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Emergency Neurologic Life Support: Meningitis and Encephalitis

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Abstract Bacterial meningitis and viral encephalitis, particularly herpes simplex encephalitis, are severe neurological infections that, if not treated promptly and effectively, lead to poor neurological outcome or death. Because of the value of early recognition and treatment, meningitis and encephalitis was chosen as an Emergency Neurological Life Support protocol. This protocol provides a practical approach to recognition and urgent treatment of bacterial meningitis and encephalitis. Appropriate imaging, spinal fluid analysis, and early empiric treatment are discussed. Though uncommon in its full form, the typical clinical triad of headache, fever, and neck stiffness should alert the clinical practitioner to the possibility of a central nervous system infection. Early attention to the airway and maintaining normotension are crucial steps in the treatment of these patients, as is rapid treatment with anti-infectives and, in some cases, corticosteroids.

Keywords Emergency neurologic life support · Neurocritical care · Meningitis · Encephalitis

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Introduction

Meningitis and encephalitis are potentially life-threatening central nervous system (CNS) diseases, which often present initially to the Emergency Department (ED). Many of these patients are critically ill and transported to the ED by Emergency Medical Services (EMS). Meningitis is strictly defined as inflammation of the meninges, while encephalitis is strictly defined as inflammation of the brain. If both are inflamed, the patient has meningo-encephalitis. Meningitis causes fever, meningismus, and pain (e.g., headache, neck pain), but, other than depressing a patient's mental status, does not affect cortical brain function (e.g., aphasia, seizure, hemiparesis). Alternately, encephalitis typically causes cortical disturbance, particularly seizures. Most patients have a predominance of one or the other, but many have features of the combined meningo-encephalitis syndrome. The two conditions that are most important to recognize in the first hour are bacterial meningitis and herpes encephalitis, as these diseases produce significant morbidity and mortality and have specific treatments that can improve patient outcome if administered quickly.

It is estimated that 500,000 cases of bacterial meningitis occur worldwide each year, of which more than 1/3 die ($\approx$170,000) and a large number of survivors are left with neurologic sequelae [1]. The incidence and common causative agents have changed considerably in developed countries since the introduction of conjugate vaccines for Haemophilus influenza B (HiB) and Meningococcus [2]. In these countries meningitis and encephalitis have become rare diseases. Because of poverty and poor health care infrastructure, they remain significantly more common in developing and poor nations [3]. The annual incidence of bacterial meningitis in the U.S. is approximately 3 cases per 100,000 [1] and the highest incidence occurs in

children under 1 year of age (76.7/100,000) [1]. While accurate estimates of incidence are difficult to obtain, encephalitis is a less common disease than meningitis. The non-herpes varieties display seasonal variation.

Bacterial meningitis and bacterial or viral encephalitis are medical, neurologic, and, occasionally, neurosurgical emergencies which carry substantial morbidity and mortality despite modern medical management. In one study, 48% of patients with bacterial meningitis presented within 24 h of the onset of symptoms [4]. Therefore, patients who have a hyper-acute (hours) to acute (hours to days) onset of headache and altered mental status should be considered as potentially having meningitis or encephalitis. While children present similarly to adults, neonates are more likely to present with non-specific findings including decreased feeding, irritability, and lethargy [3].

Fever is a major feature of these infectious illnesses. Additional symptoms include stiff neck (typically elicited by neck flexion), fever, new rash, focal neurological findings, or new seizures. Meningitis should be considered in the differential diagnosis of any lethargic, vomiting, irritable neonate. In a large series of 696 adult patients with bacterial meningitis, the classic triad of fever, neck stiffness, and change in mental status was present in only 44% of patients, but 95% of patients had at least two symptoms when a fourth symptom—headache—was added to the classic triad [4]. In contrast, another report pooling adult studies of patients with meningitis demonstrated that 95% of patients had at least two of the three elements of the classic triad [5]. The absence of fever, altered mental status, and neck pain in an immunocompetent patient essentially eliminates the diagnosis of meningitis and suggests other diagnoses should be pursued [5].

