
# FACULTY

# BOARD REVIEW SESSION BOOK

**COURSE DIRECTORS:**
John Bennett, MD
Henry Masur, MD

**COURSE CO-DIRECTORS:**
Paul Auwaerter, MD
David Gilbert, MD
Roy Gulick, MD, MPH
Andrew Pavia, MD
Richard Whitley, MD

**COURSE ORGANIZERS:**

GW | Office of Continuing Education in the Health Professions

# CONTENTS

*This page left blank intentionally.*

# SESSION 1 | SATURDAY, AUGUST 22, 2020

**Session Moderator:** Dr. Masur

**Session Panelists:** Drs. Bloch, Chambers, Dhanireddy, Scheld, Pavia, and Saag

| Question # | Topic | Speaker |
|---|---|---|
| 1 | Conjunctivitis | Bennett |
| 2 | Candiduria: Fungus | Bennett |
| 3 | Bacterial Sinusitis | Bloch |
| 4 | Clostiridium perfringens | Bloch |
| 5 | Gas gangrene | Bloch |
| 6 | UTI | Chambers |
| 7 | Staph aureus | Chambers |
| 8 | Meningococcus | Gandhi |
| 9 | Endocarditis | Gandhi |
| 10 | Joint infections-cutibacterium | Nelson |
| 11 | CRMO(chronic ost) | Nelson |
| 12 | DRESS | Nelson |
| 13 | Bordatella | Pavia |
| 14 | VZV | Pavia |
| 15 | Rickettsia Africae | Masur |

*This page left blank intentionally.*

## 1 | CONJUNCTIVITIS | BENNETT

A 50 year old woman who wears contact lenses has had redness, itching and burning in her right eye for one week. When she awakes in the morning, her right eyelids are stuck together. She separates the lids with a warm, moist towel. Examination of her right eye reveals diffusely injected bulbar and palpebral conjunctivae, and purulent discharge on the lid margins.

She otherwise feels well, and has no fever, cough, wheezing, or nasal discharge. She is not sexually active.

She notes no change in her visual acuity, and has no problem reading the newspaper or looking at her computer screen. Her ophthalmologist reports she has no keratitis or anterior uveitis. He has sent a conjunctival swab for bacterial culture and a multiplex PCR panel to detect Chlamydia, adenovirus and other viruses. He recommends soft compresses and a return in 3-5 days, when the results will be available. Instead, the patient didn't want to wait and sought your advice because you had seen her recently for a urinary tract infection.

She stopped wearing her contact lens after several days of symptoms, but her symptoms continue.

What would you prescribe?

A. Azithromycin orally for 5 days Surgical exploration
B. Levofloxacin orally for 5 days
C. Await treatment until PCR panel results are available
**D. Moxifloxacin eye drops**
E. Antihistamine eye drops

**Correct answer: Moxifloxacin eye drops**

The purulent discharge and use of contact lenses suggest that this is acute bacterial conjunctivitis rather than viral, chlamydial or allergic conjunctivitis. Absence of sexual activity weighs against Chlamydia trachomatis conjunctivitis. Gonorrheal conjunctivitis is hyper acute, extremely painful and purulent. The likely pathogen is Hemophilus influenzae or Streptococcus pneumonia.

An ophthalmologist has performed a slit lamp exam to be sure there is no corneal involvement and keratitis is usually more painful than this case.

For patients who wear contact lenses, bacterial conjunctivitis can lead to severe manifestations, especially when due to gram negative bacilli or acanthamoeba. Other water borne organisms also can be the causative agents.

Some cases of mild conjunctivitis are likely viral and will resolve if the patient discontinues wearing the contact lenses. However, if symptoms are severe or persist for several days after the patient stops using contact lenses, topical antibiotic therapy is appropriate.

Eye drops containing moxifloxacin, trimethoprim-polymyxin, neomycin-polymyxin or sulfacetamide are commonly used. Oral drugs are not recommended. Waiting for the culture and PCR was a reasonable

request by the ophthalmologist but empiric therapy with fluoroquinolone eye drops has high chance of success, based on her risk factors.

Antihistamine eye drops would be appropriate if there were other manifestations suggesting allergic conjunctivitis.

Steroid eye drops are not appropriate to manage infectious conjunctivitis.

Keep in mind that if the conjunctivae are diffusely injected, these findings indicate inflammation. This should be distinguished from a "ciliary flush", where there is a halo of injected vessels around the cornea (corneal limbus). A ciliary flush is caused by anterior uveitis or keratitis. Conjunctival injection, or dilated conjunctival vessels in the absence of discharge, is not conjunctivitis but can occur from many causes, including systemic infections, like leptospirosis or scrub typhus.

## 2 | CANDIDURIA: FUNGUS | BENNETT

An 80-year-old resident of a nursing home has severe dementia, type 2 diabetes mellitus and a chronic indwelling Foley catheter, which is in place to manage his persistent incontinence. He has no remarkable medical history and is quite healthy except for his dementia. He has received antibiotics for presumed urinary tract infection twice in the last year.

The nursing home staff decided to obtain a urinalysis and urine culture: they call you because the urine culture is growing Candida albicans with a colony count of 100,000 cfu/ml. His UA shows 30-40 WBC and 10-20 RBC per HPF, with a 1+ leukocyte esterase

He is in his usual state of health with no fever, no urinary symptoms that you can elicit from him, and no flank tenderness.

What would you recommend?

**A. Observe and do nothing more unless the patient becomes symptomatic**
B. Observe but obtain repeat urinalysis and culture in one week
C. Change Foley catheter and give oral fluconazole for 1 week
D. Change Foley catheter and IV caspofungin for 1 week
E. Change the Foley catheter and order Amphotericin B deoxycholate bladder washes daily for 5-7 days

**Correct answer: Observe and do nothing more unless the patient is symptomatic**

Asymptomatic candiduria, like asymptomatic bacteriuria, is common in patients with urinary catheters. Diabetes mellitus and antibiotic use predispose to candiduria in both catheterized and non-catheterized patients. Candiduria usually represents colonization in this population. The white and red cells in the UA are likely due to the catheter rather than active inflammation from a true urinary tract infection. The presence of pseudo hyphae or colony count, if that is reported, also is of no help in distinguishing colonization from infection.

This patient does not need to be treated, although changing the Foley can be helpful regarding colonization or infection but is not mandatory or necessary. Repeating the UA and urine culture in a week will not provide any additional information that will help with management.

Many providers will treat such patients as the one described here with fluconazole, but the candiduria usually returns promptly. The same is true with amphotericin B bladder washes.

When candida is found in the urine, there is sometimes concern about a fungus ball in the urinary collecting system. These are unusual, in the absence of diabetes mellitus, antibiotic therapy and renal obstruction or urologic abnormalities. If there is such a concern, a renal ultrasound or abdominal CT is appropriate. Renal papillary necrosis is usually present. The "ball" is typically a sloughed renal papilla invaded by Candida.

Note that candiduria in a patient about to have a urologic bladder procedure is an indication for therapy. Many (but not all) experts routinely treat candiduria in renal transplant recipients, especially in the setting of transplant rejection, though that is not in the IDSA Candida guidelines.

If the indwelling catheter was not necessary to relieve obstruction, a preventive measure to be considered is removal of the indwelling bladder catheter and use of a condom catheter, which may yield a lower risk of infection, or use of a recently developed external, sluice-like collection system.

## 3 | Bacterial Sinusitis| Bloch

In the month of January in Chicago, a 30-year-old woman in excellent health has had purulent nasal drainage, fevers to 38.5 C, sore throat, and chills for the past 14 days.

She has been able to work and to exercise on the treadmill as usual, but she feels tired in addition to her other symptoms.

She saw her primary care physician after 3 days of symptoms, who was insistent that she did not need antibiotics because her symptoms were of short duration and likely would resolve without antibiotics.

She comes to you as an ID physician for another opinion a week after seeing her primary care physician.

On exam, she has a temperature of 38.3C with intermittent chills, moderate pain over her sinuses, and purulent looking nasal discharge. Her CBC is still normal. She has no drug allergies.

What would be the best choice for management?

A. Cephalexin (Keflex)
B. Nasal decongestant and nasal irrigations with saline twice daily for 3-5 days but no antibiotics unless her clinical syndrome worsens
C. Clindamycin (Cleocin)
**D. Amoxicillin-clavulanate (Augmentin)**
E. Ciprofloxacin (Cipro)

**Correct answer: Amoxicillin-clavulanate**

With fever, chills and rhino sinusitis lasting for over 10 days, this patient likely has bacterial rhino sinusitis even though the white blood count is normal.

This patient may well have had a viral syndrome initially, and the primary care physician likely made a wise decision after only 3 days of symptoms. At that point, the syndrome might have resolved without antimicrobials. However, now with 10 days of facial tenderness, fever, and chills, it is likely this is a bacterial process.

While different guidelines provide different recommendations, IDSA recommends amoxicillin-clavulanate and not amoxicillin because of the likelihood of a beta lactamase producing organism such as Moraxella or Hemophilus. Staphylococcus aureus is such an uncommon cause of community-acquired acute bacterial sinusitis that it does not figure in choice of empirical antibiotics.

Pneumococci are often resistant to ciprofloxacin, so "e" would not be a good choice. Cephalexin and clindamycin lack useful activity against Hemophilus influenzae and Moraxella catarrhalis, major pathogens in bacterial sinusitis.

Rising resistance of pneumococci to penicillins and macrolides is causing concern but the IDSA guidelines still recommend amoxicillin clavulanate.

Admittedly, there are no adequately powered clinical trials to prove that amoxicillin-clavulanate is superior to other options such as azithromycin or amoxicillin, but amoxicillin-clavulanate is plausibly the best option, especially of the options listed here.

## 4 | CLOSTIRIDIUM PERFRINGENS| BLOCH

A 45-year-old male is 10 days post-chemotherapy with cytarabine plus daunorubicin for acutemyeloidleukemia. He presents to the ED with profound weakness, fever, and watery diarrhea.

Due to a known absolute neutrophil count of <500 cells/mcL, he has been taking prophylactic once daily levofloxacin since starting chemotherapy.

Three days prior to admission, WBC was 0.1 K/mcL, hgb 9 gm/dL and platelets 26,000/mcL.

In the ED, T 103°F, BP 79/42 mm Hg, P 144/min.

Immediate empiric therapy was started with meropenem and vancomycin.

The lab was unable to measure hgb due to massive hemolysis.

Peripheral smear shows "ghost" RBCs (RBCs without a cytoplasm).

Lactic acid 14 mmol/L

Total bilirubin 13.6 mg/dl, creatinine 48 mg/dL and LDH 17,000 units/L.

Which one of the following is the most likely pathogen causing the clinical syndrome?

**A. Clostridium perfringens**
B. Clostridium sordellii
C. Escherichia coli shiga toxin
D. Group A Streptococcus
E. Bacteroides fragilis

**Correct Answer: Clostridium perfringens**

This syndrome was due to C. perfringens sepsis.

The presumed source was bowel "mucositis" secondary to the chemotherapy..

Massive hemolysis occurs in 2-15% of patients with C. perfringens bacteremia. The organism's alpha toxins (phospholipase C and sphingomyolinase) hydrolyze RBC membranes with loss of their hemoglobin and resultant appearance as 'ghost" cells.

Alpha toxin also activates capillary bed adhesion molecules, which leads to sequestration of neutrophils and platelets. The mortality is 74-91% with survival times of only a few hours.

Treatment includes combination of penicillin and clindamycin for the Clostridium, but these infections can be polymicrobial requiring additional agents.

Of interest, with the exception of delafloxacin, Clostridia species are resistant in vitro to fluoroquinolones.

The toxins of C. sordellii produce a different clinical picture, i.e. a leukemoid reaction due to toxin-mediated damage to receptors for capillary endothelium neutrophil adhesion molecules. In addition, another toxin damages intracellular adhesion, which results in capillary leakage and massive edema and hemoconcentration.

Ref: Clin Infect Dis 2019;69:2193-4.

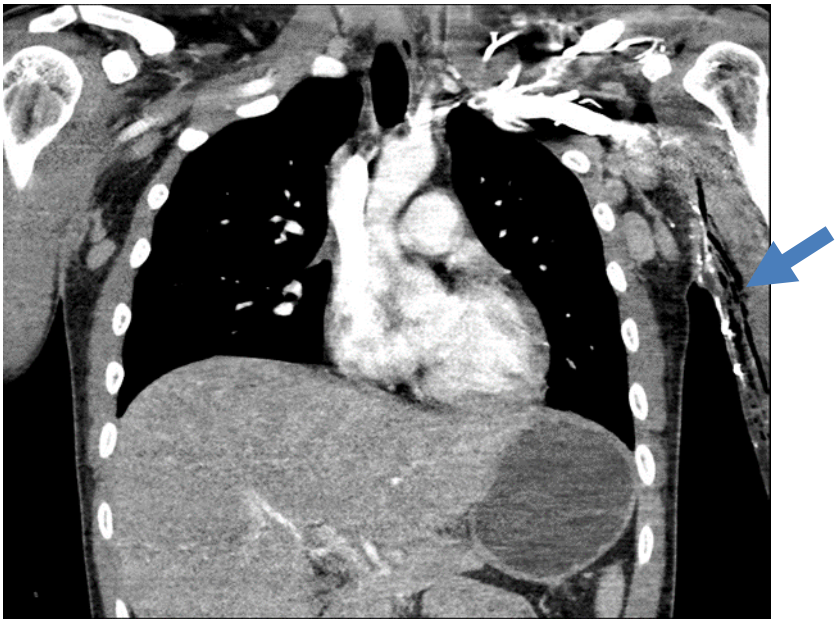
## 5 | GAS GANGRENE| BLOCH

A 56-year-old man was admitted to the ICU with sepsis. His family notes that the previous day he complained of diffuse myalgias and chills and he stayed home from work. The next morning, he was unarousable. EMS was called and patient was intubated at the scene.

Physical exam was pertinent for T=34.7 C, BP=77/42 (unresponsive to fluid resuscitation), HR=126. He was unresponsive to voice, but grimaced with palpation of left upper extremity, and bilateral lower extremities. Scleral icterus was present. Extremity exam was without erythema, swelling or fluctuance, but note was made of left upper extremity crepitus on palpation.

Labs revealed WBC=28.9 (96% seg), H/H=6.9/20.3, platelets=50, Cr=2.7, AST/ALT=521/312, Bil=7.2, LDH=842

CT scan of the chest is displayed below:



What is the most likely predisposing factor for his illness?

**A. Colon cancer**
B. Poorly controlled diabetes
C. Hypogammaglobulinemia
D. Tick Bite
E. Tinea pedis

**Correct Answer: Colon cancer**

This patient has a multifocal necrotizing soft tissue infection associated with hemolysis, consistent with Clostridial myonecrosis (colloquially known as gas gangrene).

Clostridial myonecrosis may occur as a complication of trauma with inoculation of environmental bacteria, or, as in this case, spontaneously. Spontaneous clostridial infection is usually caused by C. septicum, which is part of the normal gastrointestinal microbiome. Colonic defects allow translocation of bacteria into the bloodstream, with secondary infection of musculature. Case series have identified colon cancer in 1/3 to ½ of all cases of spontaneous clostridal myonecrosis. Other predisposing factors include inflammatory bowel disease, diverticulitis, neutropenia and lymphoproliferative disorders.

Features suggestive of this diagnosis include acute onset of fever, muscular pain out of proportion to the physical findings, and rapid clinical deterioration. Gas is typically present on imaging (as demonstrated in this patient's CT) and crepitus may be appreciated with palpation. Toxin production is associated with local tissue necrosis and hemolysis, often leading to profound anemia.

Mortality for clostridial myonecrosis exceeds 50%, and survival is dependent on early and aggressive surgical debridement with ancillary antibiotic therapy including clindamycin to inhibit toxin production. Survivors should be screened for occult GI malignancy after recovery.

Differentiating clostridial myonecrosis from other causes of necrotizing soft tissue infection can be difficult in the absence of diagnostic cultures.

Diabetics are at increased risk for perineal necrotizing fasciitis, also known as Fournier's gangrene. This is typically due to mixed infection with aerobic and anaerobic enteric bacteria.

Tinea pedis is a risk factor for Streptococcus pyogenes skin infection, especially in the setting of prior saphenous vein graft harvest or lymphedema. While group A streptococcus is the leading cause of necrotizing fasciitis, tinea predisposes to erysipelas, a more superficial skin infection.

Hypogammaglobulinemia increases the risk of infection with encapsulated bacteria but is not a predisposing factor for clostridial infection.

Babesiosis, a tick-borne protozoal infection, is associated with sepsis and hemolysis, but does not cause necrotizing soft tissue infection.

## 6 | UTI | CHAMBERS

A 57-year-old female is admitted for alcohol intoxication.

She has symptoms of an upper respiratory tract infection, is mildly tremulous, but otherwise has no complaints.

Temperature is 37oC, heart rate 110, blood pressure 145/95, respiratory rate 16. The exam is normal except for tremulousness.

Admission labs include serum sodium 132 mEq/L, serum potassium 3.2 mEq/L, serum chloride 98 mEq/L, bicarbonate 23 mEq/L, blood urea nitrogen 30 mg%, serum creatinine 1.6 mg%.

CXR is normal.

She responds well to fluids and lorazepam.

After 3 days labs have normalized and she is ready for discharge.

Two blood cultures obtained on admission grew nothing, urine culture from admission 104 cfu/ml of pan-susceptible MSSA (contemporaneous urinalysis 10-20 WBCs, 1+ protein, trace ketones and a few squamous cells).

You are asked by the primary team to provide recommendations on antimicrobial therapy. Which is the following would you recommend?

**A. No antimicrobial therapy**
B. A 7-day course of cefazolin 1 g IV q8h
C. A 7-days course of cephalexin 500 mg po q6h
D. TMP/SMX 160/800 mg po twice daily for 3 days
E. Penicillin VK 500 mg po q6h for 7 days

**Correct answer: No antimicrobial therapy.**

No therapy is needed in this case.

The patient either has asymptomatic bacteruria or the urine is contaminated given the presence of squamous cells on the UA. The presence of white cells in the urine does not make a urinary tract infection more likely in the absence of symptoms of a urinary tract infection.

The blood cultures, which is it appropriate to obtain to exclude a bacteremia, are negative and reassuring that there is no on-going serious infection.

## 7 | STAPH AUREUS | CHAMBERS

A 28-year-old male who injects drugs is admitted for fever and left hip pain. On physical examination the temperature is 39.50C , heart rate 130, blood pressure 110/60, respiratory rate 22.

He has a 2/6 systolic murmur at the left sternal border and difficulty moving his left hip because of pain. Renal function is normal.

CXR is normal and CT of the left hip shows a large left gluteal abscess. The abscess is drained with Gram-stain of the pus showing Gram-positive cocci in clusters.

He is empirically started on vancomycin. The next day 2 of 2 blood cultures from admission are positive for Gram-positive cocci in clusters. A transthoracic echocardiogram is normal.

What empirical therapy would you recommend for this patient?

A. Continue vancomycin
B. Continue vancomycin and add rifampin
C. Continue vancomycin and add nafcillin
D. Discontinue vancomycin and start daptomycin
E. Discontinue vancomycin and start linezolid

**Correct answer: Continue vancomycin**

Antimicrobial therapy for MRSA is appropriate pending results of culture and susceptibility testing. Vancomycin is a drug of choice in this setting.

80% of patients with S. aureus bacteremia will clear blood cultures within 24-48h of starting effective therapy and given that there is an identified source of infection, there is no need to alter therapy at this point.

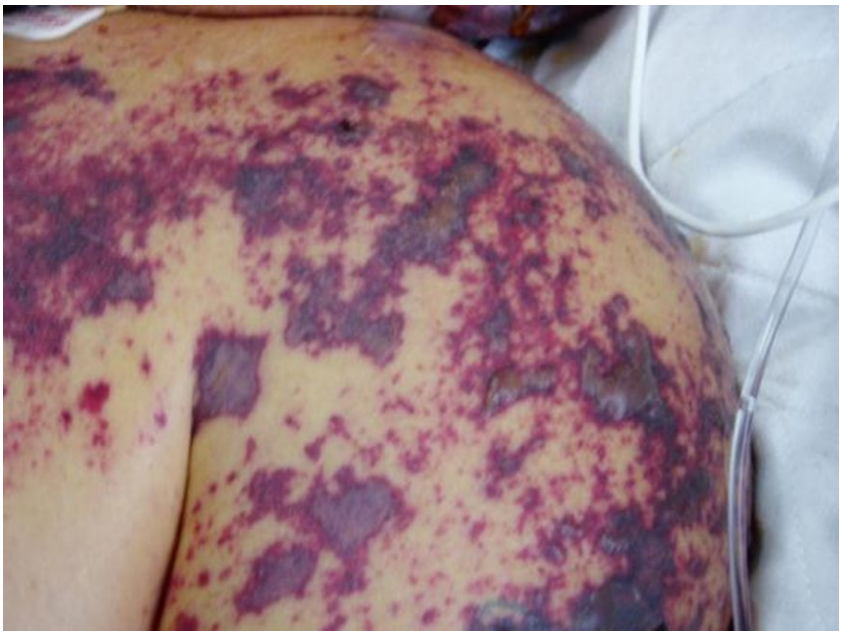
Daptomycin is a suitable alternative, but there is no compelling reason and little to be gained to change to this.

Linezolid is appropriate for treatment of skin and soft tissue infection, but because endocarditis has not been ruled out it is not a good choice at this juncture.

Two randomized controlled trials have shown no benefit in combination therapy with an anti-staphylococcal penicillin or rifampin for S. aureus infections complicated by bacteremia.

Ceftaroline along could be used as initial therapy but has no clear benefit over vancomycin alone or daptomycin alone.

## 8 | MENINGOCOCCUS | GANDHI



This rash was found on a stuporous adult one morning. He had appeared well the night before other than some "flu like" symptoms.

