



Editing file

Practice file



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Resources

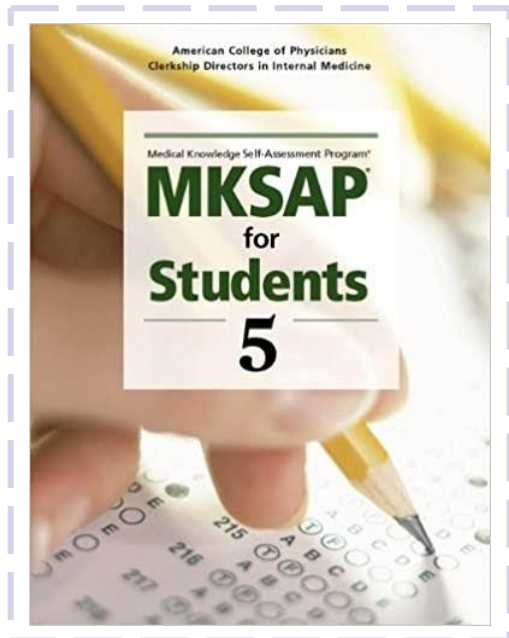
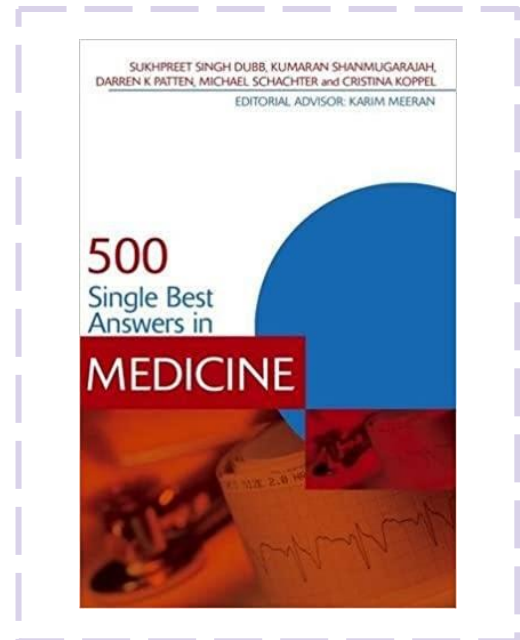
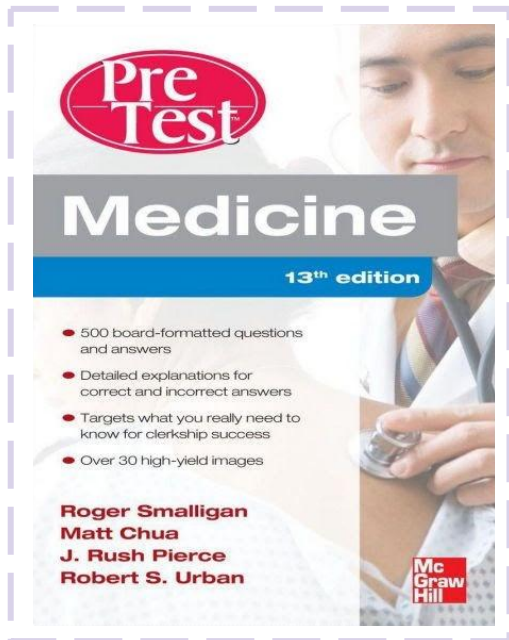


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AIDS/HIV

Q1 (Pretest): A 22-year-old male patient complains of fever and shortness of breath. There is no pleuritic chest pain or rigors and no sputum production. A chest x-ray shows diffuse perihilar infiltrates. The patient worsens while on azithromycin. A methenamine silver stain shows cyst like structures. Which of the following is correct?

- A. Definitive diagnosis can be made by serology.
- B. The organism will grow after 48 hours.
- C. History will likely provide important clues to the diagnosis.
- D. Cavitory disease is likely to develop.
- E. The infection is unlikely to recur.

Explanation: Patients with *Pneumocystis jirovecii* (formerly *carinii*) frequently present with shortness of breath and no sputum production. The interstitial pattern of infiltrates on chest x-ray distinguishes the pneumonia from most bacterial infections. Diagnosis is made by review of methenamine silver stain. Serology is not sensitive or specific enough for routine use. The organism does not grow on any media. Cavitation is quite unusual. The history is likely to suggest a risk factor for HIV disease. The disease commonly recurs in patients with CD4 counts below 200/ μ L unless prophylaxis (usually with trimethoprim-sulfamethoxazole) is employed.

Q2 (Pretest): A 27-year-old man has fever, macular rash, and lymphadenopathy. He had unprotected sex with a male partner 2 weeks before the onset of these symptoms and has just learned that the partner is infected with HIV. The patient's rapid HIV test is negative. What is the best test to evaluate this patient for HIV infection?

- A. HIV enzyme-linked immunoabsorbent assay (ELISA)
- B. PCR for HIV RNA
- C. Western blot testing
- D. Glycoprotein 120 using ELISA
- E. PCR for HIV DNA

Explanation: HIV infection is usually diagnosed by the detection of HIV-specific antibodies using rapid HIV test or a conventional enzyme-linked immunoabsorbent assay (ELISA), which are highly sensitive tests, and confirmed by Western blot or indirect immunofluorescence assay, which are highly specific tests. Antibodies appear in few weeks after infection, sometimes after the development of acute HIV infection (acute retroviral syndrome). Clinicians should maintain a high level of suspicion for acute HIV infection in all patients who have a compatible clinical syndrome and who report recent high-risk behavior. When acute retroviral syndrome is a possibility, a plasma RNA polymerase chain reaction (PCR) should be used in conjunction with an HIV antibody test to diagnose acute HIV infection. Although HIV DNA testing is available, it offers no added advantages over the more readily available and FDA-approved HIV RNA testing. The patient's HIV serology (antibody testing) is negative, so repeating the serology testing by ELISA or ordering Western blot is not indicated at this point. It is appropriate to repeat the serology testing in 4 to 6 weeks.

Q3 (MKSAP): A 38-year-old man is admitted to the hospital with a 1-week history of progressive dyspnea, cough, and low-grade fever. He has a history AIDS and has found it difficult to take all of his medications. His CD4 count measured 6 months ago was 80/ μ L. He has no allergies. On examination, he appears dyspneic. Temperature is 39.2°C (102.5°F), blood pressure is 110/70 mm Hg, pulse rate is 110/min, and respiration rate is 32/min. Oxygen saturation by pulse oximetry is 82% on ambient air. Cardiopulmonary examination is normal. Arterial blood gas results are: pH, 7.41; PO₂, 58 mm Hg (7.7 kPa); PCO₂, 32 mmHg (4.3 kPa); HCO₃⁻, 20 meq/L (22 mmol/L). Chest x-ray revealed bilateral interstitial infiltrates. A silver stain of induced sputum is positive for *Pneumocystis jirovecii*. Which of the following is the best initial treatment regimen for this patient?

- A- Dapsone
- B- Dapsone plus corticosteroids
- C- Trimethoprim-sulfamethoxazole
- D- Trimethoprim-sulfamethoxazole plus corticosteroids

Explanation: The best initial treatment regimen for this patient is trimethoprim-sulfamethoxazole plus corticosteroids. *Pneumocystis jirovecii* pneumonia remains the most common AIDS-defining illness and cause of death in patients with AIDS. The diagnosis should be considered in any patient with a CD4 cell count of less than 200/ μ L who presents with fever, dry cough, and dyspnea developing over several days or weeks. The chest radiograph typically shows bilateral interstitial infiltrates, but findings can vary from a normal film to consolidation or a pneumothorax. The diagnosis is established by silver stain examination of induced sputum or a bronchoscopic sample showing characteristic cysts. A 3-week course of trimethoprim-sulfamethoxazole is the standard treatment. Corticosteroids are required for patients with evidence of hypoxia (arterial PO₂ <70 mmHg [9.3 kPa] or an alveolar-arterial gradient >35 mm Hg [4.7 kPa]) and should be continued for the entire course of treatment. Dapsone can be an adjunctive treatment to trimethoprim in acute *Pneumocystis jirovecii* and can be used alone as a prophylactic agent for patients with a CD4 count less than 200/ μ L in patients who are intolerant of trimethoprim-sulfamethoxazole, but it is not recommended as single drug therapy for *Pneumocystis jirovecii* pneumonia.

AIDS/HIV

Q4 (MKSAP): A 28-year-old woman is evaluated following the diagnosis of HIV infection discovered during a routine screening examination. On examination, the patient appears well. Temperature is 37.1°C (98.8°F), blood pressure is 105/70 mm Hg; pulse rate is 88/min, and respiration rate is 10/min. The remainder of her examination is normal. Her CD4 cell count is 77/uL and her HIV-1 RNA level is 200,000/mL. Her toxoplasma antibody is positive, and her tuberculin skin test is negative. All of her immunizations are up to date. The patient agrees to begin antiretroviral drug therapy.

Which of the following treatments is also indicated at this time?

- A- Trimethoprim-sulfamethoxazole
- B- Trimethoprim-sulfamethoxazole plus azithromycin
- C- Trimethoprim-sulfamethoxazole plus fluconazole
- D- Trimethoprim-sulfamethoxazole plus isoniazid
- E- Trimethoprim-sulfamethoxazole plus valganciclovir

Explanation: This patient should receive trimethoprim-sulfamethoxazole. Several drugs have been shown to provide effective prophylaxis against opportunistic infections in patients with HIV infection and to prolong life in some patients. The CD4 cell count is an indicator of immune competence. Recommendations regarding when to initiate prophylaxis are based on CD4 cell count levels. The threshold for Pneumocystis and toxoplasmosis prophylaxis is 200/uL and 100/uL, respectively. The patient's CD4 cell count is 77/uL, and she should receive prophylaxis for Pneumocystis and for toxoplasmosis if her antibody titer is positive (demonstrating previous infection but not immunity) Trimethoprim-sulfamethoxazole is the first-line agent for both.

Azithromycin is used for prophylaxis against Mycobacterium avium complex in patients with a CD4 cell count less than 50/L. This patient's CD4 cell count is not at this threshold and, therefore, prophylactic azithromycin therapy is not recommended. Fluconazole is not recommended for the primary prophylaxis of Candida infections despite its effectiveness in this role. The potential for drug resistance, numerous potential drug-drug interactions, the case and effectiveness of treating infection when it does occur, and lack of survival benefit argue against prophylactic use. Isoniazid would be indicated if the patient were found to have a positive tuberculin skin test greater than 5mm and a negative chest x-ray excluding active tuberculosis. There is no reason to provide prophylactic isoniazid therapy for patients who have not been exposed to Mycobacterium tuberculosis. Although valganciclovir is effective in preventing cytomegalovirus (CMV), infection, decisions regarding prophylaxis are complex. Valganciclovir is expensive, a theoretical concern about the development of drug resistance exists, it is toxic to the bone marrow, and treatment of early infection is very effective. Finally, no proven survival benefit is associated with CMV prophylaxis.

Q5 (MKSAP): A 28-year-old man is evaluated at a community health center for a 10-day history of sore throat, headache, fever, anorexia, and muscle aches. Two days ago, a rash developed on his trunk and abdomen. He had been previously healthy and has not had any contact with ill persons. He has had multiple male and female sexual partners and infrequently uses condoms. He has been tested for HIV infection several times, most recently 8 months ago; all results were negative. On physical examination, temperature is 38.6°C (101.4°F). There are several small ulcers on the tongue and buccal mucosa and cervical and supraclavicular lymphadenopathy. A faint maculopapular rash is present on the trunk and abdomen. A rapid plasma reagin test is ordered.

Which of the following diagnostic studies should also be done at this time?

- A- CD4 cell count measurement
- B- Epstein-Barr virus IgG measurement
- C- HIV RNA viral load and HIV antibody measurements
- D- Skin biopsy

Explanation: The most appropriate additional test is an HIV RNA viral load and HIV antibody measurement. This patient's prolonged febrile syndrome in the setting of HIV risk factors should raise concerns for recent infection with HIV. Detection of HIV RNA is the most sensitive test for detecting HIV infection during the acute symptomatic phase. Tests for HIV-specific antigens, such as p24, can also detect the presence of virus in the acute setting. Antibodies to HIV do not commonly occur until about 6 weeks after infection and may therefore be negative during the acute symptomatic phase. Patients diagnosed with acute HIV infection on the basis of an HIV viral load measurement should have confirmatory serologic antibody testing performed at a subsequent point in time.

In addition to the acute retroviral syndrome, this patient must be evaluated for secondary syphilis using the rapid plasma reagin test. Secondary syphilis and acute retroviral syndrome should always be considered in sexually active patients with rash, fever, and generalized lymphadenopathy. Other causes of a mononucleosis syndrome (for example, Epstein-Barr virus and cytomegalovirus infections) should also be considered if these tests are inconclusive. The CD4 cell count may be profoundly depressed in patients with acute HIV infection, but the CD4 cell count can be both insensitive in the diagnosis of acute infection and depressed by various other, non-HIV-1 infectious agents.

Although acute HIV infection can mimic the signs and symptoms of mononucleosis, testing for Epstein-Barr virus infection is a less immediate concern in this patient who has multiple risk factors for HIV infection. Furthermore, acute infection would be detected with an elevated IgM antibody titer, not IgG.

The histopathology of the rash in acute HIV infection is nonspecific and is not useful in diagnosis; therefore, a skin biopsy is not indicated.

AIDS/HIV

Q6 (MKSAP): A 38-year-old man is evaluated for a 3-week history of progressive right-sided weakness of the upper and lower extremities, difficulty with balance, and slurred speech. Medical history includes syphilis 12 years ago that was treated with benzathine penicillin G. On physical examination, vital signs are normal. The Mini-Mental State Examination score is 22 (normal >24/30). Speech is dysarthric. There is right-sided hemiparesis with increased muscle tone on the right. Serologic testing for HIV antibodies is positive. CD4 cell count is 80/uL. MRI of the brain reveals numerous ring-enhancing lesions in the basal ganglia and the corticomedullary junction, predominantly on the left side, with mass effect. Which of the following is the most likely diagnosis?

