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PHOTO OPPORTUNITY I: PHOTOS & QUESTIONS TO TEST YOUR BOARD PREPARATION  ANSWER KEY

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NOTE ABOUT MATERIALS
See the recording or your syllabus for the images.

Case 1
60 year old man was well until day of admission when he developed lethargy and confusion. Over the course of the day, his hands and feet grew cold and numb and he developed a rash. He lived in a rural area (mountain-lion territory) and drank well-water. He had a history of alcohol abuse. He rode horse and has dogs, one of whom bit him a few days prior to his presentation. On exam, he was febrile (38.7 C). He had nonblanching, nonpalpable, purpuric patches on scalp, trunk, thighs; puncture wounds on dorsal aspect of hand; edema, cyanosis of nose (shown). The most likely diagnosis is which of the following:

A. *E. coli* 0157:H7
B. *Yersinia pestis*
C. *Pasteurella*
D. *Capnocytophaga*
E. Leptospirosis

Answer: D

Discussion: This patient has sepsis and purpura fulminans due to *Capnocytophaga canimorsus*. *Capnocytophaga canimorsus* is a facultative, fastidious gram-negative bacillus found in the mouth of dogs and cats. Risk factors for infection include male sex, dog-bite, alcohol abuse, asplenia, and immunosuppression. In *Capnocytophaga* septicemia, 20-40% of patients develop a rash which, as in this case, may initially be maculopapular with rapid progression to purpura fulminans. Treatment of *Capnocytophaga* is generally with a 3rd generation cephalosporin, a beta-lactam/beta-lactamase inhibitor or a carbapenem. Because serious *Capnocytophaga* infection may follow a dog or cat bite in asplenic patients, antibiotic prophylaxis with amoxacillin/clavulanate should be considered in this situation.
The other diagnoses in the differential are less likely. *E. coli* 0157:H7, which may be complicated by hemolytic uremic syndrome, usually presents with abdominal cramping followed by diarrhea; fever is typically absent. In this case, gastrointestinal symptoms were not prominent and he had a high fever, which makes *E. coli* 0157:H7 less likely. In the U.S., most cases (80-85%) of *Yersinia pestis* present as bubonic plague, in which regional lymphadenitis is present; this patient did not have swollen lymph nodes. *Pasteurella* infections may follow cat or dog bites but septicemia is uncommon and most patients have a primary source of infection, such as cellulitis. Leptospirosis usually occurs through contact with urine or tissues of infected animals; this patient lacked features of the acute phase of leptospirosis, such as conjunctival suffusion; moreover, purpura fulminans, as was seen in this case, would be quite unusual in leptospirosis.

**Case 2**

49 year old man with AIDS (CD4 count 43, HIV RNA 225,000) presented with 4 weeks of pain on defecation. His exam notable was for a tender, boggy prostate. A urinalysis showed 5-10 WBC/hpf. Urine culture was without growth. Pelvic CT showed a prostate abscess. The patient underwent aspiration of the abscess; a silver stain and a hematoxylin and eosin stain of the prostatic aspirate are shown. The most likely diagnosis is which of the following:

- **A. Blastomyces dermatitidis**
- **B. Pneumocystis jiroveci**
- **C. Histoplasma capsulatum**
- **D. Candida albicans**
- **E. Cryptococcus neoformans**

Answer: **E**

Discussion: This patient has a cryptococcal prostate abscess. The silver stain shows cryptococcal organisms; the hematoxylin and eosin stain shows yeast with a surrounding capsule, an appearance characteristic of Cryptococcus. Culture of prostate aspirate grew *Cryptococcus neoformans*.

*Cryptococcus neoformans* enters body via the respiratory route. The organism has a tropism for the central nervous system. Other focal sites of cryptococcal involvement may include skin, bone and prostate. Many cases of cryptococcal prostate infection are asymptomatic. The prostate may serve as a sanctuary from antifungal therapy; prolonged antifungal therapy may be required to clear the infection.

The other infections on the differential diagnosis are less likely. Although *Blastomyces* infection may involve the prostate, the morphology of the organism is different than seen in this case; the yeast forms of *Blastomyces* usually have a thick wall and reproduce by single buds which have a broad-based bud between parent and bud ("broad-based bud of Blasto") (see case later in the session for an example). The yeast form of *Histoplasma capsulatum* is smaller than Blastomyces and reproduces by multipolar budding, sometimes with narrow-based buds; the organism, despite its name, is not surrounded by a capsule. In tissue, both the yeast and hyphal forms of *Candida albicans* may be present. Although extra-pulmonary *Pneumocystis jiroveci* infection occurs in...
patients with advanced AIDS who are not taking prophylaxis or who are receiving inhaled pentamidine, involvement of the prostate is not typically seen.

