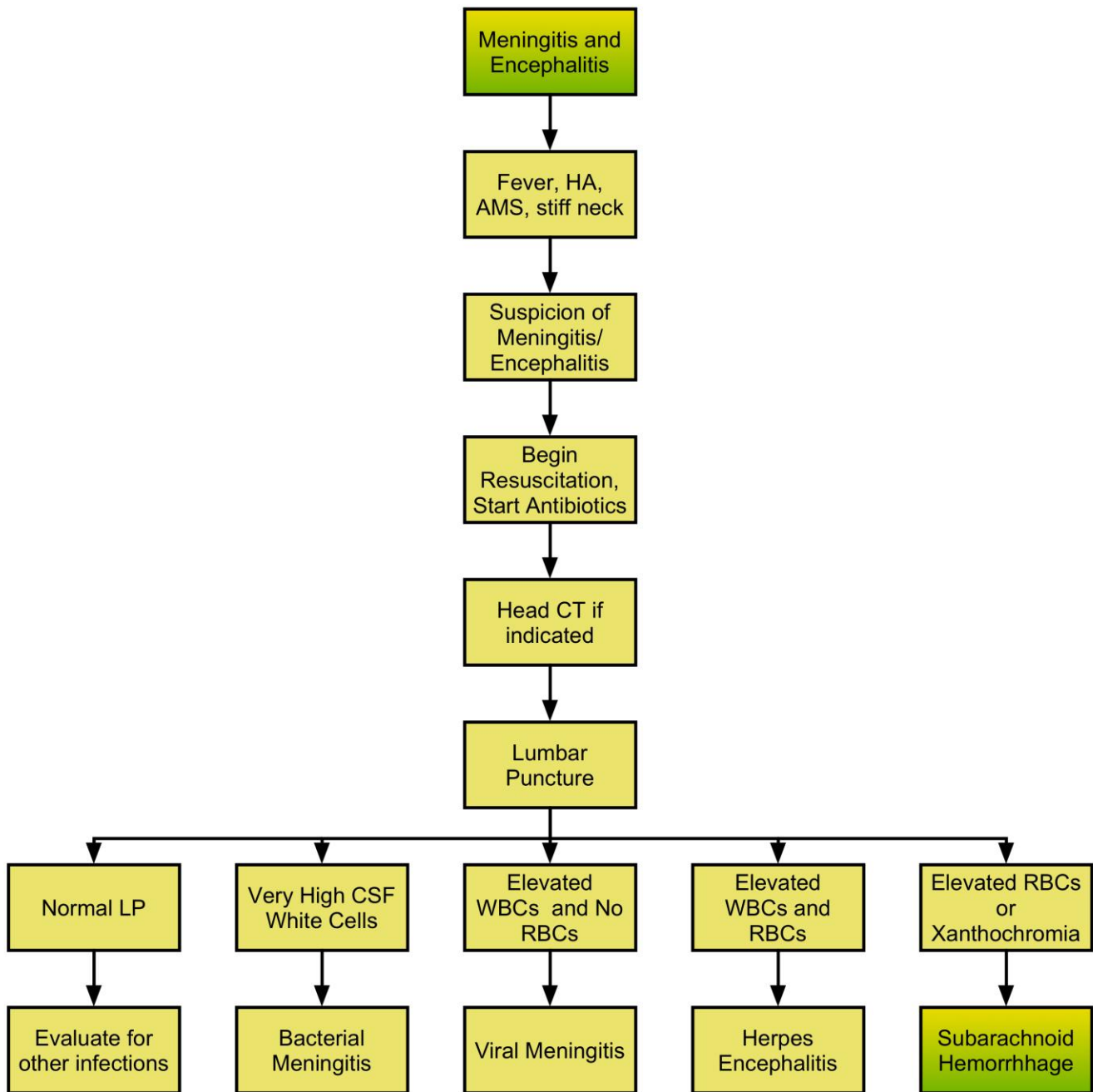


Emergency Neurological Life Support

Meningitis and Encephalitis

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[Checklist & Communication](#)

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Checklist

- Vital signs, history, examination
- IV access, draw labs, blood cultures and lactate
- Labs: CBC, platelets, PT/PTT, chemistries, blood cultures, lactate
- IV fluids, treat shock
- Immediate administration of dexamethasone followed by appropriate antibiotics for presumptive bacterial meningitis
- Consider acyclovir (if HSV a possibility)
- Obtain head CT if altered mental status or focal neurological findings.
- Perform lumbar puncture (after head CT results available, if CT necessary)
- If meningococcus, remember exposure prophylaxis

