Question #1

A 34-year-old woman in Columbus, Ohio was admitted to the hospital because of high fever, prostration, and extreme malaise of increasing severity over the past week.

Her past history was notable for Crohn’s disease being treated with adalimumab (Humira) for the past two months. Prior prednisone therapy had been discontinued.

She was born in Nicaragua but had lived in the United States with her husband and children for the past five years, working in a daycare center.

On examination, she was flushed and dyspneic, with pulse oximetry at 92% saturation. Chest x-ray showed a faint diffuse infiltrate.

Admission studies found her long standing anemia has worsened, with a hematocrit of 25%, platelet count 30,000, WBC 2,500 with a normal differential, alkaline phosphatase 250, ALT 120, AST 89 and creatinine 2.0.

She was transferred to intensive care and given intravenous cefipime and levofloxacin plus oral doxycycline. Admission and subsequent daily blood cultures remained negative. At the end of the first week, micafungin was begun because yeast cells were seen in her peripheral blood smear.

The most likely source of her infection was which of the following:

A. A human in Nicaragua
B. A human in her daycare center
C. Intravenous drug use
D. Pigeon droppings
E. Soil

Correct Answer: E

Rationale:

Patients receiving TNF-alpha inhibitors are at increased risk of disseminated, severe intracellular infections, including tuberculosis and histoplasmosis.

Although the clinical picture is compatible with either infection, yeasts in the peripheral blood smear provide strong evidence for acute disseminated histoplasmosis.

Candidemia rarely causes visible yeast on smear, would have grown from routine blood cultures and would not explain her admission findings. An echinocandin such as micafungin, is not effective and immediate institution of amphotericin B is indicated.

Azotemia, probably from her histoplasmosis, would suggest use of liposomal amphotericin B (Ambisome) would be better tolerated than conventional amphotericin B.
Question #2

A 21-year-old college student was admitted to the hospital in July with a fever of 40°C, dry cough, dyspnea and prostration of increasing severity over the past 24 hours.

He had been previously healthy and was spending his summer on Martha’s Vineyard as a groundskeeper for a golf course. He was living in a beach house with some college friends, with no pets in the house.

He did not use alcohol or tobacco and had no history of recent travel.

On admission he had crackles over both lung fields but no other abnormalities on physical examination.

Bilateral pneumonia was present on chest xray. WBC was 4,100 with a normal differential. Hemoglobin was 15 and platelets 150,000. His AST and ALT were 2 x normal.

He said his coworker at the golf course had been admitted with a similar illness the prior day to another hospital.

Among the possible inhalation exposures that must be considered in the management of this patient, which of these is the most likely?
   A. Ticks or small rodents ground up by the lawn mower
   B. Cleaning out rodent nests from under the tool shed
   C. Scraping pigeon droppings off the patio
   D. Scrubbing the shower floor at the swimming pool
   E. Spreading compost on the flowers

Correct answer: A

Rationale:

The geography should suggest Tularemia as more likely than some of the other options, especially hantavirus pulmonary syndrome (rodent nests) that would be more likely in the Southwest. Tularemia is usually acquired from an infected small animal through cutaneous inoculation of the animal’s blood into a small cut or from a tick bite. However, machines that cut grass and brush can aerosol tissue or ticks from infected animals and cause pulmonary tularemia. When there is aerosol exposure, pulmonary infiltrates are bilateral, the wbc is often normal, and the transaminases are often mildly elevated.

Diagnosis is usually made retrospectively by serology but effective treatment requires an aminoglycoside or perhaps a fluoroquinolone.

- **Rodent nests** can be a source of hantavirus pulmonary syndrome through the urine and feces. In this case there is no hemoconcentration, or biphasic illness, or geographic clue to make this the most likely diagnosis
- **Pigeon droppings** can be found to contain Cryptococcosis but rarely appear to trace to cases of cryptococcosis.
• **Aerosolized water** can be a source of legionnaires' disease. Outbreaks of legionnaire’s disease are uncommon: since this is an outbreak, and there are no specific clues, Legionnaire’s is a less likely cause than tularemia.

• **Compost** can lead to aspergillosis in patients with impaired immunity. Aspergillus does not cause invasive pulmonary disease in immunocompetent patients.

**Question #3**

A 61-year-old man has had fever for 10 days with temperatures as high as 103°F. He also notes intermittent headaches, muscle aches, and anorexia.

Eight weeks before his febrile illness began he had hunted feral swine in Florida with two friends. They butchered six feral swine, and, while dressing one of animals, the patient cut his hand with a knife. The meat was brought home and stored in a freezer.

Two weeks before his illness began, the patient boiled and ate some of the swine meat. His hunting companions are well.

