Acute Encephalitis

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Acute encephalitis means inflammation of the brain. Acute encephalitis associated with viral infections includes two distinct clinical-pathological diseases. The form referred to simply as acute viral encephalitis is direct infection of neural cells with perivascular inflammation, neuronal destruction, neuronophagia, and tissue necrosis, and this pathology is centered primarily in the gray matter. The other disease, postinfectious encephalomyelitis (acute disseminated encephalomyelitis), is an illness that follows a variety of viral and some bacterial infections; there is no evidence of direct infection of neural cells, but there is widespread perivascular inflammation and demyelination localized to the white matter of the brain.

Clinically, the distinction is often difficult unless the demyelinating disease complicates an exanthem. Historically, approximately two-thirds of the fatal cases of encephalitis were acute viral encephalitis, and one-third were postinfectious encephalomyelitis. The number of cases of postinfectious encephalomyelitis has decreased greatly, however, with the elimination of the use of vaccinia virus for prevention of smallpox and the institution of immunization against measles, mumps, and rubella.

The reported incidence of acute encephalitis is between 3.5 and 7.4 cases per 100,000 patient-years [1, 2]. It is more common in children, among whom the incidence is >16 cases per 100,000 patient-years [3]. Nearly 100 different agents have been associated with encephalitis, but the most important life-threatening causes of acute neuronal and glial infection are herpes simplex virus and the arthropod-borne viruses (arboviruses); the most common antecedent illness related to postinfectious encephalomyelitis is nonspecific respiratory disease. The most important issues in the differential diagnosis of encephalitis are to rule out nonviral diseases, which may require urgent treatment, and to properly identify cases due to herpes simplex virus, where morbidity and mortality can be greatly reduced with specific antiviral therapy.

Acute Viral Encephalitis

In addition to the arboviruses and herpes simplex virus (which will be discussed below), many other viruses can cause encephalitis, but in most cases, the encephalitis is milder, has fewer sequelae, and is associated with lower mortality rates (table 1). The enteroviruses (coxsackieviruses and echoviruses) are the commonest causes of acute viral meningoencephalitis, but <3% of CNS complications due to these viruses have obtundation or focal signs sufficient for classification as encephalitis [4]. Fatal encephalitis can occur, however, in neonates infected with some coxsackieviruses and echoviruses. Adenoviruses also can cause severe encephalitis in children, and encephalitis occasionally accompanies exanthem subitum due to human herpesvirus 6.

Rare fatalities have been described in children with encephalitis due to adenovirus or human herpesvirus 6 [5, 6]. Acute self-limited encephalitic symptoms have also been reported at the time of primary HIV disease and seroconversion to HIV infection. These symptoms are not described in patients with chronic progressive HIV encephalitis and patients with AIDS and dementia. In older children and adults, mumps virus and lymphocytic choriomeningitis virus are common causes of mild encephalitis.

CNS infections due to rabies virus in nonimmunized individuals are uniformly fatal, but only one to five persons die of rabies each year in the United States. The early localization of this infection to limbic structures in many patients leads to characteristic behavioral changes; however, some patients may have ascending paralysis simulating acute polineuritis (Guillain-Barré syndrome) or obtundation resembling other viral encephalitides.

Nonviral infectious diseases must be considered in the differential diagnosis of acute encephalitis (table 2). Noninfectious diseases, such as gliomatosis cerebri, carcinomatous meningitis, sarcoidosis, systemic lupus erythematosus, vasculitis, ruptured intracerebral cysts, and the oculocephalic syndromes, also must be considered. For patients with AIDS and those with profound immunodeficiency, a different differential diagnosis needs consideration. In these patients, cytomegalovirus encephalitis and ependymitis, toxoplastic encephalitis, and fungal infections become major causes of encephalitic signs and symptoms.

A definitive diagnosis of acute viral encephalitis is dependent on virus isolation or results of immunocytochemical studies of tissue or serological studies. Nevertheless, evaluation of historical data and systemic physical findings can lead to a
Table 1. Viruses causing acute viral encephalitis (in order of increasing severity).