A challenge in diagnosing meningitis or encephalitis is that there is no single definitive clinical symptom or sign. A review of papers on adult meningitis published between 1966 and 1997 found that Kernig's sign was the sign most frequently elicited when evaluating a patient for possible meningitis. Kernig's sign is elicited with the patient lying supine, and his hips and knees flexed to 90°. The clinician then extends the patient's knee, straightening the leg [5]. A positive sign is present when extension of the leg at the knee produces significant lower back or posterior thigh discomfort due to meningeal irritation. Brudzinski's sign, in contrast, is elicited by placing the patient in a supine position and passively flexing the patient's neck. The clinician observes whether this action triggers flexion at the hips and knees. Despite the common teaching of these maneuvers, their sensitivity and specificity for diagnosing meningitis is unknown. Therefore, the absence of these signs should not be used to rule out meningitis [6]. Another test that has been studied in patients suspected of having meningitis is the jolt accentuation test. The clinician instructs the patient to rotate their head horizontally at a frequency of two rotations per second. A positive jolt accentuation test produces exacerbation of the patient's headache [5]. In a small study, this maneuver had a sensitivity of 100% and a specificity of 54% for identification of meningitis.

The Emergency Neurological Life Support (ENLS) suggested algorithm for the initial management of meningitis and encephalitis is shown in Fig. 1. Suggested items to complete within the first hour of evaluating a patient with meningitis and encephalitis are shown in Table 1.

Prehospital Considerations

In the prehospital setting, EMS personnel should approach the patient based upon the chief complaint, assess the basic ABCs of resuscitation (i.e., Airway, Breathing, Circulation), and begin management as appropriate for the severity of the patient's presentation and the training level of the EMS providers. This may include obtaining basic vital signs, formal assessment of mental status utilizing the Glasgow Coma Score (GCS), measurement of serum glucose levels, placement of intravenous (IV) access, initiation of IV fluid resuscitation, and airway management. If IV access cannot be rapidly obtained in an unstable patient, placement of an intra-osseous (IO) cannula should be considered. Prehospital resuscitation of patients with life-threatening infections can expedite achievement of resuscitation goals including adequate mean arterial pressure (MAP) [7]. In a population-based retrospective study, prehospital IV placement and fluid administration were associated with a decreased likelihood of in-hospital mortality [8].

Initial Assessment

As with all acute medical and neurological events, the basic ABCs of resuscitation should be evaluated immediately on presentation to the ED. Vital signs (including temperature, blood pressure, heart rate, and respiratory rate, along with peripheral oxygen saturation), a pain scale, assessment of GCS, and a rapid check of the patient's serum glucose level should be quickly obtained at triage and compared to those obtained by prehospital personnel.

In most instances, an oral temperature is adequate. Patients who are markedly tachypneic may not be able to keep their mouths closed during an oral temperature reading and may require a rectal temperature to ensure accuracy. Both fever (temperature > 38 °C) and hypothermia (temperature < 36 °C) are compatible with CNS infection.

