emDocs

The EM Educator Series

The EM Educator Series: Meningitis – Unusual Headache and Fever

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Case 1: A 37-year-old male with a history of polysubstance abuse presents with confusion and unilateral weakness. Vital signs reveal fever.

Case 2: A 22-year-old female presents with fatigue, headache, and neck pain. She recently completed a course of antibiotics for sinusitis, but she otherwise has no past medical history.

Questions for Learners:

1. What are the major risk factors for meningitis?
2. How can patients present with meningitis?
3. What are high yield components of the history and exam?
4. What labs should be obtained?
5. When is CT recommended?
6. What are considerations with antibiotics?
7. When are steroids recommended?

Suggested Resources:

- Articles
  - IBCC – Meningitis
  - emDOCs – Why we miss meningitis and how to improve
  - emDOCs – Myths in EM: When is CT before LP needed?
  - emDOCs – Meningitis
- Journal Articles
  - American Journal of EM – High Risk/Low Prevalence Diseases: Meningitis

Answers for Learners:

1. What are the major risk factors for meningitis?

Immunocompromised
Immunocompromised patients are at higher risk for all types of infectious meningitis. While obvious populations include HIV positive patients, patients with autoimmune diseases, and cancer patients undergoing active chemotherapy or radiation therapy, patients with chronic steroid use, diabetes, obesity, chronic alcoholism, blood dyscrasias, and prior splenectomy patients should be considered immunocompromised. HIV patients have been shown to be 6 to 324-fold more susceptible to meningitis.

Age
Pediatric (particularly neonates) and elderly patients >age 65 are at increased risk for meningitis infections 11. Additionally, these patients can present with non-specific symptoms, such as trouble hearing or issues with balance. Neonates are especially susceptible to meningitis partly due to their cellular and humoral immune immaturity as well as increased permeability of the blood-brain barrier. A potential confounder in the extremes of age may be the difficulty in obtaining an accurate medical history and disease course. While there is an abundance of neonatal fever workups with geographic variances, typically, all patients under 21 to 28 days of life require a lumbar puncture.

Exposure
ENT infections increase the risk of meningitis, given the close proximity of the infection to the blood-brain barrier. Subsequently, an accurate history of recent head and neck infections or antibiotic use is important. Additionally, any history of neurosurgical procedures or placement of hardware such as a VP shunt, puts a patient at significantly increased risk. Cancer patients who underwent neurosurgery accounted for 75% of the cancer patients who developed meningitis. History of intravenous drug use, and a history of endocarditis can also increase a patient's risk of meningitis. Travel to endemic regions of meningitis also increases the risk of meningitis, possibly due to the lack of regional vaccination. In addition, young adults living in close quarters to college freshmen or military recruits may also be at increased risk for some serogroup subtypes of Neisseria meningitides.

Vaccination History
Vaccination history is key in evaluating a patient with possible meningitis. Since the introduction of vaccines, rates of bacterial meningitis have dropped significantly. More recently the group B Neisseria meningitidis vaccine and the pneumococcal vaccine have led to decreased rates of meningitis in all age groups. The introduction of the PCV7 vaccine led to significant decreases in bacterial meningitis in children aged 1-23 months. Subsequently, patients electing to forego vaccinations are at higher risk compared to the general vaccinated population.

2. How can patients present with meningitis?

frequency of symptoms in patients with bacterial meningitis *(27062097)*

- **Headache** ~80%
- **Neck stiffness** ~80%
    - Nuchal rigidity is resistance to passive flexion. Stiffness to flexion-extension reflects meningeal irritation, whereas stiffness to *rotation* does not. (LaHue 2021)

- **Fever** (>38C): ~80%
- **Nausea/vomiting** ~70%
    - Often present, but under recognized as a symptom of CNS infection.(Louis 2021)
- **Altered mental status** ~60%
    - Coma in ~15%
- Focal neurologic deficits ~30%

symptom* combinations *in meningitis

- The classic **triad** of meningitis is **fever**, **nuchal rigidity**, and **altered mental status**.
    - All three features are only seen in about 40% of patients.(27062097) If encountered this combination is highly suggestive, but it has a low sensitivity.
    - Nearly all patients with meningitis (~99%) will have at least one of these three features. However, only one feature is quite nonspecific.(8416268)
- 95% of patients with bacterial meningitis will have at least two of the following four cardinal symptoms: **fever**, **nuchal rigidity**, **altered mental status**, and **headache**.(34798976)
- When in doubt, it's generally better to err on the side of getting a lumbar puncture (especially among intubated patients who can't be closely observed for deterioration).

3. What are high yield components of the history and exam?

No single physical exam finding is accurate enough to clearly identify meningitis. However, a constellation of exam findings suggestive of meningitis in conjunction with laboratory and vital sign abnormalities may raise its suspicion. For these reasons, we highlight some classic exam findings below.

