Meningitis

This disease is notifiable in the UK, see NOIDs article for more detail. Meningitis is an inflammation of the leptomeninges and underlying subarachnoid cerebrospinal fluid (CSF). The inflammation may be caused by infection with viruses, bacteria, other micro-organisms, or non-infective causes.

Viral meningitis is more common and usually more benign than bacterial meningitis but all cases of suspected meningitis should be managed as though having bacterial meningitis, until proven otherwise. Meningococcal disease is the leading infectious cause of death in early childhood. It presents as bacterial meningitis (15% of cases), septicaemia (25% of cases), or as a combination of the two presentations (60% of cases).

See also separate article Sepsis (Septicaemia).

Epidemiology

- Meningitis occurs in people of all age groups but infants, young children and the elderly are more predisposed to meningitis.
- Viral meningitis is the most common cause.
- Every year around 3,200 cases of bacterial meningitis occur in the UK. 3,000 cases of viral meningitis were reported between 2009-2010 but the actual incidence is likely to be far higher.
- The epidemiology of bacterial meningitis in the UK has changed dramatically over a period of two decades following the introduction of vaccines to control Haemophilus influenzae type b, serogroup C meningococcus and pneumococcal disease.
- The Joint Committee on Vaccination and Immunisation has recommended the introduction of a new vaccine against group B meningococcal disease to the immunisation schedule at 2, 4 and 12 months.
- The quadrivalent (A, C, W, Y) vaccine is now given to all 17-18 year olds.

Risk factors

- Patients with CSF shunts or dural defects (eg, staphylococcal).
- Patients having spinal procedures (eg, spinal anaesthetics) are at increased risk and Pseudomonas spp. may then be the cause.
- Other risk factors include bacterial endocarditis, diabetes mellitus, alcoholism and cirrhosis, intravenous drug abuse, renal insufficiency, adrenal insufficiency, malignancy (increased risk of listerial infection), hypoparathyroidism, thalassaemia major and cystic fibrosis.
- Splenectomy and sickle cell disease increase the risk of meningitis secondary to encapsulated organisms.
- Crowding (eg, military recruits and college students) increases the risk of outbreaks of meningococcal meningitis.

Causes

- Neonates: group B streptococci, Listeria monocytogenes, Escherichia coli.
- Infants and young children: H. influenzae type b, if younger than 4 years and unvaccinated; Neisseria meningitidis, Streptococcus pneumoniae.
- Elderly and immunocompromised: S. pneumoniae, L. monocytogenes, tuberculosis (TB), Gram-negative organisms.
- Hospital-acquired and post-traumatic meningitis (may often be multidrug-resistant), Klebsiella pneumoniae, E.coli, Pseudomonas aeruginosa, Staphylococcus aureus.
- N. meningitidis: usually local outbreaks among young adults; there is increased incidence in late winter or early spring. Meningococcal meningitis is endemic in parts of Africa, India and other developing nations. Periodic epidemics occur in sub-Saharan Africa as well as among religious pilgrims travelling to Saudi Arabia for the Hajj.
Neonatal meningitis\[6\]
See also separate general article Congenital, Perinatal and Neonatal Infection.

- Neonates are at greater risk of meningitis. Risk factors for the development of meningitis include low birth weight (below 2500 g), premature delivery, premature rupture of membranes, traumatic delivery, fetal hypoxia and maternal peripartum infection.
- Intrapartum prophylactic antibiotics in pregnant mothers who carry, or who are at risk of colonising, group B streptococci, have been effective in reducing the risk of neonatal group B streptococcal meningitis.
- Caesarean section reduces the risk of transmission of herpes simplex virus (HSV).
- The initial presentation is usually nonspecific with features including raised or unstable temperature, respiratory distress, episodes of apnoea and bradycardia, hypotension, feeding difficulty, irritability and reduced activity.\[7\]
- Meningitis should therefore be considered and included in the urgent investigations of any acutely ill neonate.
- In developed countries, the rate of mortality from bacterial meningitis among neonates has decreased but there has not been a significant decrease in long-term complications such as cerebral palsy, learning disability, seizures and hearing impairment.
- Mortality following HSV infection of the central nervous system is 4-14%. HSV-1 and HSV-2 have the same risk of mortality but HSV-2 is more often associated with long-term complications such as cerebral palsy, general learning disability, seizures, microcephaly and visual impairment.\[8\]

