

## Educational Case: Neisseria Meningitis

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*The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see <http://journals.sagepub.com/doi/10.1177/2374289517715040>.<sup>1</sup>*

### Keywords

pathology competencies, organ system pathology, nervous system, central nervous system, brain, meningitis, disseminated intravascular coagulation, Waterhouse-Friderichsen syndrome

Received October 30, 2020. Received revised June 27, 2021. Accepted for publication August 08, 2021.

### Primary Objective

*Objective NSC2.4: Suppurative Meningitis and Abscess.* Describe the gross and microscopic features of acute suppurative meningitis and brain abscess; and name the organisms most commonly associated with each.

Competency 2: Organ System Pathology; Topic NSC: Nervous System—Central Nervous System; Learning Goal 2: Infection

### Secondary Objective

*Objective HPCD2.7: Disseminated Intravascular Coagulopathy.* Discuss disseminated intravascular coagulopathy (DIC) in terms of etiologies, pathogenesis, clinical presentation, and course.

Competency 2: Organ System Pathology; Topic HPCD: Hematopathology—Platelets and Coagulation Disorders; Learning Goal 2: Hemostasis

### Patient Presentation

An 18-year-old college student who lives in the campus dormitory presents to the emergency department (ED) with fever and a stiff neck that began a few hours earlier. He also describes a headache and nausea that started at the same time. Past medical history is noncontributory. He has not seen a

physician since the age of 13. His social history reveals recreational marijuana use and periodic alcohol ingestion.

### Diagnostic Findings, Part I

Physical examination reveals a well-nourished individual who is confused and in moderate distress. Vital signs are temperature 103 °F, heart rate 120 beats per minute, blood pressure 95/60 mm Hg, and respiratory rate of 20 breaths per minute. Cardiac examination reveals a normal S1 and S2 with regular rhythm without murmurs, heaves, or gallops. Lungs are clear to auscultation. The abdomen is soft, nontender with positive bowel sounds and no masses on palpation. A petechial rash is noted on his trunk. His skin is cold and clammy. Kernig and Brudzinski signs are positive. He is oriented to person and place but not time and has no focal neurological deficits. The remaining examination is within normal limits.

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## Questions/Discussion Points, Part I

### *What Is the Differential Diagnosis Based on the Clinical History and Physical Examination?*

The differential diagnosis for the combination of a headache and a stiff neck is broad and includes infectious, neurological, and musculoskeletal causes. Neck and upper back muscle stiffness or spasms can cause neck stiffness and secondary cervicogenic headache. Migraines classically cause a unilateral pulsating headache and can be accompanied by neck pain. The combination of neck stiffness and headache can also indicate meningeal irritation from subarachnoid hemorrhage or infection.

Patients with subarachnoid hemorrhage classically present with “the worst headache of my life.” Hemorrhage into the cerebrospinal fluid (CSF) can cause meningeal irritation and neck stiffness. Infection of the meninges by bacteria, viruses, or fungal entities can also cause meningeal irritation and present with fever, headache, and neck stiffness. The classic triad of fever, stiff neck, and altered mental status, that is, seen with meningitis, has low (44%) sensitivity for meningitis; however, nearly all patients have at least 2 of the 3 signs.<sup>2</sup>

### *What Are the Kernig and Brudzinski Signs?*

The Kernig and Brudzinski signs are physical examination findings that suggest meningeal irritation and are manifested as the body’s way to avoid stretching the meninges. The Kernig sign is resistance to passive extension of the flexed legs when the patient is lying supine. The Brudzinski sign is involuntary flexion of the hip and knee when the examiner passively flexes the patient’s neck. These signs are classically used to test for meningitis.

It is important to note that both of these physical examination findings have low sensitivity (Kernig 7%-18%; Brudzinski 7%-14%) and high specificity (Kernig 93%-98%, Brudzinski 94%-98%) for meningitis. In cases of all kinds of meningitis, the Kernig or Brudzinski signs are seen with only 61% frequency.<sup>3</sup> A study analyzing the presence of Kernig and Brudzinski signs in 297 patients with suspected meningitis found a combined positive likelihood ratio of 0.97, indicating that the tests lack diagnostic value.<sup>4</sup>

### *What Is the Differential Diagnosis for the Petechial Rash?*

A petechial rash is a rash made up of flat, nonblanching, reddish-purple dots <2 mm in diameter. If these spots are  $\geq 3$  mm in diameter, they are called purpura.<sup>5</sup> Note that there is a gray area in size between 2 and 3 mm in the definition of petechiae and purpura. Petechiae and purpura are caused by hemorrhage. The differential diagnosis is broad. Causes include infectious diseases, autoimmune diseases, coagulopathies, and minor trauma. It is also important to note the distribution and extent of petechiae. The more widespread and

numerous, the more likely there is a significant derangement in platelet count and/or function.

