Emergency Neurological Life Support Meningitis and Encephalitis Protocol Version 5.0

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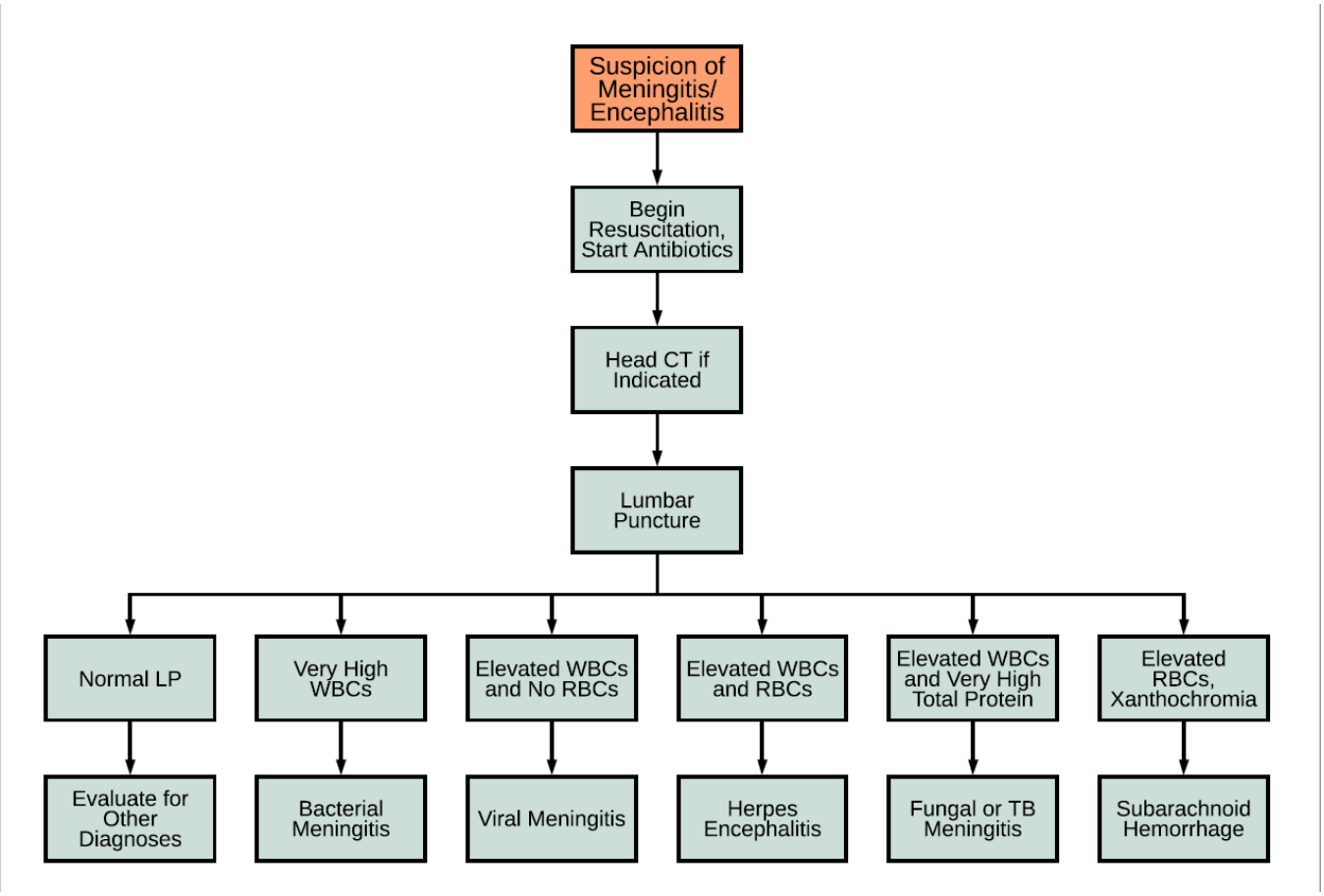
Meningitis and Encephalitis Algorithm



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Suspicion of Meningitis or Encephalitis

Fever, headache, altered mental status, stiff neck

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.