Communication

- Presenting signs, symptoms, vital signs on arrival
- Pertinent past medical history and history of the present illness
- Relevant laboratory results including white blood cell count, bicarbonate level, lactate level, and renal function
- Whether head CT was obtained and results
- Antibiotics administered and time started
- IV fluid given
- Results of LP, including opening pressure
- Current vital signs
- Ongoing concerns, active issues, outstanding studies/tests
- Last physical and neurological exam finding prior to transfer
- Need for exposure prophylaxis if meningococcus

Bacterial Meningitis

Likely bacterial meningitis

- Continue antibiotics
- Stop acyclovir
- Continue dexamethasone
- Adjust antibiotics based on finalized gram stain and culture results and sensitivities

In addition to antibiotics and dexamethasone, supportive care and management of other systems is important in patients with bacterial meningitis. Some patients may have a concomitant bloodstream infection with the offending pathogen and may require early goal directed therapy for sepsis. If the lumbar puncture demonstrates elevated intracranial pressure, the patients should be monitored closely for signs of persistent increased ICP. There is no evidence that intracranial pressure monitoring devices are safe or helpful in this patient population and the risks, including the potential of a superinfection with the foreign body, must be weighed with the potential benefits. Likewise, no evidence exists as to the appropriate treatment of increased ICP. Hyperventilation should probably be avoided as these patients already may suffer from some degree of decrease cerebral vessel diameter due to vasculopathy. Mannitol or hypertonic saline may be reasonable considerations.

Age factors:

- Children and young adults with suspected bacterial meningitis are at risk for *Haemophilus influenzae* (if not vaccinated), *Neisseria meningitidis*, and *Streptococcus pneumoniae*. As such, they should be started on a 3rd generation cephalosporin and vancomycin at doses appropriate for CNS penetration
- Middle aged adults are at highest risk for *Streptococcus pneumoniae*. As such they should be started on a 3rd generation cephalosporin and vancomycin at doses appropriate for CNS penetration. Vancomycin can be used alone in patients with a severe penicillin allergy.
- The elderly and immunosuppressed are at risk for *Streptococcus pneumoniae* and *Listeria monocytogenes*. As such, they should be started on Ampicillin, a 3rd generation cephalosporin and vancomycin at doses appropriate for CNS penetration. Vancomycin and trimethoprim-sulfamethoxazole can be used in patients with a severe penicillin allergy.

Begin Resuscitation, Start Antibiotics

Empirical treatment

If the patient meets SIRS criteria (hypotension, fever) an initial fluid bolus of 20-30 ml/kg of crystalloid solution should be immediately infused over 20-30 minutes and the patient's vital signs, mental status, and airway should be reassessed every 5 min during this phase of treatment. If IV access cannot be obtained within a few minutes of presentation, interosseous access should be placed.

There is evidence for the use of dexamethasone in bacterial meningitis, particularly in *Streptococcus pneumoniae* meningitis. Unless there is clear clinical evidence that the cause is NOT *Streptococcus pneumoniae*, dexamethasone is recommended.

Give:

- dexamethasone 10 mg IV now. Ideally the steroid should be given 15 minutes prior to the start of antibiotic therapy, but should not delay the administration of IV antibiotics.

Next:

Administer IV antibiotics as soon as possible. Select the appropriate antibiotics/antivirals based on a) the course of the suspected CNS infection, b) age of the patient, and c) other infectious risk factors

- Children < 3 months are at risk for group B streptococci, *Escherichia coli*, *Listeria monocytogenes*, *Streptococcus pneumoniae*, and *Neisseria meningitidis*. Use IV ampicillin, gentamycin, and cefotaxime.
- In older infants, children, and adolescents, the causes are typically *Streptococcus pneumoniae* (which may be penicillin resistant), *Neisseria meningitidis* and *Haemophilus influenzae*. Administer vancomycin plus either cefotaxime or ceftriaxone. The empiric antibiotic regimen should be broadened in infants and children with immune deficiency, recent neuro- surgery, penetrating head trauma, or other anatomic defects
- Young adults with suspected bacterial meningitis are at risk for *Haemophilus influenzae* (if not vaccinated), *Neisseria meningitidis*, and *Streptococcus pneumoniae*. As such, they should be started on a 3rd generation cephalosporin and vancomycin at doses appropriate for CNS penetration.
- Middle aged adults are at highest risk for *Streptococcus pneumoniae*. As such they should be started on a 3rd generation cephalosporin and vancomycin at doses appropriate for CNS penetration. Vancomycin can be used alone in patients with a severe penicillin allergy.