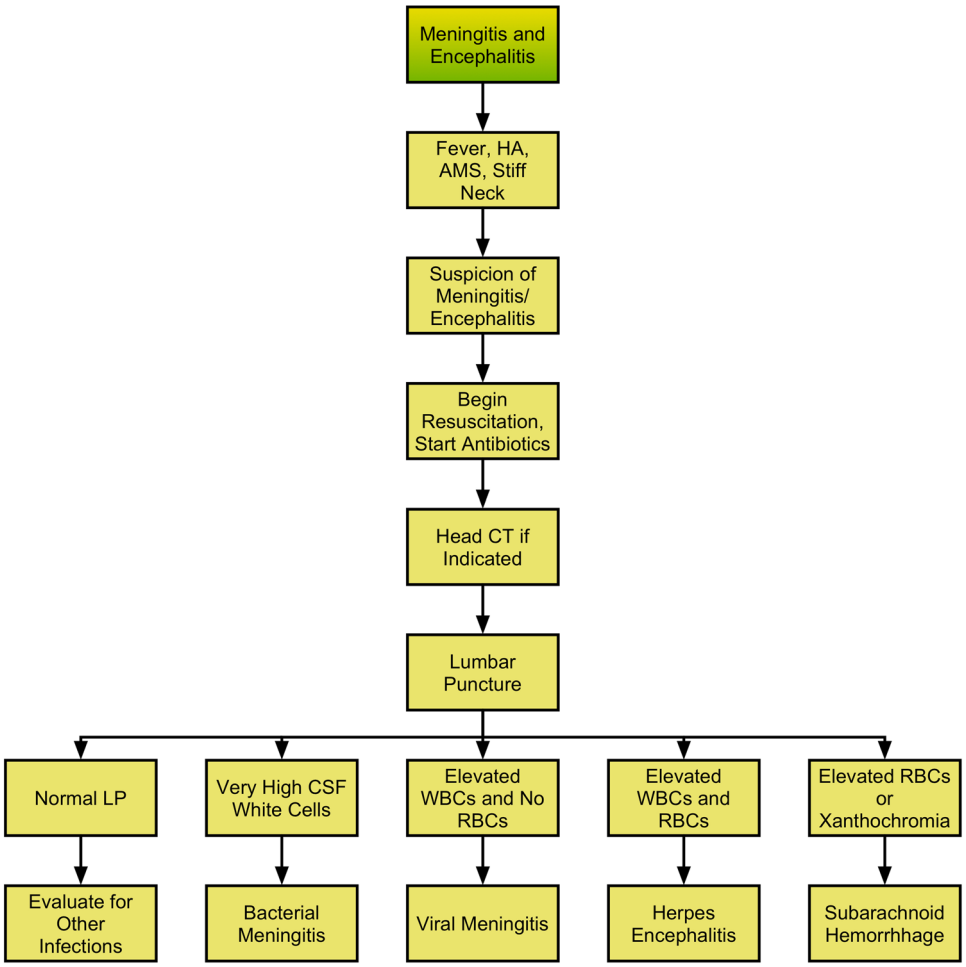

Fig. 1 ENLS meningitis and encephalitis protocol

Table 1 Meningitis and encephalitis checklist for the first hour

Checklist
☐ Vital signs, history, examination
☐ IV access
☐ Labs: CBC, 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 herpes simplex virus a concern)
☐ Head CT, if patient neurological exam abnormal
☐ Lumbar puncture (LP), if CT results available
☐ If meningococcus remember exposure prophylaxis

If the patient is normothermic, the pre-test probability of bacterial meningitis or herpes simplex encephalitis (HSE) encephalitis is decreased. However, newly immunocompromised patients, patients with viral meningitis, and even an occasional patient with bacterial meningitis may present to the ED without fever. In an evaluation of 696 patients with community-acquired acute bacterial meningitis, the mean reported temperature was 38.8 °C, and 77% of patients were febrile. The evaluation did not report the number of patients who were hypothermic [4].

Patients with altered mental status are at risk for aspiration, have decreased ability to maintain a patent airway, and should be monitored for the need for endotracheal intubation. Intubation should be considered for any patient with a GCS $\leq$8 for airway protection. Patients with bacterial meningitis are at risk for lung or bloodstream infections with the same pathogen, further reinforcing the need to closely monitor vital signs and hemodynamics.

Immediately after vital signs are assessed in triage, patients at high risk for meningitis should have adequate IV access (i.e., a minimum of two 18 gauge or larger peripheral IVs) placed, and blood samples sent for laboratory analysis, including a peripheral white blood cell (WBC) count and differential, basic metabolic panel, serum lactate, and blood cultures. An initial fluid bolus of 20–30 mL/kg of crystalloid solution should be immediately infused over 20–30 min and the patient's vital signs, mental status, and airway should be reassessed every 5 min during the proximal phase of treatment. If IV access cannot

be obtained within a few minutes of presentation, IO access should be placed.

Similar to patients with other bacterial infections, some patients with bacterial meningitis will be hypotensive. This may result from sepsis or increased insensible fluid losses from fever, tachypnea, diaphoresis, and vomiting. In addition, bacterial meningitis, like other diseases causing septic shock, can trigger a pronounced inflammatory response, leading to vasodilation, capillary leak, and, in some cases, myocardial dysfunction.

The initial resuscitation strategy in critically ill patients with suspected meningitis or encephalitis should be identical to that recommended for other sepsis and septic shock patients. For example, in guidelines focusing on initial resuscitation, the Surviving Sepsis Campaign recommends beginning resuscitation immediately in patients with hypotension (systolic blood pressure < 90 mmHg; MAP < 65 mmHg) or a serum lactate of ≥ 4 with an initial fluid challenge of 30 ml/kg of crystalloid in the first 3 h. These recommendations changed from the strict algorithmic resuscitation model of the prior iterations to a more flexible model stressing rapid diagnosis and rapid administration of fluids and antibiotics, followed by careful monitoring and reassessment of hemodynamic status with further fluid boluses as needed [9, 10].

The above changes came in light of recent randomized trials of alternative resuscitation strategies in patients with severe sepsis and septic shock suggesting that early identification, rapid fluid resuscitation, timely antibiotic administration, and careful monitoring may be more important than the specific resuscitation algorithm and goals [11–13].

One liter boluses of crystalloid over 15 min should be given repeatedly until these goals are reached or the patient is stabilized, volume replete, and no longer fluid responsive. The rate of fluid infusion should be reduced to a maintenance level once goals are achieved or when the patient demonstrates no further fluid responsiveness [2, 9]. Norepinephrine should be used to support MAP if the patient remains hypotensive despite initial resuscitation.

