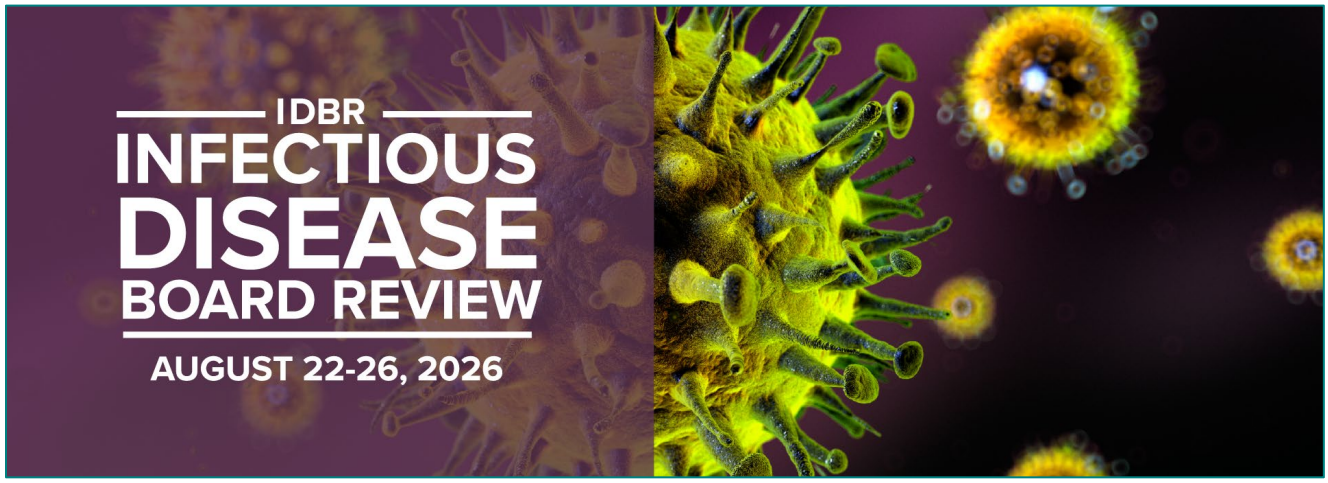


2026 IDBR Faculty Board Review Session Book

Course Directors:
John Bennett, MD
Henry Masur, MD

Course Co-Directors:
Barbara D. Alexander, MD, MHS
David Aronoff, MD
Paul Auwaerter, MD
Roy Gulick, MD, MPH
Robin Patel, MD
Andrew Pavia, MD
Richard Whitley, MD

IDBR Question Editor
Karen Bloch MD, MPH

Course Accredited by:

GW | Office of Continuing Education in the Health Professions

Contents

SESSION 1 | SATURDAY, AUGUST 22, 2026

Session Moderator: Dr. Patel

Session Panelists: Drs. Alexander, Pavia, Saullo, and Tamma

Question #	Topic	Speaker
1	Cytomegalovirus Prophylaxis	Alexander
2	*Blastomyces* Stain	Patel
3	Influenza Rx	Pavia
4	Disseminated Toxoplasmosis	Saullo
5	Cellulitis Therapy	Tamma
6	*Cunninghamella*	Alexander
7	Culture Negative Endocarditis	Patel
8	Phlebovirus Disease	Pavia
9	HHV 6 Encephalitis and Rx	Saullo
10	Metronidazole	Tamma
11	Latent TB Rx	Alexander
12	Cryptococcal Meningitis	Patel
13	Hantavirus	Pavia
14	Household Measles Contact	Saullo
15	Sinusitis Rx	Tamma

This page left blank intentionally.

1 | CYTOMEGALOVIRUS PROPHYLAXIS | ALEXANDER

A CMV seronegative renal transplant recipient received an allograft from a CMV seropositive donor. Valganciclovir prophylaxis was started. After one month, he developed refractory leukopenia despite optimal dosing of valganciclovir for renal function and stopping mycophenolate.

What is the best option for CMV prophylaxis?

A. Stop valganciclovir; start every other week preemptive monitoring with a blood-based CMV PCR test

B. Stop valganciclovir and start valacyclovir

C. Stop valganciclovir and start letermovir

D. Stop valganciclovir and start maribavir

E. Decrease to half dose valganciclovir

Correct answer: Stop valganciclovir and start letermovir

Rationale

This kidney transplant recipient is at high serologic risk for CMV (donor positive, recipient negative). Accordingly, prophylaxis against CMV is recommended for the first 6 months post-transplant. Valganciclovir is the most frequently used drug for CMV prophylaxis following solid organ transplant. Leukopenia is a relatively common side effect.

Preemptive prophylaxis requires weekly monitoring; less frequent screening results in higher rates of CMV disease and inferior long-term graft survival compared with universal prophylaxis. Thus, every other week screening is not the correct option here.

While valacyclovir has excellent activity against VZV and HSV, the activity against CMV is less and requires high doses. Long-term follow-up also shows a higher incidence of acute rejection and allograft fibrosis at 3 years after transplant in those receiving valacyclovir compared with valganciclovir. Thus, transitioning to valacyclovir is not optimal.

Maribavir is an oral antiviral that prevents phosphorylation of essential viral proteins, preventing CMV replication. It is also active against EBV, although not against other herpes group viruses (HSV, VZV). Maribavir is an option to treat refractory or resistant CMV infection but is not approved for CMV prophylaxis in solid organ transplant recipients.

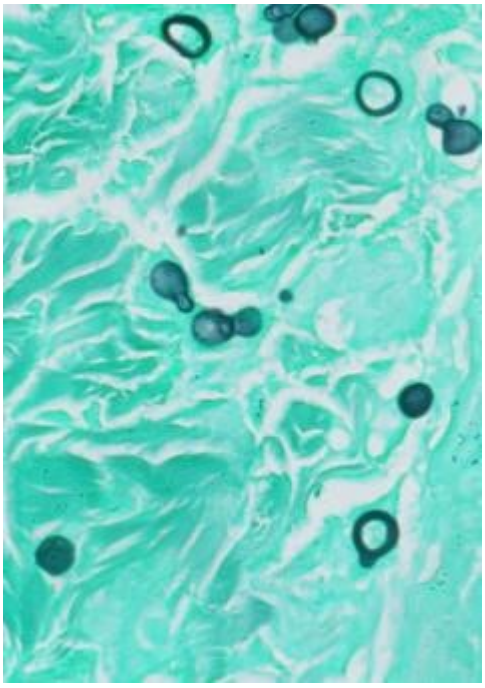
Subtherapeutic antiviral drug exposure during prophylaxis can lead to breakthrough infection with drug-resistant CMV. A large study showed that breakthrough infection on prophylaxis is more likely to occur in recipients with valganciclovir doses renally adjusted below the manufacturer's recommendations. Thus, low dose valganciclovir prophylaxis is not recommended; dosing should be according to renal function.

Letermovir was approved by the FDA in 2023 based on a clinical trial that demonstrated it to be non-inferior to valganciclovir for prophylaxis of CMV disease in renal transplant recipients at high serologic risk for CMV. The trial also showed less leukopenia in the letermovir arm. Thus, letermovir is the best alternative option in the setting of leukopenia. Acyclovir should be added for herpes simplex virus prophylaxis.

2 | *BLASTOMYCES* STAIN | PATEL

A 32-year-old woman in Wisconsin who worked as a farmer, presents to her family physician in June with a 3-week history of low-grade fever, myalgias, and a productive cough, and a skin lesion on her arm that developed over the previous week. The physician found an infiltrate on chest x-ray and collected sputum and a biopsy from the skin lesion for culture and histopathology.

The organisms shown here were seen when the tissue was stained with a silver stain. After 14 days, a mold grew in the fungal culture.



Which of the following is the most likely pathogen?

- **A. *Blastomyces* species**
- B. *Candida* species
- C. *Coccidioides* species
- D. *Cryptococcus* species
- E. *Histoplasma* species

Correct answer: *Blastomyces* species

Rationale

This patient has blastomycosis with dissemination to the skin, a common site of dissemination. *Blastomyces* species are dimorphic fungi with yeast cells observed in tissue and grow as filamentous molds in culture.

The large yeasts are characterized by a thick wall and a broad base when budding is observed.

Candida and *Cryptococcus* species are not dimorphic, growing as yeasts in tissue and culture.

Coccidioides and *Histoplasma* species are dimorphic fungi; in tissue, *Coccidioides* species appear as non-budding spherules and *Histoplasma* species as yeast with narrow based buds; both grow as molds in culture. (*Candida* species may form pseudohyphae.)

3 | INFLUENZA RX | PAVIA

A 72-year-old retired firefighter who has a history of chronic obstructive lung disease is seen in the emergency department because of 96 hours of cough, chills, sore throat, and body aches. He lives in an assisted care facility where he has his own room but takes meals in a congregate dining room.

He reports that several other residents and servers in the dining room have been coughing. In the emergency department, a test for influenza is positive. He is hypoxemic and admitted to the intensive care unit.

Regarding treatment for influenza, what should he receive?

A. No specific anti-viral because the patient has been ill for substantially more than 48 hours

B. Baloxavir

C. Peramivir

D. Oseltamivir

E. Zanamivir

Correct answer: Oseltamivir

Rationale

Although 48 hours is used as a symptom interval beyond which specific anti-viral treatment is not recommended for outpatients, this interval is waived for patients who are sick enough to be hospitalized. So, this patient should be treated.

Zanamivir is given by inhalation and would be difficult to administer in this hypoxemic, acutely ill patient with lung disease.

Peramivir's effectiveness is similar to oseltamivir. The advantage of peramivir is that it is given intravenously and thus is the appropriate option for patients that cannot take any medications enterally. Peramivir is much more expensive and no more effective than oseltamivir. There is no indication in the question that the patient cannot take oral medications; hence, oseltamivir is preferred.

Baloxavir is single-dose oral option for influenza but almost all experience to date is with treating outpatients, so it is not a first-line option for this hospitalized patient. In addition, some data suggest that the barrier to acquired resistance is low which further diminishes enthusiasm to use this agent as monotherapy for severe disease in vulnerable patients.

CDC statements are extremely helpful, but do not always guide practice: however, in terms of the "correct" answer for an exam, keep in mind this 2025 CDC communication (IDSA 2019 guidelines are similar):

"For hospitalized patients with suspected or confirmed influenza, initiation of antiviral treatment with oral or enterically administered oseltamivir is recommended as soon as possible.

For outpatients with complications or progressive disease and suspected of confirmed influenza, initiation of antiviral treatment with oral oseltamivir is recommended as soon as possible.

For outpatients with suspected or confirmed uncomplicated influenza, oral oseltamivir, inhaled zanamivir, intravenous peramivir, or oral baloxavir may be used for treatment, depending upon approved age groups and contraindications. In one randomized controlled trial, baloxavir had greater efficacy than oseltamivir in adolescents and adults with influenza B virus infection."

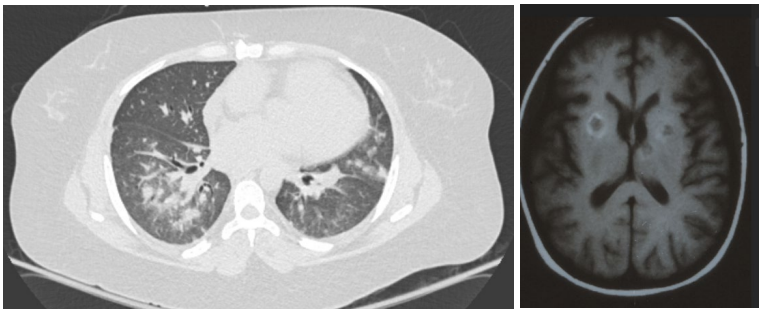
4 | DISSEMINATED TOXOPLASMOSIS | SAULLO

A 50-year-old woman is admitted with 1 month of fever, dyspnea, and confusion. She underwent heart transplantation 15 months ago from a donor who was seropositive for cytomegalovirus (CMV), Epstein-Barr virus (EBV), and *Toxoplasma*, while she was seropositive for CMV but seronegative for EBV and *Toxoplasma*.

She completed 3 months of valganciclovir prophylaxis and 12 months of sulfamethoxazole-trimethoprim prophylaxis and is on chronic immunosuppression with tacrolimus, prednisone, and mycophenolate.

On presentation: T 39.0°C, HR 130, BP 100/60, and RR 30, SpO_2 82% on room air.

Relevant computed tomography (CT) imaging of the lungs (left) and brain magnetic resonance imaging (MRI, right) are below.



Initial microbial testing, including blood cultures, serum cryptococcal antigen, and CMV quantitative plasma PCR, is negative.

Which of the following prophylactic antimicrobial therapies would most likely have prevented this complication?

A. Acyclovir
B. Valganciclovir
C. Letermovir
D. Fluconazole
E. Sulfamethoxazole-trimethoprim

Correct answer: Sulfamethoxazole-trimethoprim

Rationale

The patient is experiencing disseminated toxoplasmosis following heart transplantation.

Toxoplasmosis represents a severe and potentially fatal opportunistic infection in transplant recipients. During post-transplant immunosuppression, encysted bradyzoites from either the donor or recipient may proliferate into tachyzoites, which destroy infected cells and can result in localized or disseminated infection.

Heart transplant recipients represent the solid organ transplant population most commonly affected by toxoplasmosis. The highest risk occurs during the first post-transplant year, particularly for donor-derived infection in seronegative recipients paired with seropositive donors, due to the absence of preexisting immunity.

Reactivation of infection is also observed in seropositive recipients. Prophylaxis is therefore essential. Although the first year is the period of greatest risk, infection can occur beyond one year, especially in high-risk mismatched patients after discontinuation of prophylaxis, as demonstrated in this case.

Toxoplasmosis may present as pneumonitis, myocarditis, meningoencephalitis, chorioretinitis, or disseminated disease, as seen.

CT findings supporting toxoplasmosis in this case include bilateral ground-glass and nodular opacities on chest imaging. Characteristic central nervous system findings, such as ring-enhancing lesions in the basal ganglia, were also observed.

Sulfamethoxazole-trimethoprim (SMX-TMP) is the preferred agent for toxoplasmosis prevention in heart transplant recipients. Due to the risk of late-onset and severe toxoplasmosis in high-risk donor seropositive/recipient seronegative (D+/R-) heart transplant recipients, the American Society of Transplantation guidelines recommend consideration of lifelong prophylaxis in this population (2019, weak, low evidence). If prophylaxis is discontinued, ongoing clinical monitoring, including diagnostic testing with polymerase chain reaction (PCR), and early empiric therapy are advised.

Acyclovir is used to prevent herpes simplex virus (HSV) and varicella zoster virus (VZV) infections following transplantation. Although these viruses can cause severe, disseminated infections, such as pneumonitis and meningoencephalitis, the severity, timeline, and clinical course in this case are more consistent with toxoplasmosis.

Valganciclovir is used to prevent cytomegalovirus (CMV) infection and provides protection against HSV and VZV. Although CMV infection can occur in the late post-transplant period, the infection timeline, recent discontinuation of SMX-TMP, and negative CMV quantitative plasma PCR make CMV infection unlikely.

Letermovir is similarly used for CMV prophylaxis and is not the most appropriate choice for the same reasons as valganciclovir. Additionally, letermovir is FDA-approved for CMV prophylaxis in high-risk (CMV D+/R-) renal transplant recipients, but not in heart transplant recipients, although off-label use does occur.

Fluconazole is an azole antifungal that can be used to prevent fungal infections, but is not typically administered for extended periods after heart transplantation. Although disseminated cryptococcal infection could explain some aspects of this presentation, it is not the most likely diagnosis. Furthermore, while a negative serum cryptococcal antigen test does not fully exclude this diagnosis, it reduces its likelihood.

Relevant reference: La Hoz RM, Morris MI. Clin Transplant. 2019 Sep;33(9):e13546. PMID: 30900295.

5 | CELLULITIS THERAPY | TAMMA

A 46-year-old man presents for follow-up after being diagnosed with non-purulent cellulitis of the lower leg. Three days ago, he was started on cephalexin. At that time, he had fever, localized erythema, and tenderness over the anterior shin.

Today, he reports that his fever and malaise have resolved, and that his leg is less painful. On examination, the affected area remains warm and erythematous. The area of erythema is slightly larger than at the initial visit. There are no bullae, fluctuance, or necrosis, and vital signs are normal.

Which of the following is the most appropriate next step in management?

A. Switch to intravenous antibiotics

B. Continue the current oral antibiotic regimen to complete a 5-day course

C. Add trimethoprim–sulfamethoxazole for MRSA coverage

D. Refer the patient to the emergency department for further evaluation

E. Continue the current oral antibiotic regimen to complete a 10-day course

Correct answer: Continue the current oral antibiotic regimen to complete a 5-day course

Rationale

Early during the treatment of non-purulent cellulitis, the area of erythema may appear unchanged or even expand slightly despite appropriate therapy. This phenomenon can occur due to toxin-mediated inflammation or local edema and does not necessarily indicate treatment failure.

Clinical improvement is best assessed by resolution of systemic symptoms (e.g., fever, malaise), decreased pain or tenderness, and stabilization or improvement of local findings.

In this case, the patient's systemic symptoms have improved, and the erythema is less intense, suggesting an appropriate response to therapy.

The duration is important here and antibiotic utilization is a relevant topic for the boards. The American College of Physicians has published best practice advice outlining common scenarios when short-course antibiotics are appropriate (Lee RA et al; Appropriate Use of Short-Course Antibiotics in Common Infections: Best Practice Advice From the American College of Physicians. Ann Intern Med. 2021 Jun;174(6):822-827). This includes a recommendation that a 5–6-day course of anti-streptococcal therapy for non-purulent cellulitis is sufficient if the patient is clinically improving.

Intravenous therapy is typically reserved for patients who are systemically ill or unable to take oral or failing oral therapy. MRSA coverage is generally not required for non-purulent cellulitis, which is most commonly caused by β-hemolytic streptococci. Emergency department evaluation is warranted if there are findings of rapid progression, systemic toxicity, necrosis, or bullae, none of which are present in this patient.

6 | *CUNNINGHAMELLA* | ALEXANDER

A 68-year-old man underwent heart transplant and is maintained on mycophenolate mofetil, tacrolimus, and prednisone, as well as valganciclovir, atovaquone and nystatin swish & swallow.

He was previously diagnosed with invasive pulmonary aspergillosis. At the time of diagnosis, blood and BAL galactomannan were positive/above the upper limit of the assay, and 1,3 beta-D-glucan was >500 pg/ml positive.

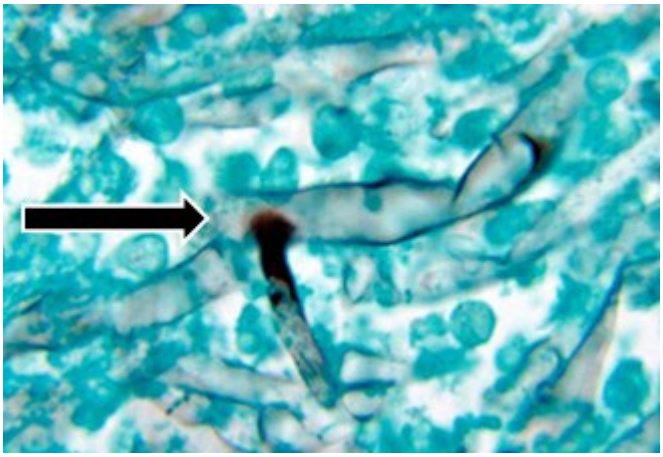
His pulmonary lesions improved, and he became afebrile on voriconazole.

Three months later, while still on voriconazole, he became febrile, and a new large pulmonary lesion appeared on CT in a different location. The earlier lesions had nearly resolved.

1,3 beta D glucan had fallen to 216 pg/ml and serum galactomannan was negative.

Bronchoalveolar lavage fluid cultures were negative and the bronchoalveolar lavage fluid galactomannan was negative.

A biopsy of the new lung lesion was performed; the GMS stain is shown below.



Grocott-Gömöri methenamine silver (GMS) 400x

What is the most likely pathogen?

A. *Cryptococcus neoformans*
B. *Aspergillus terreus*
C. *Scedosporium apiospermum* complex
D. *Cunninghamella bertholletiae*
E. *Fusarium solani*

Correct answer: *Cunninghamella bertholletiae*

Rationale

This patient developed a new lung lesion during successful treatment for pulmonary aspergillosis with voriconazole. Hyphae on the biopsy indicate a mold infection.

While breakthrough mold infections in patients taking prophylactic azoles or echinocandins are most often due to aspergillosis, this patient's prior aspergillosis is responding to therapy, meaning that another infection should be considered, including mucormycosis, scedosporiosis or fusariosis.

Members of the *S. apiospermum* complex are typically susceptible to voriconazole and have narrower, septate hyphae.

Fusarium species are more resistant to azoles but also have narrow, septate (hyphomycete-type) hyphae.

The broad, aseptate, ribbon-like hyphae shown are consistent with mucormycosis.

You should recognize the common genus designations of the Mucorales that cause mucormycosis: *Rhizopus, Mucor, Rhizomucor, Cunninghamella, Apophysomyces,* and rarely, Lichtheimia and *Syncephalalastrum*. Without the pathology result, the pulmonary lesion could have been caused by a variety of fungi, nocardia, mycobacteria, etc.

A negative serum beta D glucan and negative galactomannan would be characteristic of mucormycosis.

The negative serum galactomannan is a weak clue to think of something other than aspergillosis. The galactomannan test, while relatively specific for *Aspergillus* species (false positives can occur rarely with *Fusarium* species), has low sensitivity in the solid organ transplant population.