Minor trauma causes petechiae through the breakage of small capillaries, causing hemorrhage into the surrounding tissue. Coagulopathies are derangements of the clotting cascade and platelets that can lead to hemorrhage. The etiology of such disorders is varied. Autoimmune disorders causing petechiae include idiopathic thrombocytopenic purpura and immunoglobulin A vasculitis (formerly referred to as Henoch-Schönlein purpura). Infectious diseases that present with petechiae include Rocky Mountain spotted fever (*Rickettsia rickettsii* infection) and meningococcal meningitis (*Neisseria meningitidis* infection). Disseminated intravascular coagulation (DIC) is an acquired coagulopathy that results from a variety of etiologies such as major trauma, sepsis, obstetrical complications, and malignancy. It also presents with a petechial rash.<sup>6</sup>

### *What Further Testing Is Indicated for the Patient?*

The patient described in the clinical vignette has a fever, signs of meningeal irritation, and petechiae indicating coagulopathy. A complete blood count (CBC) would be useful to evaluate the patient for infection and thrombocytopenia. Coagulation studies should also be ordered, including prothrombin time/international normalized ratio (PT/INR), activated partial thromboplastin time (aPTT), and D-dimer. There is a concern for meningeal irritation, so a lumbar puncture (LP) should be obtained if there is a low risk for herniation to assess for opening pressure, cell count, chemistries, culture, and cytology. A CSF-PCR (polymerase chain reaction) panel for CNS pathogens should be obtained. Blood cultures should also be obtained to assess for systemic infection.

The American College of Emergency Physicians states a neuroimaging study, such as a computed tomography (CT) scan of the head, is needed before LP only if the patient is exhibiting signs suggestive of increased intracranial pressure such as papilledema, altered mental status, focal neurologic deficits, and signs of meningeal irritation in order to assess for increased intracranial pressure and reduce the risk of brain herniation prior to LP. Otherwise, a neuroimaging study does not need to be obtained before LP.<sup>7,8</sup>

Controversy exists regarding diagnosis of suspected viral meningitis. Viral meningitis is largely self-resolving and treatment is supportive.<sup>9</sup> Some argue that LP is not needed when viral meningitis is suspected due to risks of LP outweighing the benefits in the more benign clinical course of viral meningitis,<sup>9</sup> while others argue that LP needs to be done to rule out an atypical presentation of bacterial meningitis, which requires prompt antibiotic therapy.<sup>10</sup>

## Diagnostic Findings, Part 2

An initial CBC is remarkable for a white blood cell (WBC) count of  $18,000/\text{mm}^3$  ( $4,500\text{--}11,000/\text{mm}^3$ ) and platelet count of  $90,000/\text{mm}^3$  ( $150,000\text{--}400,000/\text{mm}^3$ ). The PT is 17 seconds

(11-15 seconds), INR is 1.4 (0.9-1.1), aPTT is 38 seconds (25-40 seconds), and the D-dimer is 1,100 ng/mL (<500 ng/mL). Following an unremarkable CT scan of the head, an LP is performed with an opening pressure of 250 mm H<sub>2</sub>O (70-180 mm H<sub>2</sub>O). The CSF has a yellowish, cloudy appearance. Results of the CSF analysis show a WBC count of 10,000 cells/mm<sup>3</sup> (0-5 cells/mm<sup>3</sup>), 99% neutrophils; protein 200 mg/dL (20-45 mg/dL); and glucose of 20 mg/dL (45-65mg/dL). The CSF gram stain shows gram-negative diplococci (Figure 1). CSF culture, CSF-PCR panel, and blood cultures are pending.

Four hours later, a repeat CBC is remarkable for a WBC count of 22,000/mm<sup>3</sup> and a platelet count of 40,000/mm<sup>3</sup>. Repeat coagulation studies are remarkable for a PT of 25 seconds, aPTT of 45 seconds, INR of 2.4, and a D-dimer of 3,500 ng/mL. The fibrinogen level is 0.1 g/L (0.2-0.4 g/L).

