

Viral meningitis and encephalitis

Philip Rice

Abstract

Meningitis and encephalitis due to virus infections occur at all stages of life from the neonate to the elderly and may represent disease due to the primary site of replication, e.g. rabies, or be part of a wider infection syndrome, e.g. HIV. A large proportion of cases go unconfirmed by laboratory diagnosis despite use of sensitive techniques (such as the polymerase chain reaction). They may be both sporadic and epidemic in nature, but with changing environmental and societal conditions, agents may emerge anew, e.g. Nipah and Hendra viruses, or reappear after a period of good control through vaccination, e.g. mumps and poliovirus. Specific anti-viral treatment is very limited at present. Prevention is by public health measures and vaccination.

Keywords enteroviruses; Hendra; herpes simplex encephalitis; HSV; Japanese encephalitis; Nipah; rabies; viral encephalitis; viral meningitis; West Nile virus

Viral meningitis

Definition and epidemiology – the term ‘aseptic meningitis’ was introduced because it seemed to represent a specific aetiological entity, namely patients with symptoms and signs of meningitis in whom bacterial cultures were negative. It is now known that almost all such cases are caused by a wide range of viruses, though most cases are caused either by enteroviruses (70–90%), herpes simplex virus (HSV-1, HSV-2) acquired genitally or mumps virus (Table 1).

The exact incidence of viral meningitis is unknown but it is grossly under-reported. In the UK a total of 2898 patients were admitted to hospital in 2005–2006 with such a diagnosis, more than 10 times the number formally notified to the Health Protection Agency. Whilst any age group can be affected, childhood disease is most common; a study from Finland found an annual incidence of 219 per 100,000 in infants aged <1 year compared with 28 per 100,000 in those <14 years old.

Transmission occurs by droplet infection, close personal and kissing contact or faeco-orally. Zoonotic infection is seen with lymphocytic choriomeningitis virus, an arenavirus related to Lassa fever that is excreted in the urine of small rodents; transmission of this organism occurs by inhalation when changing bedding contaminated with urine.

Clinical features – the typical syndrome of viral meningitis comprises a triad of symptoms and signs of acute onset: fever, headache and accompanying signs of meningeal irritation (photophobia, neck stiffness, Kernig’s sign and jolt accentuation of

headache). Non-specific symptoms include arthralgia and myalgia, sore throat, rash, and lethargy. Other symptoms and signs are specific to the causative agent. Clues to the possible organism may be obtained based on other information revealed in the history: sexual orientation, travel, vaccination status, animal exposure, etc.

Enteroviruses

The enteroviruses comprise over 70 serotypes, including poliovirus, Coxsackievirus A and B, and echovirus. Most infections are asymptomatic and occur seasonally in late summer and autumn. Outbreaks may also occur in nurseries and day-care centres. Rarely, outbreaks on neonatal units have been described; these can occasionally have a high mortality.

A rash may be seen; this may be erythematous and maculopapular, vesicular on the palms, soles of feet and inside the mouth (as in hand, foot and mouth disease), or an exanthem in the oral cavity (seen in herpangina). Enterovirus serotype 71 can also induce acute flaccid paralysis identical to that caused by poliovirus; there was an extensive outbreak in SE Asia several years ago. Aside from this complication full recovery is the rule. In patients with agammaglobulinaemia, chronic, relapsing meningitis may result requiring administration of intravenous immunoglobulin. There are no licensed anti-viral agents, though the novel anti-viral agent, pleconaril, was shown to have some small benefit in a subgroup of patients with severe headache.

HSV and varicella-zoster virus

Primary genital HSV infection can occur with either HSV-1 or HSV-2. The risk of clinically apparent meningitis is greatest in a primary genital infection, with approximately 30% of women and 13% of men developing this complication. However, if a non-primary genital infection occurs (infection with one virus type in an individual who possesses pre-existing antibody to the other type), clinical meningitis is unusual. As the prevalence of oral HSV-1 infection appears to be decreasing at least in the UK, we may see more cases of HSV-induced meningitis. There is also a syndrome of benign recurrent aseptic meningitis that has been shown to be caused by reactivation of genitally acquired HSV infection, most commonly HSV-2. This syndrome occurs predominantly in women (female:male ratio 6:1), and episodes can occur as much as 20 years apart. The average number of episodes recorded by patients is four. In one study, the recurrence rate in those presenting with a first episode of HSV meningitis was found to be 19%. Headache may be associated with genital recurrences. However, the risk of recurrent meningitis after genital infection, and the host and viral factors underlying its development, remain poorly understood.

Reactivation of varicella-zoster virus (VZV) usually presents as shingles, but can also present as meningitis without a cutaneous component. Such patients may suffer excruciating headaches.

Mumps virus

Mumps meningitis is manifested in 1–10% of cases of mumps, typically about five days after onset of parotitis though abnormalities in the cerebrospinal fluid (CSF) are seen in approximately 50% of cases of infection. The meningitis may however precede parotitis by a week or even follow it after two weeks.

