

# Meningitis in a young woman

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**When a young woman presents with fever, headache and photophobia, the emergency doctor suspects meningitis. The steps to diagnosis and treatment of this life-threatening emergency are outlined.**

**A**s a GP working in the local hospital emergency department, you may assess and treat adult patients presenting with headache and fever. An important differential diagnosis is bacterial meningitis, which is a life-threatening emergency requiring prompt administration of antibiotics. The steps to expediting diagnosis and treatment of meningitis are illustrated by the following case.

## The case

One evening, a young woman is brought by ambulance to the emergency department. You note that she has placed her hands over her eyes and she looks unwell. You immediately go to assess her. Her blood pressure is 95/40 mmHg, heart rate 105 beats per minute and regular, respiratory rate 24 breaths per minute and temperature 39.1°C.

She reports that she has a severe headache and does not like looking at the light. While you take a history, you insert an intravenous cannula and prescribe a one-litre bolus of normal saline. You send samples for venous blood gas analysis, a full blood count, measurement of electrolytes and creatinine, liver function tests, coagulation profile and blood culture.

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## The history

You learn that the woman has a history of well-controlled asthma and endometriosis. She takes salbutamol, paracetamol and ibuprofen as needed. She has no allergies. She currently works in finance and lives with her partner and two young children, aged 2 and 4 years, who are all well. She is an ex-smoker, drinks two standard drinks per week and does not use any recreational drugs. She has not travelled recently.

The patient reports that she has had nasal congestion and a sore throat over the past few days and has felt her sinuses have been blocked. She has had some maxillary pain and has been using salbutamol more often than usual. She experienced chills and sweats the previous night, and this morning developed a severe headache, which she describes as coming on gradually. She reports that she does not usually experience headaches. She also reports that she cannot tolerate bright light but has no weakness, no visual changes and no speech disturbance.

She has no history of immunosuppression, and her family history is unremarkable. She has not had the influenza vaccination this year.

You think that this presentation may represent meningitis and ask your colleague to quickly gather the lumbar puncture equipment. You also ask for ceftriaxone, vancomycin and dexamethasone to be prepared immediately. As you are considering the diagnosis of meningitis, you place the patient under droplet precautions in case it is caused by *Neisseria meningitidis* or *Haemophilus influenzae* type B (Hib). According to local hospital guidelines, these precautions can be lifted 24 hours after commencement of effective therapy that will clear nasopharyngeal carriage.<sup>1</sup> The other common causes of meningitis generally require standard precautions.<sup>1</sup>

## Physical examination

While nursing staff prepare the equipment and antibiotics, you continue your examination. You notice neck stiffness and objective photophobia, but do not observe a rash. The patient is fully alert despite keeping her eyes closed. Results of a cranial nerve examination are normal, and her upper limb and lower limbs have normal

### 1. FACTORS THAT SHOULD PROMPT CEREBRAL IMAGING BEFORE LUMBAR PUNCTURE<sup>3</sup>

- New-onset seizures
- Focal neurological signs
- Papilloedema
- Impaired consciousness
- Immunocompromised
- History of focal neurological disease

### 2. RISKS OF LUMBAR PUNCTURE

- Headache
- Bruising and bleeding
- Infection
- Cerebrospinal fluid leak
- Allergy to local anaesthetic
- Nerve injury

power, tone, reflexes and sensation. She has no papilloedema. She has some mild maxillary sinus tenderness. Her ears, nose and throat appear normal on examination. Results of the rest of the examination are unremarkable.

### Test results and provisional diagnosis

You are extremely concerned about the possibility of bacterial meningitis in this young woman. You are also considering the possibility of viral meningitis; however, a definitive diagnosis requires analysis of cerebrospinal fluid (CSF), and the consequences of missing a bacterial infection are great. The lack of neurological symptoms and signs makes encephalitis or raised intracranial pressure unlikely. You consider other diagnoses such as subarachnoid haemorrhage, migraine and venous sinus thrombosis but believe they would be unlikely in this patient.