<u>Fever</u>

Measuring oral temperature is adequate. Both fever (temperature > 38°C) or hypothermia (temperature < 35°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.

<u>Headache</u>

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). Neonates may be lethargic, stop eating, and become irritable, have pale or marble skin and hypo or hypertonia. As an individual ages, children may have symptoms more defined than a neonate such as headache, nausea, vomiting, seizures. Adults typically become somnolent then stuporous. Adults may also have more specific signs such as neck stiffness and fever. 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 erector spinae 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 their 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.

Begin Resuscitation, Start Antibiotics

Empirical treatment

If the patient meets SIRS criteria (hypotension, fever), an initial fluid bolus of 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. Antibiotics should be given concomitantly with IV fluids, or immediately after starting IV fluids, and should never be delayed.

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 < 2 months are at risk for group B *streptococci* (GBS), *Escherichia coli*, *Listeria monocytogenes, Streptococcus pneumonia, Haemophilus influenzae and Neisseria meningitidis*. Use IV ampicillin, gentamycin, and cefotaxime.
- In older infants (2 to 23 months), children, and adolescents, the causes are typically *Streptococcus pneumoniae* (which may be penicillin resistant), *Neisseria meningitides,* and *Haemophilus influenzae*. In the younger patients in this group, GBS may still occur. Administer vancomycin plus either cefotaxime or ceftriaxone. The empiric antibiotic regimen should be broadened in infants and children with immune deficiency, recent neurosurgery, 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. (Vancomycin plus Moxifloxacin or levofloxacin or Meropenem can be used in case of penicillin allergy or resistance.
- 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 for *S. pneumoniae*, and trimethoprim-sulfamethoxazole for *Listeria*, 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 euvolemia. 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 fungal CNS disease or systemic fungal infections, and rapid disease progression, empiric amphotericin B can be considered.

- TB meningitis is another CNS infection to be considered in the early differential diagnosis, especially if there has been a subacute and more protracted course of onset of illness: In a patient presenting with a symptom duration of more than 5 days, particularly if the patient is immunocompromised, the diagnosis of TB meningitis should be considered. Tuberculosis is more prevalent in high-risk groups, including the homeless, nursing home residents, ethnic minorities, and persons infected with HIV. Empiric treatment regimens are largely based on those for pulmonary TB.

There is evidence supporting the use of dexamethasone in bacterial meningitis, particularly in CNS infections caused by *Streptococcus pneumoniae, and Haemophilus influenzae.* In a Cochrane systematic review and meta-analysis, it was found that corticosteroids overall reduced the rate of any hearing loss, severe hearing loss, and neurological sequelae. Subgroup analyses showed that corticosteroids a) prevented hearing loss in children with bacterial meningitis b) reduced severe hearing loss only in children with meningitis due to H. influenzae, c) reduced mortality in Streptococcus pneumoniae but not for other bacteria and d) protected against severe hearing loss and short-term sequelae for children in high-income countries, but not for those in low-income countries. Adjunctive corticosteroids are also recommended for TB meningitis regardless of disease severity.

Give dexamethasone 10 mg IV, ideally given 10 to 20 minutes before antibiotics, or with the first dose of antibiotics, until up to 4 hours after the first antibiotic dose. Corticosteroid administration should not delay the administration of IV antibiotics. Other corticosteroids can be used in equivalent doses if dexamethasone is not available. Dexamethasone is the preferred corticosteroid, when these agents are used, due to superior penetration into the cerebrospinal fluid (CSF) and a longer half-life. There is insufficient data to recommend starting corticosteroids in neonates.

