

# ENCEPHALITIS

---

Diana Montoya Melo

4 yo female patient, brought to the ED after having a GTC seizure 30 mins ago, which lasted up to a min.

Mom reports that he has a ho 3 days of fever and runny nose, associated with decreased activity level and 1 day history of lethargy. Mom has been treating the fever at home, and the last dose of Tylenol was given 1 hour ago.

On arrival, VS: T: 37.9, PR: 135/min, RR: 26, BP: 87/59. O2 Sat 100%. Patient is obtunded, tolerates RA, Moist mucous membranes, nasal congestion, pink TM bilaterally, tonsillar erythema, no exudates, oropharynx with few small pustules. LCTAB. Abd:soft, ND, NT. Skin: cap refill prolonged. Small pustules over palms and soles. Neuro: appears obtunded but arouses with painful stimuli. Neurologic exam reveals no focal findings. No neck stiffness, neg meningeal signs

- PMH: unremarkable
- Immunizations UTD

# PARTIAL VS FULL SEPSIS WORKUP?

---

Besides getting a full sepsis workup, what other diagnostic tools should be included:

- a) Brain imaging
- B) CMP
- C) Coags
- C) EEG
- E) all of the above

Besides getting a full sepsis workup, what other diagnostic tools should be included:

- a) Brain imaging
- B) CMP
- C) Coags
- C) EEG
- *E) all of the above*

WHAT ELSE CAN BE  
INCLUDED AS PART OF  
THE WORKUP?

---

## Initial evaluation and management of suspected encephalitis in children older than one month of age

### History

Symptoms: fever; depressed or altered level of consciousness; lethargy; personality change; emotional lability; seizure; ataxia

Travel

Exposure (animals, insects, freshwater swimming, toxins)

Immunizations

Immune status

### Physical findings

Vital signs and general examination

Neurologic examination, particularly for focal findings and GCS

### Laboratory studies

Screening laboratories: CBC; glucose; electrolytes; BUN; creatinine; ammonia; blood pH; blood cultures; LFTs; urinalysis; urine drug screen; save a sample of acute serum

Lumbar puncture: perform emergently, often after neuroimaging if a focal lesion is suspected; obtain opening pressure when clinically feasible; send CSF for cell count/differential, glucose, protein, bacterial culture, HSV PCR, enterovirus PCR; save a sample of CSF

Other laboratory tests to consider: influenza testing during influenza season; tests for toxic metabolic encephalopathy and inborn errors of metabolism (see text); antibody studies for NMDAR and VGKC (see text)

### Ancillary studies

Neuroimaging: MRI preferred, but CT if MRI not promptly available, impractical, or cannot be performed

EEG: as soon as is feasible (for evidence of encephalitis or nonconvulsive seizure)

## Suggested initial laboratory evaluation for children and adolescents with encephalitis

For nonimmunocompromised patients
<b>Blood</b>
Complete blood count with differential count and platelets
Blood culture
Serum electrolytes, glucose, ammonia, blood urea nitrogen, creatinine; blood pH
Serum aminotransferases (alanine aminotransferase, aspartate aminotransferase)
Coagulation studies
Serology for EBV, HIV
Anti-NMDAR and anti-VGKC antibodies if clinically indicated
Acute serum sample (to hold for subsequent serologic testing if necessary)
<b>CSF</b>
Opening pressure (when feasible)
Cell count, differential, protein, glucose, Gram stain, acid fast stain
Bacterial culture; <i>M. tuberculosis</i> culture (if clinically indicated)
PCR: HSV, enterovirus (PCR for other <i>Herpesviridae</i> , WNV, influenza, and other pathogens, as indicated by history and epidemiology)
CSF sample (to hold for subsequent testing)

**Respiratory samples**

Respiratory panel (PCR) (influenza, adenovirus, human metapneumovirus, and respiratory syncytial virus)

Viral culture of respiratory secretions and nasopharynx

Throat swab for HSV, enterovirus

**Stool (or rectal swab)**

Viral culture of stool

Enterovirus PCR

**Urine**

Urinalysis

Urine toxicology screen

**Skin lesions (if present)**

Biopsy for DFA and PCR for *R. rickettsia*

Culture and/or DFA of skin lesions for HSV, VZV, and enteroviruses

**For immunocompromised patients****Above tests, plus:**

Blood: Serum cryptococcal antigen, *Toxoplasma gondii* IgG

CSF: Cryptococcal antigen, Histoplasma antigen; PCR for CMV, CJ, HHV6, WNV

Urine: Histoplasma antigen

CSF results are back, which of the following would you expect to find in this patient?