However, the optimal translation of these recommendations to the management of patients with CNS infections is unclear, and, in particular, the relationship between aggressive early volume resuscitation and cerebral edema should be systematically investigated. The results of the recently completed ProCESS, ProMISe, and ARISE studies contribute little to this discussion since less than 1% of the patients enrolled in ProCESS and $<2\%$ of the patients enrolled in ARISE and ProMISe trials had meningitis [11–13].

CBC and CT

In compliance with the Infectious Disease Society of America (IDSA) Practice Guidelines for the Management of Bacterial Meningitis [14], cranial computed tomography (CT) should be done prior to LP if the patient is at least 60 years of age, has a history of CNS disease (e.g., mass lesion, stroke, and focal infection), presents in an immunocompromised state (e.g., HIV infection or AIDS, immunosuppressive therapy, or transplantation), has had a history of seizure within 1 week before presentation, or possesses certain specific abnormal neurologic findings (e.g., an abnormal level of consciousness, an inability to answer two consecutive questions correctly or to follow two consecutive commands, gaze palsy, abnormal visual fields, facial palsy, arm drift, leg drift, abnormal language). These clinical features at baseline are associated with abnormal findings on a CT scan of the head. However, there are data showing that altered mental status alone, in the absence of focal neurological signs, or new onset seizures is not a contraindication to LP prior to CT scan, and these data resulted in a revision of the Swedish guidelines on acute bacterial meningitis in 2009 in which moderate to severe impairment of mental status and new onset seizures as contraindications to initial LP were deleted [15–17]. The IDSA guidelines on meningitis were last updated in 2004 [14]. If circumstances permit, cranial CT should occur prior to LP in patients with any of these concerning clinical signs. Obtaining a cranial CT and performing an LP should delay neither antibiotic administration nor initial resuscitation.

Much like body temperature, peripheral WBC can be elevated or depressed in patients with CNS infection, and blood frequently possesses increased immature forms [18]. A normal WBC count does not rule out meningitis.

Depending on body temperature, presenting symptoms, complete blood count (CBC), and the results of the head CT scan, the exploration of CNS infection may potentially include performance of a LP. A LP is helpful in evaluation of viral meningitis, so a patient without classic symptoms of neck stiffness, impaired alertness, and an elevated WBC may still benefit from cerebrospinal fluid (CSF) analysis.

Suspicion of Infection

In patients in whom there is a moderate to high suspicion of CNS infection and for whom LP has not yet been performed, parenteral antimicrobials should not be delayed while waiting for a CT scan of the brain. With the most sensitive organisms, CSF sterilization occurs only after 4–6 h following initiation of antimicrobials.

As described in the Initial Management and CBC and CT sections above, head CT prior to LP should be performed in the patient with suspected CNS infection when any of the following are present: papilledema or loss of venous pulsations on funduscopic examination; focal neurological signs; immunocompromised patients; known mass lesions; or seizures within 1 week of the presentation.

In patients who do not present with these signs, have normal mental status, and have no focal neurologic deficits, a head CT is not always required prior to LP. However, in most patients who have a clinical presentation consistent with acute bacterial meningitis or encephalitis, there will be enough diagnostic uncertainty that CT is advisable prior to LP.

In a study of the need for head CT prior to LP among 301 patients with suspected bacterial meningitis, 78% of patients had a head CT performed prior to LP [19]. Of these patients, 24% had an abnormality on the CT reading, and 5% had evidence of mass effect. Age $>$ 60 years; immunocompromised state; history of CNS disease; altered level of consciousness; and focal neurologic deficits were predictive of abnormal CT findings. If CT scans were ordered only on those individuals with a predictive sign of CT abnormality, the rate of CT acquisition would have been decreased by 41% [19]. A normal head CT does not preclude the development of a herniation syndrome. 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 response to antibiotic administration, and not necessarily as a result of the diagnostic intervention.

Known or suspected immunocompromised patients may present with less classic signs of meningitis or encephalitis. For such patients, the clinician should lower his or her pretest probability for these diagnoses and err on the side of a more complete work-up, including emergent brain imaging and LP.

If the head CT shows a mass lesion or another condition, such as a *subarachnoid hemorrhage* (SAH), that adequately explains the patient's mental status, then the evaluation of bacterial meningitis can be aborted.

In cases with a normal (if performed) head CT in the presence of fever, abnormal WBC count, headache, and altered mental status, there should be moderate to high suspicion for meningitis or encephalitis (see the section Start Antibiotics). There is evidence for the use of dexamethasone in bacterial meningitis, particularly in CNS infections caused by *Streptococcus pneumoniae* [20]. In situations where it is clearly evident that the suspected organism is something other than *Streptococcus pneumoniae*, then dexamethasone may be withheld. Otherwise, empiric use of dexamethasone until cultures return is reasonable [20]. In a meta-analysis, corticosteroids reduce hearing loss in children with *H. influenzae* type b meningitis, but not in children with meningitis due to non-*Haemophilus* species, whereas mortality was improved in the subgroup of meningitis caused by *Streptococcus pneumoniae*, but not by other bacteria [21].