TARGET	AGENT	CHILDREN	ADULTS
BACTERIAL			
Group B *Streptococci* *Listeria* Gram-negative bacteria *(E. coli)*	Ampicillin	0 to 7 days: 100 mg/kg/dose IV every 8-12 h	2 g IV every 4 h
		8 to 28 days: 75 mg/kg/dose IV every 6 h	
		> 28 days: 100 mg/kg/dose IV every 6 h (MAX: 2 g/dose)	
H. influenzae *N. meningitidis* *P. aeruginosa* *S. pneumoniae*	Ceftazidime	0 to 7 days: 50 mg/kg/dose IV every 8-12 h	2 g IV every 8 h
		8-28 days: 50 mg/kg/dose IV every 8 h	
		≥28 days: 50 mg/kg/dose IV every 6-8 h (Maximum dose: 6g/day)	
H. influenzae *N. meningitides* *P. aeruginosa* *S. pneumoniae*	Cefotaxime	0-7 days: 50 mg/kg/dose IV every 8-12 h	2 g IV every 4-6 h
		8-28 days: 50 mg/kg/dose IV every 6-8 h	
		>28 days: 75 mg/kg/dose IV every 6-8 h (maximum dose: 12 g/day)	
H. influenzae *N. meningitidis* *S. pneumoniae*	Ceftriaxone*	Neonatal:	2 g IV every 12h
		< 14 days: 50 mg/kg IM once daily	
		14-28 days: 100 mg/kg x1, then 80-100 mg/kg/day IV once daily	
		Infants/children:	

		80-100 mg/kg/day divided every 12-24 hours (Maximum dose: 4 g/day)	
S. aureus *S. pneumoniae*	Vancomycin	0-7 days: 10 mg/kg/dose IV every 8-12 h 8-28 days: 10mg/kg/dose IV every 6-8 h >28 days: 15mg/kg/dose IV every 6 h	15-20 mg/kg/dose IV every 8 -12 h
Enterococcus species *Listeria monocytogenes* *S. agalactiae* *P. aeruginosa*	Gentamicin	0-7 days: 4 mg/kg/dose IV every 24 h 8-60 days: 5 mg/kg/dose IV every 24h 60 days-10 years: 2.5 mg/kg/dose IV every 8 h >10 years: 5 mg/kg/*day* IV divided every 8 h	5 mg/kg/day IV in divided doses every 8 h
H. influenzae *N. meningitidis* *S. pneumoniae*	Meropenem	40 mg/kg/dose IV every 8 h (maximum dose: 2 g/dose)	2 g IV every 8 h
Alternative in penicillin allergy - component of empiric therapy - *H. influenzae* *Enterobacteriaceae* *P. aeruginosa*	Aztreonam	0-7 days: 30 mg/kg/dose IV every 8 h ≥8 days: 30 mg/kg/dose IV every 6-8 h (MAX: 8 g/day)	2 g IV every 6-8 h

TARGET	AGENT	CHILDREN	ADULTS
VIRAL			
Herpes simplex virus	Acyclovir	0-90 days: 20 mg/kg/dose IV every 8 h	10 mg/kg/dose IV every 8 h
		90 days-12 years: 10-15 mg/kg/dose IV every 8 h	
		≥12 years: 10 mg/kg/dose IV every 8 h (Maximum dose 8 g/day)	
Varicella-Zoster virus	Acyclovir Or	Acyclovir dosing: see above Ganciclovir dosing: see below	10 mg/kg/dose IV every 8 h
	Ganciclovir		5 mg/kg/dose IV every 12 h
Cytomegalovirus (in HIV-infected)	Ganciclovir	0-3 months: 6 mg/kg/dose every 12 h ≥3 months:5 mg/kg/dose every 12 h. Add foscarnet until symptoms improve	5 mg/kg/dose every 12 h plus foscarnet until symptoms improve*
*off-label			

TARGET	AGENT	CHILDREN	ADULTS
FUNGAL			
Candida species *Aspergillus* species *Mucorales* *Mycoses* Molds *Leishmania* species Histoplasmosis Coccidiomycoses	Amphotericin B	<28 days: use conventional formulation: 1mg/kg/dose IV once daily ≥28 days: use liposomal formulation:5 mg/kg/dose IV daily (may premedicate with acetaminophen + antihistamine to prevent infusion reactions)	Use lipid complex formulation:5 mg/kg/dose IV daily (may premedicate with acetaminophen + antihistamine to prevent infusion reactions)
Cryptococcus Empiric in febrile neutropenic patients	Liposomal amphotericin B	dosing as above	3-6 mg/kg/day IV daily (may premedicate with acetaminophen + diphenhydramine to prevent infusion reactions)