<table>
<thead>
<tr>
<th>Virus(es)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coxsackieviruses and echoviruses</td>
<td>Rare fatal encephalitis in neonates</td>
</tr>
<tr>
<td>Human herpesvirus 6</td>
<td>Mild encephalitis in children</td>
</tr>
<tr>
<td>HIV</td>
<td>Rare acute encephalitis at the time of primary infection</td>
</tr>
<tr>
<td>Adenoviruses</td>
<td>Occasional serious encephalitis in children</td>
</tr>
<tr>
<td>Epstein-Barr virus*</td>
<td>Occasional encephalitis with infectious mononucleosis</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Occasional encephalitis with infectious mononucleosis</td>
</tr>
<tr>
<td>Mumps virus*</td>
<td>Common mild encephalitis; rare deaths</td>
</tr>
<tr>
<td>Lymphocytic choriomeningitis virus</td>
<td>Common mild encephalitis; rare deaths</td>
</tr>
<tr>
<td>Arboviruses</td>
<td>1%–50% of cases are fatal* (dependent on virus and age of host)</td>
</tr>
<tr>
<td>Herpes simplex viruses</td>
<td>&gt;70% of cases are fatal (if untreated)</td>
</tr>
<tr>
<td>Rabies virus</td>
<td>&gt;99% of cases are fatal</td>
</tr>
</tbody>
</table>

* Some fatal cases have the pathology of postinfectious encephalomyleitis. Some viruses may cause acute encephalitis and postinfectious encephalomyleitis.

**California encephalitis is fatal in <1% of children; western equine encephalitis, 10% of infants; St. Louis encephalitis, 20% of elderly persons; and eastern equine encephalitis, 50% of individuals of all ages.**

presumptive clinical diagnosis for many patients (table 3). All agents cause fever, headache, and nuchal rigidity.

The wide variety of neurological signs depends only to a very limited extent on the etiologic agent. Consciousness is generally altered, and mild lethargy may progress to confusion, stupor, and coma. Focal neurological signs usually develop; seizures are common. Motor weakness and accentuated deep tendon reflexes and extensor plantar responses are often present. Occasionally, abnormal movements or tremor develops. When the hypothalamic-pituitary area is involved, hyperthermia and poikilothermy are seen. The involvement of the spinal cord may lead to superimposed flaccid paralysis with loss of tendon reflexes and paralysis of the bladder and bowel. Increased intracranial pressure is common.

Pathological studies of patients dying during this period show either diffuse or multifocal areas of inflammation and neuronophagia particularly in the cerebral and cerebellar cortex; deep nuclei of the basal ganglia, thalamus, and hypothalamus; brain stem nuclei; and gray matter of the spinal cord. Inclusions may be seen in herpesvirus and rabies virus infections.

**Arbovirus Encephalitis**

Arbovirus infections occur at different rates in different parts of the world. For example, each year in Asia about 20,000 people have Japanese encephalitis, the world’s most widespread arbovirus encephalitis [7]. All arboviruses have geographic limitations, since they are restricted to specific species of mosquitoes or ticks and to specific ecological systems. Human illnesses are seasonal since they depend on the breeding and feeding seasons of the arthropod host.

Globally, >20 arboviruses cause human encephalitis. In the United States, four arboviruses are important: California encephalitis (LaCrosse strain), St. Louis encephalitis, western equine encephalitis, and eastern equine encephalitis viruses.

Venezuelan equine encephalitis, Colorado tick fever, and Powassan, Jamestown Canyon, and snowshoe hare viruses are rare causes of encephalitis in North America [8]. Each North American arbovirus has a specific geographic distribution, is associated with a different ratio of inapparent-to-clinical infections and distinct age-dependent effects, and causes encephalitis of variable severity.