- The elderly and immunosuppressed are at risk for *Streptococcus pneumoniae* and *Listeria monocytogenes*. As such they should be started on ampicillin, a 3rd generation cephalosporin and vancomycin at doses appropriate for CNS penetration. Vancomycin and trimethoprim-sulfamethoxazole can be used in patients with a severe penicillin allergy.
- For suspected CNS infections that evolve over days consider viral encephalitis, particularly Herpes Simplex encephalitis: Treatment should begin with acyclovir at 10mg/kg every 8 hours. IV hydration should be sufficient to achieve normovolemia. This avoids the complication of acyclovir associated renal failure.
- For suspected CNS infections that evolve over days in an immunosuppressed patient, consider fungal meningitis. If there is a high index of suspicion for fungal meningitis, such as prior history of the disease or systemic fungal infections, and the patient is progressing rapidly, empiric Amphotericin B can be considered.



Elevated RBCs and WBCs

Consider herpes encephalitis

If the following is true:

- Elevated RBC
- WBCs in the hundreds
- Glucose greater than two-thirds serum glucose, or sometimes lower
- Protein < 50 mg/dL or elevated
- No organisms on gram stain

Then, the patient may have herpes encephalitis. The presence of seizures is also compatible with this diagnosis.



Elevated RBCs no WBCs

Likely SAH

If the following is true:

- Elevated RBC
- WBC < 5
- Glucose greater than two-thirds serum glucose
- Protein < 50 mg/dl
- No organisms on gram stain
- Xanthochromia

Then, the patient likely has a subarachnoid hemorrhage that was not detected on the CT scan. Xanthochromia may be absent if the LP was done within the first few hours of headache onset (and so one typically only sees RBCs).



Elevated WBC no RBCs

Probably viral meningitis

Mild elevation in WBCs without RBCs is suggestive of viral meningitis or viral (not herpes) encephalitis. If the following is true:

- Normal RBC
- WBCs 10-100s
- Glucose greater than two-thirds serum glucose
- Protein < 50 mg/dl
- No organisms seen on gram stain

Then the patient likely has a viral meningitis or viral (not herpes) encephalitis. Seroconversion of HIV should also be considered.



Evaluate for Other Infections

A normal LP is highly predictive of absent bacterial infection of the meninges. Pure encephalitis, and perhaps early Herpes Simplex encephalitis can have a normal lumbar puncture since the inflammation is within the brain parenchyma and may not communicate with the subarachnoid space. However, given the constellation of fever, leukocytosis and altered mental status, it is most likely the patient is suffering a depressed mental status from systemic inflammation rather than direct involvement of the central nervous system itself.

This is termed “metabolic encephalopathy” and is common in patients with preexisting brain disorders or atrophy. Once the true infection is found and treated (urinary tract, lungs, sepsis) the patient’s mental status improves to baseline. Prolonged poor mental status after systemic signs of treatment appear (defervescence, falling WBC count) may prompt additional investigation as to cause.



Herpes Encephalitis

Empirical treatment and diagnosis

- Continue acyclovir 10 mg/kg every 8 hours IV
- Send CSF for HSV PCR
- Continue other antibiotics until cultures/PCR results back
- MRI of the brain
- Achieve and maintain euvolemia to prevent acyclovir associated renal failure



Immunocompromised Patient

Confirmed or suspected

Immunocompromised patients, or patients suspected of being immunocompromised, may present with less classic signs of meningitis or encephalitis.

- For such patients, lower your pretest probability for these diagnoses and err on the side of a more complete work-up including LP and brain imaging.



Head CT if Indicated

In patients where there is a moderate to high suspicion of CNS infection and the lumbar puncture has not yet been done, parenteral anti-infectives **SHOULD NOT BE DELAYED** while waiting for a CT scan. CSF sterilization occurs only after 4-6 hours in the most sensitive organisms, and patient outcomes are linked to earlier antibiotic treatment. Therefore presumptive treatment in a patient who later has a normal LP is far better than waiting to give antibiotics for the CT, then LP results confirm severe bacterial meningitis.