TARGET	AGENT	CHILDREN	ADULTS
MYCOBACTERIAL	**(Initial intensive phase)**		
Empiric for strong suspicion of tuberculous meningitis: combination regimen (4 drugs)	Ethambutol	Weight-based:	
		<15 years or ≤ 40kg: 15 to 25 mg/kg/dose PO once daily (maximum dose: 1g/dose) 40- 55 kg: 800 mg PO once daily	<15 years or ≤40 kg: 15 to 25 mg/kg/day 40-55 kg: 800 mg PO daily
		56-75 kg: 1200 mg PO once daily	56-75 kg: 1200 mg PO daily
		76-90 kg: 1600 mg PO once daily	76-90 kg: 1600 mg PO daily
	Isoniazid	<15 years *and* ≤40 kg: 10-15 mg/kg/dose PO once daily (Maximum dose: 300 mg/dose) <15 years *and* >40 kg, or ≥15 years: 5mg/kg/day	5 mg/kg/dose PO once daily
	Pyrazinamide	<40 kg: 35 mg/kg/day	40-55 kg: 1000 mg PO once daily
		40-55 kg: 1000 mg daily	56-75kg: 1500 mg PO once daily
		56-75 kg: 1500 mg daily	76-90kg: 2000 mg PO once daily
		76-90 kg: 2000 mg daily	

	Rifampin/rifampicin	<28 days: 2.5-10mg/kg/dose IV every 12 h <15 years *and* ≤40kg: 10-20 mg/kg/dose IV once daily <15 years *and* >40kg, or ≥15 years: 10 mg/kg once daily (maximum: 600 mg/dose)	10 to 20 mg/kg once daily (maximum: 600 mg/dose)

* Neonates should only receive intramuscular formulations of ceftriaxone. Intravenous formulations have potential for fatal lung and kidney damage in preterm and term neonates.

Table 4

Neonate (<28 days)	Infants/Children (≥28 days)	Adults - immunocompetent	Adults - immunocompromised	Healthcare associated
Ampicillin (0-7 d: 100 mg/kg/dose IV every 8 h; 8-28 d: 75 mg/kg/dose IV every 6 h)	Ceftriaxone (80-100 mg/kg/day IV divided every 12-24 hours; maximum dose: 4 g/day)	Ceftriaxone (2 g IV every 12 h)	Cefepime (2 g IV every 8 h)	Cefepime (2 g IV every 8 h)
	Or	Or	Or	Or
	°Cefotaxime (75 mg/kg/dose IV q6-8h)	Cefotaxime (2 g IV every 4-6 h)	Meropenem (2 g IV every 8 h)	Ceftazidime (2 g IV every 8 h)
Plus	Plus	Plus	Plus	Or
Gentamicin (0-7 d: 4 mg/kg/dose IV every 24 h; 8-28 d: 5 mg/kg/dose IV every 24 h)	Vancomycin (15 mg/kg/dose IV q6h)	Vancomycin (15-20 mg/kg/dose IV every 8-12 h	Vancomycin (15-20 mg/kg IV every 8-12 h)	Meropenem (2 g IV every 8 h)
Or		Plus (if >50 yrs)	Plus	Plus
°Cefotaxime (0-7 d: 50 mg/kg/dose IV every 8-12 h; 8-28 d: 50 mg/kg/dose IV every 6-8 h)		Ampicillin (2 g IV every 4 h)	Ampicillin (2 g IV every 4 h)	Vancomycin (15-20 mg/kg IV every 8-12 h)
Or				
Ceftazidime (0-7 d: 50mg/kg/dose IV every 8-12 h; 7-28 d: 50mg/kg/dose IV every 8 h)				
	*Dexamethasone (0.15mg/kg IV q6h) – give before or with first dose of antibiotic	*Dexamethasone (10mg IV every 6 h) – give before or with first dose of antibiotic		

Notes on Table 4

*in patients with certain risk factors (e.g., unimmunized patients, young children [age ≥ 6 weeks to 5 years], children with sickle cell disease, asplenic patients) or if there is known or suspected Haemophilus influenzae or S. pneumoniae infection (e.g., based on Gram stain results).