- A- Cryptococcal meningitis
- B- Mycobacterium avium complex infection
- C- Progressive multifocal leukoencephalopathy
- D- Toxoplasmosis encephalitis

Explanation: The most likely diagnosis is toxoplasmosis encephalitis. Toxoplasmosis almost always presents as reactivation disease in patients with HIV infection and typically occurs when the CD4 cell count is less than 100/uL. Additional findings are fever, neurologic deficits, and an MRI showing ring-enhancing lesions, often with associated edema.

Sulfadiazine plus pyrimethamine and folinic acid are given initially. Follow-up MRI is critical to assess treatment response. If there is no therapeutic response after 14 days, stereotactic brain biopsy is recommended to rule out other causes, especially a primary central nervous system lymphoma.

Cryptococcal meningitis is the most common form of meningitis in patients with AIDS, who typically present with symptoms such as headache, irritability, and nausea that can mimic other disorders. Most patients have a CD4 cell count of less than 100/uL. The diagnosis is based on detection of cryptococcal antigen in the cerebrospinal fluid or culture of *Cryptococcus neoformans* in the cerebrospinal fluid. Cryptococcal meningitis is not usually associated with ring-enhancing lesions on brain MRI.

Disseminated *Mycobacterium avium* complex (MAC) infection is common in patients with advanced-stage HIV infection and a CD4 cell count of less than 50/uL. Symptoms include fever, weight loss, hepatosplenomegaly, lymphadenopathy, malaise, and abdominal pain. The diagnosis is generally confirmed by recovering the pathogen from sterile tissue (usually blood). MAC infection is not associated with ring-enhancing lesions on MRI. This patient's CD4 count also helps exclude this diagnosis.

Progressive multifocal leukoencephalopathy is a demyelinating disease of the central nervous system caused by the polyomavirus JC virus. It occurs almost exclusively in severely immunocompromised patients, including those with advanced HIV-1 infection. Clinical findings of progressive multifocal leukoencephalopathy include dementia, hemiparesis or paralysis of one extremity, ataxia, hemianopia, and diplopia. The characteristic MRI appearance of these lesions is hyperintense (white) areas on T2-weighted images and fluid-attenuated inversion recovery (FLAIR) sequences and hypointense (dark) areas on T1-weighted images. There is usually no mass effect.

Q7 (500Best): A 42-year-old man presents to accident and emergency with a 3-week history of shortness of breath, dry cough, fevers and malaise. He has presented as his exercise tolerance has deteriorated. He mentions that he has been HIV positive for ten years. On examination, there are fine crackles throughout both lung fields. Chest x-ray demonstrates bilateral perihilar interstitial shadowing. What is the most likely causative organism?

- A. *Pneumocystis jiroveci*
- B. Herpes simplex virus type 1
- C. Herpes simplex virus type 2
- D. *Streptococcus pneumoniae*
- E. *Mycoplasma pneumoniae*

Explanation: *Pneumocystis jiroveci* (A), formerly known as *Pneumocystis carinii*, is a fungal infection that is the most common life-threatening opportunistic infection for people with AIDS. It presents with dry cough, exertional dyspnoea, fever and malaise. Chest x-ray may be normal or show bilateral perihilar interstitial shadowing. On CT scan of the chest, there might be a characteristic ground-glass appearance. Herpes simplex virus type 1 (B) and type 2 (C) cause oral and genital ulcers. *Streptococcus pneumoniae* (D) is the most common cause of pneumonia, but the clinical signs of exertional dyspnoea and dry cough in a patient with HIV make *Pneumocystis jiroveci* far more likely in this question. *Mycoplasma pneumoniae* (E) is a cause of atypical pneumonia, which presents with dry cough, fever and malaise. The patient subgroup, presence of fine crepitations in both lung fields and the x-ray findings make this option incorrect.

AIDS/HIV

Q8 (500Best): A 42-year-old man presents to accident and emergency with a 3-week history of retrosternal discomfort after swallowing. He mentions that he has been unable to keep any food down at all. He has been HIV positive for ten years. He is admitted and endoscopy shows areas of ulceration throughout the oesophagus. What is the most likely causative organism?

- A. Staphylococcus aureus
- B. Cryptosporidium parvum
- C. Candida albicans
- D. Pneumocystis jiroveci
- E. Cryptococcus neoformans

Explanation: Candida albicans (C) is a fungal infection that may colonize the oesophagus of patients with HIV, causing dysphagia and retrosternal discomfort. It is treated with fluconazole or ketoconazole. However, resistance to these organisms is becoming increasingly common. Staphylococcus aureus (A) does not colonize the oesophagus and causes ulceration in patients with HIV. Cryptosporidium parvum (B) is a protozoal infection that presents with abdominal pain, nausea or vomiting and profuse watery diarrhoea. Pneumocystis jiroveci (D) causes pneumocystis pneumonia in HIV patients. Cryptococcus neoformans (E) causes meningitis in patients with HIV; these patients present with fever, headache and drowsiness. Cryptococcus neoformans may then be identified from the cerebrospinal fluid obtained at lumbar puncture.

Q9 (500Best): A 42-year-old man presents to his GP with 'blotches' over his legs. He has been HIV positive for ten years. On examination, there are multiple purple and brown papules over his legs and his gums. What is the most likely diagnosis?

- A. Malignant melanoma
- B. Squamous cell carcinoma
- C. Basal cell carcinoma
- D. Kaposi's sarcoma
- E. Toxoplasmosis

Explanation: Kaposi sarcoma lesions are characteristically well-defined pigmented papules. Lesions may also have surrounding soft tissue swelling and, in patients with HIV, they often occur in the mouth. Within the HIV population, Kaposi's sarcoma has a predisposition for homosexual men and tends to be more aggressive. Kaposi's sarcoma may also involve the gastrointestinal tract and the respiratory system. This visceral Kaposi's sarcoma has a worse prognosis than disease just confined to the skin. Malignant melanoma (A) and basal cell carcinoma (C) are not associated with HIV, making this answer incorrect. Squamous cell carcinoma (B), however, is associated with HIV, but presents with ulcerated lesions with raised edges. Toxoplasmosis (E) is caused by Toxoplasma gondii and normally presents with cerebral abscesses or encephalitis in patients with HIV.

Q10 (500Best): A 42-year-old man presents to his GP with 'blotches' over his legs. He has been HIV positive for ten years. On examination, there are multiple purple and brown papules over his legs and his gums. A diagnosis of Kaposi's sarcoma is suspected. What is the most likely causative organism?

- A. Herpes simplex virus type 1
- B. Herpes simplex virus type 2
- C. Human herpes virus type 3
- D. Human herpes virus type 8
- E. Pneumocystis jiroveci

Explanation: Human herpes virus type 8 (D) is associated with Kaposi's sarcoma. Kaposi's sarcoma is derived from vascular endothelial cells and fibrous tissue. Herpes simplex virus type 1 (A) and herpes simplex virus type 2 (B) cause oral and genital ulcers. Human herpes virus type 3 (C) is also known as VZV and causes chicken pox and shingles. It is important to note that the herpes viruses occur more frequently and with a greater severity in patients who are HIV positive. Pneumocystis jiroveci (E) causes pneumocystis pneumonia in patients with HIV.

AIDS/HIV

Q11 (500Best): A 42-year-old man presents to his GP complaining of deterioration in his vision in the right eye and the presence of floaters. The change in his vision has been causing him to suffer from headaches. He has been HIV positive for ten years. Fundoscopy reveals haemorrhages and exudates on the retina. What is the most likely diagnosis?

- A. Retinal detachment
- B. CMV retinitis
- C. Kaposi's sarcoma
- D. Optic atrophy
- E. Diabetic retinopathy

Explanation: Cytomegalovirus can cause varying pathology in patients with HIV including retinitis, colitis, oesophagitis and pneumonitis. CMV retinitis (B) causes varying symptoms, depending on which part of the retina is involved. The common presenting features include loss of visual acuity, floaters, headache and eye pain. If the macular is involved, there may be complete loss of vision. The characteristic appearance on fundoscopy is the presence of haemorrhages and exudates, described as a 'pizza-pie' appearance. Treatment of CMV retinitis should be started as soon as possible to prevent the infection from spreading and compromising the vision. Retinal detachment (A) should be considered in patients who give a history of floaters. However, the appearance on fundoscopy is characteristic of CMV retinitis, thus making retinal detachment (A) the incorrect answer. Kaposi's sarcoma (C) does not involve the retina, but there may be lesions around the eye. Optic atrophy (D) presents with decreased visual acuity, but pale optic disks are seen on fundoscopy. There is no history to suggest that this patient has diabetes, thus making diabetic retinopathy (E) the incorrect answer.

Q12 (500Best): A 42-year-old man presents to accident and emergency with a 1-day history of headache and fevers. He presents with his partner who says he has been becoming increasingly confused and disorientated. On examination, his temperature is 38.5°C. On cranial nerve examination there is a right-sided superior quadrantanopia. An urgent CT scan of the head is organized which shows multiple ring enhancing lesions. What is the most likely diagnosis?

- A. Toxoplasmosis
- B. Meningitis
- C. Cryptosporidiosis
- D. CMV encephalitis
- E. Histoplasmosis

Explanation: Toxoplasmosis (A) is caused by the protozoa *Toxoplasma gondii*. In patients with HIV, it may present with encephalitis. Clinical features include fever, headache confusion and convulsions. As in this case, there may be focal neurological signs on examination. The multiple ring enhancing lesions are the characteristic CT finding. Meningitis (B) may present with a high fever, headache and confusion. However, the focal neurological signs and the presence of multiple ring-enhancing lesions on CT make this answer incorrect. Cryptosporidiosis (C) may affect HIV patients and presents with abdominal pain, nausea and vomiting and profuse diarrhoea. While CMV encephalitis (D) may produce the clinical features described in this question, the CT finding of the multiple ring enhancing lesions makes this answer incorrect. Histoplasmosis (E) may affect HIV patients and presents with respiratory symptoms.

Concepts in infection prevention

Q1 (Pretest): A 60-year-old female patient is admitted to the hospital in septic shock secondary to a urinary tract infection. The patient is started on antibiotics awaiting culture results. She improves with complete resolution of her symptoms. The patient continues to have a urinary catheter in place. On the 10th hospital day, the patient is discharged to a rehabilitation facility. As a part of the routine admission orders, urinalysis and culture are ordered. The patient denies fever, abdominal pain, nausea, or vomiting. The urinalysis shows 5 to 10 white blood cells and a negative dipstick for nitrite and leukocyte esterase, but the culture grows more than 105 colonies of *Candida albicans*. Which of the following is the best course of action?

- A. Start antifungal therapy with fluconazole.
- B. Continue broad-spectrum antibiotics.
- C. Remove the urinary catheter.
- D. Encourage water intake and continue to observe.
- E. Remove the urinary catheter and start liposomal amphotericin B.

Explanation: Every positive culture requires interpretation. A positive culture could represent a pathogen, a colonizer, or a contaminant. The presence of symptoms and signs of infection in addition to supportive laboratory and radiologic data makes a cultivated microbe a pathogen. The patient has no symptoms or signs of infection and her urinalysis shows no pyuria. In this case, *C. albicans* is a colonizer, and no antifungal therapy is indicated. Predisposing risk factors need to be eliminated to reduce the chances of colonization and to prevent a colonizer from becoming a pathogen. Removing a Foley catheter, controlling hyperglycemia and stopping broad-spectrum antibiotics, when feasible, represent some examples of risk factor elimination. Antifungal therapy (such as with fluconazole or amphotericin B) is inappropriate for fungal colonization alone.

Q2 (MKSAP): A 32-year-old woman is evaluated for an upper respiratory infection. She was well until 5 days ago when she developed a fever, sore throat, nonproductive cough, and runny nose. She has no ear pain or nasal congestion. Her medical history is otherwise unremarkable. She has no allergies and takes no medications. She lives at home with her husband and 8-year-old twin boys. On physical examination, her vital signs are normal. Her ears, nose, and oropharynx appear normal. She has no lymphadenopathy and her lungs are clear to auscultation.

Which of the following is the best prevention strategy for her family?

- A- Echinacea
- B- Frequent hand washing
- C- Penicillin G
- D- Surgical face mask
- E- Vitamin C

Explanation: Handwashing with soap and water has proven efficacy in removing viruses from the hands and helps prevent the spread of infections. Contact with secretions is probably the principal mode of upper respiratory viral infection transmission. A meta-analysis of 30 studies assessing hand hygiene showed a reduction in respiratory illness of 21%. Although commonly used to prevent upper respiratory tract infections, prevention studies using echinacea have failed to show consistent benefit and it cannot be recommended. Antibiotics, such as penicillin G, are ineffective in the treatment or prevention of viral diseases. In addition, the inappropriate use of antibiotics increases the risk of bacterial resistance and exposes the patient to unnecessary risks, such as allergic reactions, and complications, such as vaginal yeast infection and gastrointestinal upset, including the possibility of *Clostridium difficile* infection. Commonly used in Asia to prevent respiratory infections, the benefit of face masks is undocumented. In one trial in Japan, use of surgical face masks did not result in a lower incidence of upper respiratory tract infections but was associated with a greater incidence of headache. Prevention studies using vitamin C have failed to show consistent benefit in the general community; however, a subgroup of studies that included persons exposed to significant cold or physical stress showed a reduction in the incidence and duration of colds. Multivitamin and multimineral supplementation are commonly used in men and women aged 65 years or older; however, prevention studies using daily multivitamin and multimineral supplementation in this population have failed to show consistent benefit on the incidence of upper respiratory tract infections.

Concepts in infection prevention

Q3 (AMBOSS): Two hours after admission to the intensive care unit, a 56-year-old man with necrotizing pancreatitis develops profound hypotension. His blood pressure is 80/50 mm Hg and he is started on vasopressors. A central venous access line is placed. Which of the following is most likely to decrease the risk of complications from this procedure?