California encephalitis viruses cause about 70 reported cases of encephalitis each year [8]. Cases are most prevalent in the midwestern states, where the LaCrosse strain causes encephalitis. Over the past three decades, >90% of cases have been in...
Western equine encephalitis virus causes disease in adults and children west of the Mississippi River; the sequelae in children younger than 1 year of age are more severe, and the mortality is higher. For unknown reasons, the numbers of major epidemics and interepidemic cases of this disease have markedly decreased in recent years. The inapparent infection-to-encephalitis ratio is about 1,000:1.

Eastern equine encephalitis virus is restricted largely to the Atlantic and gulf coasts and is dependent on a natural cycle between marsh birds and mosquitoes that do not bite large mammals. Only when there are ecological changes in the marsh as well as changes in bird and mosquito populations does the virus spill over into other mosquito species that do bite and infect horses and humans. It is fortunate that there are so few human infections, because this virus is associated with the highest infection-to-illness ratio (20:1) and causes the most severe disease (mortality rate, >50%; 70% of surviving children have severe sequelae).

Rapid diagnosis of arbovirus encephalitis is possible by testing for virus-specific IgM in spinal fluid by means of a simple antibody-capture ELISA. Antibody is usually present at the time of medical presentation. The absence of IgM in the spinal fluid of patients with Japanese B encephalitis on the day of admission predicts a poor prognosis [10].

Treatment of arbovirus encephalitis is supportive with fluid restriction to passively dehydrate the brain, anticonvulsant administration if seizures occur, and artificial ventilation for respiratory failure. Vigorous avoidance of hypothermia may be counterproductive, since modest temperature elevations may serve as a natural defense against thermolabile viruses. The respiratory tract, urinary tract, intravenous catheter sites, and skin should be checked assiduously for evidence of infection. Prophylaxis for deep vein thrombosis and gastrointestinal ulceration should be used for patients with prolonged inactivity. Corticosteroid therapy is not routinely indicated [11].

**Herpes Simplex Virus Encephalitis**

A diffusely form of herpes simplex virus encephalitis occurs in babies infected perinatally, and herpes simplex virus type 2 is usually involved in this form. The localized sporadic form of encephalitis in otherwise healthy children and adults that will be discussed here is due predominantly to herpes simplex virus type 1. This encephalitis has no seasonal preference, and there are ~2,000 cases per year in the United States. The distinctive pathology (localization of inflammation and necrosis to the medial-temporal and orbital-frontal lobes) determines the clinical manifestations and suggests the diagnosis. Since death occurs in >70% of individuals who are not treated with antiviral agents and since survival rates and quality of survival are related to the mental status at the time that treatment is instituted, early diagnosis and treatment are imperative.

More than 90% of adults have antibody to herpes simplex virus type 1, and about 25% of patients who have encephalitis

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**Table 3. Historical data and systemic physical findings that suggest the cause of acute encephalitis.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Virus(es)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical data</td>
<td>Arboviruses in tick and mosquito season; mumps virus in spring; enteroviruses in late summer and fall; lymphocytic choriomeningitis virus in winter (Borrelia burgdorferi in summer)</td>
</tr>
<tr>
<td>Travel</td>
<td>Other arboviruses, exotic viruses (regional bacteria, fungi, and parasites)</td>
</tr>
<tr>
<td>Family illnesses</td>
<td>Enteroviruses cause family outbreaks of varied disease (Mycobacterium tuberculosis)</td>
</tr>
<tr>
<td>Recreational activity</td>
<td>California encephalitis virus in woodlands (Leptospira in farm ponds; Naegleria in quarry water)</td>
</tr>
<tr>
<td>Animal exposures</td>
<td>Lymphocytic choriomeningitis virus carried by mice or hamsters; rabies virus transmitted by bat, wild carnivore, dog, or cat bites</td>
</tr>
<tr>
<td>Immunization and drugs</td>
<td>Viruses causing childhood exanthems, enteroviruses, human herpesvirus 6 (Rickettsia rickettsii, B. burgdorferi)</td>
</tr>
<tr>
<td>Rash</td>
<td>Coxsackieviruses</td>
</tr>
<tr>
<td>Herpangina</td>
<td>HIV, Epstein-Barr virus, cytomegalovirus (agents of cat-scratch disease, Brucella)</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>Mumps virus, lymphocytic choriomeningitis virus</td>
</tr>
<tr>
<td>Parotitis and/or orchitis</td>
<td>Adenoviruses, lymphocytic choriomeningitis virus (Mycoplasma)</td>
</tr>
</tbody>
</table>