- A) WBC: 328, L: 18% N: 82%, RBC:0, prot: 250, Glucose: 38
- B) WBC: 128, L: 78% N: 22, RBC:0, prot: 140, Glucose: 68
- C) WBC: 328, L: 88% N: 12, RBC:0, prot: 300, Glucose: 10
- D) none of the above

# CSF results are back, which of the following would you expect to find in this patient?

- A) WBC: 328, L: 18% N: 82%, RBC:0, prot: 250, Glucose: 38
- B) WBC: 128, L: 78% N: 22, RBC:0, prot: 140, Glucose: 68
- C) WBC: 328, L: 88% N: 12, RBC:0, prot: 300, Glucose: 10
- D) none of the above

## Cerebrospinal fluid analysis in central nervous system infection

	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell count (cells/microL)		
	<10*	10-45*	>250 <sup>Δ</sup>	50-250 <sup>◇</sup>	>1000	100-1000	5-100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Lyme disease Neurosyphilis	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Early bacterial meningitis Viral meningitis Neurosyphilis TB meningitis
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections (such as mumps and LCMV)	TB meningitis		Some cases of mumps and LCMV	Encephalitis	Encephalitis

LCMV: lymphocytic choriomeningitis virus; TB: tuberculosis.

\* <0.6 mmol/L

• 0.6-2.5 mmol/L

Δ >2.5 g/L

◇ 0.5-2.5 g/L

# CSF AND VIRAL ENCEPHALITIS

- The CSF indices in viral encephalitis are similar to those in viral meningitis and meningoencephalitis and may overlap with those of bacterial meningitis
- 3 to 5%, CSF findings are completely normal
- CSF findings in viral encephalitis are as follows:
  - CSF pleocytosis. WBC typically ranges from 0 to 500 cells/microL with a lymphocytic predominance; however, a predominance of neutrophils can be seen during the first 24 to 48 hours of infection.
  - RBC are usually absent (except in traumatic tap), but their presence can indicate HSV encephalitis, La Crosse virus encephalitis, or other necrotizing encephalitides (eg, Eastern equine encephalitis, amebic encephalitis)
  - Protein is usually slightly elevated (generally <150 mg/dL)
  - Glucose is usually normal and >50 percent of blood value

## Possible infectious etiologies of meningoenceph

Viruses
<b>Herpes simplex type 1</b>
<b>Herpes simplex type 2</b>
<b>Enteroviruses</b> (echovirus, parechovirus, coxsackievirus A and B, poliovirus, and the numbered enteroviruses)
<b>Varicella zoster virus</b>
<b>Epstein-Barr virus</b>
<b>Cytomegalovirus</b>
<b>Human herpesvirus 6</b>
Human immunodeficiency virus
<b>Arboviruses</b> (LaCrosse virus, West Nile virus, <b>St. Louis encephalitis virus</b> , Eastern and Western equine encephalitis virus, Japanese encephalitis virus)
Rabies virus
Influenza virus
Measles virus
Mumps virus
Rubella virus
Murray Valley encephalitis virus
Nipah virus
Hendra virus
Tick-borne encephalitis virus
Powassan virus
Herpes B virus
Hepatitis E virus
Creutzfeldt-Jakob disease

Bacteria
<i>Mycoplasma pneumoniae</i>
<i>Listeria monocytogenes</i>
<i>Mycobacterium tuberculosis</i>
<i>Treponema pallidum</i>
<i>Bartonella henselae</i> (cat scratch disease)
<i>Bartonella quintana</i> ("trench fever")
<i>Borrelia burgdorferi</i> (Lyme disease)
<i>Coxiella burnetii</i> (Q fever)
<i>Rickettsia rickettsii</i> (Rocky Mountain spotted fever)
<i>Ehrlichia chaffeensis</i> (human monocytotropic ehrlichiosis)
<i>Anaplasma phagocytophilum</i> (human granulocytotropic ehrlichiosis)
<i>Tropheryma whipplei</i>

Fungi
<i>Cryptococcus neoformans</i>
<i>Coccidioides species</i>
<i>Histoplasma capsulatum</i>
Parasites
<i>Toxoplasma gondii</i>
<i>Plasmodium falciparum</i>
<i>Naegleria fowleri</i>
<i>Acanthamoeba spp</i>
<i>Balamuthia mandrillaris</i>
<i>Taenia solium</i> (cysticercosis)
<i>Baylisascaris procyonis</i>
<i>Gnathostoma spinigerum</i>
<i>Trypanosoma brucei gambiense</i>

# What would be the best empiric therapy in this case:

- A) Vancomycin
- B) Acyclovir
- C) Vancomycin + Ceftriaxone
- D) Doxycycline
- E) Bactrim

What would be the best empiric therapy in this case:

- A) Vancomycin
- **B) *Acyclovir***
- C) Vancomycin + Ceftriaxone
- D) Doxycycline
- E) Bactrim