## Questions/Discussion Points, Part 2

*Given the Patient's Age and Laboratory Results, What Is the Diagnosis?*

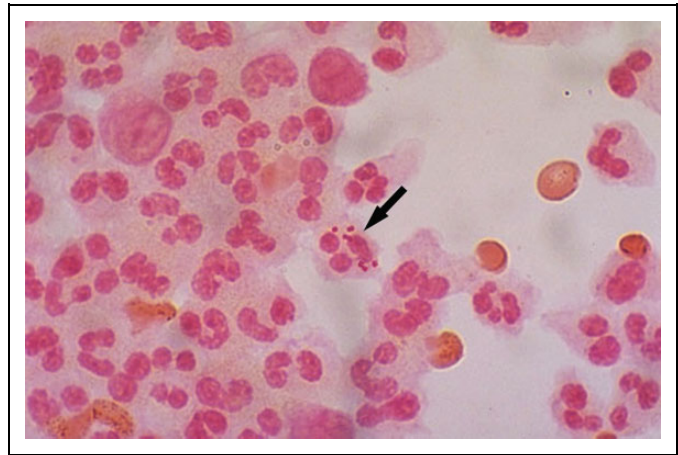
Given the patient's young age, presentation of fever and stiff neck, positive Kernig and Brudzinski signs on physical examination, elevated WBC count, and CSF findings, this patient has acute bacterial meningitis. The patient is also likely septic. The patient's coagulation studies, including increased PT, INR, aPTT, and D-dimer over a 4-hour period, combined with his progressive thrombocytopenia, indicate a consumptive coagulopathy (DIC).

*What Organism Is the Most Likely Culprit?  
List the Most Common Causative Agents  
in Neonates and the Elderly Patients*

*Neisseria meningitidis*, a significant cause of bacterial meningitis in young otherwise healthy individuals with sepsis, is the most obvious causative organism for this patient's meningitis. Meningitis caused by *N meningitidis* is called meningococcal meningitis.

*Neisseria meningitidis* is an encapsulated gram-negative diplococcus bacteria with several serotypes that colonizes the nasopharynx in up to 40% of the population.<sup>11</sup> This patient currently lives in dormitory housing, which likely exposed him to a strain of *N meningitidis* that he was not immune to.<sup>12</sup> Others who are at high risk for developing *N meningitidis* infection are those with asplenia and complement deficiencies.

The most common causative agents of meningitis differ based on a patient's age. Both neonates and the elderly patients are more prone to developing meningitis. The causative organism differs in each population.<sup>13</sup> Group B *Streptococcus* and *Escherichia coli* are common causative agents in neonates, as compared to the elderly patients in whom *Streptococcus pneumoniae* and *Listeria monocytogenes* are common.



**Figure 1.** Cerebrospinal fluid (CSF) gram stain reveals numerous neutrophils. The neutrophil at the arrow demonstrates several gram-negative diplococci within the cytoplasm, a feature consistent with *Neisseria meningitidis* infection. Republished with permission from web path (<https://webpath.med.utah.edu/CNSHTML/CNSI91.html>).

*What Are the Typical Cerebrospinal Fluid Findings in the First 24 to 48 Hours of Bacterial Meningitis?*

Cerebrospinal fluid analysis is useful for determining the etiology of meningitis. In bacterial meningitis, the opening pressure upon LP is usually markedly elevated. There is typically a pleomorphic leukocytosis with a differential of main neutrophils. Because bacteria are present within the CSF itself, the CSF will have low glucose. The CSF protein content is elevated due to inflammation. A CSF gram stain may demonstrate the etiologic organism.<sup>2</sup>

*What Is the Most Common Causative Agent for Viral Meningitis, and How Would the Cerebrospinal Fluid Findings Differ From Bacterial Meningitis?*

The most common causative agents for viral meningitis (a common cause of aseptic meningitis) are enteroviruses, which account for 80% of cases.<sup>13</sup> A CSF-PCR panel identifies common pathogens associated with meningitis from 1 mL of CSF and is useful in identifying the etiologic agent within hours. At our institution, this panel tests for *E coli*, *Haemophilus influenzae*, *L monocytogenes*, *N meningitidis*, *Streptococcus agalactiae*, *S pneumoniae*, cytomegalovirus, Enterovirus, Herpes simplex virus (HSV)1, HSV2, human herpesvirus 6, human parechoviruses, Varicella-zoster virus, and *Cryptococcus neoformans/gattii*. The CSF can also be cultured for bacteria and fungus, and a separate Cryptococcal antigen test to identify a protein made by *Cryptococcus* can be performed. Cerebrospinal fluid findings as well as presentation are usually milder in viral meningitis when compared to bacterial meningitis. Typically, leukocytosis is less prominent in the CSF and is composed of lymphocytes. The glucose can be normal or low, but the protein is still high. The opening pressure is only slightly elevated above normal (Table 1).