Beta D glucan tests are nonspecific. Keep in mind that many processes can cause false positive beta glucan tests, including hemodialysis, intravenous immunoglobulin, gauze packing of wounds, bacterial infections, and albumen. While most fungi produce 1,3 beta D glucan, the Mucorales and *Cryptococcus* species do not. Sensitivities of serum beta D glucan tests for invasive fungal infections range from 50-90% depending on the hosts' underlying disease and the fungus being assessed (most studies focus on invasive *Candida* species, invasive *Aspergillus* species, or *Pneumocystis jirovecii*). In the case presented, the positive serum beta glucan result may also be due to the notoriously slow and variable clearance from the prior *Aspergillus* infection.

C. neoformans would be unlikely to develop on voriconazole and would appear as yeasts, not hyphae.

This case highlights several important points:

- The beta D glucan test does not detect Mucorales or *C. neoformans*
- *Fusarium* and *Scedosporium* species have hyphae that resemble *Aspergillus* species on histopathology
- Patients on voriconazole may develop mucormycosis or infection with other unusual voriconazole-resistant molds or yeasts.

7 | CULTURE NEGATIVE ENDOCARDITIS | PATEL

A 64-year-old man with a prosthetic aortic valve presents with fever and general malaise of four weeks duration. He lives in an urban area of the US and has no unusual exposures.

He denies having taken any recent antibiotics.

Echocardiography shows a 2 mm vegetation on his aortic valve with mild aortic regurgitation.

Three sets of blood cultures are negative after five days of incubation.

Which of the following is most likely to be helpful?

A. **Serologic testing for *Bartonella* species and *Coxiella burnetii***
B. Fungal and mycobacterial blood cultures
C. Three further sets of blood cultures
D. Blood PCR for *Tropheryma whipplei*
E. Serologic testing for *Mycoplasma pneumoniae* and *Legionella* species

Correct answer: Serologic testing for *Bartonella* species and *Coxiella burnetii*

Rationale

This is a case of culture-negative endocarditis.

Blood cultures are always the first microbiologic test for endocarditis diagnosis, but in this case, they are already negative, and the patient has not received antibiotics. The next most reasonable step is therefore serologic testing for *Bartonella* species and *Coxiella burnetii*.

Further blood cultures are unlikely to be positive; fungal or mycobacterial endocarditis would be distinctly unusual; *Candida* species would grow in routine blood cultures. Whipple endocarditis could be diagnosed by blood PCR, but this is not a highly sensitive approach and could be done in addition to testing for *Bartonella* and *Coxiella* species.

Endocarditis caused by *M. pneumoniae,* or *Legionella* species would be unusual; if positive, serologic testing for these organisms is likely to be falsely positive, confounding the clinical picture.

Another type of test that could be considered (but is not offered as an answer) is 16S ribosomal RNA gene PCR/sequencing or shotgun metagenomic sequencing of blood. Both methods use next-generation sequencing. Metagenomic sequencing refers to the application of sequencing techniques to analyze the totality of the genomic material present in a sample.

8 | PHLEBOVIRUS DISEASE | PAVIA

A 42-year-old Tennessee farmer is seen for fever that has been present for five days. He is also experiencing pronounced fatigue and intermittent diarrhea.

For the two weeks before he became ill, he had been working in a field clearing brush and reported removing numerous ticks from his body on an almost daily basis. His exam is unremarkable except for fever.

He is leukopenic, thrombocytopenic, and has elevated aminotransferases. A presumptive diagnosis of ehrlichiosis is made.

PCR studies for *Ehrlichia* and *Anaplasma* are sent, and he is given doxycycline. After five days of doxycycline therapy, he is not improved.

Which of the following is the most likely cause of his illness?

A. **Phlebovirus**
B. Babesia
C. Scrub typhus (*Orientia tsutsugamushi*)
D. *Rickettsia typhi* (Murine typhus)
E. Adenovirus

Correct answer: Phlebovirus

Rationale

The syndrome of fever, leukopenia, thrombocytopenia, and elevated liver enzymes after a tick bite is strongly suggestive of ehrlichiosis or anaplasmosis, but one would have expected a clinical response to doxycycline.

In 2012, two cases of a new phlebovirus infection with a clinical picture mimicking ehrlichiosis, were described in Missouri. It appears to be tickborne. The virus was subsequently named, "Heartland Virus" (N Engl J Med 2012; 367:834-841).

In September 2014, a fatal case was reported from Tennessee. As of 2022, Heartland virus disease cases have been identified in residents from Arkansas, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Missouri, North Carolina, Oklahoma, Pennsylvania, Tennessee, and West Virginia.

This virus should be considered when a patient with suspected ehrlichiosis does not respond to doxycycline within a few days, especially if they are *Ehrlichia* PCR negative. There is no known treatment for the Heartland virus.

- Babesiosis is spread by the *Ixodes* tick and would be unlikely in Tennessee; leukopenia is uncommon with this infection

- Murine typhus caused by *R. typhi* would respond to doxycycline
- Adenovirus in a normal host would be unlikely to cause the clinical picture seen here
- Scrub typhus, due to *O. tsutsugamushi*, does not occur in the Western Hemisphere and responds to doxycycline

9 | HHV 6 ENCEPHALITIS | SAULLO

A 30-year-old woman with acute myelogenous leukemia underwent allogeneic hematopoietic cell transplantation from a matched unrelated donor. She has myeloid engraftment on day 10 but post-transplant course has been complicated by skin graft-versus-host disease for which she has been receiving high-dose corticosteroids and tacrolimus.

Her prophylaxis includes acyclovir, letermovir, inhaled pentamidine, and posaconazole.

She is admitted on post-transplant day +45 with progressive confusion and irritability. She is initially afebrile with stable vitals, but soon after admission develops a generalized tonic-clonic seizure.

MRI demonstrates bilateral symmetric hyperintensities in the medial temporal lobes.

Labs demonstrate a sodium of 126 mEq/L, creatinine of 0.7 mg/dL, a normal hepatic panel, and a WBC of 1.9 x 10^3/μL.

Lumbar puncture demonstrates a normal opening pressure and a lymphocyte-predominant pleocytosis (30 nucleated cells/μL – 95% lymphocytes), a mildly elevated CSF protein, and normal CSF glucose. Additional CSF studies are pending.

Which of the following is the most appropriate next step in management?

A. Intravenous liposomal amphotericin B plus flucytosine

B. Intravenous IV foscarnet

C. Cessation of tacrolimus

D. Intravenous IV acyclovir

E. Rituximab

Correct answer: Intravenous IV foscarnet

<u>Rationale</u>

The clinical presentation is most consistent with human herpesvirus 6 encephalitis (HHV-6), which is a cause of viral encephalitis following allogeneic hematopoietic cell transplantation.

High-risk features for HHV-6 reactivation and encephalitis are present, including being early post-transplantation (within the first 100 days), and administration of high-dose corticosteroids

for graft-versus-host disease. The clinical syndrome aligns with HHV-6 encephalitis, as evidenced by progressive confusion, irritability, seizures, and hyponatremia (sodium 126 mEq/L), consistent with the syndrome of inappropriate antidiuretic hormone secretion, which often precedes HHV-6 encephalitis. MRI findings of bilateral medial temporal and hippocampal hyperintensities (limbic encephalitis pattern), along with cerebrospinal fluid (CSF) lymphocytic pleocytosis and mild protein elevation, further support this diagnosis.

Empiric treatment should be initiated promptly when clinical suspicion is high, without waiting for confirmatory testing, such as CSF HHV-6 polymerase chain reaction (PCR) analysis.

Amphotericin B plus flucytosine is appropriate for central nervous system (CNS) cryptococcal infection; however, the CNS imaging and clinical presentation are more consistent with HHV-6 encephalitis. Additionally, posaconazole prophylaxis reduces the likelihood of breakthrough cryptococcal infection.

Cessation of tacrolimus is indicated for the management of posterior reversible encephalopathy syndrome (PRES), also referred to as reversible posterior leukoencephalopathy syndrome (RPLS). However, the clinical course and MRI findings in this case are most consistent with HHV-6 encephalitis. PRES typically presents with MRI abnormalities in the posterior, particularly parieto-occipital, region due to bilateral, typically symmetric vasogenic edema.

Intravenous acyclovir has good activity against herpes simplex virus (HSV) and varicella zoster virus (VZV) but does not reliably treat HHV-6. Further, her ongoing acyclovir prophylaxis makes HSV and VZV less likely viral culprits.

The primary antivirals applied for the treatment of HHV-6 include intravenous ganciclovir and foscarnet. Given the patient's early post-transplant status and leukopenia, foscarnet would be an appropriate choice given the association of ganciclovir with myelosuppression.

Rituximab is used to treat Epstein-Barr virus-mediated post-transplant lymphoproliferative disorder. However, the timeline, acuity of presentation, and absence of enhancing mass lesions on MRI make HHV-6 encephalitis the more likely diagnosis.

Relevant references: Kampouri E et al. Transplant Cell Ther. 2025 Aug;31(8):480-493. PMID: 40409689.

10 | METRONIDAZOLE | TAMMA

A 63-year-old man with type 2 diabetes mellitus and peripheral neuropathy presents with several weeks of progressive left foot pain, intermittent fevers, and a chronic plantar ulcer. On admission, his temperature is 38.3°C, heart rate is 102 beats/min, blood pressure is 132/76 mm Hg, and oxygen saturation is 98% on room air. Examination demonstrates a 2-cm ulcer over the plantar aspect of the left first metatarsal with surrounding erythema and probing to bone. Laboratory studies reveal a white blood cell count of 10,800 cells/μL, erythrocyte sedimentation rate of 84 mm/hour, serum creatinine of 0.9 mg/dL, and normal liver enzyme levels.

MRI of the left foot demonstrates osteomyelitis involving the first metatarsal. Bone biopsy cultures grow *Escherichia coli* and *Bacteroides fragilis*. Blood cultures remain negative. Because the patient declines surgical amputation, he is treated medically with a planned 6-week course of intravenous ceftriaxone plus oral metronidazole for chronic diabetic foot osteomyelitis.

Four weeks after initiating therapy, he returns to the infectious diseases clinic with several days of progressive gait instability, dizziness, slurred speech, and increasing confusion noted by his family. He denies headache, fever, or new focal weakness. Vital signs are normal. Neurologic examination demonstrates dysarthria and truncal and gait ataxia without focal motor or sensory deficits. Complete blood count, comprehensive metabolic panel, serum glucose, and renal and hepatic function are unchanged from baseline.

MRI of the brain demonstrates bilateral symmetric T2/FLAIR hyperintense lesions involving the cerebellar dentate nuclei without evidence of acute infarction or mass effect.

Which of the following is the most appropriate next step in management?

A. Discontinue ceftriaxone

B. Discontinue metronidazole

C. Obtain blood cultures

D. Perform lumbar puncture

Correct answer: Discontinue metronidazole

Rationale

Metronidazole neurotoxicity is a rare but well-recognized adverse effect that typically occurs after prolonged administration or high cumulative doses of metronidazole, often after several weeks of treatment.

Clinical manifestations can include ataxia, dysarthria, peripheral neuropathy, confusion or encephalopathy, and occasionally seizures. MRI findings often show symmetric T2 hyperintensities in the cerebellar dentate nuclei, although other regions of the brain may also be involved.

The most important management is immediate discontinuation of metronidazole. Neurologic symptoms typically improve over days to weeks after the medication is stopped.

Neurotoxicity with cefepime is well recognized but is not typically seen with ceftriaxone.

It is unlikely that this patient would develop bacteremia while on directed antibiotics, making blood cultures low yield.

Similarly, secondary seeding of the central nervous system infection while on appropriate treatment is unlikely.

11 | LATENT TB RX | ALEXANDER

A 62-year-old patient with end stage renal disease requiring hemodialysis is scheduled for a living related kidney transplant in one month.

He is referred to you for a positive interferon-gamma release assay. He denies fevers, weight loss, cough, or shortness of breath.

CXR showed a calcified pulmonary granuloma.

What would you recommend?

A. **Isoniazid plus pyridoxine daily for 9 months starting now**
B. Isoniazid plus pyridoxine daily for 9 months beginning one month after transplant
C. Pyrazinamide plus rifampin daily for 2 months
D. Levofloxacin daily for 6 months

Correct answer: Isoniazid plus pyridoxine daily for 9 months starting now

Rationale

Solid organ transplant recipients have a substantially increased risk of developing active tuberculosis (TB) compared with the general population. While cases of donor-transmitted TB have occurred, most cases of active TB in solid organ transplant recipients are thought to arise by reactivation of latent or healed untreated primary infection.

Treatment of latent tuberculosis infection (LTBI) significantly reduces TB reactivation in solid organ transplant recipients.

Indications for LTBI treatment in solid organ transplant candidates include:

- Untreated LTBI (e.g., initial or boosted tuberculin skin test with $\geqslant$5 mm induration or positive interferon-gamma release assay without evidence of active TB)
- History of inadequately treated LTBI
- History of TB contact before transplantation
- Receipt of organ from a donor with a history of untreated TB infection

Therapy for latent TB should ideally be initiated prior to transplant but does not need to delay transplant. Options for LTBI treatment in solid organ transplant candidates include:

- Isoniazid for 9 months given daily or twice weekly by directly observed therapy; 9 months of treatment confers additional benefit over 6 months. Pyridoxine (vitamin B6) 25-50 mg daily should be administered concomitantly to reduce the risk of neuropathy
- Rifampin daily for 4 months; rifampin is limited by drug-drug interactions that preclude continuation of post-transplant treatment; thus, it is preferable to complete the course of

rifampin prior to transplantation. In the case presented, the patient is scheduled for transplantation in one month, and therefore rifampin would not be a viable choice

- Isoniazid plus rifapentine weekly for 12 weeks; this regimen has been used successfully in renal transplant candidates, although use of this regimen after transplantation is limited by severe drug interactions between rifamycins and immunosuppressive agents

Pyrazinamide plus rifampin daily for 2 months has been associated with a high rate of hepatotoxicity and is no longer recommended.

A clinical trial of levofloxacin for LTBI therapy in transplant candidates was stopped due to development of tenosynovitis; therefore, fluoroquinolones are not recommended as first-line LTBI treatment.

References: Holty JE, Gould MK, Meinke L, Keeffe EB, Ruoss SJ. Tuberculosis in liver transplant recipients: a systematic review and meta-analysis of individual patient data. Liver Transpl. 2009; 15(8): 894-906; Subramanian, AK and Theodoropoulos NM. Clinical Transplantation. 2019;33:e13513.

12 | CRYPTOCOCCAL MENINGITIS | PATEL

A 34-year-old man who underwent renal transplantation for end stage renal disease due to focal sclerosing glomerulonephritis two months prior to presentation, presents to the Emergency Department in January with headache and fever of five days duration.

His post-transplant course was uncomplicated, and he is receiving prednisone, tacrolimus, mycophenolate mofetil and trimethoprim-sulfamethoxazole.

He and his donor were cytomegalovirus and Epstein-Barr virus seropositive.

He lives in Minnesota and has been at home since the transplant. He has no personal history of or exposure to tuberculosis.

There is no history of travel to the desert Southwest of the United States, or outside of the United States and no animal exposure.

A lumbar puncture is performed revealing 50 cells/ml (90% lymphocytes, 10% neutrophils), a protein of 75 mg/dL and a glucose of 35 mg/dL. Gram stain of cerebrospinal fluid is negative, and bacterial cultures are in progress.

His cerebrospinal fluid is submitted to testing with a multiplex PCR panel, and returns the results shown below (i.e., all results are negative).

Viruses	**Bacteria**	**Fungi**
Cytomegalovirus NEGATIVE	*Escherichia coli* K1 NEGATIVE	*Cryptococcus neoformans/gattii* NEGATIVE
Enterovirus NEGATIVE	*Haemophilus influenzae* NEGATIVE	
Herpes simplex virus 1 NEGATIVE	*Listeria monocytogenes* NEGATIVE	
Herpes simplex virus 2 NEGATIVE	*Neisseria meningitidis* Negative	
Human herpes virus 6 NEGATIVE	*Streptococcus agalactiae* NEGATIVE	
Human parechovirus NEGATIVE	*Streptococcus pneumoniae* NEGATIVE	
Varicella zoster virus NEGATIVE		

Which test is most urgent to perform on his cerebrospinal fluid next?

A. Mycobacterial culture
B. West Nile virus PCR
C. Zika virus PCR
D. Cryptococcal antigen
E. Smear for *Naegleria fowleri*

Correct answer: Cryptococcal antigen

<u>Rationale</u>

The patient's clinical presentation is consistent with cryptococcal meningitis.

The PCR is negative for *Cryptococcus* species; however, PCR is less sensitive than antigen testing for detection of *C. neoformans/gattii* in cerebrospinal fluid; therefore, cryptococcal antigen testing of cerebrospinal fluid is recommended.

Also, of the options, cryptococcal meningitis is the most likely to benefit from prompt institution of therapy.

While tuberculous meningitis is possible, it is less likely than cryptococcal meningitis.

His exposure history (or lack thereof) and the time of the year argue against West Nile virus, Zika virus or *Naegleria fowleri*.

13 | HANTAVIRUS | PAVIA

A 29-year-old man is admitted with rapid onset of shortness of breath and hypoxemia. He reports that about a week ago he developed a headache, fevers, myalgias and abdominal pain. He was seen in an urgent care clinic where influenza, and COVID-19 testing was negative.

Three weeks ago, he returned from a prolonged trip to South America where he was backpacking and climbing in Chile and Argentina. The rest of his exposure history is hard to obtain because of his dyspnea.

On exam, he is tachypneic and tachycardic with diffuse rales.

- Chest Xray shows diffuse fluffy infiltrates
- O_2 saturation could not be maintained on high flow oxygen, and he was intubated and placed on mechanical ventilation

Laboratory studies reveal the following:

- HCT: 52%
- WBC: 9000 cells/μl with 50% immature neutrophils and 2+ atypical lymphocytes
- Platelet count: 70,000/μl
- PT/INR 19/1.9
- AST/ALT: 90/105 U/L

What is the most likely cause of this syndrome?

A. Dengue
B. Malaria
C. *Staphylococcus aureus* pneumonia
D. Hantavirus pulmonary syndrome
E. Argentine hemorrhagic fever virus

Correct answer: Hantavirus pulmonary syndrome

Rationale
This young man presents with sudden severe respiratory distress and pulmonary infiltrates after a non-specific prodrome, with evidence of hemoconcentration, thrombocytopenia and coagulopathy.

The laboratory findings of thrombocytopenia, coagulopathy, left shifted white count with immunoblasts (aka atypical lymphs) combined with rapidly progressive pulmonary edema is typical of hantavirus pulmonary syndrome. It should more properly be referred to as cardiopulmonary syndrome since there is cardiac dysfunction and primarily non cardiogenic pulmonary edema from capillary leak.

Volume resuscitation can make these patients worse and inotropic support is critical. ECMO is often required.

New world hantaviruses are widely distributed and there are several different species. You should be familiar with the two most prevalent.

- In North America Sin Nombre virus is the most common, carried by the deer mouse (*Paromyscus maniculatus*).
- In South America the most important is Andes virus, found predominantly in Chile and Argentina, and carried by the long tailed pygmy rat (*Oligoryzomys longicaudatus*). Inhalation of rodent urine or feces accounts for most infections. Only Andes virus has been documented to have human-to-human transmission.

There are European hantaviruses as well: these largely manifest as hemorrhagic fever with renal syndrome (HFRS) and are also transmitted by rodents. This patient gave no history of being in Europe.

Infection with a second genotype of dengue can result in dengue hemorrhagic fever, but pulmonary findings this severe and sudden would be very uncommon.

The prodromal symptoms could be consistent with malaria, but the coagulopathy, unusual CBC and rapid development of respiratory distress don't fit.

Staphylococcal pneumonia following a viral respiratory illness is plausible but less likely. More focal CXR findings would be more typical, and *S. aureus* would not explain the atypical lymphs.

Argentine hemorrhagic fever is a distractor here: it's too obscure to be a correct answer on an exam one would hope!! Argentine hemorrhagic fever is present in Argentina and could explain the fever and coagulopathy but not the acute pulmonary findings. This is not due to a hantavirus. This is due to an Arenavirus, Junin virus, transmitted by rodents, which occurs mostly in rural agricultural workers during plowing or similar activities. While this is a hemorrhagic fever, only a minority of patients develop clinical hemorrhagic features.

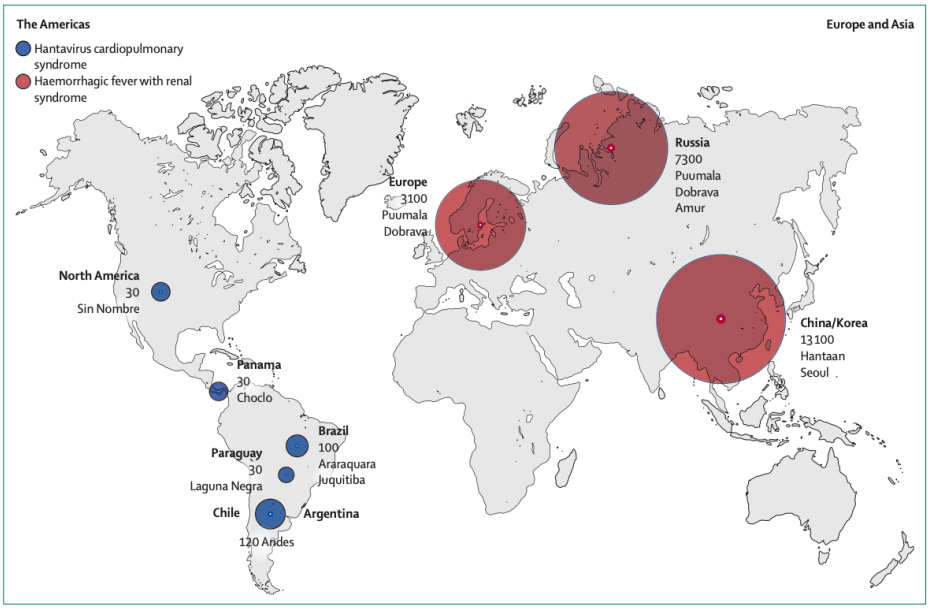


Figure 2: **Mean annual number of reported hantavirus cases in different regions and countries (2000–20)**
Unrecognised cases exceed reported cases for Puumala, Seoul, and Choclo virus.[8,23,28,39-41]

Vial et al. Lancet Infect Dis 2023; 23: e371–82

14 | HOUSEHOLD MEASLES CONTACT | SAULLO

A 47-year-old male arrives for clinic follow-up. He alerts you that five days ago, his brother and 10-year-old niece came to stay with him in his home. Yesterday, his niece was diagnosed with measles after developing high fevers, cough, conjunctivitis, and a rash.