**Case 3**
A 30 year old woman presented with a 4 week history of word-finding difficulties, expressive aphasia and right upper extremity weakness. She lived in New England. She denied recent travel or known insect bites. She stated that she is not sexually active. On exam, she was afebrile. She had oral thrush. She had difficulty naming objects and had right-sided weakness. Her WBC count was 2.2 (44% P, 45% L). Head MRI showed abnormal T2 signal involving white matter, most prominently in the left frontoparietal region. There was no enhancement, edema, or mass effect.

Her clinical syndrome is most likely to be caused by:

A. An arbovirus  
B. A polyomavirus  
C. A herpes virus  
D. A spirochete  
E. A dematiaceous fungus

Answer: B

Discussion: This patient has progressive multifocal leukoencephalopathy (PML), which is demyelinating disease of the central nervous system caused by reactivation of JC virus, a polyoma virus. Her HIV antibody test was positive. Her CD4 cell count was 20/mm3, the HIV-1 RNA level was 182,000 copies/mL. CSF: no pleocytosis. JC virus PCR was positive.

PML usually affects immunocompromised hosts, including those with hematologic malignancies, HIV, or patients who receive agents such as natalizumab or rituxamab. PML typically presents with rapidly progressive focal neurologic deficits, usually due to cerebral white matter disease. MRI generally shows multiple foci of increased T2 signal intensity involving white matter, without edema or enhancement—as was seen in this case. Treatment of PML consists of reversal of immunodeficiency; in HIV+ patients, this is achieved by administering antiretroviral therapy.

This patient is unlikely to have an arboviral infection, such as West Nile Virus encephalitis, because of the absence of features such as confusion, headache, meningeal signs or symptoms or paralysis. Herpes simplex virus infection typically involves the temporal lobe. Syphilitic infection can cause gumma, which was not seen in this case, or a stroke-like syndrome related to meningovascular disease. A dematiaceous fungus is unlikely because the patient does not have risk factors for such an infection (e.g. adjacent paranasal sinus infection, penetrating trauma) and lack of enhancement of the brain lesion on head imaging.

**Case 4**
A 30 year old man in the southern highlands of Peru was well until 3 months prior to evaluation when he developed a firm nodule on his hand. Several weeks later, the nodule ulcerated. He
subsequently developed a lesion on his forearm. The patient worked in construction and occasionally harvested crops. He owned cats, dogs and chickens. On exam, he was afebrile and appeared well. His skin lesions are shown. The CBC and CXR were normal. The most likely diagnosis is which of the following:

A. *Mycobacterium ulcerans* (Buruli ulcer)  
B. Cutaneous anthrax  
C. Sporotrichosis  
D. Tularemia  
E. Coccidioidomycosis

Answer: C

Discussion: This patient has sporotrichosis. Fungal culture of a skin biopsy grew filamentous colonies with a dark brown appearance. Microscopy demonstrated hyphal forms consistent with *Sporothrix schenckii*.

Cutaneous sporotrichosis presents with a papulonodular lesion, typically occurring on a distal extremity at the site of minor trauma. The initial lesion may be smooth or verrucous, and it often ulcerates. Secondary lesions may develop proximally along lymphatic channels, in a so-called “sporotrichoid spread”. The lesions are typically painless. Therapy is usually with itraconazole.

Other infections that can present with a “sporotrichoid” pattern of lesions include:

1. *Nocardia*: found in soil, organic matter, water; may present after direct inoculation, e.g. gardening, minor trauma  
2. *Sporothrix schenckii*: found in similar geographic environs as Nocardia, and has a similar incubation period of up to 2 weeks.  
3. *Mycobacterium marinum*: usually follows exposure to the organism growing in a pool, ocean or aquarium.  
4. *Leishmaniasis*: inoculation by the bite of a sand fly; usually occurs in Central or South America  
5. *Francisella tularensis*: ulcer is often particularly painful and patients may have fever and systemic symptoms.

The other diagnoses in the differential are less likely. Buruli ulcer (caused by *Mycobacterium ulcerans*) usually starts with a painless, mobile skin nodule and an area of induration and may progress to massive ulcers with undermined borders. Cutaneous anthrax typically gives a shallow necrotic ulcer with extensive surrounding edema; this was not seen in this case. In tularemia, the ulcer is often particularly painful and patients may have fever and systemic symptoms; these features were not present in this patient. Coccidioidomycosis usually gives pulmonary disease and at times meningeal infection; a lymphocutaneous pattern of lesions is not typical for this infection.

Case 5
A 30 year old man presented with a rash after recently returning from a 4-week trip to India. Two days before presentation, he had developed vesicular skin lesions that were followed by malaise and fever. The rash had started on his head and spread to involve the trunk, extremities, and genitalia. He had a history of genital HSV. He denied sexual contact with anyone other than his wife, and he did not have any exposure to animals.