His examination is unremarkable except for a temperature of 102.2°F and a pulse of 110.

A complete blood count (including differential), routine blood chemistries and a chest x-ray are all normal.

Which one of the following is the most likely diagnosis?

- A. Brucellosis
- B. Tularemia
- C. Leptospirosis
- D. Trichinellosis
- E. Q Fever

**Correct Answer: A**

**Rationale:**

Historically **brucellosis** due to B. suis occurred in swine slaughterhouse workers. In 1972, the Department of Agriculture Brucellosis Eradication Program was expanded to cover swine herds resulting in elimination of brucellosis in commercial swine herds and a decrease in human B. suis infection. In the United States now, swine-associated brucellosis in humans occurs predominantly in those who hunt feral swine. There also is some Brucella in bison in the western United States.

Brucellosis often results in a non-specific febrile illness as in this patient, following an incubation period of 2-10 weeks (may be months).

So-called **typhoidal tularemia** may produce a prolonged, non-specific febrile illness, but it is associated with hunting and skinning rabbits or rodents, not swine; and the incubation period here is too long.

**Leptospirosis** may produce a non-specific febrile illness in hunters who encounter animal urine from a variety of animals, but swine would be an unlikely source of infection, and the eight week interval from hunting to illness far exceeds the incubation period of leptospirosis.
Feral swine could be a source of trichinellosis following ingestion of contaminated meat, but boiling the meat should have killed the parasites, and, after ten days of illness, this patient should have obvious eosinophilia.

The incubation period is too long for Q fever; the normal chest x-ray also makes this less likely.

**Question #4**

A 32-year-old female was admitted for fever and neutropenia following remission induction therapy of acute myelogenous leukemia. She had been receiving levofloxacin prophylaxis and G-CSF.

On admission, she appeared ill and had a temperature of 39°C. Multiple 5-10mm painful, tender red papules and plaques were present on her arms and trunk. Oral mucosa and conjunctivae were normal.

A Hickman catheter site in her right infraclavicular region appeared normal. Her routine blood studies were notable for a rise in her absolute neutrophil count ANC of 500/cu mm, a rise since her last clinic visit a week prior. Ceftazidime was begun. A chest CT was normal.

On the third hospital day her fever and rash were unchanged but she was clinically stable. Blood cultures were negative. ANC was now 750/cu mm.

A skin biopsy was reported as showing numerous neutrophils without leukocytoclastic vasculitis or organisms on fungal stains or on routine culture at 48 hours.

The most appropriate treatment is which of the following:

A. Add micafungin
B. Add prednisone
C. Stop G-CSF
D. Change ceftazidime to meropenem
E. Add amphotericin B

**Correct answer: B**

**Rationale:**

The patient’s painful skin lesions, leukocytic infiltrate and fever are most compatible with Sweet’s syndrome, also called neutrophilic dermatosis, often seen in patients with AML, myelodysplastic syndrome or other malignancies.

Appearance as the neutrophils return during G-CSF treatment is a common timing. Were the lesions fungal in origin, the fungal stains of the biopsy would have shown the fungi and culture of the biopsy would have been positive for Candida and or occasionally moulds (e.g. fusarium) at 48 hours. A short, tapering course of prednisone leads to rapid improvement in Sweet’s syndrome, though relapse can occur.

G-CSF does not cause skin lesions, though some have postulated a role in increasing the incidence of Sweet’s syndrome.
**Question #5**

A 19-year-old woman is seen for fever and swollen lymph nodes in the neck. She was completely well until 11 days earlier when she had the onset of fever and vague neck discomfort. She had no sore throat and no dental or scalp problems.

Her physician found prominent anterior and posterior adenopathy on the left side of the neck. Her temperature was 100.4°F, and the rest of her examination was normal. Her WBC count was 4800 with 12% atypical lymphocytes; the doctor suspected mononucleosis.

A Monospot test was negative; IgG antibodies to Epstein-Barr virus (EBV) viral capsid antigen and Epstein-Barr nuclear antigen (EBNA) were present.

The patient was very anxious because her cousin had been diagnosed with a lymphoma two years earlier, so the physician obtained an excisional biopsy of one of the posterior cervical nodes.

Pathology of the node showed preserved architecture and a necrotizing lymphadenitis with histiocytic infiltrate and phagocytosed debris.

Which one of the following is the most likely diagnosis?