Aseptic meningitis
CSF has cells but is Gram-stain negative and no bacteria can be cultured on standard media. Causes include:

- Partly treated bacterial meningitis.
- Viral infection - eg, mumps, echovirus, Coxsackievirus, HSV and herpes zoster virus, HIV, measles, influenza, arboviruses.\[9\]
- Fungal infection: fungal meningitis is rare but can be life-threatening. People with immunodeficiency (eg, AIDS, leukaemia, immunosuppressant medication) are at higher risk. Fungal causes of meningitis include infection with Cryptococcus, Histoplasma and Coccidioides species.
- Parasites - eg, eosinophilic meningitis caused by angiostrongyliasis.
- Other possible causative organisms include atypical TB, syphilis, Lyme disease, leptospirosis, listeriosis and brucellosis.
- Kawasaki disease.
- Mollaret's meningitis.

Non-infective meningitis
Meningeal inflammation can be caused by meningeal infiltration by:

- Malignant cells (leukaemia, lymphoma, other tumours).
- Chemical meningitis (intrathecal drugs, contaminants).
- Drugs (non-steroidal anti-inflammatory drugs (NSAIDS), trimethoprim).
- Sarcoidosis.
- Systemic lupus erythematosus.
- Behçet's disease.

Presentation
See also separate articles Ill and Feverish Child and Fever and Night Sweats.

Invasive meningococcal disease\[2, 10\]
Invasive meningococcal disease may present with septicaemia, meningitis or a combination of both. See separate article Meningococcal Disease.

- A generalised petechial rash, beyond the distribution of the superior vena cava, or a purpuric rash in any location, in an ill child, is strongly suggestive of meningococcal septicaemia and should lead to urgent treatment and referral to secondary care.
The following features in an ill child should prompt consideration of a diagnosis of invasive meningococcal disease: petechial rash, altered mental state, cold hands and feet, extremity pain, fever, headache, neck stiffness, skin mottling.

Meningococcal meningitis and/or septicaemia may also present with capillary refill time more than two seconds, unusual skin colour and hypotension.

Meningococcal septicaemia without meningitis does not tend to present with stiff neck, back rigidity, bulging fontanelle, photophobia, Kernig's sign, Brudzinski's sign, paresis, focal neurological deficits or seizures.

Clinical presentation of meningitis may include:\[2\]
- Fever, headache.
- Stiff neck (generally not present in children under the age of one year or in patients with altered mental state), back rigidity, bulging fontanelle (in infants), photophobia, opisthotonus (if severe).
- Altered mental state, unconsciousness, toxic/moribund state.
- Shock: signs of shock include tachycardia and/or hypotension, respiratory distress, altered mental state and poor urine output.
- Kernig's sign (pain and resistance on passive knee extension with hips fully flexed).
- Brudzinski's sign (hips flex on bending the head forward).
- Paresis, focal neurological deficits (including cranial nerve involvement and abnormal pupils).
- Seizures.

Viral meningitis may be clinically indistinguishable from bacterial meningitis but features may be more mild and complications (eg, focal neurological deficits) less frequent. Any person presenting with suspected meningitis should therefore be managed as having bacterial meningitis until proved otherwise.

Classic symptoms are not evident in infants and also not often seen in the elderly.

Some children and young people will present with mostly nonspecific symptoms or signs and the conditions may be difficult to distinguish from other less important infections presenting in this way. Children and young people under the age of 16 with more specific symptoms and signs are more likely to have bacterial meningitis or meningococcal septicaemia and the symptoms and signs may become more severe and more specific over time.\[2\]

A study of children aged 16 years or younger with meningococcal disease found that classical signs such as haemorrhagic rash, meningism and impaired consciousness did not tend to appear until after 13-22 hours. However, more nonspecific features such as leg pain, cold hands and feet and abnormal skin colour appeared much earlier with a median onset of 7-12 hours. These earlier features are thus very important in early diagnosis and therefore earlier initiation of potentially life-saving treatment.\[11\]

One study found that the classic triad of fever, neck stiffness and a change in mental status was present in only 44% of adults presenting with community-acquired acute bacterial meningitis. However, 95% had at least two of the four symptoms of headache, fever, neck stiffness and altered mental status.\[12\] Most patients with viral meningitis present with subacute neurological symptoms developing over 1-7 days. Chronic symptoms lasting longer than one week suggest meningitis caused by some viruses as well as TB, syphilis or fungi.