The Infectious Disease Society of America's practice guidelines state: "some authorities would initiate dexamethasone in all adults with suspected bacterial meningitis because the etiology of meningitis is not always ascertained at initial evaluation" [14]. Patients should be given 10 mg of IV dexamethasone immediately and every 6 h thereafter for a duration of 2–4 days for adults, and 0.15 mg/kg every 6 h for 2–4 days for children [20]. Ideally, the steroid should be given 10–20 min prior to or at the start of antibiotic therapy or concomitantly with the first dose of antibiotic. Dexamethasone should not be given to patients who have already received antibiotics due to lack of efficacy data.

Start Antibiotics

Appropriate antimicrobials should be started as soon as possible after a patient with suspected CNS infection presents for medical care. In patients with septic shock, each hour delay in the administration of appropriate antimicrobials after onset of hypotension increases mortality an average of 7.6% [22]. These results were confirmed by another study of 261 patients treated with a protocolized resuscitation strategy [23]. When appropriate antimicrobials were administered within 1 h of triage, mortality was 19.5%, whereas delays longer than 1 h after triage resulted in an increase in mortality to 33.2% [23].

The applicability of these findings to patients with bacterial meningitis is limited by the small percentage of patients in each study who had primary CNS infections. Prior, less rigorous studies have demonstrated an association between time to antibiotic administration in bacterial meningitis and mortality [24]. Delays in antibiotic administration are common. In a cohort of 122 patients with documented bacterial meningitis, one study found a mean time from triage to antibiotics of 3 h (interquartile range, or IQR 1.6–4.3 h) with 90% of this time occurring after the initial physician encounter [24]. In the recent study examining the impact of the 2009 changes in Swedish recommendations regarding CT before LP, the relative increase in mortality was 12.6% per hour of treatment delay in acute bacterial meningitis after adjusting for all confounding factors [16].

The choice of empiric antimicrobials is based on several factors, including the time course of symptom progression, patient age, and other infectious risk factors. For suspected CNS infections that evolve over hours, bacterial

meningitis, viral meningitis, and, less commonly, viral encephalitis may be considered.

Worldwide, *Streptococcus* pneumoniae and *Neisseria meningitides* account for the majority of cases of meningitis. Neonates have a permeable blood brain barriers and are at risk of infection caused by Group B streptococcus, *Listeria monocytogenes,* and *E. coli.* Children and young adults with suspected bacterial meningitis are at risk for *Haemophilus influenzae* (if not vaccinated), *Neisseria meningitidis*, and *Streptococcus pneumoniae*. Middle-aged adults are at highest risk for *Streptococcus pneumoniae*. As such, both groups should be started on a third generation cephalosporin and vancomycin at doses appropriate for CNS penetration and renal function. The elderly and immunosuppressed population, including alcoholics, are at risk for *Streptococcus pneumoniae* and *Listeria monocytogenes*. As such, they should be started on ampicillin, a third generation cephalosporin, and vancomycin at doses appropriate for CNS penetration and renal function [14]. Common initial antibiotic dosing for adults with normal renal function suspected of having bacterial meningitis are as follows: Ceftriaxone 2 g IV q 12 h, Vancomycin 15–20 mg/kg IV every 8–12 h (not to exceed 2 g per dose or daily total of 60 mg/kg; adjust to achieve trough concentration of 15–20 mcg/ml), and Ampicillin 2 g IV q 4 h.

Vancomycin and trimethoprim–sulfamethoxazole can be used in patients with a severe penicillin allergy (aztreonam may be used for Gram-negative coverage). If there is a high suspicion for viral encephalitis (cortical deficits, lymphocytic predominance in the CSF) treatment should begin with acyclovir at the doses listed below.

For suspected CNS infections that evolve over days, viral encephalitis and, particularly, HSE should be considered. For patients with normal renal function, treatment should begin with IV acyclovir at 10 mg/kg (based on ideal body weight) every 8 h. The frequency of acyclovir administration will need to be adjusted for patients with renal insufficiency or end stage renal disease. Hydration should be sufficient to achieve normovolemia, avoiding the complication of acyclovir-associated renal failure.