The patient has acute myelogenous leukemia and underwent a matched-related donor allogeneic hematopoietic cell transplant 2 months ago. His course has been complicated by skin and gastrointestinal graft-versus-host disease, for which he is on tapering doses of high-dose prednisone and tacrolimus. The patient was up to date on all vaccines prior to transplant, including 2 doses of the measles, mumps, and rubella (MMR) vaccine.

What is the best next step in management?

A. Administer the MMR vaccine immediately

B. Administer intravenous immunoglobulin immediately

C. Start prophylactic vitamin A immediately

D. Check measles serologies, and if negative, then administer intravenous immunoglobulin

E. No intervention required as the window has passed for any preventative measures. Closely monitor the patient for signs or symptoms of measles

Correct answer: Administer intravenous immunoglobulin immediately

Rationale

This question emphasizes the importance of recognizing measles exposure in an immunocompromised patient who is only two months post-allogeneic hematopoietic stem cell transplant and is functionally non-immune to measles, regardless of previous vaccination or serologic status.

Measles is a highly transmissible virus, mainly spread through the airborne route when people cough, sneeze, or breathe. It can also be transmitted by contact with contaminated objects. Having an infected person in the same household poses a serious risk, as infectious droplets can stay in the air for up to two hours. In addition, people are contagious from at least four days before to four days after the onset of rash.

Prompt and effective management is critical to prevent complications, as immunocompromised patients are at increased risk for severe outcomes from measles, including respiratory failure and life-threatening neurological complications.

Although administering the measles, mumps, and rubella (MMR) vaccine within 72 hours of exposure can serve as post-exposure prophylaxis in eligible non-immune patients, it is not appropriate for this patient.

The MMR vaccine is a live-attenuated vaccine and is generally not given until patients are at least 24 months post-transplantation and off immunosuppression, and/or not receiving certain relapse prophylaxis or maintenance therapies.

Earlier MMR vaccination at 12 to 24 months post-transplant can be considered during measles outbreaks in patients who meet specific criteria. Therefore, immediate administration of the MMR vaccine is not indicated in this scenario.

Administering intravenous immunoglobulin (IVIG) to at-risk individuals within six days of exposure is the recommended intervention. This patient is still within the effective window for IVIG, but since 5 days have already passed since exposure, administration should be prompt.

Measuring measles serologies would unnecessarily delay IVIG administration and isn't reliable for assessing immunity in this situation; management decisions should be based on exposure risk.

Vitamin A does not have a role in post-exposure prophylaxis for measles; its use is reserved for the treatment of measles, particularly in children with severe disease.

Relevant references: Pergam SA et al. Biol Blood Marrow Transplant. 2019 Nov;25(11):e321-e330. PMID: 31394271.

15 | SINUSITIS RX | TAMMA

A 42-year-old woman presents to a primary care clinic with nasal congestion, facial pressure, and purulent nasal discharge that began 11 days ago.

She initially had symptoms of a common cold, including sore throat and rhinorrhea. Although most of her symptoms have improved slightly, right sided nasal congestion and facial pressure have worsened. She denies shortness of breath or chest pain.

Her temperature is 37.2°C (99.0°F).

Physical examination reveals right maxillary sinus tenderness and purulent nasal drainage from the right nares.

What is the most appropriate next step in management?

A. Supportive care with decongestants and saline nasal lavage

B. Obtain a plain film of the sinuses

C. Refer to otolaryngology for sinus cultures

D. Start empiric antibiotics

Correct answer: Start empiric antibiotics

Rationale

Most cases of acute rhinosinusitis are caused by viral infections and resolve without antibiotics.

Clinical guidelines recommend reserving antibiotics for patients who meet criteria suggesting acute bacterial rhinosinusitis. According to recommendations from the Infectious Diseases Society of America, antibiotics should be considered when any one of the following three clinical presentations is present: (1) persistent symptoms: nasal discharge or daytime cough lasting $\geqslant$ 10 days without improvement, (2) severe symptoms: fever $\geqslant 102^{\circ}$ F (39° C) or purulent nasal discharge or facial pain lasting $\geqslant 3-4$ consecutive days, or (3) worsening symptoms: initial improvement from a typical viral upper respiratory infection followed by worsening sinus symptoms after $5-6$ days. These clinical features help distinguish bacterial sinusitis from viral upper respiratory infections, reducing unnecessary antibiotic use.

Supportive care is appropriate for patients who don't meet the criteria above, as most of these patients have a viral process.

Plain films of the sinuses are insensitive for the diagnosis of acute bacterial rhinosinusitis and are not indicated.

Patients who fail to improve on empiric antibiotics warrant referral to otolaryngology for further evaluation including possible cultures to guide antibiotic therapy.

SESSION 2 | SUNDAY, AUGUST 23, 2026

Session Moderator: Dr. Auwaerter

Session Panelists: Drs. Bell, Bennett, Mitre, Platts-Mills, and Tunkel

Question #	Topic	Speaker
16	*Borrelia hermsii*	Auwaerter
17	*Acinetobacter* Sepsis	Bell
18	Winterbottom Sign	Bennett
19	*Dibothriocephalus latus*	Mitre
20	*Entamoeba histolytica* Liver Abscess	Platts-Mills
21	CNS Shunt Rx	Tunkel
22	HIV CAP	Auwaerter
23	Cavitary Pneumonia ICU Rx	Bell
24	Chagas Serology and Pregnancy	Bennett
25	Babesiosis	Mitre
26	Scombroid at Banquet	Platts-Mills
27	Rhombencephalitis	Tunkel
28	Tracheal Culture	Bell
29	*Wuchereria bancrofti*	Mitre
30	CSF Rhinorrhea	Tunkel

This page left blank intentionally.

16 | *BORRELIA HERMSII* | AUWAERTER

This is the blood smear from a previously healthy commercial photographer with a fever after visiting Tanzania and Colorado.

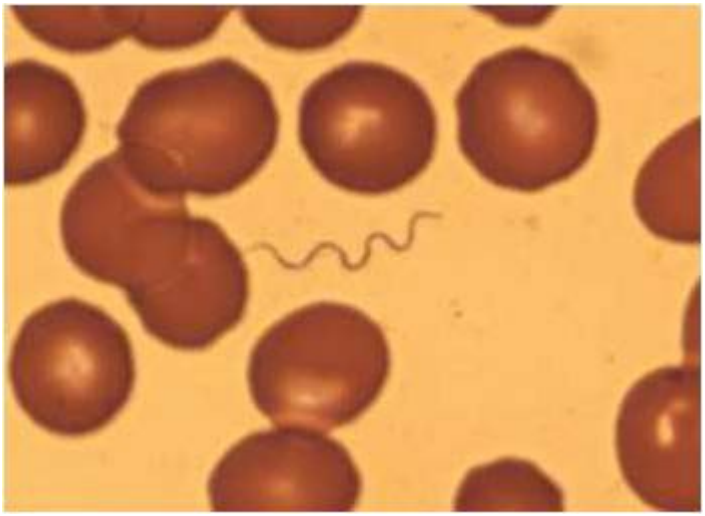
He went to Tanzania 42 to 35 days before the presentation. He spent most of the time in the city but did go to a rural orphanage where he took some photographs. He saw many rats near his hotel and in the rural area.

After returning to Chicago, he left for a week-long trip to Colorado in early July, from 14 days previously to 7 days before the presentation. He slept with his friends in his first of the season opening uncle's rustic cabin in the Rocky Mountains, white water rafting and driving an all-terrain vehicle through the woods.

About 3 days after returning to Chicago, he developed a fever, headache and myalgia.

He came to a travel clinic the next day after developing a fever (4 days after returning from Colorado), where a blood film exam to evaluate for malaria was done.

The blood for complete blood cell count and routine chemistries was clotted.



His blood smear is shown. When he was called about his blood smear results, he said he was feeling OK, was busy, and wouldn't return to the clinic.

What is the most likely identity of this organism?

A. ***Borrelia hermsii***
B. *Borrelia recurrentis*
C. *Leptospira interrogans*
D. *Borrelia burgdorferi*
E. *Spirillum minus*

Correct answer: *Borrelia hermsii*

Rationale

The organism shown is an extracellular spirochete consistent with relapsing fever *Borrelia*. The species cannot be determined reliably from smear morphology alone, but the epidemiologic setting makes *Borrelia hermsii* the best answer.

The tip-off in this stem is that the patient slept in a rustic cabin in the Rockies. Relapsing fever, caused by spirochetes of the *Borrelia* genus, is an arthropod-borne infection and occurs as tick-borne and louse-borne infections. Incubation periods are important: both types of relapsing fever (louse-borne and tick-borne) have a customary incubation period of 7-18 days. Thus, the incubation period is too long for African-derived *Borrelia recurrentis* (and this patient is not a likely candidate for a louse-borne disease, which usually afflicts those in poor living conditions). Of the other four options, seeing *Borrelia* in the blood would be most unlikely except for *Borrelia hermsii, which is* transmitted in this case by a soft tick (*Ornithodoros* hermsi) at elevations of 4,000-10,000 feet in the Rockies, Sierra Nevadas, Cascades and higher elevation forests in Utah and Nevada in the US.

Tick-borne relapsing fever (TBRF) is a zoonosis that occurs worldwide and involves multiple tick species and at least 15 *Borrelia* species. The two main *Borrelia* species in North America are *Borrelia hermsii* (in the Western mountains) and *Borrelia turicatae* (in the South) would be the organisms to be considered in North America. However, TBRF can also be acquired in Africa, particularly in West Africa, where it is caused by several species, including *Borrelia crocidurae* and *B. duttonii*. During untreated febrile episodes, relapsing-fever spirochetes may reach high concentrations and can be visualized on stained peripheral blood smears; PCR can confirm the diagnosis and help determine the species.

Only one species causes louse-borne relapsing fever. *Borrelia recurrentis* is spread only by lice from human to human and is associated with socioeconomic factors, now largely being found in refugee camps, most recently in Sub-Saharan Africa. However, this was a considerable problem in post-World War II Europe and Northern Africa (50,000 deaths).

Neither *Leptospira interrogans* nor *Borrelia burgdorferi* are typically seen in blood smears, as the bacterial burden in blood is very low (an exception in the US *Borrelia* spectrum is *Borrelia mayonii,* which could be a board question as discovered in 2016 and may see spirochetemia).

Relapsing fever may resolve after a few febrile episodes of decreasing intensity. Jarisch-Herxheimer reactions occur during therapy (tetracyclines, macrolides, or penicillin).

Spirillum minus is an uncommon cause of rat bite fever and has not been reported in the Western Hemisphere; there is no history of rat bites. This organism has been seen in blood smears.

17 | *ACINETOBACTER* SEPSIS | BELL

A 52-year-old man with 35% total body surface area burns has been in the ICU for 3 weeks and recently underwent tracheostomy for prolonged mechanical ventilation. After a period of stability off antibiotics, he develops fever, hypotension, and new bilateral infiltrates on chest radiograph.

Blood cultures and endotracheal aspirate both grow *Acinetobacter baumannii*.

The isolate is preliminarily reported as carbapenem-resistant. The patient is hemodynamically unstable and requires norepinephrine.

Which of the following is the most appropriate empiric antimicrobial regimen pending susceptibility results?

A. Ceftazidime–avibactam
B. Meropenem–vaborbactam
C. Sulbactam–durlobactam plus meropenem
D. Colistin plus imipenem
E. Colistin monotherapy

Correct answer: Sulbactam–durlobactam plus meropenem

Rationale

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) represents one of the most challenging multidrug-resistant organisms encountered in the ICU. Sulbactam–durlobactam is a novel β-lactam/β-lactamase inhibitor combination specifically developed for CRAB. Unlike other β-lactamase inhibitors, sulbactam itself has intrinsic activity against *A. baumannii* through high-affinity binding to penicillin-binding proteins 1 and 3. Durlobactam protects sulbactam from degradation by class A, C, and D β-lactamases, which are commonly expressed by CRAB strains. The ATTACK trial demonstrated that sulbactam–durlobactam, when used in combination with imipenem, provided improved clinical outcomes and reduced nephrotoxicity compared to colistin-based therapy. Meropenem is a reasonable alternative to imipenem in settings where imipenem is not available. Pending susceptibilities, empiric therapy with sulbactam–durlobactam plus a carbapenem is now considered the preferred regimen for suspected CRAB infections in the ICU.

Ceftazidime–avibactam and meropenem–vaborbactam have no reliable activity against *A. baumannii*, as the β-lactamases responsible for carbapenem resistance (OXA-type enzymes) are not inhibited by avibactam or vaborbactam.

Colistin was previously used as salvage therapy for CRAB but carries a high risk of nephrotoxicity and suboptimal lung penetration, particularly in pneumonia. Inhaled colistin has been to reduce nephrotoxicity of IV colistin but aerosol drug has poor lung penetration, and is not recommended as part of therapy for CRAB.

Therapy with intravenous colistin can be considered in resource-limited settings without viable alternatives.

18 | WINTERBOTTOM SIGN | BENNETT

A 23-year-old college student is seen for intermittent fevers, headaches and arthralgias.

He came to the US from the Central African Republic (central Africa) two months ago to attend college.

He says his symptoms have been present for at least the last four months, and it is hard for him to concentrate on his studies.

On exam his temperature is 100.6F; he has a soft, moveable posterior cervical node 3 cm by 3 cm; and his liver and spleen are palpable.

Which one of the following is the most likely diagnosis?

A. Malaria
B. Rift Valley fever
C. *Rickettsia africae* infection
D. Typhoid fever
E. African trypanosomiasis

Correct answer: African trypanosomiasis

Rationale

West African trypanosomiasis due to *Trypanosoma brucei gambiense* is seen in West and Central Africa and is more chronic in presentation than the East African form due to *Trypanosoma brucei rhodesiense*.

- Patients may have intermittent fevers, headaches, and arthralgias for months before developing central nervous system infection (sleeping sickness).
- Posterior cervical adenopathy is common in the West African form. Patients may have hepatosplenomegaly.

Malaria may cause hepatosplenomegaly but is not associated with adenopathy.

This illness is too long in duration for Rift Valley fever*, Rickettsia africae* infection, or typhoid fever.

19 | *DIBOTHRIOCEPHALUS LATUS* | MITRE

A 56-year-old male from Pittsburgh, PA presents to his primary care physician with fatigue. He reports no fevers, chills, sweats, chest pains, respiratory symptoms, abdominal pain, or diarrhea.

Chest/abdomen/pelvis CT scan with contrast is normal. Blood tests reveal normal thyroid function tests as well as a normal white blood cell count and differential.

His Hgb level is low at 9 g/dL with an MCV of 106 fL.

He reports spending two weeks every summer at Lake Como in Italy where he enjoys fishing and eating freshly caught perch.

Which of the following is the most likely cause of his fatigue?

A. *Ancylostoma duodenale*
B. *Entamoeba histolytica*
C. *Anisakis simplex*
D. *Wuchereria bancrofti*
E. *Dibothriocephalus latus (*aka *Diphyllobothrium latum)*

Correct answer: *Dibothriocephalus latus (*aka *Diphyllobothrium latum)*

Rationale

This patient most likely has *Dibothriocephalus latus* (aka *Diphyllobothrium latum*), the broad fish tapeworm.

Individuals at high risk are those with a history of eating freshly caught, undercooked lake fish.

In contrast to most helminth infections, *D. latus* is more prevalent in temperate and cold climates. Endemic regions include the United States and Canada, Scandinavian countries, Central and Eastern Europe, Chile, Argentina, and Japan. Individuals become infected by eating undercooked freshwater fish.

A 2016 study of sub-alpine lakes in the northern areas of Italy found that 25% of perch and over 80% of pike in Lake Como harbored the parasite (PMID: 27491055). Despite the high prevalence of this parasite in some lakes, the prevalence of *D. latus* infection in humans is low.

Once larvae are ingested it takes a couple of months for the adult tapeworms to mature. While these tapeworms can grow very large (to more than 20 meters in length), most patients are asymptomatic. A subset develop fatigue, lightheadedness, abdominal pain, salt-craving, and, rarely, loose stools and diarrhea. Long-lasting infections of several years can result in vitamin B12 deficiency (and corresponding macrocytic anemia).

D. latus causes vitamin B12 deficiency by directly taking up substantial amounts of vitamin B12 and by reducing human absorption because of parasite-mediated disruption of vitamin B12 and intrinsic factor.

Incorrect answers

- *Ancylostoma duodenale* (A) and *Entamoeba histolytica* (B) can both cause an iron-deficiency anemia due to intestinal bleeding, but this results in microcytic anemia.
- *Anisakis simplex* (C) is typically acquired by ingestion of undercooked saltwater fish such as cod, herring, and mackerel. Salmon (which spend most of their life in saltwater but some of their life in freshwater) can also carry *A. simplex*. *A. simplex* causes an acute abdominal pain syndrome in which the larval forms invade the gastric or intestinal epithelium. *A. simplex* can also cause acute allergic reactions. While gastric or intestinal anisakiasis could potentially lead to sufficient bleeding that causes anemia, this would be iron-deficient and microcytic.
- *Wuchereria bancrofti* (D) is the most common cause of lymphatic filariasis. It can cause lymphedema, hydrocele, and elephantiasis, but does not typically cause anemia.

20 | *ENTAMOEBA HISTOLYTICA* LIVER ABSCESS | PLATTS-MILLS

A 45-year-old man previously healthy man presents with two weeks of right upper quadrant pain, fever, and weight loss. He returned from a month-long trip to rural Mexico ten weeks ago. He recalls a self-limited episode of diarrhea while he was there that has fully resolved.

Laboratory tests show a white blood cell count of 12,000/microL with normal eosinophil percentage. Liver enzymes are notable for an elevated alkaline phosphatase.

Ultrasound reveals a solitary 6 cm fluid-filled mass in the right lobe of the liver.

Which of the following is most likely to be diagnostic?

A. Bacterial blood cultures

B. Percutaneous aspiration of the liver cyst

C. Serology for *Entamoeba histolytica*

D. Stool microscopy for ova and parasites

E. Echinococcal serologies

Correct answer: Serology for *Entamoeba histolytica*

<u>Rationale</u>

The travel history, subacute duration of symptoms, and solitary right-lobe abscess are highly suggestive of an amebic liver abscess caused by *Entamoeba histolytica*.

- Antibody tests are almost invariably positive after the first week of symptoms and provide laboratory confirmation
- Treatment includes metronidazole to eradicate tissue invasive trophozoites followed by a luminal agent (paromomycin or iodoquinol) to eliminate colonization and prevent future relapse

Percutaneous drainage is rarely necessary for the diagnosis of amoebic liver abscesses but may be indicated for cysts that are >10 cm or when symptoms persist despite antibiotic therapy. The contents of the cyst are classically described as having an "anchovy paste" appearance. Trophozoites are infrequently present microscopically, but *E. histolytica* antigen testing or PCR may be used to confirm the diagnosis when serologic testing is inconclusive.

Stool microscopy may be diagnostic with amoebic colitis, but in the absence of diarrhea it is significantly less sensitive than serology for diagnosing invasive disease of the colon. While the presence of cysts in the stool may suggest the possibility of an amoebic liver abscess, a more specific test for liver disease is needed.

Hydatid cysts caused by echinococcal infection of the liver are typically more indolent, with symptoms rarely occurring until the cyst is >10 cm in size. Pain is the most common presenting symptom, but systemic complaints, such as fever or weight loss are rare in the absence of cyst rupture. Ultrasound may show septations or daughter cysts, which differentiate this from amoebic liver abscess.

21 | CNS SHUNT RX | TUNKEL

A 50-year-old man was admitted for replacement of a non-functioning ventriculoperitoneal shunt that had been placed when he had obstructive hydrocephalus from cryptococcal meningitis.

A low-grade fever began several days after replacing the ventricular end and valve of the shunt.

Cerebrospinal fluid (CSF) from the shunt reservoir revealed a WBC count of 150 cells/mm^3, glucose of 40 mg/dL, and protein of 100 mg/dL. Gram stain was negative, but culture of CSF revealed a light growth of *Staphylococcus epidermidis*, susceptible to vancomycin and linezolid.

The patient's entire shunt was removed, a ventricular drain placed, and intravenous vancomycin started.

Which of the following is recommended prior to placing a new CSF shunt?

A. Continue vancomycin for ten days

B. Continue vancomycin, add linezolid, and treat for ten days

C. Continue vancomycin until drain cultures have been negative ten days

D. Add intraventricular vancomycin and treat for ten days

Correct answer: Continue vancomycin until drain cultures have been negative ten days

Rationale

The duration of antimicrobial therapy for CSF shunt infections is not completely defined. The timing of reimplantation should be individualized based on the isolated microorganism, severity of ventriculitis, and improvement of CSF parameters and CSF sterilization in response to antibiotic therapy.