- A. Preparation of the skin with chlorhexidine and alcohol
- B. Replacement of the central venous line every 7-10 days
- C. Initiation of periprocedural systemic antibiotic prophylaxis
- D. Placement of the central venous line in the femoral vein

Explanation: Proper hand hygiene and preparing the skin with chlorhexidine is the most effective strategy in decreasing the risk of infection (e.g., CLABSI) from CVL placement. Chlorhexidine has proven superior to iodine-based compounds for antiseptics.

Q4 (AMBOSS): An 82-year-old man with alcohol use disorder is brought to the emergency department from his assisted living facility because of fever and cough for 1 week. The cough is productive of thick, mucoid, blood-tinged sputum. His temperature is 38.5°C (101.3°F) and respirations are 20/min. Physical examination shows coarse inspiratory crackles over the right lung field. Sputum cultures grow gram-negative, encapsulated bacilli that are resistant to amoxicillin, ceftriaxone, and aztreonam. Which of the following infection control measures is most appropriate for preventing transmission of this organism to other patients in the hospital?

- A- Require all staff and visitors to wear droplet masks
- B- Transfer patient to a positive pressure room
- C- Require autoclave sterilization of all medical instruments
- D- Isolate patient to a single-occupancy room

Explanation: Multidrug-resistant strains of bacteria, such as ESBL-producing strains, are a greater public health hazard than infections with organisms of a normal resistance spectrum, and thus need stricter infection control measures. In addition to the standard contact precautions and strict hand hygiene, patients should be isolated in single-occupancy rooms.

Q5 (AMBOSS): Five days after admission to the hospital for treatment of community-acquired pneumonia, a 76-year-old man develops watery diarrhea and cramping lower abdominal pain. Today, he has had three episodes of foul-smelling, nonbloody diarrhea without nausea or vomiting. He has hypertension and hyperlipidemia. His medications include lisinopril, atorvastatin, cefotaxime, and clarithromycin. His temperature is 37.5°C (99.5°F), pulse is 95/min, respirations are 16/min, and blood pressure is 140/85 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 97%. Crackles are heard over the right lower lung base. Abdominal examination shows mild tenderness throughout the lower quadrants. Leukocyte count is 13,000/mm³. Stool analysis is pending. In addition to isolating the patient and wearing gloves and a gown upon room entry, which of the following infection control measures is most appropriate for preventing transmission of the organism responsible for this patient's gastrointestinal symptoms?

- A- Wear an N95 respirator
- B- Use an alcohol-based hand rub
- C- Wash hands with soap and water
- D- No further infection control measures are required

Explanation: Adequate hand hygiene, which is a standard precaution, should always be performed by health care providers (HCPs) for infection control before and after contact with a patient, regardless of whether or not the patient has an infection. In most instances, the use of alcohol-based hand rubs (ABHRs) alone is a quicker and superior method of hand hygiene than washing hands with soap and water. However, hand hygiene with soap and water rather than an ABHR is required if the HCP's hands are visibly soiled or when caring for patients with acute infectious diarrhea or infections due to spore-forming organisms such as *C. difficile*, because ABHRs are ineffective against spores. Wearing gloves and a gown is an important adjunct in preventing contamination with spores but is not a substitute for hand hygiene. HCPs should wash hands with soap and water before putting on gloves and gowns as well as after removing them.

When caring for patients with contact-transmitted diseases such as *C. difficile* infection, in addition to standard precautions, HCPs should follow contact precautions (e.g., isolating patients, wearing gloves and a gown upon room entry).

Other infections requiring airborne precautions include measles, varicella, smallpox, and severe acute respiratory syndrome (SARS) infections (e.g., COVID-19).

Concepts in infection prevention

Q6 (AMBOSS): A 46-year-old man who is a prisoner comes to the county jail urgent care clinic because of a 1-month history of productive cough, malaise, and right-sided chest pain. During this time, he also has had shortness of breath and a 6-kg (13-lb) weight loss. Three weeks ago, he was treated with amoxicillin for pneumonia but his symptoms did not improve. He worked as a construction worker for 15 years. He has HIV infection and hypertension. Medications include lisinopril and antiretroviral therapy. His temperature is 38.4°C (101.1°F) and blood pressure is 142/88 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 91%. On pulmonary examination, scattered crackles are heard bilaterally; there is dullness to percussion at the right lung base. Chest x-ray shows right-sided hilar lymphadenopathy, a fibrous, cavitory lesion in the right lower lobe, and right-sided pleural effusion. CD4 count is 600 cells/mm³.

- A- Droplet precautions
- B- Airborne precautions
- C- Standard precautions
- D- Contact precautions

Explanation: Patients with active tuberculosis (TB) disperse bacilli-containing droplet nuclei (aerosols) while coughing or sneezing, warranting airborne precautions in addition to standard precautions. Patients with suspected or confirmed active TB must be placed in airborne infection isolation rooms (AIIRs) because droplet nuclei can remain suspended in the air and travel long distances. The negative air pressure in AIIRs prevents contaminated air from escaping. Furthermore, patients with active TB must wear surgical face masks in an ambulatory care setting or while being transported to another facility. Health care personnel should wear an N95 respirator (or a higher-level respirator) before entering the AIIR. Airborne precautions for active TB are usually terminated only after the patient has significant clinical improvement, three consecutive negative smears on sputum microscopy (collected 8–24 hours apart), a negative sputum culture, and received treatment for 2–3 weeks.

Other infections requiring airborne precautions include measles, varicella, smallpox, and severe acute respiratory syndrome (SARS) infections (e.g., COVID-19).

Healthcare associated infection

Q1 (Pretest): A 59-year-old man undergoes coronary bypass surgery. He receives cefazolin prophylactically for 24 hours. On the ninth postoperative day, he develops a fever of 39.8°C with a heart rate of 115 beats/minute and a blood pressure of 105/65 mm Hg. The surgical site is healing well with no redness or discharge. His white blood cell count is 14,000/mm³ and urinalysis reveals many white blood cells per high power field. Blood and urine cultures grow a non-lactose fermenting oxidase-positive gram-negative rod. Which of the following antibiotics is most appropriate to treat this infection?

- A. Moxifloxacin
- B. Ceftriaxone
- C. Doripenem
- D. Trimethoprim-sulfamethoxazole
- E. Tigecycline

Explanation: The patient has a healthcare-associated urinary tract infection complicated by gram-negative bacteremia. The complete identification of gram-negative rods might take 48 hours. Knowing the ability of the growing bacteria to ferment lactose might help in the early prediction of the likely pathogen at hand. Among lactose fermenting gram-negative rods, enterobacteriaceae like E coli are most common. Among non-lactose fermenting oxidase-positive gram-negative bacteria, P aeruginosa is most common. Ceftriaxone, doripenem, and trimethoprim-sulfamethoxazole can be used to treat urinary tract infections while moxifloxacin and tigecycline do not achieve high enough concentration in urine to be used for this indication. Of the listed antibiotics, doripenem, which is a carbapenem beta-lactam antibiotic, is the only one with antipseudomonal activity. Antibiotics with antipseudomonal activity include certain penicillins (piperacillin/tazobactam and ticarcillin/clavulanate), cephalosporins (ceftazidime and cefepime), carbapenems (imipenem, meropenem, and doripenem), fluoroquinolones (ciprofloxacin and levofloxacin), and aminoglycosides (gentamicin, tobramycin, and amikacin).

Q2 (MKSAP): A 69-year-old man is admitted to the cardiac intensive care unit with an exacerbation of heart failure. Notable clinical findings include elevated central venous pressure, an S₃, pulmonary crackles, and pedal edema. Intravenous furosemide and lisinopril are initiated, and a urinary catheter is placed to measure urine output. In addition to meticulous hand hygiene, which of the following measures is most effective in preventing a catheter-associated urinary tract infection?

- A- Antibiotic prophylaxis
- B- Changing the urinary catheter every 72 hours
- C- Minimizing manipulation and irrigation of the catheter
- D- Promptly discontinuing urinary catheter use
- E- Using silver impregnated urinary catheters

Explanation: The most effective way to prevent catheter-associated urinary tract infections (UTIs) is to decrease catheter use. Devices should be used for specific indications, not for convenience and should be removed as soon as possible. Examples of appropriate use include diagnosing pathological findings in the lower urinary tract or the cause of urinary retention, monitoring fluid status in acutely ill patients when this directly impacts medical treatment, and managing patients with stage 3 or 4 pressure ulcers on the buttocks. However, urinary catheters often are used for convenience, which significantly increases the risk for UTIs. If the catheter is needed, measures are required to decrease the risk of bacteriuria and subsequent infection. These include handwashing, using an aseptic technique and sterile equipment for catheter insertion and care, securing the catheter properly, maintaining unobstructed urine flow and closed sterile drainage, and considering use of antibacterial-coated catheters. Manipulation and irrigation should be minimized. Specimens should be collected using the drainage bag valve. Antibiotics should not be used as prophylaxis for the prevention of UTIs because such use promotes antibiotic resistance.

Q3 (MKSAP): A 36-year-old woman is admitted to the intensive care unit from the emergency department after intentionally ingesting an overdose of a long-acting barbiturate. Endotracheal intubation was performed in the emergency department and the patient was placed on mechanical ventilation. Other than being minimally arousable and mechanically ventilated, the patient is stable. Which of the following measures will reduce the risk of ventilator-associated pneumonia?

- A- Changing the endotracheal tube every 2 days
- B- Nasal placement of the endotracheal tube
- C- Prophylactic antibiotics
- D- Semi-erect (45°) positioning in bed

Explanation: Semi-erect position will most likely reduce the risk of ventilator-associated pneumonia (VAP). Even when a cuffed tube is in place, bacteria from the stomach can reach the lungs and cause pneumonia. Semi-erect positioning in bed at 45° is useful because it reduces the risk of excursion of bacteria from the stomach into the upper airways. Changing endotracheal tubes seems logical, but reintubation is associated with certain risks (for example, intubating the esophagus or precipitating hypoxia during the procedure). Reintubation may also increase the risk of nosocomial pneumonia. Careful inspection and management of the tubing can help reduce infections slightly. Because the tubing has a tendency to collect water, careful drainage of accumulated condensate into patient-specific drainage containers is advocated. Oral placement of endotracheal tubes is currently believed to be superior to nasal placement because nasogastric and nasotracheal tubes cause some degree of obstruction of the ostia in the nose, which can predispose to nosocomial sinusitis. Whether all nasal tubes should be replaced by oral tubes is unclear. However, no benefit will be gained by changing from an orotracheal tube to a nasotracheal tube to prevent a case of health-care associated pneumonia. Reducing the density of gastric bacteria by use of prophylactic antibiotics is tempting. However, this approach is ineffective and serves to select for resistant strains.

Healthcare associated infection

Q4 (MKSAP): A 68-year-old man is diagnosed with *Clostridium difficile* infection 5 days after elective hip replacement surgery. This hospital has recently reported a high incidence of *C. difficile* infections. The patient was in a two-bed hospital room. In addition to bleach for enhanced room cleaning, which of the following "bundled" measures would be most effective in preventing the spread of *C. difficile* in this hospital setting?

- A. Airborne precautions and alcohol hand sanitizer
- B. Airborne precautions and soap and water for hand hygiene
- C. Barrier precautions and alcohol hand sanitizer
- D. Barrier precautions and soap and water for hand hygiene
- E. Droplet precautions and soap and water for hand hygiene

Explanation: The most effective bundled measures to prevent the spread of *Clostridium difficile* infection are barrier precautions and soap and water for hand cleaning. Environmental contamination with vegetative *C. difficile* and *C. difficile* spores frequently occurs. *C. difficile* is transmitted to other patients through the hands and clothes of health care workers and from common equipment that is used on patients without cleaning. A combination of interventions "bundled" together have been shown to be effective at reducing many hospital-acquired infections. The use of a *C. difficile* bundle consisting of barrier precautions, enhanced cleaning with bleach, and traditional soap-and-water hand hygiene is useful in preventing the spread of *C. difficile*. Soap and water are not sporicidal, but the mechanics of hand washing effectively removes spores. Alcohol-based hand hygiene products do not kill spores and are ineffective at removing them from hands.

Barrier precautions such as wearing nonsterile gloves and a gown and using dedicated equipment have been recommended for *C. difficile* control by the Centers for Disease Control and Prevention and have been shown to be effective.

Airborne precautions are recommended for patients with known or suspected illnesses transmitted by airborne droplet nuclei, such as tuberculosis, measles, varicella, or disseminated varicella zoster virus infection. Patients must be isolated in a private room with negative air pressure, the door must remain closed, and all entering persons must wear masks with a filtering capacity of 95%. Transported patients must wear masks.

Droplet precautions are recommended for patients with known or suspected illnesses transmitted by large-particle droplets, such as *Neisseria meningitidis* infections and influenza. Patients are isolated in private rooms, and hospital personnel wear face masks when within 3 feet of the patient.

Q5 (500Best): A 42-year-old man presents to accident and emergency with a 3-week history of retrosternal discomfort after swallowing. He mentions that he has been unable to keep any food down at all. He has been HIV positive for ten years. He is admitted and endoscopy shows areas of ulceration throughout the oesophagus. What is the most likely causative organism?

- A- *Staphylococcus aureus*
- B- *Cryptosporidium parvum*
- C- *Candida albicans*
- D- *Pneumocystis jiroveci*

Explanation: is a fungal infection that may colonize the oesophagus of patients with HIV, causing dysphagia and retrosternal discomfort. It is treated with fluconazole or ketoconazole. However, resistance to these organisms is becoming increasingly common. *Staphylococcus aureus* (A) does not colonize the oesophagus and causes ulceration in patients with HIV. *Cryptosporidium parvum* (B) is a protozoal infection that presents with abdominal pain, nausea or vomiting and profuse watery diarrhoea. *Pneumocystis jiroveci* (D) causes pneumocystis pneumonia in HIV patients. *Cryptococcus neoformans* (E) causes meningitis in patients with HIV; these patients present with fever, headache and drowsiness. *Cryptococcus neoformans* may then be identified from the cerebrospinal fluid obtained at lumbar puncture.

