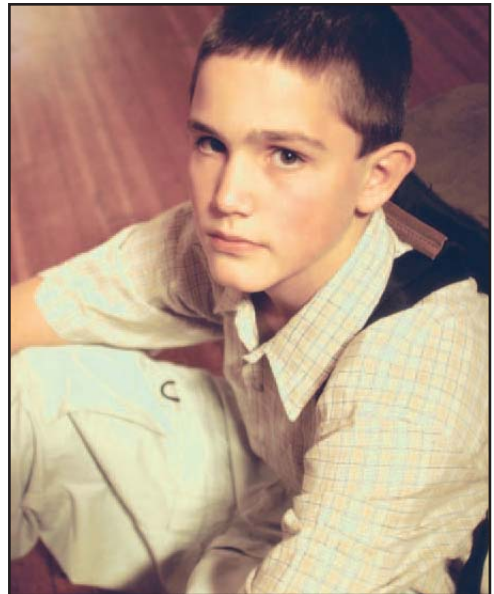


# Meningitis and Encephalitis On the Brain

By Michael R. Achong, MB, BSc, FRCPC



### Michael's history

Michael is brought to the emergency department (ED) because of fever, headache and vomiting. The 15-year-old high school student's illness began about 12 hours previously.

In the ED, he is confused, febrile, and has neck stiffness; a petechial eruption is noted on his trunk and extremities.

### *What causes meningitis?*

The most common causes of bacterial meningitis in adults are *Streptococcus pneumoniae* and *Neisseria meningitidis*. During this era of childhood immunization against invasive *Haemophilus influenzae* infection, it has become rare for meningitis to be caused by this organism. *Listeria monocytogenes* should be considered in certain age groups (infants under a year old, and adults over 60), while group B streptococci (*Streptococcus agalactiae*) and *Escherichia coli* are the most common culprits in neonates. Immunocompromised patients may present with a wider range of microbial infection, e.g., toxoplas-

### In this article:

1. Should the patient have a CT scan of his head before a lumbar puncture?
2. Should I wait for blood and CSF results before starting antibiotic therapy?
3. What is the best initial, empirical antibiotic therapy for bacterial meningitis?
4. What should I do about his contacts, at home and at school?

mosis or cytomegalovirus in patients with acquired immune deficiency syndrome (AIDS).

### *Do the new vaccines prevent meningitis caused by these organisms?*

The new heptavalent pneumococcal conjugate vaccine (Prenar<sup>®</sup>) decreases the incidence of invasive pneumococcal disease caused by the seven serotypes in children.<sup>1</sup> It is not clear, however, whether the medication will have an impact on the incidence of pneumococcal meningitis in

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Table 1

## Quick facts on invasive meningococcal disease

- There are usually about 300 cases of invasive meningococcal disease reported in Canada each year, with a case fatality rate of about 10% to 20%, even with prompt and appropriate medical treatment.
- Most cases occur between late winter and early spring, although sporadic cases may occur year round.
- Infants under the age of one are at greatest risk, but no age group is immune.<sup>6</sup>

Adapted from: National Advisory Committee on Immunization: Statement on recommended use of meningococcal vaccines. Canada Communicable Disease Report 2001; 27: 2-36.

Table 2

## Useful clinical clues to invasive meningococcal disease include:

- A hemorrhagic rash
- A "flea-bitten" maculopapular rash that blanches on pressure
- The abrupt onset and rapid evolution of the illness
- Marked systemic toxicity with headache, fever, vomiting, neck stiffness and photophobia
- A patient in a high risk age group or contact with a meningococcal-diseased patient.<sup>5</sup>

Adapted from: Yung AP, McDonald MI: Early clinical clues to meningococemia. Med J Australia 2003; 178:134-7.

adults. Early reports indicate the monovalent meningococcal serogroup C conjugate vaccine (MenC-conjugate or Menjugate<sup>®</sup>) has decreased the incidence of meningococcal infection caused by serogroup C.<sup>2</sup>

## What are the clues?

Early diagnosis and treatment of meningococcal infection is crucial as this infection may be rapidly fatal (Table 1). Every effort should be made to give antibiotics promptly; this may mean giving antibiotics before the patient is transferred to hospital and avoiding delays in the

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ED.<sup>3</sup> A hemorrhagic rash (petechial or purpuric) is often cited as an early clue to the presence of meningococcal disease, but less than half of all patients with invasive meningococcal disease may have a rash (Table 2). Even when present, a petechial eruption is not specific for invasive meningococcal disease.<sup>4</sup>

