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**OBJECTIVES-** Meningitis

1. In the patient with a non-specific febrile illness, look for meningitis, especially in patients at higher risk (e.g., immuno-compromised individuals, alcoholism, recent neurosurgery, head injury, recent abdominal surgery, neonates, aboriginal groups, students living in residence).
2. When meningitis is suspected, ensure a timely lumbar puncture.
3. In the differentiation between viral and bacterial meningitis, adjust the interpretation of the data in light of recent antibiotic use.
4. For suspected bacterial meningitis, initiate urgent empiric IV antibiotic therapy (i.e., even before investigations are complete).
5. Contact public health to ensure appropriate prophylaxis for family, friends and other contacts of each person with meningitis.

Meningitis is defined as inflammation of the meninges, the membranes covering the brain and spinal cord. It is most commonly due to infection, either bacterial or viral. This can happen through hematogenous spread, when bacteria invade the bloodstream (often from the upper airway), and gradually make their way to the subarachnoid space.

However, it can also happen through direct contiguous spread. This is when organisms gain entry into the cerebrospinal fluid from adjacent infections (think sinusitis, brain abscess, otitis media) or directly through penetrating traumatic injury, congenital defects, or during neurosurgical procedures.

It can at times be accompanied by inflammation of the brain tissue itself, which is called meningoencephalitis. But for today, we will focus on the meninges themselves.

The good news is that since the most common causative bugs of meningitis are:

- *Streptococcus pneumoniae*,
- *Neisseria meningitidis*, and
- *Haemophilus influenzae*,

The incidence of meningitis has declined significantly since the initiation of vaccination programs.



The bad news is that despite modern medical therapy, meningitis remains associated with a high case fatality rate of anywhere between 10-30%. And this doesn't include unfavourable neurological outcomes.

**Objective 1- In the patient with a non-specific febrile illness, look for meningitis, especially in patients at higher risk.**

When we think of meningitis, we often think of the classic meningitis triad:

- Fever,
- nuchal rigidity, and
- altered mental status.

That's right! That being said, all three features of this triad are only seen in about 40% of patients so although this triad is highly suggestive, it is far from being sensitive. Nearly all patients (~99%) will have at least one of these features, but just one is pretty non-specific.

However, in a study of 696 patients with confirmed bacterial meningitis (van de Beek et al.), they demonstrated that at least two of fever, headache, neck stiffness, and altered mental status were present in 95% of cases.

Other symptoms can include:

- nausea and/or vomiting,
- focal neurologic deficits,
- septic arthritis or
- palpable purpura.

In other words, if you've got an unexplained fever, always consider meningitis, especially if it's accompanied by nuchal rigidity, altered level of consciousness, headache or nausea/vomiting.

And especially if they are at increased risk. This includes:

- Immuno-compromised individuals (think of diabetes, chronic steroid use, splenectomy ect)
- Patients struggling with alcohol use disorder
- Recent neurosurgery or abdominal surgery
- Indwelling neurological device or cochlear implant
- Head injury, especially if suspected basal skull fracture (which can lead to a CSF leak)
- Unvaccinated folks (to H. flu, Strep penumo or N. meningitidis). This includes neonates too young for their vaccines. Here in the NWT, they receive their first doses at 2 months of age.
- Individuals living in shelters or crowded spaces, daycare, college dorms



What about those physical exam findings they always mentioned in med school?

These are the Kernig and Brudzinski signs.

#### The Kernig sign

Is described as resistance to full extension of the leg when the hip is flexed while the

#### Brudzinski sign

Is described as flexion of both hips and knees when the neck was passively flexed.

The short story is that they may not even be worth the google. There is very limited supporting evidence and low sensitivity (I mean less than 10%) of these "classic signs".

You may also hear talk of the jolt accentuation sign. It was initially thought that a negative jolt accentuation in a non-ill appearing patient would be sufficient to rule out meningitis, however multiple studies with larger cohorts demonstrated largely ranging specificities and sensitivities. All in all, it has limited diagnostic value and is not reliable to rule out meningitis.