Q6 (AMBOSS): Five days after undergoing right hemicolectomy for colon cancer, a 62-year-old man has fever, abdominal pain, nausea, and urinary frequency. The surgery was uncomplicated. An indwelling urinary catheter was placed intraoperatively. His temperature is 39.4°C (102.9°F), pulse is 91/min, and blood pressure is 118/83 mm Hg. There is tenderness to palpation of the costovertebral angle. The urine collected in the catheter bag appears cloudy. Which of the following measures is most likely to have prevented this patient's current condition?

- A- Early removal of catheter
- B- Antimicrobial prophylaxis
- C- bladder irrigation
- D- Daily catheter replacement

Explanation: The most effective measures for the prevention of catheter-associated urinary tract infections (UTIs) are avoidance of unnecessary catheterization, sterile technique during catheter placement, and early removal of urinary catheters when they are no longer indicated; patients undergoing surgery not involving the urinary tract should have their catheters removed as soon as possible (preferably within 24 hours postoperatively).

Use of antibiotics

Q1 (Pretest): A 35-year-old previously healthy man develops cough with purulent sputum over several days. On presentation to the emergency room, he is lethargic. Temperature is 39°C, pulse 110, and blood pressure 100/70. He has rales and dullness to percussion at the left base. There is no rash. Flexion of the patient's neck when supine results in spontaneous flexion of hip and knee. Neurologic examination is otherwise normal. There is no papilledema. A lumbar puncture is performed in the emergency room. The cerebrospinal fluid (CSF) shows 8000 leukocytes/ μL , 90% of which are polys. Glucose is 30 mg/dL with a peripheral glucose of 80 mg/dL. CSF protein is elevated to 200 mg/dL. CSF Gram stain is pending. Which of the following is the correct treatment option?

- A. Begin acyclovir for herpes simplex encephalitis.
- B. Obtain emergency MRI scan before beginning treatment.
- C. Begin ceftriaxone and vancomycin for pneumococcal meningitis.
- D. Begin ceftriaxone, vancomycin, and ampicillin to cover both pneumococci and Listeria.
- E. Begin high-dose penicillin for meningococcal meningitis.

Explanation: This previously healthy male has developed acute bacterial meningitis as evident by meningeal irritation with a positive Brudzinski sign, and a CSF profile typical for bacterial meningitis (elevated white blood cell count, high percentage of polymorphonuclear leukocytes, elevated protein, and low glucose). The patient likely has concomitant pneumonia. This combination suggests pneumococcal infection. Because of the potential for beta-lactam resistance, the recommendation for therapy prior to availability of susceptibility data is ceftriaxone and vancomycin. Though herpes simplex can be seen in young healthy patients, the clinical picture and CSF profile are not consistent with this infection. The CSF in herpes simplex encephalitis shows a lymphocytic predominance and normal glucose. Listeria monocytogenes meningitis is a concern in immunocompromised and elderly patients. Gram stain would show gram-positive rods. Neisseria meningitidis is the second commonest cause of bacterial meningitis but rarely causes pneumonia (the portal of entry is the nasopharynx). Although penicillin G still kills the meningococcus, empiric therapy should cover all likely pathogens until Gram stain and culture results are available. Because the patient has no papilledema and no focal neurologic findings, treatment should not be delayed to obtain an MRI scan.

Q2 (Pretest): A 70-year-old nursing home resident had been admitted to the hospital for pneumonia and treated for 10 days with levofloxacin. She improved but developed diarrhea 1 week after discharge, with low-grade fever, mild abdominal pain, and 2 to 3 watery, nonbloody stools per day. A cell culture cytotoxicity test for Clostridium difficile-associated disease was positive. The patient was treated with oral metronidazole, but did not improve after 10 days. Diarrhea has increased and fever and abdominal pain continue. What is the best next step in the management of this patient?

- A. Obtain C difficile enzyme immunoassay.
- B. Continue metronidazole for at least 2 more weeks.
- C. Switch treatment to oral vancomycin.
- D. Hospitalize patient for fulminant C difficile-associated disease.
- E. Use synthetic fecal bacterial enema.

Explanation: The diagnosis is very consistent with C difficile disease. The patient is elderly, has been in both a nursing home and hospital setting and received more than a week of a fluoroquinolone antibiotic. Mild fever, abdominal pain, and watery diarrhea are all consistent with the diagnosis, and the cell culture cytotoxicity test is the most specific of diagnostic tests. Failure on metronidazole is increasingly reported, with at least a 25% failure rate. Switching to oral vancomycin is recommended. The patient does not have fulminant disease which usually presents as an acute abdomen, sepsis, or toxic megacolon; so hospitalization is not necessary. Synthetic fecal bacterial enema is one potential treatment being studied for recurrent C difficile disease but is not standard treatment.

Q3 (MKSAP): A 25-year-old woman who is 28 weeks pregnant has asymptomatic bacteriuria detected during a routine prenatal visit. She has not had fever, urinary frequency, or dysuria and is not taking any medications other than prenatal vitamins. She has never had a urinary tract infection before and has no medical problems. On physical examination, vital signs, including temperature, are normal. There is no costovertebral angle tenderness.

Which of the following is the most appropriate management?

- A- Ampicillin
- B- Ciprofloxacin
- C- Trimethoprim
- D- Observation

Use of antibiotics

Explanation: The most appropriate management is to begin ampicillin. Pregnant women are screened for asymptomatic bacteriuria, which is associated with low birth weight, prematurity, and an increased risk for pyelonephritis. This pregnant woman has asymptomatic bacteriuria that now requires treatment. An appropriate antibiotic for this patient is ampicillin, amoxicillin, or nitrofurantoin. These antibiotics are Food and Drug Administration pregnancy risk category B drugs. Ciprofloxacin and trimethoprim are both pregnancy risk category C drugs and are therefore not indicated. Urine cultures should be obtained after treatment in pregnant women with asymptomatic bacteriuria to confirm eradication of bacteria. Confirming the sterility of the urine can be done by repeating urine cultures at intervals until delivery.

Q4 (MKSAP): A 77-year-old woman is evaluated during a routine physical examination. She is asymptomatic and has a history of hypertension, type 2 diabetes mellitus, and hyperlipidemia. Medications are aspirin, lisinopril, hydrochlorothiazide, a glyburide, and lovastatin. She has no allergies. Her physical examination is unremarkable. Laboratory studies including serum creatinine, blood urea nitrogen, electrolytes, liver function tests, and a fasting lipid panel are normal. Her hemoglobin A1c is 6.3%. Urinalysis shows 15 leukocytes per high-power field and bacteria; no erythrocytes, protein, or glucose are noted. Urine culture grows Escherichia coli of at least 10⁵ colony-forming units (cfu)/mL.

Repeat urinalysis and urine culture confirm these results.

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

- A. Ciprofloxacin for 3 days
- B. Ciprofloxacin for 7 days
- C. Trimethoprim-sulfamethoxazole for 3 days
- D. No treatment

Explanation: The most appropriate management for this patient's asymptomatic bacteriuria is no treatment. For asymptomatic women, bacteriuria is defined as 2 consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts of at least 10⁵ cu/mL. Escherichia coli remains the single most common organism isolated from women, but other organisms, such as Proteus mirabilis, are more common in men. Treatment of asymptomatic bacteriuria in women with diabetes is not indicated. A randomized, controlled trial of antibiotic therapy or no therapy for women with diabetes and asymptomatic bacteriuria showed antibiotic therapy did not delay or decrease the frequency of symptomatic urinary tract infection, nor did it decrease the number of hospitalizations for urinary infection or other causes. However, women who received antibiotic therapy had significantly more adverse antimicrobial effects.

Screening for asymptomatic bacteriuria is recommended only for pregnant women and before transurethral resection of the prostate, urinary tract instrumentation involving biopsy, or other tissue trauma resulting in mucosal bleeding. Women with diabetes, premenopausal nonpregnant women, older persons living in the community, elderly institutionalized persons, persons with spinal cord injury, and patients with catheters while the catheter remains in situ should not be screened or treated for asymptomatic bacteriuria. Screening is also not recommended for simple catheter placement or cystoscopy without biopsy. Unless indicated, screening and treatment for asymptomatic bacteriuria should be discouraged.

Q5 (MKSAP): A 22-year-old woman is evaluated in September for the acute onset of fever, myalgia, arthralgia, and nonproductive cough. Medical history is noncontributory. On physical examination, the patient is not ill-appearing. Temperature is 38.0°C (100.5°F), blood pressure is 114/62 mm Hg, pulse rate is 90/min, and respiration rate is 18/min. A few crackles are heard at the right lung base. The leukocyte count is 12,000/uL (12 × 10³/L), and the remaining laboratory studies are normal. Chest radiograph reveals a right middle lobe infiltrate.

Which of the following oral antimicrobial agents should be initiated?

- A- Azithromycin
- B- Moxifloxacin
- C- Penicillin
- D- Zanamivir

Explanation: Oral azithromycin should be initiated. The most common pathogens identified from recent studies of patients with mild community-acquired pneumonia (CAP) were Streptococcus pneumoniae, Mycoplasma pneumoniae, and Chlamydia pneumoniae. Macrolides have long been commonly prescribed for treatment of outpatients with CAP, and numerous randomized clinical trials have demonstrated the efficacy of clarithromycin or azithromycin as monotherapy. Erythromycin is a less expensive macrolide but not generally recommended owing to the need for more frequent dosing, more gastrointestinal upset, and lack of coverage for Haemophilus influenzae.

The use of fluoroquinolones to treat ambulatory patients with CAP without comorbidities is discouraged because of the concern that widespread use would lead to the development of resistance.

Penicillin would not be effective in treating M. pneumoniae or C. pneumoniae and is therefore not appropriate in this patient.

Influenza virus symptoms typically consist of fever (usually high), headache, extreme fatigue, nonproductive cough, sore throat, nasal congestion, rhinorrhea, myalgia, and occasionally, gastrointestinal symptoms, with most cases of influenza occurring from November through April in the Northern Hemisphere. Because the patient's symptoms and findings are more consistent with CAP than influenza virus infection, antiviral therapy with zanamivir is not indicated.

Use of antibiotics

Q6 (500Best): A 19-year-old medical student presents to his GP during fresher's fortnight. He is complaining of neck stiffness, headache and sensitivity to light. On examination, a non-blanching, petechial rash is observed on the trunk. What is the most appropriate immediate management?

- A. Send the patient to accident and emergency immediately
- B. Send him home with advice to rest and return if the symptoms worsen
- C. Administer 1.2g of intramuscular benzylpenicillin
- D. Give 500mg of ciprofloxacin
- E. Take a full set of blood tests

Explanation: This case is describing the presentation of a patient with bacterial meningitis. Typical features on presentation include signs of meningism, such as neck stiffness and photophobia, decreased consciousness and a non-blanching petechial rash over the trunk and lower limbs. The immediate management of this life-threatening condition is crucial knowledge as it will save lives, and drugs and doses are worth remembering. The best management is administration of 1.2mg of IM or IV benzylpenicillin (C) and then immediate transfer to a hospital. Sending this patient home (B) is thus inappropriate. Ciprofloxacin (D) is a usually given to contacts of the patient as prophylaxis against infection, rather than in the treatment. Bloods (E), blood cultures and, if possible, a lumbar puncture are all necessary investigations, but the patient must be given the initial dose of antibiotic and then sent urgently to accident and emergency (A).

Q7 (500Best): Following a colonic resection, a 72-year-old woman becomes unwell with acute confusion, pyrexia, tachycardia and hypotension. The patient has had a difficult postoperative period, which has included an admission to ITU for the management of a chest infection. Blood cultures are sent and grow methicillin-resistant Staphylococcus aureus (MRSA). The patient is placed in isolation and barrier nursing is implemented. What is the most appropriate management of this patient?

- A. Manage conservatively
- B. Start intravenous vancomycin
- C. Start intravenous co-amoxiclav
- D. Start intravenous co-amoxiclav and gentamicin
- E. Start oral metronidazole

Explanation: MRSA is a hospital-acquired infection which may colonize the skin, cause wound infections, pneumonias or septicaemia. The case in this question is describing sepsis as a result of MRSA. The most appropriate management of this patient is with isolation, barrier nursing and intravenous vancomycin (B). The patient is septic and thus conservative management (A) is inappropriate. Co-amoxiclav (C), gentamicin (D) and metronidazole (E) are not used in the treatment of MRSA. Isolation, barrier nursing, hand washing and removal of lines when possible are needed to prevent the spread of MRSA.

Q8 (500Best): A 20-year-old man presents to accident and emergency with extreme pain in the right knee. On examination, his temperature is 38.5°C and the knee is hot and swollen. He is unable to move his knee due to pain. The joint is aspirated and blood cultures are taken. The patient is admitted and started on intravenous antibiotics. Gram staining of the joint aspirate shows gram-negative diplococci. What is the most likely responsible organism?

- A- Chlamydia trachomatis
- B- Neisseriae gonnorrhoeae
- C- Haemophilus influenzae
- D- Streptococcus pneumoniae

Explanation: The case in this question describes a patient presenting with septic arthritis. The most common cause of septic arthritis in young fit adults is gonococcal arthritis. The results of the Gram stain should also identify Neisseriae gonnorrhoeae (B) as the correct answer. Chlamydia trachomatis (A) may cause reactive arthritis and is a gram-negative bacteria. However, it does not cause septic arthritis and the Gram stain finding of diplococci means that this is the incorrect answer. Haemophilus influenzae (C) is a gram-negative bacteria that causes septic arthritis in children. Streptococcus pneumoniae (D) is a gram-positive bacteria that commonly causes pneumonia. It is possible for this bacteria to cause septic arthritis. However, the result of the Gram stain and the age of the patient make the answer incorrect in this question. Streptococcus viridans (E) is a gram-positive bacteria that is commonly responsible for infective endocarditis.