Your patient has now been in the emergency department for 10 minutes. You are aware that delayed treatment of bacterial meningitis is associated with higher mortality.<sup>2</sup> Ideal management involves a

lumbar puncture to obtain a CSF sample for analysis followed promptly by administration of empirical antibiotics. However, some patients are at risk of raised intracranial pressure (Box 1).<sup>3</sup> These patients should be given empirical antibiotic therapy and then undergo cerebral CT before lumbar puncture.<sup>4</sup> If findings on imaging confirm the presence of raised intracranial pressure then lumbar puncture should be deferred.

Your patient does not have any features to suggest raised intracranial pressure, and you decide to proceed with lumbar puncture without imaging after gaining informed consent. Possible side effects of lumbar puncture are listed in Box 2. The patient has no history of coagulopathy and is not haemodynamically unstable – features which may preclude lumbar puncture.

You work quickly and successfully perform a lumbar puncture, followed immediately by administration of empirical intravenous dexamethasone 10 mg (first), ceftriaxone 2 g and a loading dose of vancomycin 25 mg/kg. It is important to measure the opening pressure while performing a lumbar puncture, as it can assist in diagnosis and has therapeutic implications in some types of meningitis, such as cryptococcal meningitis.

You are pleased you have been able to perform all investigations and administer antibiotics within 25 minutes of your patient arriving. You know that any delay in treating bacterial meningitis is deleterious, and it is recommended that treatment be started within 30 minutes. If there will be a delay in performing lumbar puncture or there is a high suspicion of bacterial meningitis then empirical antibiotics should be given before lumbar puncture.<sup>4</sup> If meningococcal sepsis is suspected then empirical antibiotics should be given immediately.<sup>5</sup> Empirical antibiotics should also be given if the patient presents out of hospital (benzylpenicillin 2.4 g or ceftriaxone 2g intravenously or intramuscularly if meningococcal disease is suspected).<sup>4</sup>

After administration of the fluid bolus, the patient's blood pressure has improved

**TABLE 1. RELEVANT INVESTIGATION RESULTS IN A PATIENT WITH SUSPECTED MENINGITIS**

Investigation	Result
<i>Cerebrospinal fluid</i>	
Opening pressure (mmHg)	22
White cell count (cells/L)	250 x 10 <sup>6</sup> (95% polymorphs)
Protein (g/L)	0.75
Glucose (mmol/L)	2.3
<i>Blood</i>	
Haemoglobin (g/L)	115
Platelets (cells/L)	414 x 10 <sup>9</sup>
White cell count (cells/L)	22.2 x 10 <sup>9</sup>
Neutrophils (cells/L)	14.1 x 10 <sup>9</sup>
Potassium (mmol/L)	3.8
Sodium (mmol/L)	146
Urea (mmol/L)	13.8
Creatinine (µmol/L)	110
INR	1.1

to 105/60 mmHg and the tachycardia has resolved. The CSF examination results are reported and are consistent with bacterial meningitis (Tables 1 and 2).<sup>5-7</sup> Gram stain of the CSF is negative for bacteria. You also asked for India ink staining of the CSF, which shows no cryptococci. CSF testing for cryptococcal antigen is also negative. You continue treating the patient with ceftriaxone 2 g twice daily, vancomycin (consult local guidelines for dosing recommendations), and dexamethasone 10 mg every six hours.

### Management and discussion

Meningitis and encephalitis are serious presentations, and a good outcome requires early diagnosis and treatment. It is often difficult to differentiate between viral and bacterial meningitis based on clinical findings alone. The classic triad of presentation

of bacterial meningitis in adults is headache, fever and neck stiffness. Altered mental status is also common. Most patients (95%) present with at least two of these four features.<sup>8</sup> Signs such as Brudzinski's sign and Kernig's sign, although reasonably specific, are not sufficiently sensitive to be relied on to rule out meningitis.<sup>3</sup>