A. Tuberculosis  
B. EBV Mononucleosis  
C. Histiocytic Lymphoma  
D. Systemic Lupus Erythematosus  
E. Kikuchi Disease

**Correct answer: E**

**Rationale:**
The pathology here is characteristic of Kikuchi Disease, a benign condition of unknown cause. It is most often seen in young adults (mostly women) and characterized by fever and cervical adenopathy (especially posterior; usually unilateral). Diagnosis is made by seeing the lymph node histology showing preserved architecture with necrotizing histiocytic infiltrate (not neutrophils) and fragments of nuclear debris. Although the other diagnoses here can manifest with fever and lymphadenopathy; the pathology is only consistent with Kikuchi. The presence of IgG antibody to VCA and anti-EBNA antibody indicates past EBV infection.
Question #6

This 34 year old female with AIDS (CD4 = 20 cells) was brought to a Washington DC emergency room by her husband because of fever and somnolence. There is no history of travel outside the locality. Her only medications had been naturopathic.

The figure shows her contrast-enhanced CT.

Which of the following would most likely be effective?

A. Azithromycin  
B. Metronidazole  
C. Quinine + clindamycin  
D. Pyrimethamine + clindamycin  
E. Primaquine + clindamycin

Correct answer: D

Rationale:
The lesions in this HIV-infected patient would be consistent with toxoplasmosis or lymphoma.

Only one of the drug choices would treat toxoplasmosis and, of course, none would treat lymphoma.

The usual treatment of cerebral toxoplasmosis would be sulfadiazine plus pyrimethamine but pyrimethamine plus clindamycin gave comparable therapeutic results in one randomized trial.

Trimethoprim-sulfamethoxazole has been reported useful in a few case reports. is also acceptable and has the advantage of being the only regimen in which both drugs can be given IV.
Question #7

You are called at 9 pm to the surgical floor to see a 29-year-old male with a fever of 40°C who returned 7 hours previously from the operating room where his dislocated shoulder was repaired. He is a healthy male with no underlying disease and was injured playing soccer. The patient is somnolent, flushed, diaphoretic, and rigid. His blood pressure was elevated from 150/80 to 180/100 twenty minutes ago. Now the BP is 110/60. He is given one ampule of Narcan, but does not respond.

Which of the following is true?
   A. This syndrome should be treated with IVIG.
   B. This syndrome should be treated with high-dose corticosteroids.
   C. Dantrolene should be part of acute therapy.
   D. Subcutaneous or IV epinephrine should be given immediately.
   E. None of the above.

Correct answer: C

Rationale:
This could be either an example of the neuroleptic malignant syndrome (NMS) or malignant hyperthermia both of which should be treated with dantrolene. Neuroleptic malignant syndrome is due to an idiosyncratic reaction to neuroleptics and certain antiepileptics and is characterized by four characteristics: mental status change, rigidity, fever, and dysautonomia. Extremities are described as "lead pipes." Labile hypertension, arrhythmias, and elevated liver function tests and CPK, plus hypoxia are characteristic. Look for this also in association with withdrawal or changes in anti Parkinson medications where an NMS like syndrome occurs.

Look for these drugs:

Neuroleptic Agents
- Aripiprazole
- Chlorpromazine
- Clozapine
- Fluphenazine
- Haloperidol
- Olanzapine
- Perphenazine
- Quetiapine
- Risperidone
- Thioridazine
- Ziprasidone

Antiemetic agents
- Domperidone
- Droperidol
- Metoclopramide
- Prochlorperazine
- Promethazine
Certain overdoses can overlap with NMS especially cocaine and ecstasy.

Treatment should include treating the muscle rigidity (benzodiazepines), hyperthermia (cooling blankets), arrhythmias, and hypertension. Drug therapy is dantrolene or bromocriptine, non-depolarizing paralytic agents and dopamine, and muscle relaxants. This syndrome is distinct from malignant hyperthermia syndrome, which usually occurs in the operating room and is related to halothane or a depolarizing paralytic agent. The malignant hyperthermia syndrome occasionally occurs as late as 24 hours after the offending drug, so this patient with high fever and muscular rigidity could well have malignant hyperthermia.

This syndrome can be confused with Serotonin syndromes that are associated with serotonin uptake inhibitors. Patients often have nausea and vomiting as a prodrome and then are agitated and hyperreflexive with myoclonus and ataxia. The drugs associated with serotonin syndrome include:

- Cocaine
- Droperidol
- Ondansetron
- SSRIs (Citalopram, Paroxetine)
- Fentanyl

In a question or a patient if there is rigidity, think of NMS; if there is a prodrome of nausea and vomiting followed by hyperreflexia and tremor or clonus, think of serotonin syndrome. For the boards you should look for malignant hyperthermia, malignant neuroleptic syndrome, and serotonin syndrome (see table below).