*Neisseria meningitidis* has a polysaccharide capsule whose chemical composition defines the serogroup of the organism. Five serogroups (A, B, C, Y and W135) are responsible for almost all cases of meningococcal disease. Since 1989, serogroups B and C have been responsible for most cases of endemic meningococcal infection in Canada, with serogroup C becoming increasingly responsible for clusters or outbreaks in schools. Early vaccines have provided protection against serogroups A, C, Y, and W135, but have limited immunogenicity in early childhood and provide a relatively short period of protection. A new vaccine to protect against serogroup C became available in Canada in 2001. This monovalent serogroup C conjugate vaccine (MenC-conjugate- and Menjugate<sup>®</sup>) has been recommended for the routine vaccination of infants to young adults.<sup>5,6</sup>

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As the serogroup B polysaccharide is poorly immunogenic, there is no currently available effective vaccine against this serogroup. The quadrivalent vaccine against serogroups A, C, Y, and W 135 has been used for several years to control outbreaks and epidemics, however, the quadrivalent vaccine is not recommended for routine immunization. This is because it provides relatively short-term protection and has a low efficacy in children under 10 and is ineffective in children under two.

Laboratory diagnosis of meningococcal disease traditionally depends on Gram stain and culture of blood, CSF, or a skin lesion aspirate. Identification of meningococcal DNA in blood or CSF using polymerase chain reaction (PCR) is becoming available and will help with more rapid diagnosis, and identification of serogroup. It may be particularly helpful if there has been prior administration of antibiotics.

***One of my patients shared a school bus with the teenager who died of meningococcal meningitis yesterday. Should my patient receive prophylactic antibiotics and, if so, with what drug schedule?***

The attack rate for household contacts exposed to patients who have sporadic meningococcal disease has been estimated to be about four cases per 1,000 persons exposed, which is 500 to 1,000 times greater than in the general population.<sup>7</sup> Physicians should have quick access to the recommended antibiotic prophylaxis schedules using rifampin, ciprofloxacin, or parenteral cef-

triaxone for household and close social contacts of cases of meningococcal infection.<sup>8</sup> Prompt, consistent advice may help to defuse the anxiety in those who have come into contact with someone who has sporadic meningococcal disease.

***I have heard so much about increasing antibiotic resistance among bacteria. Has this affected our choice of empirical early therapy for bacterial meningitis?***



Emergence of penicillin and cephalosporin resistance in *Streptococcus pneumoniae* has prompted more complex antibiotic regimens. Essentially, third generation cephalosporins (cefotaxime or ceftriaxone) are the first line treatment of bacterial meningitis, with the addition of ampicillin for those patients in whom the possibility of *Listeria monocytogenes* is a concern.

Vancomycin, with or without rifampin, is added if there is concern over drug resistant pneumococci for the initial empirical treatment of meningitis.<sup>6</sup>

Adjunctive dexamethasone therapy may be of benefit in children with *Hemophilus influenzae* meningitis but the current recommendation of the Canadian Pediatric Society is not to prescribe dexamethasone routinely for bacterial meningitis in children.<sup>9</sup> Although the value of steroids in adults with bacterial meningitis (other than tuberculosis) is still being debated,<sup>10</sup> recent British guidelines<sup>6</sup> support the use of dexamethasone 10 mg every six hours for four days, with the first dose given just before or at the same time as the first dose of antibiotics.

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Table 3

## Certain clinical features may suggest HSV encephalitis

- The onset is usually abrupt with a high fever and the tempo of the illness rapid with deteriorating level of consciousness.
- HSV 1 has a predilection for involvement of the temporal and inferior frontal lobes. Such involvement of the temporal lobe may manifest clinically as bizarre behaviour, speech difficulties and gustatory or olfactory hallucinations.

### *How do I distinguish between bacterial and viral meningitis?*

One diagnostic dilemma is to distinguish between bacterial and viral meningitis. Apart from the CSF findings of viral meningitis (modest increase in leukocytes with a predominance of lymphocytes, a normal CSF glucose concentration), patients with viral meningitis tend to appear less ill than those with bacterial meningitis.

Enteroviruses are the most common cause for viral meningitis.<sup>11</sup> Detection of a range of pathogens (enteroviruses, Herpes simplex virus (HSV), and Mycobacterium tuberculosis) by PCR on CSF will probably emerge as the “gold standard” diagnostic test for central nervous system (CNS) infections. For enteroviruses, the technique is highly sensitive and specific. Results are potentially available within 24 hours, and only small volumes of CSF are required. Such use of PCR for the diagnosis of enteroviral meningitis may allow the discontinuation of antimicrobial therapy and decrease costs by facilitating early discharge from hospitalization.

HSV (HSV-1 in about 95 % of cases) is the most common cause of severe viral encephalitis

in North America.<sup>12</sup> The illness may be fulminant and life-threatening. Intravenous acyclovir (10 mg/kg every eight hours for up to 14 days) affords the best results if given early in the disease (before the patient is unconscious).