On exam, he appeared ill, but not toxic. The temperature was 101 degrees F. He had conjunctival injection. He had a vesicular rash with lesions on his face, back, and chest. The most likely diagnosis is which of the following:

A. VZV
B. Disseminated HSV
C. Monkeypox
D. Rickettsialpox
E. Acute HIV

Answer: A

Discussion: This patient has varicella infection (chickenpox). Most cases of varicella infection occur in childhood. However, 10% of those older than age 15 are susceptible. In tropical areas, up to 30% of individuals are susceptible at age 20 and 5-10% susceptible at age 30. For this reason, screening of immigrants who do not report a history of chickenpox may be cost-effective (Merrett, CID, 2007). The clinical presentation of varicella is with maculopapules, vesicles, pustules, scabs in various stages of evolution. Successive crops of lesions appear over 2-4 days and crusts completely fall off in 1-2 weeks. Complications of varicella—such as pneumonitis, hepatitis, encephalitis—are more frequent in adults.

Other diagnoses in the differential include monkeypox, rickettsialpox, disseminated HSV and acute HIV infection. Disseminated HSV usually occurs in immunocompromised patients. He had no known risk factors for HIV infection and other features, such as pharyngeal symptoms, were absent. He did not have known exposure to animals that carry monkeypox, such as prairie dogs; moreover, he did not have adenopathy, which is often seen in cases of monkeypox. Other features that distinguish chickenpox (varicella) from monkeypox and rickettsialpox are summarized in the tables below.

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Chickenpox</th>
<th>Smallpox</th>
<th>Monkeypox</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Superficial vesicular lesions in different stages of development</td>
<td>Lesions at same stage of development</td>
<td>Lesions at same stage of development</td>
</tr>
<tr>
<td>Adenopathy</td>
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<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Prodrome</td>
<td>None or mild</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Rickettsialpox</th>
<th>Chickenpox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eschar</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lesions in crops</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of lesions</td>
<td>Relatively sparse (20-40)</td>
<td>Many</td>
</tr>
</tbody>
</table>
Case 6
40 year old man with diabetes mellitus was well until 6 weeks before admission when he developed fever and malaise. Chest X-ray showed RLL infiltrate. He was treated with 2 wks of azithromycin. Initially felt better, but after stopping his antibiotics again felt poorly. On day of admission, he awoke to find vision in left eye was almost completely gone. He also complained of mild pain in the left eye. On exam, he was ill-appearing. T: 38.3°C. Left eye (shown): conjunctival injection, reduced vision (hand motion only). Decreased breath sounds over right base. Tachycardic, S1/S2/S3 audible with soft diastolic murmur at RUSB. Chest X ray showed a RLL infiltrate, right pleural effusion. The most likely diagnosis is which of the following:

A. Staphylococcal keratitis  
B. Herpes simplex keratitis  
C. Bacterial endogenous endophthalmitis  
D. Pulmonary tuberculous with chorioretinitis  
E. Cytomegalovirus retinitis

Answer: C

Discussion: This patient has bacterial endogenous endophthalmitis in the setting of endocarditis. Transesophageal echo revealed large aortic root abscess and fistulous tract to the right atrium. Blood cultures grew penicillin-sensitive *Streptococcus pneumoniae*.

Endogenous endophthalmitis results from hematogenous spread of bacterial or fungal infection to eye. Endogenous bacterial endophthalmitis is most commonly due to gram-positives (*S. aureus, Strep*), although gram-negative infection may occur. The clinical presentation generally consists of acute onset of systemic illness, decreased visual acuity, eye pain, and hypopyon (a layer of pus in inferior portion of anterior chamber of eye). Patients with endocarditis should be monitored for visual symptoms and promptly evaluated for endophthalmitis if those symptoms develop.

Staphylococcal and HSV keratitis are unlikely given the absence of corneal symptoms as well as the evidence for systemic infection in this case. Pulmonary TB with chorioretinitis and cytomegalovirus (CMV) retinitis would not explain his initial improvement with azithromycin or the presence of a diastolic heart murmur. Although CMV immune recovery uveitis has been reported to mimic endogenous endophthalmitis in an HIV+ patient who initiated antiretroviral therapy, this was not the case in this patient.

Case 7
A 50 year old woman was well until 7 days prior to admission when she noted a “bite” on her left thigh. The lesion enlarged over several days. Four days prior to admission, she developed fatigue, arthralgias, myalgias, fever, and headache. On the day of admission (in July), she developed a generalized rash on extremities, trunk, back. The patient lived in New England.
had seen a mouse in her basement. She had a dog. She denied sexual activity. On exam, she appeared well. Her temperature was 100.5 F. No adenopathy. Lesion present on her left thigh (shown). A papular erythematous rash was present on her extremities, back, chest. The infection was most likely transmitted by:

A. Another person  
B. An infected prairie dog  
C. An animal hide  
D. Mouse mite  
E. Deer tick

Answer: D

Discussion: This patient has rickettsialpox, caused by *Rickettsia akari*, which is transmitted by the mouse mite. Serologic testing at the CDC showed a titer of 1:256 against *Rickettsia rickettsiae* and other members of the spotted fever group of rickettsiae, including *Rickettsia akari*. The patient was treated with doxycycline, with rapid improvement in her fever and rash.