Blood cultures of this patient are likely to grow which of the following:

A. **Gram negative cocci**
B. Gram positive cocci
C. Gram negative bacilli
D. Gram positive bacilli

**Correct answer: Gram negative cocci**

This patient has purpura fulminans, usually due to Neisseria meningitidis.

Purpura are nonblanchable, hemorrhagic skin lesions that result from the leakage of red blood cells into the skin.

There are many processes that can cause similar lesions.

- Idiopathic thrombocytopenic purpura (ITP)
- Thrombotic thrombocytopenic purpura (TTP)
- Warfarin and heparin
- Cryoglobulins
- Calciphylaxis
- Sepsis and DIC due to a wide variety of bacteria

Purpura fulminans is a severe complication of meningococcal disease characterized by the acute onset of cutaneous hemorrhage and necrosis due to infection of capillary endothelial cells with subsequent vascular thrombosis and disseminated intravascular coagulopathy.

The first manifestation is usually cutaneous pain followed by erythema and petechiae. Ecchymoses develop and evolve into painful indurated, purple papules with erythematous borders and then evolve into necrosis, bullae and vesicles. Patients often have concurrent meningitis.

Meningococcal disease is one of the most devastating infections. Disease due to Neisseria meningitidis attacks young, previously well individuals and can progress over hours to death.

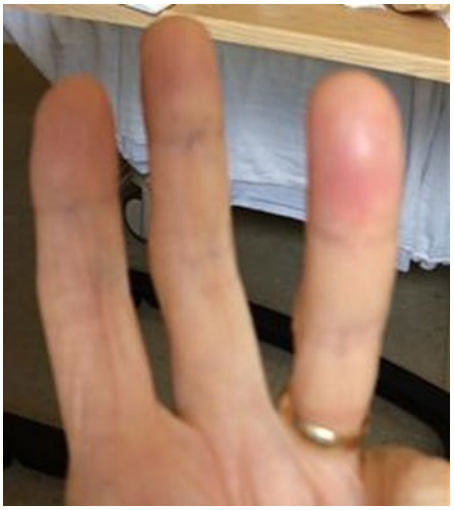
Mortality can be very high and long-term sequelae can be severe. The mortality and morbidity from meningococcal disease has changed very little since the 1950s.

Keep in mind that complement deficiency involving early and late components of the complement system have been associated with increased susceptibility. Eculizumab, a monoclonal antibody complement inhibitor used for treatment of hemolytic uremic syndrome and paroxysmal nocturnal hemoglobinuria, predisposes to meningococcemia. There may also be an association between HIV infection and meningococcemia, but this is controversial.

## 9 | ENDOCARDITIS| GANDHI

A 74-year-old female presented with a 4-month history of fatigue and one month of dull, non-radiating lumbar back pain. She had low-grade fever four months ago which resolved with three weeks of amoxicillin-clavulanate, given for sinusitis.

She has lost 10 pounds of weight, has sweating at night and recently noticed a tender swelling on her finger.



She had a mitral valve repair with a prosthetic ring implanted 20 years prior and has mitral regurgitation on transthoracic echocardiogram, unchanged from 8 months prior. The finger nodule in the above photo, is suggestive of which of the following:

A. Staphylococcal felon
**B. Osler's node**
C. Rheumatoid nodule
D. Polymyalgia rheumatica
E. Janeway lesion

**Correct answer: Osler's node**

This is a typical appearance of an Osler's node and should suggest the diagnosis of subacute bacterial endocarditis, which this patient had.

Relatively uncommon clinical manifestations that are highly suggestive of IE include:

- Osler nodes – Tender subcutaneous violaceous nodules most often seen on the pads of the fingers and toes, but also occur on the thenar and hypothenar eminences
- Janeway lesions – Nontender erythematous macules on the palms and soles
- Roth spots – Hemorrhagic lesions of the retina with pale centers

Rheumatologic complaints are common in SBE and can mislead the diagnosis, particularly in the elderly, who may have preexisting cardiac murmurs.

Staphylococcal felon is an infection of the pulp of the terminal digit, arising by direct inoculation. Polymyalgic rheumatica does not cause finger lesions.

Nothing in the history is consistent with rheumatoid arthritis.

Janeway lesions occur in SBE but are nontender red macules, most often on the palm.

## 10 | JOINT INFECTIONS-CUTIBACTERIUM | NELSON

A 55-year-old male carpenter consulted his orthopedic surgeon about increasing pain and stiffness in his right shoulder over the past three months. Fifteen months previously the surgeon had performed a right shoulder arthoplasty because of severe arthritis in the shoulder. The patient had been able to return to work and reported no fever, redness or swelling.

The surgeon aspirated about a milliliter of cloudy fluid from the joint which had a WBC of 2500 and a negative Gram stain, routine aerobic and anaerobic culture. Because of concern for infection in the prosthetic joint, the surgeon plans on a two-stage joint replacement and seeks your advice about intraoperative cultures..

You recommend which of the following:

**A. Obtain 3-5 pieces of tissue from the infected site and request the lab hold aerobic and anaerobic cultures for 14 days**
B. Inoculate any fluid found in the joint into aerobic and anaerobic blood cultures for routine processing
C. Send swabs of the prosthetic ball and socket for aerobic and anaerobic culture
D. Request that all intraoperative cultures be stained for acid fast organism and cultured for Mycobacteria as well as routine aerobic and anaerobic cultures
E. Ask the lab to hold some of the intraoperative specimen for possible PCR testing in case the routine cultures are negative

**Correct answer:** Obtain 3-5 pieces of tissue from the infected site and request the lab hold aerobic and anaerobic cultures for 14 days

Routine wound cultures are incubated by most labs for only 3 days, whereas Cutibacterium acnes requires up to two weeks of anaerobic incubation to grow. C. acnes is the single most common cause of shoulder prosthetic joint infection and infects other prosthetic joints as well.

The median time for presenting with C. acnes infection of a shoulder prothesis is 15 months. Pain and stiffness, without fever or leukocytosis, is the most common presentation. Patients often have normal ESR and CRP, and fewer inflammatory cells than seen with infection due to other organisms.

Culturing multiple sites from the operative wound helps distinguish contamination from infection by common skin flora, such as Staphylococcus epidermidis and C. acnes. Inoculating joint fluid into blood culture bottles is useful if the bottles are incubated up to two weeks, not the usual five days. Broth cultures can be overgrown by a small inoculum of rapidly growing organisms, losing the discrimination and quantitation an agar plate provides.

Mycobacteria are a possible but much less common infecting organism in shoulder prostheses.

PCR has been invaluable in the diagnosis of septic arthritis due to fastidious organisms, such as Kingella kingae in infants, but the ubiquitous presence of skin flora in operative specimens has made this sensitive technique less valuable than in joint aspirates.

Swabs of removed hardware are insensitive and not recommended.

If the microbiology lab can place prosthetic parts in an ultrasound bath to remove biofilm, that sonicated fluid is the most sensitive culture source.

## 11 | CRMO(CHRONIC OST) | NELSON

A 20-year-old woman presents with progressive pain and swelling over her right medial clavicle.

She first noticed discomfort several weeks ago that was most apparent when she used her right arm. Over the last week she became aware of swelling in this area. She has had occasional low-grade fevers over this period of time which respond to ibuprofen.

When she was 18 years old, she developed subacute osteomyelitis of her left femur. Blood cultures and bone cultures were negative. She received a course of oral antibiotics and reports that the pain in her leg improved over several months.

She lives on an organic dairy farm. She denies any history of injection drug use.

On exam she is well appearing. The medial clavicle is prominent with tenderness and erythema overlying the sternoclavicular junction. ESR is 32 and CRP 14.6 mg/dL.

Plain films demonstrate lytic areas within the medial clavicle with periosteal thickening and areas of sclerosis. The sternum was normal.

What do you suggest next?

**A. MRI of the clavicle and bone scan**
B. Percutaneous needle biopsy of the clavicle for histopathology and culture
C. Open surgical debridement of the clavicle with cultures and biopsy
D. Administer vancomycin and ceftriaxone for a six-week course
E. Administer ciprofloxacin and doxycycline for a 12-week course

**Correct answer: MRI of the clavicle and bone scan**

This young woman has chronic recurrent multifocal osteomyelitis, a benign non-infectious condition. This entity is more common in children and adolescents but can be seen in younger adults, most commonly in women. It is characterized by sterile osteomyelitis, most commonly involving the long bones and clavicle.

Treatment is with anti-inflammatory therapy; antibiotics are not effective. When the diagnosis is suspected, MRI may demonstrate lytic lesions with hyperostosis and sclerosis.

Bone scan may identify asymptomatic foci of the disease, supporting the diagnosis.

Clinical clues to CRMO include the indolent presentation, the prior history of culture-negative osteomyelitis, and the anatomic location (medial clavicle). CRMO may also be associated with the SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis).

Spontaneous hematogenous osteomyelitis of the clavicle is rare, particularly in adults. Sternoclavicular septic arthritis may be seen in the setting of injection drug use but is otherwise uncommon in healthy adults; additionally the radiographic findings are not supportive of SC joint arthritis.

## 12 | DRESS | NELSON

A 59-year-old male is being treated for MSSA sternal osteomyelitis after undergoing coronary artery bypass grafting. He has been home receiving outpatient parenteral antimicrobial therapy (OPAT) with IV oxacillin.

Two weeks after discharge, fever develops. On OPAT laboratory surveillance, the following results are noted:

- WBC: 18.4
    - neutrophils: 32%
    - eosinophils: 18%
- HCT: 31.3
- PLT: 512
- BUN: 24
- Creatinine: 1.4 (baseline 1.1)
- AST: 380
- ALT: 475
- Alk Phos: 166
- Bili: 1.0

Oxacillin is stopped, but fever persists, and he develops a diffuse erythematous maculopapular rash on his torso and limbs.

What is your best management option?

A. Start nafcillin; advise oral diphenhydramine and continue outpatient monitoring
B. Start cefazolin and IV diphenhydramine; continue outpatient monitoring
**C. Start vancomycin; hospitalize and consider corticosteroid therapy**
D. Test dose cefazolin; if tolerated start IV cefazolin
E. Penicillin skin testing and test dose of nafcillin; if negative start nafcillin

**Correct answer: Start vancomycin; hospitalize and consider corticosteroid therapy**

This patient with eosinophilia, hepatitis, fever and rash has DRESS syndrome (Drug Reaction, Eosinophilia, and Systemic Symptoms), a type IV hypersensitivity reaction. DRESS is an idiosyncratic reaction that occurs between two and eight weeks of initiation of a drug. Among antimicrobials, vancomycin, sulfonamides, minocycline, and beta-lactams are the most common agents to cause DRESS. In addition to fever, eosinophilia, and rash, patients with DRESS may have hepatitis, nephritis, myocarditis, leukocytosis and/or lymphadenopathy. DRESS is a severe cutaneous adverse reaction (SCAR) and has a fatality rate of 2-10%.

Patients who have SCARs while on beta-lactam therapy should not be re-challenged with beta-lactam therapy.

While the rate of cross-reactivity between penicillins and cephalosporins is known for type I reactions, the rate of cross-reactivity for type IV reactions is not known. For patients with severe type IV reactions (including severe cutaneous adverse reactions), challenge with beta-lactam therapy is not recommended.

Penicillin skin testing is useful in patients who have suspicion for a type I IgE-mediated hypersensitivity reaction (urticaria, anaphylaxis) but is not useful to predict type IV mediated reactions.

Patients with DRESS syndrome usually require hospitalization; systemic corticosteroids are often administered to mitigate the inflammatory reaction.

## 13 | BORDATELLA | PAVIA

A 31-year-old male first grade school teacher developed fever, rhinorrhea, and malaise for several days, followed by a progressively worsening dry cough. He has now been sick for 12 days.

His chest x-ray was normal.

An empirical 5 day course of azithromycin treatment was begun on day three of his illness (he has now completed treatment 4 days ago), but he has continued to cough.

A nasopharyngeal swab, sent for Bordetella pertussis PCR, was positive.

He was previously in excellent health. He received all of his childhood immunizations but nothing subsequently.

The best advice for this patient would be which one of the following:

A. His clinical syndrome is not due to pertussis if his chest x-ray is normal.
B. He should not return to the classroom until his PCR is negative.
C. His students should be offered macrolide chemoprophylaxis. Students who refuse a macrolide should be excused from school for 21 days.
D. If the teacher was immunized as a child, this is likely a false positive PCR.
**E. All his household contacts, regardless of age and vaccine status, should receive prophylaxis.**

**Correct answer: All his household contacts, regardless of age and vaccine status, should receive prophylaxis.**

About a fourth of the cases of pertussis are in adults. Under diagnosis is common. Duration of vaccine immunity has been estimated as 4-12 years, so that adults become susceptible.

Chest x-rays are usually normal unless bacterial super-infection occurs.

This teacher was no longer infectious after about five days of azithromycin and can continue to teach school.

As a routine practice, all the first grade students should have received the required 3 to 5 doses of acellular pertussis vaccine and are at a low enough risk to make prophylaxis unnecessary, though their vaccine status should be reviewed. Children in the teacher's household should take prophylaxis or stay out of school for 21 days.

The usual incubation is 1 to 3 weeks, so that any student he infected may already be symptomatic.

Post-exposure antibiotics are intended to reduce disease rather than transmission: All the teacher's household members and other close contacts, regardless of age and vaccination status, should take azithromycin daily for 5 days at this time (or clarithromycin for 7 days): prophylaxis is useful within the first 3 weeks of onset of disease in the index case. If a contact does not wish to take a macrolide, they should avoid close contact with susceptible persons, particularly children under age 7, for 21 days.

Adults, including healthcare personnel, are vaccinated to prevent disease in these adults and to prevent their transmitting disease to susceptible household members. The ACIP has recommended that all adults receive a dose of Tdap (Tetanus toxoid, reduced dose diphtheria toxoid, acellular pertussis) and that this vaccine should be given instead of Td for wound prophylaxis. Individual decisions can be made about using pertussis booster immunizations during outbreaks. Revaccination is not, however, a substitute for chemoprophylaxis of those with appropriate exposure.

Outbreaks are occurring which involve fully vaccinated children and adults. 18,166 cases were reported in the US in 2015 and many additional cases were likely undiagnosed or not reported.

## 14 | VZV | PAVIA

A 70-year-old male presents to the Emergency Room with confusion, slurred speech and a right sided weakness of 3 hours duration.

He had previously been healthy except taking methotrexate and infliximab for rheumatoid arthritis.

He has no history of headaches and no pain on palpation of his forehead.

MRI with gadolinium contrast showed restricted diffusion in the left posterior basal ganglia extending to the internal and external capsule, compatible with an acute stroke.

LP showed:

- 90 wbc (90% mononuclear)
- 5 rbcs
- Glucose: 50 mg/dl
- Protein: 60 mg/dl

The patient's wife reports that he had shingles on his left forehead and around his eye 7 weeks ago. This began while he was on a Mediterranean cruise, delaying medical attention. While extremely painful, the rash had improved over three weeks with famciclovir and prednisone.

If this lesion were caused by an infectious agent, which of the following would be the most likely etiologic agent?

A. West Nile virus
B. CMV
C. HSV
**D. VZV**
E. Tick borne encephalitis virus

**Correct answer: E. Granulomatous angiitis from VZV**

Clinicians must be aware of neurologic complications of zoster. This case is most likely large vessel vasculitis (granulomatous arteritis) characterized by the development of acute stroke weeks or months after zoster ophthalmicus. Most patients are over 60 years old, immunosuppressed or normal and typically have their event 7 weeks after the localized zoster, although intervals up to 6 months are documented.

Transient ischemic attacks may also occur with granulomatous arteritis, as will less well-defined cognitive changes. The lesion is due to focal constriction and segmental narrowing of the internal carotid, or anterior or medial cerebral arteries. Histology reveals multinucleated giant cells, inclusion bodies, and viral particles. Other vessels can be involved if the zoster occurs in other cranial distributions. LP, if done, shows a modest lymphocytosis, less than 100 cells/cu mm.

Although there are not controlled trials, given the pathology, acyclovir for 7-10 days and prednisone (60-80mg qd x 3-5 d) is recommended.

For the ID boards, remember CNS complications of VZV, such as Ramsey Hunt syndrome (zoster of the geniculate ganglion presenting as vesicles in the internal or external ear or palate or tongue associated with cranial nerve VII palsy and treated with acyclovir/prednisone), cerebellar ataxia, transverse myelitis and encephalitis in immunocompetent adults, and small vessel disease encephalitis, especially in HIV infected patients.

Some of these syndromes occur in the absence of a clinically apparent rash.

Other parts of the differential, not listed here, would be an ischemic stroke or temporal arteritis. An MR angiogram should define the arterial abnormalities and are distinct for temporal arteritis vs ischemic stroke vs granulomatous arteritis.

Tickborne encephalitis occurs in Europe as well as Siberia and the Far East, mostly in campers or workers exposed to ticks. However, focal cerebral lesions are uncommon, and there are no clues here about a biphasic illness or tick exposure.

West Nile causes encephalitis and muscle weakness, not hemiplegia. On MRI, but look for basal ganglia or thalamic lesions as well as extrapyramidal signs for the encephalitis manifestation of this infection.

HSV encephalitis should not present with hemiparesis and the lesion on imaging should be in the temporal lobe.

HSV encephalitis should be associated with bizarre behavior and a temporal lesion, at least classically.

## 15 | RICKETTSIA AFRICAE | MASUR

A 29-year-old man is referred to you for evaluation of fever and a rash, which have lasted 5 days. He returned from vacationing in South Africa 3 days ago. While there he spent most of his time at the beaches around Capetown. On the last day of his vacation, he had the onset of fever, mild headache, and myalgias. These symptoms persisted and were accompanied by photophobia and the development of a diffuse papular rash last night. He was sexually active while on vacation with two different female partners. His past medical history is unremarkable and he is taking no medications.

On examination, temperature is 100.6°F, BP 110/78 mm Hg, pulse 94/min, respirations 14. There is a diffuse, papular erythematous rash on the trunk that extends onto the extremities. There are five dark red, 0.5–1.0-cm lesions on the right lower extremity. A few shotty cervical and inguinal lymph nodes are palpable bilaterally. The conjunctivae are mildly injected. The oropharynx is normal as are the ears and nose. The remainder of the examination is normal.

Which of the following is the most likely cause of this patient's current illness?

A. Rickettsia prowazekii
B. Rickettsia rickettsii
**C. Rickettsia africae**
D. Measles
E. Treponema pallidum

**Correct answer: Rickettsia africae**

The combination of a rash associated with a tache noire or eschar in a febrile patient should always suggest a vector-borne disease.

In this case, the recent travel to South Africa especially with exposure to the tall grasses around the beaches is characteristic of R. africae infection.

R. conorii causes an identical disease but is uncommon in South Africa. The syndrome caused by R. conorii and R. africae are often hard to distinguish. A study in NEJM (May, 2001) suggested that R. africae is much more common than R. conorii among visitors to South Africa. Both organisms cause self-limiting diseases with short incubation periods although fatalities do occur in 2–3% of R. conorii infections. Both are often associated with rashes although a substantial fraction of patients infected with R. africae have no rash, or the rash appears late.

R. africae infection characteristically has multiple tache noires (eschars) while R. conorii infections usually have only one tache noire.

R. rickettsii causes RMSF, a severe disease that does not occur in South Africa. There is no eschar. R. africae shares considerable homology with R. rickettsii, but it causes a much milder illness that is usually self-limited.

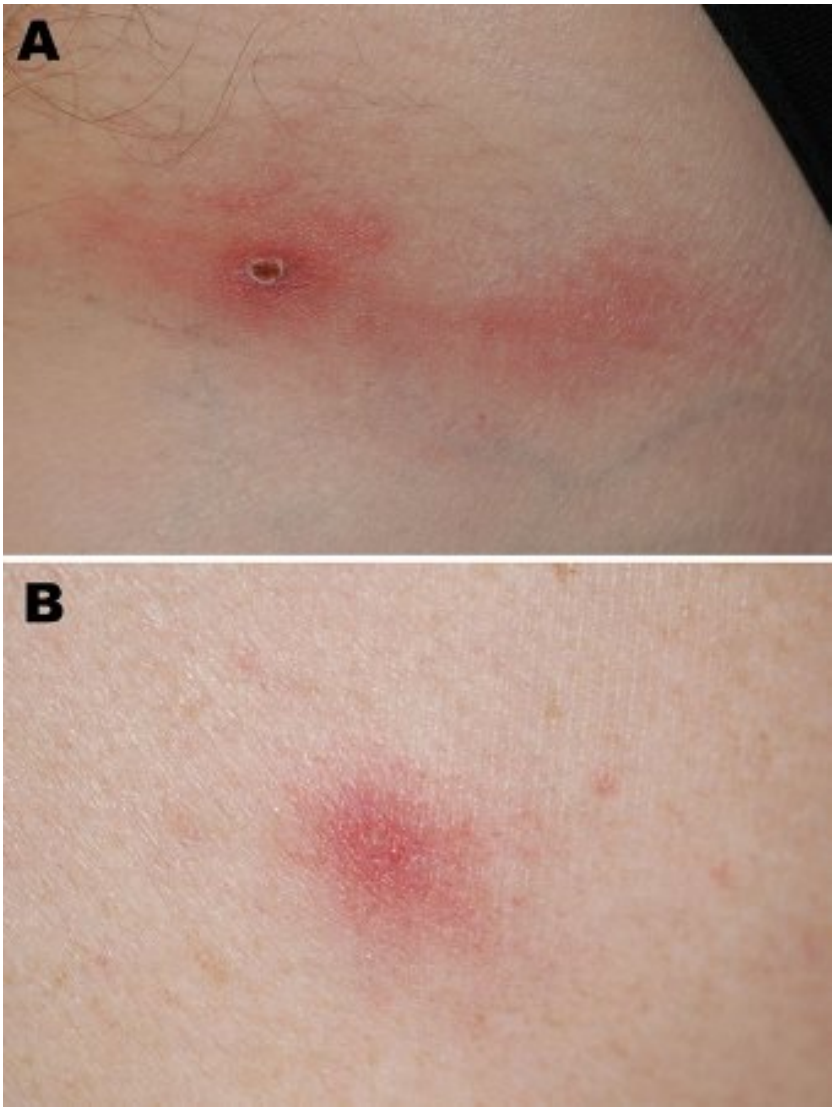
Primary HIV infection would be a consideration in this patient except for the tache noire.