A head CT is **NOT** always required prior to an LP. The logic of performing a head CT prior to LP is to prevent cerebral herniation from an intracranial mass lesion. In this setting, lowering lumbar pressure could cause downward herniation of the brain. Therefore, a head CT should be performed prior to the LP when the presentation includes papilledema/loss of retinal venous pulsations or focal neurological signs, or in patients with known mass lesion. A normal head CT does not protect the patient from a herniation syndrome after the LP as diffuse brain swelling can occur rapidly from the underlying infection.

In a patient with no focal findings, and no papilledema, LP prior to head imaging is likely safe. However, in most patients who have a clinical presentation consistent with meningitis or encephalitis, there will be enough uncertainty as to the exact intracranial process, so it is incumbent on the examiner to perform a CT prior to the LP.

If the head CT shows a mass lesion or other condition that adequately explains the patient's mental status, then that cause should be diagnostically evaluated and LP avoided.



Lumbar Puncture

Rapid assessment of spinal fluid

An LP is essential for both establishing a diagnosis and tailoring therapy.

The opening pressure should be measured with a manometer prior to the collection of CSF in the lateral decubitus position. CSF should be collected in (at least) 4 tubes.

- Send tube 1 and tube 4 for red and white cell counts
- Send tube 2 for protein and glucose
- Send tube 3 for gram stain and culture (and India ink if fungal infection is suspected).

If there is a suspicion for Herpes encephalitis, a small amount of CSF from tube 2 or 3 should be sent for Herpes PCR. Some laboratories perform bacterial antigen assays which may be useful. Additional laboratory tests that may be performed by some centers include bacterial PCR (particularly for Mycobacterium), enterovirus PCR, fungal antigens and viral culture.

 Flowchart

Normal LP

Rules out meningitis and encephalitis

An LP is considered normal if

- No RBCs
- WBCs < 5
- Glucose greater than two-thirds serum glucose
- Protein < 50 mg/dl
- No organisms seen on gram stain

If all of the above are true, meningitis is ruled out. However, a normal LP is consistent with non-herpetic encephalitis but other than medical support there is no emergency intervention that is necessary. Evaluation for systemic infection should also ensue.



Subarachnoid Hemorrhage

Management of SAH

Review the head CT to look for subarachnoid blood (this can be absent after SAH approximately 5% of the time, particularly with small hemorrhages and imaging obtained long after symptom onset).

See the ENLS protocol [Subarachnoid Hemorrhage](#).

Suspected Meningitis or Encephalitis

Headache and altered mental status

Patients that have a hyper-acute (hours) and acute (hours to days) onset of headache and altered mental status should be considered to have meningitis or encephalitis. Additional signs of meningismus, fever, new rash, focal neurological findings or new onset seizure significantly increase the suspicion of CNS infection.

Infants often have non-specific manifestations of CNS infection such as fever, hypothermia, lethargy, irritability, respiratory distress, poor feeding, vomiting, or seizures. In older children, clinical manifestations include fever, headache, photophobia, nausea, vomiting, and decreased mental status.

As with all acute medical and neurological events, the basics of ABC (airway, breathing and circulation) should be evaluated early in the Emergency Department course. Patients with altered mental status are at high risk for airway compromise and should be monitored closely for needing intubation. Likewise, patients with bacterial meningitis are at risk for lung or bloodstream infections with the same pathogen, and as such, vital signs and hemodynamics need to be monitored closely to diagnose sepsis.

Meningitis is defined as inflammation of the meninges (and will have an abnormal LP) while encephalitis is defined as inflammation of the brain (and the LP is usually normal). If both are inflamed, the patient has meningoencephalitis. Meningitis causes fever, meningismus (flexion limitation of neck when fully supine), and pain (head and/or neck) but other than depressing a patient's mental status, does not affect any cortical function. Encephalitis on the other hand typically causes cortical disturbances (seizures, aphasia, hemiparesis, etc.). In pure encephalitis, the spinal fluid is free of white cells but protein may be elevated. Once white cells are found in the spinal fluid, some form of meningitis is also present.

The two conditions that are most important to recognize in the first hour are bacterial meningitis and herpes encephalitis as these diseases have specific treatments that can improve patient outcome if administered quickly.