**Objective 2: When meningitis is suspected, ensure a timely lumbar puncture.**

**Objective 3: In the differentiation between viral and bacterial meningitis, adjust the interpretation of the data in light of recent antibiotic use.**

**Objective 4: For suspected bacterial meningitis, initiate urgent empiric IV antibiotic therapy (i.e., even before investigations are complete).**

The diagnosis of meningitis is based on cerebrospinal fluid results obtained by timely lumbar puncture. The key word being "timely" here. The CSF sample is then sent for Gram stain and culture, cell count with differential, glucose, and protein.

If the patient is immunocompromised, consider adding PCR for HSV or other viral pathogens. The CSF analysis will confirm meningitis (via WBC elevation) and can help distinguish bacterial vs. viral meningitis.

When bacterial meningitis is considered, **never** withhold empiric antibiotics in order to collect the cerebrospinal fluid sample. Delaying antibiotic therapy until the LP is completed is the most common error in the acute management of meningitis.

That being said, sterilization of CSF is possible within 2 hrs, highlighting the importance of a timely LP. Empiric antibiotics should **not**, I repeat, should not be delayed if an LP cannot be obtained in a timely manner.

Early antimicrobial therapy is associated with a mortality benefit and reduced incidence of unfavourable outcomes.



Current North American adult guidelines recommend:

- a 3rd generation cephalosporin, commonly ceftriaxone 2g IV, with
- vancomycin 15 mg/kg IV with
- the addition of ampicillin 2g IV for listeria coverage for patients who are:
  - aged >50,
  - who are immunocompromised,
  - or who struggle with alcohol use disorder.
- You can also consider adding acyclovir if HSV encephalitis is suspected.

The use of dexamethasone 10mg IV given before or with the first dose antibiotics is generally supported as a 2015 Cochrane review demonstrated a lower incidence of short-term neurological sequelae, mortality in patients with *S.pneumoniae*, and hearing loss in children with *H.influenzae*.

If not given before or with the first dose of antibiotics though, forget about the steroids as there is concern that they may reduce antibiotic penetration into CSF and cause further harm.

As long as there are no contraindications to an LP. For example, you would want to withhold the LP if there is evidence of coagulopathy, until it is corrected due to the risk of bleeding complications such as an epidural hematoma.

What about a head CT prior to the LP?

We have historically been preoccupied with identifying which patients with suspected meningitis may have an intracranial mass lesion, which would put them at risk for post-lumbar puncture herniation. This has largely been driven by several case reports finding a temporal link between LP and herniation.

The concern with over-reliance on CT is that patients often do not receive antibiotics prior to their CT scan. This practice has been associated with delays in therapy and an associated increase in mortality.

So again, ensure you've got antibiotics onboard first, then order a head CT prior to LP in patients with high risk criteria. These include:

- Altered mental status or deteriorating level of consciousness
- Focal neurological deficit
- New-onset seizure
- Papilledema
- Immunocompromised state



- Malignancy
- Hx of focal CNS disease (stroke, focal infection, tumor)
  - Concern for mass CNS lesion
  - Age >60 years

So we've got antibiotics onboard, potentially a CT, with an LP within 2 hours or less of giving empiric antibiotics.

Now once you've got your CSF analysis results, you can confirm your diagnosis. Generally put, a bacterial meningitis will have:

- An elevated opening pressure
- A very high WBC, over 1000/mm<sup>3</sup>,
- With a neutrophilic predominance (usually >80%)
- Reduced glucose
- Elevated protein
- And a positive Gram stain

In viral meningitis, which tends to be more benign and for which treatment is mostly supportive, you will have:

- A normal opening pressure
- An elevated WBC, but not as impressive as a bacterial infection, usually below 300/mm<sup>3</sup>
- With a lymphocytic predominance
- Normal glucose
- Normal protein
- And a negative Gram stain

It is important to note that you may have to adjust the interpretation of the CSF data in light of recent antibiotic use. Despite a negative CSF culture, cessation of antibiotics is generally not recommended in these patients if they are suspected of having bacterial meningitis based on clinical and other lab findings. Review the other CSF parameters (eg, glucose, protein, WBC count) and review or request (if not done) CSF PCR analysis for viruses that may cause meningitis.