Syphilis and measles would also be a consideration were it not for the eschar. Measles is also accompanied by coryza, cough and conjunctivitis.

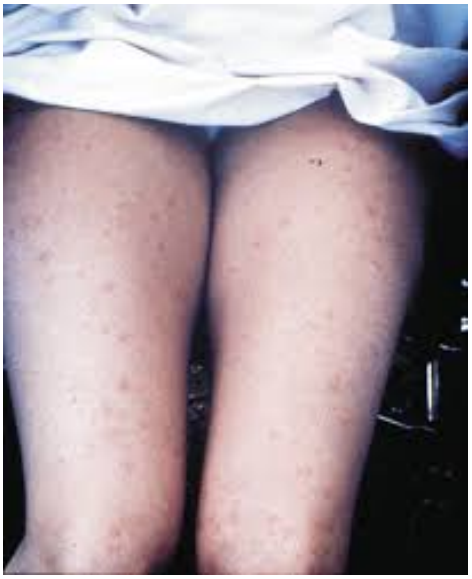
Of note, the Rickettsia mentioned here have different vectors; Amblyomma ticks (R. africae), lice (R. prowazekii), and Dermacentor ticks (R. rickettsii).

R. prowazekii (epidemic typhus) is louse-borne and very rare among vacationers.

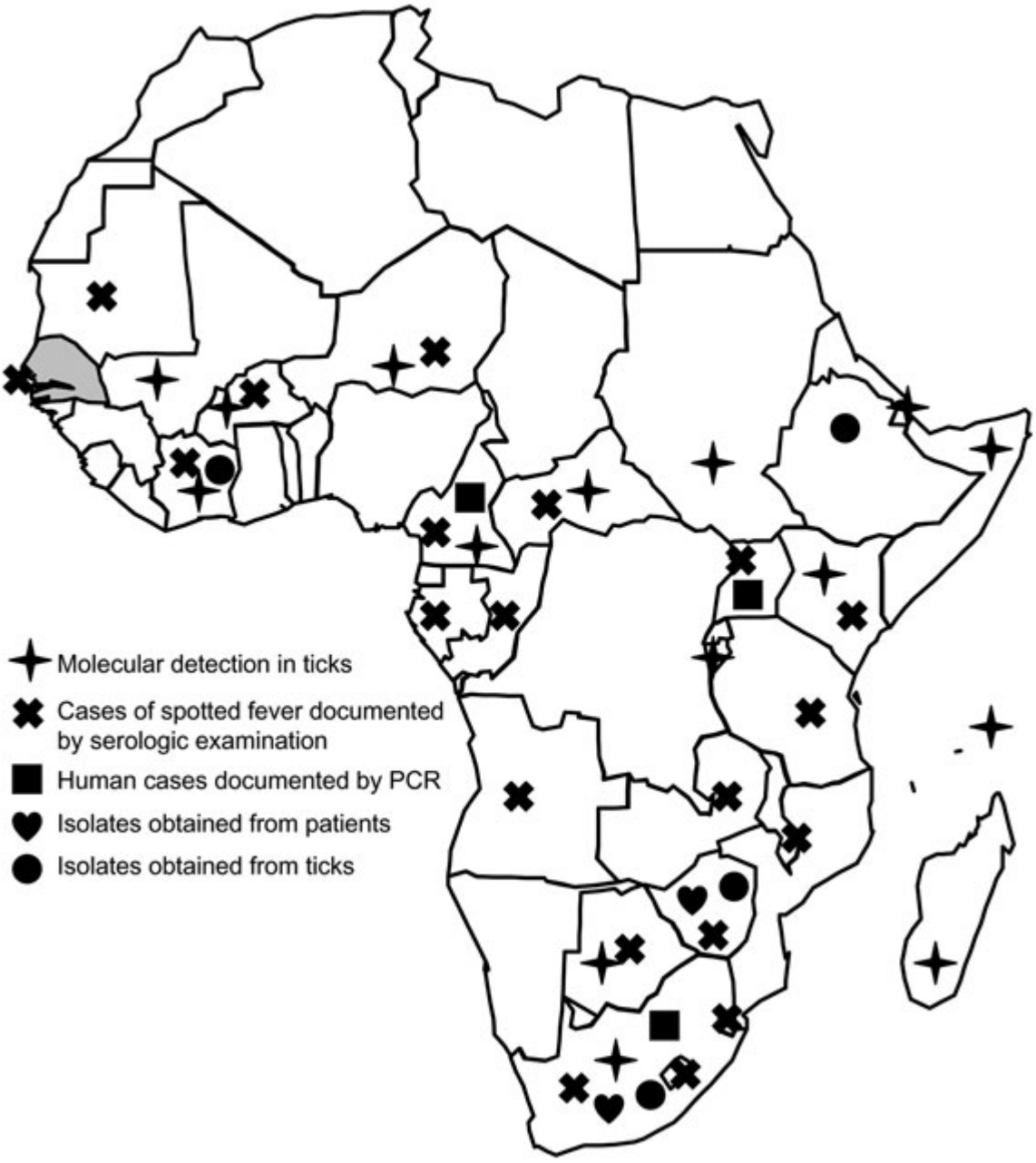
Here is a tache noire (eschar) (A) and a rash-skin lesion (B) of the tick bite for R. africae: (Emerging Infections, 2009)



Below, Rash in patient with R. Africae (SA Fam Pract 2008;50(2):33-35)



Here is a map suggesting where in Africa this infection can likely be acquired (Emerg Infect Dis 16:571 2010)



*This page left blank intentionally.*

# SESSION 2 | SUNDAY, AUGUST 23, 2020

**Session Moderator:** Dr. Whitley

**Session Panelists:** Drs. Dhanireddy, Dorman, Ghanem, Gnann, Thomas and Tunkel

| Question # | Topic | Speaker |
|---|---|---|
| **16** | Varicella | Whitley |
| **17** | HSV | Whitley |
| **18** | Eculizumab | Dhanireddy |
| **19** | Influenza | Dhanireddy |
| **20** | TB and HIV | Dorman |
| **21** | Bedaquiline Toxicity | Dorman |
| **22** | Gonococcal Infection | Ghanem |
| **23** | Trichomonas Relapse | Ghanem |
| **24** | CMV Colitis | Gnann |
| **25** | CMV Alemtuzumab | Gnann |
| **26** | CLL and HBV | Thomas |
| **27** | Household Transmission | Thomas |
| **28** | Relapse After Rx | Thomas |
| **29** | Cavernous Sinus | Tunkel |
| **30** | Listeria | Tunkel |

*This page left blank intentionally.*

## 16 | VARICELLA | WHITLEY

You are called by a 41-year-old friend who two days ago visited a religious community in central Pennsylvania that doesn't believe in vaccination. Today he learned that, right after his visit, several members of that community had been diagnosed with chicken pox (varicella). Your friend is well and has no chronic health problems. He can't remember ever having had chicken pox but is sure he didn't get the varicella vaccine.

Which one of the following is the most appropriate intervention for your friend?

A. Varicella-zoster immune globulin
B. Valacyclovir
**C. Varicella vaccine**
D. Measure varicella antibody titer
E. intravenous immune globulin

**Correct answer: Varicella vaccine**

The chickenpox (Varicella) vaccine his recommend for all healthy adults who are exposed to chicken pox and don't know their immune status.

Beginning immunization within 3-5 days of exposure makes infection less likely or less severe. Varicella-zoster immune globulin (VariZIG) is recommended for susceptible pregnant women and susceptible immunosuppressed individuals who have had a significant exposure. VariZIG no longer needs IRB approval but is expensive and most effective if given in the first 72-96 hours post exposure. Intravenous immune globulin is not recommended.

Valacyclovir is not indicated as prophylaxis for healthy adults. If used to protect immunosuppressed persons from chickenpox, it should be started no sooner than day 3 post exposure. You also can use acyclovir, valacyclovir or famciclovir to treat chickenpox in normal adults if begun in the first 24 hours of infection.

Give varicella vaccine to HIV infected persons with a CD4 count of >200; if <200 give acyclovir. Measuring titers to see if exposed person was previously infected may not provide an answer in time to give vaccine and not cost effective.

## 17 | HSV | WHITLEY

You are consulted about three rugby players from the same team who have skin lesions. The skin lesions have been present for two to three days.

Each player has 10 to 20 raised, clustered lesions on the face, neck, and arms that are about 2 to 5 mm in diameter and filled with a clear yellow fluid; there is a small ring of erythema around the base of each lesion.

The athletes say the lesions are mildly uncomfortable but not pruritic; they are very minimally tender.

Three days before the lesions were noted by the first athlete, they had engaged in a rugby match after which they attended a party and bathed in a hot tub.

Which one of the following is the most likely cause of the skin lesions?

A. Pseudomonas
B. Mycobacterium
**C. Herpes simplex**
D. Contact dermatitis
E. Molluscum

**Correct Answer: Herpes simplex**

Uncomfortable vesicular lesions suggest a herpes virus. However, the cluster of lesions is the key to the clinical presentation.

So-called "herpes gladiatorum" refers to outbreaks of herpes simplex skin lesions seen in wrestlers and rugby players who have prolonged traumatic skin-to-skin contact. Lesions are most common on the head, neck and arms.

Pseudomonas folliculitis causes pruritic lesions in areas covered by bathing suits (also known as "hot tub buns," which are pruritic but not painful).

Mycobacterial infectious can occur associated with hot tubs but the lesions are not vesicular, cases are sporadic, and the incubation period is longer than seen here.

Contact dermatitis may produce small vesicular lesions but they are pruritic. Molluscum lesions are not vesicular and not readily transmitted person to person. MRSA can spread among football players and wrestlers but would not cause clusters of vesicular lesions.

## 18 | ECULIZUMAB | DHANIREDDY

A 50-year-old patient presents to the Hematology Service with paroxysmal nocturnal hemoglobinuria. They elect to treat the patient with eculizumab, and consult you for infectious disease advice. It is likely that the eculizumab therapy, if effective, will be continued for a long time, perhaps lifelong.

The patient has never had any significant illnesses and has no history of prior infection, has normal serum immunoglobulin levels, is HBV and HCV seronegative, and has no unusual occupational exposure.

What preventive strategy would you recommend to reduce the infectious disease risks of eculizumab?

A. Trimethoprim-sulfamethoxazole to prevent pneumocystis
B. Fluconazole to prevent candidiasis

C. Acyclovir to prevent HSV and VZV
**D. Meningococcal quadrivalent and B vaccines**
E. Test for latent tuberculosis

**Correct Answer: Meningococcal quadrivalent and B vaccines**

Eculizumab is a humanized monoclonal antibody that is a terminal complement inhibitor that is licensed for use to treat paroxysmal nocturnal hemoglobinuria, and some forms of hemolytic uremic syndrome, but is increasingly used for other indications. The antibody binds to the complement component C5 and prevents its cleavage to C5a and C5b.

Eculizumab therapy is associated with a 1000-2000 fold increase incidence of meningococcal disease. The risk for invasive meningococcal disease is substantial and prior immunization with both the MenACWY and Men B vaccines is recommended (at least two weeks prior if possible), but the risk is not completely mitigated by prior meningococcal immunization especially since many of the cases associated with eculizumab have been non typable meningococci, i.e., not covered by the vaccine. Also, antibody from vaccination does not correct the loss of complement-mediated bactericidal activity.

Many providers recommend antimicrobial prophylaxis with penicillin V (such as 500 mg orally twice daily) for the duration of eculizumab therapy. Breakthrough on this regimen have been reported, perhaps due to intermediate penicillin resistance (0.12-1 mcg/ml), currently present in about 10% of US isolates.

If eculizumab is started before meningococcal vaccination is begun, ciprofloxacin 500 mg po twice daily can be given until 2-4 weeks after vaccination is begun. Revaccination with MenACWY every 5 years is recommended as long as eculizumab is continued.

Eculizumab does not appear to increase the risk of infection by the pneumococcus or Haemophilus influenzae, nor increase reactivation of tuberculosis or hepatitis B.

Ravulizumab is another complement inhibitor licensed under restricted conditions for treatment of paroxysmal nocturnal hemoglobinuria. Ravulizumab carries the same risk of meningococcal infection as eculizumab and requires the same immunization.

## 19 | INFLUENZA | DHANIREDDY

A 47-year-old female in excellent health comes to consult you for a possible vaccine related complication. She reports that she received an influenza immunization and a TdAP immunization on the instructions of her younger sister who had a newborn and wanted all visitors vaccinated.

Immediately after receiving the vaccinations in her left arm two weeks ago, her shoulder hurt. She has moderately severe pain on lifting her arm which is not relieved by non-steroidal anti-inflammatory drugs. The shoulder still hurts. She reports no fever and redness in the area of her shoulder. She has no trouble with strength in her arm or hand unless she raises her shoulder.

On examination, there is no warmth or redness of the shoulder but the patient has considerable pain when raising her left arm. No other joint is painful.

The patient is afebrile with a normal complete blood count.

What diagnostic test would you order next?

A. Plain film of shoulder
B. Magnetic resonance image (MRI) of shoulder
C. Serum uric acid test
D. Joint washout for culture
**E. Observation only for the next several weeks**

**Correct answer: Observation only for the next several weeks**

Shoulder pain is a rare complication of immunization when antigenic material in the vaccine is inadvertently injected into the bursa and joint space of the shoulder. The pain characteristically occurs within 24-72 hours of the immunization, and results in limitation in the range of motion of the shoulder. This is well described in individuals with no prior shoulder pathology. Patients may recall that the immunization site was "higher than usual."

Imaging may reveal bursal or synovial fluid, but in this case that finding would not be helpful in terms of management: Inflammation from a vaccine is a likely diagnosis given the close temporal relation of the immunization to the symptom onset. Some patients have fever and increased white blood count due to the sterile inflammation, but the patient described here did not.

A patient with a more serious vaccine related complication may be eligible for compensation by the National Vaccine Injury Compensation Program.

If this were an infection due to non-sterile immunization material or introduction of skin flora, the pain would not have started within the first 48 hours, there likely would be fever and warmth of the shoulder joint and an elevated white blood count. On the exam, if there is a potential shoulder joint infection, look for clues especially for Cutibacterium acnes infection following some sort of orthopedic procedure but that is a very different scenario from the one described here.

The pain from inadvertent injection of the bursa or joint can last for many months or lead to permanent joint damage. Steroid injections are often used to reduce the inflammation.

Gout seems unlikely in this patient given the onset of pain immediately after the immunization. Gout is usually (but not invariably) mono articular, but more typically involves the lower extremities, and would result in a more inflamed joint. A serum uric acid may be high, normal, or low, so a serum uric acid level by itself is not that helpful. Leukocytosis and elevated ESR are typical. If there is no joint fluid in which to look for urate crystal, there are scoring systems that can help establish a clinical diagnosis.

## 20 | TB AND HIV | DORMAN

A 33-year-old man who emigrated from South Africa 2 years ago presents with fever, hemoptysis and a right apical cavity on CXR and is diagnosed with pulmonary tuberculosis. Additional testing reveals he is HIV+ with an HIV RNA 122,000 copies/ml and a CD4 cell count of 47.

What do you recommend?

**A. Start TB meds first, then start ART within 2 weeks**
B. Start TB meds first, then start ART within 8 weeks
C. Start ART first, then start TB meds within 2 weeks
D. Start ART first, then start TB meds within 8 weeks

**Correct answer: Start TB meds first, then start ART within 2 weeks**

Tuberculosis is the most common AIDS-related opportunistic infection worldwide. In any patient with concomitant TB and HIV disease, the TB should be treated first and then the HIV disease.

The timing of starting antiretroviral therapy depends on the stage of HIV disease – in this case, with a CD4 cell count <50, the man is profoundly immunosuppressed and ART should be started within 2 weeks – this strategy is potentially life-saving according to large randomized controlled clinical trials. For patients with higher CD4 cell counts, ART should be started within 8 weeks.

When starting TB and HIV treatment at the same time, drug-drug interactions and the immune reconstitution inflammatory syndrome (IRIS) should be anticipated and managed.

## 21 | BEDAQUILINE TOXICITY | DORMAN

You are consulting on a hospitalized 53 y/o man with cavitary pneumonia.

Yesterday the result of a GeneXpert MTB/RIF test performed on sputum showed "MTB detected" and "rifampin resistance detected".

You started him on moxifloxacin, linezolid, clofazimine, pyrazinamide, and ethambutol for presumed multidrug-resistant (MDR)-TB, pending additional information about drug susceptibility. In discussions with the local health department TB program, the plan is to add bedaquiline.

What additional bedaquiline-specific periodic safety monitoring will be required while the patient is receiving bedaquiline?

A. Periodic audiology examination to assess for high frequency hearing loss
B. Periodic serum bedaquiline drug levels to ensure that concentrations are within an established target range
**C. Periodic electrocardiogram to assess for QTc prolongation, and serum electrolytes**

D. Visual acuity testing
E. 6 minute walk tolerance

**Correct Answer: Periodic electrocardiogram to assess for QTc prolongation, and serum electrolytes**

Bedaquiline (Sirturo) is an oral diarylquinoline that was approved by the FDA in 2012 for treatment of MDR-TB, when administered as a component of a multidrug regimen. Bedaquiline has a novel mechanism of action – inhibition of the mycobacterial ATP synthase. It has an exceedingly long terminal half-life, estimated at 4 to 5 months.

Bedaquiline has been associated with prolongation of the QTc interval, and an ECG should be obtained before initiation of treatment and periodically thereafter.

Serum potassium, calcium, and magnesium also should be assessed (and repleted if abnormal) at baseline and periodically thereafter. Guidelines recommend discontinuation of bedaquiline if the QTcF interval is greater than 500 ms, or in the event of a clinically significant ventricular arrhythmia.

Serum bedaquiline levels are not routinely available or monitored and therefore (b) is incorrect. Periodic audiology exam is indicated if a parenteral aminoglycoside is used, but bedaquiline has not been associated with auditory changes.

## 22 | Gonococcal Infection | Ghanem

An asymptomatic male with HIV (CD4= 500 cells/mm3, Viral Load <20 copies/uL), on dolutegravir-lamivudine, has had multiple anonymous sexual exposures (oral, rectal and genital) over the past few weeks and requests that he be screened for sexually transmitted diseases.

You perform the following tests:

Syphilis
- RPR negative

Chlamydia: NAAT for rectal, and first catch urine:
- both negative

Gonorrhea: NAAT for oral, rectal, and first catch urine:
- urine positive

What is the best regimen for this patient's gonococcal infection?

A. Ceftriaxone 250 mg IM
**B. Ceftriaxone 250 mg IM and azithromycin 1 gram PO**
C. Cefixime 400 mg PO
D. Azithromycin 2 grams PO
E. Doxycycline 100 mg PO

**Correct answer: Ceftriaxone 250 mg IM and azithromycin 1 gram PO**

Because of increasing antimicrobial resistance with gonococcal isolates, treatment of gonococcal infections in the U.S. should include the use of two agents (a third generation cephalosporin PLUS azithromycin or doxycycline) to treat all gonococcal infections, regardless of the results of chlamydia testing. This is the major teaching point of this question.

Another important point: Ceftriaxone IM is preferred over the use of oral cephalosporins, such as cefixime, as the cephalosporin component of therapy. Ceftriaxone provides higher treatment efficacy than oral cephalosporins and also is the only regimen that reliably eradicates pharyngeal infection, although in this case there was no evidence of pharyngeal GC.

Although a regimen of 2 grams of azithromycin may be considered to treat GC for persons who have a severe allergy prohibiting the use of cephalosporins, this regimen is no longer recommended, even as an alternative treatment, due to the increasing prevalence of resistance to macrolides among gonococci. For such persons, intramuscular gentamicin (240 mg) + 2g of oral azithromycin is recommended.

## 23 | TRICHOMONAS RELAPSE | GHANEM

A 42-year-old recently divorced woman presents complaining of a vaginal discharge. She reports a new sex partner in the past month. She denies abdominal pain, nausea, vomiting, or a rash. She has a history of gastric reflux but is otherwise healthy. On examination, a thin grey vaginal discharge is noted. Her cervix appears normal and there is no evidence of cervical motion tenderness or adnexal tenderness. A wet mount examination of a drop of the vaginal discharge reveals motile trichomonads but is otherwise normal. Testing for HIV performed two months earlier was negative.

Which of the following is the most appropriate treatment for her infection?

A. Boric acid vaginal suppository
B. Metronidazole, single oral 2g dose
**C. Metronidazole, 500 mg orally twice daily for one week**
D. Paromomycin 6% topical vaginal cream
E. No therapy

**Correct Answer: Metronidazole, 500 mg orally twice daily for one week**

The patient is symptomatic and testing confirms trichomonas vaginitis. A recent study (Kissinger P, et al. Lancet Infectious Diseases 2018) suggests that the most appropriate therapy for trichomoniasis in women is 7 days of oral metronidazole. This regimen is more effective than single dose metronidazole even in HIV uninfected women. Boric acid and paromomycin topical cream have been used in resistant trichomonas infections but limited data preclude their routine use. It would be inappropriate not to treat this symptomatic patient.

## 24 | CMV COLITIS | GNANN

A 62-year-old male computer engineer from Seattle is 90 days post allo-HSCT for myelodysplastic syndrome and has been receiving valacyclovir prophylaxis because of a positive pretransplant test for antiHSV antibody. The patient has had several episodes of severe graft versus host disease, two being associated with CMV detection in the blood by PCR, for which valganciclovir was substituted for valacyclovir for 2 to 3 week periods, ending 4 weeks ago.