Kernig Sign: The inability to straighten the leg past 135 degrees at the knee without pain, once the hip is flexed.

Brudzinski Sign: The involuntary flexion of the hips and knees in response to the neck being flexed.

Nuchal Rigidity: Resistance to passive flexion of the neck.

Jolt Accentuation: Worsening of headache when the head is rotated with a frequency of 2-3 times per second in the horizonal axis.

A 2019 meta-analysis of nine studies looked at the sensitivity and specificity of these 4 exam findings. The results are shown below:

	Sensitivity (99% CI)	Specifitity (99% CI)	LR+ (99% CI)	LR- (99% CI)	OR (99% CI)	P values
Nuchal Rigidity	46.1% (40.5-51.7)	71.3% (67.6-74.9)	1.60 (1.35-1.91)	0.76 (0.67-0.85)	2.52 (1.21-5.27)	0.001
Jolt Accentuation	52.4% (46.2-58.6)	71.1% (66.7-75.5)	1.81 (1.5-2.2)	0.67 (0.58-0.77)	3.62 (1.13-11.60)	0.004
Kernig's sign	22.9% (17.9-28.0)	91.2% (88.8-93.6)	2.61 (1.83-3.71)	0.84 (0.79-0.91)	2.37 (0.76-7.36)	0.05
Brudzinski's sign	27.5% (21.5-33.4)	88.8% (85.8-91.7)	2.44 (1.74-3.44)	0.82 (0.75-0.89)	2.91 (1.23-6.87)	0.001

The tests have low sensitivity and are poor at ruling out meningitis. We emphasize that the absence of a specific sign should not prevent physicians from initiating a workup for meningitis.

Other notable findings on exam may include photophobia, phonophobia and a petechial rash on the extremities.

4. What labs should be obtained?

Cerebral spinal fluid (CSF) should be analyzed with cell count, gram stain, glucose, protein, and cytology. Xanthochromia will often be determined by the laboratory technician or the operator of the lumbar puncture. Opening pressure, especially in cases where the patient is immunocompromised, can be helpful in the diagnosis of Cryptococcal meningitis23. Other less commonly used but potentially helpful tests include latex agglutination and polymerase chain reaction (PCR) panels. PCR panels may test for many different infections such as HSV, VZV, EBV, CMV, enterovirus, and tuberculosis but are often expensive and only available in large institutions. More advanced testing such as for West Nile Virus, Zika, Dengue and Chikungunya is often obtained in conjunction with infectious disease specialists in the setting of a known exposure.

Of note, the Biofire meningitis PCR panel can be helpful in assisting with diagnosis and need for hospitalization. Please see this ACEP Now article by Dr. David Talan.

5. When is CT recommended?

The best available evidence suggests some association between LP and brainstem herniation in patients with intracranial mass effect lesions. However, this risk is small, and there is no evidence that deferring LP prevents herniation in patients with these lesions. Decision rules that attempt to identify patients most likely to have intracranial lesions with risk for post-LP herniation have several limitations and have not been validated. Patients with significant pre-test probability for intracranial mass effect lesion or bacterial meningitis based on clinical assessment should receive head CT.

6. What are considerations with antibiotics?

In adults, the primary empiric therapy is 2g IV of either ceftriaxone or cefotaxime (due to concern for Neisseria meningitidis), with 15-20 mg/kg IV vancomycin (to cover for resistant Streptococcus pneumoniae). If the patient is immunocompromised or >50 years old, then 2g of IV ampicillin is added due to concern for Listeria monocytogenes.

Treatment of neonatal meningitis should cover both Group B Streptococcus, Listeria spp., and E. coli. Often this is performed with 100mg/kg Q8H IV ampicillin, with gentamicin 4mg/kg Q24H IV. For young infants (28-90 days), cefotaxime 100mg/kg IV can be an alternative to gentamycin.

For older infants, the recommended treatment is vancomycin 15mg/kg Q6H, with either ceftriaxone 50mg/kg Q12H or cefotaxime 100mg/kg Q8H.

Due to concern for HSV encephalitis, 20mg/kg IV acyclovir is also usually added if at all suspected. In neonates, if there is suspicion for HSV infection in the mother this should also be added.

7. When are steroids recommended?

In addition to use of antibiotics and antivirals, steroids have been shown to reduce CSF inflammation, reduce morbidity and mortality in adults, and reduce downstream neurologic dysfunction in children. The dose is 10mg IV dexamethasone (0.6mg/kg for pediatric patients) every 6 hours for adults. If bacterial meningitis is suspected and the patient is ill appearing or has neurologic findings such as altered mental status or seizures, administration of steroids should be given before or with the first dose of antibiotics. Ideally an LP would be performed prior to administration of antibiotics to obtain an appropriate specimen for culture and sensitivity results, but if an LP cannot be performed in a timely manner do not delay administration of therapeutic medications.