* Nonviral agents are in parentheses.
have a history of cold sores, an incidence that is the same as that among the general population. Therefore, encephalitis is thought to be due either to reactivation of virus (which lies latent in the trigeminal and other cranial and high cervical ganglia) or to reinfection. In either case, the occurrence in an immune host potentially explains the spread of virus from cell to cell and consequently the localization to the brain with the pia mater innervated by trigeminal fibers or to the brain adjacent to the olfactory bulbs where reinfection might occur from the olfactory mucosa.

Herpes simplex virus encephalitis may have an insidious or abrupt onset. Fever is almost always present. Headache is a prominent early symptom, and 90% of patients have signs that suggest a localized lesion in one or both temporal lobes. This localization often takes the form of personality changes, which may dominate the clinical picture for a few days or even 1 week before other signs evolve. Patients may have acute episodes of terror, may experience hallucinations, or may exhibit bizarre behavior. Such behavior may lead to initial admission to the psychiatric department.

These early behavioral changes are followed by other signs such as seizures, which are often focal and occur early in the disease in 40% of patients. Hemiparesis is seen in one-third of patients, and greater involvement of the face and arm corresponds to inferior frontal and temporal localization of the disease. Aphasia, superior quadrant visual field defects, and paresis suggest the same localization. The conditions of some patients progress very rapidly from stupor to coma to death, with few clinical clues suggesting localization.

Examination of CSF often shows an increase in pressure and mononuclear cell pleocytosis (10–1,000/mL), but early in the disease, there may be no cells or a significant number of neutrophils. RBCs are frequently present; however, their presence does not clearly indicate herpetic encephalitis, nor does their absence exclude it. The protein level in the CSF is elevated, but the sugar content is usually normal or only slightly lowered.

An electroencephalogram may show only diffuse slowing of brain waves, but often unilateral or bilateral periodic discharges in the temporal lobes suggest localization. For some patients, characteristic slow-wave complexes are seen at regular intervals of two to three per second; these complexes are highly characteristic of herpes simplex virus encephalitis. Abnormalities on CTs tend to appear later in the disease, and the major finding is a low-density abnormality in one or both temporal lobes. MRI with enhancement demonstrates lesions earlier and is superior to CT in localizing these lesions to the orbital-frontal and temporal lobes.

Cerebral biopsy with virus isolation has been the gold standard for diagnosis; the specificity of this diagnostic technique is 100%. Recently, PCR analysis for herpes simplex virus DNA has become available in many laboratories. If done with optimal techniques in an experienced laboratory, the specificity of PCR analysis of CSF is 100%, and the sensitivity is 75%–98% in different studies. False-positive results still plague some diagnostic laboratories. Isolation of virus or detection of DNA in specimens from nonneural sites has a very low specificity. Attempts to detect viral antigen in spinal fluid have shown poor sensitivity. Because herpetic encephalitis is a reactivation or reinfection, IgM antibodies are usually not present. Responses of IgG antibodies in spinal fluid occur too late to be of value in making therapeutic decisions.