If the CSF PCR is positive for a viral etiology, then antibiotics can generally be discontinued.

This is also a good time to assess alternative diagnoses and remember that meningitis can also be caused by fungal infections or neoplastic processes which would require specific CSF analyses. Consider TB meningitis in patients with a history of pulmonary TB or who live in areas with high prevalence. This would most likely be guided by your helpful specialist if needed.

And since bacterial meningitis is spread by droplets, they are admitted on contact precautions, which is important to mention as it brings us to our final objective.



**Objective 5: Contact public health to ensure appropriate prophylaxis for family, friends and other contacts of each person with meningitis.**

The risk for developing bacterial meningitis post-exposure is actually estimated to be 500-800X higher than the general population. Luckily, chemoprophylaxis has been shown to decrease transmission of *N. meningitidis* by 89% in close contacts.

Chemoprophylaxis is recommended for individuals who have been in close contact with patients diagnosed with *N. meningitidis* and *H. influenzae*. It is not recommended for patients diagnosed with pneumococcal meningitis. Close contacts include housemates, individuals exposed to secretions (shared utensils or toothbrushes, kissing, mouth-to-mouth), and individuals who intubated the patient without a facemask.

To be most effective, chemoprophylaxis should be initiated within 24 hrs of contact. Risk of infection after a period of 2 weeks from exposure is considered rare, and prophylaxis is not recommended after this time period.

Treatment options for high-risk contacts include rifampin 10 mg/kg IV (to a max of 600 mg per dose) q12H for four doses, ciprofloxacin 500 mg PO once, or ceftriaxone 250 mg IM once. Although it would be prudent to contact your local public health agency to ensure appropriate treatment.

It would also be important to advise these contacts to seek medical attention immediately if they develop any symptoms of illness or meningitis.

Alright, and that is it! That's meningitis.

Shall we do a quick review.

I do love spaced repetition..

Our main take home messages today are...

1. Meningitis is defined as inflammation of the meninges, most commonly caused by infection.
2. If you've got an unexplained fever, always consider meningitis, especially if it's accompanied by nuchal rigidity, altered level of consciousness, headache or nausea/vomiting.

And especially if they are at increased risk, think immunocompromised, heavy EtOH use, recent neurosurgery or head trauma...



3. The Kernig and Brudzinski signs as well as jolt accentuation are generally unhelpful signs.
4. The diagnosis of meningitis is based on cerebrospinal fluid results showing elevated WBC obtained by **timely** lumbar puncture. Timely meaning within 2 hours of antibiotic administration. Always give antibiotics first and consider a CT head prior to LP in those at risk of a brain mass.
5. For suspected bacterial meningitis, initiate urgent empiric IV antibiotic therapy, prior to investigations. Delaying antibiotic therapy until the LP is completed is the most common error in the acute management of meningitis.

Think we pressed this enough?

IV Ceftriaxone and vancomycin are a good place to start, with consideration of adding ampicillin for those at risk of listeria. You want to give dexamethasone before or with this first dose of antibiotics, otherwise not at all.

6. To differentiate bacterial vs viral meningitis, look at the CSF analysis results. Bacterial meningitis will have a higher WBC with a neutrophilic predominance, positive gram stain, decreased glucose and increased protein. Viral meningitis will show a less impressive elevated WBC with a lymphocytic predominance, negative gram stain and normal glucose and protein.

And remember, IV antibiotics given 2 hours or less before the LP will not affect the CSF results.

7. And finally, ensure appropriate chemoprophylaxis is administered to close contacts of meningitis patients diagnosed with *N. meningitidis* and *H. influenzae*, ideally within 24 hours of contact. Check in with your local public health agency for help.