Rickettsialpox should be considered in patients with fever and rash. An outbreak of rickettsialpox occurred in New York City in the 1980s; there is a high seroprevalence (16%) of infection in injection drug users in Baltimore. After the bite of infected mite, *R. akari* proliferates locally resulting in papule, which ulcerates to form an eschar; approximately 3-7 days later, high fever, chills and headache ensue; 2-3 days after onset of fever, a generalized papulovesicular rash (not involving palms, soles) may develop. Diagnosis is generally made by serologic testing. Treatment is with doxycycline.

Other infections listed in the differential diagnosis include varicella (transmitted from another person), monkeypox (which has been associated with prairie dogs), cutaneous anthrax (which can be found in contaminated animal products, such as hides) and Lyme disease (a deer tick-borne infection). The presence of an eschar helps distinguish rickettsialpox (in which an eschar is present) from chickenpox (in which an eschar is not present). (See previous case for an example of chickenpox.) Other features that distinguish rickettsialpox from chickenpox are summarized in the table below:

<table>
<thead>
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<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lesions in crops</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of lesions</td>
<td>Relatively sparse (20-40)</td>
<td>Many</td>
</tr>
<tr>
<td>Mature lesion</td>
<td>Papulovesicle</td>
<td>Vesicle</td>
</tr>
</tbody>
</table>

Monkeypox is unlikely because she did not have known exposure to animals that carry monkeypox, such as prairie dogs, and she did not have adenopathy, which is often pronounced in cases of monkeypox. Cutaneous anthrax typically gives a shallow necrotic ulcer with extensive surrounding edema; this was not seen in this case. Deer ticks can transmit Lyme disease or Anaplasmosis. The rash of Lyme disease looks much different than the one this patient had; in

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disseminated Lyme, there may be multiple annular skin lesions. Rash is present in <10% of cases of anaplasmosis.

Case 8
A 50 year old woman with a history of psoriatic arthritis presented with 2 weeks of cough, dyspnea, fever, and malaise. She had been treated with prednisone and methotrexate for several years, and had started inflixamab about 10 months prior to this illness. On exam, she appeared fatigued and short of breath. RR 32. 02 sat 96-100% on 100% FiO2 supplemental O2. Lungs had coarse rales bilaterally with decreased breath sounds at each base. CXR showed bilateral pulmonary infiltrates. After not responding to levofloxacin, she underwent lung biopsy (the pathology is shown). The most likely diagnosis is which of the following:

A. PCP  
B. Coccidioidomycosis  
C. Cryptococcosis  
D. Histoplasmosis  
E. Blastomycosis

Answer: D

Discussion: The patient has disseminated histoplasmosis in the setting of TNF inhibitor (infliximab) use. Her blood isolator and BAL cultures grew *Histoplasma capsulatum*. She was treated with amphotericin B, and gradually improved. She was discharged on a prolonged course of oral itraconazole.

Histoplasmosis, the most prevalent endemic mycosis in the U.S., has been reported in patients treated with TNF blockers. The morphology of the organism in the pathologic specimen is one of the keys to distinguishing between the potential diagnoses. The aspirate shows the typical narrow-based budding morphology of *Histoplasma*. By contrast, *Blastomyces* typically has broad-based budding and is larger than *Histoplasma*. (Another case in this presentation shows an example of *Blastomyces*). *Coccidioides* usually appears as a large spherule (another case in this presentation shows an example of *Coccidioides*). *Cryptococcus* has a surrounding capsule (see previous case in the slide set for an example). Although *Pneumocystis jiroveci* pneumonia has been reported in the setting of TNF antagonist use, the histologic appearance of the organism’s trophozoites and cysts are distinct from that of the morphology of *Histoplasma*.

An increased risk of serious infection has been observed among patients treated with TNF inhibitors. These infections include:
- Mycobacterial: TB, non-tuberculous mycobacteria
- Bacterial: listeriosis, nocardiosis
- Viral: HBV reactivation; possibly zoster (with TNF mAb)
- Fungal infections: PCP, histoplasma, coccidioides, cryptococcus, aspergillus, candida

The rate of granulomatous infection appears to be higher with infliximab than with etanercept (Wallis CID (2004) 38:1261), often occurring within 3 months in patient receiving infliximab.
Patients should be screened for latent TB before initiating TNF antagonist. If the tuberculin skin test (TST) or interferon-gamma release assay (IGRA) is positive, or if there is evidence of remote TB on CXR, treat with INH for at least 1-2 months before starting TNF antagonist and complete 9 months of INH. Precautions to prevent food-borne infections, such as listeria, should be taken, including avoiding unpasteurized milk products, soft cheeses, raw meat, fish, poultry, hot dogs, deli meats, etc. PCP prophylaxis should be considered in patients who are receiving TNF antagonists, especially if steroids are also being given.