Differential diagnosis

- Other causes of pyrexia and severe infection.
- Intracranial abscess.
- Other causes of altered mental state and coma - eg, encephalitis, subarachnoid haemorrhage, brain tumours.

Investigations

Investigations must not delay treatment.

Lumbar puncture (LP)

See separate articles Lumbar Puncture and Cerebrospinal Fluid for normal values and interpretation of abnormal CSF findings.
LP is performed immediately provided there are no signs of raised intracranial pressure (reduced consciousness, very bad headache, frequent fits) or focal neurology. CT scan is an unreliable investigation to detect raised intracranial pressure:  
- Samples of CSF are usually sent for Gram stain, Ziehl-Neelsen stain (TB), cytology, virology, glucose, protein, culture, rapid antigen screen or polymerase chain reaction (PCR) if available and India ink for cryptococci.
- CSF may be normal in the early stages of meningitis so the LP is usually repeated if symptoms and signs persist.

Tests performed in secondary care for children and young people[2]  
If a child or young person under the age of 16 has an unexplained petechial rash and fever (or history of fever) the following investigations are often performed in secondary care:
- FBC.
- CRP.
- Coagulation screen.
- Blood culture.
- Whole-blood polymerase chain reaction (PCR) for *N. meningitidis*.
- Blood glucose.
- Blood gases.

Other investigations for all ages  
Apart from the above, other tests often required include:
- Renal function tests
- Coagulation profile: especially if disseminated intravascular coagulation is suspected.
- CXR (lung abscess).
- Culture urine, nasal swabs and stool (virology).
- CT scan is usually reserved for those with specific adverse clinical features or when an underlying cause such as mastoiditis is suspected.[14]
- MRI can be extremely useful for detecting and monitoring the complications of meningitis.[14]
- Other possible investigations:
  - Serum cryptococcal antigen, especially if the baseline is known (less diagnostic than India ink and CSF cryptococcal antigen).
  - Serology of blood, urine and CSF for specific bacterial antigens is occasionally recommended if there is diagnostic doubt or in patients with partially treated meningitis.
  - Serum test for syphilis if neurosyphilis is suspected.

Management  
Management includes supportive treatment (including fluids, antipyretics, antiemetics), treatment of the causative organism and treatment of any complications - eg, seizures, raised intracranial pressure. See also the articles on specific infections for management of rarer causes of meningitis such as tuberculosis, fungi and parasites.

Management of viral meningitis[15]  
- The general principles of management for all viral meningitis include supportive therapy - eg, analgesia, antipyretics, nutritional support and hydration.
- Enteroviral meningitis: usually self-limiting and no specific therapy is required unless there is hypogammaglobulinaemia (immunoglobulins required).
- Aciclovir is considered beneficial in treating herpetic viral infections but only if given very early in the course of the infection and evidence for benefit is limited. Intravenous aciclovir should be started immediately if there is any suspicion of herpes simplex encephalitis.
- Ganciclovir is effective for cytomegalovirus (CMV) infections but it has significant renal toxicity and close monitoring is mandatory.

Management of bacterial meningitis[2]  
- Transfer any patient with suspected bacterial meningitis or suspected meningococcal septicaemia to secondary care as an emergency by telephoning 999/112/911.
Intramuscular or intravenous benzylpenicillin should be given before urgent transfer to hospital only if there is suspected meningococcal septicemia with a non-blanching rash. Benzylpenicillin should not be given if there is a history of anaphylaxis associated with penicillins or if giving antibiotics will delay urgent transfer to hospital. If urgent transfer to hospital is not possible (eg, remote locations or adverse weather conditions), antibiotics should be given to any person with suspected bacterial meningitis.