Use of antibiotics

Q9 (AMBOSS): A 51-year-old man with alcohol use disorder comes to the physician because of a fever and productive cough. An x-ray of the chest shows a right lower lobe consolidation and a diagnosis of aspiration pneumonia is made. The physician prescribes a drug that blocks peptide transfer by binding to the 50S ribosomal subunit. Which of the following drugs was most likely prescribed?

- A. Clindamycin
- B. Doxycycline
- C. Levofloxacin
- D. Metronidazole

Explanation: Clindamycin is a bacteriostatic antibiotic that inhibits bacterial protein synthesis by preventing peptide translocation at the 50S (large) ribosomal subunit. It targets anaerobic organisms and is commonly used for the treatment of aspiration pneumonia and lung abscess, which are typically polymicrobial. Clostridioides difficile colitis is a potential complication of clindamycin.

Q10 (AMBOSS): An 8-year-old girl is brought to the emergency room for a 6-hour history of fever, sore throat, and difficulty swallowing. Physical examination shows pooling of oral secretions and inspiratory stridor. Lateral x-ray of the neck shows thickening of the epiglottis and aryepiglottic folds. Throat culture with chocolate agar shows small, gram-negative coccobacilli. The patient's brother is started on the recommended antibiotic for chemoprophylaxis. Which of the following is the primary mechanism of action of this drug?

- A. Inhibition of peptidoglycan crosslinking
- B. Inhibition of the 30S ribosomal subunit
- C. Inhibition of the 50S ribosomal subunit
- D. Inhibition of DNA-dependent RNA-polymerase

Explanation: Inhibition of prokaryotic DNA-dependent RNA polymerase is the mechanism of rifampin, the drug of choice for prophylaxis for Haemophilus influenzae. Side effects of rifampin include hepatotoxicity, development of red/orange bodily fluids, and cytochrome P450 enzyme induction. Rifampin may also be used for prophylaxis of meningococcal meningitis.

Q11 (AMBOSS): A 69-year-old woman comes to the emergency department because of a 2-day history of cough and dyspnea. The cough is productive of small amounts of green phlegm. She has stage IV colon cancer and chronic obstructive pulmonary disease. Her medications include 5-fluorouracil, leucovorin, a fluticasone-salmeterol inhaler, and a tiotropium bromide inhaler. Her temperature is 39°C (102.2°F), pulse is 107/min, respirations are 31/min, and blood pressure is 89/68 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 87%. Pulmonary examination shows diffuse crackles and rhonchi. An x-ray of the chest shows a left upper-lobe infiltrate of the lung. Two sets of blood cultures are obtained. Endotracheal aspirate Gram stain shows gram-negative rods that are oxidase-positive. Two large bore cannulas are inserted and intravenous fluids are administered. Which of the following is the most appropriate pharmacotherapy?

- A- Cefepime and levofloxacin
- B- Ceftriaxone and azithromycin
- C- Clarithromycin and amoxicillin-clavulanate
- D- Vancomycin

Explanation: The case in this question describes a patient presenting with septic arthritis. The most common cause of septic arthritis in young fit adults is gonococcal arthritis. The results of the Gram stain should also identify Neisseriae gonorrhoeae (B) as the correct answer. Chlamydia trachomatis (A) may cause reactive arthritis and is a gram-negative bacteria. However, it does not cause septic arthritis and the Gram stain finding of diplococci means that this is the incorrect answer. Haemophilus influenzae (C) is a gram-negative bacteria that causes septic arthritis in children. Streptococcus pneumoniae (D) is a gram-positive bacteria that commonly causes pneumonia. It is possible for this bacteria to cause septic arthritis. However, the result of the Gram stain and the age of the patient make the answer incorrect in this question. Streptococcus viridans (E) is a gram-positive bacteria that is commonly responsible for infective endocarditis.

Use of antibiotics

Q12 (AMBOSS): A 3-year-old girl is brought to the physician for a well-child visit. Her father is concerned about the color and strength of her teeth. He says that most of her teeth have had stains since the time that they erupted. She also has a limp when she walks. Examination shows brownish-gray discoloration of the teeth. She has lower limb length discrepancy; her left knee-to-ankle length is 4 cm shorter than the right. Which of the following drugs is most likely to have been taken by this child's mother when she was pregnant?

- A. Ciprofloxacin
- B. Gentamicin
- C. Chloramphenicol
- D. Tetracycline

Explanation: Tetracycline crosses the placenta and accumulates in developing teeth and bones because of its tendency to form complexes with calcium salts. In utero exposure can lead to discoloration of deciduous teeth and inhibition of bone growth, as seen in this patient. For this reason, tetracyclines are contraindicated during pregnancy and in children < 8 years of age.

Common endemic infections

Q1 (Pretest): A 29-year-old man presents with a 4-day history of fever, headache with retro-orbital pain, severe musculoskeletal and lumbar back pain and rash. The symptoms began 3 days after he returned from a 2-week vacation to the Caribbean islands. The rash developed on his face before spreading over his trunk and extremities. The patient reports receiving appropriate vaccination, including hepatitis A virus vaccine, hepatitis B virus vaccine, and typhoid vaccine. Laboratory tests reveal normal kidney and liver function tests but leukopenia and thrombocytopenia. Which of the following organisms is the most likely cause of this infection?

- A. Leptospira
- B. Plasmodium falciparum
- C. Salmonella typhi
- D. Dengue virus
- E. Hepatitis A virus

Explanation: All the listed diseases can be acquired during travel, but the severe myalgias, skin rash, and thrombocytopenia are most consistent with dengue. Dengue fever is characterized by fever, severe frontal headache, retro-orbital pain, and severe musculo-skeletal and lumbar back pain. A macular or scarlatiniform rash develops within 3 to 4 days of the illness. Virtually all cases respond to conservative measures with bleeding, hepatitis, and myositis reported as potential rare complications. Dengue hemorrhagic fever is a more severe form of the disease. It is more common among infants and elderly people. It is characterized by increased vascular permeability with hypovolemic shock and thrombocytopenia with spontaneous ecchymoses and mucosal bleeding. Dengue is a mosquito-borne illness. Leptospirosis is a spirochetal disease that has two phases. The bacteremic phase is characterized by sudden onset fevers, rigors, headache, photophobia, and severe myalgias. Four to 30 days later, the immunologic phase ensues and is characterized by conjunctivitis, photophobia, retrobulbar pain, neck stiffness, diffuse lymphadenopathy, hepatosplenomegaly, and aseptic meningitis. The most severe form is called Weil disease; it is associated with up to 40% mortality and is characterized by high direct bilirubin and mild elevation in alkaline phosphatase and transaminase values, combined with a high creatine phosphokinase. Malaria is a parasitic disease usually caused by *P. falciparum*. Patients present with influenza-like symptoms, jaundice, and in its most severe forms with obtundation and confusion. Hepatitis A causes markedly elevated transaminase values and jaundice. *S. typhi* causes typhoid fever. Patients present with influenza-like illness with abdominal discomfort and constipation. Mild, bloody diarrhea could develop in some cases. The patient might develop small rose-colored macules called "rose spots" on the trunk, but thrombocytopenia is not a common feature of typhoid fever.

Q2 (MKSAP): A 75-year-old man with type 2 diabetes mellitus is evaluated in the emergency department for a draining chronic ulcer on the left foot, erythema, and fever. Drainage initially began 3 weeks ago. Current medications include metformin and glyburide. On physical examination, he does not appear ill. Temperature is 37.9°C (100.2°F); other vital signs are normal. The left foot is slightly warm and erythematous. A plantar ulcer that is draining purulent material is present over the fourth metatarsal joint. A metal probe makes contact with bone. The remainder of the examination is normal. The leukocyte count is normal, and an erythrocyte sedimentation rate is 70 mm/h. A plain radiograph of the foot is normal. Gram stain of the purulent drainage at the ulcer base shows numerous leukocytes, gram-positive cocci in clusters, and gram-negative rods. Which of the following is the most appropriate management now?

- A- Begin imipenem
- B- Begin vancomycin and ceftazidime
- C- Begin vancomycin and metronidazole
- D- Perform bone biopsy

Explanation: : The most appropriate management is to perform a bone biopsy. Contact with bone (when using a sterile, blunt, stainless steel probe) in the depth of an infected pedal ulcer in patients with diabetes mellitus is strongly correlated with the presence of underlying osteomyelitis, with a positive predictive value of 90%. Patients with diabetes require bone biopsy to obtain deep pathogens, identification of which is the only way to establish a definitive diagnosis and guide therapy. Although it may seem intuitive that drainage from a superficial site such as an ulcer or a sinus tract would contain the causative pathogens, superficial cultures usually do not include the deep organisms responsible for the infection. Failure to identify the causative deep-bone pathogens may lead to spread of infection to adjacent bones or soft tissues and the need for extensive debridement of amputation. The one exception is *Staphylococcus aureus*, which, if found in superficial cultures, correlates well with findings on deep cultures. This patient appears well enough to wait for the bone biopsy to be completed before starting empiric antibiotic therapy and adjusting the antibiotics based on culture results. Empiric therapy should include activity against streptococci, methicillin-resistant *S. aureus* (MRSA), aerobic gram-negative bacilli, and anaerobes. Therapy with imipenem alone will not adequately cover MRSA, vancomycin and ceftazidime will not adequately cover anaerobic bacteria, and vancomycin and metronidazole will not adequately cover gram-negative organisms.

Common endemic infections

Q3 (500Best): A 51-year-old man presents to accident and emergency with a lesion on his forearm. He mentions that he has spent the past three months travelling around South America and only returned home 3 days ago. While his lesion has been present for a few weeks he was reluctant to see a doctor in South America. On examination, there is a 3 × 3 cm erythematous ulcer on the left forearm with a raised edge. What is the most likely diagnosis?

- A. Leishmaniasis
- B. African trypanosomiasis
- C. Herpes zoster
- D. Schistosomiasis
- E. Cryptosporidiosis

Explanation: Leishmaniasis (A) is caused by the Leishmania protozoa, transmitted by sandflies, and is seen in areas of Africa, Europe, Asia, Central and South America. The case described in this question is of cutaneous leishmaniasis. In cutaneous leishmaniasis, lesions develop at the bite site. These start as an itchy papule and develop into erythematous ulcers with raised edges. In visceral leishmaniasis, the protozoa spread from the cutaneous lesions, via the lymphatics to the reticuloendothelial system. Onset of symptoms may be insidious and features include fever, sweats, cough and arthralgia. The liver, spleen and lymph nodes are usually enlarged on physical examination. Mucocutaneous leishmaniasis occurs when primary cutaneous lesions spread to the mucosa of the nose, palate, pharynx or larynx. African trypanosomiasis (B) is sleeping sickness and is caused by Trypanosoma gambiense. Herpes zoster (C) is shingles, which presents with a blistering rash across a well-demarcated dermatomal distribution. Schistosomiasis (D) is caused by water-borne fluke worms and does not result in the cutaneous lesions described in this question, making the answer incorrect. Cryptosporidiosis (E) is a parasitic disease that results in fever and watery diarrhoea.

Q4(500Best): Which of the following statements is most accurate regarding leishmaniasis?

- A- It is transmitted by the anopheles mosquito
- B- Leishmania are bacteria
- C- Leishmaniasis is usually a self-limiting condition
- D- It is transmitted by the tsetse fly
- E- The presence of Leishman–Donovan bodies confirms the disease

Explanation: Leishman–Donovan bodies (E) may be seen in bone marrow, spleen, lymph node or skin lesions in patients with leishmaniasis and confirms the disease. Leishmania is transmitted by the phlebotomine sandfly, making options (A) and (D) incorrect. Leishmania are not bacteria (B), they are protozoa. There are multiple Leishmania species found in different parts of the world that result in cutaneous, mucocutaneous and visceral leishmaniasis. The clinical picture produced is dependent on the Leishmania species and the reaction of the host immune system. Visceral leishmaniasis is not a self-limiting condition (C) and, if left untreated, may result in pancytopenia which can be life threatening.

Q5 (500Best): A 26-year-old Bangladeshi man presents to accident and emergency with a 1-week history of fever, headache, malaise and dry cough. He returned to the UK 2 weeks ago, having spent his summer in Bangladesh. On examination, his temperature is 39°C and a patchy maculopapular rash is seen over his trunk. On examination of the abdomen, there is splenomegaly. Blood tests reveal a low white cell count. What is the most likely diagnosis?

- A- Tetanus
- B- Malaria
- C- Typhoid
- D- Cholera

Explanation: The case in this question describes the presentation of a patient with typhoid (C). This is caused by infection with Salmonella typhi. The features in the question that should alert the diagnosis of typhoid are the patchy maculopapular rash (known as rose spots), which occur in approximately 40 per cent of cases, and the low white cell count, due to a leukopenia. The patient may initially be constipated and subsequently develop diarrhoea. Complications of disease include meningitis, pneumonia, osteomyelitis and intestinal perforation. Diagnosis of typhoid is confirmed on culture of blood, bone marrow, urine or stool. Tetanus (A) may initially present with fevers and malaise, but the rash on the trunk, splenomegaly and low white cell count are not features, making this answer incorrect. Malaria (B) should be considered in returning travellers with a pyrexia and thick and thin blood films sent. However, the maculopapular rash is not seen in malaria, thus making this answer incorrect. Cholera (D) presents with diarrhoea, which is occasionally profuse and watery. Primary syphilis (E) does not present with a fever, rash or splenomegaly making this answer incorrect.