Case 9
A HIV+ pregnant F in her 40s presented with five days of tinnitus, left ear fullness and decreased hearing. She also noted a burning sensation on her left cheek and ear. On exam, vesicles were seen in the external auditory canal (shown) and there was fluid noted behind the tympanic membrane. Hearing was decreased in left ear. Tender adenopathy was present in the left cervical and submandibular region. Studies showed CD4 cell count 480, HIV RNA undetectable (the patient was receiving therapy). Audiogram: conductive and high frequency sensorineural hearing loss on the left. Wound culture: coagulase-negative Staph. The most likely diagnosis is which of the following:

A. Staphylococcal cellulitis  
B. Pseudomonas malignant otitis externa  
C. Varicella zoster virus  
D. Contact dermatitis  
E. Syphilis

Answer: C

Discussion: This patient has Ramsay Hunt Syndrome (Herpes zoster oticus). This syndrome is due to reactivation of VZV infection in the geniculate ganglion of the CN VII (facial nerve). The classic triad consists of vesicles in the external auditory canal and auricle; ear pain; facial nerve palsy (may be severe). Herpes zoster oticus may also affect taste (branch of the facial nerve to anterior tongue), hearing and vestibular function (CN VIII).

The appearance of grouped vesicles is typical for herpes zoster and is not generally seen in the other diagnoses listed in the differential diagnosis (staphylococcal cellulitis, contact dermatitis, syphilis). Pseudomonas malignant otitis externa was first described in elderly patients with diabetes mellitus, but may occur in patients with AIDS; however, this patient has a normal CD4 cell count.

Case 10
A 40 year-old woman from China developed fever, epigastric pain, and nausea. One week later, she was brought to the emergency department because of confusion and fever. On examination, her temperature was 101°F. She had right upper quadrant abdominal tenderness. An abdominal
CT scan showed a 10 cm hypoattenuated liver lesion. An aspirate was performed; the culture showed mucoid colonies with a positive string test. The most likely organism is:

A. Entamoeba histolytica  
B. E. coli  
C. Streptococcus milleri  
D. Actinomyces  
E. Klebsiella pneumoniae

Answer: E

Discussion: A hypermucoid strain of Klebsiella has been associated with a distinctive clinical syndrome in Southeast Asia that includes primary liver abscess, bacteremia, and metastatic infection. Risk factors for this infection include diabetes and Asian ancestry. The Klebsiella colonies exhibit extreme “stickiness” on agar plates (“hypermucoviscosity phenotype”), and the string test is positive (i.e. a “string” of more than 5 millimeters is formed when one touches the colony). The other organisms on this list would not be expected to have a hypermucoid phenotype or a positive string test; Entamoeba histolytica would not grow and form colonies on a bacterial culture plate.

Case 11

A 60 year old man presented with a few hours of severe pain in the right upper extremity. The exam was normal and he was discharged. Over the next few hours, he developed progressive swelling of the right upper extremity. On exam, the right upper extremity was diffusely swollen with a deep-red discoloration; there were several bullae (shown). No pulses were palpable in the right upper extremity. WBC 8,900 (47% polys, 38% bands). An X-ray showed air in the soft tissues. The most likely diagnosis is which of the following:

A. Vibrio vulnificus  
B. Group A streptococcal necrotizing fasciitis  
C. Mixed aerobic/anaerobic necrotizing fasciitis  
D. Clostridial gas gangrene  
E. Bullous pemphigoid

Answer: D

Discussion: This patient has spontaneous gas gangrene. Surgical cultures grew Clostridium septicum. In retrospect, patient reported a several month history of bright red blood per rectum. Subsequent evaluation revealed an invasive colonic carcinoma.

Gas Gangrene (Clostridial Myonecrosis) may present with acute onset of severe pain, sometimes without abnormal physical findings. The patient generally appears quite ill. There is subsequent rapid progression of skin discoloration, tense edema, crepitus and development of bullae containing thin, serosanguinous or hemorrhagic fluid. Gram stain of fluid or surgical specimen demonstrates large gram-positive or gram-variable rods.
Traumatic gas gangrene is generally due to *C. perfringens*, and sometimes other Clostridial species. Spontaneous (non-traumatic) gas gangrene is most commonly due to *C. septicum*. Predisposing factors for spontaneous gas gangrene include intestinal disease (tumor, ulceration, inflammation) or systemic factors (malignancy, cirrhosis, neutropenia, diabetes mellitus). *C. septicum* infection is associated with malignancy: In one series, 81% of patients had malignancy and in 37% the cancer was occult (Kornbluth et al. Medicine (1989) 68:30). The most common cancers associated with *C. septicum* are colorectal and hematologic malignancies.