Management includes supportive treatment with analgesia, antipyretics, nutritional support and hydration. Do not restrict fluids unless there is evidence of raised intracranial pressure or increased antidiuretic hormone (ADH) secretion.[2] The choice of antibiotics and the duration of therapy should be guided by the microbiological diagnosis but initial 'blind' antibiotic therapy must be started immediately. The National Institute for Health and Care Excellence (NICE) recommendation to children (over 3 months old) is for dexamethasone to be given for suspected or confirmed bacterial meningitis as soon as possible.[2] Corticosteroids given to patients of all ages with bacterial meningitis have been shown to reduce hearing loss and neurological sequelae significantly but there is no evidence that they reduce overall mortality.[16] Choice of antibiotic is usually determined by local guidelines and close liaison with a microbiologist.

Initial 'blind' therapy

- Children 3 months and older and young people should be given intravenous ceftriaxone as empirical treatment before identification of the causative organism. If calcium-containing infusions are required at the same time, cefotaxime is preferable.
- Children younger than 3 months should be given intravenous cefotaxime plus either amoxicillin or ampicillin. NB: ceftriaxone should not be used in premature babies or in babies with jaundice, hypoalbuminaemia or acidosis, as it may exacerbate hyperbilirubinaemia.

Meningitis caused by meningococci

- Intravenous ceftriaxone for at least seven days is usually used.
- Prevention of secondary case of meningococcal meningitis is usually with rifampicin or ciprofloxacin.[17]

See also separate article Meningococcal Disease.

Meningitis caused by pneumococci[18]

- Vancomycin and a third-generation cephalosporin (either cefotaxime or ceftriaxone) should be used, pending isolation of the organism and in vitro susceptibility testing.
- Benzylpenicillin may be given if the organism is penicillin-sensitive but penicillin resistance is becoming an increasing problem.

Meningitis caused by H. influenzae type b

- Children aged 3 months and older and young people - intravenous ceftriaxone for 10 days in total unless directed otherwise by the results of antibiotic sensitivities.

Meningitis caused by group B streptococci

- This mainly occurs in babies between the ages of 7-90 days.[19] Intravenous cefotaxime for at least 14 days should be given.[2]

Meningitis caused by listeriosis

- For children under the age of 3 months, intravenous amoxicillin or ampicillin for 21 days in total, plus gentamicin for at least the first seven days.
Complications

- **Immediate**: septic shock, including disseminated intravascular coagulation, coma with loss of protective airway reflexes, cerebral oedema and raised intracranial pressure, septic arthritis, pericardial effusion and haemolytic anaemia (*H. influenzae*).
- Subdural effusions: reported in 40% of children aged 1-18 months with bacterial meningitis. Risk factors include young age, rapid onset of illness, low peripheral white cell count and high CSF protein.
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH).
- Seizures: occur more commonly during the acute stage of the disease. Studies reported that this occurred in 47% of children and 17% of adults with acute bacterial meningitis.\[20, 21\]
- Delayed: decreased hearing, or deafness; other cranial nerve dysfunction, multiple seizures, focal paralysis, subdural effusions, hydrocephalus, intellectual deficits, ataxia, blindness, Waterhouse-Friderichsen syndrome and peripheral gangrene.

Prognosis

- Meningitis kills more UK children under the age of 5 than any other infectious disease.\[2\]
- Prognosis depends on the pathogen, the patient's age and condition and the severity of acute illness.
- Patients with severe neurological impairment on presentation or with extremely rapid onset of illness, even if treated immediately, have a 50-90% mortality rate and an even higher rate of morbidity.
- Pneumococcal meningitis is associated with a high rate of mortality and morbidity.\[22\]
- Meningococcal disease has a better prognosis when meningitis accompanies the septicaemia than when it does not.
- The prognosis for viral meningitis is usually excellent, with complete resolution usually within 10 days.

Prevention

See separate articles Immunisation Schedule (UK), Hib Vaccination, Meningococcal Vaccines and Pneumococcal Vaccination.

- Vaccination against *H. influenzae* type b, meningococcus groups B and C and *S. pneumoniae*. Quadrivalent vaccine (A, C, W, Y) for 17-18 year olds.
- Appropriate prophylaxis of people in close contact with those diagnosed.

Further reading & references

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