Two weeks ago the patient had the onset of fever and severe diarrhea. Reappearance of CMV in the blood by PCR has led to initiation of intravenous ganciclovir on the third day of diarrhea. Persistence of diarrhea for seven days despite high dose steroids for presumed GVHD of the colon led to infectious disease consultation. Stool was negative for Clostridium difficile toxin by PCR and the CMV PCR in blood was unchanged over the first five days.

What would be the most appropriate next step?

A. Oral metronidazole
B. Oral vancomycin
C. Change from ganciclovir to foscarnet
**D. Colonoscopy**
E. Stool for Strongyloides

**Correct answer: Colonoscopy**

Separating CMV colitis from graft-versus host disease is difficult clinically and both may coexist. This patient has a positive blood PCR for CMV, but this is not diagnostically definitive and one would want to rule out concurrent GVHD and confirm CMV disease prior to committing to therapy for either or both. A colon biopsy is needed.

Blood CMV PCR can be followed as a marker for response to therapy, but it may take 10 days or so for the CMV viral load to fall during ganciclovir treatment. Five days is too early to change to a more toxic drug, foscarnet.

Colonoscopy with biopsy may show apoptotic bodies of GVH or may show CMV by immunoperoxidase staining of colonic submucosa.

C. difficile is unlikely in view of the negative PCR assay on stool.

Strongyloides stercoralis is unlikely since there is no stated exposure history.

Ganciclovir resistance can arise with repeated ganciclovir and valganciclovir exposure but is unusual in stem cell transplant recipients. A mutation in the UL97 ORF, coding for the protein which monophosphorylates ganciclovir, is the most common mechanism when it occurs, and foscarnet is still effective against such mutants.

Norovirus is another possible cause of diarrhea in stem cell transplant recipients. Reports have suggested that it can mimic GVHD, with a persistent course of chronic diarrhea. This argues for sending stool for a gastrointestinal PCR panel.

## 25 | CMV ALEMTUZUMAB | GNANN

A 73-year-old woman with T cell prolymphocytic leukemia has been treated with alemtuzumab (Campath) for 10 weeks and is awaiting a stem cell transplant. She is receiving trimethoprim-sulfamethoxazole and acyclovir prophylaxis.

During the tenth week of therapy, she develops low-grade fever and non-specific fatigue and myalgias. Her physical examination is unremarkable except for new shotty cervical adenopathy and some mild enlargement in her liver and spleen. Her hemoglobin, white blood count, and platelet count have fallen but she is not neutropenic. Her chest x-ray is normal.

She has not traveled since her diagnosis of leukemia and has no unusual exposures.

What would be the next best step for diagnosing the likely cause of this syndrome?

A. Bone marrow biopsy
B. Serum PCR for toxoplasma
**C. Serum PCR for CMV**
D. Lymph node biopsy
E. CT scan of chest and abdomen

**Correct answer: Serum PCR for CMV**

This is a typical case of CMV reactivation during alemtuzumab (Campath) which probably should have been recognized and averted by prospective PCR monitoring. CMV viremia should be measured by quantitative polymerase chain reaction (PCR) weekly during alemtuzumab treatment: valganciclovir prophylaxis/preemptive therapy should be used if viremia is present although some would wait for rising PCR titers. Reactivation typically occurs after 4-6 weeks of therapy. It may be prudent in the setting of CMV reactivation to suspend alemtuzumab if that is feasible in terms of the underlying condition.

Treatment is usually at least 2-3 weeks of ganciclovir or valganciclovir with therapy ending when symptoms are resolved and the PCR is negative.

Alemtuzumab (Campath) is an anti CD52 T cell antibody that could be a topic for a board question because it is used in so many settings: B cell chronic lymphocytic leukemia, multiple sclerosis, aplastic anemia, graft vs host disease, hemophagocytic syndrome/HLH, and HSCT and solid organ transplants.

Alemtuzumab binds to CD52, a nonmodulating antigen present on the surface of B and T lymphocytes, a majority of monocytes, macrophages, NK cells, and a subpopulation of granulocytes.

Serious infections (bacterial, viral, fungal, and protozoan) have been reported. The label recommends prophylactic medications for PCP and herpes viral infections during treatment and for at least 2 months following the last dose or until CD4+ counts are ≥200 cells/$mm^3$, (whichever is later)—this patient was receiving TMP-SMX and acyclovir.

Severe and prolonged lymphopenia may occur; CD4+ counts usually return to ≥200 cells/mm3 within 2 to 6 months; however, CD4+ and CD8+ lymphocyte counts may not return to baseline levels for more than 1 year.

Toxoplasma could present with febrile lymphadenopathy especially in immunocompetent patients. This patient was receiving TMP-SMX prophylaxis which makes toxoplasma unlikely and would more typically have manifested cerebral or visceral disease

EBV could cause a syndrome like this but CMV is more common.

A lymph node biopsy would be diagnostic but there is no reason to make this invasive procedure the first diagnostic test.

## 26 | CLL AND HBV | THOMAS

A 64-year-old female with a history of chronic lymphocytic leukemia (CLL) for several years was recently diagnosed with Richter's transformation to diffuse large B cell lymphoma.

Her oncologist recommended starting R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy given the advanced stage disease.

The patient has a history of recurrent and severe sinopulmonary infections and hypogammaglobulinemia. As a result, she has been on monthly intravenous immunoglobulin (IVIG) for the past two years.

The patient's hepatitis B serology obtained a year ago showed:

- HBsAg: nonreactive
- Total HBc Ab: positive
- HBsAb: positive
- HBV viral load: negative

Her oncologist referred her to be seen by you for further recommendations about the patient's hepatitis B.

What is the most appropriate next step?

A. Treat only if monthly serum quantitative HBV viral load becomes positive while she gets treated with R-CHOP
B. Start tenofovir plus emtricitabine pre-R-CHOP
C. Start entecavir pre-R-CHOP
D. Administer a single hepatitis B vaccine booster dose
**E. Review pre-IVIG hepatitis B serology before making a decision**

**Correct answer: Review pre-IVIG hepatitis B serology before making a decision**

Due to risk of HBV reactivation in patients receiving chemotherapy, highest in those treated with anti-CD20 (rituximab or ofatumumab)-based chemotherapy and/or corticosteroids, it is recommended that patients undergo testing with hepatitis B serology, and risk-stratified to determine if they should receive antiviral prophylaxis during and after treatment.

In cases where patients truly have a current (+HBsAg) or previously resolved infection (negative HBsAg with +HBcAb and +/- HBsAb), antiviral prophylaxis initiated concurrently or prior to immunosuppressive therapy has been shown to decrease risk of HBV reactivation and HBV hepatitis.

However, it is important to recognize that administration of immunoglobulin products (IVIG, subcutaneous Ig) has been associated with transmission of HBV antibodies (PMID: 27076567), which should be taken into consideration of diagnostic tests in patients receiving immunoglobulin treatment. Patients with false positive cAb results from receiving IVIG may thus receive unnecessary antiviral prophylaxis and potentially needless monitoring.

If the patient has a baseline (pre-IVIG) hepatitis B serology that is negative (HBcAb and HBsAb both negative), especially if a repeat hepatitis B serology off IVIG is negative, this strongly suggests false positive HBc and HBsAb.

However, if a baseline (pre-IVIG) hepatitis B serology is not available for comparison, especially given the time-sensitive need for initiating R-CHOP, there is not a reliable way of differentiating false positivity from previous hepatitis B infection. Initiating antiviral prophylaxis with entecavir or tenofovir or lamivudine is the most prudent course of action.

There is no additional benefit to using tenofovir/emtricitabine over tenofovir alone.

## 27 | HOUSEHOLD TRANSMISSION | THOMAS

A 32-year-old woman is referred for 'hepatitis' recognized by her primary care physician. She is otherwise well. She was born in Philippines but has lived in the USA for 2 years. She is a nurse on a medicine floor. Married with 2 children: 7 and 5 years old.

She brings a lab slip with the following:

- Total anti-HAV pos;
- IgG anti-HBc pos;
- IgM anti-HBc neg;
- HBsAg pos; HBeAg pos;
- anti-HBe neg;
- HBV DNA 8.2 log IU/ML;
- ALT 24 U/L; AST 18 U/L;
- anti-HCV neg.

Which of the following recommendations is most appropriate:

A. HBV vaccinate husband and children
B. Advise to use condoms
**C. Test husband and children for HBsAg**
D. Advise to stop work and initiate look-back investigation of a sample of patients
E. Advise against future pregnancies

**Correct answer: Test husband and children for HBsAg**

She has chronic hepatitis B that is most likely in what is often called the immunotolerant stage.

She has most likely been infected from birth. If nothing was done to prevent transmission, there is a high chance her husband and children are already infected. Vaccinating them now would not detect or prevent transmission that already occurred, making it most reasonable to test for HBsAg and anti-HBs.

If negative for both markers, then vaccination would be appropriate. There is no reason she cannot have additional pregnancies as transmission can be prevented by birth-dose vaccination and HBIG. If pregnant, she would also qualify for tenofovir to further reduce the risk of transmission.

The risk of a health care worker spreading HBV infection to patients is very low but depends on the type of exposures and viral load.

SHEA and CDC guidelines stratify risk on viral load above 2,000 IU (~10,000 genomes/ml) and only recommend restrictions for HBV infected health care workers who have exposure prone procedures, chiefly surgeons. Although her viral load is high enough, there have never been HBV transmissions from nurses.

## 28 | Relapse After Rx | Thomas

You treated a 54-year-old man for chronic HCV infection with a direct acting regimen.

At baseline he was genotype 1a and HCV RNA was 6.5 log IU/ml. Baseline ALT was 92 U/L. He was HCV RNA undetectable after 4 weeks of treatment and again 12 weeks after treatment was done. ALT was 28 U/L
He is otherwise well.

Now he returns 2 years later because his primary tested him and his ALT is 84 U/L and HCV RNA is 6.8 log IU/ml and genotype 1a.

Which is most likely?

A. He has HBV relapse from DAA treatment
B. He has HCV relapse
**C. He was reinfected by HCV**

D. He has steatohepatitis

**Correct answer: He was reinfected by HCV**

Once a viral response to treatment is sustained 12 weeks after treatment is stopped, recurrence of HCV infection is rare, occurring in only 1% overall.

Recurrent HCV infection is much more likely in persons with ongoing HCV risk, strongly suggesting it typically represents reinfection not late relapse.

This inference is further substantiated by viral sequence testing that often shows a different infection.

On the other hand, detection of the same genotype, such as in this case, does not mean it is relapse since genotype 1a is the most common in the United States and one can be reinfected by the same source.

Steatosis is common but doesn't cause his HCV RNA to be positive again.

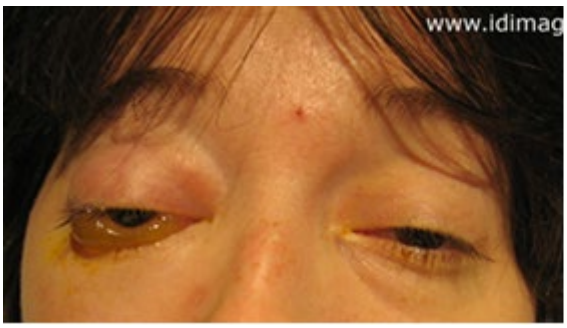
## 29 | Cavernous Sinus | Tunkel

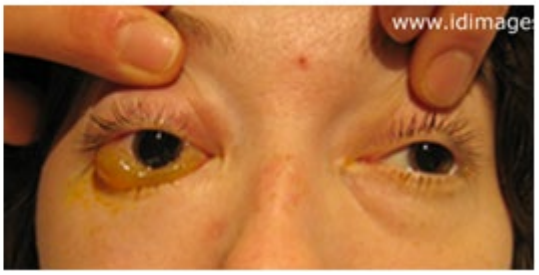
A previously healthy 30-year-old woman presented with right temporal headache, eye pain, diplopia and decreased vision in the right eye.

On exam, her temperature was 102°F. Her left eye had normal extraocular movement and vision. On the right, there was periorbital edema, proptosis, chemosis, and ptosis; the right eye was fixed in the midline.

Vision in the right eye was reduced to count fingers at 3 feet. She underwent a lumbar puncture; CSF analysis revealed glucose 69 mg/dL, protein 180 mg/dL, 3,000/$mm^3$ WBC (82% P, 18% L).

An MRI is ordered.




The most likely diagnosis is:

A. Superior sagittal sinus thrombosis
**B. Cavernous sinus thrombophlebitis**
C. Bacterial endophthalmitis
D. Mucormycosis

E. Right ethmoid sinusitis

**Correct Answer: Cavernous sinus thrombophlebitis**

The patient underwent MR angiography of the head, which revealed thrombosis of the right cavernous sinus. Cultures of blood and CSF grew methicillin-sensitive *Staphylococcus aureus.* The source was unknown.

The facial veins and pterygoid plexus drain into the cavernous sinus via the inferior and superior ophthalmic veins; as a result, infections of the face can spread to the cavernous sinus. The cavernous sinus encompasses CN III, IV and VI. Cavernous sinus thrombosis presents with headache, chemosis, proptosis, diplopia, and ptosis; the findings often become bilateral as thrombosis spreads to the contralateral sinus through a venous plexus that crosses the midline. Orbital abscess, extending from the ethmoid sinus, can present with similar findings, though with early visual loss, and can be distinguished on MRI or CT.

The other diagnoses on the list would not be expected to give such prominent proptosis, ptosis, and ophthalmoplegia. Moreover, the CSF formula is consistent with a parameningeal focus; the other diagnoses on the list would not be expected to have such a CSF formula. Mucormycosis would not be expected in a nondiabetic.

## 30 | LISTERIA | TUNKEL

A previously healthy 60-year-old woman presents to the emergency room complaining of 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 is 38.3°C, blood pressure is 120/60 mmHg, heart rate is 109 beats/minute, and respiratory rate is 13 breaths/minute. She is alert and oriented but appears 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 CSF examination revealed a lymphocytic pleocytosis with 500 white blood cells/$mm^3$ (94% lymphocytes). CSF glucose level was normal and protein level 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. Behcet's disease
B. Cytomegalovirus (CMV)
C. Herpes simplex virus type 2
**D. Listeria monocytogenes**
**E.** Mycobacterium tuberculosis

**Correct Answer: Listeria monocytogenes**

The most likely diagnosis is rhombencephalitis.

The most common infectious cause is *L. monocytogenes* that often affects otherwise healthy individuals. Other causes of infectious rhombencephalitis are enterovirus 71, HSV-1, HSV-2, HHV-6, EBV, and *M. tuberculosis*. Behcet's 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.

The majority of 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%).

MRI is superior to CT for demonstrating rhombencephalitis. Finding abscesses with ring enhancement can be useful in making a diagnosis of Listeria-associated rhombencephalitis. Immediate antimicrobial therapy is the most important predictor of a favorable outcome (Clauss and Lorber. Curr Infect Dis Rep. 2008;10(4):300-6).

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

Neither CMV nor HSV are likely to present with ring-enhancing abscesses of the brainstem in an immunocompetent adult.

While *M. tuberculosis* is a rare cause of rhombencephalitis, the involvement of the basal cisterns with leptomeningeal enhancement after intravenous injection of contrast is the finding most characteristic of tuberculosis-associated rhombencephalitis. She has no known risk factors for TB.

She does not have any other clinical manifestations to suggest Behcet's disease.

*This page left blank intentionally.*

# Session 3 | Monday, August 24, 2020

**Session Moderator:** Dr. Gulick

**Session Panelists:** Drs. Bell, Dupont, Maldarelli, Saag, and Weinstein

| Question # | Topic | Speaker |
|---|---|---|
| **31** | HBV and ART | Gulick |
| **32** | PREP | Gulick |
| **33** | Post Exp Prophylaxis | Gulick |
| **34** | PrEP Acute HIV | Gulick |
| **35** | Staph Epi Blood Contaminant | Bell |
| **36** | Hyperserotonin | Bell |
| **37** | Shigellosis | Dupont |
| **38** | Irritable Bowel | Dupont |
| **39** | HIV Testing | Maldarelli |
| **40** | Initiating Rx | Maldarelli |
| **41** | Raltegravir Resistance | Maldarelli |
| **42** | ART Renal Toxicity | Saag |
| **43** | Pregnancy | Saag |
| **44** | Flu Exposure | Weinstein |
| **45** | PPE | Weinstein |

*This page left blank intentionally.*

## 31 | HBV AND ART | GULICK

A 55-year-old female has been HIV infected for 15 years, and is well suppressed with an undetectable viral load during this period on efavirenz, tenofovir, and emtricitabine (Atripla).

She has heard about the new dolutegravir and lamivudine two drug regimen and would like to try this two drug combination instead of Atripla (efavirenz, tenofovir, emtricitabine) which she has tolerated well for many years.

She has been Hepatitis B surface antigen positive since she started her antiretroviral regimen. She has never had a positive plasma HBV DNA or elevated liver function tests.

What would you recommend?

A. Switching to dolutegravir-lamivudine is a good option
B. Switching to dolutegravir-lamivudine following long term efavirenz is unlikely to control the HIV infection and thus not a good option
**C. Switching to dolutegravir-lamivudine would control the HIV infection but would likely lead to HBV breakthrough unless another HBV drug were added**
D. Switching to dolutegravir-lamivudine would be a good option for HIV suppression but would suppress HBV only if ribavirin were added

**Correct Answer: Switching to dolutegravir-lamivudine would control the HIV infection but would likely lead to HBV breakthrough unless another HBV drug were added**

There is growing evidence that some two-drug regimens are effective in maintaining virologic control in patients who initiated therapy and achieved virologic suppression with three-drug regimens, provided the HIV is susceptible to both ARV drugs in the new regimen. However, caution should be taken in patients with HBV coinfection, as these simplified regimens may not have adequate anti-HBV activity.

Dolutegravir plus lamivudine is a good option for treatment of ART based on clinical trials. It is unlikely this patient has integrase resistance given the fact she has been on Atripla since prior to the introduction of integrase inhibitors (2007).

In terms of controlling the HIV, this would be reasonable but…the patient also has HBV infection which has been well suppressed by the tenofovir plus emtricitabine components of Atripla.

Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) have activity against both HIV and HBV, an ART regimen for patients with both HIV and HBV should be include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen.

If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen. Entecavir could be used in addition to a fully suppressive ARV regimen for patients with HBV/HIV-coinfection.

Other HBV treatment regimens, including adefovir alone or in combination with 3TC or FTC and telbivudine, are not recommended for patients with HBV/HIV coinfection.

Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and be carefully monitored during interruptions in HBV treatment.

If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression.

If this patient were of childbearing potential, she would have to be well informed about pregnancy risks if she were interested in taking dolutegravir.

- DTG is not recommended for those of childbearing potential who are planning to become pregnant or who are sexually active and not using effective contraception.
- For those who are using effective contraception, use of a DTG-based regimen can be considered after discussing the risks and benefits of this drug with the patient.

## 32 | PREP | GULICK

A 33-year-old woman has a male sexual partner who is known to be living with HIV and intermittently takes his medications and sometimes refuses to wear condoms. She is requesting HIV pre-exposure prophylaxis (PrEP) but is not sure she can comply with a daily pill.

What do you offer her?

**A. Daily tenofovir disoproxil fumarate (TDF)/emtricitabine**
B. Daily rilpivirine
C. "On demand" TDF/emtricitabine – 2 pills within 2-24 hours before sex followed by 1 pill 24 and 48 hours after
D. "On demand" TAF/emtricitabine – 2 pills within 2-24 hours before sex followed by 1 pill 24 and 48 hours after
E. Improve condom use to 100%

**Correct Answer: Daily TDF/emtricitabine**

This woman is at-risk for acquiring HIV and not in control of her partner's choices (to take his antiretrovirals or to use condoms), so she is a candidate for HIV PrEP. The ONLY HIV PrEP regimen that demonstrates efficacy in heterosexual women (and FDA-approved on that basis) to date is (a) daily tenofovir disoproxil fumarate/emtricitabine.

There are concerns about lower drug concentrations in the female genital tract than in male or female rectal tissues. Daily TAF/emtricitabine was non-inferior to daily TDF/emtricitabine in the DISCOVER studies,

but these studies only enrolled men. TAF/FTC was approved for PrEP but NOT for those having receptive vaginal sex "On demand" TDF/emtricitabine showed excellent efficacy in the IPERGAY study, that study again only enrolled men. "On demand" TAF has not been studied and cannot be recommended for men or women.

Given her concerns about taking a daily pill, you should counsel her about the available data and offer her adherence strategies.

Long acting oral and injectable options will hopefully be available in the near future.

## 33 | POST EXPOSURE PROPHYLAXIS | GULICK

A 37-year-old man with no past medical history except HBV surface antibody positive after vaccination presents the morning after an episode of receptive anal intercourse with another man where the condom broke. He is unaware of his sexual partner's medical history or whether he takes medications.

In addition to offering testing for HIV, hepatitis C, and bacterial STIs.

What do you advise?

A. No specific prophylaxis
B. 2-drug prophylaxis with tenofovir disoproxil fumarate (TDF)/emtricitabine.
C. 2-drug prophylaxis with tenofovir alafenamide (TAF)/emtricitabine
**D. 3-drug prophylaxis with TDF/emtricitabine + dolutegravir**
E. 3-drug prophylaxis with TAF/emtricitabine + efavirenz

**Correct answer: 3-drug prophylaxis with TDF/emtricitabine + dolutegravir**

This man has experienced a significant recent potential exposure to HIV and should be offered antiretroviral prophylaxis. 2-drug prophylaxis is indicated for pre-exposure prophylaxis (PrEP); 3-drugs are indicated for post-exposure prophylaxis (PEP).

Current PEP guidelines recommend a well-tolerated drug with a high barrier to resistance: the integrase inhibitors, bictegravir, dolutegravir, or raltegravir and the protease inhibitor, darunavir (boosted). Antiretroviral drugs with a lower barrier to resistance -- NNRTIs (including efavirenz) and the integrase inhibitor, elvitegravir -- are NOT recommended.