Common endemic infections

Q6 (AMBOSS): A 14-year-old girl is brought to the physician by her father because of fever, chills, abdominal pain, and profuse nonbloody diarrhea. Her symptoms began 1 week ago when she had several days of low-grade fever and constipation. She returned from Indonesia 2 weeks ago, where she spent the summer with her grandparents. Her temperature is 39.3°C (102.8°F). Examination shows diffuse abdominal tenderness and mild hepatosplenomegaly. There is a faint salmon-colored maculopapular rash on her trunk and abdomen. Which of the following is the most likely causal organism?

- A- Salmonella typhi
- B- Clostridioides difficile
- C- Clostridium perfringens
- D- Vibrio cholerae

Explanation: Salmonella typhi is most likely to have caused this patient's symptoms, who has recently traveled to an endemic region. Typhoid infection is characterized by a fluctuating fever and malaise followed by profound fatigue, high fever, and relative bradycardia. Initial constipation can be followed by profuse diarrhea (pea-soup diarrhea), a salmon-colored maculopapular rash (rose spots), and hepatosplenomegaly, usually in the second week after onset. Salmonella typhi is transmitted via the fecal-oral route, with the bacteria initially entering the host through intestinal Peyer patches. After a period of replication, the organism enters the bloodstream and can seed several organs (e.g., the liver and spleen).

Treatment with a third-generation cephalosporin (e.g., ceftriaxone) or a fluoroquinolone is indicated. The WHO recommends typhoid fever vaccination, which contains the Vi capsular polysaccharide antigen, to those traveling to high-risk areas (East and Southeast Asia, Latin America, Africa).

Q7 (AMBOSS): A previously healthy 32-year-old man, who is a military veteran, comes to the emergency department because of high-grade fever and malaise for 3 days. He has severe generalized joint and body pains refractory to acetaminophen. He also has a severe stabbing pain behind his eyes. One week ago, he returned from deployment for a peace-keeping mission in Taiwan. He is sexually active and uses condoms inconsistently. His temperature is 38.7°C (101.7°F), pulse is 102/min, and blood pressure is 100/70 mm Hg. Examination shows nontender inguinal lymphadenopathy. There is a maculopapular rash over the trunk and extremities. Abdominal examination shows no abnormalities. Urinalysis is normal. An ELISA test for HIV is negative. Which of the following is most likely to have prevented this patient's condition?

- A- Prophylaxis with doxycycline
- B- Safe sexual practices
- C- Vaccination
- D- Mosquito repellent

Explanation: Dengue virus is transmitted through the bite of an infected mosquito, most commonly from the species Aedes aegypti. The use of mosquito repellent is the most effective measure for preventing dengue virus infection in patients traveling to endemic areas. Although a vaccine has already been approved for children living in endemic areas, it is currently not indicated for travelers because of its limited efficacy.

Because infections with dengue virus, Chikungunya virus, and Zika virus can have similar clinical presentations, including arthralgia, fever, and a diffuse maculopapular rash, a single PCR that simultaneously tests for all three viruses should be performed.

Common endemic infections

Q8 (AMBOSS): A 26-year-old man comes to the physician because of a 3-week history of malaise and recurrent fever. He has also had a 4.5-kg (10-lb) weight loss over the past 3 months. He came back from his honeymoon in Kenya 6 months ago. He appears ill. His temperature is 39°C (102.2°F). He is alert and oriented to person, time, and place. Physical examination shows generalized lymphadenopathy and hepatosplenomegaly. Laboratory studies show a hemoglobin concentration of 9.1 g/dL, leukocyte count of 2,900/mm³, and platelet count of 108,000/mm³. Which of the following is the most likely vector of this patient's condition?

- A- setse fly
- B- Sand fly
- C- Freshwater snail
- D- Anopheles mosquito

Explanation: Visceral leishmaniasis, a parasitic disease caused by protozoans of the *Leishmania* genus, is transmitted by infected phlebotomine sand flies. Most leishmaniasis infections are asymptomatic. However, they can cause fever, malaise, weight loss, lymphadenopathy, hepatosplenomegaly, and pancytopenia, as seen in this patient. Cutaneous leishmaniasis is also a possible manifestation. The diagnosis of leishmaniasis is confirmed with microscopic visualization of macrophages containing amastigotes in blood smears and/or tissue. Amphotericin B is the treatment of choice.

Tuberculosis

Q1 (Pretest): A 22-year-old male patient, recently incarcerated and now homeless, has received 1 week of clarithromycin for low-grade fever and left upper-lobe pneumonia. He has not improved on antibiotics, with persistent cough productive of purulent sputum and flecks of blood. Repeat chest x-ray suggests a small cavity in the left upper lobe. Which of the following statements is correct?

- A. The patient has anaerobic infection and needs outpatient clindamycin therapy.
- B. Sputum for acid fast bacilli stain and culture is required.
- C. The patient requires glove and gown contact precautions.
- D. Isoniazid to treat latent tuberculosis should be started if PPD is positive.
- E. Interferon-gamma release assay should be ordered.

Explanation: The patient is high risk for tuberculosis due to his history of incarceration and homelessness. The location of the infiltrate in the upper lobe, as well as the formation of a cavity, further suggests reactivation tuberculosis. Sputum smear and culture for AFB are mandatory. The patient requires respiratory isolation precautions in a negative pressure room, not contact precautions. Anaerobic infection would be in the differential diagnosis of upper lobe infiltrate with cavity formation, but evaluation for tuberculosis is critical because of the risk of person-to-person spread. Single-drug therapy with INH is a good prophylactic regimen but is inappropriate until active TB is excluded. Monotherapy for active TB leads to the rapid development of drug resistance. The pneumococcus rarely causes cavitory pneumonia. Interferon-gamma release assay and tuberculin skin testing with purified protein derivative are used to diagnose latent TB infection, not active TB disease like the patient presented in the vignette.

Q2 (MKSAP): A 65-year-old man recently immigrated to the United States from Africa. He is evaluated in the emergency department for a 3-week history of cough and dyspnea, now with hemoptysis. He has also had fevers, night sweats, and a 13.6-kg (30-lb) weight loss over the past 3 months. On physical examination, he is thin and coughs frequently. Temperature is 38.3°C (101.0°F), blood pressure is 100/60 mm Hg, pulse rate is 101/min, and respiration rate is 30/min. Pulmonary examination reveals crackles over the right upper lung field.

Which of the following is the most important initial infection-control option in this setting?

- A- Chest radiograph
- B- Institution of airborne precautions
- C- Sputum for acid-fast bacilli stain and culture
- D- Tuberculin skin testing

Explanation: The most important infection control measure is the institution of airborne precautions. This foreign-born patient most likely has reactivation of pulmonary tuberculosis. Tuberculosis is a communicable disease and is inhaled into the respiratory system via airborne droplets. A diagnosis of pulmonary tuberculosis should be considered in any patient with cough for longer than 3 weeks, loss of appetite, unexplained weight loss, night sweats, hoarseness, fever, fatigue, or chest pain. The index of suspicion should be substantially high for patients who have spent time in developing countries, geographic areas of the United States such as Miami or New York City, or in a correctional facility.

Initially, the most important management is protection from potential tuberculosis exposure with airborne precautions, including placement of the patient into a negative-pressure room and use of respiratory protection by health care workers. Acceptable protection includes a "respirator," which refers to an N95 or higher filtering facepiece respirator or a powered air-purifying respirator. Within health care settings, tuberculosis airborne precautions should be immediately initiated in patients with symptoms or signs consistent with tuberculosis or in those with documented infectious tuberculosis who have not completed antituberculosis treatment. Such patients should continue to be managed with airborne precautions until they are determined to be noninfectious (clinical response to a standard multidrug anti tuberculosis treatment regimen or until an alternative diagnosis is made).

Although chest radiograph and sputum acid-fast bacilli stain and culture would be performed in a setting such as this, they would not be done before implementation of effective airborne precautions to reduce the risk for transmission of infection to health care workers and other patients. Performing tuberculin skin testing can help to establish a diagnosis of tuberculosis; however, such testing would not differentiate active from latent tuberculosis and should not be performed before airborne precautions are instituted.

Tuberculosis

Q3 (MKSAP): A 45-year-old woman is evaluated because of a tuberculin skin test result of 11-mm induration discovered yesterday following a hospital pre-employment examination. She is otherwise healthy. Her HIV test result is negative. She relocated 3 months ago to the United States from El Salvador where she worked as a bank teller. She feels well and reports no fever, cough, or weight loss. She takes no medications. On physical examination, the vital signs and cardiopulmonary examinations are normal. Which of the following is the most appropriate next management step?

- A. Chest radiograph
- B. Four-drug antituberculous therapy
- C. Isoniazid therapy
- D. Clearance for employment

Explanation: The most appropriate next management step is to obtain a chest radiograph. The most common tuberculosis testing procedure is the tuberculin skin test (ST). The procedure involves injecting purified protein derivative (PPD) intradermally and assessing the skin response to the antigen load. The induration- not the erythema resulting within 48 to 72 hours is then measured. Various cutoff values are used, based on the patient's risk status, to increase the specificity of the test results. Because of her recent arrival from a high-prevalence area, an induration greater than 10 mm is considered a positive test result and is indicative of latent or active tuberculosis infection.

Consequently, this patient should receive a chest radiograph to exclude the presence of active tuberculosis disease. If radiographic results are negative, treatment for latent tuberculosis infection consisting of isoniazid therapy with vitamin B₆ (pyridoxine) supplementation should be offered. A tuberculin skin test with an induration greater than 10mm is also considered positive in the following high-risk groups: injection drug users, residents or employees of high-risk congregate settings (such as prisons and jails, nursing and homeless shelters), mycobacteriology laboratory personnel, persons with clinical conditions that put them at high risk for active disease, children younger than 4 years or children exposed to adults in high-risk categories.

Standard therapy for active tuberculosis includes at least 6 months of three- to four-drug therapy (isoniazid, rifampin, pyrazinamide, and ethambutol). This therapy would be inappropriate if the patient has a normal chest radiograph and no symptoms of active infection.

Treatment of latent tuberculosis infection substantially reduces the risk that tuberculosis infection will progress to active disease; therefore, providing no additional evaluation or therapy and clearing the patient for employment would not be appropriate.

Q4 (MKSAP): A 32-year-old healthy female physician is beginning a post graduate fellowship at a university hospital and must undergo tuberculin skin testing. She grew up in Africa and completed medical school and residency training in London. She received the bacille Calmette-Guerin (BCG) vaccine at age 6 years. Tuberculin skin testing indicates a 16-mm area of induration at the tuberculin skin testing site. Physical examination is normal.

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

- A- Chest radiograph
- B- Isoniazid, rifampin, pyrazinamide, and ethambutol
- C- Repeat tuberculin skin testing in 2 weeks
- D- No additional therapy or evaluation

Explanation: This patient should receive a chest radiograph. She received bacille Calmette-Guerin (BCG) vaccination in Africa more than 20 years ago. Receipt of this vaccination should not influence interpretation of the tuberculin skin test. BCG vaccination is used in many countries with a high prevalence of tuberculosis to prevent childhood tuberculous meningitis and miliary disease. Tuberculin reactivity caused by BCG vaccination wanes with the passage of time and is unlikely to persist more than 10 years after vaccination in the absence of Mycobacterium tuberculosis infection; therefore, tuberculin skin testing reactions in persons vaccinated with BCG should be interpreted using the same criteria as used in those who have not received the vaccine. This patient's tuberculin skin testing result should be interpreted as positive (16 mm) and is indicative of latent or active tuberculosis infection. Consequently, she should receive a chest radiograph to exclude the presence of active tuberculosis disease. If radiographic results are negative, treatment for latent tuberculosis infection consisting of isoniazid therapy should be initiated. Vitamin B₆ (pyridoxine) supplementation should also be considered as 2% of patients treated with isoniazid will develop peripheral neuropathy that is preventable with supplemental pyridoxine therapy. Supplemental pyridoxine is especially important in patients at high risk for neuropathy (those with diabetes, uremia, alcoholism, malnutrition, HIV infection, pregnancy, or seizure disorders).

Four-drug therapy (isoniazid, rifampin, pyrazinamide, and ethambutol), which is appropriate in patients with active tuberculosis, is not indicated in this patient. Treatment of latent tuberculosis infection substantially reduces the risk that tuberculosis infection will progress to active disease; therefore, providing no additional evaluation or therapy would not be appropriate. Patients exposed to tuberculosis in the distant past may have an initial negative skin test; performing a second test 7 to 21 days after the first may be helpful in reducing the false-negative response rate. Such two-step testing often "boosts" a negative test result to positive as the immune system recalls its previous exposure, thus divulging a true-positive result. Two-step testing may be particularly helpful in older persons and in distinguishing new from old exposures in annual employee-testing programs. Because this patient has a positive tuberculin skin test, repeating the tuberculin skin test is unnecessary and will not alter management.

Tuberculosis

Q5 (MKSAP): A 32-year-old man is evaluated in the office for a 2-month history of fever, night sweats, weight loss, and cough. He works as a pharmacy technician in an extended care facility for veterans. On physical examination, he has a prominent cough and appears ill. Temperature is 38°C (100.4°F); other vital signs are normal. Fine crackles are auscultated over the right posterior thorax. The remainder of the physical examination is normal. A chest radiograph shows a right upper lobe infiltrate with a small cavity. A stained sputum specimen is positive for acid-fast organisms; sputum culture results are pending. HIV testing is negative.

Which of the following is the most appropriate initial therapy for this patient?

- A. Isoniazid
- B. Isoniazid, pyrazinamide, and ethambutol
- C. Isoniazid, rifampin, pyrazinamide, and ethambutol
- D. No therapy until cultures confirm *Mycobacterium tuberculosis*

Explanation: The initial treatment of this patient with active tuberculosis must include four antituberculous drugs. Because of increasing concerns of drug resistance, all patients with suspected or confirmed tuberculosis are treated with four-drug therapy with the first-line agents isoniazid, rifampin, pyrazinamide, and ethambutol for 2 months, followed by de-escalation of antimicrobial therapy once drug susceptibility of isoniazid and rifampin is established. These agents are then continued for 7 months, totaling a 9-month treatment course.