# EMPIRIC THERAPY OF VIRAL ENCEPHALITIS

- Empiric acyclovir —prompt initiation of intravenous (IV) [acyclovir](#) for children (beyond the neonatal period) and adolescents with suspected encephalitis
- Dose
  - >28 days to <3 months – 20 mg/kg per dose every eight hours
  - ≥3 months to <12 years – 10 to 15 mg/kg per dose every eight hours
  - ≥12 years – 10 mg/kg per dose every eight hours
- Duration
  - If HSV is confirmed or probable, should be continued for 21 days
  - LP should be performed near the end of acyclovir treatment to ensure that HSV PCR is negative; acyclovir therapy should be continued if CSF HSV PCR remains positive.
- The decision to continue [acyclovir](#) therapy for patients in whom HSV PCR is negative must be individualized.
- HSV PCR in the CSF can be negative during the first few days of the illness

# EMPIRIC THERAPY OF VIRAL ENCEPHALITIS

- 2012 shortage of IV acyclovir — in agreement with the AAP Committee on ID
  - IV [ganciclovir](#) 6 mg/kg every 12 hours for patients  $\leq 90$  days of age and 5 mg/kg every 12 hours for patients  $> 90$  days of age
  - If ganciclovir cannot be given, IV [foscarnet](#) 60 mg/kg every 12 hours
- Empiric antibiotics — If clinically and/or epidemiologically indicated, empiric treatment should be provided for bacterial meningitis, rickettsial infection, and ehrlichiosis, pending the results of cultures and other diagnostic studies

## Suggested initial therapy for agents that cause encephalitis

Agent	Specific therapy
<b>ADEM</b>	Corticosteroids
<b>Bacteria</b>	
<i>Listeria monocytogenes</i>	Ampicillin plus gentamicin; trimethoprim-sulfamethoxazole
<i>Tropheryma whipplei</i>	Ceftioxone, followed by either trimethoprim-sulfamethoxazole or cefime
<b>Fungi</b>	
<i>Coccidioides</i>	Fluconazole, itraconazole, voriconazole, amphotericin B
<i>Cryptococcus neoformans</i>	Amphotericin B plus flucytosine
<i>Histoplasma capsulatum</i>	Liposomal amphotericin B
<b>Helminths</b>	
<i>Baylisascaris procyonis</i>	Albendazole plus diethylcarbamazine
<i>Gnathostoma</i>	Albendazole or ivermectin
<i>Taenia solium</i> (cysticercosis)	Albendazole and corticosteroids
<b>Mycobacteria</b>	
<i>Mycobacterium tuberculosis</i>	4 drug regimen; consider addition of corticosteroid
<b>Protozoa</b>	
<i>Acanthamoeba</i>	Trimethoprim-sulfamethoxazole plus rifampin plus ketoconazole
<i>Balamuthia mandrillaris</i>	Pentamidine plus macrolide and fluconazole and sulfadiazine and flucytosine and phenothiazine
<i>Naegleria fowleri</i>	Amphotericin B and rifampin
<i>Plasmodium falciparum</i>	Quinine, quinidine or artemether
<i>Toxoplasma gondii</i>	Pyrimethamine plus sulfadiazine or clindamycin
<i>Trypanosoma brucei gambiense</i>	Eflornithine
<i>Trypanosoma brucei rhodesiense</i>	Melarsoprol

<b>Rickettsioses and ehrlichioses</b>	
<i>Anaplasma phagocytophilum</i>	Doxycycline
<i>Ehrlichia chafeensis</i>	Doxycycline
<i>Rickettsia rickettsii</i>	Doxycycline
<b>Spirochetes</b>	
<i>Borrelia burgdorferi</i>	Ceftriaxone, cefotaxime
<i>Treponema pallidum</i>	Penicillin G
<b>Viruses</b>	
Cytomegalovirus	Ganciclovir plus foscarnet
Epstein-Barr	No specific treatment
Herpes B virus	Valgancyclovir
Herpes simplex	Acyclovir
Human herpesvirus 6	Gancyclovir or foscarnet
Human immunodeficiency virus	HAART
JC virus	Reversal of immunosuppression if possible
Measles	Ribavirin
Nipah	Ribavirin
St. Louis encephalitis	Interferon-2 alpha
Varicella-zoster	Acyclovir
West Nile	No specific treatment

# REFERENCES

- **Acute viral encephalitis in children and adolescents: Clinical manifestations and diagnosis.** edited by Denise S. Basow, published by UpToDate in Waltham, MA.
- **Acute viral encephalitis in children and adolescents: Treatment and prevention.** edited by Denise S. Basow, published by UpToDate in Waltham, MA.