The recommended course of PEP is 4 weeks (along with counseling and repeat testing) – given that length of time and the low potential for toxicity, there is no reason to use the newer tenofovir alafenamide (TAF) as opposed to tenofovir disoproxil fumarate (TDF).

## 34 | PrEP Acute HIV | Gulick

A 34-year-old gay man presents requesting HIV pre-exposure prophylaxis (PrEP).

His past medical history is notable only for gonorrhea two months ago that was treated with IM ceftriaxone; he has had repeated negative HIV tests.

He notes "a few days of feeling feverish" but has not taken his temperature. On physical exam his temperature is 38.6 C. (101.5 F.), he has a non-tender 1 cm oral ulcer and a faint macular red rash, the remainder of the exam in normal.

A rapid HIV oral test in the office is negative.

In addition to routine blood work and HIV testing, what do you recommend

A. Start PrEP with tenofovir disoproxil fumarate (TDF)/emtricitabine
B. Start PrEP with tenofovir alafenamide (TAF)/emtricitabine
C. Start PrEP with generic tenofovir disoproxil fumarate (TDF)/lamivudine
D. Start PrEP with tenofovir disoproxil fumarate (TDF)
**E. Hold PrEP until laboratory results return**

**Correct Answer: Hold PrEP until laboratory results return**

This gay man is at risk for HIV infection on the basis of his recent episode of gonorrhea and should be strongly considered for PrEP. However, his current fever, oral ulcer, and rash although non-specific could be compatible with acute HIV infection – the rapid HIV oral test only detects HIV antibodies that may not have developed yet.

Starting PrEP is never an emergency and acute HIV infection should be ruled out with an HIV antigen/antibody combination test and/or HIV RNA test prior to starting PrEP.

Starting a 2-drug PrEP regimen in someone with acute HIV infection will likely lead to the selection of drug-resistant viral strains, as seen in the large phase 3 PrEP studies.

## 35 | Staph Epi Blood Contaminant | Bell

You are asked to see a 62-year-old female admitted for acute myocardial infarction.

1 of 2 blood cultures drawn from a central venous catheter for a new fever on hospital day 3 was positive on day 4 for Gram-positive cocci in clusters, later identified as Staphylococcus epidermidis. The aerobic bottle was positive at 33 hours but the anerobic bottle remained negative. Two peripheral blood cultures were obtained on day 4, the central venous catheter was replaced, and she was started empirically on vancomycin.

The Staph. Epidermidis from hospital day 3 (before the line was removed and before antibiotics were started) is growing coagulase-negative staphylococcus with the following MICs in mcg/ml:

- vancomycin 2 mcg/ml
- daptomycin MIC 0.5
- linezolid 2
- clindamycin 1
- TMP/SMX 0.5/5

The other 3 blood cultures prior to starting vancomycin have no growth at 48 hours. Since removing the line and starting vancomycin, the patient is afebrile with no localizing signs or symptoms.

White blood count remains normal.

What would you recommend?

A. Continue vancomycin for 5 days
B. Switch to IV daptomycin and complete 5 days of therapy
C. Switch to oral linezolid to complete 5 days of therapy
D. Discontinue vancomycin and start daptomycin
**E. Discontinue vancomycin**

**Correct answer: Discontinue vancomycin**

This patient had one of four pretreatment blood cultures growing Staphylococcus epidermidis. If this were a catheter-acquired bloodstream infection, it is unlikely that the other blood culture drawn from the same catheter, even from a different port, would be negative. Also, Staphylococcus epidermidis is a facultative anaerobe, meaning it can grow aerobically or anaerobically; but it failed to grow from the anaerobic bottle of the same blood culture. The 33 hours to positivity is also consistent with the low inoculum one might find with a contaminant.

Transient culture positivity with a low inoculum can occur from a deep focus of infection but the patient rapidly became afebrile, the WBC was normal and there was no clinical evidence of a deep focus.

In this case with one of two blood cultures positive in a clinically stable immunocompetent patient, it would have been reasonable to repeat the cultures and observe the patient. Laboratories with MALDI-tof or Biofire can often identify the isolate directly from the positive blood culture bottle, which assists treatment decisions.

## 36 | HYPERSEROTONIN | BELL

A 56-year-old alcoholic woman with adult onset diabetes mellitus and depression fractured her right hip falling down the stairs.

She had an open reduction and internal fixation repair one week ago, but developed redness and drainage of the wound secondary to a vancomycin resistant *E. faecium* (VRE) infection of the operative site.

She was started on linezolid. You are called to see her on day 10 of hospitalization (day 8 of linezolid) because of anxiety, tremulousness, fever to 39.6°C, agitation and confusion.

The patient takes metformin (Glucophage) and glipizide for her diabetes mellitus and citalopram (Celexa) for her depression.

If this is a drug reaction, which one of the following is most likely?

A. Delirium tremors
B. IgE mediated allergic reaction
C. IgG mediated allergic reaction
**D. Hyper-serotonin syndrome**
E. Malignant hyperthermia

**Correct answer: Hyper-serotonin syndrome**

This patient most likely has a serotonin excess syndrome due to the combined effects of linezolid and citalopram SSRI.

Linezolid is a weak monoamine oxidase inhibitor (MAOI) and can rarely interact with selective serotonin reuptake inhibitors (SSRI's) such as citalopram causing a hyper-serotonin syndrome. You should be aware of this interaction since intervention can be lifesaving, and since this is easy to test on the board examination.

This is too late to be delirium tremens assuming that she has not been drinking in the hospital: delirium tremens occurs within 2-4 days of alcohol cessation and while it may last for 5-7 days, it would not start on the tenth day of hospitalization.

Malignant hyperthermia is usually related to inhalational anesthetics (halothane) or succinylcholine and occurs in the operating room or recovery room in most instances.

This could be neuroleptic malignant syndrome that would be related to a neuroleptic (citalopram) but which would have nothing to do with linezolid. This was not offered as a choice.

## 37 | SHIGELLOSIS | DUPONT

A 40-year-old businessman develops diarrhea while traveling to Thailand.

The illness progresses to passage of grossly bloody stools. He has been ill three days when he returns home. He is still passing bloody stools and is weak, febrile and tachycardic when you see him.

What treatment do you recommend while you are awaiting culture results?

A. a single dose of ciprofloxacin (500 mg)
B. a single dose of tinidazole (2 grams)
C. rifaximin 200 mg three times a day for three days
D. only oral rehydration therapy
**E. single dose of azithromycin (1,000 mg)**

**Correct Answer: Single dose of azithromycin (1,000 mg)**

Acute febrile and dysenteric diarrhea in a single adult traveling to a developing region is most likely caused by strains of *Shigella*, *Campylobacter* or *Salmonella*.

Treatment of choice must be guided by antibiograms of likely organisms in the geographic region where the pathogen was acquired.

In South Asia ciprofloxacin-resistant *Campylobacter* is the most likely cause of febrile dysentery. Tinidazole is useful for giardiasis not *Campylobacter* diarrhea.

Rifaximin is not effective in treating mucosally invasive bacterial infections.

A single dose of azithromycin is effective in treating the major causes of febrile dysentery of travelers. The illness is significantly shortened by azithromycin making oral rehydration alone an inadequate management strategy.

## 38 | Irritable Bowel | DuPont

Six months after an otherwise healthy young international traveler returns home to the United States from India, she presents for medical evaluation. She has been sick since she visited India although her symptoms have changed.

She initially had a bout of diarrhea, passing grossly bloody stools that responded to three days of ciprofloxacin.

During the next six months, she experienced recurrent bouts of abdominal pain, abdominal bloating and loose stools without frank diarrhea. The abdominal pain is cramping and exacerbated by eating.

What do you suspect is the diagnosis?

**A. Post-infectious irritable bowel syndrome (IBS)**
B. Chronic Cyclospora infection
C. Chronic norovirus infection
D. Clostridium difficile diarrhea
E. Celiac disease

**Correct answer: Post-infectious irritable bowel syndrome (IBS)**

**Post-infectious IBS** has been reported to occur in between 5% of travelers' diarrhea, particularly that due to inflammatory pathogens such as *Campylobacter* and *Shigella*.

Symptoms of **celiac disease**, also called gluten-sensitive enteropathy, overlap post-infectious irritable bowel syndrome but the proximity to an episode of diarrhea and the absence of extraintestinal symptoms are more consistent with IBS.

While ***Cyclospora*** infection can be protracted the illness is chronic diarrhea with abdominal pain and discomfort not related to eating. Moreover, cyclosporiasis will present with more systemic symptoms like nausea, anorexia, fatigue and weight loss.

**Norovirus gastroenteritis** is not a chronic process outside of immunocompromised patients.

***C. difficile*** can present with recurrent diarrhea but liquid stools would be reported, not only abdominal discomfort.

## 39 | HIV TESTING | MALDARELLI

A 22-year-old woman recently underwent HIV testing done as part of a routine annual check-up. She's had 3 prior male sexual partners and used condoms "most of the time"; her last episode of intercourse was 3 months ago.

Testing reveals:

HIV antigen/antibody screening test: positive

HIV-1 Supplemental immunoassay: negative

HIV-2 Supplemental immunoassay: negative

HIV-1 RNA: 12 copies/ml

What's the correct interpretation?

A. She has chronic HIV-1 infection
B. She has chronic HIV-2 infection
C. She has acute HIV-1 infection
D. She has HIV, but is a long-term non-progressor
**E. She does not have HIV**

**Correct Answer: She does not have HIV**

The HIV testing algorithm changed in the last few years moving from a screening antibody test (ELISA) with a confirmatory Western Blot to a screening combined antigen/antibody test with a confirmatory immunoassay.

Her positive screening test was NOT confirmed with the immunoassay which leaves 2 possibilities – she's either got acute HIV infection or both the screening test and the nucleic acid (viral load) tests are false positives.

Given her history with no recent exposure and her very low viral load copy number (<100), is a false positive result. If she had acute infection, the viral load level would be in the hundreds of thousands or even more than a million copies/ml.

## 40 | INITIATING RX | MALDARELLI

A 26-year-old man who had a negative HIV test 6 months ago presents to urgent care following unprotected sex with another man 10 days ago. He feels "flu-ish" and has a fever of 101.2 F; the rest of his physical examination is normal. A rapid test for HIV is positive. He is willing to start antiretroviral therapy if you recommend it.

While awaiting further lab testing, you would recommend:

A. Start tenofovir disoproxil fumarate/lamivudine/doravirine
B. Start tenofovir alafenamide/emtricitabine/elvitegravir/cobicistat
C. Start abacavir/lamivudine/dolutegravir
**D. Start tenofovir alafenamide/emtricitabine/bictegravir**
E. Hold ART until testing returns

**Correct Answer: Start tenofovir alafenamide/emtricitabine/bictegravir**

This man is at risk for acquiring HIV and presents with a new positive rapid HIV test. While the flu-like symptoms and fever are non-specific, in this scenario acute HIV infection is suspected. While in past years, many would have delayed starting ART, there is growing consensus to start ART while awaiting the results of laboratory testing. Starting ART now will reduce his likelihood of transmitting to others, will likely improve his chance of following-up with medical care, and will limit his seeding of tissue reservoirs.

Once the decision to start ART (while laboratory testing is pending) is made, you need to select a regimen with a high barrier to resistance (which rules out NNRTI-based regimens like [a] and elvitegravir-based regimens like [b]).

Both dolutegravir and bictegravir (and the HIV protease inhibitor darunavir) have high barriers to resistance, but dolutegravir is combined here with abacavir a drug that requires screening for the genetic marker HLA B*5701 to reduce the risk of hypersensitivity reaction. So, the correct regimen choice is (d).

## 41 | RALTEGRAVIR RESISTANCE | MALDARELLI

A 23 yo man with HIV and pre-treatment HIV RNA 2.2 million copies/ml started tenofovir alafenamide (TAF)/emtricitabine + raltegravir and suppressed his HIV RNA to <20 copies/ml by 6 months; subsequent HIV RNA levels were <20 copies/ml at 9 months and 12 months, but 1507 copies/ml at 15 months, repeated at 5440 copies/ml.

When questioned, the patient admitted to missing occasional doses but vows to improve his adherence.

Genotype shows RT: M184V, PR: L63P, Integrase: Y143R and N155H.

Which of the following regimens would you recommend?

**A. TAF/FTC + dolutegravir (double-dose)**
B. TDF/FTC/doravirine
C. TDF/FTC/efavirenz
D. TAF/FTC/elvitegravir/cobicistat

**Correct answer: TAF/FTC + dolutegravir (double-dose)**

This patient experienced confirmed virologic failure after initial suppression on a raltegravir-based regimen, most likely due to intermittent adherence.

Confirmed virologic failure should prompt a change in regimen, based on antiretroviral therapy history and genotyping. This was his first regimen and current genotype shows reverse transcriptase (RT) substitution M184V, conferring resistance to emtricitabine (FTC) and lamivudine (3TC) but "resensitizing" (enhancing virologic activity) to tenofovir.

The protease substitution listed, L63P, is a common polymorphism and a distractor here. The integrase substitutions at Y143R and N155H confer resistance to raltegravir (and elvitegravir), but importantly, not to dolutegravir.

Given the demonstrated resistance to FTC (emtricitabine) here, choices (b) and (c) that include 3$^{rd}$ drugs with low barriers to resistance (the NNRTIs doravirine and efavirenz) are poor choices because of the risk for the development of rapid resistance.

Choice (d) also is a poor choice both because the integrase inhibitor elvitegravir also has a low barrier to resistance and because the patient's emergent viral strain demonstrates cross-resistance to elvitegravir.

The best choice is (a) because both TAF and dolutegravir (given at double-dose according to prior clinical trials in participants with integrase inhibitor resistance) are fully active drugs. Alternative regimens (e.g. protease inhibitor-based) also would work, but are not listed here.

## 42 | ART Renal Toxicity | SAAG

A 59-year-old MSM with hypertension controlled on an ACE inhibitor takes PrEP with daily tenofovir disoproxil fumarate (TDF)/emtricitabine. His pre-PrEP creatinine was 1.1 mg/dL (creatinine clearance ~75 cc/min). On routine follow-up testing, his creatinine is now 1.4 mg/dL (creatinine clearance ~55 cc/min).

A urinalysis is negative for protein, glucose, or cells.

What do you advise?

A. Stop PrEP, use condoms
B. Repeat labs in 3 months
C. Change to every other day TDF/emtricitabine
**D. Change to daily tenofovir alafenamide (TAF)/emtricitabine**
E. Change to "on demand" TAF/emtricitabine

**Correct answer: Change to daily tenofovir alafenamide (TAF)/emtricitabine**

This man may have some renal disease from his hypertension as demonstrated by his mildly reduced creatinine clearance prior to starting PrEP. Tenofovir disoproxil fumarate (TDF) can cause proximal renal tubular dysfunction (Fanconi's like syndrome, characterized by proteinuria, glycosuria, hypophosphatemia, and subsequently, increased creatinine) and is contraindicated with a creatinine clearance <50 cc/min.

The newer tenofovir alafenamide (TAF) is associated with less renal toxicity and labeled for use down to a creatinine clearance of 30 cc/min – changing to daily TAF/emtricitabine (d) would be the best choice here for an individual with MSM risk. TAF/FTC is not indicated for PrEP for individuals at risk for HIV from receptive vaginal sex because its effectiveness in that population has not been evaluated

"On demand" PrEP would result in less drug exposure and could be another strategy with TDF/emtricitabine (although that choice was not given) – "on demand" dosing with TAF/emtricitabine has not been studied.

## 43 | Pregnancy | SAAG

A 25-year-old woman is 3 months pregnant and is found to be HIV+, HIV RNA is 96,000 copies/ml and CD4 cell count is 625 cells/µL. She is willing to start ART if you recommend it.

What is the most appropriate strategy?

A. Hold ART until the 3rd trimester
B. Start tenofovir alafenamide/emtricitabine/bictegravir
**C. Start tenofovir disoproxil fumarate/emtricitabine + dolutegravir**
D. Start tenofovir disoproxil fumarate/lamivudine/doravirine

**Correct answer: Start tenofovir disoproxil fumarate/emtricitabine + dolutegravir**

ART is indicated for all pregnant women with HIV, both for their own health and to prevent HIV transmission to their child. The DHHS Perinatal Guidelines recommend individual antiretroviral drugs and drug regimens; providers also are encouraged to report pregnancy outcomes to the Antiretroviral Pregnancy Registry www.apregistry.com that periodically updates the available safety data.

As expected, there is limited data on many of the newer HIV drugs in pregnancy (e.g., bictegravir, doravirine, tenofovir alafenamide) and these cannot be recommended.

The best choice here (per the guidelines) is (c) tenofovir disoproxil fumarate/emtricitabine + dolutegravir – there is some experience and available data with all 3 of these drugs during pregnancy.

## 44 | Flu Exposure | Weinstein

A 21-year-old college student is seen in the University Health Service for symptoms of abrupt onset, including headache, myalgia, fever (T 102.2°F) and cough. Some of her friends have been ill with similar symptoms. The student has just returned from winter break in the last week from her home in state. She has had symptoms for three days. Her roommate, who is otherwise in good health, does not have respiratory symptoms.

She is a non-smoker and has no significant past medical history. She is on an oral contraceptive as her only prescription medicine, but she has taken some of her roommate's guaifenesin. Her last influenza immunization was while in high school.

On exam, she has a temperature of T 100.0°F, unlabored respirations with a rate of 16, BP 100/70 and pulse of 88. Her lung fields are clear.

According to the CDC and state Health Department reports, seasonal influenza is circulating in the state, and there is a high incidence of influenza-like illness.

Which of the following is the best recommendation?

A. Perform a rapid influenza diagnostic test (RIDT)
B. Perform a rapid point-of-care molecular test for influenza
C. Prescribe either oseltamivir or baloxivir
**D. Recommend student stay in her room until at least 24 hours after resolution of fever (and not using antipyretics)**
E. Recommend her roommate receive oseltamivir chemoprophylaxis for influenza

**Correct Answer: Recommend student stay in her room until at least 24 hours after resolution of fever (and not using antipyretics)**

When seasonal influenza is circulating at high levels within local communities, patients with fever and cough may be diagnosed clinically with influenza without the need for diagnostic testing. Although the CDC and IDSA now recommend molecular testing for influenza due to vastly superior sensitivity over RIDTs, testing should only be carried out when the results would influence the management of the patient or household.

In this case, neither A nor B would be correct, and C is also wrong as this patient has a clinical diagnosis of uncomplicated influenza, but with symptoms beyond 48 hours, antivirals are not recommended. Her roommate could be advised that she could seek early evaluation if she has an onset of symptoms. As the roommate is not known to be in a high-risk category (such as a highly immunosuppressed individual, lacking influenza immunization), she would not fall into the group one could consider influenza chemoprophylaxis. If the roommate did fall into this high-risk category, testing of the ill patient to secure an influenza diagnosis would then be helpful to decide if chemoprophylaxis should be prescribed.

## 45 | PPE | WEINSTEIN

You are asked to examine a person under investigation (PUI) for COVID-19. Your gown and garb should be which of the following?

A. Cover gown, surgical mask, and gloves
B. Cover gown, N-95 respirator, and gloves
C. Cover gown, N-95 respirator, gloves, and disposable shoe covers
**D. Cover gown, N-95 respirator, gloves, and goggles**
E. Cover gown, N-95 respirator, gloves, disposable shoe covers, and goggles

**Correct answer: Cover gown, N-95 respirator, gloves, and goggles**

Although COVID-19 likely is spread by large droplets and maybe by contaminated environmental surfaces, the rapid spread of the virus and the 2-3% mortality have led to more heightened containment recommendations. Specifically, CDC recommends that personal protective equipment (PPE) include a single pair of disposable patient examination gloves (change gloves if they become torn or heavily contaminated), disposable isolation gown, respiratory protection (i.e., N-95 or higher-level respirator), and eye protection (i.e., goggles or disposable face shield that fully covers the front and sides of the face). PPE for Ebola were more inclusive of garb to control exposure to environmental contamination, including more extensive coverings, such as use of disposable booties and covers for the lower leg.

*This page left blank intentionally.*

# SESSION 4 | TUESDAY, AUGUST 25, 2020

**Session Moderator:** Dr. Auwaerter

**Session Panelists:** Drs. Alexander, Boucher, Marr, Mitre, and Winthrop

| Question # | Topic | Speaker |
|---|---|---|
| **46** | Acute Prostatitis | Auwaerter |
| **47** | Ludwig's Angina | Auwaerter |
| **48** | Nitrofurantoin Pneumonitis | Auwaerter |
| **49** | Symphysis Pubis Osteitis | Boucher |
| **50** | Voriconazole Periostitis | Boucher |
| **51** | Urinary Tract Infection | Alexander |
| **52** | Donor Syphilis and Renal Tx | Alexander |
| **53** | Ibrutinib | Marr |
| **54** | Mucormycosis and Car T | Marr |
| **55** | Lenalidomide Pulmonary Toxicity | Marr |
| **56** | Cryptosporidium | Mitre |
| **57** | Babesia | Mitre |
| **58** | Schistosoma | Mitre |
| **59** | M. mucogenicum | Winthrop |
| **60** | M. marinum | Winthrop |

*This page left blank intentionally.*

## 46 | ACUTE PROSTATITIS | AUWAERTER

A 55-year-old male is referred to you because of a three-day history of spiking fevers, myalgias, dysuria, and vague perineal pain. He has some urinary dribbling which is new.

His prostate is tender on palpation. A urinalysis reveals many white blood cells and gram negative rods. The urine culture grows E. coli (CFU >105/ml) which is sensitive to multiple antibiotics including ciprofloxacin.

CBC reveals a white blood count of 15,000 cells/uL with 90% neutrophils.

He is treated with ciprofloxacin for ten days which he took as prescribed, stopping a week ago. He initially resolved all symptoms, but now has myalgias again as well as more deep pelvic pain and a return of his fever, which is 38-39C.