Other forms of viral encephalitis, such as those caused by the Arboviruses, including West Nile virus, may also have a sub-acute presentation [25]. There are no pharmacotherapeutic interventions for these encephalitides, but until exclusion of HSE can be verified, empiric acyclovir is reasonable. For suspected CNS infections that evolve over days in an immunosuppressed patient, fungal meningitis should be considered. Prior history of the CNS disease or systemic fungal infections and rapid disease progression should raise the index of suspicion for fungal meningitis. Empiric amphotericin B should be administered during diagnostic testing.

Lumbar Puncture (LP)

An LP is essential for both establishing a diagnosis and tailoring therapy. Informed consent should be obtained, when possible, and the clinical team should perform a "time-out" prior to starting the procedure.

Optimally the patient should be positioned in the left lateral decubitus position, as an opening pressure (OP) cannot be measured if the patient is sitting up. After prepping and draping the patient in the usual, sterile fashion, and accessing the sub-arachnoid space with a spinal needle, the OP should be measured with a manometer prior to the collection of CSF. An elevated OP is indicative of elevated intracranial pressure. In order to avoid CSF leakage and post LP headache, instruct patient to keep head of bed less than 15° following procedure.

CSF should be collected in a minimum of four tubes. Tubes 1 and 4 should be sent for red blood cell (RBC) and WBC counts; tube 2 for protein, glucose, and lactic acid; tube 3 for Gram's stain, antigens, and culture (and India ink if fungal infection is suspected). If there is a suspicion for herpes encephalitis, a small amount of CSF from either tube 2 or 3 should be sent for herpes polymerase chain reaction (PCR).

Larger volumes of CSF increase the sensitivity of a Gram's stain and culture. Some laboratories perform bacterial antigen assays, which may be useful in certain circumstances. Additional laboratory tests that may be performed at some centers include bacterial PCR (particularly for Mycobacterium), Herpes simplex PCR, enterovirus PCR, immunoglobulin M (IgM) for arboviruses, fungal antigens, and viral culture. Clinicians should be aware of local laboratory policies regarding minimum amounts of CSF required for Gram's stain and culture.

If the spinal fluid OP is found to be greatly elevated (e.g., >400 mm H_2O), expert opinion recommends that the needle stylette should be left in place and mannitol administered. It may be prudent to recheck the pressure after a few minutes to determine that it has declined, before removing the needle.

Normal LP

An LP is considered normal if there are no RBCs/high-powered field (HPF), fewer than five WBCs/HPF, the CSF glucose/serum glucose ratio is >0.67, the CSF protein <50 mg/dL, and no organisms are seen on Gram's stain. If all of the above are true, meningitis is excluded, as is encephalitis in most cases.

Very High CSF White Cells

The finding of a marked elevation in WBCs (neutrophils of 100–1000 per HPF or higher without a significant number of RBCs) is consistent with bacterial meningitis. In addition, the CSF/serum glucose ratio will usually be significantly reduced (<0.67), and the CSF protein is usually markedly elevated and almost always >50 mg/dL. Organisms are seen on Gram's stain in approximately 70% of cases.

Mildly Elevated WBC and No RBCs

A mild elevation in CSF WBCs without RBCs is consistent with a viral meningitis or viral (not herpes) encephalitis. WBCs often range from 10 to several 100 and the CSF possesses a normal CSF glucose/serum glucose ratio, and protein <50 mg/dL. Organisms are absent on the Gram's stain. Although patients with the above findings are unlikely to have bacterial meningitis, in many cases they will be admitted to the hospital and continued on antibiotics until the CSF culture results are negative and clinical improvement is demonstrated.

Elevated WBCs and RBCs

A patient with herpes encephalitis will typically have an elevated CSF RBC count (10–100/HPF or higher), WBCs in the hundreds/HPF (typically with a lymphocytic predominance), CSF glucose/serum glucose ratio >0.67, a protein level that may either be <50 mg/dL or elevated, and no organisms on Gram stain. The presence of seizures and findings of uni- or bilateral hypodensities in the temporal lobes on brain MRI, and rarely on brain CT scans, are also compatible with this diagnosis.

Elevated RBCs or Xanthochromia

If the CSF reveals an elevated RBC count (100–1000/HPF or higher), either a WBC count <5/HPF or fewer than 1 WBC/500 RBC, a CSF glucose/serum glucose ratio >0.67, and a protein <50 mg/dL; no organisms are seen on Gram's stain; and xanthochromia is detected, then the patient likely has suffered 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 (when RBCs are typically not seen).

Bacterial Meningitis

In patients with CSF demonstrating bacterial meningitis, clinicians should continue antibiotics, stop acyclovir, and continue dexamethasone. Subsequently, they should adjust antibiotics based on final Gram stain, culture results, and sensitivities.