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Suspicion for CNS Infection

Moderate to high suspicion

Based on the previous findings above, clinical suspicion of meningitis or encephalitis is increased and one needs to rapidly treat presumptively and ultimately diagnose the cause. If the patient has meningitis they are at high risk of sepsis as well so both antibiotics and fluid resuscitation becomes paramount.

- Place at least 1 large bore (18 gauge) IV
- Draw blood cultures, CBC, basic metabolic panel, and lactate quickly

Peripheral white count

A peripheral leukocytosis is often present in patients with meningitis. In cases of *Neisseria* meningitis one may actually see bacteria on the gram stain of whole blood. If the white count is not elevated, then bacterial meningitis is less likely. Depending on body temperature, you may stop here and work up non-infections causes of headache and altered mental status with the same caveats mentioned in "Fever, HA, AMS, Stiff Neck". For example, the patient may still have a viral meningitis without a leukocytosis so LP may still be indicated to establish a diagnosis.

Based on the presence of fever and elevated white count, along with headache and altered mental status, one should have moderate to high suspicion for meningitis or encephalitis.

Fever, Headache, Altered Mental Status, Stiff Neck

Classic symptoms and signs of meningitis

Fever

Measuring oral temperature is adequate. Both fever (temperature $> 38^{\circ}\text{C}$) or hypothermia (temperature $< 35^{\circ}\text{C}$) are compatible with CNS infection. If the patient is euthermic, the pretest probability of bacterial meningitis or HSV encephalitis is decreased. However, newly immunocompromised patients, patients with viral meningitis, and even a rare patient with bacterial meningitis may present euthermic. Depending on other signs and symptoms, it may be appropriate to stop here and work-up other causes of headache.

Headache

The presence of a new, never experienced headache is a significant symptom that needs work-up on its own merits. If the headache is sudden in onset (i.e. a thunderclap headache within seconds) this suggests subarachnoid hemorrhage (SAH). Patients with SAH can have fever because blood in the meninges causes a chemical meningitis. If the headache is typical of the patient's usual headache, one should not completely dismiss this symptom's importance as meningitis and encephalitis will cause exacerbation of a pre-existing headache disorder. Lastly, it is quite uncommon to have meningitis without headache or neck pain, but less uncommon in encephalitis.

Altered Mental Status

CNS infections typically depress the level of consciousness (see the ENLS protocol [Coma](#)). Infants may be lethargic, stop eating, and become irritable. Adults typically become somnolent then stuporous. Delirium is common with the chief objective sign of inattentiveness (can't repeat back serial digits). Sepsis can compound the mental status if significant hypotension is present. Elderly patients or patients with pre-existing neurological conditions may become agitated and combative.

Stiff Neck/Meningismus

Meningitis causes reflex contraction of the spinea erector muscles causing limitation in passive neck flexion (meningismus). Patient may complain of neck stiffness or pain, but many do not, so this symptom has poor negative predictive value. To test for the sign of meningismus, place the patient fully supine (completely flatten the bed and remove the pillow), then rotate the head on neck. You should feel no resistance to rotation if the patient is fully relaxed. Then, ask the patient to not resist, place you hand under there head, and slowly flex the head on the neck and see if you can fully flex the neck so that the chin touches the manubrium. If it does, meningismus is absent. If there is a limitation, it typically occurs at a specific degree of flexion and beyond. Measure the distance from the chin to the chest with your fingers and report the degree of flexion limitation as the number of finger breadths you can place in-between. If the patient resists flexion to all degrees, especially if there is resistance to head rotation,

meningismus may be present but this finding is less specific. Do not test for neck flexion limitation if the patient is standing or sitting as this produces false negatives; the patient must be fully supine.



Very High WBCs

WBCs > 100-1000

Marked elevation in WBCs without RBCs is highly suggestive of bacterial meningitis. So, if the following is true:

- No RBC
- WBCs 100-1000 or higher
- Glucose less than two-thirds serum glucose, but rarely normal
- Protein > 50 mg/dl
- Organisms seen on gram stain

Then, the patient likely has bacterial meningitis.



Viral meningitis or Viral (non Herpes) Encephalitis

Treatment

Treatment of viral meningitis or viral (non herpes) encephalitis:

- Discontinue acyclovir and antibiotics
- Discontinue dexamethasone
- Treat headache
- For West Nile Virus, there is risk of respiratory decompensation from spinal cord involvement so admission to the ICU for observation may be appropriate