In those with shunt infections caused by coagulase-negative staphylococci and initially normal CSF findings, the presence of negative CSF cultures for 48 hours after externalization generally confirms that removal of the hardware effected a cure and that early reimplantation (after the third day) is reasonable.

If the coagulase-negative staphylococcus was isolated along with abnormal CSF parameters, a true infection was likely present and reimplantation should not be done until CSF cultures have remained negative for 7-10 days.

If the patient is responding to therapy with intravenous vancomycin, there is no reason to add linezolid or intraventricular vancomycin.

22 | HIV CAP | AUWAERTER

A 68-year-old man with HIV (CD4 = 35 cells/mm^3; viral load 50,000 copies/mL) and emphysema is brought to the emergency department with 3 days of cough productive of purulent sputum, progressive shortness of breath, and fevers. He recently completed a course of amoxicillin-clavulanate and a steroid dose pack for a COPD exacerbation.

Medications include taking bictegravir/emtricitabine/tenofovir and prophylactic TMP-SMX, although he admits to poor adherence.

On physical exam his temperature is 39° C, respiratory rate is 30/min, and BP is 96/58. Room air O_2 saturation is 85% and soon required high-flow oxygen.

Initial evaluation is notable for:

- WBC 8700 cells/ mL with 85% neutrophils (prior WBC 3000 cells/mL)
- Sputum Gram stain and sputum and blood cultures: pending from offsite lab
- Chest x-ray: dense, alveolar infiltrates in the left lower and R middle lobes
- MRSA nasal swab: negative

Empiric coverage for community-acquired pneumonia should include which pathogen in this patient?

A. *Bordetella bronchiseptica*

B. Methicillin-resistant *Staphylococcus aureus*

C. *Rhodococcus equi*

D. Pseudomonas aeruginosa

E. *Acinetobacter baumannii*

Correct answer: *Pseudomonas aeruginosa*

Rationale

For patients with advanced HIV infection with risk factors presenting with community-acquired pneumonia, the teaching point here is to recognize that *P. aeruginosa is* over-represented as a causative agent in this setting. HIV infection alone does not require routine antipseudomonal treatment, but this patient has several recognized risk factors: a CD4 count of ≤50 cells/mm^3, COPD, recent hospitalization, recent antimicrobial, and corticosteroid exposures.

Methicillin resistant *S. aureus* is more common in people with HIV and nasal testing is recommended in patients presenting with severe pneumonia. The negative predictive value of a rapid MRSA nasal test is quite high, and this makes MRSA unlikely.

Empiric therapy is not indicated for *B. bronchiseptica* (the etiologic agent of kennel cough), *R. equi*, or *A baumannii* regardless of HIV status given their rarity. Additionally, a question with MRSA as an answer would typically include issues such as post-influenza history, injection drug use, cavitary or necrotizing features.

Risk Factors for *Pseudomonas* pneumonia include CD4 count ≤50 cells/mm^3, underlying neutropenia, preexisting lung disease, use of corticosteroids, severe malnutrition, hospitalization within the past 90 days, residence in a health care facility or nursing home, and chronic hemodialysis. Of note, with effective ART, *P. aeruginosa* as a concern lessen, however, if other risk factors remain, patient may still be at risk.

His pneumonia would be categorized as severe based on his need for high flow oxygen and multilobar disease on chest radiograph.

The NIH Opportunistic Infection in Persons with HIV Infection Guidelines recommend:

Empiric Therapy for Patients with Severe CAP at Risk of *Pseudomonas* Pneumonia

- **Severe CAP**
    - PaO_2/FiO_2 ≤250
    - ICU admission
    - Hypotension requiring aggressive fluid resuscitation
    - Multilobar infiltrates
    - Need for high-flow oxygen

- **Preferred Empiric Therapy**
    - An IV anti-pneumococcal, **antipseudomonal** beta-lactam +IV antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) (AI)
        - Preferred IV beta-lactams: piperacillin-tazobactam, cefepime, imipenem, or meropenem
- **Alternative Therapy**
    - An IV anti-pneumococcal, **anti-pseudomonal** beta-lactam (as above) + IV azithromycin or
    - An IV anti-pneumococcal, **anti-pseudomonal** beta-lactam (as above) + an IV anti-pneumococcal fluoroquinolone (moxifloxacin or levofloxacin)

When the microbiologic diagnosis is established, therapy can be de-escalated.

23 | CAVITARY PNEUMONIA ICU RX | BELL

A 74-year-old woman with chronic obstructive pulmonary disease and prior stroke with residual dysphagia is admitted from home via the emergency department for acute hypoxemic respiratory failure requiring supplemental oxygen.

On hospital day 2, she has a witnessed aspiration event and develops fever (39.1°C), worsening oxygenation, and hypotension requiring vasopressors. She is intubated and transferred to the ICU. Chest radiograph shows new right lower lobe consolidation.

Bronchoalveolar lavage (BAL) fluid cultures grow *Streptococcus intermedius*.

She is started on piperacillin–tazobactam. Over the next 72 hours, her oxygenation stabilizes and vasopressor requirements plateau, but she remains intermittently febrile with persistent leukocytosis.

CT scan of the chest reveals multiple cavitary lesions in the right lower lobe, the largest measuring 2.1 cm, with surrounding consolidation. No single collection is amenable to percutaneous drainage.

Which of the following is the most appropriate next step in management?

A. Escalate antibiotics to meropenem plus vancomycin

B. Add clindamycin

C. Continue piperacillin tazobactam monotherapy

D. Consult thoracic surgery for surgical drainage

E. Perform another bronchoalveolar lavage

Correct answer: Continue piperacillin tazobactam monotherapy

Rationale

This patient has aspiration-related necrotizing pneumonia with multiple small lung abscesses, a recognized complication in older adults with impaired airway protection. Typically, the microbiology of lung abscesses is polymicrobial with anaerobes as a typical finding, but BAL fluid is not routinely cultured for anaerobes unless a protected brush or similar approach is used. Most multiplex panels for pneumonia do not detect anaerobic bacteria. A Gram stain could be helpful to assess the possibility of anaerobes especially if aerobic cultures are negative. Thus, a BAL would not identify anaerobic bacteria: a percutaneous drainage of a lung abscess typically is cultured for anaerobes as well as aerobes but…this was not done in this case.

In this patient *S. intermedius* (a member of the *Streptococcus anginosus* group, historically referred to as "S. milleri") was identified in the BAL. This organism has a special predilection for causing abscesses. Lung abscesses are typically polymicrobial.

While anaerobes appear to be less common pathogens than previously thought with aspiration pneumonia, anaerobes (e.g., *Fusobacterium* species) are often involved in lung abscesses.

Although this patient remains intermittently febrile with persistent leukocytosis, her oxygenation has stabilized and vasopressor requirements have plateaued. Importantly, persistence of fever and inflammatory markers within the first 48–72 hours does not constitute treatment failure, as clinical improvement often precedes laboratory normalization and radiographic resolution may take weeks. Accordingly, there is no role for a repeat bronchoalveolar lavage.

Most lung abscesses resolve with medical therapy alone, particularly when collections are small (<3 cm), multifocal, and not amenable to percutaneous drainage. In this setting, continued antimicrobial therapy with close clinical monitoring is the most appropriate management strategy.

Escalation of antibiotics to meropenem plus vancomycin is unlikely to improve outcome, as the identified organism is already well covered by piperacillin–tazobactam, and broader therapy does not accelerate resolution of established abscesses.

Addition of clindamycin offers no additional benefit when adequate anaerobic coverage is already provided and increases the risk of *Clostridioides difficile* infection without improving clinical outcomes.

Surgical consultation for drainage is not indicated, as no dominant cavity is present and invasive intervention is generally reserved for abscesses ≥6 cm, failure of medical therapy, or development of complications such as empyema or bronchopleural fistula.

24 | CHAGAS SEROLOGY AND PREGNANCY | BENNETT

A 27-year-old woman is referred to your office because the blood bank where she recently donated notified her that a test for Chagas disease was positive, as was a confirmatory test they performed. She is concerned because she is 8 weeks pregnant. She lived in a rural area of El Salvador until age 12 before moving to the USA and returned twice to visit relatives since then. She is in good health and takes no medications.

What is the most appropriate next step in management?

A. Start benznidazole to protect the fetus from becoming infected

B. She needs two confirmatory serologic tests to confirm chronic infection before further action

C. *Trypanosoma cruzi* PCR on her blood now and prior to delivery to detect fetal infection

D. Prescribe benznidazole after delivery to decrease the likelihood of maternal disease later in life

E. Perform serology for *T. cruz*i infection on the infant after delivery

Correct answer: She needs two confirmatory serologic tests to confirm chronic infection before further action

Rationale

All blood banks in the USA perform a screening or a screening and confirmatory serologic test on donor blood for *T. cruzi*. When the screening or screening and confirmatory tests are positive, the patient is notified. Blood bank tests are designed to be as sensitive as possible to the various strains of *T. cruzi* but are not specific. This patient has a high pretest probability of having chronic Chagas and needs further testing with a different confirmatory serologic test. PCR or blood smears are too insensitive to diagnose chronic, asymptomatic Chagas disease. Patients with confirmed chronic Chagas disease have a low but definite risk of developing cardiomyopathy or megacolon/megaesophagus later in life or acute Chagas disease if immunosuppressed.

Treatment of asymptomatic or pregnant healthy patients with benznidazole is not recommended because of the toxicity of benznidazole, low incidence of later disease and uncertain efficacy in preventing later disease or fetal transmission. Mothers with chronic Chagas disease have a 1-5% risk of transmitting infection to their fetus.

The infant should be checked at birth and periodically afterwards by PCR for infection and if PCR is positive (preferably twice), the infant should be treated to prevent acute disease. The period of highest risk is the first six months after birth. Maternal antibody interferes with serologic testing of the infant during this period, but the infant could be tested by serology later.

Other answers are wrong because the patient's diagnosis needs confirmation. Her infant would not need treatment without further clinical or laboratory evidence of infection.

25 | BABESIOSIS | MITRE

A 45-year-old man living on Eastern Long Island, New York had been ill for 5 days with fever (T102.7°F) and flu-like symptoms including headache. Two days ago, when he noticed an enlarging oval red rash of about 10 cm on the back of his right thigh, he was started on doxycycline for presumed Lyme disease.

Today, while fevers have not abated though the rash is fading, he became faint on standing at home, and he is brought to the emergency department where his blood pressure is normal, but he is quite anemic.

His past medical history is only remarkable for a motorcycle accident 10 years earlier which he suffered splenic injury requiring splenectomy.

On examination, he appears ill with pulse 100/minute, blood pressure 98/70 and temperature recorded as 101°F. There is an ovoid homogenous rash over the posterior right thigh and a left upper quadrant abdominal scar.

Laboratories:

- Leukocyte count 3.3 x 10^9/L (50% neutrophils, 35% lymphocytes, 15% monocytes)
- Hemoglobin 4.7 gm/dL
- Platelet count 105,000 x 10^9/L
- Total bilirubin 3.8mg/dL
- ALT 110 U/L
- LDH 650 IU/mL

He develops adult respiratory distress syndrome (ARDS), progressive renal failure and disseminated intravascular coagulation.

Which of the following is the most likely cause of his progressive problems indicative of severe sepsis?

A. *Borrelia burgdorferi*

B. *Francisella tularensis*

C. *Babesia microti*

D. *Anaplasma phagocytophilum*

E. *Rickettsia rickettsii*

Correct answer: *Babesia microti*

Rationale

This patient is most likely to have babesiosis as a cause of severe anemia with evidence of hemolysis, followed by ARDS, renal failure, and disseminated intravascular coagulation.

Splenectomized patients are at enhanced risk for severe sepsis due to encapsulated bacteria (e.g., *Streptococcus pneumoniae, Haemophilus influenzae*, *Neisseria meningitidis*) and also for other pathogens including *Capnocytophaga canimorsus* and the intraerythrocytic parasite *B. microti*, which behaves like malaria. As this patient's rash is consistent with erythema migrans acquired in New York, this means he was bitten by an *Ixodes scapularis* tick (also known as the black-legged tick, sometimes also colloquially called a deer tick), putting him at risk of babesiosis as a co-infection of Lyme disease. His laboratory studies reveal a characteristic anemia with hemolytic features including elevated bilirubin and LDH with concomitant thrombocytopenia.

Rocky Mountain spotted fever (RMSF, *R. rickettsii*) can certainly cause severe infection, but is less likely than *B. microti* since RMSF does not usually cause this degree of anemia; *R. rickettsii* is primarily transmitted by *Dermacentor* (dog) ticks. Over 90% of patients with severe RMSF will display either a diffuse maculopapular or petechial rash which is not present in this patient. As Lyme disease is not transmitted by *Dermacentor* ticks, and this patient had a characteristic erythema migrans rash, this implicates the *Ixodes scapularis* tick as the vector.

Besides *B. burgdorferi* as the cause of Lyme disease, *I. scapularis* ticks in the Northeast US can transmit other human pathogens simultaneously, although this is relatively uncommon. Other infections include *Borrelia miyamotoi* (an emerging pathogen resembling relapsing fever), Powassan or Deer Tick virus (agent of encephalitis), *Anaplasma phagocytophilum* (Human Granulocytic Anaplasmosis [HGA]), or *B. microti*. All these pathogens can produce disease after similar (but not identical) incubation periods. The incubation period of HGA is 5 days to 2 weeks. While the incubation period of Lyme related erythema migrans is 1-2 weeks (range 3-30 days), the incubation period of babesiosis is slightly longer (1-6 weeks).

The patient's prior history of trauma-related splenectomy places him at high risk of severe *Babesia* infection, but such a circumstance is not known to result in more severe Lyme disease. Although HGA can routinely cause thrombocytopenia, liver function test abnormalities, and be more severe in splenectomized patients, neither HGA nor Lyme disease causes as severe an anemia with hemolytic features.

Use of parenteral doxycycline would treat both Lyme disease and HGA, so it would be unlikely that mild illness would progress to this severity if due to HGA, even in a splenectomized patient. Not listed as a choice, Human Monocytic Ehrlichiosis (HME) is due to *Ehrlichia chaffeensis* which is transmitted by a different vector, *Amblyomma americium* also known as the lone star tick, which does overlap epidemiologically with much of the same region as the deer tick.

26 | SCOMBROID AT BANQUET | PLATTS-MILLS

A group of adults in Detroit, Michigan develops an illness during a banquet in which they are served mahi-mahi, mushrooms, wonton soup, and corn with margarine.

Eight of 16 people eating the meal have symptoms beginning within 20 minutes after eating fish that tastes peppery and unusual. They experienced a burning mouth, felt flushed, had a headache, and felt dizzy. Two experienced an urticarial reaction.

The illness lasted 10 hours.

What is the likely cause of the outbreak?

A. Ciguatera
B. Monosodium glutamate toxicity
C. Staphylococcal food poisoning
D. Scombroid
E. Mushroom poisoning

Correct answer: Scombroid

Rationale

Scombroid is caused by the release of histamine-like substances by *Proteus* and *Klebsiella* species (peppery taste) when fish is not well refrigerated. It is treated with antihistamines and is short lasting.

Most outbreaks of **ciguatera** occur in coastal areas (Caribbean or Hawaii). The lack of neurologic findings and rapid resolution points to a disease other than Ciguatera.

Monosodium glutamate (MSG) could possibly cause this type of syndrome in a few patients, but not half the exposed persons, and the much faster onset after food consumption and urticarial reaction are not consistent with MSG.

Staphylococcal food poisoning would produce vomiting without other findings, and the very short incubation period is inconsistent with staphylococcal food poisoning.

Mushroom poisoning would not explain the peppery taste of the fish and, while mushroom toxidromes are diverse, a rapid-onset urticarial reaction is not described.

27 | RHOMBENCEPHALITIS | TUNKEL

A previously healthy 60-year-old woman presents to the emergency room with headaches, fevers, nausea, and vomiting for the past 4 days. Two days prior to her ER presentation, she noted difficulty with balance.

Earlier this morning, she noted left facial numbness. She denied any night sweats, photophobia, or neck stiffness. She has not traveled outside of the United States and has lived her entire life in Baltimore, Maryland.

She lives with her husband and two daughters in a row house. They own 2 cats and a dog. She denies smoking, alcohol use, or injection drug use.

On physical examination, her temperature was 38.3° C, blood pressure 120/60 mmHg, heart rate 109 beats/minute, and respiratory rate 13 breaths/minute. She was alert and oriented but appeared uncomfortable. Higher cortical functions, extraocular movements and visual fields were intact. Limb tone, motor strength and reflexes were normal. Plantar responses were flexor.

Abnormalities included left facial hypoesthesia, right facial weakness and left gaze-evoked nystagmus. She was noted to have gait ataxia. The remainder of her physical examination was unremarkable.

Her peripheral white cell count, and differential were normal.

- A comprehensive metabolic panel was normal.
- Lumbar puncture and cerebrospinal fluid (CSF) examination revealed a lymphocytic pleocytosis with 500 white blood cells/mm^3 (64% lymphocytes). CSF glucose was normal, and protein was slightly elevated. No organisms were visualized on Gram stain of the CSF. CT scan without IV contrast was unremarkable.
- Postgadolinium T1-weighted MRI images of the brain showed multiple ring-enhancing abscess-like lesions in the brainstem with mild meningeal enhancement.

Which of the following is the most likely etiology of her clinical presentation?

A. Behçet disease
B. Cytomegalovirus
C. Herpes simplex virus type 2
D. *Listeria monocytogenes*
E. *Streptococcus pneumoniae*

Correct answer: Listeria monocytogenes

Rationale

Involvement of the brainstem is diagnostic of a rhombencephalitis.
The most common infectious cause is *L. monocytogenes*. Unlike *Listeria* meningitis, which typically occurs in older or immunocompromised individuals, *Listeria* rhomboencephalitis often

affects otherwise healthy individuals. Other infectious causes of rhombencephalitis are enterovirus 71, herpes simplex virus types 1 and 2, human herpesvirus 6, Epstein Barr virus, and *Mycobacterium tuberculosis*. Behçet disease is the most common non-infectious cause. Rhombencephalitis as a result of a paraneoplastic process also occurs. The classic clinical syndrome of *L. monocytogenes*-associated rhombencephalitis is a biphasic illness characterized by a prodrome of fever, headache, nausea, and vomiting, followed by the sudden onset of progressive asymmetrical cranial nerve abnormalities, cerebellar signs, and hemiparesis or hemisensory defects, with or without meningeal signs.

Most patients have a lymphocytic CSF pleocytosis (only 40% have a CSF dominated by polymorphonuclear cells). Blood cultures are more likely to be positive (~60%) than CSF cultures (~30%). CSF PCR for *L. monocytogenes* may be diagnostic.

MRI is superior to CT for demonstrating rhombencephalitis. Finding abscesses with ring enhancement can be useful in making a diagnosis of *L. monocytogenes*-associated rhombencephalitis. Immediate antimicrobial therapy is the most important predictor of a favorable outcome.

None of the other pathogens listed can explain the entirety of the clinical presentation:

Neither cytomegalovirus nor herpes simplex virus are likely to present with ring-enhancing abscesses of the brainstem in an immunocompetent adult.

While *M. tuberculosis* is a rare cause of rhombencephalitis, involvement of the basal cisterns with leptomeningeal enhancement after intravenous injection of contrast is the finding most characteristic of tuberculosis-associated rhombencephalitis.

She does not have any other clinical manifestations to suggest Behçet disease.

28 | TRACHEAL CULTURE | BELL

A 60-year-old man has been in intensive care unit for the past three weeks with a flare of lupus erythematosus for which he has received a short course of methylprednisolone and cyclophosphamide. His hospital course was complicated by hospital acquired pneumonia, requiring intubation and mechanical ventilation.

He completed a one-week course of vancomycin and meropenem four days ago.

After a tracheostomy, he was febrile for several hours but then defervesced with unchanged ventilatory support, PEEP of 10 and an FIO_2 of 0.4. A tracheal aspirate and blood cultures were obtained, and he was restarted on meropenem and vancomycin.

Blood cultures were negative but tracheal aspirate had a heavy growth of *Stenotrophomonas maltophilia*, susceptible to trimethoprim-sulfamethoxazole, levofloxacin, and minocycline.

What do you recommend?

A. **Stop meropenem and vancomycin and observe**
B. Add trimethoprim-sulfamethoxazole
C. Add minocycline
D. Add minocycline and trimethoprim-sulfamethoxazole
E. Add levofloxacin

Correct answer: Stop meropenem and vancomycin and observe

Rationale

S. maltophilia is a frequent bronchial colonizer in ventilated patients given broad spectrum antibiotics. This patient has none of the criteria of ventilator-associated pneumonia: new fever, increased ventilatory support or new infiltrates in the lung. This patient had a transient fever after a procedure but was otherwise stabile. Meropenem and vancomycin can be safely stopped; no further treatment is needed for *S. maltophilia*.

29 | *WUCHERERIA BANCROFTI* | MITRE

A 31-year-old man presents with a chief complaint of enlarged scrotum. He reports having worked as a missionary in rural areas in the northern regions of Nigeria for the past three years.

While in Nigeria he took atovaquone/proguanil daily for malaria prophylaxis during the rainy seasons. He had two episodes of *Giardia* infection and one febrile episode that resolved with empiric treatment for both typhoid fever and malaria.

He did substantial work outdoors and reports having been frequently bitten by mosquitoes. He routinely ate fresh produce and meats, and recalls having eaten a few dishes prepared with fresh goat milk.