Treatment of herpes simplex virus encephalitis includes supportive care that was mentioned above for arbovirus encephalitis. Temporal lobe swelling can encroach on the perimesencephalic cistern with lateral shift and compression of the brain stem. Therapy with intravenous steroids is usually employed in hopes of decreasing this swelling. No adverse effect of steroids on the infectious process has been documented, but the value of steroids in this crisis is questionable. Historically, surgical decompression of temporal lobes was used, and it must be kept in mind that most studies validating the use of antiviral therapy employed temporal lobe biopsy as a criterion for study entry. Thus, the efficacy shown in these studies may have resulted from drug therapy plus surgical decompression.

The best antiviral drug now available is acyclovir; therapy with this agent reduces the mortality rate to 19% 6 months after treatment, compared with 50% among those patients treated with vidarabine and >70% among those patients treated with placebo in prior studies. The patient’s age and level of consciousness at the beginning of therapy are important prognostic factors. For example, in an initial study [12], patients younger than 30 years of age who had a Glasgow coma score of >6 all survived, and eight of 13 had only mild or no long-term morbidity. In contrast, all three patients older than 30 years of age who had a Glasgow coma score of ≤6 died or had severe sequelae.

It is also important to note that of biopsies of >200 patients in the acyclovir study, only 33 were positive, compared with 50% of biopsies in a prior comparison of vidarabine and placebo [13]. In an attempt to consider the diagnosis earlier, the threshold of suspicion was lowered, and the accuracy of diagnosis was reduced.

Even with extensive clinical experience, one cannot anticipate an accuracy of >50% in the diagnosis of herpes simplex virus encephalitis by clinical examination, spinal fluid examination, and imaging early in the course of the disease. Although it is the only encephalitis that characteristically presents with signs and symptoms suggesting a temporal lobe localization, herpes simplex virus causes only about 10% of the cases of viral encephalitis. Enteroviruses, arboviruses, and other infectious agents may by chance provoke signs pointing to the temporal lobe. Nonviral illnesses, many of which are treatable, also may be localized to the temporal lobe and mimic herpes simplex virus encephalitis [14].

Patients who survive herpetic encephalitis may have severe debilitating sequelae, including major motor and sensory deficits, aphasia, and often an amnestic syndrome (Korsakoff’s psychosis). Even after early acyclovir treatment and good re-
Table 4. Viruses associated with postinfectious encephalomyelitis.

<table>
<thead>
<tr>
<th>Virus(es)</th>
<th>Frequency</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinia virus</td>
<td>1:60 to 1:100,000</td>
<td>Eliminated by eradication of smallpox</td>
</tr>
<tr>
<td>Measles virus</td>
<td>1:1,000</td>
<td>Almost eliminated by introduction of vaccine</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
<td>1:4,000</td>
<td>Largely associated with acute cerebellar ataxia</td>
</tr>
<tr>
<td>Rubella virus</td>
<td>&lt;1:20,000</td>
<td>Reduced 99% in the United States by vaccine</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>Rare</td>
<td>In early weeks of infectious mononucleosis</td>
</tr>
<tr>
<td>Mumps virus</td>
<td>Rare</td>
<td>Reduced 99% in the United States by vaccine</td>
</tr>
<tr>
<td>Influenza viruses</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>Nonspecific</td>
<td>Rare</td>
<td></td>
</tr>
</tbody>
</table>

* Occurred with variola virus infection (smallpox), but the frequency was never accurately determined.

† Although acute demyelination has been reported in a few fatal cases, mumps virus meningitis and/or encephalitis usually represents direct infection of neural cells.

covery of normal performance on standard clinical mental status tests, more detailed clinical cognitive testing may show mild dysnomia and impaired new learning.

Relapse of encephalitis is occasionally seen 1 week to 3 months after initial improvement and completion of 10–14 days of acyclovir therapy. The infection may be chronic with enhancement of the local and adjacent cortical ribbon. Virus can be reisolated from specimens obtained during repeated biopsy, and thus far these isolates have not proved to be acyclovir-resistant mutants. Retreatment with acyclovir or acyclovir and vidarabine is indicated in these cases.