*Vibrio vulnificus* can cause a rapidly progressive soft tissue infection but usually afflicts patients with liver disease, iron overload or an immunocompromising condition. Group Streptococcal necrotizing fasciitis would not result in air in the soft tissues. Mixed aerobic/anaerobic necrotizing fasciitis often occurs after trauma or surgery. Bullous pemphigoid would not present in such a fulminant manner nor would gas be present in the tissues.

**Case 12**

A 60 year old man with L4-L5 and L5-S1 diskectomy for disc herniation in the remote past and benign prostatic hypertrophy presented with a 6-month history of fever to 102-104°F, chills and headache. He subsequently developed lower back pain, which worsened until it awoke him from sleep. He also noted anorexia and 12 lb weight loss. Patient was from the Middle East, where he lived in an urban area. He had eaten cheeses while in Europe several months earlier. He denied animal exposure and known exposure to TB. On exam, he had point tenderness over the lumbar spine with associated paravertebral muscle spasm. The WBC was 5.1. The ESR was 80. Blood cultures were sterile. MRI: high signal intensity in the L5 vertebrae with extension into the L4-5 disk space and the lower half of L4. Signal changes in the soft tissues anterior to L4-5 and S1, which enhanced with gadolinium. Pathology showed epithelioid histiocytes, and intracellular organisms. The most likely diagnosis is which of the following:

A. Anaerobic bacterial vertebral osteomyelitis  
B. Tuberculous vertebral osteomyelitis (Pott’s)  
C. Staphylococcal vertebral osteomyelitis  
D. *Brucella* vertebral osteomyelitis  
E. Fungal vertebral osteomyelitis

Answer: D

Discussion: This patient has brucella spondylitis. A L4 laminectomy with decompression and aspiration of the epidural abscess produced free-flowing malodorous purulent material. Pathological exam showed focal epithelioid histiocytes with intracellular coccobacilli. Operative culture grew small gram-negative coccobacilli, identified as *Brucella melitensis* biovar 3 by the CDC. The *Brucella* standard agglutination test was positive with a titer of 1:320. Testing for *Brucella* antibodies was also positive (IgM 1:320, IgG 1:640).

Brucella spondylitis is prevalent in the Mediterranean, Arabian peninsula, South Asia, Central and South America. Although a systemic infection, localized osteoarticular complications may occur. Lumbosacral spondylitis and sacroiliitis are the most common sites of osteoarticular
disease. Although Staphylococcal infection, tuberculosis and, less commonly, fungal and anaerobic infections can cause vertebral osteomyelitis, he is from an endemic area (the Middle East) and has a typical presentation (involvement of the lumbosacral spine; presence of intracellular organisms) for *Brucella* vertebral osteomyelitis.

**Case 13**

A 30 year old woman presented with right temporal headache, eye pain, diplopia. She lived in New England in a wooded area. On exam, her temperature was 102°F. Her left eye had normal extraocular movement. On the right, there was periorbital edema, proptosis, chemosis, ptosis; the right eye had impaired medial adduction and no lateral, superior or inferior motion. She underwent a lumbar puncture; CSF glucose 69, protein 180, 3,000 WBC (82% P, 18% L).

The most likely diagnosis is:

A. Lyme disease  
B. Cavernous sinus thrombosis  
C. Whipple’s disease  
D. Cryptococcal meningitis  
E. Orbital cellulitis

Answer: B

Discussion: The patient underwent CT angiography of the head, which revealed thrombosis of both cavernous sinuses, both superior ophthalmic veins; and the right sigmoid sinus and internal jugular vein. Cultures of blood and CSF grew methicillin-sensitive *Staphylococcus aureus*. The patient treated with nafcillin; her symptoms and signs improved.

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, V1, V2; CN VI is located more medially, near the internal carotid. Cavernous sinus thrombosis presents with headache, eye swelling, proptosis, diplopia, ptosis; the findings may become bilateral as thrombosis spreads to the contralateral sinus.

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.

**Case 14**

60 year old woman with a history of diabetes mellitus presented with a month of anorexia and nausea followed by 1 week of fever and right upper quadrant abdominal pain. She had undergone an endoscopy with biopsy of a gastric ulcer 2 months before. On exam, she was febrile (101 F). She had RUQ abdominal tenderness. WBC count: 12,000. Alkaline phosphatase: 195. An abdominal CT scan showed hypoattenuated lesions in the liver. A gram stain of the aspirate is shown. The most likely diagnosis is:
A. *M. tuberculosis*
B. Nocardia
C. *Streptococcus milleri*
D. Actinomyces
E. Aspergillus

Answer: D

Discussion: This patient has hepatic actinomycosis. Direct fluorescent antibody stain and culture of the liver aspirate were positive for *Actinomyces israelii*.

