585-5.

Although there are many areas of neurology where disease classification is in its infancy, syndromes attributable to mitochondrial abnormalities are the most neonatal in this regard. This book aims, and largely succeeds, in assimilating a huge volume of data which tries to correlate biochemical, clinical and molecular defects. From migraine to myopathy and peripheral neuropathy to Parkinson's disease there are few areas for which a mitochondrial aetiology has not been sought, and even fewer to which an acronym has not been assigned. MEPOP, MNGIE, MiMyCa and NARP are perhaps less well known than LHON, MERRF and MELAS to name but a few. The inescapable bottom line is well pointed out by Lewis Rowland in his excellent chapter which attempts to synthesise the field: the same mutation can cause a varied phenotype and yet the same phenotype may be associated with a variety of mitochondrial DNA abnormalities.

In seeking to approach this problem from different angles there is inevitably a degree of repetition. Some of the chapters are more useful to molecular biologists and neurochemists within the field and yet there is much here for the interested clinician. However, whilst occasional photographs of gels may illustrate points, the absence of a single ragged red fibre is rather an oversight. Perhaps we have all seen enough of these beasts but a chapter on the pathology of mitochondrial disease would have been useful. Having said this, there are some excellent diagrams and tables which sum-up current research and allow the non-molecular biochemist to understand some of the intricacies of these difficult but important disorders. Overall this is a unique and invaluable reference book for all those interested in mitochondrial diseases.

JOHN ZAJICEK

Dementia. Editors: ALISTAIR BURNS and RAYMOND LEVY. Publisher: Chapman and Hall, London 1994. (Pp 874; £125.00.) ISBN 0-412-54740-6.

After decades of neglect, the last twenty years has seen a blossoming of interest in

dementia and principally in Alzheimer's disease. Excellent though the late Professor C E Wells book on dementia is, the recent rapid advances in research methodology, principally in molecular biology and in imaging techniques, mean that a replacement is timely. The editors (two academic psychogeriatricians) "aim to encompass in a single volume, all aspects of all types of dementia", a Herculean task. They admit that they could not hope to succeed in such an aim and have therefore concentrated on "providing a solid core of information which is likely to remain part of the main stream view of the field." Let us see if they have achieved this aim.

The book is divided into two main sections, dementia of the Alzheimer type and non-Alzheimer dementia. Considering the large number of authors, there is little repetition. There are some excellent sections in the Alzheimer section and I would recommend the overview by Absher and Cumming on cognitive and non-cognitive aspects of dementia. The chapters on cholinergic and non-cholinergic neurotransmitter systems as well as the careful and detailed chapter on the molecular pathobiology of Alzheimer's disease are excellent. The chapters on the assessment of memory failure and dementia are thorough and well referenced but the section on imaging is disappointing. The chapters on computed tomography and neurophysiology exemplify the dictum that experts should write on their own subject.

However, the first two-thirds of the book, the section on Alzheimer's disease, deals only with the elderly patient. Alzheimer's original patient was 51 and this is acknowledged but then the younger demented patient is ignored. This is particularly true in the section on services. The chapter on services in the U.K. does not mention the younger patient nor does it mention the services provided by voluntary organisations and it does not reflect the situation in the U.K. as I know it.

The last third of the book describes the non-Alzheimer dementias. There is a lucid account of vascular dementia by O'Brien and a chapter on pathology of vascular dementia by Brun. He regards Binswanger's disease as identical with *état lacunaire*, a concept with which many British neurologists would disagree. Towards the end of the book, almost as an appendage, are chapters on unusual causes of dementia. These are the chapters of most interest to neurologists. Perhaps in a later edition these chapters together with the excellent chapter on prion diseases could be expanded and placed earlier in the book. As it stands, the balance seems wrong, too little attention is given to younger patients and to non-Alzheimer causes of dementia and yet it is these patients who deserve accurate diagnoses and for whom a different management might be appropriate. The indexing and proof reading is careless—look up the nomenclature of Binswanger's disease and you would be directed to Page 624, which is blank.

So have the authors succeeded in their aim? For geriatricians and psychogeriatricians this book will become the standard reference book. For neurologists however, this book has serious flaws and does not achieve its potential. Perhaps it will if there is a second edition.

MYFANWY THOMAS

Neuropsychiatric Disorders. By GARETH W ROBERTS, P NIGEL LEIGH, DANIEL R WEINBERGER. Published by Mosby Europe Ltd, London 1993. ISBN 1-56375-510-6.

The neurology-psychiatry distinction is being rendered obsolete by strident advances in neuroscience. Basic neuroscience and clinical neurology have much to offer each other, and this book, written by distinguished neuroscientists and clinicians, aims to increase cross-fertilisation.

The broad areas of study are the dementias, motor disorders, epilepsy and the psychoses. Within these areas, all of the major diseases are covered.

Each main disease has a chapter in which neuroscience and clinical aspects are seamlessly integrated. Chapters follow the same overall structure of clinical features, pathology, investigation and treatment. Pathological and imaging illustrations are of high quality, while the accompanying text is a distillate of current thought, clearly explained for those new to the area.

It is difficult to fault the book. If pushed to do so, there is little regarding the role of neuropsychology in diagnosis and disease staging. The reference section is also somewhat brief. Advances, such as the role of superoxide dismutase in motor neurone disease, and the trinucleotide repeat sequences in the diagnosis of Huntington's disease, have occurred too recently for inclusion.

The book is likely to succeed in its aim of breaking down boundaries between neurology and psychiatry, and between clinical and basic neuroscience. Its main value is in introducing the clinician and neuroscientist to the other's discipline.

JOHN GREENE

CORRECTION

Anderson M. Management of cerebral infection. *J Neurol Neurosurg Psychiatry* 1993;56:1243-1258 (neurological emergency). The dosage of dexamethasone should be 0.15 mg/kg body weight every six hours for four days.