### How Should Bacterial Meningitis Be Treated?

Empiric intravenous (IV) antibiotics should be started as soon as possible after the diagnosis of bacterial meningitis is suspected or proven. Although LP and CSF analysis is desirable and should be done immediately if feasible, it should not delay the administration of antibiotics. Delays in antibiotic treatment >6 hours after presentation are associated with adverse outcomes.<sup>14</sup> A retrospective review of 123 cases of adult acute bacterial meningitis found that the risk of death in patients was 8.4 times higher when antibiotics were delayed >6 hours after presentation, with delay in antibiotic administration for CT and LP being a common cause of delay.<sup>15</sup> The Infectious Disease Society of America recommends that at least blood cultures should be obtained before empiric antibiotics are administered if an LP will be delayed.<sup>16</sup>

For patients <50 years old and with no risk factors for *L monocytogenes* infection, the empiric antibiotic regimen should include vancomycin and a third-generation cephalosporin such as ceftriaxone. If the patient is >50 years old, ampicillin should be added to this regimen.<sup>17</sup> The antibiotic regimen can be narrowed when the causal organism is identified by culture. For example, if *N meningitidis* is identified, patients can be switched to IV aqueous penicillin G.<sup>11</sup>

Dexamethasone, a corticosteroid, should also be initiated before or with IV antibiotics. The use of dexamethasone has been shown to decrease mortality rates and to decrease the complications of infection.<sup>17</sup>

### What Are Some Possible Complications of Acute Bacterial Meningitis?

The complications of acute bacterial meningitis are initially related to the effects of the infection at the focal neurological level; however, if the infection becomes systemic, widespread complications can result. Neurological complications include seizures, brain abscess, mental retardation, both sensorineural and conductive hearing loss, cranial nerve abnormalities principally of the third, fourth, sixth, or seventh cranial nerves, and fibrosis of the meninges and brain parenchyma, which can obstruct CSF circulation. Focal neurological signs such as hemiparesis and visual field defects occur in approximately one-third of adults with community-acquired bacterial meningitis.<sup>18</sup> Widespread complications can result from seeding of the infection and include endocarditis and pyogenic arthritis. Shock and sepsis can occur, leading to limb ischemia and gangrene. Disseminated intravascular coagulation is also seen.

### What Is the Most Likely Diagnosis for This Patient's Coagulopathy?

The most likely cause for this patient's progressively worsening coagulopathy is DIC. Disseminated intravascular coagulation is an acquired coagulopathy characterized by the abnormal

**Table 1.** CSF Findings in Bacterial Versus Viral Meningitis.<sup>2</sup>

Test	Normal	Bacterial	Viral
Cells/mm <sup>3</sup>	0-5	200-20,000 neutrophils	25-2,000 lymphocytes
Glucose (mg/dL)	45-85	<45 (low)	Normal or low
Protein (mg/dL)	15-45	>50 (high)	>50 (high)
Opening pressure (mm H <sub>2</sub> O)	70-180	Markedly elevated	Slightly elevated

Abbreviation: CSF, cerebrospinal fluid.

**Table 2.** International Society on Thrombosis and Hemostasis (ISTH) Score for Diagnosis of DIC.<sup>19</sup>

Test	Results	Score
Platelet count, (platelets × 10 <sup>9</sup> /L)	>100	0
	50 to <100	+1
	<50	+2
D-dimer	No increase	0
	Moderate increase	+2
	Severe increase	+3
Prolonged PT over normal value, seconds	<3	0
	>3 to <6	+1
	>6	+2
Fibrinogen level, g/L	>1	0
	<1	+1