He had intermittent interactions with livestock but no animal bites or scratches and reports that he was careful to only drink boiled or bottled water.

Ultrasound reveals a collection of anechoic fluid around both testes, consistent with a bilateral hydrocele.

Which of the following is the most likely cause of this condition?

A. ***Wuchereria bancrofti***
B. *Brugia malayi*
C. *Loa loa*
D. *Onchocerca volvulus*
E. *Dirofilaria immitis*

Correct answer: *Wuchereria bancrofti*

Rationale

All the answers listed are filarial parasites.

This patient most likely has lymphatic filariasis due to *W. bancrofti*, the species responsible for 90% of all cases of lymphatic filariasis.

- Other causes of lymphatic filariasis include *B. malayi* (which accounts for most of the remaining 10% of cases) and *Brugia timori* (which accounts for less than 1% of all cases).

While the Global Program to Eliminate Lymphatic Filariasis has had tremendous success in reducing overall world prevalence, at least 50 million individuals are still infected and over 35 countries remain endemic, including Nigeria. Transmission is via mosquitoes and disease in travelers usually occurs after long-term exposure, as described in this case. Some individuals develop episodes of adenolymphangitis (aka filarial fevers) that manifest as fevers with retrograde lymphangitis and swelling of the leg, arm, or breast for several days. More commonly, fevers in filariasis are due to recurrent bacterial skin and soft tissue infections associated with anterograde lymphangitis. Over time, lymphatic dysfunction caused by the parasite can lead to hydrocele, lymphedema, and frank elephantiasis. Hydrocele is quite common, and it is estimated that over 20 million men in the world today have hydrocele due to lymphatic filariasis.

Incorrect Answers

- *B. malayi* is incorrect because it is not endemic in Africa. *B. malayi* occurs predominantly in Southeast Asia and does not occur in Africa.
- *L. loa* presents is the cause of “African eye worm”, which presents as movement of adult worms in under the conjunctiva of the eye. Loa loa also causes transient migratory swellings (aka Calabar swellings) but does not cause hydrocele.
- *O. volvulus* is the cause of river blindness. It is transmitted by blackflies and causes dermatitis, subcutaneous skin nodules (containing nests of adult worms), anterior eye disease (initially a punctate keratitis and then over time a sclerosis keratitis, this occurs due to an inflammatory reaction to dying microfilariae), and retinitis (much less common than anterior eye disease, this occurs via a not well understood mechanism). It does not typically cause hydrocele.
- *D. immitis* causes heartworm disease in dogs and cats. It primarily causes pulmonary nodules in humans.

30 | CSF RHINORRHEA | TUNKEL

A 45-year-old man with no significant past medical history is involved in a motor vehicle accident in which he suffers a high-impact blunt force trauma to the head.

On evaluation, he is found to have a basilar skull fracture and is medically managed. Three days later, he is noted to have fluid coming out of his right nostril.

Testing of the fluid is positive for beta-2-transferrin confirming that it is cerebrospinal fluid (CSF). The patient is doing well and is recovering well from his skull fracture.

On physical examination, he is afebrile and vital signs are normal. He is alert and oriented to person, place and time, and has no neurological deficits. His laboratory studies reveal a normal leukocyte count. MRI of the brain does not show a fluid collection or air fluid level.

Which of the following interventions is appropriate?

A. Immediate surgical intervention to repair the leak

B. Surgical intervention if the leak does not stop after 7 days

C. Administration of prophylactic intravenous vancomycin

D. Administration of prophylactic intravenous vancomycin and cefepime

Correct answer: Surgical intervention if the leak does not stop after 7 days

Rationale

This patient has suffered a basilar skull fracture and has developed a CSF leak manifesting as rhinorrhea. These patients may have persistent dural defects that can lead to episodes of bacterial meningitis.

Many leaks will cease spontaneously, but surgery is indicated for leaks that persist for several weeks or in patients who present with delayed or recurrent infection.

Surgery is not indicated in the acute phase (before 7 days) of leakage as there are no differences in outcome in patients with acutely repaired leaks compared with those whose leaks stop spontaneously within 7 days.

About administration of prophylactic antibiotics in patients with basilar skull fracture and CSF leak, the interpretation and comparison of studies examining this question are confounded by multiple variables, including patient selection, choice of antimicrobial agents and definition of infection. Although no prospective controlled trials have examined the efficacy of prophylactic antimicrobials for these patients, meta-analyses have suggested that prophylaxis does not prevent meningitis in patients with basilar skull fracture and has the potential to result in the selection and growth of antibiotic-resistant organisms.

SESSION 3 | MONDAY, AUGUST 24, 2026

Session Moderator: Dr. Aronoff

Session Panelists: Drs. Boucher, Dhanireddy, Dorman, Ghanem, and Klompas

Question #	Topic	Speaker
31	*Capnocytophaga canimorsus* S/P Dog Bite	Aronoff
32	MRSA and Ceftobiprole	Boucher
33	Japanese Encephalitis Vaccines	Dhanireddy
34	LFTs on INH	Dorman
35	Gonorrhea Tenosynovitis	Ghanem
36	Arthroplasty Surgical Prophylaxis	Klompas
37	Psittacosis	Aronoff
38	*Staphylococcus aureus* Nafcillin Toxicity	Boucher
39	Zoster Vaccines Normal Host	Dhanireddy
40	Linezolid	Dorman
41	Chlamydia Fitz-Hugh-Curtis	Ghanem
42	Norwegian Scabies	Klompas
43	TB Prophylaxis	Dorman
44	Bacterial Vaginosis	Ghanem
45	Diphtheria Prophylaxis	Klompas

This page left blank intentionally.

31 | *CAPNOCYTOPHAGA CANIMORSUS* S/P DOG BITE | ARONOFF

A 58-year-old man with a history of alcohol use disorder presents to the emergency department with fever, hypotension, and diffuse purpura fulminans involving both lower extremities.

His partner reports that three days ago he was bitten on his forearm by his neighbor's German shepherd while trying to separate the dogs during a fight. The bite wound was cleaned and bandaged at an urgent care clinic and was not sutured.

On examination, he is febrile (40.1°C), hypotensive (BP 82/48 mm Hg), and tachycardic. The bite wound on his forearm appears only mildly erythematous, but his lower legs and feet have extensive dark purple, nonblanching lesions.

Laboratory testing reveals thrombocytopenia (platelets 28,000/μL), elevated INR and PTT, and elevated D-dimer consistent with disseminated intravascular coagulation (DIC).

Blood cultures are pending. He is started on broad-spectrum empiric antibiotics.

Which of the following organisms is most likely to be identified on blood culture?

A. *Pasteurella multocida*

B. *Streptococcus canis*

C. *Capnocytophaga canimorsus*

D. *Clostridium perfringens*

E. *Neisseria meningitidis*

Correct answer: *Capnocytophaga canimorsus*

Rationale

C. canimorsus is a Gram-negative fusiform rod that is a normal commensal of the oral microbiota of dogs and, to a lesser extent, cats. It is one of the most important organisms to recognize in the setting of a dog bite wound with subsequent systemic infection, particularly in immunocompromised hosts.

The classic at-risk patient is one with **asplenia, alcoholism, or liver disease**. In these patients, even a trivial bite or scratch—or sometimes no identifiable wound at all—can lead to overwhelming sepsis with DIC and purpura fulminans within 24–72 hours. Mortality is high without prompt treatment. The organism may be difficult to identify on routine culture and may be misidentified as a diphtheroid or other organism on Gram stain. MALDI-TOF MS is a reliable method for identification.

The standard first-line antibiotic treatment for *C. canimorsus* infection is amoxicillin-clavulanate (oral) or a β-lactam–β-lactamase inhibitor combination (e.g., ampicillin-sulbactam, piperacillin-tazobactam for inpatients). Although penicillin or ampicillin alone have historically been considered the drugs of choice, the emergence of β-lactamase-producing strains has shifted recommendations toward β-lactamase inhibitor combinations as preferred empiric therapy.

Carbapenems are also effective. The organism is **generally** resistant to aztreonam and trimethoprim-sulfamethoxazole.

P. multocida is also transmitted by dog or cat bites but typically causes a rapidly progressive wound infection or cellulitis rather than the fulminant sepsis with purpura fulminans seen here.

C. perfringens could cause gas gangrene following a deep wound but would not typically present with purpura fulminans and DIC in this fashion.

N. meningitidis can cause purpura fulminans but is not associated with animal bites.

S. canis is a rare zoonotic pathogen from dogs that can cause neonatal sepsis but is not a common cause of post-bite sepsis in adults.

32 | MRSA AND CEFTOBIPROLE | BOUCHER

A 58-year-old man with poorly controlled type 2 diabetes mellitus is admitted for fever.

He was most recently admitted 6 weeks ago for hyperosmolar coma. That hospitalization was complicated by a central-line associated MRSA bacteremia for which he was treated with vancomycin for 14 days.

Two of two blood cultures obtained at this admission are again positive for MRSA with the following MIC results:

- Linezolid 2 mg/ml (susceptible)
- Vancomycin 4 mg/ml (intermediate)
- Daptomycin 2 mg/ml (non-susceptible)
- Ceftaroline 1mg/ml (susceptible)
- Ceftobiprole 2 mg/ml (susceptible)
- Rifampin 0.25 mg/ml (susceptible)
- Gentamicin 1 mcg/ml (no breakpoint established)

Which antibiotic regimen would you recommend for this patient?

A. Linezolid

B. Vancomycin + rifampin

C. Daptomycin + gentamicin

D. Ceftobiprole

Correct answer: Ceftobiprole

Rationale

Of the four antibiotic choices listed, only three, vancomycin, daptomycin, and ceftobiprole, are FDA-approved for treatment of MRSA bacteremia.

Linezolid is approved for MRSA infections, but not bacteremia and is not a first-line agent for this reason and because it lacks bactericidal activity.

Because the isolate is not susceptible to vancomycin or daptomycin, both are contraindicated as single agents.

Whether adding rifampin to vancomycin would be effective against a VISA strain is unknown; evidence supporting use of adjunctive rifampin for *S. aureus* bacteremia is lacking, and with non-susceptibility of the strain to vancomycin, there is a risk of emergence of rifampin resistance on therapy. So, this is not a good choice.

Evidence of improved efficacy is lacking for adding gentamicin to daptomycin, particularly when the strain is non-susceptible to the latter.

The combination of daptomycin with a beta-lactam, typically ceftaroline, has been used to treat MRSA bacteremia, principally as salvage therapy, but evidence supporting its use, or that it is any better than ceftaroline alone, is of low quality. In any case, this combination was not listed as an option.

Ceftaroline has been used to treat MRSA bacteremia, but it is not FDA approved for this indication.

This contrasts with ceftobiprole, which has been compared to daptomycin in a randomized controlled trial of bacteremia, and is FDA approved for this indication as well as for right-sided endocarditis due *to S. aureus*. Thus, ceftobiprole is the best choice for this patient. Patients with left-sided *Staphylococcus aureus* endocarditis were excluded from the ceftobiprole bacteremia study and it is not FDA approved for this indication.

33 | JE VACCINE | DHANIREDDY

A 35-year-old agricultural consultant in good health is returning to India for 3 months where she will inspect crops in rural areas. There is known to be Japanese encephalitis in the area.

Three years ago, when she had visited the same area, she was vaccinated for Japanese B encephalitis with the standard two dose regimen.

What advice should you give her for protection against Japanese B encephalitis?

A. Immunization is ineffective and therefore no immunization was needed 3 years ago or is needed now

B. Immunization is associated with a substantial risk for encephalitis and therefore should not be given

C. Since she was immunized three years ago, she should receive a booster dose

D. She should receive a booster only if titers demonstrate no measurable IgG antibodies against JE

Correct answer: Since she was immunized three years ago, she should receive a booster dose

Rationale

Japanese B encephalitis can be a devastating disease. Thus, for people likely to be exposed, immunization is appropriate. People likely to be exposed should take precautions to minimize mosquito bites.

The JE vaccine is likely to be effective based on antibody studies. Since she was immunized three years ago, and she is now going to an endemic area where she likely will be exposed, she should receive a booster dose.

The JE vaccine is an inactivated product and quite safe. No serious hypersensitivity, neurologic, or other serious adverse events have been identified.

There is no guideline recommendation to determine a need for vaccination by measuring antibody levels.

Background from MMWR:

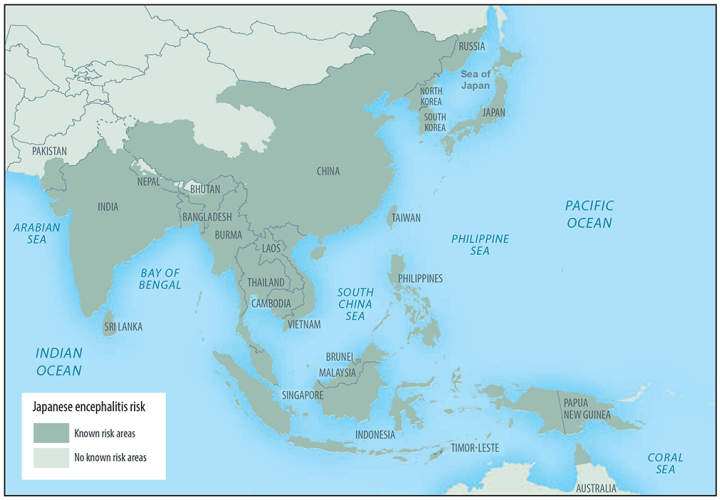
"JE virus, a mosquito borne flavivirus, is the most common vaccine-preventable cause of encephalitis in Asia. JE occurs throughout most of Asia and parts of the western Pacific."

"The majority of JE virus infections in humans are asymptomatic, and <1% of persons infected with JE virus develop encephalitis. Acute encephalitis is the most commonly identified clinical syndrome among people with JE virus infection, although milder forms of disease (e.g., aseptic meningitis or undifferentiated febrile illness) also can occur. Among patients who develop clinical symptoms, the incubation period is 5–15 days. Approximately 20%–30% of patients die, and 30%–50% of survivors have neurologic, cognitive, or behavioral sequelae. No antiviral treatment is available." MMWR July 19, 2019 / 68(2);1–33.

JE virus infections are usually confirmed by detection of virus-specific antibody in CSF or serum.

"JE vaccine is recommended for persons moving to a JE-endemic country to take up residence, longer-term (e.g., ≥1 month) travelers to JE-endemic areas, and frequent travelers to JE-endemic areas. JE vaccine also should be considered for shorter-term (e.g., <1 month) travelers with an increased risk for JE on the basis of planned travel duration, season, location, activities, and accommodations and for travelers to JE-endemic areas who are uncertain about their specific

travel duration, destinations, or activities. JE vaccine is not recommended for travelers with very low-risk itineraries." MMWR July 19, 2019 / 68(2);1–33.



34 | LFTs ON INH | DORMAN

A 40-year-old HIV-uninfected male returns from a State Department assignment in India where he was well other than occasional episodes of self-limited diarrhea.

PPD was negative when he departed.

PPD is positive upon return, with 20 mm of induration. He has no symptoms; a chest radiograph is normal.

Baseline laboratory values, including liver function tests, are normal.

He has been vaccinated for HBV and HAV and is HCV seronegative.

He is started on a regimen of isoniazid 300 mg plus pyridoxine 25 mg per day since his physician is more comfortable with that regimen than newer, CDC recommended regimens.

He returns after 4 weeks of taking isoniazid and pyridoxine. He is asymptomatic and reports taking his drugs daily and missing very few doses.

Upon routine lab testing his ALT is 65 IU/L (ULN=33) and his AST is 90 units (ULN=48 IU/L). Total bilirubin is 0.6 mg/dl.

What is the best option for management at this point?

A. **Continue the current regimen with the patient told to report any symptoms immediately and recheck enzymes in 2-4 weeks**
B. Continue the current regimen but measure the patient's acetylation rate to determine safety of continuation
C. Double the dose of pyridoxine
D. Perform an interferon-gamma release assay (IGRA) to determine if prophylaxis is really needed
E. Abandon plan to treatment of latent tuberculosis infection (LTBI); monitor the patient closely for symptoms and obtain a chest x-ray every 6 months for 3 years

Correct answer: Continue the current regimen with the patient told to report any symptoms immediately and recheck enzymes in 2-4 weeks

Rationale

All regimens for treatment of LTBI are associated with hepatotoxicity with the risk of hepatotoxicity greatest with INH monotherapy and less for rifamycin-based regimens.

This patient should continue INH: small increases in transaminase levels (less than 5x upper limit of normal) are common and almost always improve or resolve within a few weeks. Therefore, continuation is safe if the patient is asymptomatic.

If the patient starts to feel ill, such as loss of appetite or flu-like symptoms, he should be told to stop isoniazid and come in promptly for liver function testing.

In regard to changing regimens, switching to rifampin alone would be confusing for two reasons. It would leave undecided whether isoniazid is safe for possible future use and, if hepatic enzymes continued upward it would leave open the possibility that rifampin could be causing hepatotoxicity.

Starting a once-a-week dose of isoniazid of 900 mg, along with rifapentine, would be even more confusing. The current regimen is satisfactory and will prove likely to not be hepatotoxic.

Pyridoxine is given to prevent peripheral neuropathy, not to hepatotoxicity, so increasing the dose is not warranted. Either 25 or 50 mg is appropriate.

CDC does not recommend confirming a positive PPD with an IGRA, or vice versa. The only recommendation for using both a PPD and IGRA is when the first test is negative and a strong suspicion of exposure to tuberculosis exists.

Here are some important points about INH hepatitis:

- Isoniazid monotherapy has a higher risk of hepatotoxicity than the rifamycin-based regimens, although the risk for INH is low (about 1%).
- Pretreatment liver function tests should be obtained in high-risk patients, such as those with liver disease, regular alcohol consumption, pregnancy or HIV infection.

- At-risk patients and those with pretreatment abnormal liver function may need periodic monitoring of liver function tests. Monthly visits are important to monitor symptoms and adherence.
- Patients most at risk for hepatitis are >65 years old, are regular alcohol users, and/or take other hepatotoxic drugs such as acetaminophen, statins or certain herbal supplements. Viral hepatitis, genetic predisposition including acetylation status, female sex and pregnancy are associated with hepatitis, as is immunocompromise. Interestingly, HIV infection does not appear to be a risk factor.
- Patients present with fatigue, malaise, right upper quadrant pain, asymptomatic jaundice, and/or flu-like symptoms. This typically occurs within 2-3 months of starting INH, but cases have been reported many months after starting INH. Aminotransferase levels are often 10x upper limits of normal; bilirubin and alkaline phosphatase levels are variable.

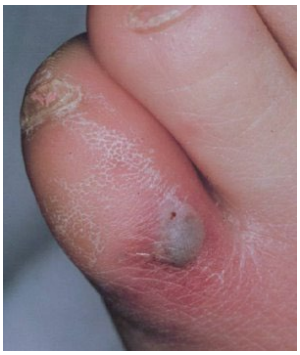
Once INH hepatitis is suspected, all hepatotoxic drugs should be discontinued if bilirubin is ≥3 mg/dL or serum transaminases are more than five times the upper limit of normal.

There are numerous examples of acute INH hepatitis necessitating liver transplantation.

35 | GONORRHEA TENOSYNOVITIS | GHANEM

A 38-year-old marine sergeant reports to sick bay a week after shore leave with acute onset of fever, malaise and five pustular skin lesions, including the one shown here.

He appears acutely ill, but his vital signs (other than temperature) are normal.



He has pain on flexion and slight swelling in the right wrist; his wrist flexor tendons are quite tender. His left ankle was tender the day before but is now asymptomatic.

While on shore leave in a port city in Mexico, he had sex with a commercial sex worker, consumed alcohol and passed out in an alley infested with rats and mice.

On hospital day 3 the lab reports a positive blood culture.

Which of the following would be the most likely organism?

A. Spirochete
B. Gram negative bacillus
C. Gram negative coccus
D. Gram positive bacillus
E. Endemic mycosis

Correct answer: Gram negative coccus

Rationale

The key: Tenosynovitis (inflammation of the lining of the sheath that surrounds a tendon) as opposed to arthralgias or arthritis should make you consider gonorrhea before any other infection.

Since the patient was unconscious in a rat-infested alley, a spirochete in the blood would suggest rat bite fever due to *Spirillum minor*, but this organism is rarely seen in the Western hemisphere and doesn't grow in blood cultures.

A Gram-negative rod could be rat bite fever due to *Streptobacillus moniliformis*, but this doesn't grow well in blood cultures.

A Gram-negative coccus could be *Neisseria gonorrhoeae* or *Neisseria meningitidis*, either of which is possible in this setting, although the former is more likely than the other.

A Gram-positive bacillus might be *Erysipelothrix*, *Listeria* or *Bacillus* species, none of which fit the epidemiology or clinical situation.

Growth in a blood culture at three days is not likely to be histoplasmosis, blastomycosis, or coccidioidomycosis.

This case is typical of disseminated gonorrhea: the acute stage of illness is characterized by fever, chills, and generalized malaise. Skin lesions are few and usually disappear spontaneously. Patients are ill but do not typically have hypotension or septic shock.

Tenosynovitis should always suggest disseminated gonorrhea above any other infection. Often multiple tendons are simultaneously inflamed, especially the wrist, fingers, ankle, and toes.

If there are skin lesions, they are painless and few in number.

There are many viral and bacterial causes of septic arthritis, including gonorrhea and rat bite fever, but this patient did not have septic arthritis.

36 | ARTHROPLASTY SURG PROPHYLAXIS | KLOMPAS

A 69-year-old woman requires a hip replacement after fracturing her greater trochanter.