Actinomyces most commonly involves the jaw, the lung and intra-abdominal sites. Hepatic actinomycosis represents about 5% of cases of actinomycosis and may result either from direct extension from contiguous focus or hematogenous spread. It is usually related to a breach in the gastrointestinal mucosa, although extension from pleuro-pulmonary infection is sometimes seen. Other companion organisms may be present.

The gram stain of the liver aspirate shows branching, filamentous gram positive rods, a characteristic appearance for Actinomyces. Although Nocardia can have a similar appearance on gram stain, it usually infects immunocompromised hosts; moreover, Nocardia is modified AFB positive whereas Actinomyces is not. The other organisms on the list (*M. tuberculosis, Aspergillus, Streptococcus milleri*) would not have the morphologic appearance of branching, filamentous gram positive rods on gram stain.

Case 15
A 25 year-old man presented with nine days of vomiting, diarrhea, fever, headaches. He lived on farm, and had contact with goats, chickens, guinea pigs, turkeys, cats, and dogs. On exam, he appeared acutely ill. T 104.4°F; the exam was otherwise normal. Laboratory studies were notable for an AST 111, ALT 79, and an alkaline phosphatase of 146. He underwent liver biopsy; pathology showed a granuloma consisting of a dense fibrin ring with a central lipid vacuole.

The most likely diagnosis is:

A. Coxiella
B. Cryptococcus
C. Histoplasma
D. Cyclospora
E. Bartonella

Answer: A

Discussion: The patient’s Coxiella serology was strongly positive. He was treated with doxycycline and rifampin, and his symptoms and liver function test abnormalities resolved.
Coxiella burnetii, the agent of Q fever, is contracted through exposure to infected ruminants (parturient goats, cattle, sheep). Transmission usually occurs by inhalation. Acute disease usually presents with high fever, pneumonia and/or hepatitis.

The “doughnut” granuloma seen this case is characteristic of Q fever, although it may also be seen in Hodgkin's disease, EBV and CMV infections, and drug hypersensitivity. The other organisms listed would not be expected to be associated with a “doughnut” granuloma.

**Case 16**
A 63 year old man with a history of myelodysplastic syndrome developed small pruritic pustules on his lower extremities, which progressed over several months to nodular, ulcerating lesions. He received two short courses of cephalexin with transient but non-sustained improvement. He lived in the U.S. and had not traveled overseas. On exam, he was afebrile. He had several nodular erythematous lesions with superficial ulcerations on the lower extremities (shown). Studies were notable for WBC count of 15,000 with 12% blasts. Skin biopsy showed a neutrophilic infiltrate with eosinophilic granules. The most likely diagnosis is which of the following:

A. Botryomycosis  
B. Sweet’s Syndrome  
C. Cutaneous Leishmaniasis  
D. Mycobacterium chelonae  
E. Blastomycosis

**Answer:** A

**Discussion:** The histopathologic appearance is characteristic of botryomycosis. Skin biopsy showed granules consisting of basophilic staining cocci surrounded by an eosinophilic coat (the Splendore Hoeppli phenomenon). The culture of the skin biopsy grew *Staphylococcus aureus*.

Botryomycosis is a bacterial disease that clinically and histologically mimics actinomycosis. It is characterized by the microscopic formation of eosinophilic granules surrounding densely packed microorganisms in a suppurative focus (Splendore Hoepli phenomenon). There are two categories of botryomycosis: cutaneous and visceral. Cutaneous disease consists of scattered papular and nodular lesions that develop subacutely. This is usually caused by *S. aureus*. A prolonged antibiotic course is often necessary.

Sweet’s syndrome, a neutrophilic dermatosis, often presents with fever and tender papules which can progress to form plaques. Cutaneous leishmaniasis may present with an ulcerative lesion or nodular lymphangitis; this patient had not traveled to an endemic area. *Mycobacterium chelonae* and Blastomycosis would be expected to be associated with granulomatous inflammation.

**Case 17**
A 72 yo M with bioprosthetic aortic valve presents to the hospital with fever, dyspnea, anorexia. He lives in Boston, and has not traveled outside of the city. On exam, his temperature is 101°F. He has a hyperpigmented macular lesion on his thumb, which is not tender.
The most likely diagnosis is:
A. Herpetic whitlow
B. Herpes zoster
C. Tache noir (Rickettsial infection)
D. Fusariosis
E. Endocarditis

Answer: E

Discussion: The patient’s blood cultures grew *Staphylococcus aureus*. Echocardiogram revealed a vegetation on the prosthetic aortic valve. The patient has a Janeway lesion in the setting of endocarditis. Janeway lesions, which can be seen in patients with endocarditis, are non-tender, macular, erythematous lesions usually involving the palms and soles.