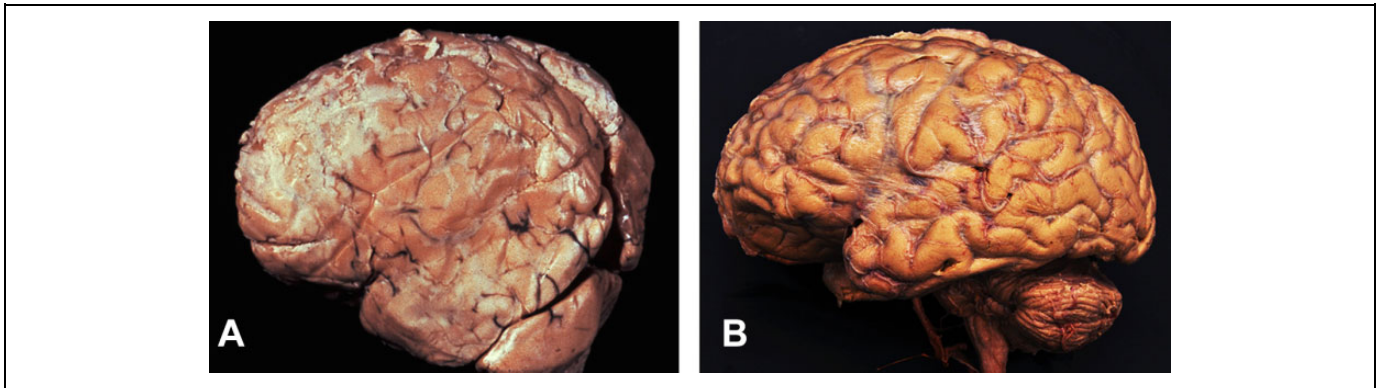
Abbreviation: DIC, disseminated intravascular coagulation.

activation of coagulation factors that causes both thrombosis and hemorrhage. Risk factors for the development of DIC include sepsis, severe trauma, obstetrical complications, and malignancy. This patient's overwhelming bacterial infection and sepsis likely triggered DIC. Disseminated intravascular coagulation is reported in 10% to 20% of critical care admissions, and the mortality rate is as high as 46%.<sup>6</sup>

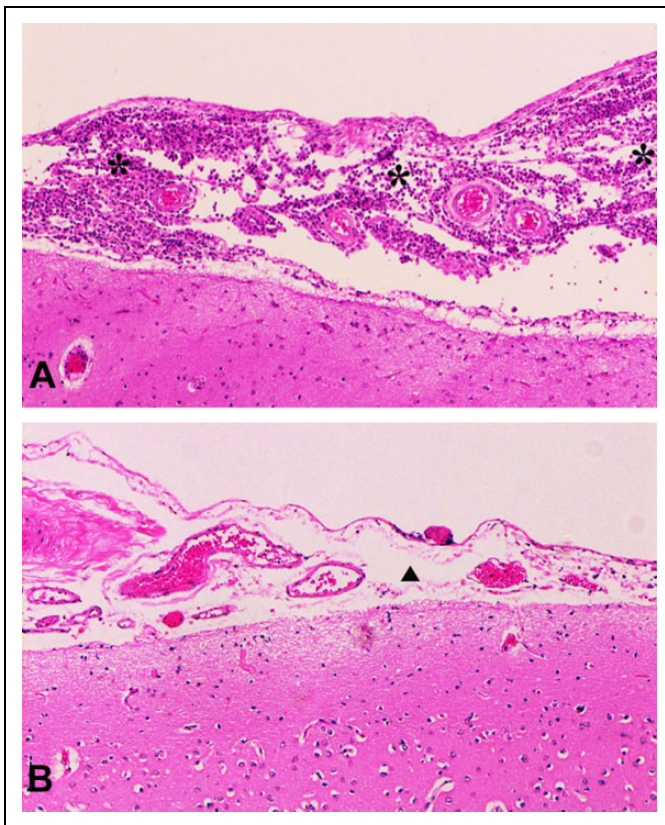
The International Society on Thrombosis and Hemostasis (ISTH) score can be used to diagnose DIC (Table 2). A score of >5 points correlates with DIC, and a score of <5 points means that DIC is less likely.<sup>6,19</sup> The ISTH score has a sensitivity of 93% and a specificity of 98%.<sup>6</sup>

For the patient in the clinical vignette above and using his second set of lab values, our patient would score 7 points (platelets 40,000/mm<sup>3</sup>, D-dimer moderately increased at 3,500 ng/mL, PT 25 seconds, fibrinogen 0.1 g/L), which is consistent with the diagnosis of DIC.

Treatment of DIC consists of treating the underlying cause and supportive measures. Patients with serious bleeding can be given blood, platelet, and fresh frozen plasma transfusions as indicated. Thrombosis can be treated with heparin.<sup>20</sup> However, both blood products and anticoagulants should be given with caution. Their use may be detrimental because DIC features both simultaneous clotting and bleeding, with either bleeding or clotting potentially being exacerbated by treatment of the other.