### *HSV is a feared cause of viral encephalitis. Are there any early clues that would help me to make this diagnosis, and facilitate early acyclovir therapy?*

As early treatment is crucial, acyclovir should be given on suspicion of HSV encephalitis. HSV encephalitis shows no particular predilection for any age group or season; there is no person-to-person transmission (Table 3).

The presence of herpes labialis is not helpful in the diagnosis of HSV encephalitis. It is seen in < 10 % of cases and it may be merely a non-specific feature of a febrile illness. This contrasts with the almost invariable presence of mucocutaneous lesions in HSV-2 encephalitis. The use of PCR to detect viral DNA is a very sensitive and specific test for HSV encephalitis and has replaced brain biopsy.

### *When do I have to consider the possibility of encephalitis caused by West Nile virus?*

With the summer season on us, the specter of West Nile virus has become a major concern.<sup>13</sup> Less than 1% of patients infected with West Nile virus develop neurologic problems, with patients over 50 being at greatest risk.

Asymmetrical weakness without pain or sensory findings are important clues to the diagnosis of WNV infection causing a neurologic syndrome (Table 4).

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Table 4

## Several clinical patterns should prompt consideration of West Nile virus CNS infection

- Uncomplicated aseptic meningitis, and
- Encephalomyelitis of grey matter that involves the cerebral cortex, diencephalons, brainstem and spinal cord.

### *Patients may show a combination of:*

- Decreased level of consciousness;
- Brain stem involvement: Locked-in syndrome, swallowing difficulties, facial weakness
- Cerebellar involvement: Ataxia
- Anterior horn cell and motor axonal neuropathy: Flaccid paralysis or a polio-like syndrome.

## Don't forget tuberculosis

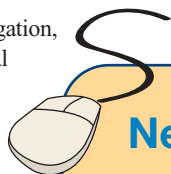
Tuberculous meningitis is usually thought of as a subacute lymphocytic meningitis, but clinical presentations are varied.<sup>14</sup> Clues include cranial nerve palsies reflecting basal meningitis, hydrocephalus, CSF pleocytosis with a lymphocytic predominance and an abnormal chest X-ray in about half the patients.

A remote or recent contact with tuberculosis or extra-meningeal tuberculosis should prompt a consideration of tuberculous meningitis. CME

### References

1. Canadian Paediatric Society: Pneumococcal vaccine for children. *Paediatr Child Health* 2002; 7:417-8.
2. De Wals P, DeSerres G, Niyonsenga T: Effectiveness of a mass immunization campaign against serogroup C meningococcal disease in Quebec. *JAMA* 2001; 285: 177-81.
3. Begg N, Cartwright KA, Cohen J, et al: Consensus statement on diagnosis, investigation, treatment, and prevention of acute bacterial meningitis in immunocompetent adults. *J Infection* 1999; 39:1-15.
4. Gold R: Fever and petechiae in children. *Pediatr Child Health* 1997; 2:260-1.

5. Canadian Paediatric Society: Meningococcal vaccine for children. *Paediatr Child Health* 2002; 7:425-6.
6. Heyderman RS, Lambert HP, O'Sullivan I, et al: Early management of suspected bacterial meningitis and meningococcal septicemia in adults. *J Infection* 2003; 46:75-7.
7. National Advisory Committee on Immunization: Statement on recommended use of meningococcal vaccines. *Canada Communicable Disease Report* 2001; 27:2-36.
8. Weir E: Meningococcal disease: Oh no, not another childhood vaccine. *Can Med Assoc J* 2002; 166:1064-6.
9. Canadian Paediatric Society Infectious Disease and Immunization Committee: Therapy of suspected bacterial meningitis in Canadian children six weeks of age and older. *Paediatr Child Health* 2001; 6:147-52.
10. Tunkel AR, Scheld WM: Corticosteroids for everyone with meningitis? *N Engl J Med* 2002; 347:1613-5.
11. Redington JJ, Tyler KL: Viral infections of the Nervous System, 2002. *Arch Neurol*. 2002; 59:712-18.
12. Kennedy PGE, Chaudhuri A: Herpes simplex encephalitis. *J Neurol Neurosurg Psych* 2002; 73:237-38.
13. Pepperell C, Rau N, Kraiden S et al: West Nile virus infection in 2002: Morbidity and mortality among patients admitted to hospital in southcentral Ontario. *Can Med Assoc J* 2003; 168:1399-1405.
14. Thwaites G, Mai NTH, Drobniewski F, et al: Tuberculous meningitis. *J Neuro Neurosurg Psychiatry* 2000; 68:289-99.



## Net Readings

1. [www.ninds.nih.gov/health\\_and\\_medical/disorders/encmenin\\_doc.htm](http://www.ninds.nih.gov/health_and_medical/disorders/encmenin_doc.htm)
2. <http://www.musa.org/>
3. <http://www.nmaus.org/info/>