¶Dexamethasone, if given, should be administered before or immediately after the first

dose of antibiotics. Duration of treatment: 2-4 days for adults and children

◦Cefotaxime: currently on shortage in U.S.

Vancomycin: not to exceed 2 g per dose or a total daily dose of 60 mg/kg; adjust dose to achieve vancomycin serum trough concentrations of 15 to 20 mcg/mL

If Beta lactam allergic:

For Listeria: trimethoprim-sulfamethoxazole - 5mg/kg (based on the trimethoprim component) IV every 6 to 12h

For S. Pneumoniae, N. Meningitidis, H. influenzae: replace the Beta lactam with moxifloxacin 400mg po daily or levofloxacin 750mg IV daily

Suspected healthcare associated meningitis: replace Beta lactam with Aztreonam (2g IV every 6 to 8h) or Ciprofloxacin (400mg IV every 8 to 12h)

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 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.

Indications for neuroimaging prior to lumbar puncture:

- ✓ Patient is ≥ 60 years
- ✓ History of CNS disease
- ✓ Immunocompromised state
- ✓ History of seizure (within one week of presentation)
- ✓ Abnormal neurologic exam findings
  - Impaired level of consciousness
  - Abnormal language
  - Cranial nerve findings
  - Motor findings
  - Papilledema or loss of venous pulsations on fundoscopic examination

A normal head CT does not necessarily protect the patient form a herniation syndrome. Brain herniation after LP occurs in approximately 5% of cases or less. CT scan can detect brain shift and findings of impending herniation, contraindicating an LP. However, CSF pressure may be elevated, even to levels where herniation may occur, in absence of abnormalities on CT. Meningitis can be fulminant and characterized by progressive inflammation of the meninges and brain swelling. Patients can herniate after LP because of disease progression, or due to the inflammatory response to bacterial proinflammatory substances liberated after antibiotic administration (especially if steroids are not given around the time of first antibiotic administration), and not necessarily as a result of the LP. Vice versa, CSF pressure can be normal in patients with space occupying lesions causing brain shift seen on CT scan, even in the stage of herniation, and the LP may lead to herniation even with the CSF having normal pressure.

In a patient with none of the above indications, doing an 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 diagnostic uncertainty that CT may be advisable prior to LP to rule out other etiologies. Although MRI is preferable for encephalitis but CT with and without contrast can be performed.

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 left lateral decubitus position. CSF should be collected in (at least) 4 tubes.

- Send tube 1 and tube 4 for RBCs and WBC count and differential (if tube 1 was turbid, and tube 4 is clear, this suggests a traumatic tap)
- Send tube 2 for protein, glucose, and lactic acid
- Send tube 3 for gram stain and culture; India ink if fungal infection is suspected; antigens, PCR (For viruses, especially herpes viruses. May also be sent in tube 2), IgM for viruses, viral culture

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.

Normal LP

Rules out meningitis and encephalitis

An LP is considered normal if:

- No RBCs/HPF or up to ≤ 5
- WBCs ≤ 5/HPF
- CSF glucose/serum glucose ratio >0.6
- 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 may be 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.

Evaluate for Other Diagnoses

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 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 appears (defervescence, falling WBC count) may prompt additional investigation as to cause.

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/HPF or higher
- CSF glucose/serum glucose ratio <0.6, but rarely normal
- Protein > 50 mg/dl
- Organisms seen on gram stain in approximately 70% of cases

Then, the patient likely has bacterial meningitis.