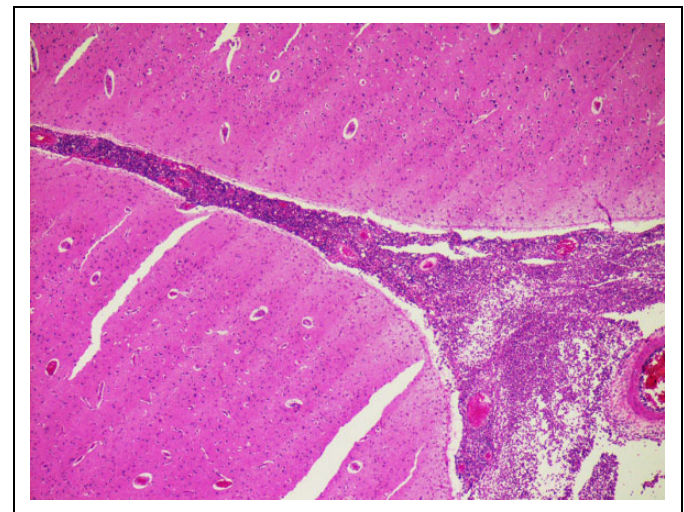
**Figure 2.** A, Acute bacterial meningitis. Brain shows a prominent white exudate involving the leptomeninges most prominent over the frontal lobe, compared to the normal translucent leptomeninges covering the fixed brain in B.



**Figure 3.** A, The subarachnoid space in acute bacterial meningitis is distended by a prominent neutrophilic infiltrate (\*) compared to the subarachnoid space (arrowhead) in the normal leptomeninges in B (hematoxylin and eosin [H&E], intermediate magnification).

### Diagnostic Findings, Part 3

Empirical intravenous ceftriaxone and vancomycin are started in the ED and the patient is admitted to the intensive care unit. The patient's mental status continues to deteriorate and aggressive fluid resuscitation and pressors are needed to maintain his blood pressure. The CSF-PCR panel is positive for *N meningitidis*. Cerebrospinal fluid and blood cultures both grow *N meningitidis*.



**Figure 4.** The subarachnoid and perivascular (Virchow-Robin) space is distended with an acute inflammatory infiltrate. Brain parenchyma is not involved (hematoxylin and eosin [H&E], intermediate magnification).

After admission, the patient starts bleeding from his venipuncture and IV sites. His skin becomes mottled, and he suddenly has a grand mal seizure and then becomes unresponsive. Despite aggressive resuscitation efforts, the patient dies. An autopsy is performed.

### Questions/Discussion Points, Part 3

*Describe the Gross and Histologic Findings Seen in the Brain and Adrenal Gland*

Figures 2 through 4 are images of the brain and Figures 5 and 6 are images of the adrenal gland. There is prominent vascular congestion with perivascular exudate on the brain surface (Figure 2). A histological section through the leptomeninges shows an intense neutrophilic infiltrate distending the subarachnoid and perivascular (Virchow-Robin) space (Figures 3 and 4). The brain parenchyma is uninvolved. The gross



**Figure 5.** A, Waterhouse-Friderichsen syndrome. Hemorrhage replaces the entire adrenal gland on cross section compared to the normal adrenal gland in B.

appearance of the adrenal gland on cross section demonstrates marked hemorrhage compared to the normal adrenal gland (Figure 5). Hemorrhagic infarction of the adrenal cortex is present on histologic examination (Figure 6).

#### ***Based on the Images, What Is the Cause of Death?***

The subarachnoid and perivascular neutrophilic exudate distending the leptomeninges is diagnostic of acute bacterial meningitis as the underlying cause of death. The presence of bilateral adrenal hemorrhage leading to acute adrenocortical insufficiency is a complication of bacterial meningitis.