There are no vesicles to suggest herpes or zoster infection. The patient has not been in a wooded area, so is not at particular risk for rickettsial infection. He has not been neutropenic, so fusariosis is not likely.

Case 18
A 40 year-old man with AML who was undergoing salvage chemotherapy with high-dose Ara-C developed scattered pruritic erythematous papules across his trunk, axillae and upper extremities in the setting of profound neutropenia. He was originally from Peru. Family members, including 2 young children, had visited recently. His skin lesion is most likely caused by:

A. Leukemia
B. Non-tuberculous mycobacterium
C. Drug reaction
D. Filamentous fungus
E. An ectoparasite

Answer: E

Discussion: The patient had scabies, an ectoparasite. Skin biopsy revealed a scabies mite within a parakeratotic scale. The patient was treated with 5% permethrin cream, with reapplication 1 week later. On further evaluation, his young children who had recently visited were also found to have scabies infestation. The other entities on the differential diagnosis might present with papules but the biopsy clearly shows the scabies mite.

Case 19
A 35 year old man of Ethiopian descent cut his left thumb with a knife while slaughtering a lamb as part of Easter festivities. He washed the wound with water and applied lemon juice and alcohol. One week later, he developed swelling and tenderness and a fluctuant lesion at the site. Two weeks after the injury, he underwent incision and drainage; cultures grew *S. aureus* (oxacillin sensitive). Treated with cephalexin but the lesion did not improve. On exam, he was
afebrile. He had a 2 x 2 x 2 cm firm lesion on his thumb (shown), without discoloration, purulent discharge, fluctuance, or bleeding. The most likely diagnosis is which of the following:

A. Botryomycosis due to \textit{S. aureus}
B. Nocardia
C. Brucella
D. Orf
E. Salmonella

Answer: D

Discussion: The patient’s lesion was removed surgically. Pathology showed hyperkeratosis, epidermal necrosis, dermal infiltrate of mixed inflammatory cells; the surface keratinocytes had eosinophilic inclusions. PCR testing at CDC was positive for orf virus DNA.

Ecythma contagiousum (orf) is a zoonotic infection caused by a dermatropic parapox virus of goats and sheep. It is transmitted by contact with an infected animal or fomites. Cases have been reported in animal handlers and children after visiting petting zoos or livestock fairs. Clusters have also been reported after Eid and other festivities involving lamb sacrifice, such as Passover and Easter. Following a 3-7 d incubation period, patients may develop a macule or papule which then progresses to form a nodule with red center, white halo and peripheral erythema. The lesion may then ulcerate and form a regenerative papilloma. Most infections resolve in 4-8 weeks. Human-to-human transmission has not been reported. Protective immunity is incomplete; persons can be infected multiple times. For more information, see MMWR (April 13, 2012) which highlighted 4 cases of orf associated with household meat processing or animal slaughter.

Case 20. Bonus Question

50 year old man was admitted with nephrolithiasis and \textit{E. coli} urosepsis. His course was complicated by acute respiratory distress syndrome, requiring prolonged ventilatory support and a tracheostomy. During the hospitalization, he developed a nosocomial pneumonia due to MRSA, treated with vancomycin. One week later, he developed a new rash and fever. On exam, he had erythematous areas over the trunk and thighs as well as bullae, which expressed yellow, serous, nonpurulent fluid when opened. The most likely diagnosis is which of the following:

A. Dermatitis herpetiformis
B. Bullous pemphigoid
C. Linear IgA bullous disease
D. Herpes zoster
E. Staph scalded skin syndrome

Answer: C
Discussion: Linear IgA bullous disease (LABD) is a rare autoimmune subepidermal blistering disorder which is usually idiopathic. The syndrome is characterized by a vesiculobullous eruption of the skin and mucous membrane. On pathology, there is linear IgA deposition along the basement membrane zone, as was seen in this case. Drug-induced LABD is most often due to iv vancomycin use. It generally resolves with discontinuation of vancomycin, but may recur with rechallenge.

The other entities in the differential diagnosis are less likely. Herpes zoster presents with grouped vesicles which are very different in appearance than the large bullae seen here. Dermatitis herpetiformis is usually extremely pruritic and is characterized by grouped exoriations, erythematous plaques and papules with vesicles. Bullous pemphigoid may be precipitated by drugs but the immunofluorescent staining is different than that of LABD. Staphylococcal scalded skin syndrome (SSSS) is a toxin-mediated disease, usually in children, in which the skin easily detaches by rubbing (Nikolsky’s sign); in this condition, the toxin acts on the stratum granulosum of the epidermis.