Latent tuberculosis (positive tuberculin skin test result but no evidence of active disease) can be treated with a 9-month course of isoniazid. However, this patient has symptoms, an abnormal chest radiograph, and a positive sputum stain for acid-fast organisms, excluding latent tuberculosis. Three-drug therapy with isoniazid, pyrazinamide, and ethambutol is insufficient therapy for potentially drug-resistant tuberculosis. Therapy cannot be delayed until a definitive diagnosis of tuberculosis is made because this may take weeks, and the infection could worsen or spread to other persons in the interim.

Q6 (MKSAP): A 39-year-old woman is recently diagnosed with systemic lupus erythematosus after investigation of a fever, fatigue, arthralgia, a Coombs-positive hemolytic anemia, and leukopenia. She requires treatment with prednisone at an initial dosage of 1 mg/kg/day. She weighs 60 kg (132 lbs). Hemoglobin is 7.5 g/dL (750 g/L) and leukocyte count is 1900/uL ($1.9 \times 10^9/L$). Chest radiograph is normal. Tuberculin skin testing reveals 8 mm of induration.

Which of the following is the most appropriate next step in this patient's management?

- A- Isoniazid for 9 months
- B- Isoniazid, pyrazinamide, rifampin, and ethambutol for 12 months
- C- Rifampin for 1 month
- D- No antituberculous therapy

Explanation: Isoniazid therapy for 9 months is recommended for this patient and pyridoxine (vitamin B₆) is typically added to prevent isoniazid-induced peripheral neuropathy. This patient was screened for tuberculosis because of concerns regarding immunosuppression due to her disease and her impending therapy with prednisone. Malnutrition, immunosuppressed states, and stress are risk factors for primary progression or reactivation of quiescent tuberculosis. Various cutoff values are used, based on the patient's risk status, to increase the specificity of tuberculin skin test results. Three cut-points have been defined for a positive tuberculin reaction: 5 mm, 10 mm, and 15 mm of induration. An induration of 5 mm or more is considered positive in persons at highest risk of developing active tuberculosis (HIV-infected patients, immunosuppressed patients, persons with close contact with anyone with active tuberculosis, or those with a chest radiograph consistent with prior tuberculosis). This patient is immunosuppressed, and the 5-mm threshold for initiating therapy for latent tuberculosis applies to her. In addition, the American Thoracic Society recommends that patients who use prednisone (215 mg/d) or any other immunosuppressive agent and who have a 5 mm or larger area of induration in tuberculin skin testing begin prophylactic therapy with isoniazid. An induration of 10 mm or more is considered positive in persons who have immigrated to the United States from high-risk countries within the past 5 years; injection drug users; prisoners; health care workers; and patients with silicosis, diabetes mellitus, chronic renal failure, leukemia or lymphoma, carcinoma of the head or neck or lung, recent significant weight loss, or a history of gastrectomy or jejunioileal bypass. Healthy adolescents who are exposed to adults in high-risk categories should also be screened using this 10-mm cut-off. A cut-off point of 15 mm is used for all low-risk persons. Because this patient has no evidence of active tuberculosis, four-drug treatment for 1 year is not needed. The use of rifampin for the treatment of latent tuberculosis has not been extensively studied. Rifampin for 3 months seems to be as effective as longer treatment with isoniazid; one month of rifampin therapy is insufficient. No antituberculous therapy places the patient at risk for reactivation tuberculosis because of her immunosuppressed state and would not be appropriate.

Tuberculosis

Q7 (MKSAP): A 35-year-old woman is evaluated in the office before the initiation of infliximab for rheumatoid arthritis. She was diagnosed with rheumatoid arthritis 5 years ago, and her disease is inadequately controlled on methotrexate and naproxen. She has no other complaints or medical problems and has no risk factors for tuberculosis. She has never been screened for tuberculosis. Her physical examination is unremarkable except for changes compatible with active rheumatoid arthritis involving her hands and feet. A chest radiograph is normal. Forty-eight hours after administering the tuberculin skin test, there is 7 mm of induration at the injection site.

Initiation of which of the following is the most appropriate next step in this patient's treatment?

- A. Infliximab
- B. Isoniazid
- C. Isoniazid and infliximab
- D. Isoniazid, rifampin, pyrazinamide, and ethambutol

Explanation: The most appropriate next step in this patient's management is to initiate isoniazid. Screening for latent tuberculosis is indicated in patients prior to solid organ transplant, initiation of chemotherapy or tumor necrosis factor a (TNF-a) inhibitors, or in the presence of other major immunocompromising conditions. Adverse effects of TNF-a inhibitors include the risk for serious infection. Infliximab, adalimumab, and etanercept are associated with an increased incidence of reactivation tuberculosis, particularly extrapulmonary tuberculosis. Therefore, all patients being considered for such therapy should undergo screening for latent tuberculosis infection, which includes a full medical history, physical examination, and tuberculin skin testing with purified protein derivative (PPD) or an interferon- γ release assay. If screening is positive, appropriate treatment for latent tuberculosis is indicated before beginning therapy with a TNF- α inhibitor. The Centers for Disease Control and Prevention recommend treatment of latent tuberculosis infection for all patients planning to take a TNF-a inhibitor who have a PPD result of 5 mm or more of induration or a positive interferon- γ release assay. Therefore, the most appropriate treatment for this patient is isoniazid for 9 months. Although the most appropriate duration of treatment with isoniazid before beginning infliximab is unknown, most experts recommend at least 2 months of isoniazid therapy before initiating a TNF-a inhibitor. Four-drug antituberculous therapy is indicated for active tuberculosis when a patient's drug resistance status is unknown but is not appropriate for this patient, who has no evidence of active tuberculosis.

Q8 (500Best): A 40-year-old Indian man presents to accident and emergency with a one-month history of haemoptysis. He is a non-smoker. On further questioning, he mentions that he has also been having fevers and night sweats. Chest x-ray shows nodular shadowing in the right upper zone. What is the most likely diagnosis?

- A. Sarcoidosis
- B. Small cell carcinoma of the lung
- C. Primary tuberculosis
- D. Post-primary tuberculosis
- E. Pneumocystis pneumonia

Explanation: The symptoms of fevers, night sweats and weight loss in an Indian male are characteristic of post-primary pulmonary tuberculosis (D). Initial infection with *Mycobacterium tuberculosis* is known as primary tuberculosis (C) and is usually asymptomatic. The bacilli reaching the lung causes an initial reaction, resulting in the granulomatous lesions (with central caseating, necrotic material) walled in by surrounding epithelioid cells). These lesions may contain the tubercle bacilli, which can become reactivated later in life, usually caused by depression in host immunity, resulting in post-primary tuberculosis. Post-primary tuberculosis may manifest itself in a number of ways, the most common of which is pulmonary tuberculosis. Fever and night sweats are not a feature of sarcoidosis (A). Furthermore, the cough in sarcoid is usually dry and characteristic chest x-ray findings are bilateral hilar lymphadenopathy with pulmonary infiltrates. Small cell carcinoma of the lung (B) should be considered in patients with haemoptysis and chest x-ray changes. However, the patient is a non-smoker, making this diagnosis less likely than tuberculosis. Pneumocystis pneumonia (E) is caused by *Pneumocystis jirovecii* and is seen in immunocompromised patients. While night sweats and fevers may occur, the cough in *Pneumocystis pneumoniae* is usually non-productive. In addition, chest x-ray usually shows widespread pulmonary infiltrates. Thus, this is the incorrect answer.

Q9 (500Best): A 39-year-old Indian man presents to his GP with a 5-week history of haemoptysis, night sweats and weight loss. Which of the following investigations can be used to confirm the diagnosis of tuberculosis?

- A. Tuberculin skin testing
- B. Blood cultures
- C. Chest x-ray
- D. Ziehl–Nielsen sputum staining
- E. Computed tomography pulmonary angiogram (CTPA)

Explanation: This is a straightforward question. The diagnosis of tuberculosis is confirmed on staining of sputum with Ziehl–Nielsen staining (D) for acidfast bacilli. Tuberculin skin testing (A) is when the tuberculosis antigen is injected intradermally and the size of the reaction is measured 48–72 hours later. While this test indicates immunity to tuberculosis, it does not help confirm a diagnosis of the disease. Blood cultures (B) are not useful in the diagnosis of tuberculosis. Sputum cultures however, which are grown on Lowenstein–Jensen medium for up to 12 weeks, can confirm the diagnosis. This test has the added advantage that antibiotic sensitivity can also be determined. Chest x-ray (C) is highly useful and may demonstrate a cavitating lesion of pulmonary tuberculosis. However, a diagnosis on microscopy or culture is needed to confirm the x-ray findings. CTPA (E) is the investigation of choice in the diagnosis of pulmonary embolism.

Tuberculosis

Q10 (500Best): A 56-year-old man attends your clinic with a three-month history of a productive cough with blood-tinged sputum, following his return from India. Associated symptoms include lethargy, night sweats and decreased appetite. He is normally fit and healthy with no past medical history. On examination, the patient's chest has good air entry bilaterally with no added sounds and his temperature is 37.3°C. A sputum sample sent from the patient's GP reveals a growth of acid fast bacilli. From the list below, which is the most likely diagnosis?

- A. Pulmonary embolism
- B. Tuberculosis
- C. Bronchitis
- D. Pneumonia
- E. Bronchogenic carcinoma

Explanation: Although answers A–E can all cause haemoptysis, the clue in this question points towards the sputum analysis report which shows a growth of acid fast bacilli seen in tuberculosis (TB) (B) which can be categorized into pulmonary (75 per cent of cases) and extrapulmonary (25 per cent of cases). The gram-positive aerobic bacterium (*Mycobacterium tuberculosis*) is usually airborne, transmitted by people suffering from active pulmonary TB (e.g. via coughing, sneezing, speaking, spitting, etc.), sharing of needles among intravenous drug users, within high-risk racial or ethnic minority populations and people suffering from immunocompromised conditions. Most people (90 per cent) infected with the bacterium are asymptomatic (latent TB) with an approximately 10–15 per cent lifetime chance that the latent infection will progress to full blown TB. Once the mycobacteria reach the alveoli (primary TB), replication of the bacteria occur with formation of a Ghon focus (granuloma formation), which is usually located in the upper or lower lobes of the lung. Granuloma formation occurs (aggregation of macrophages, T- and B-lymphocytes and fibroblasts) in an attempt to kill the mycobacteria but this is not always efficient, especially with dormant bacteria. The bacteria can spread via the lymphatic system or bloodstream to other organs causing secondary TB (refer to Section 11, Infectious diseases, for further reading). Symptoms of primary pulmonary TB include chronic cough, haemoptysis, pyrexia, night sweats, loss of appetite, weight loss and lethargy. Chest x-ray may show a 'coin lesion' in the upper or lower lobes of the lung, sputum analysis may show growths of mycobacterium but can sometimes be difficult to culture in vitro and may take from 4 to 12 weeks. Interferon gamma release assays (IGRAs) can also be performed where the detection of interferon gamma release, from the blood, is tested against certain mycobacterial proteins. Tuberculin skin tests, although widely performed, produce false negatives and therefore making the IGRAs more favourable in diagnostic capability due to the reduced number of false negatives. Bronchoscopy can also be performed with BAL specimens sent to the laboratory for culture and sensitivity.

Q11 (500Best): Your clinic patient has been diagnosed with pulmonary tuberculosis (TB) following a three-month history of haemoptysis and fever. The patient is due to start on treatment and you are asked by your registrar which of the following regimes is the most suitable. The patient has no known drug allergies and, in addition, liver function tests and urea and electrolytes results are all within normal ranges. From the list below, which of the following answers is the most appropriate and recommended treatment regimen for this patient?

- A. Three months of isoniazid, rifampicin, ethambutol and pyrazinamide, followed by three months of isoniazid and rifampicin
- B. Four months of isoniazid and rifampicin, followed by two months of isoniazid, rifampicin, ethambutol and pyrazinamide
- C. Six months of isoniazid, rifampicin, ethambutol and pyrazinamide
- D. Six months of isoniazid and rifampicin
- E. Two months of isoniazid, rifampicin, ethambutol and pyrazinamide, followed by four months of isoniazid and rifampicin

Explanation: NICE guidelines (March 2006; Clinical diagnosis and management of tuberculosis and measures for its prevention and control) recommend a standard regimen of six months which includes:

- The use of four drugs initially (e.g. isoniazid, rifampicin, ethambutol and pyrazinamide) for a total of two months.
- This is then followed by four months treatment with isoniazid and rifampicin.

This regimen is viewed as first choice daily dosing and given in fixed-dose combination tablets. This standard regimen is usually used for fully drug-susceptible TB at all sites except for the CNS, all ages (children and adults) and patients with negative or positive HIV status.

Second-line drugs (e.g. amikacin, capreomycin, cycloserine, azithromycin, clarithromycin, moxifloxacin and levofloxacin) are used in special situations such as bacterial resistance and drug intolerance. For further information, please consult the NICE guidelines mentioned above.

Tuberculosis

Q12 (500Best): A 45-year-old man with diabetes, diagnosed with pulmonary TB who started treatment two months ago, presents to you with a week's history of pins and needles in his hands and feet with associated numbness. He tells you that his symptoms started since he stopped taking the vitamins given to him at the start of his TB treatment. From the list below, which of the following drugs is responsible symptoms described by the patient?

- A. Pyrazinamide
- B. Rifampicin
- C. Ethambutol
- D. Isoniazid
- E. None of the above

Explanation: This patient is suffering from peripheral neuropathy secondary to isoniazid (D) administration. Isoniazid is associated with depletion of vitamin B6 (pyridoxine) and therefore results in peripheral neuropathy. Other side effects include rash, deranged liver function (due to the fact that this drug is metabolized in the liver by acetylation and dehydrazination and converted to ammonia compounds which can cause hepatitis), CNS effects and sideroblastic anaemia.