<table>
<thead>
<tr>
<th>Onset</th>
<th>SEROTONIN SYNDROME</th>
<th>NEUROLEPTIC</th>
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<tr>
<td>Onset</td>
<td>&lt;1 day</td>
<td>1st dose to many weeks</td>
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<tr>
<td>Neuromuscular Exam</td>
<td>Hyperreactivity (tremor, clonus)</td>
<td>Muscular rigidity, bradyreflexia</td>
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<tr>
<td>Causative Drugs</td>
<td>Serotonin agonists</td>
<td>Antipsychotics</td>
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<tr>
<td>Treatment</td>
<td>Stop offending agent&lt;br&gt;<strong>Benzodiazepine, Cyproheptadine</strong></td>
<td>Stop offending agent&lt;br&gt;<strong>Bromocriptine, Dantrolene, Amantadine</strong></td>
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<tr>
<td>Resolution</td>
<td>&lt; 24 hours</td>
<td>Days to weeks</td>
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Question #8

A prospective renal transplant recipient and related donor, both from rural Egypt, await renal transplantation in New York City. Both were previously diagnosed with schistosomiasis, S. mansoni and S. haematobium and both were treated for schistosomiasis on multiple occasions in the past. The transplant surgeon asks your advice about how he should proceed.

Which one of the following is correct?

A. Serology would be helpful in ruling out active infection.
B. Praziquantel can kill the schistome worms but not the eggs.
C. Absence of eggs by multiple O&P examinations of stool and urine effectively rules out active Schistosomiasis.
D. If any worms are alive at transplantation in the recipient, they can multiply to cause a massive infection.
E. Schistosoma haematobium is likely to be transmitted by the donor kidney.

Correct answer: B

Rationale:
Schistosomiasis has a complicated life cycle and cannot multiply in the definitive host, humans. Immunosuppression does not result in worm multiplication and in fact is more likely to negatively affect them. Likewise, schistosome ova do not multiply in the body. Active infections are characterized by the excretion of live eggs. However, absence of eggs in microscopy examinations of stool and urine does not rule out active infection as patients with low worm burdens frequently do not excrete enough eggs to be routinely detected by standard O&P exams. Dead eggs in S. haematobium and to some extent in S. mansoni are retained in the tissues and shed in the feces or urine but do not constitute an active infection and require no treatment. Available serologic tests remain positive in inactive chronic infections.

There is no reason not to treat active infections. Treatment is fast, safe and reasonably effective in killing the worms. Although the eggs are not killed, egg production stops with killing of the worms. The transplant has no bearing on treatment of the donor: his kidney will not transmit schistosomes to the recipient. He should be treated only to eradicate live worms in his body which might still be excreting eggs.
Question #9

You are consulted to see a patient who recently underwent resection of a solitary pulmonary nodule. The patient is a 58-year-old nurse who recently moved from North Carolina to Ohio and began a new job as a case manager in a hospital. She was completely without symptoms; her last chest x-ray was 18 years earlier and was normal. She eats sushi and, on weekends prior to her move, volunteered for many years at a dog shelter. Because of her age and a 42-year history of cigarette smoking she had resection of the nodule.

The reason for the infectious diseases consultation is that the pathology of the nodule revealed a worm with a muscularis layer surrounded by a granulomatous reaction.

The nodule was most likely due to which one of the following?

A. Echinococcus
B. Anisakis
C. Toxoplasma
D. Strongyloides
E. Dirofilaria

Correct answer: E

Rationale:
Dirofilaria, the dog heartworm, may present as a solitary nodule in humans. The larval forms of the worm which are transmitted to man from dogs by mosquito bites wind up in the right heart but, in humans, cannot develop into mature worms; the larvae die and are embolized to the lung, inducing a granulomatous reaction. Typically the diagnosis is made when a nodule is resected and the worm is seen.

- **Echinococcus** may cause asymptomatic lung infection but typically produces cystic disease.
- **Anisakis** is a roundworm that can cause human GI illness following ingestion of raw fish such as sushi, but would not cause a pulmonary nodule.
- Cysts and tachyzoites of **Toxoplasma** do not resemble worms and have no muscularis structures.
- **Strongyloides** larvae migrate through the lung and may cause a diffuse infiltrate in the hyperinfection syndrome but do not form solitary nodules in the lung.
Question #10

You are asked to see a 45-year-old male with abdominal pain, who underwent endoscopy where several inflammatory masses were seen in the proximal small bowel and resected.

On pathologic examination, round worms consistent with anisakiasis were seen. The patient travels extensively and enjoys eating raw fish in his travels to various countries including the Japan and China three weeks ago.

What therapy for anisikiasis is the best choice for patients with abdominal pain such as this patient?