#### ***What Is Waterhouse-Friderichsen Syndrome?***

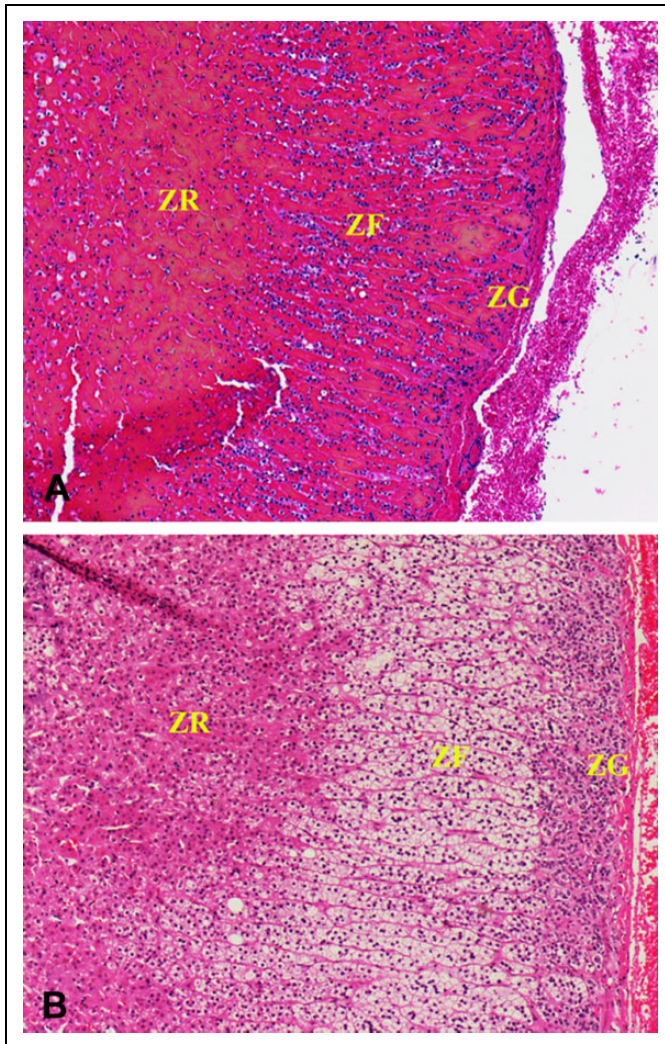
Waterhouse-Friderichsen syndrome is a disorder characterized by adrenal gland hemorrhage that results in primary adrenal insufficiency. It occurs as a complication of overwhelming bacterial infection, classically from *N meningitidis*. The

syndrome is associated with the development of DIC, widespread purpura, and rapidly progressive hypotension that leads to shock. The hypotension is due in part to the lack of catecholamine secretion from the adrenal medulla. The lack of epinephrine and norepinephrine leads to loss of the stress response, most important the loss of blood vessel tone.

Waterhouse-Friderichsen syndrome is characterized histologically by widespread hemorrhage that starts in the adrenal medulla near the venous sinusoids. The hemorrhage then extends peripherally into the cortex, through the zona reticularis, zona fasciculata, and the zona glomerulosa.<sup>21</sup>

#### ***What Is a Brain Abscess and Which Bacterial Organisms Most Commonly Cause it in Immunocompetent Patients?***

A brain abscess is a focal point of necrosis and inflammation of brain tissue that is most commonly caused by a bacterial infection. The bacteria reach the brain by direct implantation (eg, ventriculoperitoneal shunt), local extension from adjacent sites



**Figure 6.** A, The adrenal gland shows hemorrhagic infarction of the adrenal cortex compared to the normal adrenal gland in B (hematoxylin and eosin [H&E], intermediate magnification). ZF indicates zona fasciculata; ZG, zona glomerulosa; ZR, zona reticularis.

(eg, mastoiditis), or via hematogenous spread (eg, endocarditis). The most common organisms implicated in immunocompetent patients are streptococci and staphylococci.<sup>13</sup> Anaerobes, including *Fusobacterium*, *Prevotella*, and *Actinomyces*, as well as polymicrobial infections, are also commonly implicated in brain abscess formation when tested for.<sup>22</sup>

#### What Postexposure Prophylaxis, If Any, Should be Given to His Close Contacts?

With cases of confirmed *N meningitidis* infection, the patient's close contacts should be given prophylactic antibiotics to prevent secondary cases. Different antibiotic regimens are available for prophylaxis.<sup>11</sup> Close contacts are people that the patient lives with and shares space with for extended periods

**Table 3.** CDC Guidelines for Childhood Vaccinations.<sup>24</sup>

Vaccine	Pathogen	Recommended administration
Meningococcal conjugate (MenACWY)	<i>Neisseria meningitidis</i>	All persons 1st dose: 11-12 years old  Booster: 16 years old *High-risk persons
Serogroup B meningococcal (MenB)	<i>Neisseria meningitidis</i> serogroup B	*High-risk persons
Hib vaccination	<i>Haemophilus influenzae</i> type B	All persons 1st dose: 2 months 2nd dose: 4 months 3rd dose: 6 months 4th dose: 12-15 months
PCV13 (pneumococcal conjugate)	<i>Streptococcus pneumoniae</i>	All persons 1st dose: 2 months 2nd dose: 4 months 3rd dose: 6 months 4th dose: 12-15 months
PPSV23 (pneumococcal polysaccharide)	<i>Streptococcus pneumoniae</i>	*High-risk persons

\* See CDC guidelines.

of time, such as family or dorm mates. School and work contacts do not need to be treated.