In addition to antibiotics and dexamethasone, supportive care and management of other organ systems is important in patients with bacterial meningitis. Some patients may have a concomitant bloodstream infection with the offending pathogen and may require focused resuscitation for severe sepsis or septic shock. If the LP demonstrates an elevated opening pressure ICP, monitoring and treatment of intracranial hypertension may be required.

Viral Meningitis and Viral Encephalitis

The treatment for herpes encephalitis has been discussed above. The treatment of viral meningitis or non-herpetic viral encephalitis is primarily supportive in nature. Many of these patients will have a significantly depressed level of consciousness, making close observation and airway management crucial. For West Nile virus, there is risk of respiratory decompensation from neuromuscular weakness secondary to spinal cord involvement and depression of consciousness. Oxygen saturation may fall first due to aspiration, but more likely the patient's pCO_2 will rise as an early indicator of ventilatory failure. Admission to the ICU for observation is frequently warranted.

Pediatric Considerations

Bacterial meningitis is an important contributor to pediatric morbidity and mortality [26]. Diagnosis can be difficult in infants who often have non-specific manifestations 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 [27]. The major pathogens involved are dependent on the age of the child [26]:

- <2 months—Group B Streptococcus, *Listeria monocytogenes*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*
- 2–23 months—*Streptococcus pneumoniae*, Group B Streptococcus, *N. meningitidis*, *Haemophilus influenzae* [14, 21]
- 2–10 years—*Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*

- 11–17 years—*Neisseria meningitidis*, *Streptococcus pneumoniae*

Bacterial meningitis is a true pediatric medical emergency and immediate diagnostic and therapeutic steps must be taken in these children (Fig. 2). The initial management should include evaluation and restoration of normal oxygenation, ventilation, and perfusion. Supportive care should also include detection and management of hypoglycemia, acidosis, and coagulopathy. LP and blood cultures should be performed without delay, and empiric antibiotics should be given immediately following its completion. If performance of blood cultures or the LP is not possible or must be delayed (i.e. due to the need to obtain brain imaging), initiation of antibiotic therapy should not be postponed. Children with mass effect on brain imaging or sings of intracranial hypertension are at higher risk of cerebral herniation when a LP is performed. In such cases, neurosurgical consultation may be warranted prior to the procedure. An empiric antibiotic regimen for infants <3 months of age should include ampicillin, gentamycin and cefotaxime [14]. In older infants, children, and adolescents, the appropriate empiric treatment regimen should cover penicillin resistant *S. pneumoniae* and *N. meningitidis*. This can be accomplished with administration of vancomycin 60 mg/kg/day IV in 4 divided doses (maximum 4 g/day) plus either cefotaxime 300 mg/kg/day IV in 3–4 divided doses (maximum 12 g/day) or ceftriaxone 100 mg/kg/day IV in 1–2 divided doses (maximum 4 g/day) [21].

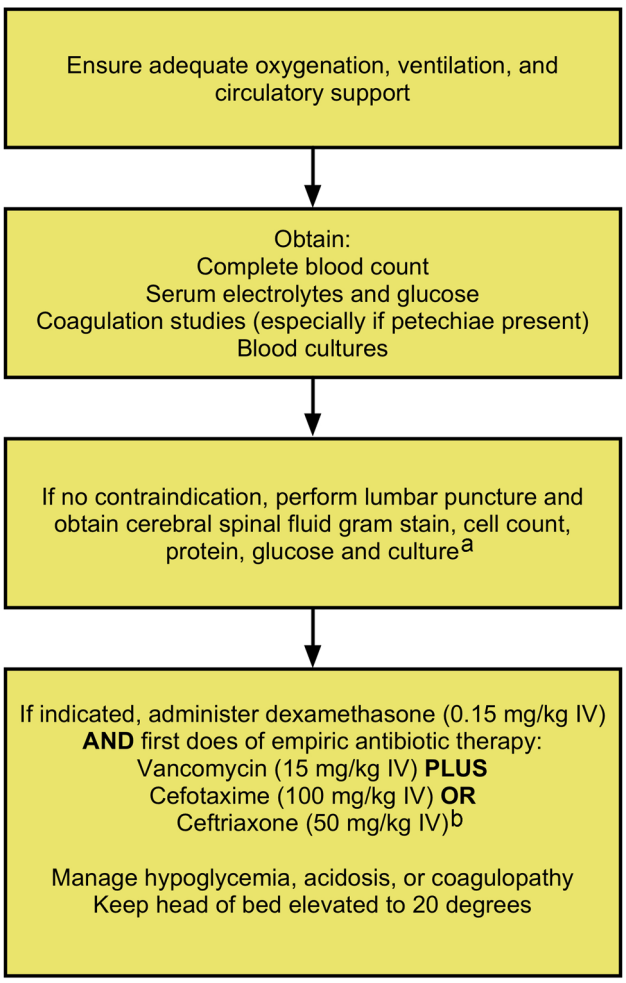

Fig. 2 Approach to suspected CNS infection in infants and children

The empiric antibiotic regimen should be broadened in infants and children with immune deficiency, recent neurosurgery, penetrating head trauma, or other anatomic defects