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Viral causes of meningitis

- Mumps
- Enteroviruses
 - Poliovirus types 1, 2 and 3
 - Coxsackievirus type A (23 serotypes)
 - Coxsackievirus type B (6 serotypes)
- Echovirus (31 serotypes)
- Others
 - Enterovirus 71 (hand, foot and mouth disease)
 - Enterovirus 70 (epidemic conjunctivitis)
- Genital herpes simplex virus types 1 and 2
- Other herpes viruses
 - Cytomegalovirus
 - Epstein–Barr virus
 - Varicella-zoster virus
- HIV
- Lymphocytic choriomeningitis virus
- Adenovirus types 3 and 7
- ARBO viruses

ARBO, arthropod-borne.

Symptoms last for 7–10 days but it is essentially benign with no long-term complications. The epidemiology of viral meningitis has changed dramatically since the introduction of the MMR vaccine in the UK 1988. Before this, mumps virus was the most common cause of meningitis (annual incidence 5–11/100,000 population, 1200 hospital admissions each year); the current incidence is about 0.3/100,000 population. Outbreaks still continue to occur despite the good uptake rates of vaccine seen primarily in the UK and USA. This is thought to be due to a mixture of primary and secondary vaccine failure and the relatively high transmissibility of mumps virus.

HIV

Headache occurs in about 50% of patients during primary HIV infection, and symptoms of meningitis are seen in 17% with HIV seroconversion. Higher HIV RNA concentrations in the CSF also correlate with neurological symptoms. Early diagnosis of primary infection by either 4th generation Ab/Ag assays or viral load testing in clinically highly suspected cases may enable post-exposure prophylaxis to be given to sexual contacts.

Viral encephalitis

Definition and epidemiology – encephalitis is an uncommon outcome of many common viral infections (Figure 1 and Table 2). Infection of the brain parenchyma can have devastating consequences; mortality is high, and there is long-term morbidity in many survivors. A diverse range of agents is responsible, and infection may occur at any time from the neonatal period to old

Table 1

Viral causes of encephalitis

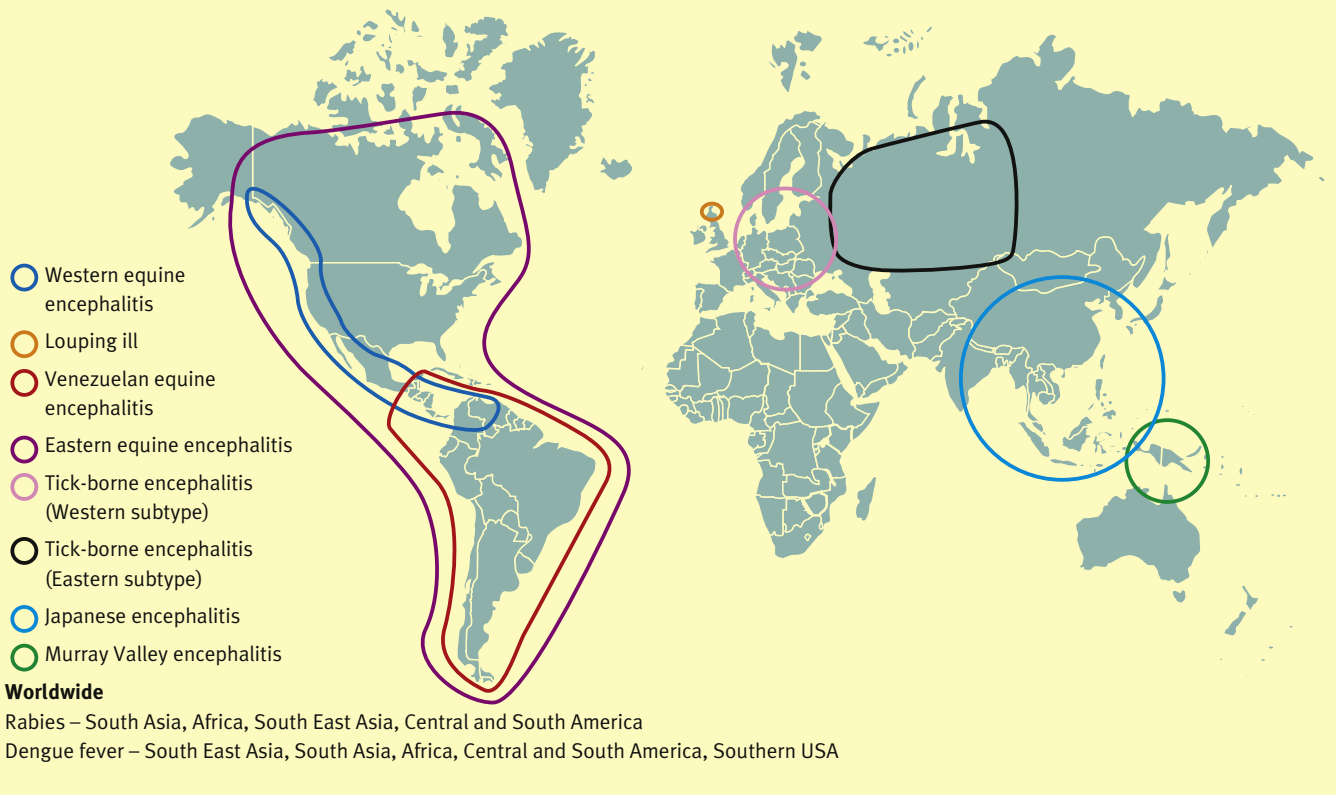


Figure 1

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