Assuming that the prostate is the source of the fever and pelvic pain, the best management option would be:

A. Perform prostatic massage in order to obtain a quantitative culture of urine collected in initial post-massage, midstream and remaining urine and treat based on result
B. Repeat a urinalysis and culture and treat based on results; no other evaluation is necessary
**C. Retreat with ciprofloxacin**
D. Order trans rectal ultrasound
E. Order trans rectal biopsy

**Correct answer: Retreat with ciprofloxacin**

This patient's relapse probably occurred because he received less than the recommended 4-6 weeks of treatment for bacterial prostatitis.

It would be reasonable to resume twice-daily ciprofloxacin or switch to once daily levofloxacin and continue for 4-6 weeks. The original isolate was susceptible to ciprofloxacin and secondary drug resistance is unusual in this situation.

A repeat urine culture will delay treatment and is unlikely to find another organism. Quantitative urine cultures, separating early from late micturition, are recommended in the differential diagnosis of recurrent urinary tract infections when the prostate is suspected as the source.

Prostatic massage is painful and may induce bacteremia in acute bacterial prostatitis.

If the patient had not responded initially, a trans-rectal ultrasound, CT or MRI would determine whether a prostatic abscess caused failure, requiring drainage for response... A prostate biopsy can assist evaluation of patients with chronic pelvic pain (prostadynia) but has no role in this patient.

Keep in mind that the causative agents almost always enter via the urethra. Acute prostatitis can present in the setting of cystitis, urethritis, or a variety of urogenital tract infections. Anatomical abnormalities need to be considered.

Prostatitis also occurs after any kind of urethral instrumentation (catheterization, transurethral prostate surgery etc.). The organisms are typical pathogens of UTIs (E coli, proteus etc.) and Enterococci.

HIV is a risk factor for reasons that are not clear (consider GC or even Salmonella in addition to the more common pathogens).

Keep in mind that while short courses of antibiotics are part of antibiotic stewardship, most experts suggest that acute prostatitis requires 4-6 weeks of therapy.

## 47 | LUDWIG'S ANGINA | AUWAERTER

A 19-year-old college-sophomore develops a sudden fever to 103°F, chills, malaise, hoarseness, painful swallowing, neck soreness and swelling over two days.

She is evaluated at a local emergency department. She had a WBC 15,300 with 88% PMNs, negative rapid Group A strep screen and negative rapid influenza test (RIDT). She is discharged with an amoxicillin prescription for pharyngitis.

Two days later she is evaluated by otolaryngology because of persistent symptoms. She is thought to have a ranula (mucous filled sublingual cyst) as an explanation. Her primary care physician prescribes levofloxacin in addition to the amoxicillin.

The physician arranges for an infectious diseases evaluation, when she is unimproved 6d into her illness.

Her symptoms have continued, but she describes some shortness of breath and chest pain but no cough. On exam, temperature 101.7°F, pulse 113, BP 94/70, respirations 22 and mildly labored. She appears ill and is slightly anxious.

Her oropharynx has no lesions or exudates, but the tongue appears slightly enlarged.

Her neck has bilateral anterior swelling with tenderness with erythema (see photo).

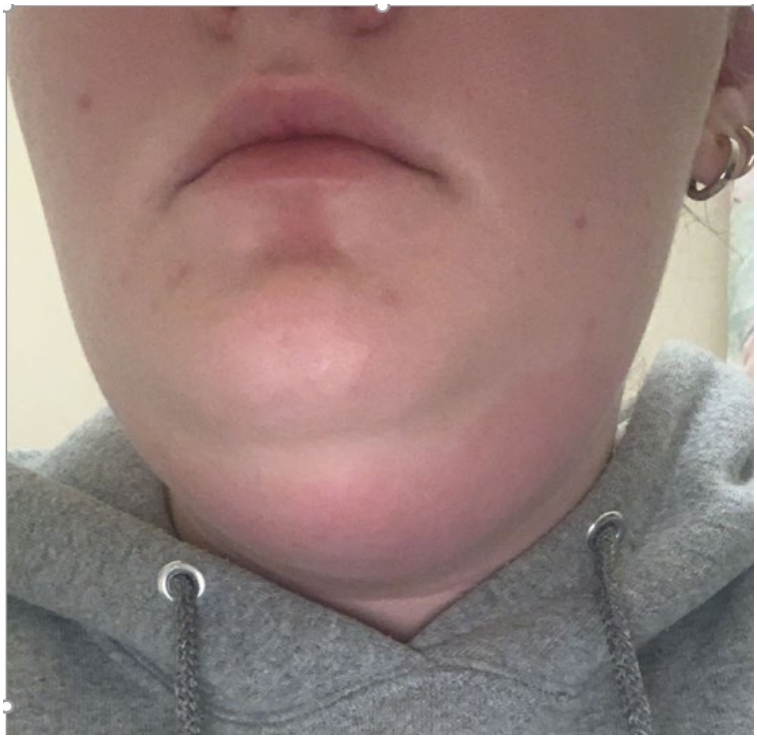


Photo provided by P.G. Auwaerter MD (patient authorized)

Which of the following answers reflect what should be should be pursued next?

A. Monospot test for Mononucleosis
B. Chest CT with angiography
**C. Neck and chest CT**
D. Lateral neck film
E. TSH (Thyroid Stimulating Hormone)

**Correct answer: Neck and chest CT**

The patient's symptoms are consistent with infection of the submandibular space, which is also known as Ludwig's angina. Imaging in this patient did detect multiple small abscesses in her geniohyoid muscle. A chest CT and chest pain suggested early superior mediastinitis.

Typically arising from dental infections of the second or third mandibular molar teeth, Ludwig's angina is an aggressive infection that develops without lymphadenopathy but includes a cellulitic component. The neck swelling is often described as having an overlying woody or brawny cellulitis.

Progression can lead to airway obstruction Infection can also spread rapidly into buccopharyngeal gap and neck muscles that may then lead to the parapharyngeal space, retropharyngeal space, and into the mediastinum. Life-threatening complication includes septic shock, airway compromise and mediastinitis.

Imaging of the neck by CT or MRI will delineate deep cervical space infections and is the test of choice to secure a diagnosis of Ludwig's angina. Additionally, a chest CT is needed to assess whether the infection has spread into the mediastinum in this patient with chest pain.

If abscesses are present, they tend to develop later, they should be aspirated or drained by surgery if of sufficient size. Other critical management issues include maintenance of the airway, institution of antibiotics to cover normal oral flora that he is immunocompetent patients should be covered by regimens such as ampicillin/sulbactam, ceftriaxone with metronidazole or clindamycin plus levofloxacin.

The patient did not have typical drooling, muffled voice, stridor or sitting in a tripod position, as seen with epiglottis, an infection in which a lateral neck film may suggest the diagnosis.

Chest CT with angiography is useful for detecting bland pulmonary emboli, or septic pulmonary emboli that frequently complicate Lemierre's disease that presents with unilateral, not bilateral neck pain and/or swelling.

The patient appears too ill for DeQuervain's thyroiditis wherein fever, neck pain and central swelling may occur with erythema over the thyroid (Maroni sign).

## 48 | Nitrofurantoin Pneumonitis | Auwaerter

A 35-year-old woman is seen for 5 weeks of progressive cough paroxysms, pleuritic pains, chest tightness and dyspnea.

Her primary care provider had tried albuterol as well as a course of amoxicillin/clavulanate with no benefit.

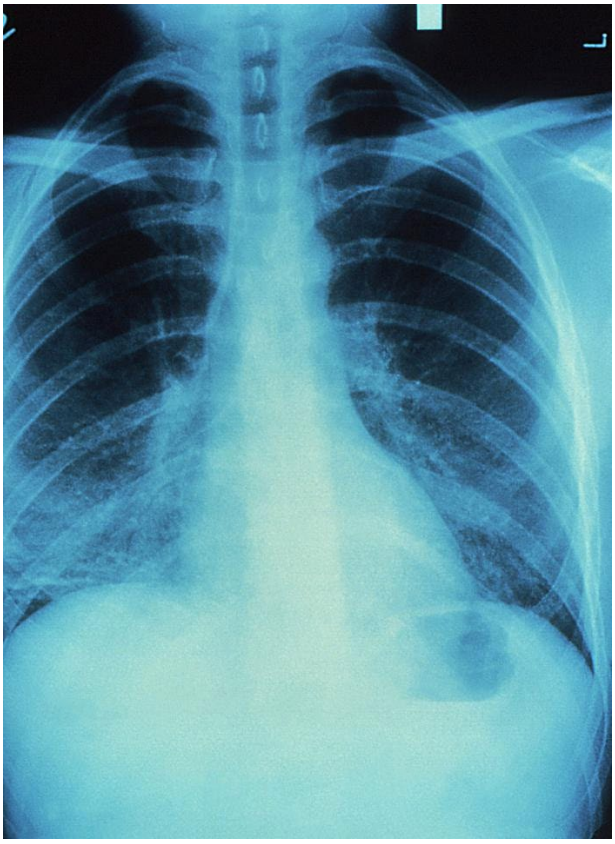
Her past medical history includes early menopause with the institution of estrogen replacement, recurrent urinary tract infections, insomnia, and depression.

Her current medications include Premarin, vaginal estrogen, venlafaxine and nitrofurantoin and have been unchanged for 3 months.

Physical examination: largely unremarkable. On the pulmonary exam, she has no percussive dullness but does have fine bibasilar crackles bilaterally

Her laboratories are remarkable for a white blood cell count of 11,800 cells/mL with 63% neutrophils, 36% lymphocytes and 1% eosinophils. Her chemistry profile is normal. The urinalysis is acellular. An erythrocyte sedimentation rate is 48 mm/h.

The chest x-ray is seen below.



Which treatment decision will most likely lead to the resolution of her symptoms?

A. Initiate Azithromycin x 5 days
B. Start INH, RIF, PZA, ETB
C. Start Ceftaroline x 7 days
**D. Discontinue nitrofurantoin**
E. Prednisone 60 mg daily with taper

**Correct Answer: Discontinue nitrofurantoin**

This patient has nitrofurantoin-induced pneumonitis. This process can present as either atypical pneumonia or interstitial fibrosis picture. This drug-induced pneumonitis may start acutely as soon as 7 to 8 days after drug initiation in these patients often are febrile accompanying their dyspnea and dry cough symptoms.

A subacute presentation is described if someone has symptoms for a month or more and is similar to acute presentations thought with less prominent fever.

Early, acute hypersensitivity reactions and subacute presentations typically have ground-glass appearances on chest imaging and display eosinophilia identified either circulating in the periphery or upon sampling by bronchoalveolar lavage.

Pneumonitis arising after chronic administration often more than 12 months on nitrofurantoin tends to be seen more in elderly populations. In one large study, chronic presentations comprised nearly 50% of all nitrofurantoin-induced pneumonitis. These later presentations may be described as interstitial pneumonitis, bronchiolitis obliterans or mixed ground-glass appearance with fibrosis and/or consolidation.

Treatment of drug-induced pneumonitis by nitrofurantoin is simple and includes discontinuing the drug. Corticosteroids have no proven role but are sometimes used when severe hypoxemia is present. Patients who are on nitrofurantoin should be monitored for potential pulmonary effects.

- Other drugs that may cause acute hypersensitive pulmonary hypersensitivity syndromes include
    - daptomycin,
    - sulfonamide antibiotics
    - minocycline
    - ampicillin
    - isoniazid.
    - Other drugs also causing similar problems include
        - amiodarone, flecainide, bleomycin, phenytoin, and nonsteroidal anti-inflammatory drugs.

Azithromycin is a macrolide antibiotic that covers many of the so-called atypical pneumonia pathogens that have intracellular lifestyles such as *Legionella*, *Mycoplasma* and *Chlamydia* species. The 5-week duration of symptoms would be an unusual presentation.

Dry cough and an interstitial CXR pattern could be due to tuberculosis; however, this would be an atypical picture except for someone who is immunosuppressed or with HIV given the lower lobe orientation.

The anti-MRSA cephalosporin, ceftaroline, is without compelling rationale given the subacute respiratory symptoms as well as the case that nitrofurantoin is not known to skew towards MRSA colonization.

## 49 | Symphysis Pubis Osteitis | Boucher

An 88-year-old man is evaluated in referral for a history of prostate cancer and recurrent urinary tract infections who has severe groin and suprapubic pain, limiting his walking and physical activities.

His history is significant for prostate cancer diagnosed 12 years earlier treated with brachytherapy. He had a transurethral resection of the prostate 6 months earlier for urinary retention with relief. He has had several urinary tract infections, including an ESBL-E. coli and K. pneumoniae over the past years that resolved with treatment. His last antibiotic received was four months ago, ten days of ciprofloxacin.

He otherwise has only hypertension. He is a widower and lives alone with a pet dog in Northern Virginia. He has no known history of TB or potential contacts.

Over the last three months, he has had progressive pain with walking or standing. His family has noted that he now walks with a waddle and requires a cane for stability. He has had no recent dysuria or unusual frequency.

A CT scan suggested abnormalities at the symphysis pubis, and a subsequent MRI showed extensive bone marrow edema in this region with some bony erosions symmetrically at the symphysis, along with edema in surrounding abductor muscles. He was hospitalized at an outpatient facility. Two fine needle aspirations of the affected area were negative for bacterial or fungal pathogens. Urinalysis was without pyuria, and urine culture was negative. Following the second aspiration and based on the imaging, that patient received six weeks of vancomycin and meropenem.

The patient states it has had little impact on his pain syndrome. Repeat MRI imaging is slightly worse, according to the radiologist. Erythrocyte sedimentation rates have continued to range between 45-60 mm/h (normal < 30 mm/h), and a C reactive protein remains elevated 1.5 mg/dL (normal 0.0-0.5 mL). He now sees you one week after completing his outpatient parental antibiotic therapy (OPAT).

Which course of action will likely lead to durable improvement for this patient?

**A. Employing a course of NSAIDs or corticosteroids over six weeks**
B. Arrange for an open biopsy of bone and tissue for bacterial, fungal and AFB cultures
C. Resume vancomycin and meropenem to complete a 12-week total course
D. Change to linezolid and ceftazidime/avibactam
E. Obtain a full-body triple-phase bone scan

**Correct answer: Employing a course of NSAIDs or corticosteroids over six weeks**

The best answer is that this scenario represents symphysis pubis osteitis [PO]of a noninfectious etiology. This uncommon condition can arise following sports-related injuries, vaginal childbirth, and in patients who have undergone genitourinary procedures. It is often confused with osteomyelitis of infectious nature. Symphysis pubis osteitis is defined by a painful inflammatory process resulting in bony destruction of the margins of the symphysis pubis. It is a self-limiting process, treated conservatively by anti-inflammatory drugs. The main difference between osteitis pubis and osteomyelitis is the negative culture on biopsy and, as in this case, there is no response to broad-spectrum antibiotic therapy for putative culture-negative osteomyelitis. Symphysis pubis osteitis may cause bony erosions as well as abnormalities in surrounding musculature that may be interpreted as due to osteomyelitis by radiologists. Urologists and gynecologists may be unfamiliar with this entity.

A trial of nonsteroidal anti-inflammatory agents or corticosteroids yields relief of PO symptoms, often combined with physical therapy. An open biopsy may be a morbid procedure in a man of this age and is unlikely to be rewarding. Rarely, fistulae arising from the bladder in patients with bladder neck deformities or strictures occur, but usually, these also cause fluid collections. Additional antibiotics do not have a role in symphysis pubis osteitis. The cause of the PO remains unknown.

A bone scan is a relatively insensitive study to detect bone inflammation. Additionally, if with displaying abnormal uptake, the study would not distinguish infectious from non-infectious inflammation, therefore not adding any clinical information to MRI imaging results.

## 50 | VORICONAZOLE PERIOSTITIS | BOUCHER

A 42-year-old male had a heart lung transplant 2 years prior and was doing well when he presented to his transplant team complaining of diffuse body aches, particularly in the extremities. He had no arthritis on examination and full range of motion in joints.

The patient was afebrile, and his routine CBC, chemistry profile, cardiac echo, and pulmonary function tests were unchanged except for a serum alkaline phosphatase which was for the first time twice the upper limit of normal. Other liver function tests were normal.

A bone scan showed numerous scattered areas of uptake. Routine films of the extremities showed patches of periosteal thickening and a few calcified excrescences.

He had been followed for 18 months for pulmonary nodules which had been associated with an elevated serum galactomannan test. He had been treated ever since the nodules were recognized 18 months previously with voriconazole.

He is receiving tacrolimus (Prograf) and mycophenolate mofetil (CellCept) plus trimethoprim-sulfamethoxazole prophylaxis for PCP, acyclovir for recurrent orolabial Herpes simplex and once daily multivitamins with vitamins A and D.

A repeat chest CT showed no change from the small nodules seen two months prior.

The most likely cause of these joint manifestations is:

A. Drug interaction with Vitamin D
B. Drug interaction with Vitamin A
**C. Voriconazole toxicity**
D. Tacrolimus toxicity
E. Mycophenylate mofetil toxicity

**Correct Answer: Voriconazole toxicity**

ID physicians are familiar with the common adverse effects associated with voriconazole: vision changes, rash, nausea and vomiting, abnormal liver function tests, and hallucinations.

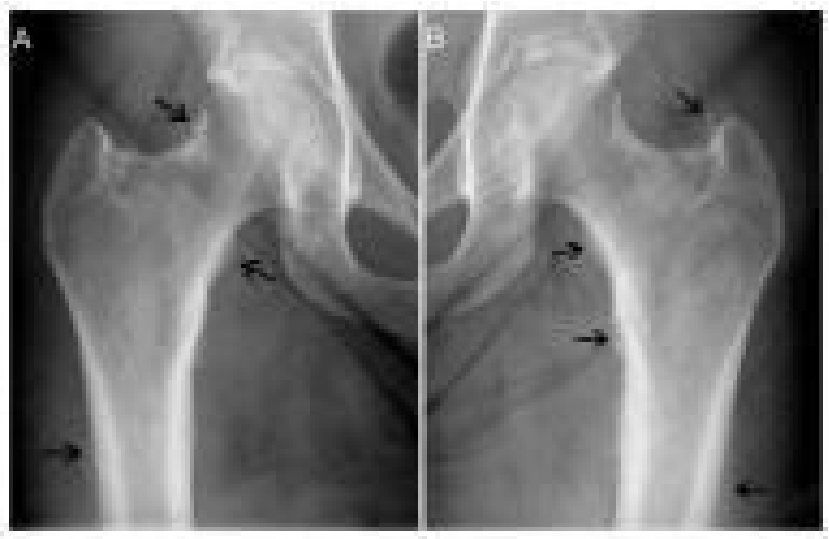
Periostitis has been associated with long term voriconazole therapy, presenting as in this patient with diffuse body aches, elevated alkaline phosphatase, and patches of periosteal thickening on routine x-ray which are positive on bone scan. Calcified excrescences are sometimes seen. This syndrome typically

occurs after at least 6 months of therapy, although cases have been reported after 6 weeks of therapy. Serum fluoride levels are characteristically elevated as well as serum alkaline phosphatase.

The syndrome is important to recognize because it usually resolves gradually after stopping voriconazole.

Voriconazole is the only azole in current use to have three fluorines in the molecule; other azoles have two fluorines. One hypothesis for the periostitis caused by voriconazole but no other azoles is that the third fluorine can be released into the blood stream during metabolism of the drug and cause fluorosis.

The differential diagnosis of the x-ray and clinical findings includes hypertrophic osteoarthropathy (often associated with malignancies or chronic infections), venous stasis associated periosteal reaction, thyroid acropachy (an autoimmune thyroid disorder associated with periosteal reactions, clubbing, and digital swelling) , and hypervitaminosis A. Voriconazole induced periostitis seems most likely.



https://www.aspergillus.org.uk

## 51 |Urinary Tract Infection| Alexander

A 50-year-old woman underwent a successful renal transplant 7 years ago. She has had no complications, and is taking tacrolimus, prednisone and mycophenolate. There have been no changes to her regimen, and she has been doing well.

During the past two weeks, she has had intermittent diarrhea without fever. The biofire screen for stool pathogens was negative (22 target pathogens including *Clostridioides difficile* toxin a/b and an array of bacteria, viruses, and parasites).

She is referred to you for evaluation, with her primary care physician pointing out that she as two urine cultures that each show >100,000 E coli, with 5-10 wbc. Ultrasound shows no dilatation of renal pelvis or ureter in the transplanted kidney.

The E. coli is sensitive to cephalosporins and quinolones. The patient denies any urinary symptoms such as frequency or dysuria.

What would you recommend with regard to the urine findings?

**A. No treatment**
B. Ciprofloxacin for 3 days
C. Ciprofloxacin for 14 days
D. Ceftriaxone x 1 dose followed by 6 days of cephalexin
E. MR scan of pelvis before a therapeutic decision is made

**Correct answer: No treatment**

This patient has asymptomatic bacteriuria, and merits no treatment even though she has a renal transplant. There may be some differences of agreement about bacteriuria during the first month post-transplant, but there is consensus against treating asymptomatic bacteriuria after that first month, assuming that the transplant went well and there are no complicating factors.

**Note the IDSA GUIDELINE:** *In renal transplant recipients who have had renal transplant surgery >1 month prior, we recommend against screening for or treating asymptomatic bacteriuria (strong recommendation, high-quality evidence).*

*The patients who merit treatment of asymptomatic bacteriuria include only pregnant women and patients undergoing invasive urologic procedures that will disrupt the mucosa. Pregnant women should at least be screened for asymptomatic bacteriuria once during an initial visit and treated for 4-7 days with an appropriate antibiotic if positive and then probably screened periodically again.*

- *In patients undergoing elective non-urologic surgery, we recommend against screening for or treating asymptomatic bacteriuria*
- *In patients who will undergo endoscopic urologic procedures associated with mucosal trauma, we recommend screening for and treating asymptomatic bacteriuria prior to surgery*
- *In patients planning to undergo surgery for an artificial urine sphincter or penile prosthesis implantation, we suggest not screening for or treating asymptomatic bacteriuria*

Diabetes or neutropenia or an indwelling Foley or cystoscopy catheter are not reasons to treat asymptomatic bacteria although sometimes non-specific symptoms such as low-grade fever or vague abdominal pain lead to clinicians using clinical judgement and electing to treat.