She has a history of recurrent urinary tract infections typically treated with nitrofurantoin or fosfomycin, but is otherwise healthy.

To reduce the likelihood of an infection involving her surgical site, what antibiotics do you recommend for preoperative prophylaxis?

A. Cefazolin
B. Vancomycin
C. Vancomycin plus cefazolin
D. Ceftriaxone
E. Cefepime

Correct answer: Cefazolin

Rationale

Cefazolin alone is recommended for perioperative prophylaxis in patients undergoing arthroplasty.

A randomized trial of pre-operative prophylaxis using cefazolin alone versus cefazolin plus vancomycin in adults without known methicillin-resistant *Staphylococcus aureus* (MRSA) colonization who were undergoing arthroplasty reported similar or fewer infections amongst patients randomized to cefazolin alone (NEJM 2023;389:1488-98).

The patient's history of recurrent urinary tract infections does not contribute to risk in this case – joint infection secondary to urinary tract infection is exceedingly rare and nitrofurantoin/fosfomycin are not associated with increased risk of MRSA - in fact both are typically active against MRSA.

37 | PSITTACOSIS | ARONOFF

A 34-year-old woman presents to her physician with a 10-day history of nonproductive cough, fever, headache, and myalgias. She has no history of recent travel, and has been otherwise healthy.

She works as a clerk at a pet supply store. Two weeks ago, she began helping to care for a recently purchased flock of parakeets after a previous employee became ill with a similar respiratory illness.

On examination, her temperature is 39.1°C, heart rate is 72 beats per minute, and she has diffuse crackles on auscultation.

A chest X-ray reveals patchy bilateral infiltrates. Routine sputum cultures are negative.

Which of the following is the most likely diagnosis?

A. Legionnaires disease
B. *Mycoplasma pneumoniae*
C. Psittacosis
D. Q fever
E. Influenza

Correct answer: Psittacosis

Rationale

This patient has psittacosis, caused by *Chlamydia psittaci*, an obligate intracellular bacterium transmitted to humans through inhalation of aerosolized infectious particles from infected birds. The classic epidemiologic clue is occupational or recreational exposure to psittacine birds

(parrots, parakeets, cockatiels), although other avian species, including pigeons, hawks, and waterfowl, can serve as sources.

The incubation period is typically 7–14 days. Psittacosis classically presents as a pneumonia with high fever, severe headache (often out of proportion to respiratory symptoms), and relative bradycardia—a temperature-pulse disparity that should raise suspicion for this diagnosis. The chest X-ray may show patchy or lobar consolidation.

Routine bacterial sputum cultures will not grow *C. psittaci*. Diagnosis is made by serology (detection of antibodies by indirect immunofluorescence or microimmunofluorescence) or by PCR. The treatment of choice is **doxycycline** for 10–14 days. Macrolides are an alternative.

Legionnaires disease also presents as pneumonia with temperature-pulse disparity and negative routine sputum cultures and must always be in the differential. However, the strong link to avian exposure and the occupational history of a coworker with a similar illness point to psittacosis. *Legionella* species are acquired from contaminated water systems, not birds.

Mycoplasma pneumoniae is the most common cause of pneumonia in young adults, but is not acquired from birds and does not typically produce this degree of systemic illness.

Q fever presents similarly with pneumonia and temperature-pulse disparity, but is acquired from livestock (cattle, goats, sheep) or their parturition products, not from birds.

Bonus nugget: Relative bradycardia (aka, Faget sign) is classically associated with typhoid fever, brucellosis, legionellosis, psittacosis, Q fever, and certain viral infections, including dengue and yellow fever. This phenomenon occurs when infections fail to produce the expected tachycardic response to fever (typically 10 beats per minute increase per degree Celsius).

38 | *STAPHLYOCOCCUS AUREUS* NAFCILLIN TOXICITY | BOUCHER

A 57-year-old man presents with 1 week of fever, chills, and low back pain.

A transesophageal echocardiogram shows a 6 mm mobile mass on the mitral valve. MRI of the spine shows evidence of discitis between the 3rd and 4th lumbar vertebrae.

Admission blood cultures are positive for *Staphylococcus aureus* resistant only to penicillin.

He is treated with nafcillin 2 gm IV every 4 hours with resolution of fever but little change in back pain. Follow-up blood cultures from hospital days 4 and 5 are negative.

The white blood cell count is 18,000/mm^3 with 90% neutrophils on admission; on hospital day 20, the white blood cell count is 3,000/mm^3 with 30% neutrophils. Renal function is normal.

Which of the following options is most appropriate for this patient?

A. **Cefazolin 2 gm IV every 8 hours**
B. Ceftriaxone 2 gm IV every 12 hours
C. Linezolid 600 mg IV every 12 hours
D. Nafcillin 1 gm IV every 4 hours
E. Vancomycin 1 gm IV every 12 hours

Correct answer: Cefazolin 2 gm IV every 8 hours

Rationale

The neutropenia is due to bone marrow maturation arrest caused by nafcillin and necessitates discontinuing this antibiotic.

Reducing the dose of nafcillin might resolve the neutropenia but would provide subtherapeutic levels if 1 g IV q 4h were administered, as described in the answer above. Thus, this is not a good strategy.

Neutropenia is a well-recognized toxicity of nafcillin in particular, and not a contraindication for use of cephalosporins or other beta-lactam antibiotics. Neutropenia often occurs with relatively high doses after weeks of therapy (i.e., it is time and dose dependent).

Cefazolin is recommended treatment of invasive methicillin-susceptible *S. aureus* (MSSA) infections, including bacteremia and endocarditis, and is preferred over either vancomycin or ceftriaxone. This drug would be a good option since neutropenia is not a common adverse effect of cefazolin.

Ceftriaxone is a poor choice due to its marginal activity against MSSA, high level of protein binding, absence of any controlled trials of its use in the treatment of *S. aureus* osteomyelitis, endocarditis, or bacteremia, and observational studies suggesting that it is less efficacious than cefazolin or anti-staphylococcal penicillins, particularly for endocarditis.

Linezolid is not FDA approved to treat endocarditis. It is a static drug, and long courses cause bone marrow suppression, which is already an issue here. Given its long-term toxicity, linezolid is a poor option.

39 | ZOSTER VACCINES NORMAL HOST | DHANIREDDY

A 70-year-old woman in good health had an episode of zoster 20 years ago which was diagnosed clinically and resolved uneventfully with acyclovir treatment. When she went to a new internist 15 years ago, that internist recommended Zostavax-- Zoster Vaccine Live (ZVL) -- which the patient received.

She now wants to know if she should receive Shingrix (recombinant zoster vaccine-RZV)). She remains in good health.

What would you advise her?

A. Since she had a clinical case of zoster, she did not need Zostavax 15 years ago and does not need Shingrix (recombinant zoster vaccine) now
B. Since she had Zostavax, she does not need Shingrix
C. She should only get Shingrix if her IgG titers against zoster are below the level of detection
D. She should receive Shingrix (recombinant zoster vaccine)

Correct answer: She should receive Shingrix (recombinant zoster vaccine)

Rationale

Recombinant zoster vaccine (RZV-Shingrix) is indicated in adults aged ≥50 years, irrespective of prior receipt of varicella vaccine or ZVL, and does not require screening for a history of chickenpox (varicella). This is a two-dose series: Following the first dose of RZV, the second dose should be given 2–6 months later.

Adults should receive RZV regardless of history of herpes zoster.

If a patient is experiencing an episode of herpes zoster, vaccination should be delayed until the acute stage of the illness is over, and symptoms abate.

Screening for a history of varicella (either verbally or via laboratory serology) before vaccination for herpes zoster is not recommended.

However, in persons known to be VZV negative via serologic testing, ACIP guidelines for varicella vaccination should be followed.

RZV (Shingrix) is not indicated for prevention of chickenpox (varicella) although some experts would expect Shingrix-RZV to be effective for prevention of varicella.

40 | LINEZOLID | DORMAN

You are treating a 66-year-old man for pulmonary disease due to *Mycobacterium abscessus* complex that is resistant to macrolides. He completed 8 weeks of IV imipenem, IV amikacin, and oral omadacycline and one week ago he was transitioned to oral omadacycline, oral linezolid, and inhaled amikacin.

He also has COPD, hypertension, and depression, and takes an inhaled combination beta agonist and muscarinic antagonist, lisinopril, and sertraline.

This morning his wife called reporting that over the past few days he has had increasing agitation, and this morning is confused, with fever, sweating, loose stools, and tremors.

On exam in the emergency department, he is agitated; his temperature is 101°F, pulse 110/minute and regular, there is marked diaphoresis, and there is muscle clonus in the lower extremities.

Lab testing shows normal WBC and creatinine.

Which of the following best explains this situation?

A. *Clostridioides difficile* colitis

B. Monoamine oxidase inhibition by linezolid

C. Sertraline-mediated inhibition of linezolid metabolism

D. Side effect of inhaled liposomal amikacin

Correct answer: Monoamine oxidase inhibition by linezolid

Rationale

Linezolid acts as a reversible, nonselective monoamine oxidase inhibitor (MAOI). Monoamine oxidase is responsible for the breakdown of serotonin. When a person already taking an SSRI (like sertraline) starts linezolid, the combination of inhibited serotonin reuptake and inhibited serotonin metabolism can lead to excessive synaptic serotonin levels.

Excess serotonin can precipitate serotonin syndrome, typically characterized by the triad of:

- Neuromuscular hyperactivity (tremor, hyperreflexia, clonus)
- Autonomic instability (tachycardia, fever, diaphoresis)
- Altered mental status

The primary management of serotonin syndrome is immediate discontinuation of the offending agents (in this instance linezolid and sertraline).

C. difficile colitis can cause severe illness, including fever, tachycardia, and diarrhea. However, the absence of diarrhea and leukocytosis argue against *C. difficile* as a cause of this patient's current illness.

Inhaled liposomal amikacin mainly causes local side effects including hoarse voice and, in some people, dyspnea temporally associated with inhalation and those are not mentioned here. Sertraline does not meaningfully inhibit linezolid metabolism.

41 | CHLAMYDIA FITZ-HUGH-CURTIS | GHANEM

A 17-year-old adolescent cis-gender woman presented for care because of a ten-day history of increasing abdominal pain, accompanied by low grade fever the past two days.

The pain was mostly in the right upper quadrant, worse on deep breathing. On deep inspiration, the pain was felt in her right shoulder. She also reported abnormal yellow vaginal discharge. Her menses have been normal. No dysuria was reported.

She reported condomless vaginal intercourse with a several male partners.

On exam, her vital signs were normal except for a temperature of 38.5°C. She had marked tenderness in the right upper quadrant and some dull tenderness over the lower abdomen bilaterally.

Her WBC was 11,800/mm^3 with normal liver chemistries. Abdominal ultrasound showed no evidence of cholecystitis or liver abscess. A urine pregnancy test was negative.

Which test is most likely to establish the correct diagnosis?

A. CT of abdomen and pelvis with oral and IV contrast
B. Laparoscopy
C. Cervical NAAT for herpes simplex virus
D. Liver biopsy
E. Cervical NAAT for *Chlamydia trachomatis*

Correct answer: Cervical NAAT for *Chlamydia trachomatis*

Rationale

You might have recognized this as a case of Fitz-Hugh-Curtis syndrome. The right upper quadrant tenderness and right shoulder pain on deep inspiration indicate irritation of the diaphragm, more likely in or around the liver.

Hepatitis or liver abscess seem unlikely and leave unexplained her vaginal discharge and lower abdominal tenderness (the ultrasound was also unrevealing).

Pelvic exam has not been done, so a tuboovarian abscess remains possible, though does not explain her right upper quadrant abdominal pain and shoulder pain with inspiration.

A unifying diagnosis would be perihepatitis due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, the Fitz-Hugh-Curtis syndrome. She should be treated for pelvic inflammatory

disease (PID), and the perihepatitis-related pain can be managed with a nonsteroidal anti-inflammatory drug.

Laparoscopy might show adhesions between the liver and adjacent tissue from perihepatitis but not explain them.

Liver biopsy is not indicated with normal liver function and sonogram.

CT of the abdomen and pelvis is unlikely to identify the cause of the infection, but a positive NAAT of a cervical swab for *C. trachomatis* would explain the vaginal discharge and open the possibility that infection had spread from the tuboovarian area into the peritoneum, causing perihepatitis.

Herpes simplex virus (HSV) would not present like this although HSV can occasionally cause acute hepatitis.

Fitz-Hugh-Curtis syndrome (perihepatitis) is associated with PID. There is inflammation of the liver capsule and peritoneal surfaces of the right upper quadrant. Because the liver parenchyma is not involved, liver function tests are normal or minimally elevated. Women present with right upper quadrant abdominal pain with a remarkable pleuritic component, which sometimes can be referred to the right shoulder. There is tenderness in the right upper quadrant which can overshadow the pelvic pain of PID.

This syndrome has been associated with PID and specifically with *Neisseria gonorrhoeae* (historically) and more recently with *Chlamydia trachomatis* as well.

Outpatient therapy is often sufficient: A single intramuscular dose of a long-acting cephalosporin [ceftriaxone (500 mg if <150 kg or 1 g if $\geqslant$150 kg)] plus doxycycline (100 mg orally twice daily for 14 days) plus metronidazole (500 mg orally twice daily for 14 days).

42 | NORWEGIAN SCABIES | KLOMPAS

A 68-year-old man with a history of schizophrenia presents to the emergency department with paranoid delusions. He is currently undomiciled and has not been taking his antipsychotics.

He says that he feels like he has tiny worms crawling all over him that are making his skin dry and flaky.

Exam is notable for a cachectic, disheveled man in dirty clothing. He has thick hyperkeratotic plaques and warty skin crusts in a patchy distribution over the entire body which are particularly pronounced on the hands, feet, and elbows.

Which of the following care providers require post-exposure prophylaxis?

A. The psychiatrist who interviewed him for 120 minutes while sitting in a chair next to his bed in a regular hospital room
B. The patient who was in an adjacent bed in the same room for 14 hours
C. The intern not wearing PPE who did a complete physical exam
D. The nurse in gown & gloves but no mask who helped him into a hospital gown
E. The registration clerk whose pen he used to sign his admission paperwork

Correct answer: The intern not wearing PPE who did a complete physical exam

Rationale

This patient most likely has crusted scabies (formerly Norwegian scabies).

Ringworm, tinea corporis, is usually not this extensive.

Patients with crusted scabies can harbor thousands to millions of mites making them highly contagious (in contrast to patients with classic scabies where only a few dozen mites are involved). Transmission is via skin-to-skin contact (+/- handling the patient's clothing or bedding).

The intern not wearing PPE likely had skin-to-skin contact during the physical exam and thus merits post-exposure treatment.

Treatment options include permethrin cream or oral ivermectin.

The others (psychiatrist, patient in next bed, nurse in gown and gloves, and registration clerk) were less likely to have had skin-to-skin contact but if they do report they had skin-to-skin contact they too should be offered scabies prophylaxis.

43 | TB PROPHYLAXIS | DORMAN

A 22-year-old patient with HIV infection (CD4 count 350 cells/ μL, viral load <50 copies/ml on dolutegravir/lamivudine) lives with his parents in an apartment.

His mother, who works as a correctional officer, is healthy but was recently diagnosed with pulmonary tuberculosis when she developed a cough, radiologic evidence consistent with tuberculosis, and has a sputum that was smear positive and NAAT (Cepheid Xpert MTB/Rif) positive for rifampin-susceptible *Mycobacterium tuberculosis*.

The patient has no symptoms consistent with TB and has an unremarkable physical examination.

Laboratory results are consistent with prior visits. Chest x-ray is normal.

The patient had a negative PPD in clinic 2 years ago when he was first evaluated for HIV infection.

What would you recommend for this patient?

A. Withhold decision until results of repeat PPD or IGRA are available from current clinic visit
B. Withhold decision until results of chest CT and PPD or IGRA are available from current clinic visit
C. If initial PPD and IGRA are negative, repeat PPD or IGRA at 3, 6 and 12 months and initiate treatment only if PPD or IGRA are positive
D. Initiate treatment for latent TB regardless of PPD or IGRA result

Correct answer: Initiate treatment for latent TB regardless of PPD or IGRA result

Rationale

People with HIV who are in close contact with anyone with infectious tuberculosis (TB) should receive LTBI treatment, regardless of their TB screening test results.

TB infection can occur at any CD4 T lymphocyte (CD4) cell count, although the risk increases with progressive immunodeficiency. Even with effective antiretroviral therapy, the risk of TB disease among people with HIV remains greater than that among the general population.

Once active TB disease is excluded and in the absence of other medical contraindications, people with HIV with a positive TB screening test should receive latent TB infection treatment unless there is documentation of prior treatment for active TB or latent TB infection.

Given the important drug–drug interactions between rifamycins and several antiretroviral agents, selection of a latent TB infection regimen will depend on a patient's current or planned ARV regimen.

This patient is receiving dolutegravir, which interacts with rifamycin drugs. The optimal regimen for treating latent TB in this patient requires careful consideration of other concurrent medications that might interact with rifamycins, including antiretroviral drugs. The optimal regimen is probably difficult to test on an exam.

How to dose dolutegravir in this patient if a rifamycin is used for treatment of latent TB is controversial: an additional dose of dolutegravir daily is advocated on the Liverpool website.

https://www.hiv-druginteractions.org/

44 | BACTERIAL VAGINOSIS | GHANEM

A 28-year-old woman presents with her fourth episode of symptomatic bacterial vaginosis (BV) within the past year. She is in a mutually monogamous relationship with her male partner. She has previously responded to standard BV therapy but experiences frequent recurrences.

In addition to standard treatment with metronidazole in this patient, what additional intervention may be considered in her male partner?

A. No treatment for the male partner; advise condom use only

B. Single 2 g dose of oral metronidazole for the male partner

C. Oral metronidazole 500 mg twice daily for 7 days plus 2% topical clindamycin cream applied to the penile glans/coronal sulcus twice daily for 7 days

D. Topical metronidazole gel applied to the penis once daily for 5 days

E. Doxycycline 100 mg twice daily for 7 days

Correct answer: Oral metronidazole 500 mg twice daily for 7 days plus 2% topical clindamycin cream applied to the penile glans/coronal sulcus twice daily for 7 days

Rationale

In the NEJM randomized trial of couples with recurrent BV, concurrent combined male-partner therapy with oral metronidazole and topical 2% clindamycin cream reduced BV recurrence in women compared with usual care without partner treatment. Single-dose metronidazole, doxycycline, penile metronidazole gel alone, or no partner therapy are not evidence-based interventions.

For the first time, ACOG recommends considering concurrent treatment of sexual partners, including male partners, alongside the patient's BV treatment in certain cases.

- Who to consider for partner treatment:
    - Women with recurrent, symptomatic BV: Concurrent male partner therapy can be offered to help reduce recurrence.
    - Shared decision-making: ACOG suggests discussing partner therapy even for patients with a first symptomatic BV episode and those with same-sex partners or non-monogamous partnerships, using shared decision-making given limited data.

More research is needed, particularly for same-sex partners, multiple partners, and asymptomatic BV. Shared decision-making is emphasized rather than strict, universal partner treatment.

45 | DIPHTHERIA PROPHYLAXIS | KLOMPAS

A previously unvaccinated immigrant from Bangladesh was seen in the emergency department for pharyngitis two days after arrival in the United States.

The patient required an emergency tracheostomy and while the differential diagnosis was extensive, the patient received broad spectrum antibiotics plus steroids.

The patient was found to have an oropharyngeal culture positive for *Corynebacterium diphtheriae*, presumably acquired in Bangladesh.

The patient was treated appropriately with penicillin and horse origin antitoxin obtained from CDC.

The emergency department team that had close contact with the patient during examination and tracheostomy inquires about prophylaxis, although they have all been immunized.

What should you recommend?

A. **A single dose of intramuscular benzathine penicillin G or a 7- to 10-day course of oral erythromycin; if last dose of toxoid was ⩾5 years ago add a single dose of diphtheria toxoid**
B. Single dose of ciprofloxacin plus a single dose of diphtheria toxoid if last dose of toxoid was 5 or more years ago
C. Four doses of rifampin plus a single dose of diphtheria toxoid if last dose was 5 or more years ago
D. No therapy unless the healthcare worker's oropharyngeal culture is positive
E. No therapy regardless of culture since they have been vaccinated

Correct answer: A single dose of intramuscular benzathine penicillin G or a 7- to 10-day course of oral erythromycin; if last dose of toxoid was ⩾5 years ago add a single dose of diphtheria toxoid

Rationale

Health care workers and non-health care workers are managed somewhat differently regarding post exposure management.