#### What Are the Childhood Vaccines Against Bacterial Meningitis? What Pathogens Do They Target, and When Are They Administered?

Several childhood vaccines provide protection against bacterial meningitis, including *N meningitidis*, *S pneumoniae*, and *H influenzae* type B. *Haemophilus influenzae* type B was a common cause of meningitis in children before the vaccine was introduced.<sup>23,24</sup> Table 3 lists Centers for Disease Control and Prevention (CDC) guidelines for childhood vaccinations.

Aside from routine administration, high-risk persons should either receive certain vaccines earlier in life or should receive vaccines that are specifically for high-risk groups. For example, HIV-positive patients, asplenic, and patients with complement deficiency should receive the meningococcal conjugate vaccine early and should also receive the serogroup B meningococcal vaccination that is not a part of the routine childhood vaccination schedule. Also, individuals at high risk for contracting meningococcal meningitis, such as working in the military, working in a microbiology lab, or travel to areas of the world where meningococcal infection is endemic (the "meningitis belt" in sub-Saharan Africa) should receive meningococcal vaccine boosters every 5 years.<sup>23</sup>

## Teaching Points

### *Neisseria meningitidis* meningitis:

- Empiric intravenous antibiotics should be started as soon as possible after the diagnosis of bacterial meningitis is suspected or proven. Although obtaining blood cultures, neuroimaging studies, and CSF analysis is desirable and should be done immediately if feasible, they should not delay the administration of antibiotics.
- Kernig and Brudzinski signs are classically associated with meningitis but have low sensitivities and high specificities. They have little diagnostic value.
- A noncontrast CT scan of the head should be done in patients with signs of increased intracranial pressure, acute mental status change or neurological deficits, and signs of meningeal irritation before lumbar puncture to avoid the risk of brain herniation when CSF is drawn.
- Bacterial meningitis is characterized by a high CSF WBC count with many neutrophils, low glucose, and high protein. In contrast, viral meningitis is characterized by a moderate WBC count with many lymphocytes, normal glucose, and high protein.
- Different organisms more commonly cause bacterial meningitis in patients of different age groups. In neonates, Group B *Streptococcus* and *Escherichia coli* are the most common pathogens, while in the elderly patients *Streptococcus pneumoniae* and *Listeria monocytogenes* are more common.
- Waterhouse-Friderichsen syndrome occurs classically with *N meningitidis* infection and is characterized by bilateral adrenal hemorrhage and subsequent circulatory collapse.
- Bacterial meningitis, grossly, shows prominent vascular congestion with perivascular exudate on the brain surface. Frank pus can often be seen.
- The histological features of acute bacterial meningitis show a neutrophilic infiltrate in the leptomeninges that distends the subarachnoid and perivascular (Virchow-Robbin) space. The brain parenchyma is usually uninvolved.
- Postexposure antibiotic prophylaxis is needed for close contacts of patients who have *N meningitidis* infection to prevent secondary cases.
- Routine childhood vaccinations play a key role in the prevention of bacterial meningitis.

### Disseminated intravascular coagulation (DIC):

- DIC is an acquired coagulopathy with a variety of etiologies, including sepsis, malignancy, severe trauma, and obstetrical complications.
- DIC can result in both thrombosis and hemorrhage, and clinical manifestations can represent either or both of these etiologies.

- Characteristic laboratory findings in DIC include thrombocytopenia, prolonged PT and aPTT, elevated D-dimer, and decreased fibrinogen.
- The International Society on Thrombosis and Hemostasis score can be used to estimate the likelihood of the diagnosis of DIC based on laboratory findings.
- DIC is common in critical care setting admissions and the mortality is very high, highlighting the importance of DIC awareness in the acutely ill patient as well as the importance of swift diagnosis and treatment of the underlying cause.
- The gross features of Waterhouse-Friderichsen syndrome are marked bilateral adrenal hemorrhage and extensive necrosis. Histologically, the hemorrhage includes both the adrenal cortex and the medulla.

### Author's Note

Figures 2 through 6 were obtained during the scope of US government employment for Dr Conran.


### Declaration of Conflicting Interests


The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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