Suspicion of Bacterial Meningitis

- Continue antibiotics
- Stop acyclovir
- Continue dexamethasone
- Adjust antibiotics, and either continue or stop dexamethasone based on final 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 LP demonstrates an elevated OP, ICP monitoring and treatment of intracranial hypertension may be required. Details of management of intracranial hypertension can be found in the ENLS manuscript on the same topic and in the 2019 Neurocritical Care Society Guidelines for Cerebral Edema Management. Risks, including the potential of a superinfection with the foreign body, must be weighed with the potential benefits.

If the OP is found to be greatly elevated (e.g., > 400 mm H_2O), expert opinion recommends that the needle stylet should be left in place and mannitol administered. It may be prudent to recheck the pressure after a few minutes to confirm that the CSF pressure has declined, before removing the needle. Hyperventilation should probably be avoided as these patients already may suffer from some degree of decreased cerebral vessel diameter due to vasculopathy. Mannitol or hypertonic saline may be reasonable considerations.

Elevated WBCs and 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:

- No RBC per HPF
- WBCs 10-100s
- Normal CSF glucose/serum glucose ratio (>0.6)
- Protein < 50 mg/dl (if elevated, it is usually <100 mg/dL)
- No organisms seen on gram stain

Then the patient likely has a non-herpes viral meningitis or encephalitis.
Seroconversion of HIV should also be considered.

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

Elevated WBCs and RBCs

Consider herpes encephalitis

If the following is true:

- Elevated RBC (10–100/HPF or higher),
- WBCs in the hundreds/HPF, typically with lymphocytic predominance,
- CSF glucose/serum glucose ratio >0.6, or sometimes lower,
- Protein < 50 mg/dL or mildly elevated usually <100 mg/dL, and
- No organisms on gram stain,

then the patient may have herpes encephalitis. The presence of seizures and findings of uni- or bilateral hypodensities with or without hemorrhage in the temporal lobes on brain MRI, and rarely on brain CT scans, are also compatible with this diagnosis.

Empirical treatment and diagnosis of herpes encephalitis

- 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

Elevated WBCs and Very High Total Protein

Fungal or TB Meningitis

Fungal CNS infections are highly variable in clinical presentation and need to be considered in suspected CNS infections that evolve over days in an immunosuppressed patient. Prior history of CNS disease or systemic fungal infections and rapid disease progression should raise the index of suspicion for fungal meningitis.

As with other CNS infections, fast identification and treatment initiation significantly affects the odds of a better outcome. Typical CSF findings include lymphocytic pleocytosis (few to several hundred per HPF) and for certain organisms also with eosinophilic predominance. CSF glucose is decreased, and CSF protein is generally elevated (up to 250 mg/dl or beyond). If CSF acquisition via LP is difficult or impossible, it can be an indicator of very high (>1 gm/dL) CSF protein and obstructive hydrocephalus. Empiric amphotericin B should be administered during diagnostic testing.

Elevated RBCs, Xanthochromia

Likely Subarachnoid Hemorrhage

If the following is true:

- Elevated RBC (100 to 1,000/HPF or higher),
- WBC < 5/HPF or fewer than 1 WBC/500 RBC,
- CSF glucose/serum glucose ratio >0.6,
- Protein < 50 mg/dl,
- No organisms on gram stain, and
- 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).

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.

Pediatric considerations

Bacterial meningitis is a true medical emergency. Pediatric patients should be resuscitated similarly using the ABC approach with securing airway, breathing and circulation. Shock may also be a presentation in pediatric patients. IV access with rapid isotonic fluid resuscitation of 20-60 mL/kg in the first hour should be administered with a goal to restore normal peripheral perfusion, heart rate and blood pressure for age. For fluid refractory shock, epinephrine for cold shock and norepinephrine for warm shock should be started. Initiation of antibiotics should not be delayed for investigations such as imaging and LP. Age-appropriate use of antibiotics and use of dexamethasone have been discussed above.
Other conditions to keep in mind include Acute Flaccid Myelitis (AFM), which is a rare but feared problem with children presenting as acute paralysis. Decreasing vaccine coverage has also led to measles encephalitis and mumps-associated meningitis in pediatric population