The most common causes of bacterial meningitis are *N. meningitidis*, *Streptococcus pneumoniae* and Hib.<sup>9,10</sup> The incidences of Hib and certain serotypes of *S. pneumoniae* and *N. meningitidis* have been dramatically reduced by successful immunisation programs.<sup>9</sup> The backbone of bacterial meningitis empirical therapy aims to cover *N. meningitidis* and Hib with high-dose ceftriaxone; however, consideration of patient demographics will prompt additional therapy. For instance, if risk factors such as age older than 50 years, pregnancy, excessive alcohol use or immunosuppression are present, then *Listeria monocytogenes* is considered, prompting addition of benzylpenicillin.<sup>11</sup> Preceding sinusitis or otitis media prompts addition of vancomycin to cover *S. pneumoniae* as cephalosporin resistance can occur.<sup>4,10</sup> Common causes of meningitis and their treatment are shown in Table 3.<sup>4,12</sup>

Lumbar puncture results can help direct therapy, with Gram stain of the CSF having high specificity and moderate sensitivity.<sup>3</sup> Pneumococcal antigen assays and nucleic acid amplification testing of CSF for *N. meningitidis* can establish the diagnosis, especially in patients who have received antibiotics before lumbar puncture.<sup>4</sup> Once the diagnosis is made, antibiotics should be rationalised, with the selection based on antibiotic susceptibility results.

Cryptococcal meningitis should be considered in patients who are immunocompromised (caused, for example, by *Cryptococcus neoformans*). In addition, *Cryptococcus gattii* can cause meningitis in immunocompetent individuals. Cryptococcal antigen testing and India ink staining of the CSF allow diagnosis of these conditions. In Australia, other rare presentations include eosinophilic meningitis (caused, for example, by the parasite

**TABLE 2. INTERPRETATION OF CEREBROSPINAL FLUID RESULTS<sup>5-7</sup>**

	Normal range	Bacterial meningitis	Viral meningitis
Opening pressure	<25 mmHg	Elevated	Normal
White cell count	<5 x 10 <sup>6</sup> cells/L	Raised (>80% neutrophils)	Raised (<20% neutrophils)
Protein	<0.45 g/L	Raised	Normal or raised
Glucose	2.8 to 4.4 mmol/L (>0.60 of serum level)	Reduced	Normal

*Angiostrongylus cantonensis*), typically detected by the presence of eosinophils in the CSF; and tuberculous meningitis, detected by the presence of acid-fast bacilli on microscopy or growth of *Mycobacterium tuberculosis* in CSF culture.

Corticosteroids have shown mortality benefit in adults presenting with *S. pneumoniae* meningitis, but only if given before or with the first antibiotic treatment. Corticosteroids are now recommended in early management and can be discontinued if an

alternative cause to *S. pneumoniae* is found.<sup>13</sup>

Most cases of viral meningitis are caused by enteroviruses, which can be diagnosed with enteroviral polymerase chain reaction (PCR) testing.<sup>14</sup> Other viral causes include herpes simplex virus (HSV) and varicella-zoster virus (VZV), which can be diagnosed with HSV and VZV PCR tests, respectively.<sup>14</sup> HSV type 2 can cause recurrent benign lymphocytic meningitis. The mainstay of therapy for patients with viral meningitis is supportive.

**TABLE 3. COMMON CAUSES OF MENINGITIS AND ENCEPHALITIS AND THEIR TREATMENT (DOSES ASSUME NORMAL RENAL FUNCTION)<sup>4,12</sup>**