Postinfectious Encephalomyelitis

A variety of names have been used for this clinical pathologic syndrome. Postinfectious encephalomyelitis, parainfectious encephalomyelitis, postexanthematous encephalomyelitis, postvaccinal encephalomyelitis, and postinfluenzal encephalomyelitis have been used to describe its clinical setting. Acute disseminated encephalomyelitis, perivascular myelinolysis, perivenular encephalitis, and acute demyelinating encephalomyelitis have been coined to describe its pathological features. Allergic encephalomyelitis, immune-mediated encephalomyelitis, hyperergic encephalomyelitis, and disseminated vasculomyelopathy have been proposed to correspond with presumed pathogenetic mechanisms.

The incidence of postinfectious encephalomyelitis is unknown, but it now probably accounts for between 10% and 15% of cases of acute encephalitis in the United States. In the past, vaccinia and measles were the commonest causes of this infection; vaccinia was eliminated by the lack of need for a vaccine, and measles was virtually eliminated by the introduction of a vaccine. It is interesting that postinfectious encephalomyelitis also has occurred with variola virus infection (smallpox), but postinfectious encephalomyelitis has not been pathologically documented after immunization with attenuated measles virus vaccine. The highly variable rates of disease after vaccinia are in contrast to the very consistent rates of disease after measles (table 4).

The pathological changes in patients with postinfectious encephalomyelitis are remarkably similar to those in patients with acute encephalomyelitis following immunization against rabies with vaccines prepared in CNS tissues. CNS tissue alone can induce similar demyelination after repeated inoculation into an animal or after inoculation with an adjuvant; this disease is known as experimental allergic or autoimmune encephalomyelitis. Injection of CNS tissue either experimentally or in the form of a brain-derived vaccine produces a cell-mediated autoimmune reaction against a host’s myelin proteins.

What is difficult to understand is how a similar process can be initiated by a viral infection, particularly when the disease follows a variety of different viral infections so that a mechanism of molecular mimicry is probably not a factor. In recent years, measles virus infection has been shown to cause a marked disruption of normal immune regulation. Proliferative responses of lymphocytes in the presence of myelin basic protein are found in up to 15% of patients with measles and in approximately one-half of patients with postmeasles encephalomyelitis [14]. This reaction suggests that viral infection of lymphoid cells may deregulate normal immune responses and release autoimmune responses.

Clinically, many signs and symptoms of postinfectious encephalomyelitis resemble those of acute viral encephalitis. However, there is usually a history of an exanthem or a nonspecific respiratory or gastrointestinal disease for about 5 days to 3 weeks prior to the acute onset of encephalomyelitis. For example, postmeasles encephalomyelitis typically occurs 4–8 days after the rash; the child has defervesced, is feeling well, and is going back to school when headache and fever abruptly return and consciousness is compromised. Seizures and focal neurological signs are frequent. The explosiveness of the symptoms is even greater than that seen in acute viral encephalitis.

Postinfectious complications of some infections are more specific (such as the acute cerebellar ataxia that follows varicella), yet it is assumed on the basis of limited immunologic
studies of autoimmune reactivity that these complications have a similar mode of pathogenesis. The mortality and morbidity rates are very different depending on the different infective agents, but it is also striking how desperately ill children can undergo total or near total recovery.

Examination of the CSF usually shows mild mononuclear cell pleocytosis and elevated protein levels, but the results of this analysis are normal for one-third of these patients. An electroencephalogram usually reveals abnormalities with diffuse slowing of brain waves. Gadolinium-enhanced MRI has proved the most helpful test for differentiating postinfectious encephalomyelitis from viral encephalitis, since there is often very striking enhancement of multifocal white matter lesions. These imaging abnormalities resolve over many months; therefore, these lesions may be obvious and disquieting even after complete clinical recovery.