A. Praziquantel
B. Ivermectin
C. Paromomycin
D. Prednisone
E. Endoscopic removal

Correct answer: E

Rationale:
Anisakiasis can be acquired from eating raw fish, is most often reported in Japan and thus is a plausible diagnosis in this case. The parasite infects fish: when the fish is eaten raw some patients develop an allergic response within hours or a few days when the parasite comes into contact with mucosa, or begins to burrow. Some patients cough up the parasite; others develop gastritis or enteritis.

No medical therapy is clearly effective, and worms should be removed if visualized. Stool exams are not useful for diagnosis.
Question #11

A 42-year-old MSM was recently diagnosed with HIV-infection. Upon initial work-up, he was found to have a CD4 count of 560 cells/mm3, viral load of 25,000 copies/mL. He also was found to have (+) HBsAg, HBV-DNA = 200,000 IU/mL, ALT = 95, AST = 86.

His liver biopsy shows significant fibrosis but he has no signs of cirrhosis or portal hypertension. He refuses antiretroviral therapy at this time.

You decide to treat his HBV.

Which of the following treatment will be most appropriate for this patient?

A. Tenofovir/emtricitabine
B. Lamivudine
C. Peginterferon alfa 2P
D. Entecavir
E. Entecavir and peginterferon alpha 1

Correct answer: C

Rationale:
Most patients with HBV and HIV co-infection should be treated with a fully suppressive HIV regimen that includes two drugs also active against HBV. Thus, most patients will receive a regimen that includes tenofovir plus 3TC or FTC in addition to a backbone antiretroviral agent.

This patient does not want HIV therapy, but presumably is persuaded that his liver fibrosis is a reason to start therapy for HBV. There is only one option in this case that will not lead to antiretroviral resistance, i.e. treat him with interferon alone.

While the treatment of HBV in patients with HIV can be complicated, one clear principle is to avoid anti HBV regimens that are likely to induce resistance to anti HIV drugs, specifically nucleosides. In this scenario, all answers except C involve mono or dual nucleoside therapy that might be effective treatment of HBV, but would quickly lead to HIV resistance unless other potent HIV drugs were added. Even entecavir can induce HIV resistance among other nucleosides regardless of what dose is used.

When entecavir was first marketed, it was claimed that it did not have activity against HIV, and thus would be safe to use in patients who only need HBV treatment. However, entecavir can produce I84V mutations when used alone.

Peginterferon does not have substantial direct HIV activity and its use will not lead to emergence of HIV mutations that confer cross resistance to antiretroviral drugs. This would be an alternative for individuals who only will accept treatment for HBV.
**Question #12**

A 46-year-old African American male previously in excellent health presented with one week of increasing anorexia, nausea, and dark urine.

He was working regularly as a computer programmer and has not sought medical care or had blood tests done for several years. He denied drug or alcohol abuse, or receiving blood products but he had multiple sexual partners. He had donated blood six months ago and was not informed of any issues when he was screened.

On examination:

- His vital signs were normal and he was in no acute distress.
- Liver and spleen could not be palpated through his obese abdomen. There was no tremor, ascites, edema, clubbing, or visible abdominal veins.
- WBC was 4,200 with a normal differential.
- Hemoglobin, platelet count, albumin, and prothrombin time were normal.
- ALT was 1,115; AST 846 and bilirubin 6.2.

He is again HIV negative, and his hepatitis serologies showed the following:

- Hepatitis B anticore IgG and IgM positive
- Hepatitis B surface antigen and e antigen positive, antibody to surface antigen and to e antigen negative
- Hepatitis B viral load 1,000,000 copies/mL
- Antibody to HIV, hepatitis A, C and D negative

Which of the following is the most appropriate treatment?

- A. Entecavir
- B. Lamivudine
- C. Adefovir plus lamivudine
- D. Alpha interferon 2b plus ribavirin
- E. Observation only

**Correct answer: E**

**Rationale:**
This patient has hepatitis B.

Acute hepatitis B clears in >95% of immunocompetent adults, and thus treatment is not indicated for acute disease. Considerations are different for infants and children, and for immunocompromised adults.

Distinction between acute hepatitis B and an acute exacerbation of chronic hepatitis B is difficult. He had donated blood six months ago, indicating that he was likely hepatitis core IgG antibody negative at that time. Also, his anticore IgM is still positive, consistent with acute hepatitis B. Viral load is not helpful in the distinction.
This patient most likely has acute hepatitis B, acquired sexually.

Most patients will resolve acute hepatitis B spontaneously, developing antibody to surface and to e antigen and lose surface antigen positivity. Thus there is no urgent reason to treat this patient.