CDC recommendations:

For **healthcare personnel** who have an exposure to diphtheria, regardless of vaccination status:

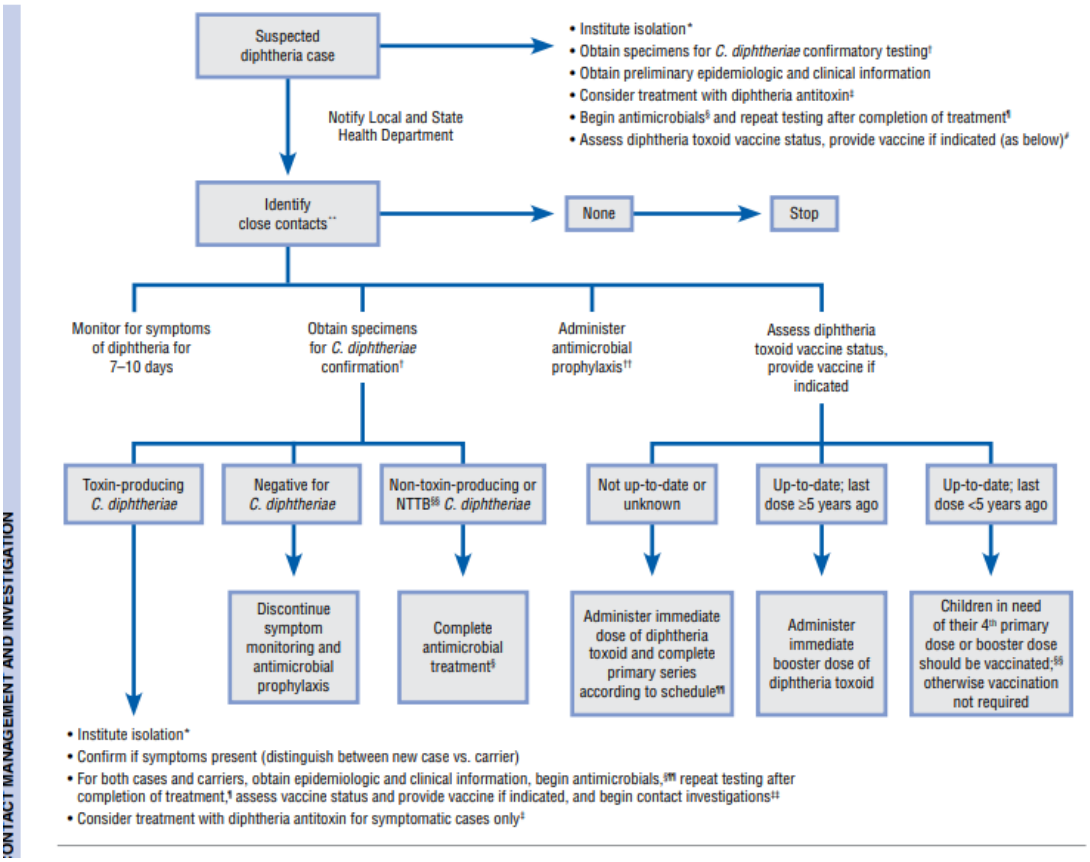
- Administer a single dose of intramuscular benzathine penicillin G or a 7- to 10-day course of oral erythromycin plus for fully vaccinated persons, and if last dose was five years ago or more, a single dose of diphtheria toxoid
- Exclude from work and obtain nasal and pharyngeal swabs for *C. diphtheriae* culture
    - If nasal AND pharyngeal cultures are negative for toxin-producing *C. diphtheriae*, healthcare personnel may return to work while completing postexposure antibiotic therapy
    - If nasal and pharyngeal cultures are positive
        - Healthcare personnel with positive cultures may return to work when:
            - Postexposure antibiotic therapy is completed AND
            - At least 24 hours after completion of postexposure antibiotic therapy
            - Two consecutive pairs of nasal AND pharyngeal cultures, obtained at least 24 hours apart, are negative for toxin-producing *C. diphtheriae*

For **household contacts**:

- Close contacts of patients with pharyngeal or cutaneous diphtheria should be monitored for development of respiratory or cutaneous illness for 7–10 days after their last exposure.
    - Close contacts include all household members, people with a history of habitual, close contact with the patient, or people directly exposed to patient secretions
    - For chemoprophylaxis, close contacts should receive a 7–10 day course of erythromycin or penicillin or a single dose of benzathine penicillin
        - Before antibiotic administration, diphtheria patients and their close contacts should have nasal, and throat swabs collected for culture to test for *C. diphtheriae* carriage
    - Clearance of the organism should be confirmed after completion of the antibiotic course by repeat swabbing and testing
        - If repeat testing is still positive, another course of antibiotics should be administered
    - Patients and close contacts who are not up to date with diphtheria vaccination should receive the recommended doses of diphtheria toxoid–containing vaccine

https://www.cdc.gov/mmwr/volumes/68/wr/mm6812a2.htm

Management of Close Contacts



https://www.cdc.gov/surv-manual/downloads/appendix-2-close-contact-form.pdf

This page left blank intentionally.

SESSION 4 | TUESDAY, AUGUST 25, 2026

Session Moderator: Dr. Gulick

Session Panelists: Drs. Bloch, Gandhi, Kotton, Maldarelli, Saag, and Whitley

Question #	Topic	Speaker
46	Calcium Pyrophosphate	Bloch
47	CMV Encephalitis	Gandhi
48	HIV Drug Interactions	Gulick
49	CAR T-Cell Therapy	Kotton
50	Persistent Low CD4 on ART	Maldarelli
51	Histoplasma Adrenal Insufficiency	Saag
52	HSV Ulcer Dx	Whitley
53	Disseminated *Strongyloides stercoralis*	Bloch
54	Mucoid *Klebsiella pneumoniae*	Gandhi
55	Non-occupational Post Exposure Prophylaxis	Gulick
56	Ganciclovir Resistant Cytomegalovirus	Kotton
57	Integrase Resistance	Maldarelli
58	Opioid Withdrawal	Saag
59	Mollaret	Whitley
60	*Mycobacterium hemophilum* HIV	Gandhi

This page left blank intentionally.

46 | CALCIUM PYROPHOSPHATE | BLOCH

An 86-year-old female is admitted with right wrist pain and fever. She was hospitalized the preceding week for pyelonephritis with urine cultures growing *Escherichia coli*, with negative blood cultures. She was discharged on a 7-day course of ciprofloxacin. She lives with her granddaughter and 2 cats.

The wrist was aspirated with 23,000 WBC/mm^3 (94% neutrophiles) but negative Gram stain and crystal exam. Empiric vancomycin and ceftriaxone were started, and she was taken to the operating room for right wrist arthrotomy with finding of purulent fluid in the midcarpal and radiocarpal joints.

On hospital day 2 she continued to be febrile with ongoing right wrist pain. On hospital day 3, she noted new onset of left wrist pain. Imaging shows chondrocalcinosis of the wrist.

Cultures from the arthrocentesis, operative cultures, and blood cultures are all no growth at 72 hours.

What is the most likely cause of her polyarticular arthritis?

A. *E. coli* bacteremia with secondary septic arthritis
B. *Borrelia burgdorferi* infection
C. *Bartonella henselae* infection
D. Parvovirus B19 infection
E. Calcium pyrophosphate deposition disease

Correct answer: Calcium pyrophosphate deposition disease

Rationale

Calcium pyrophosphate deposition disease (CPPD) is due to precipitation of calcium pyrophosphate crystals in connective tissues causing acute or subacute monoarticular or oligoarticular arthritis. The knee is the most involved joint with CPPD disease, but crystals may precipitate in any joint. As in this case, bilateral wrist involvement in an older patient should suggest the diagnosis of CPPD arthritis.

Diagnosis of CPPD is confirmed by visualization of positively birefringent calcium pyrophosphate crystals under polarized light microscopy, but these are not uniformly present. Imaging showing calcification of cartilage, or chondrocalcinosis, is suggestive of CPPD. In this patient, arthrocentesis of the left wrist confirmed the presence of calcium pyrophosphate crystals.

Fever and elevated inflammatory markers are frequent with exacerbations. These may make it difficult to differentiate CPPD from gout or septic arthritis. However, the other infectious diagnoses would not cause chondrocalcinosis and are less consistent with this presentation.

- Secondary seeding of joints is unlikely in the absence of bacteremia, especially while on appropriate antibiotic therapy
- Lyme arthritis typically causes subacute arthritis, with the knees most effected
- The history of cats in the household may be a risk factor for cat scratch disease due to *B. henselae*, but this does not cause inflammatory arthritis

Parvovirus B19 infection in adults can cause acute, symmetric arthritis or arthralgias involving the hands and feet; rash is typically present.

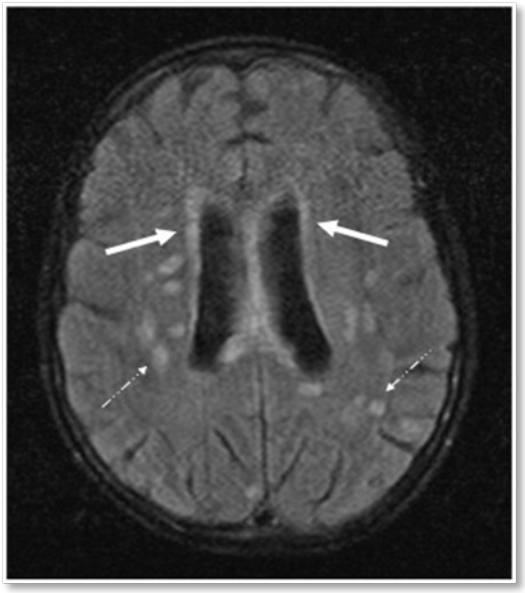
47 | CMV ENCEPHALITIS | GANDHI

A 32-year-old female with HIV infection (viral load 100,000/ml, and a CD4 count below 10 cells/mm^3) has failed all available ART regimens.

Her mother brings her to the clinic because of confusion for 1-2 weeks. She is afebrile, oriented x 1, and slow to respond.

She has nystagmus and cranial nerve VI palsy on the right.

The contrast enhanced MRI image (shown below) is read as showing ventriculitis (i.e., inflammation of the ependymal lining of the lateral cerebral ventricles).



Which PCR of CSF would most likely provide the most likely diagnosis?

A. JC virus
B. Epstein-Barr virus
C. Cytomegalovirus
D. Human herpesvirus 6
E. Human herpesvirus 8

Correct answer: Cytomegalovirus

Rationale

Cytomegalovirus encephalitis should be considered when patients fit the following.

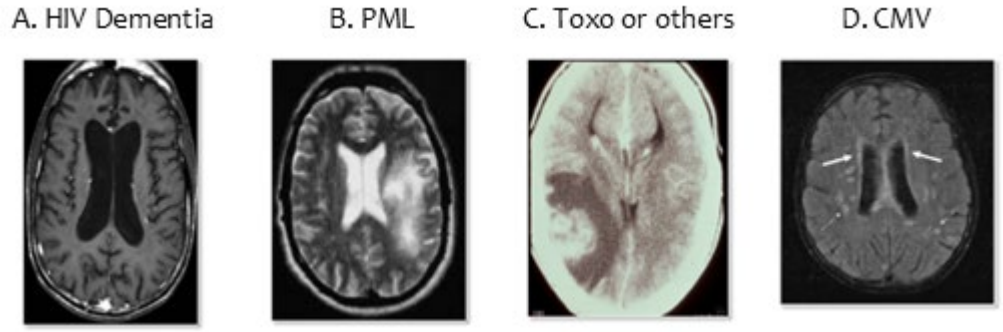
- Imaging
    - Periventricular enhancement (shown in image above) or
        - Less common: Micronodular throughout the brain

*Clinical and laboratory characteristics

- Low CD4 (<50/mm^3)
- Rapid onset (days or weeks-unlike HIV dementia)
- Focal cranial nerve findings or nystagmus
- Cerebrospinal fluid pleocytosis sometimes with polys

Hopefully the exam will not expect you to be a neuroradiologist.

However, there are several patterns you should recognize especially but which should be considered with the appropriate clinical presentation:



A. Ventriculomegaly and cerebral atrophy, typical of HIV dementia
B. White matter lesions typical of JC encephalitis (progressive multifocal leukoencephalopathy)
C. Mass lesions typical of *Toxoplasma gondii*, lymphoma and many other fungal, mycobacterial and neoplastic processes

Ventricular enhancement, characteristic of cytomegalovirus encephalitis

48 | HIV Drug Interactions | Gulick

A 43-year-old man with HIV on a dolutegravir-based regimen with excellent virologic response (CD4 720 cells/μL, HIV RNA <20 copies/mL repeatedly for years) presents for routine follow-up and is found to have a CD4 count of 456 cells/μL and viral load 10,000 copies/ml.

He states he has not missed a single dose of his antiretrovirals and did not start any new medications.

One month ago, he started a nutritional supplement from a health food store called "Vitamin-Mineral Boost" that he started before he goes to bed, the same time as he takes his antiretrovirals.

What is the most likely cause of his elevated viral load level?

A. Poor adherence

B. Taking the antiretrovirals with food

C. Calcium/magnesium in the nutritional supplement

D. Vitamin B6 in the nutritional supplement

Correct answer: Calcium/magnesium in the nutritional supplement

Rationale

The positive cations calcium and magnesium bind to dolutegravir and reduce its absorption resulting in suboptimal dolutegravir levels and subsequent virologic breakthrough. This could have been avoided by taking the supplement and the antiretrovirals either with food or 6 hours or more apart.

The patient has been adherent for many years, so poor adherence seems unlikely in this case. Some antiretrovirals (e.g., rilpivirine) should be taken with food, but a dolutegravir-based regimen can be taken with or without food.

Vitamin B6 does not interact with antiretrovirals.

49 | CAR T-Cell Therapy | Kotton

A 53-year-old man has received CAR CD19 T cell therapy with axicabtagene ciloleucel (Yescarta - a CD19-directed genetically modified autologous T cell immunotherapy) for refractory diffuse large B cell lymphoma (DLBCL). He had failed prior regimens of standard chemotherapy.

Seven days after infusion of the axicabtagene ciloleucel (Yescarta), he developed fever to 38.3°C, hypotension, hypoxemia, pulmonary infiltrates, and oliguria.

On physical examination, other than his vital signs there are no new findings other than diffuse crackles. He has a port in place that looks unremarkable.

His absolute neutrophil count in 50 cells/μl.

Which of the following would most accurately describe how to distinguish septic shock from a CAR-T cell cytokine release syndrome in this patient?

A. IL-1 level

B. IL-6 level

C. CH50

D. C reactive protein

E. There is currently no clinical or laboratory test that will distinguish sepsis from CAR-T cytokine release syndrome

Correct answer: There is currently no clinical or laboratory test that will distinguish sepsis from CAR-T cytokine release syndrome

Rationale

Axicabtagene ciloleucel (Yescarta) is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

There is no clinical or laboratory method that will distinguish sepsis from CAR-T cell cytokine release syndrome and guide the decision whether to treat for sepsis or to withhold antimicrobial therapy. Clinical judgement is needed, and while this patient most likely has CAR-T cell cytokine release syndrome, it would be a disaster to fail to treat sepsis should this be something related to the neutropenia, the port, or…some other source of infection.

CAR-T cell therapy often leads to the release of large amounts of multiple cytokines (CAR-T cell cytokine release syndrome). This cytokine release can have diverse effects on organs. Clinical manifestations usually occur 1-14 days after CAR-T infusion.

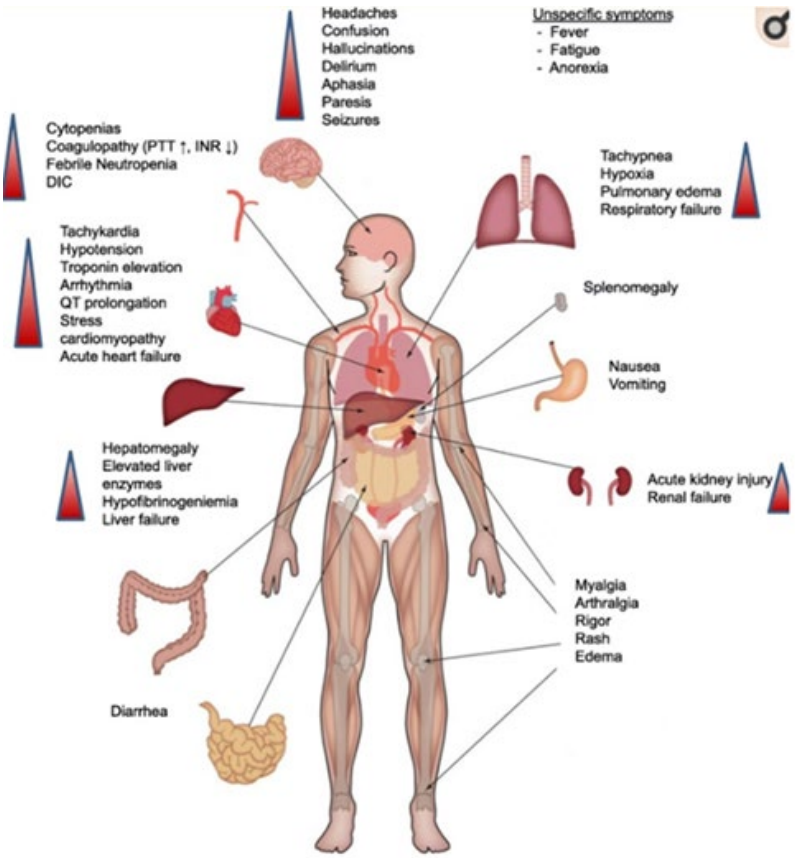
The syndrome is triggered by gamma interferon release by activated T cells or tumor cells. Interferon gamma also activates macrophages which produce IL-6, TNF-alpha and IL10 as well as IL-1, IL-2 IL-5, and GM-CSF and many other factors.

These same cytokines may be activated in sepsis, and thus there is no laboratory test that distinguishes sepsis from CAR-T cytokine release syndrome, although an aspiration of investigators is to develop a rapid test that could make that distinction. Thus, when patients present with sepsis like findings, it is prudent to treat them empirically for sepsis while getting appropriate cultures and reassessing the need for antibiotic therapy over the next several days. Patients are often treated empirically with cefepime for at least 5-7 days since it's difficult/impossible to determine if the patient had been septic. Many other options may be appropriate in certain situations, such as adding coverage for methicillin-resistant or -susceptible *Staphylococcus aureus*, or *Candida* species.

Patients treated with CAR-T cells may also get secondary hemophagocytic lymphohistiocytosis (HLH), which is also difficult to distinguish from cytokine release syndrome and from sepsis: a serum ferritin level is helpful but not definitive for HLH if >10,000 ng/ml.

There are currently several FDA approved CAR-T cell products, including tisagenlecleucel (Kymriah) for pediatric and young adults B cell acute lymphoblastic leukemia and adult DLBCL, and axicabtagene ciloleucel (Yescarta) for adult DLBCL and several other B cell malignancies. More products are being approved for a variety of solid and hematologic malignancies.

The manifestations of CAR-T cytokine release syndrome are summarized below:



Shimabukuro-Vornhagen et al. J Immunother Cancer. 2018; 6: 56

50 | Persistent Low CD4 on ART | Maldarelli

A 62-year-old man with newly diagnosed HIV infection (HIV RNA 326,000 copies/ml, CD4 205 cells/μL) starts antiretroviral therapy with tenofovir alafenamide (TAF)/emtricitabine/bictegravir. At 3 months, he had an HIV RNA is <20 copies/ml and CD4 211 cells/μL.

At 6 months, HIV RNA <20 copies/ml and CD4 203 cells/μL.

He's concerned about his CD4 cell count.

What do you recommend?

A. **Continue present ART regimen**
B. Change TAF/emtricitabine to ABC/lamivudine
C. Change bictegravir to darunavir/ritonavir
D. Add darunavir/ritonavir
E. Start filgrastim (G-CSF)

Correct answer: Continue present ART regimen

Rationale

This patient started on appropriate first-line ART and achieved maximal virologic suppression, but his CD4 cell count did not increase. This occurs in ~10% of people and is more common with older age or lower baseline CD4 cell count (and in this case, both).

Neither changing nor adding antiretroviral drugs to an already suppressive regimen has been shown to increase CD4 cell counts.

Thus, this regimen should be continued, other potential causes of lymphopenia evaluated, and the patient reassured that they are benefiting from the virologic suppression.

51 | HISTOPLASMA ADRENAL INSUFFICIENCY | SAAG

A 46-year-old man with HIV infection is seen for fever and hypotension. For the past 4 months, he has been receiving treatment for disseminated histoplasmosis.

He initially was treated with amphotericin B and is now taking itraconazole. His urine *Histoplasma* antigen is being monitored and has recently been negative. He is also receiving antiretroviral therapy according to guideline recommendations.

He has been feeling weak and tired but generally has been doing well.

Yesterday he had surgery under conscious sedation with propofol for an impacted and infected wisdom tooth. The night of surgery he developed fever and was given vancomycin and ceftriaxone by the surgical team.

This morning he was hypotensive and experienced abdominal pain. He is now on pressors.

- His temperature is 101.8°F; pulse 122/minute, BP 84/62 mmHg.
- He has mild, diffuse abdominal tenderness but no rebound, has audible bowel sounds and is otherwise unremarkable

- His leukocyte count is 6,120 cells/µl with 72% neutrophils, 23% lymphocytes and 5% eosinophils
- His sodium is 125 mEq/L; potassium is 5.7 mEq/L; creatinine is 1.9 mg/dL; HCO_3 is 20 mEq/L
- Blood cultures are negative at 18 hours
- Piperacillin- tazobactam has been started for the possibility of sepsis from an oral source

Which of the following would be the most helpful addition to his regimen to reverse his hypotension and abdominal pain?

A. Dantrolene
B. Caspofungin
C. Liposomal amphotericin B
D. Voriconazole
E. Hydrocortisone

Correct answer: Hydrocortisone

Rationale

Secondary adrenal insufficiency is classically associated with disseminated tuberculosis, disseminated histoplasmosis, and with bacterial sepsis due to meningococcus or a host of other organisms. Adrenal insufficiency has also been associated with HIV infection, itraconazole, and with hemorrhagic infarction associated with anticoagulant therapy or disseminated intravascular coagulation. Thus, this patient could have adrenal insufficiency due to his HIV disease, itraconazole, or disseminated histoplasmosis.