Adjunctive therapy with dexamethasone has been a topic of considerable debate. In a 2013 meta-analysis, the administration of dexamethasone did not affect overall mortality or long term neurological sequelae such as focal neurologic deficits, epilepsy, ataxia, and memory or concentration disturbance in children with bacterial meningitis. It did, however, reduce the incidence of severe hearing loss [21]. In subset analysis, this effect remained only in children with HiB, but not in those with meningitis caused by other organisms. Complications were similar in the steroid-treated and non-treated groups. Therefore, the American Academy of Pediatrics Committee on Infectious Diseases suggests that dexamethasone therapy may be beneficial in children with HiB meningitis if given before or at the same time as the first dose of antimicrobial therapy [28]. The committee also suggests that dexamethasone therapy be considered for infants and children with pneumococcal meningitis after weighing the potential risks and benefits. In the meta-analysis above, subgroup analysis showed an improved mortality with steroids in pneumococcal meningitis, but not with other bacteria [21]. If given, dexamethasone should be administered before or within 1 h of the first dose of antibiotics. It is probably of no benefit if given more than 1 h later, although this time interval has not been clearly defined.

Children with encephalitis present with symptoms of central nervous system dysfunction including alterations of consciousness and ataxia. Additional signs and symptoms include fever, seizures, focal neurological findings and abnormal neuroimaging [29]. As in the case of children with bacterial meningitis, the initial management includes restoration of normal oxygenation, ventilation, and perfusion, as well as detection and management of hypoglycemia, acidosis, and coagulopathy. Seizure detection and treatment are also vital.

Table 2 Empiric dosing of antimicrobial/antiviral therapy in patients with normal renal and hepatic function

Agent	Children	Adults
Acyclovir	3 months–12 years old: 20 mg/kg IV q 8 h 12 years or older: 10 mg/kg IV q 8 h	10 mg/kg IV q 8 h
Amphotericin B lipid complex	5 mg/kg IV daily	5 mg/kg IV daily
Ampicillin	0–7 days: 150 mg/kg/day IV divided q 8 h 8–28 days: 200 mg/kg/day IV divided q 6–8 h >28 days: 300 mg/kg/day IV divided q 6 h	2 g IV q 4 h
Aztreonam (for penicillin allergic patients)	30 mg/kg IV q 6–8 h	2 g IV q 6–8 h
Ceftazidime	0–7 days: 100–150 mg/kg/day IV divided q 8–12 h >7 days: 150 mg/kg/day IV divided q 8 h	2 g IV q 8 h
Ceftriaxone	80–100 mg/kg/day IV divided q 12–24 h; maximum dose: 4 g/day	2 g IV q 12 h
Liposomal amphotericin B	3–5 mg/kg IV daily	3–5 mg/kg IV daily
Meropenem	40 mg/kg IV q 8 h	2 g IV q 8 h
Vancomycin	0–7 days: 20–30 mg/kg/day IV q 8–12 h 8–28 days: 30–45 mg/kg/day divided q 6–8 h >28 days: 60 mg/kg/day IV divided q 6 h	10–15 mg/kg IV q 8 h (consider loading dose of 25–30 mg/kg IV in seriously ill patients); goal serum trough concentrations 15–20 mcg/mL; maximum dose: 2 g

Communication

Transfer of care to the accepting health care team is an important step to maintain continuity of management. Most patients with bacterial meningitis and viral encephalitis require the oversight and care that an ICU can provide. Careful observation of the patient's respiratory status and close monitoring of his or her neurological exam with attention to decline is critical.

Table 2 outlines information that is important to pass along to the accepting health care team. Knowledge of whether the presentation was hyper-acute, acute or sub-acute; the presenting and subsequent signs and symptoms; and the results of the imaging and LP (including OP) are vital pieces of information (Table 3).

Table 3 Meningitis and encephalitis communication regarding assessment and referral

Communication sign out
☐ Presenting signs, symptoms, vital signs on admission
☐ 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 if obtained
☐ Antibiotics administered and time started
☐ IV fluid administered, input/output
☐ 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

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