## 52 | Donor Syphilis and Renal Tx | Alexander

A 55-year old female has been waitlisted for a deceased donor kidney transplant for treatment of end-stage-renal disease secondary to diabetic nephropathy for the past 5 years.

She received a call stating that an appropriate deceased donor has been identified.

You are notified that the donor's RPR and TP-Ab are positive at the time of procurement.

You reviewed the donor history and it is unclear if the donor has ever been treated.

Which is the most appropriate next step?

A. Turn down the organ offer
B. Accept the kidney and recommend no treatment for the donor and recipient
C. Accept the kidney and treat the recipient only if the recipient seroconverts both RPR and FTA during monitoring monthly for 12 months
**D. Accept the kidney and treat the recipient with 2.4 million units of intramuscular benzathine penicillin G weekly for 3 weeks**

**Correct answer: Accept the kidney and treat the recipient with 2.4 million units of intramuscular benzathine penicillin G weekly for 3 weeks.**

Donor-derived infection (DDI) is defined as any infection present in the donor that is transmitted to one or more recipient. DDIs can be further categorized into expected and unexpected infections. Based on data available from the Organ Procurement and Transplantation Network (OPTN), DDIs occur in 0.2% of deceased donor organ transplants.

Serological testing for syphilis is currently recommended/mandated in donors and recipients at the time of transplantation. However, syphilis infection is not considered a contraindication to transplantation. Although in theory, syphilis may be transmitted through organ transplantation, donor-derived syphilis has only been reported in organ transplant recipients who developed seroconversion but no evidence of disease, despite appropriate post-exposure (post-transplantation) prophylaxis. Thus, option A is not appropriate.

The American Society of Transplantation Infectious Disease Community of Practice recommends treating the recipient with three weekly doses of 2.4 million units of intramuscular benzathine penicillin due to challenges in obtaining treatment histories in donors (assuming late latent syphilis). Even if the donor had neurosyphilis at the time of organ procurement, administration of intravenous penicillin to treat the transplant recipient is probably unnecessary. While in theory, if the donor is treated appropriately for late latent syphilis, the recipient does not need to be treated, it is neither ethical nor feasible to delay organ procurement for the purpose of treating the donor.

## 53 | IBRUTINIB | MARR

A 75-year-old male with chronic lymphocytic leukemia was started on ibrutinib monotherapy 20 weeks ago. He has been on trimethoprim-sulfamethoxazole and acyclovir prophylaxis since the initiation of ibrutinib therapy.

For the past week, he has had a cough non-productive of sputum. He was not febrile until today, when he noted a temperature of 38.5 C with slight worsening of his cough, and perhaps some pleuritic pain.

He lives in Annapolis, Maryland, has not traveled outside the East Coast and has no unusual exposures.

His CBC shows that his counts are stable: he is not neutropenic.

You are waiting for other lab tests to come back.

A chest CT scan shows a multiple 0.5-1.0 cm nodular lung lesions. One lesion is probably cavitating.

The most likely cause of these lung lesions is:

A. Pneumocystis resistant to TMP-SMX
B. Toxoplasma resistant to TMP-SMX
C. Candida auris
**D. Aspergillus fumigatus**
E. Nocardia brasiliensis

**Correct answer: Aspergillus fumigatus**

Although the data are still somewhat preliminary, ibrutinib has been associated with Aspergillus infections, although other fungal infections including PCP also occur.

Of note, PML has been reported to occur, and is an increased frequency of upper respiratory infections.

Ibrutinib is an oral immunomodulatory agent that could be on the exam because it is used increasingly with chronic lymphocytic leukemia, small lymphocytic lymphoma, mantle cell lymphoma, Waldenstrom macroglobulinemia and chronic graft vs host disease. Ibrutinib was the first Bruton tyrosine kinase inhibitor approved for therapy of CLL.

Ibrutinib causes hypogammaglobinemia and inhibition of B cell signaling.

There is no consensus about the need for PCP, Candida/Cryptococcus, or herpesvirus prophylaxis. As in this case, many clinicians routinely start TMP-SMX and acyclovir when using ibrutinib, although there are often, other issues related to the underlying disease or concurrent drugs that much such prophylaxis prudent.

Note also that Ibrutinib is metabolized by CYP450 enzymes and thus can be associated with numerous drug interactions.

For other tyrosine kinase inhibitors such as idelalisib and duvelisib, there are stronger recommendations for PCP and CMV prophylaxis and/or monitoring, but the data supporting these recommendations are still marginal.

PCP and Toxoplasma do not usually cause nodular pulmonary disease, and do not usually cavitate although such presentations are described. These organisms are unlikely to occur while that patient is receiving TMP-SMX prophylaxis. There is no convincing clinical data that pneumocystis or toxoplasma are resistant to

TMP-SMX, although there are interesting data regarding resistance mutations in target enzymes detected by sequencing.

Nocardia is a possible cause of these nodules, but aspergillus has been more frequently associated with ibrutinib, and TMP-SMX prophylaxis would reduce (but not eliminate) these infections.

Candida auris is frightening due to its resistance patterns (although most isolates are susceptible to echinocandins), but like other Candida species it rarely causes pneumonia.

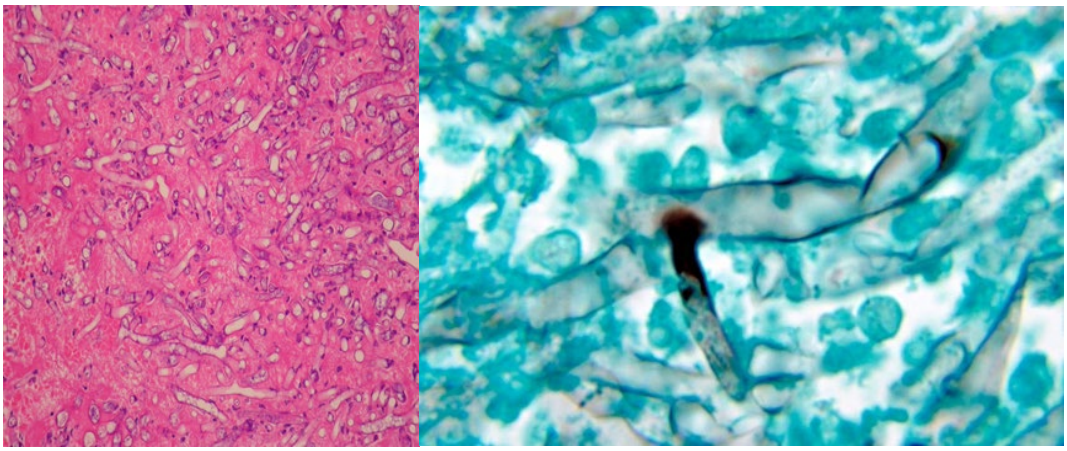
## 54 | Mucormycosis and Car T | Marr

A 63-year-old male with diffuse large B-cell lymphoma underwent CD-19 CAR-T cell therapy for treatment of underlying lymphoma.

His post-transplant course was complicated by development of grade 4 cytokine release syndrome (CRS) and neurotoxicity, requiring treatment with high dose corticosteroids (methylprednisolone 1 gram IV daily for 3 days), tocilizumab and anakinra.

On day 15 post CAR T-cell infusion, the patient was noted to have anisocoria and an MRI brain showed infarcts in both cerebral frontal lobes. He was noted to have absent brainstem reflexes and family decided to withdraw care and consented to an autopsy.

A photomicrograph (H&E stained) of his brain biopsy obtained during autopsy is shown on the left: a methenamine silver stain is shown on the right.



Which of the following would optimally be used to treat this infection?

A. Micafungin
B. Itraconazole
C. Ivermectin
**D. Amphotericin B**
E. Trimethoprim-sulfamethoxazole

**Correct answer: Amphotericin B**

This is a case of disseminated mucormycosis in an extremely immunocompromised patient who received tocilizumab (IL-6 inhibitor), anakinra (IL-1 inhibitor) and high dose corticosteroids for a known complication of CAR T-cell therapy, cytokine release syndrome (CRS).

Such patients are at increased risk of developing infections post-CAR T-cell therapy especially in those who developed grades 3 or 4 CRS, likely due to administration of conditioning chemotherapy and treatment of underlying CRS.

Among the options listed, only amphotericin B is known to be effective in mucormycosis, a diagnosis evident from the broad-based, aseptate and wide-angled branching hyphae shown in the brain biopsy photomicrographs.

## 55 | Lenalidomide Pulmonary Toxicity | Marr

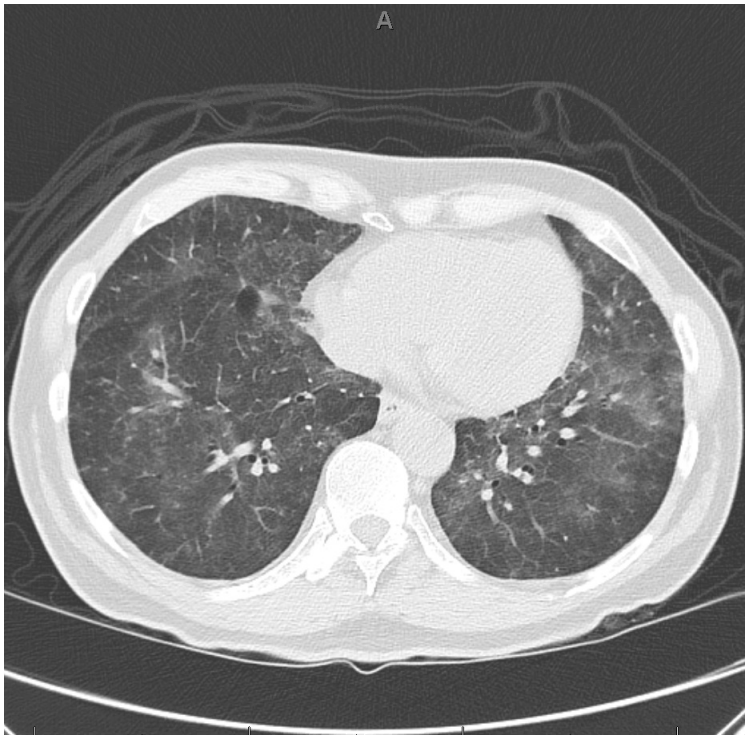
A 67-year-old male with multiple myeloma is status post autologous stem cell transplantation 9 months prior to presenting in the month of December with subacute onset of shortness of breath on exertion, which has progressively been worsening.

His post-transplant course has been uncomplicated, though the patient traveled to Arizona two months prior to admission (7 months post transplant) and he lives on a ranch in West Texas. His medication list is notable for acyclovir 800mg po BID and lenalidomide maintenance treatment.

He was seen in clinic, where he was noted to be febrile to 101F, which prompted a hospital admission for further workup.

His WBC count is 2870 (34% eosinophils). His oxygen saturation was 90% on room air.

- Respiratory viral panel on nasopharyngeal wash and BAL: negative
- Serum 1,3-beta-D-glucan: <31 ng/ml
- Bronchoalveolar lavage galactomannan: negative
- Coccidioides serology (both immunodiffusion IgG and IgM and complement fixation): negative pre stem cell transplant and currently
- Strongyloides IgG: negative pre stem cell transplant and currently. His CT chest is shown:




A bronchoscopy with bronchoalveolar lavage and transbronchial biopsy is performed.

Which of the following is the most likely finding on the biopsy?

**A. Scattered interstitial eosinophils, organizing diffuse alveolar damage in alveolar parenchyma with negative AFB and GMS stains**
B. Spherules 20 – 80 µm in diameter on fungal staining (Gomori Methenamine Silver stain-GMS) consistent with coccidioidomycosis
C. Branching, septated hyphae
D. Filariform larvae of a nematode
E. Beaded, branching, gram positive rods, positive on modified acid fast stain

**Correct answer: Scattered interstitial eosinophils, organizing diffuse alveolar damage in alveolar parenchyma with negative AFB and GMS stains**

This is a case of lenalidomide-induced pulmonary toxicity. In stem cell transplant recipients and patients with underlying hematological malignancies treated with chemotherapy and/or immunotherapy, drug-induced hypersensitivity pneumonitis should be considered on the differential diagnoses. Because it is a diagnosis of exclusion, appropriate infectious etiologies need to be excluded; thus, a transbronchial biopsy can be helpful in making the diagnosis.

This patient is at risk for pulmonary coccidioidomycosis, which is endemic in both West Texas and Arizona. However, ground-glass infiltrates and a negative serology makes coccidioidomycosis less likely.

A negative 1,3 beta-D-glucan, has modest negative predictive value for Pneumocystis jirovecii. A positive test indicates only that some fungus or inanimate substance is present. Many fungi and some inanimate substances such as gauze and dialysis membranes can produce positive results. The test is not very helpful for PCP.

Pulmonary nocardiosis typically presents with consolidative pulmonary infiltrates, and not diffuse ground-glass opacities as shown in this case.

While hyperinfection syndrome or disseminated Strongyloidiasis may present with nonspecific symptoms and radiographic findings, it usually presents shortly after conditioning chemotherapy (also known as preparative regimen) administration, not 9 months post-transplantation. The repeated negative serology makes this possibility less likely.

## 56 | CRYPTOSPORIDIUM | MITRE

You are consulted by the mother of teenage twins. She is very concerned because both of her 15-year-old daughters have had diarrhea for more than a week. Their family physician said it was a virus, but the mother is concerned that they are not getting better and are missing school. Additionally, she reports that six of the girls' friends have "the same thing."

A quick investigation discloses that six days before their gastrointestinal illness began the twins had celebrated their 15th birthday along with ten invited friends at a recreational water park. At the park they all swam in a pool and sat in a water spray. The mother, who has remained well, "didn't go near the water." No food was ingested at the park; some of the girls drank chocolate milk, others drank carbonated beverages. The six of ten girls who became ill all have watery diarrhea; none have fever. Three also report nausea and abdominal cramps. All became ill 5-7 days after the birthday celebration.

Which one of the following is most likely responsible for this outbreak of gastroenteritis?

A. Norovirus
B. Listeria
C. Giardia
**D. Cryptosporidium**
E. Rotavirus

**Correct answer: Cryptosporidium**

Cryptosporidium, a parasitic protozoan, can produce watery diarrhea lasting 1-3 weeks in healthy individuals after an incubation period of 1-12 days. Because of its resistance to chlorination, Cryptosporidium has become the leading cause of gastroenteritis outbreaks associated with treated recreational water venues.

Many such outbreaks have been reported, and attack rates among those exposed are commonly as high as 50-85%. Both the incubation period here and the duration of illness are too long for norovirus or rotavirus.

Listeria may produce gastroenteritis after ingestion of contaminated food, but fever is a prominent part of such illness; the incubation period is a day and the illness lasts 2-3 days.

Giardia outbreaks may occur following environmental exposure to water, but they are much less common in association with recreational water park exposures than are cryptosporidia.

## 57 | BABESIA | 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 Room 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, 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:

- WBC 3300 (50% PMNs, 35% lymphs, 15% monos)
- Hemoglobin 4.7gm/dL
- Platelet count 105,000
- Total bilirubin 3.8mg/dL
- ALT 110 U/L
- LDH 650 IU/mL

He develops adult respiratory distress syndrome (ARDS) and 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**

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

The splenectomized patient is at enhanced risk for severe sepsis due to encapsulated bacteria (e.g., *Streptococcus pneumoniae, Haemophilus influenzae* and *Neisseria meningitidis*) but also for other pathogens including *Capnocytophaga canimorsus* and the intraerythrocytic parasite Babesia, which behaves similarly to malaria. As his 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 laboratories reveal a characteristic anemia with hemolytic features including elevated bilirubin and LDH with concomitant thrombocytopenia.

Rocky Mountain spotted fever (RMSF, *Rickettsia rickettsii*) can certainly cause severe infection, but it is less likely than *Babesia microti* since RMSF does not usually cause this degree of anemia, and *R. rickettsii* it 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, *Ixodes 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 *Babesia microti*. All of 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 may range slightly longer (1-6 weeks).

The patient's prior history of trauma-related splenectomy places him at high risk of severe infection with Babesia, 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 human granulocytic anaplasmosis (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.

## 58 | SCHISTOSOMA | MITRE

A 48-year-old physician presents with complaints of severe fevers, abdominal pain, diarrhea, and back pain for 5 days. The patient returned from a 6-month medical mission to Sudan 2 weeks ago. The patient took doxycycline daily for malaria prophylaxis while there, but reports she would occasionally forget a dose.

She experienced frequent insect bites, especially when she took hikes along the banks of the White Nile River. She was usually careful about what she ate, but about once a week would eat home cooked meals prepared by coworkers at the medicine clinic.

On exam, her heart rate is 110 bpm, BP is 100/70, respiratory rate is 24/min, and temperature is 38.6 °C. Lung sounds are clear to auscultation bilaterally. Abdomen is soft with moderate tenderness in the right upper and right lower quadrants.

Abnormal laboratory values include a white blood cell count of 18,400/$mm^3$ with 45% neutrophils, 24% lymphocytes, 6% monocytes, 24% eosinophils, and 1% basophils. AST is 158 units/L and ALT is 144 units/L.

Ova and parasite examinations on stool and urine samples, sent by the patient's primary physician three days ago, are negative.

Which of the following organisms is most likely causing her illness?

A. Salmonella typhi
B. Plasmodium falciparum
C. Onchocerca volvulus
**D. Schistosoma mansoni**
E. Ancylostoma duodenale

**Correct Answer: Schistosoma mansoni**

The case describes a classic presentation of acute Schistosomiasis, also known as Katayama syndrome.

Findings include sudden onset of fever, abdominal pain, and marked eosinophilia in travelers with exposure to freshwater in endemic areas. In this case, the patient may have come into contact with freshwater when walking along the banks of the White Nile River.

In Schistosomiasis, cercariae released by freshwater snails directly penetrate human skin. Once inside a person, the parasites become schistosomula and migrate through the circulation to mesenteric vessels of the bowel *(S. mansoni)* or bladder *(S. haematobium)*. Acute Schistosomiasis occurs at the onset of egg laying by the mature parasites, which is typically 4 to 8 weeks after infection. The diagnosis of acute Schistosomiasis is often a clinical one, as initial diagnostic studies (including both ova and parasite exams as well as antibody studies) can be negative early in the course of infection.

*S. typhi* and *P. falciparum* can present with similar symptoms of abdominal pain and fevers. However, neither would be expected to cause a high level of eosinophilia. *O. volvulus* is the cause of river blindness

and causes skin and eye manifestations. *A. duodenale*, a cause of hookworm disease, can cause abdominal pain but is much less likely than acute Schistosomiasis to cause fever.

## 59 | M MUCOGENICUM | WINTHROP

A 27-year-old male with sickle cell disease presents with a chest syndrome crisis: he has his typical fever, chest pain, and leukocytosis. He is cultured and started on vancomycin and levofloxacin.

His initial chest radiograph shows bilateral infiltrates: an x-ray one week prior showed only some chronic scarring. Sputum gram stain, acid fast stain, and culture show only modest amounts of normal flora. His CBC and Chem 12 show a leukocytosis, hemolytic anemia, and mild LFT abnormalities.

Careful physical examination reveals no localizing physical findings: a tunneled double lumen subclavian line, in for 4 months, appears unremarkable.

After 96 hours, the laboratory reports that one blood culture is growing a non-branching beaded Gram positive bacillus that is acid fast stain positive. Three additional blood cultures are drawn (one through each lumen of the subclavian line) and one peripherally: at 48 hours they are all reported to be positive for an acid fast non branching rod.

Which of the following organisms would be most likely?

A. Nocardia asteroides
**B. Mycobacterium mucogenicum**
C. Rhodococcus equi
D. Legionella micdadei
E. Mycobacterium tuberculosis

**Correct answer: *Mycobacterium mucogenicum***

The beaded, acid fast organism appears to be some type of rapid growing mycobacterium. Microbiologically, this could be *Mycobacterium fortuitum*, *Mycobacterium chelonae*, *M. mucogenicum* or *Mycobacterium abscessus. While positive blood cultures with these organisms are rare, positive blood cultures with M. mucogenicum* particularly are associated with catheter acquired sepsis. The subclavian catheter, which has been in place for 4 months, is the likely source.

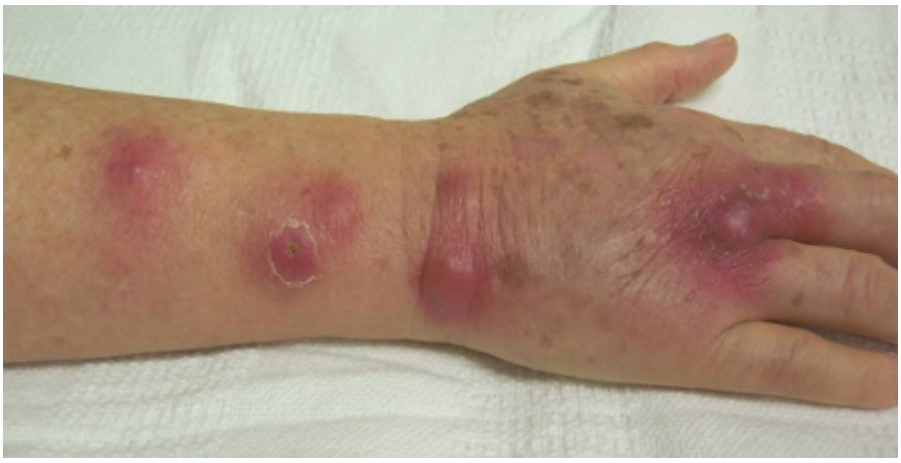
None of the listed organisms are likely to enter the bloodstream from the lung, including *Nocardia* species. Also, the acid fast smear of the sputum showed no organisms.