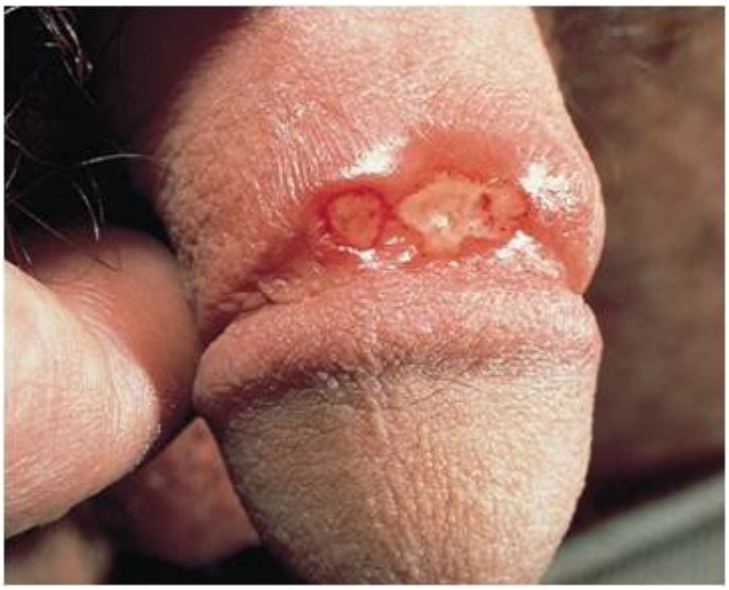
The diagnosis of adrenal crisis should be considered in someone who has had a recent stress, such as trauma or surgery, and a reason to have underlying adrenal insufficiency, such disseminated histoplasmosis or itraconazole use in this case. Supporting laboratory evidence includes hyponatremia, hyperkalemia, and mild acidemia.

The hypotension in this case is unlikely to be due to active disseminated histoplasmosis: the patient's fungal disease appears well controlled. There is no reason to switch to voriconazole, another active azole but one for which there is less experience for treating histoplasmosis than itraconazole.

There is nothing to suggest malignant hyperthermia. Malignant hyperthermia is usually triggered by a halogenated gas anesthetic or succinylcholine, neither of which would be used for conscious sedation. For malignant hyperthermia, muscle spasms, sometimes leading to rhabdomyolysis, are usual. The presence of eosinophilia, hyperkalemia and shock also make this diagnosis less likely.

52 | HSV Ulcer Dx | Whitley

An 18-year-old man presents with a history of malaise, low-grade fevers, and new-onset painful genital lesions seen in the picture below. The pain is significant.



He had unprotected sexual intercourse with a female partner 2 weeks earlier. Neither he nor his partner has traveled outside the United States. He is HIV uninfected by recent rapid test.

Which of the following diagnostic tests is most likely to yield the specific diagnosis?

A. Serum RPR
B. Antibody to herpes simplex virus-1 and -2
C. Darkfield microscopy
D. PCR for herpes simplex virus
E. Bacterial culture

Correct answer: PCR for herpes simplex virus

Rationale

Given the fairly classical clinical presentation and the lack of travel, the most likely diagnosis is primary herpes simplex virus (HSV) infection. Although syphilis is not ruled out with 100% certainty, it is much less likely because the lesion was painful.

The most sensitive and common diagnostic test would be PCR on a swab from the lesion. Tzanck smears are less sensitive and less specific. Culture for HSV infection has ~70% sensitivity, so a negative culture result would not rule out the diagnosis. NAAT (nucleic acid amplification test) is optimal for *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, but the lesion is too atypical for either.

The RPR to diagnose primary syphilis is insensitive in patients presenting with a chancre.

Chancroid is theoretically possible, but most cases occur in Sub-Saharan Africa or the Caribbean. There are cases that occur in the US, particularly among commercial sex workers and persons who exchange sex for drugs. Chancroid presents with painful ulcers (often multiple ulcers with "soft edges" and purulent exudate, sometimes with purulent lymphadenopathy and thus not like the ulcer in the image) and is diagnosed by NAAT tests done in specialty labs (the test is not FDA approved). Most labs do not perform cultures for *Haemophilus ducreyi*. Thus, this is not likely to be chancroid, and if it were chancroid, bacterial culture is not the best diagnostic test.

Remember the general rule: painful ulcers are caused by HSV and chancroid (*H. ducreyi*); painless ulcers are caused by syphilis, lymphogranuloma venereum (LGV) and granuloma inguinale (*Klebsiella granulomatis*) but that LGV inguinal adenopathy is painful.

53 | DISSEMINATED *STRONGYLOIDES STERCORALIS* | BLOCH

A 67-year-old man is admitted with confusion, headache and fever for 1 day. He has a history of polymyalgia rheumatica for which he takes prednisone 30 mg/day and trimethoprim-sulfamethoxazole single strength tablet daily *for Pneumocystis* prophylaxis. He was hospitalized 6 months previously for *Escherichia coli* bacteremia with no source identified.

He lives in rural Georgia with his wife and 3 dogs.

On exam his temperature is 103°F. He inconsistently responds to questions with yes/no answers only. He resists passive flexion of the neck.

A CBC returns with a WBC of 26 x 10^9/L (90% segmented neutrophils, 8% lymphocytes, 2% eosinophils). Urinalysis is bland. A lumbar puncture is performed with 977 WBC/μl (95% neutrophils), glucose of 25 mg/dL and protein of 130 mg/dL.

Blood and CSF cultures grow pan-susceptible *Enterococcus faecalis*.

In addition to starting treatment with ampicillin and ceftriaxone, what additional work-up is indicated?

A. Contrasted CT scan of the abdomen and pelvis

B. Colonoscopy

C. PET scan

D. Quantitative immunoglobulin levels

E. Serology for *Strongyloides stercoralis*

Correct answer: Serology for *Strongyloides stercoralis*

Rationale

This patient is likely to have chronic strongyloidiasis, with hyperinfection causing translocation of enteric flora (*E. coli* and *E. faecalis*) leading to systemic bacterial infections. *S. stercoralis* is endemic in low- and middle-income countries and also in the Southeastern United States and Appalachia.

Following infection, adult female worms burrow into small bowel mucosa where they produce ova that may mature into filariform larvae. These larvae then penetrate the intestinal mucosa, causing a phenomenon of autoinfection. Immunocompromised patients may develop hyperinfection which can manifest with abdominal symptoms (colitis/proctitis, small bowel obstruction), acute respiratory symptoms (dyspnea, chest pain), rash, or as in this case, systemic infection with enteric organisms. Community-acquired meningitis caused by enteric gram-negative bacteria or enterococci should raise suspicion for *Strongyloides* hyperinfection syndrome.

Strongyloides hyperinfection is seen almost exclusively in immunocompromised patients, with steroids being the most frequently recognized risk factor. Hyperinfection can occur even with short courses of steroid administration. While peripheral eosinophilia is common with chronic *Strongyloides* infection, this is not the case with hyperinfection and should not dissuade a clinician from the diagnosis.

Diagnosis of hyperinfection can typically be made by serology, and if this is negative but suspicion remains, by stool O&P (which notably is not an option for the multiple-choice responses). If the diagnosis is confirmed, ivermectin is typically curative but may require prolonged courses, or, when immunosuppression cannot be decreased, long term suppression with monthly dosing.

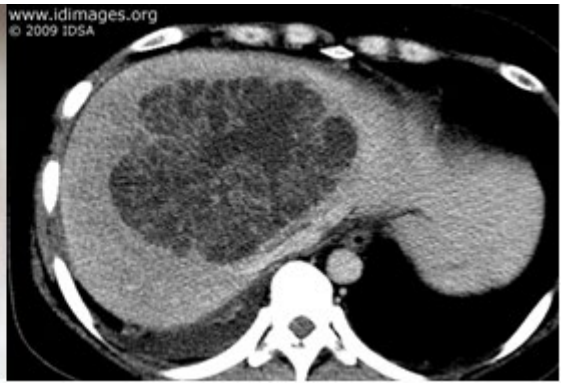
54 | MUCOID *KLEBSIELLA PNEUMONIAE* | GANDHI

A 40-year-old woman from Taiwan who was recently visiting her daughter in the US developed fever, epigastric pain, and nausea.

One week later, she was brought to the emergency department because of confusion and fever. On examination, her temperature was 101°F. She had right upper quadrant abdominal tenderness.

An abdominal CT scan showed a 10 cm hypoattenuated liver lesion (below).

An aspirate was performed; the culture showed mucoid colonies of an aerobic, Gram-negative rod with a positive string test. Her daughter likes to serve raw oysters and has a cat.



Which of the following is the most likely organism?

A. *Vibrio parahaemolyticus*
B. *Aeromonas* species
C. *Fusobacterium necrophorum*
D. *Pasteurella multocida*
E. *Klebsiella pneumoniae*

Correct answer: *Klebsiella pneumoniae*

Rationale

The only organism in the list to give a mucoid colony is *K. pneumoniae*. In addition, a hypermucoid strain of *K. pneumoniae* has been associated with a distinctive clinical syndrome in Taiwan and some other parts of Southeast Asia that includes primary liver abscess, bacteremia, and metastatic infection. Risk factors for this infection include diabetes and Asian ancestry. *K. pneumoniae* colonies can exhibit extreme "stickiness" on agar plates ("hypermucoviscosity phenotype"), and the string test is positive (i.e., a "string" of more than 5 millimeters is formed when one touches a loop to the colony).

The other organisms on this list would not be expected to have a hypermucoid phenotype or a positive string test. *F. necrophorum* is an obligate anaerobe.

V. parahaemolyticus has caused outbreaks of gastroenteritis from raw oysters but would be a rare cause of liver abscess.

Aeromonas species can cause diarrhea but would rarely be the sole organism in a liver abscess. *P. multocida* can cause sepsis after a cat bite but liver abscess would be rare.

55 | NON-OCCUPATIONAL POST EXPOSURE PROPHYLAXIS | GULICK

A 33-year-old male who has multiple sexual partners had unprotected anal intercourse for the first time last night. This new partner mentioned after the interaction that he does have HIV infection, and he "usually" takes his drugs.

In the past, you have seen the patient every 3 months for HIV testing, and he has been HIV negative to date and has never had a sexually transmitted infection.

You perform a rapid HIV test which is negative.

The patient has no symptoms other than severe anxiety, and no new physical findings.

Routine laboratory values are normal.

What would you recommend with regards to post exposure management and reducing risk of HIV infection?

A. No testing or therapy unless the patient has findings consistent with acute HIV infection

B. Follow the patient with monthly HIV antibody tests for 6 months but no therapy if he remains negative

C. Follow the patient with monthly HIV antigen/antibody tests but no therapy if he remains negative

D. Treatment with tenofovir alafenamide/emtricitabine for 12 weeks and periodic HIV serologic testing during and after prophylaxis

E. Treatment with bictegravir/tenofovir alafenamide/emtricitabine for 4 weeks (28 days) and periodic serologic testing and periodic HIV serologic testing during and after prophylaxis

Correct answer: Treatment with bictegravir/tenofovir alafenamide/emtricitabine for 4 weeks (28 days) and periodic serologic testing and periodic HIV serologic testing during and after prophylaxis

<u>Rationale</u>

Non-occupational post exposure prophylaxis (nPEP) is recommended for persons who have sexual or needle-sharing exposure to a source with HIV who does not have sustained HIV suppression or whose suppression status is unknown.

- If the source has prolonged suppression of HIV, nPEP is not routinely recommended after sexual exposure
- The preferred regimens are bictegravir/tenofovir alafenamide/emtricitabine OR dolutegravir plus tenofovir (TAF OR TDF) plus FTC OR 3TC
- nPEP should be started as soon as possible after exposure (but no later than 72 hours) and should be given for 4 weeks

- At the initial visit, HIV testing with a rapid (point-of-care) test, a laboratory-based antigen/antibody test — or both — should be performed
- HIV testing with a lab-based antigen/antibody test and a diagnostic HIV nucleic acid test should be done at 4–6 weeks (only necessary if PEP started >24 hours after exposure or missed PEP doses) and 12 weeks after exposure (for everyone).

In persons with ongoing exposure, transition from nPEP to preexposure prophylaxis should be executed as soon as the nPEP course is finished.

- Testing for syphilis, *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is indicated

Doxycycline post exposure prophylaxis (PEP) would be a consideration especially for men-who-have-sex-with men or with transgender women. Doxycycline PEP reduces (but does not eliminate) the risk of *C. trachomatis*, syphilis and *N. gonorrhoeae*, although gastrointestinal side effects and common. Doxycycline 200 mg is taken once orally within 72 hours of condomless oral, anal, or vaginal sex.

56 | GANCICLOVIR RESISTANT CYTOMEGALOVIRUS | KOTTON

A 45-year-old woman undergoes a third kidney transplant.

She is highly sensitized (has HLA antibodies that put her at higher risk of rejection) and is thus maintained on high doses of immunosuppression. Her regimen includes belatacept, mycophenolate mofetil, and prednisone.

Her donor was cytomegalovirus (CMV) IgG positive, she was CMV IgG negative (D+R-) and she was maintained on valganciclovir prophylaxis. She developed breakthrough CMV infection while on prophylaxis and was started on treatment dose valaciclovir (900mg twice a day).

She now has a rising CMV viral load (44,000 IU/ml plasma). She feels a bit fatigued and has some diarrhea, with no visual changes or other symptoms.

Her transplant doctors are reluctant to reduce immunosuppression further.

Genotyping of CMV in her peripheral blood showed a A594V mutation in the UL97 gene, which has been associated with high-level resistance to ganciclovir.

What would you recommend to treat her CMV disease?

A. High dose valacyclovir 8 grams/day
B. CMV immunoglobulin
C. High dose intravenous ganciclovir
D. Maribavir
E. Letermovir

Correct answer: Maribavir

Rationale

In view of her rising CMV viral load, she likely has ganciclovir resistant CMV, which necessitates a change to a different agent. A biopsy could be performed on her colon to confirm tissue disease, CMV colitis is the most common form of end-organ disease in solid organ transplant recipients and the rising CMV PCR in this setting is sufficiently prognostic of impending clinical disease to warrant therapy to reduce the viral load.

A good therapeutic option would be maribavir, recently approved by the FDA for drug resistant CMV and having the advantage of being an (expensive) oral drug that can be given as an outpatient. It has a different mode of action than ganciclovir and is active against ganciclovir-resistant CMV. Intravenous foscarnet and cidofovir would be other appropriate choices, although with higher potential for toxicity. These were not offered as options here. Some experts would use foscarnet for induction therapy with higher viral loads followed by maribavir, to potentially avoid the resistance seen with maribavir.

High dose ganciclovir would not be likely to overcome this resistance.

High dose valacyclovir is used for prophylaxis, but not for treatment and would not be effective.

Letermovir has shown good efficacy in prevention of CMV in bone marrow transplant recipients but has a very low barrier to resistance and is not recommended for treatment of viremic patients CMV immunoglobulin could be considered for adjunctive therapy but not primary therapy.

Maribavir has a novel mechanism of anti-CMV action that does not require intracellular phosphorylation. It is a highly specific inhibitor of the protein kinase product of the*UL97* gene. Clinically important pharmacokinetic interactions have been demonstrated during co-administration of maribavir and tacrolimus (increasing tacrolimus exposure), presumably due to inhibition of CYP3A4 or P-glycoprotein, or both.

57 | INTEGRASE RESISTANCE | MALDARELLI

A 54-year-old man living with HIV on tenofovir alafenamide (TAF)/emtricitabine/bictegravir has difficulty refilling his medications and decides to take them every other day.

On his next follow-up visit, 3 months later, his HIV RNA is 2320 copies/ml.

A repeat viral load is 4544 copies/ml, and a genotype shows reverse transcriptase M184V and integrase G140S and G148H substitutions.

What do you recommend?

A. Continue present ART regimen
B. Obtain integrase phenotype
C. Change bictegravir to darunavir/ritonavir
D. Add darunavir/ritonavir to current regimen
E. Double the bictegravir dose

Correct answer: Change bictegravir to darunavir/ritonavir

Rationale

This patient experienced virologic failure due to suboptimal adherence and developed significant viremia and drug resistance-associated mutations – including the major integrase inhibitor mutation G148H (memorize this one!) that confers resistance to the class.

You need to change his regimen, no additional testing (e.g., phenotype) is needed, and a boosted protease inhibitor (e.g., darunavir/ritonavir) would have the most activity.

Some integrase inhibitor mutations selected by raltegravir or elvitegravir retain susceptibility to bictegravir (and dolutegravir) and can be managed by doubling the dose, but not G148H. Although M184V confers complete resistance to emtricitabine (and cross-resistance to lamivudine), this mutation also "resensitizes" tenofovir, so it is reasonable to continue TAF/emtricitabine.

58 | OPIOID WITHDRAWAL | SAAG

A 41-year-old male with HIV presents for initial evaluation. His CD4 count is 141 cells/µl (9%), HIV viral load 111,580 copies/µL, CrCl 90 cc/min.

He also reports a recent history of injecting drug use with heroin, which is being treated with methadone maintenance for which he is on a stable dose.

The patient reports previous attempts at treatment with antiretroviral but was poorly adherent but now feels ready to resume treatment. No resistance mutations are found on HIV genotyping, and you decide to initiate TAF/FTC + DRV/r given the high barrier to resistance.

The patient and his counselor at the shelter where he lives report that he is adherent to the regimen prescribed by his health care team.

Ten days after initiating treatment the patient returns to your office. He reports abdominal cramping, diarrhea, rhinorrhea, piloerection and irritability.

Here is a photo of his piloerection:

What is the most likely cause of his symptoms?

A. IRIS

B. Enteric bacterial pathogen (*Salmonella* species, *Shigella* species, *Campylobacter* species)

C. Drug interaction

D. Darunavir toxicity

E. Influenza

Correct answer: Drug interaction

Rationale

Given reports of abdominal cramping, diarrhea, rhinorrhea, piloerection and irritability, the patient seems to be exhibiting findings of opioid withdrawal.

This is likely due to increased clearance (i.e., lower serum levels and/or shorter half-life) of methadone, which can result from interaction with darunavir/ritonavir. The appropriate management is to work with his methadone clinic to titrate up levels of methadone until he no longer experiences withdrawal, or switch to a regimen that does not interact with methadone.

He is not febrile or coughing, and thus influenza is less likely.

Piloerection (also known as goose bumps, erection or bristling of hairs due to the involuntary contraction of small muscles at the base of hair follicles that occurs as a reflexive response of the sympathetic nervous system) is a buzzword suggesting opioid withdrawal in this case but…there are many other causes including cold temperature, intensive emotions, other drugs. The word was mentioned in this stem for a reason! With diarrhea and cramping, he could have an enteric infection, but that would not explain piloerection or rhinorrhea.

The clinical picture is not consistent with IRIS, and IRIS typically does not occur when the baseline a CD4 count is >100/µl.

The overall clinical picture is consistent with opioid withdrawal, not infectious diarrhea.

59 | MOLLARET | WHITLEY

A 29-year-old female developed her first bout of meningitis at age 24. Since then, she has had 3 other episodes. Each is associated with headache, stiff neck, and photophobia. Each has been treated with appropriate doses of antibiotics and resolved over several days, and all cerebrospinal fluid (CSF) cultures have been negative.

Her last CSF results at the time of an acute episode revealed a WBC of 230/mm^3 (92% lymphocytes with some large and atypical appearing cells), normal glucose, and protein of 110 mg/dL. All routine bacterial cultures and Gram stains have been negative.

The patient has been well otherwise but has a history of both oral and genital herpes simplex infections, and a remote history of treated syphilis. She has refused permission for a human immunodeficiency virus test in the past.

This young woman's recurrent meningitis is most likely due to which of the following?

A. **Herpes simplex virus type 2**
B. Varicella zoster virus
C. Cytomegalovirus
D. *Treponema pallidum*
E. Human immunodeficiency virus

Correct answer: Herpes simplex virus type 2

Rationale

This is a typical presentation of benign recurrent lymphocytic meningitis – often referred to as Mollaret meningitis.

Mollaret meningitis is a type of benign recurrent lymphocytic meningitis that is most often due to herpes simplex type 2 (HSV-2) infection. Genital lesions are usually absent at the time of presentation.

None of the other choices are known to cause recurrent meningitis over a period of years.

60 | *MYCOBACTERIUM HAEMOPHILUM* HIV | GANDHI

A 35-year-old patient with substance use disorder from New York City with HIV/AIDS was seen in clinic for a 1-cm slightly tender, erythematous draining skin nodule on his left thigh. Pus squeezed from the lesion was negative on Gram stain but had unbranched bacilli on acid-fast smear. The patient failed to keep his next clinic appointment but appeared again 8 weeks later with four more lesions on the same extremity.

He had not lost weight, reported no fever, and did not seem more ill than on prior visits. Acid-fast cultures grown at 35°C on Middlebrook 7H11 agar and an automated broth system from his last visit had been reported negative for mycobacteria. Routine culture grew scant *Staphylococcus epidermidis*.

Which of the following is the most likely causative organism?

A. *Mycobacterium leprae*

B. *Mycobacterium ulcerans*

C. *Mycobacterium chelonae*

D. *Mycobacterium haemophilum*

E. *Mycobacterium malmoense*

Correct answer: *Mycobacterium haemophilum*

Rationale

M. haemophilum can cause localized cutaneous disease or disseminated disease in patients with HIV: localized skin nodules are the most characteristic presentation, as in this patient. The organism is difficult to recover on culture unless the medium contains added iron, such as ferric citrate, and is grown at 30-33° C.

M. ulcerans causes Buruli ulcer, a chronic ulcer that progresses over years and is found in tropical countries and not known to occur in the US.

The other organisms listed, other than *M. leprae*, are more likely to cause disseminated disease and should have grown on the medium used although they may take several weeks to grow.

M. leprae is not likely in this patient since no clues about geographic exposure are given and there are no suggestive findings like cutaneous anesthesia.

This page left blank intentionally.