Prevention already has been highly effective. Indeed, the eradication of smallpox has prevented disease due to vaccinia, and vaccination against measles, mumps, and rubella has decreased the incidence of postinfectious encephalomyelitis further. Once encephalomyelitis has developed, however, there is no known treatment other than supportive care. There is no indication that therapy with hyperimmune γ-globulin is of benefit. Treatment with corticosteroids and adrenocorticotropic hormone is widely used and is anecdotally reported to be effective, but in several studies of sequential patients who did or did not receive therapy with steroids or adrenocorticotropic hormone, no difference was found in clinical course or recovery.

Supportive treatment clearly is important as it is in all forms of encephalitis, including lowering the temperature with antipyretic agents, giving adequate fluids, treating seizures if they develop, reducing intracranial pressure, and using artificial ventilation when necessary. Aggressive supportive therapy is indicated, since patients with both acute viral encephalitis and postinfectious encephalomyelitis can make remarkable recoveries after prolonged periods of profound coma.

References


Suggested Reading

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1. Acute viral encephalitis and postinfectious encephalomyelitis are similar in that they both
   A. are caused by the same viruses
   B. often are associated with a history of respiratory symptoms weeks before
   C. have similar clinical signs
   D. have similar pathological changes
   E. have similar mechanisms of pathogenesis

2. The following viruses cause encephalitis almost exclusively in children except
   A. echoviruses
   B. human herpesvirus 6
   C. adenoviruses
   D. California encephalitis virus
   E. St. Louis encephalitis virus

3. In January acute encephalitis develops in a 20-year-old student in Chicago who has no travel history. Which etiology need not be considered?
   A. Mumps virus
   B. Lymphocytic choriomeningitis virus
   C. St. Louis encephalitis virus
   D. Herpes simplex virus
   E. Rabies virus

4. The arbovirus that causes the most severe cases of encephalitis in the United States is
   A. California encephalitis virus
   B. St. Louis encephalitis virus
   C. western equine encephalitis virus
   D. eastern equine encephalitis virus
   E. Japanese encephalitis virus

5. The arbovirus that has caused the largest epidemics of encephalitis in the United States is
   A. California encephalitis virus
   B. St. Louis encephalitis virus
   C. western equine encephalitis virus
   D. eastern equine encephalitis virus
   E. Japanese encephalitis virus

6. A 40-year-old man has fever, headache, odd behavior, and aphasia. Examination of the spinal fluid shows mild mononuclear cell pleocytosis, and an MRI reveals enhancement in the left temporal lobe that is consistent with herpes simplex virus encephalitis (HSVE).
   A. He has a likelihood of >90% of having HSVE.
   B. If he also had a cold sore, he would be more likely to have HSVE.
   C. He has a 50% chance of having HSVE.
   D. His age makes a diagnosis of HSVE unlikely.
   E. His lack of underlying disease makes HSVE unlikely.

7. A diagnosis of probable HSVE is made on the basis of clinical and imaging findings. Intravenous acyclovir therapy is given for 10 days; the patient's condition improves, but the patient does not fully recover. Follow-up 1 month later shows worsening confusion, and an MRI reveals increasing cortical enhancement.
   A. The original diagnosis was incorrect.
   B. A drug-resistant strain of virus has developed.
   C. Acyclovir may have failed to clear the virus even after a full course of treatment.
   D. Any of the above.
   E. None of the above.

8. The most valuable laboratory test for the diagnosis of postinfectious encephalomyelitis is
   A. a spinal fluid examination
   B. electroencephalography
   C. enhanced MRI
9. The following have been effective in reducing the morbidity and mortality due to postinfectious encephalomyelitis except
A. the use of corticosteroids
B. the elimination of smallpox
C. immunization against measles
D. the inclusion of rubella virus and mumps virus in measles vaccine
E. the improvements in intensive care

10. In August, a 3-year-old child with fever, headache, nuchal rigidity, obtundation, and a generalized seizure also has multiple vesicular blebs on the soft palate and tonsillar fossae. The most likely cause is a(n)
A. mumps virus
B. herpes simplex virus
C. coxsackievirus
D. California encephalitis virus
E. adenovirus