Organism	Initial first-line treatment recommendations*	Recommended duration of therapy†
Empirical therapy	<ul style="list-style-type: none"> <li>• Dexamethasone 10 mg every 6 hours for 4 days‡</li> <li>• Ceftriaxone 2 g twice daily or 4 g daily IV</li> <li>• ± Benzylpenicillin 2.4 g every 4 hours (if <i>Listeria monocytogenes</i> suspected)</li> <li>• ± Vancomycin IV (if <i>Streptococcus pneumoniae</i> suspected)</li> </ul>	See below
<i>Neisseria meningitidis</i>	Benzylpenicillin 1.8 g every 4 hours IV	5 days
<i>Haemophilus influenzae</i> type b	Ceftriaxone 4 g daily or 2 g twice daily IV	7 days
<i>Streptococcus pneumoniae</i>	Depends on sensitivities	10 to 14 days
<i>Listeria monocytogenes</i>	Benzylpenicillin 2.4 g every 4 hours IV	3 to 6 weeks
Herpes simplex encephalitis	Aciclovir 10 mg/kg every 8 hours IV	14 to 21 days

Abbreviation: IV = intravenous.

\* Always consider allergies, resistance and renal function and consult local guidelines.

† Always consult local guidelines.

‡ Give with or before first antibiotic dose only and stop if a cause other than *Streptococcus pneumoniae* is identified.

A patient presenting with fever, altered conscious state, seizures and/or objective neurological signs prompts consideration of encephalitis; however, the differential diagnosis can be broad and includes cerebrovascular accident, seizure disorder and cerebral abscess. Up to one-third of cases of encephalitis are immune mediated (e.g. anti-NMDA receptor encephalitis). Infectious encephalitis can be caused by the same viral organisms as viral meningitis.<sup>7</sup> HSV type 1 is the most common cause of viral encephalitis, and patients should be commenced on intravenous aciclovir promptly if this diagnosis is suspected. Other causes of infectious encephalitis include influenza, *Mycoplasma pneumoniae*, *C. neoformans*, *Toxoplasma gondii* and *Treponema pallidum*.<sup>7</sup> Murray Valley encephalitis, melioidosis and Japanese encephalitis are also important differential diagnoses.<sup>7</sup>

### Progress

The patient is admitted. When her blood results become available, they reveal prominent neutrophilia and mild acute kidney injury (Table 1). These improve with antibiotic and fluid administration. Over the first two days of admission, her fevers settle and the headache improves.

*S. pneumoniae* is isolated from the CSF culture and is sensitive to penicillin. The same organism grows in the patient's blood cultures. PCR testing of the CSF is negative for meningococcus and viruses (including HSV, VZV and enterovirus). The patient's antibiotic treatment is rationalised to high-dose benzylpenicillin, which is continued for a total of 14 days.

### Outcome

Your patient makes a full recovery and is discharged from hospital. She comes to see you at your general practice. She is grateful for your expedited and thorough care. She asks about the risk to her two children and partner. You explain that chemoprophylaxis of contacts is not recommended for *S. pneumoniae* infection, although it is

### 3. PRACTICE POINTS ON MENINGITIS

- Bacterial meningitis is a life-threatening emergency, and antibiotic administration should not be delayed
- Lumbar puncture is an essential investigation for diagnosing meningitis and encephalitis. CT can be avoided in most circumstances, to prevent delays and improve outcome
- Measure the opening pressure when performing a lumbar puncture
- Request testing of cerebrospinal fluid for protein, glucose, microscopy, Gram stain and culture and pneumococcal antigen, *Neisseria meningitidis* nucleic acid and viral PCR testing
- Consider cryptococcal antigen testing, India ink staining (for fungus), and acid-fast staining (for acid-fast bacilli) of the cerebrospinal fluid
- Consider patient factors and history when initiating empirical antibiotic therapy
- If encephalitis is suspected then aciclovir should be initiated promptly to cover herpes simplex encephalitis

used to eliminate organism carriage in contacts of patients with *N. meningitidis* and Hib infection.

### Conclusion

Bacterial meningitis is a medical emergency, and antibiotic administration should not be delayed. Practice points concerning patients with suspected meningitis are summarised in Box 3. A number of organisms can cause meningitis or encephalitis, and lumbar puncture is an important investigation for determining the causative agent. Patient characteristics should be considered in each case so that appropriate empirical antibiotics are given. MT

### References

A list of references is included in the website version of this article ([www.medicinetoday.com.au](http://www.medicinetoday.com.au)).

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