Management of catheter acquired sepsis from rapidly growing mycobacteria should involve removal of the catheter. Immunosuppressed and immunocompetent patients are often treated but metastatic foci of infection are rare. Susceptibilities can be determined in most laboratories and used to guide multi-drug

treatment if the patient is immunosuppressed or has other indications for treatment. The optimal length of therapy is unclear and is dictated by extent of infection and immune status of the host.

## 60 | M MARINUM | WINTHROP

This 55-year-old microscope repairman has an aquarium at home with tropical fish. This very slightly tender nodule appeared on the dorsum of his hand a week ago and has grown slightly larger.



He otherwise feels well.

Among the following techniques to culture the organism, which is the most important?

A. Addition of ferric citrate to mycobacterial agar
B. Use of fresh chocolate agar
C. Sabouraud's agar without antibiotics
**D. Incubation on mycobacterial agar at 30°C**
E. NNN medium

**Correct Answer: Incubation on mycobacterial agar at 30°C**

A chronic erythematous nodule on a skin surface exposed to brackish water or tropical fish tanks should suggest *Mycobacterium marinum* infection.

*M. marinum* is difficult to see in biopsy so that diagnosis depends on culture. *M. marinum* grows poorly at the usual clinical laboratory incubator temperature of 35-37°C so should be cultured on any standard mycobacterial agar at 30°C.

Iron is important for *Mycobacterium haemophilum* but not *M. marinum*.

Fresh chocolate agar is recommended for *Bartonella henselae* culture.

Sabouraud's agar is useful for sporotrichosis but not Mycobacteria. Sporotrichosis is acquired from thorny plants and not water.

NNN medium is used for culturing Leishmania but there is no exposure history for that diagnosis.

# Session 5 | Wednesday, August 26, 2020

**Session Moderator:** Dr. Gilbert

**Session Panelists:** Drs. Aronoff, Bennett, Boucher, Masur, and Patel

| Question # | Topic | Speaker |
|---|---|---|
| **61** | Ulcerative Colitis | Gilbert |
| **62** | Urinary Tract Infection | Gilbert |
| **63** | Ceftolozane Anaerobic | Boucher |
| **64** | C Diff | Aronoff |
| **65** | Actinomycosis | Aronoff |
| **66** | Recurrent UTI | Boucher |
| **67** | HIV/AIDS cryptococcal meningitis | Bennett |
| **68** | Methadone | Masur |
| **69** | HHV6 Positive | Patel |
| **70** | False Negative Crypto | Patel |

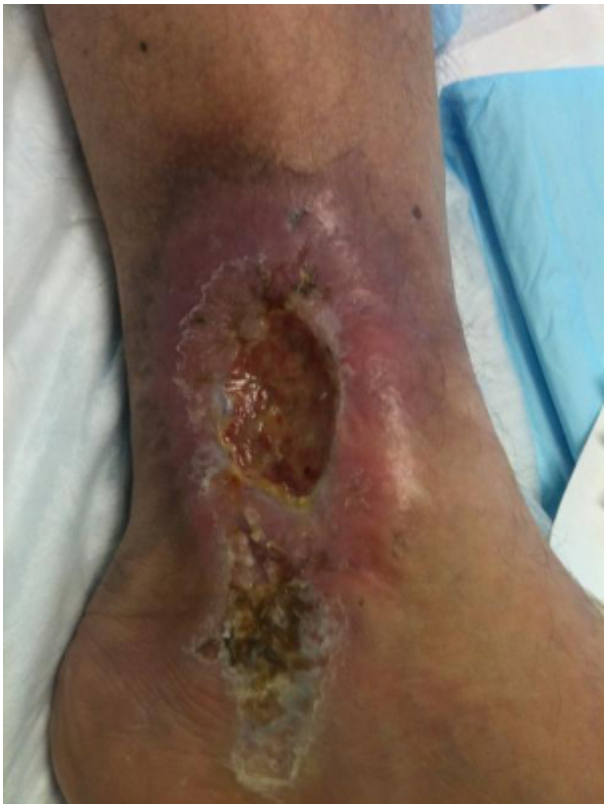
*This page left blank intentionally.*

*This page left blank intentionally.*

## 61 | Ulcerative Colitis | Gilbert

This otherwise healthy patient, who has never left the Midwestern United States, has a chronic leg ulcer. He has had a negative stains and cultures for fungi, mycobacteria, Nocardia, or viral inclusions.

This otherwise healthy patient with a chronic leg ulcer is most likely to have:



A. Common variable immunoglobulin deficiency
B. Lupus erythematosus
C. Hepatitis C
**D. Ulcerative colitis**
E. Mycobacterium ulcerans

**Correct Answer: Ulcerative colitis**

This is a typical lesion of pyoderma gangrenosa. Lesions characteristically are painful, irregular in shape, and have undermined borders. They can occur anywhere on the body but appear most often on the legs. The most common underlying disease is inflammatory bowel disease, more often due to ulcerative colitis than Crohn's, and skin lesions may precede the onset of bowel disease.

Common variable hypogammaglobulinemia would present with a history of recurrent respiratory infections, not a chronic leg ulcer.

Lupus can be associated with skin lesion but not a deep painful ulcer of this type.

Cryoglobulinemia due to hepatitis C is associated with palpable purpura, not a single large ulcerative lesion.

Mycobacterium ulcerans infection is not seen in the U.S.

## 62 | URINARY TRACT INFECTION | GILBERT

A 52-year-old man has been in the ICU following a cocaine related stroke. He was intubated following his stroke, developed staph epidermidis bacteremia from a PICC line (peripherally inserted central catheter), and is now off antibiotics (7-day course of daptomycin has been completed) ready to move to the rehabilitation floor. He has a Foley catheter and a peripheral IV line.

The patient is alert and oriented and has no new complaints.

The resident preparing to transfer the patient calls an ID consult because the urine in the Foley bag is cloudy. The patient is afebrile with normal vital signs, no new physical findings, and he does not have pain over his bladder and no flank pain.

The medical resident has obtained a urinalysis on fresh urine from the Foley catheter. there are 50-75 WBC per high power field and 5-10 RBCs with 2+ bacteria but a negative leukocyte esterase. Culture is sent.

There are no changes in his complete blood count or chemistry profile.

The patient has no known antibiotic allergies.

What would you suggest?

A. No change in regimen: follow for 48 hours with Foley in place, pending urine culture result and treat with antibiotic according to culture.
B. Replace the Foley and treat with antibiotics if urine culture is positive according to urine isolate susceptibility pattern.
C. Replace the Foley and treat empirically with ciprofloxacin.
**D. Remove the Foley and do a voiding test to determine if Foley is necessary; no antibiotic therapy.**
E. Remove the Foley and do a voiding test to determine if Foley is necessary; treat empirically with ciprofloxacin

**Correct answer: Remove the Foley and do a voiding test to determine if Foley is necessary; no antibiotic therapy.**

There is no indication that this patient has a urinary tract infection: there is no fever, no leukocytosis, no flank pain, i.e., nothing to suggest that the cloudy urine and 2+ bacteria are anything more than asymptomatic bacteriuria, a condition that does not merit antimicrobial therapy while the Foley is still in place. The diagnosis of catheter-acquired urinary tract infection (CUTI) in hospital epidemiology parlance)

require symptoms of infection. Patients with a Foley who are going to bladder surgery should be cultured and treated just prior to surgery. In regard to answer B, urine culture just prior to removing the catheter and treating the infection before catheter removal, the IDSA guidelines made no recommendation for lack of evidence for or against that practice.

Good management to reduce the likelihood of a hospital acquired UTI would be to encourage removal of the Foley catheter: a trial of voiding without the catheter would be appropriate. This can be done by following the patient with good hydration and serial ultrasounds to assure that the patient is emptying his bladder: patients who void at least 150 ml and have a residual less than 100 ml are unlikely to have urinary retention. The urinary catheter need not be replaced unless there is bladder pain or large residual volumes, i.e., >500 ml.

Asymptomatic bacteriuria in the absence of a catheter warrants treatment only in women who are pregnant or persons who are about to undergo invasive urologic procedures with mucosal bleeding.

In regard to screening for and treating asymptomatic bacteriuria in neutropenic patients, the IDSA guideline committee determined there was too little evidence to make a specific recommendation.

## 63 | CEFTOLOZANE ANAEROBIC | BOUCHER

A 55-year-old male undergoes emergency surgery for a ruptured appendix with severe bacterial peritonitis and septic shock.

He has no antibiotic allergy or intolerances.

Which one of the following antibiotics requires concomitant metronidazole IV?

A. Piperacillin-tazobactam
B. Ampicillin-sulbactam
**C. Ceftolozane-tazobactam**
D. Imipenem-cilastatin-relebactam
E. Eravacycline

**Correct answer: Ceftolozane-tazobactam**

The optimal treatment of bacterial peritonitis requires an antibacterial regimen with predictable activity vs both Enterobacteriaceae and anaerobic gram-negative bacilli (especially *Bacteroides fragilis*).

Ceftolozane-tazobactam has weak activity vs *B. fragilis* and hence, adding metronidazole is recommended.

Piperacillin-tazobactam, ampicillin-sulbactam, and all the carbapenems have activity vs anaerobic gram-negative bacilli. Note that roughly half of *E. coli* strains are now resistant, in vitro, to ampicillin-sulbactam.

Eravacycline (Xerava) is FDA-approved for complicated intra-abdominal infections based on FDA registration trials. There is limited experience in the treatment of severe peritonitis with eravacycline alone. Eravacycline antimicrobial activity includes many Enterobacteriaceae, E fecalis and E faecium, and MSSA. This in theory this can used for intra-abdominal with equivalently with carbapenems. Eravacycline has activity against ESLBL producing organisms.

## 64 | C DIFF | ARONOFF

An 86-year-old man is admitted to the hospital for treatment of community-acquired pneumonia and receives IV ceftriaxone followed by oral moxifloxacin. By day 4, his temperature is normal and he is ready for discharge when he develops loose stools with some abdominal cramping.

He is having 6-8 watery bowel movements a day. There is no blood in the stool. His albumin is 3.0, creatinine 1.9, and white blood cell count is 18,000/mm3. A stool specimen is submitted and is positive for Clostridium difficile toxin using PCR for the toxin B gene.

Which of the following drugs would you use to treat this patient assuming you were choosing monotherapy?

A. IV Metronidazole
B. PO Metronidazole
C. IV Fidaxomicin
D. PO Rifaximin
**E. PO Vancomycin**

**Correct Answer: PO Vancomycin (oral fidaxomicin would also be correct but is not a choice)**

Per the 2017 SHEA/IDSA guidelines, severe Clostridium difficile infection (CDI) is accompanied by leukocytosis (with a WBC count of ≥15,000 cells/mL) or a serum creatinine level >1.5 mg/dL. Fulminant CDI is accompanied by hypotension or shock, ileus, megacolon. This patient has high risk for severe disease due to his age.

Either oral vancomycin or oral fidaxomicin are recommended therapies for severe or refractory disease. IV fidaxomicin is not an available therapy for CDI. There is no compelling data on dose: oral vancomycin 125 mg q6h is recommended. Fulminant CDI is generally treated with high dose (500 mg q6h) vancomycin with or without IV metronidazole.

*Rifaximin* has some activity in *C. difficile* diarrhea, but has been relegated to a possible adjunctive measure in the treatment of recurrent CDI. Resistance occurs easily. Not a first line agent.

Fecal transplants are generally not appropriate for treatment of acute infection: their role is the treatment of relapses, usually in the setting of multiple relapses despite long courses of tapering vancomycin.

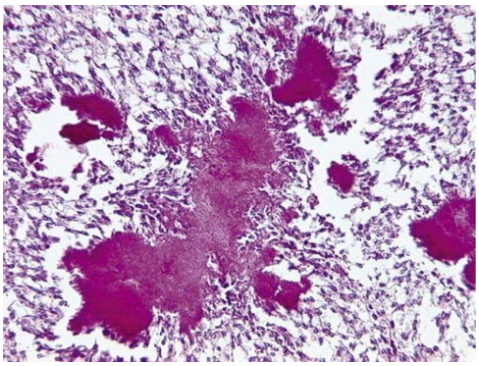
Surgery clearly has a role for patients with severe disease, but when to perform surgery or what surgical procedure to do is not easily testable. A high lactate or an ileus with abdominal distension and significant abdominal pain are ominous signs.

## 65 | Actinomycosis | Aronoff

A 42-year-old woman was referred for management of an incarcerated, indirect, inguinal hernia on the right side. She had used an IUD for many years.

Her peripheral blood white cell count, C-reactive protein and erythrocyte sedimentation rate were normal. The patient was afebrile.

During operation on the hernial sac, a putrid, inflammatory, tumorous formation associated with the right ovary was found. The histopathologic picture of the resected ovary showed a highly active zone of abscess formation, with granular conglomerates of a filamentous microorganism (Figure).



In addition to surgical resection, treatment should involve which of the following medications?

- **A. Penicillin**
- B. Voriconazole
- C. Trimethoprim-sulfamethoxazole
- D. Weekly amphotericin B
- E. Ciprofloxacin

**Correct answer: Penicillin**

This is a case of IUD-associated Actinomycosis. The case is based on a report by Wagenlehner, *et al*. published in *Clinical Microbiology and Infection*, Volume 9, Issue 8, August 2003, Pages 881-885. The image is from that case report. Actinomycetes are anaerobic, gram positive, filamentous bacteria that form sulfur granules in tissue and are highly sensitive to penicillin.

This patient had an abscess and thus obviously needed treatment. Keep in mind that Actinomyces are normal GI flora and that asymptomatic female genital colonization is not uncommon, especially if an IUD is

in place. Thus, the presence of an actinomyces like organism on a PAP smear does not require a culture for confirmation, nor is any intervention such as IUD removal necessary if the woman is asymptomatic. If the patient has pelvic inflammatory disease, the patient needs the usual work up of cervical culture, ultrasound, and antimicrobial therapy.

## 66 | Recurrent UTI | Boucher

A 27-year-old woman calls to say, "I've got another urinary tract infection." In the past six months, she was seen twice for complaints of dysuria and frequency.

The first time, a urine dipstick test was consistent with a UTI, and she responded to three days of antibiotics. The second time, which was two months ago, a culture was sent that grew a highly susceptible E. coli, and again her symptoms went away with three days of antibiotic treatment.

She is otherwise healthy, sexually active and never had any urinary symptoms before the current year.

Which one of the following is the most appropriate approach to this patient's complaint?

A. Culture her urine
B. Image her urinary tract
C. Perform a bladder emptying study
**D. Prescribe antibiotics for three days**
E. Prescribe antibiotics for 2 weeks

**Correct answer: Prescribe antibiotics for three days**

Studies show that a woman who has had a well-documented urinary tract infection and thinks she has another is almost always correct.

The fact that her UTIs responded quickly in the past, and that she never had a problem prior to the current year, means there is almost no chance that she has an anatomical or physiological reason for recurrent UTIs, so imaging or bladder emptying studies should not be done.

The fact that it has been two months since her last UTI means that it is very unlikely this new UTI represents undertreated upper tract infection, so another antibiotic course without culture for three days rather than two weeks is the correct approach.

## 67 | HIV/AIDS Cryptococcal Meningitis | Bennett

A patient with HIV infection (CD4=25 cells/µL and VL 1 million c/ml) has cryptococcal meningitis (positive serum and CSF crypt antigen) with severe headaches and blurred vision. The opening pressure on the initial

LP was not measured. Papilledema is seen on funduscopic exam. A CT scan shows no mass lesion or signs of herniation. The patient was started on Liposomal Amphotericin plus 5FC.

Which of the following would you recommend in response to her persistent severe headache and blurred vision on day 2 of therapy:

A. Immediate institution of acetazolamide and monitor for first 6 hours before adding another intervention
B. Immediate institution of dexamethasone and monitor for 24 hours
**C. Initiate daily lumbar punctures to reduce intracranial pressure**
D. Double the dose of Liposomal amphotericin B to 1.2 mg/kg/day
E. Add Fluconazole 1200 mg to the antifungal regimen

**Correct Answer: Initiate daily lumbar punctures to reduce intracranial pressure**

Among patients in whom CSF opening pressure was not initially measured, a repeat lumbar puncture should be performed with measurement of opening pressure. Reducing intracranial pressure is critical to preserving vision. Papilledema is almost always a sign of increased intracranial pressure.

For patients with high opening pressure, often defined as above 25 cm, a repeat lumbar puncture should be performed with urgency, particularly in those with vision loss. There is no guidance as to how long lumbar punctures should be continued nor when a ventriculostomy or VP shunt placed but clinical improvement is usually used to make that determination.

Answers A and B are wrong: Acetazolamide is contraindicated and dexamethasone is controversial in this clinical setting.

Answers D and E are wrong: there is no evidence that increasing the liposomal amphotericin B dose is useful, nor is there evidence that adding fluconazole to Liposomal Ampho plus 5FC is useful. There are trials where fluconazole has been used instead of 5FC in situations where 5FC was not available or not feasible, but that is not the scenario presented here.

## 68 | METHADONE | MASUR

A 67-year-old patient on methadone for chronic pain (5 mg q 8 H) for several years due to severe low back pain is admitted for pneumococcal pneumonia and an empyema. A chest tube is inserted and he is treated for pneumococcal pneumonia with bacteremia and empyema: vancomycin plus ceftriaxone is his initial regimen.

The day after his chest tube is inserted, the patient has considerable pain at the chest tube site. Acetaminophen and ketorolac are given in addition to has baseline methadone, but after 24 hours of this analgesic regimen the patient cannot sleep due to considerable, constant pain which he states in 10/10 in severity.

What would you recommend for pain relief?

A. Stopping the methadone and administering increasing doses of codeine starting at 5 mg q4h
B. **Maintaining the methadone dose and adding codeine at 5 mg q4h with increasing doses as needed**
C. Stopping the methadone and prescribing fentanyl by patient controlled analgesia (PCA)
D. Continue current regimen of methadone, acetaminophen and ketorolac for 48 hrs. more before switching the regimen

**Correct answer: Maintaining the methadone dose and adding codeine at 5 mg q4h with increasing doses as needed**

Patients should not have to tolerate severe pain and thus analgesia is appropriate. Answer 4 is thus not optimal.

Patients taking long acting opioids for chronic pain should generally have their long acting basal analgesic continued with short acting drugs added temporarily if non-narcotic drugs are not adequate. Adjusting long acting drugs for acute pain can be difficult, with the potential for under treatment of pain or over sedation and overdose. Shorter acting drugs are a better option. Thus answers 1, 3 and 4 are incorrect.

Stopping the methadone and treating with only a short acting drug such as codeine is also difficult in terms of controlling the acute and chronic pain.

This patient is taking methadone 3 times daily for pain, which is different from a high dose, once per day regimen for opioid use disorder.

## 69 | HHV6 POSITIVE | PATEL

A 22-year-old university student was in his usual state of health until the evening prior to hospital admission when he went to bed with a headache. He told his roommate that he felt feverish; the following morning his roommate found him in bed, moaning and lethargic, and brought him to the Emergency Department.

In the Emergency Department, he appeared toxic and drowsy but was oriented. His temperature was 40°C, heart rate 124/min, and blood pressure 98/60 mm Hg.

His neck was stiff and he had a purpuric non-blanching rash most prominent on the trunk, legs, and wrists.

A lumbar puncture is performed revealing 5000 cells/µl (10% lymphocytes, 90% neutrophils), a protein of 275 mg/dL and a glucose of 15 mg/dL.

Gram stain of spinal fluid shows Gram negative cocci in pairs. Bacterial cultures are pending.

His cerebrospinal fluid was submitted to testing with a multiplex PCR panel, and returned the results below.

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

Which of the following is the most appropriate antimicrobial regimen for this patient?

A. Vancomycin and cefepime
B. Vancomycin and cefepime and acyclovir
C. Ceftriaxone and ganciclovir
D. Ceftriaxone and acyclovir
**E. Ceftriaxone alone**

**Correct answer: Ceftriaxone alone**

The patient's clinical presentation is consistent with bacterial meningitis and with the rash and his age group, *Neisseria meningitidis*, which was also detected by PCR, is the likely diagnosis.

Confusion is generated by co-detection of human herpes virus 6; in this patient, this finding is clinically insignificant and should not impact therapy. Herpes virus 6, like other Herpes viruses, is a latent virus that can be found in white cells in the CSF unrelated to CNS pathology.

Either penicillin G or ceftriaxone are reasonable treatments for meningococcal meningitis.

## 70 | False Negative Crypto | 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, mycophenylate 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 spinal fluid is negative and bacterial cultures are in progress.

His spinal fluid is submitted to testing with a multiplex PCR panel, and returns the results shown below.

<table>
<tr><th>Viruses</th><th>Bacteria</th><th>Fungi</th></tr>
<tr><td>Cytomegalovirus<br>NEGATIVE</td><td>Escherichia coli K1<br>NEGATIVE</td><td rowspan="8">Cryptococcus neoformans/gattii<br>NEGATIVE</td></tr>
<tr><td>Enterovirus<br>NEGATIVE</td><td>Haemophilus influenzae<br>NEGATIVE</td></tr>
<tr><td>Herpes simplex virus 1<br>NEGATIVE</td><td>Listeria monocytogenes<br>NEGATIVE</td></tr>
<tr><td>Herpes simplex virus 2<br>NEGATIVE</td><td>Neisseria meningitidis<br>Negative</td></tr>
<tr><td>Human herpes virus 6<br>NEGATIVE</td><td>Streptococcus agalactiae<br>NEGATIVE</td></tr>
<tr><td>Human parechovirus<br>NEGATIVE</td><td rowspan="2">Streptococcus pneumoniae<br>NEGATIVE</td></tr>
<tr><td>Varicella zoster virus<br>NEGATIVE</td></tr>
</table>

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. Examination for *Naegleria fowleri*

**Correct answer: Cryptococcal antigen**

The patient's clinical presentation is consistent with cryptococcal meningitis. The PCR is negative; 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 and *Naegleria fowleri.*