The common side effects of pyrazinamide (A) (a pro-drug that inhibits growth of *M. tuberculosis*) include arthralgia, hepatotoxicity, gastrointestinal disturbances, rash, pruritus and sideroblastic anaemia.

Side effects of rifampicin (B) (a cytochrome P450 inducer) include hepatotoxicity, fever, gastrointestinal disturbances, rash and can also cause the urine and tears to become an orange-red colour which is considered a benign side effect.

The side effects associated with ethambutol (C) (a bacteriostatic drug that inhibits the formation of the cell wall in *M. tuberculosis*) include optic neuritis, red-green colour blindness, peripheral neuropathy and vertical nystagmus.

Although ethambutol could also be a possible answer here, the clue given in the question points to the patient having stopped taking his vitamins which are usually given in conjunction with isoniazid treatment.

Q13 (500Best): A 42-year-old diabetic Asian male complains of dysuria, increased urinary frequency and general malaise for the past six months. In the last few days, he has noticed blood in the urine. Examination of the urine shows the presence of neutrophils with no organisms detected on urine culture. The most likely diagnosis is:

- A. Tuberculosis
- B. Renal cell cancer
- C. Diabetic nephropathy
- D. Bladder cancer
- E. Nephritic syndrome

Explanation: affecting the renal system is often insidious and easily overlooked. Symptoms usually include pain affecting the back, flanks and suprapubic region. Non-specific symptoms including haematuria, increased frequency and nocturia should always be considered when urine examination reveals a pyuria in the absence of a positive culture, otherwise called a 'sterile pyuria'. A diabetic nephropathy (C) usually presents with increased proteinuria, initially as microalbuminuria which gradually progresses. Other signs can include a normocytic anaemia and raised erythrocyte sedimentation rate (ESR), patients do not typically have haematuria. The classic presentation in bladder cancer (D) is painless, gross haematuria, although any patient with unexplained haematuria should be investigated for bladder cancer. Important causative factors include smoking and exposure to aromatic amines present in dyes and paints. A sterile pyuria is not a feature in bladder cancer unless the patient had been recovering from a UTI infection that was partially treated. Renal cell carcinoma (B) usually involves the triad of haematuria, flank pain and an abdominal or flank mass with or without non-specific symptoms, such as weight loss, fever and malaise. Nephritic syndrome (E) does involve haematuria (micro- or macroscopic) but presents with hypertension and proteinuria which causes oedema. Dysuria and neutrophils are not usually associated.

Malaria & travel medicine

Q1 (500Best): A 27-year-old woman, who has recently returned from holiday in Africa, presents to accident and emergency with a 7-day history of fevers, sweats, headache, malaise and lethargy. On examination, her temperature is 39°C. Cardiorespiratory and gastrointestinal examinations are unremarkable. What is the most likely differential diagnosis?

- A- Malaria
- B- Tuberculosis
- C- Influenza
- D- Typhoid

Explanation: Malaria (A) should be considered as the most likely diagnosis of patients presenting with fever, having returned from malaria endemic areas. The most common presenting features are fever, malaise, headache, vomiting or diarrhoea. Tuberculosis (B) has a variable presentation, but most commonly presents with pulmonary symptoms such as cough, fever and sweats, malaise and weight loss. Tuberculosis is also an unlikely answer as the initial infection (primary tuberculosis) that may have been picked up during the trip is usually asymptomatic. Symptoms are usually manifestations of reactivation of primary tuberculosis (post-primary tuberculosis). Influenza (C) must be considered as a possible diagnosis – just because the patient has travelled to a malaria endemic area does not mean that they have not picked up flu! However, the travel history means that malaria is the more likely diagnosis, which requires investigation. Typhoid (D) presents with gastrointestinal symptoms, making this answer wrong. Finally, Dengue fever (E) is also transmitted by mosquitos and may present with abrupt onset fever. However, additional features include headache, facial flushing and retrobulbar pain. There may also be a generalized maculopapular rash. The absence of these features makes malaria the more likely diagnosis.

Q2 (500Best): A 25-year-old woman, who has recently returned from holiday in Africa, presents to accident and emergency with a 7-day history of fevers, sweats, headache, malaise and lethargy. On examination, her temperature is 39°C. A diagnosis of malaria is suspected. What is the investigation of choice to confirm the diagnosis?

- A- Blood cultures
- B- Full blood count
- C- Thick and thin blood films
- D- Ziehl–Nielson stain

Explanation: The diagnosis of malaria is usually confirmed with thick and thin blood films (C). Note that a negative result does not rule out malaria and usually three negative blood films are required to exclude the diagnosis. Blood cultures (A) should be sent in the pyrexial patient, but are not used to confirm the diagnosis. Similarly, a full set of blood tests, including the full blood count (B), should be sent. Full blood count may show a low haemoglobin or platelet count. However, the diagnosis of malaria cannot be confirmed on full blood count alone. Ziehl–Nielson staining (D) is used to detect acid-fast bacilli in the investigation of tuberculosis. A Paul–Bunnell (E) test is used in the investigation of infectious mononucleosis.

Q3 (500Best): A 30-year-old man, who has recently returned from holiday in Africa, presents to accident and emergency with a 7-day history of fever, sweats, malaise and lethargy. Thick and thin blood films detect Plasmodium falciparum. What is the most appropriate treatment?

- A- Acyclovir
- B- Omeprazole
- C- Chloroquine
- D- Quinine

Explanation: Falciparum malaria may develop into a potentially life-threatening disease if left untreated. Therefore, conservative management (A) is not the appropriate answer. Aciclovir (B) is a commonly used antiviral drug that is not used in the treatment of malaria. Widespread chloroquine (D) resistance means that this is not the first-line drug of choice for patient with falciparum malaria. Quinine (E) is used to treat falciparum malaria and can be given orally or intravenously. Omeprazole (C) is not used in the treatment of malaria.

Malaria & travel medicine

Q4 (500Best): A 45-year-old man presents to accident and emergency, having returned from a holiday to India a week ago. He has subsequently been unwell with nausea and reduced appetite. Over the past 2 days he has become jaundiced. He mentions that his two brothers with whom he went on holiday have also become jaundiced in the last 2 days. On examination, he is afebrile and there is a palpable liver edge. Liver function tests reveal a raised ALT, AST and bilirubin. All other blood tests are normal. What is the most likely diagnosis?

- A- Hepatitis A
- B- Hepatitis B
- C- Gilbert's syndrome
- D- Malaria

Explanation: Hepatitis A (A) is the most common type of viral hepatitis in the world. The hepatitis A virus is a picornavirus that is transmitted faeco-orally, usually due to the ingestion of contaminated water. The virus replicates in the liver and is excreted in the bile and then the faeces of infected individuals. Following infection, the viraemia causes the prodromal symptoms of fever, malaise, anorexia and nausea. Subsequently, jaundice may develop. As this happens, the spleen or liver may be palpable. The history of travel, the friends being affected and the clinical features should identify hepatitis A as the correct answer in this case. Gilbert's syndrome (D) is an inherited hyperbilirubinaemia that is completely asymptomatic and is normally detected as an incidental finding of a raised bilirubin with other blood results within the normal parameters. While the affected individuals in this question are brothers, the jaundice has been acquired, making Gilbert's syndrome the incorrect answer. Hepatitis B (B) is transmitted intravenously and is also sexually transmitted. In addition, it may also be transmitted vertically from mother to child. Clinical features may be similar to those seen in hepatitis A. In addition, extrahepatic features, such as rashes, arthralgia and glomerulonephritis, are more common. The outbreak of disease among three travellers makes hepatitis A the more likely option in this question. Hepatitis C (C) is transmitted by the intravenous route and is sexually transmitted. Acute infection is usually asymptomatic or mild, making this answer incorrect for this question. The majority of patients develop a chronic infection which predisposes to developing liver cirrhosis. The most common presenting features of malaria (E) are fevers, headache, vomiting or diarrhoea. While patients with malaria may develop jaundice and have a palpable liver, the absence of the other features of malaria, including pyrexia, make this answer incorrect.

Q5 (500Best): A 40-year-old man presents to accident and emergency having returned from a holiday to India a week ago. He has subsequently been unwell with nausea and reduced appetite. Over the past 2 days he has become jaundiced. On examination, he is afebrile and there is a palpable liver edge. Liver function tests reveal a raised ALT, AST and bilirubin. A diagnosis of hepatitis A is suspected. What is the most appropriate treatment?

- A- Intravenous hydrocortisone
- B- Pegylated interferon alpha plus ribavirin
- C- Conservative management
- D- Chloroquine

Explanation: Treatment of hepatitis A infection is with conservative management (C), using supportive measures where required. Hepatitis A usually has a self-limiting course and the majority of patients make a full recovery. A small minority of patients may develop fulminant hepatitis. Intravenous hydrocortisone (A) is not a treatment for hepatitis A. Pegylated interferon alpha plus ribavirin (B) is a treatment for hepatitis C. Acyclovir (D) is a guanosine analogue antiviral drug, but it is not used in the treatment of hepatitis A. Chloroquine (E) is an anti-malarial.

Q6 (500Best): A 19-year-old woman complains of general malaise and lethargy. She has recently started university after a gap year in the Western Cape of South Africa and is now returning home to visit her parents. She felt feverish with a headache which has become considerably worse by the afternoon with nausea and vomiting. Supine flexion of the patient's neck causes unassisted knee flexion. The most likely diagnosis is:

- A- Subarachnoid haemorrhage
- B- Encephalitis
- C- Bacterial meningitis
- D- Epstein-Barr virus (EBV)
- E- Malaria

Explanation: is often defined by the important triad of fever, headache and neck stiffness. Nausea, vomiting, acute malaise, severe headache, irritability and photophobia are also commonly associated features. These symptoms can progress within minutes and mild symptoms can be deceiving. A subarachnoid haemorrhage (A) is due to sudden arterial bleeding into the subarachnoid space and characteristically presents with a sudden, extremely severe headache. Other features associated with a SAH include nausea, vomiting and in severe cases a confused state or even coma. An encephalitis (B) describes an acute inflammation of the brain and can be similar to meningitis with symptoms of headache and fever. More prominent in this condition, however, are progressive drowsiness, confusion and in severe disease neurological problems such as seizures and hallucinations. EBV (D) often occurs in individuals under five years of age and is often asymptomatic. In older patients symptoms are more severe with fever, headache, lethargy and a painful throat and is otherwise known as infectious mononucleosis. Prominent in disease is the presentation of neck lymphadenopathy and splenomegaly. Malaria (E) typically causes a tertian or quartan fever shortly after infection and is associated with rigors and night sweats. Malaria is endemic in the northern and eastern parts of South Africa with low risk in the western and southern-most areas.

Malaria & travel medicine

Q7 (500Best): A 27-year-old woman visits her GP complaining of a fever. She returned from India almost 2 weeks ago and had felt unwell but attributed this to jet lag. After suffering from a fever she rested for 2 days and on recovering returned to work as an accountant. After another 2 days she now reports waking up at night again with a high fever, feeling drowsy and confused. On presentation she appears unwell, pale and sweaty. The most likely diagnosis is:

- A- Plasmodium falciparum
- B- Plasmodium vivax
- C- Plasmodium malariae
- D- Plasmodium ovale

Explanation: Human malaria is caused most often by one of four species of plasmodium which include P. falciparum, P. vivax, P. ovale and P. malariae. Transmission occurs through the bite of the female anopheline mosquito. The incidence of malaria is strongly affected by the appropriate environmental temperature which influences the temperature-dependent development of the parasite in the mosquito gut. Sporozoites, the infective stage of the plasmodium, accumulate in the salivary glands of the mosquito and enter the bloodstream when a human is bitten. Rapid uptake occurs in the liver whereby the sporozoites undergo rapid multiplication as merozoites. P. vivax and P. ovale often remain dormant in the liver as hypnozoites reactivating at a later date. The other infected hepatocyte cells rupture releasing merozoites into the bloodstream where they are taken up by erythrocyte cells. The merozoites again undergo cyclic multiplication transforming from merozoites to trophozoites to schizonts and then back to mature merozoites. At this stage, the erythrocytes rupture releasing new merozoites to infect fresh erythrocytes. This follows a tertian cycle (48 hours) in P. falciparum, P. vivax and P. ovale, while P. malariae follows a quartan cycle (72 hours), although this more often occurs in more long-standing disease. In P. vivax (B) or P. ovale (D), infection symptoms tend to be relatively mild, with a slower progression of anaemia and recovery within 6 weeks. However, hypnozoites may reactivate years after initial infection. P. malariae (C) is similarly mild in progression but is much more chronic and can last for years. P. falciparum (A) infection is distinguishable by its high parasitaemia which can cause mental state changes while elevated cytokines can cause end stage organ damage. P. knowlesi (E) is a new malarial infection in humans and can cause severe malarial symptoms. Its asexual cycle lasts around 24 hours with a typical fever following a quotidian/daily cycle.

Q8 (500Best): A 30-year-old man presents to accident and emergency with a 5-day history of fevers, sweats and lethargy. On further questioning, he mentions that he has just returned from a 6 week trip to Tanzania. On examination his temperature is 40°C. What is the most likely diagnosis?

- A- Influenza
- B- Malaria
- C- Typhoid
- D- Infectious mononucleosis

Explanation: should be considered as the most likely diagnosis of a patient presenting with fevers, having travelled to a malaria endemic area. Patients usually present with fever, malaise, headache, vomiting or diarrhoea. This patient should have thick and thin blood films sent off, in addition to a full set of blood tests to confirm the diagnosis of malaria. Influenza (A) is a possible differential diagnosis. However, the travel history should identify malaria as the most likely differential. Typhoid (C) usually presents with gastrointestinal symptoms. Infectious mononucleosis (D) would present with fevers, sweats and malaise. However, in addition, there is likely to be a sore throat. Examination would reveal inflamed tonsils and widespread lymphadenopathy in addition to splenomegaly and hepatomegaly. Cholera (E) presents with profuse watery diarrhoea.

Q10 (AMBOSS): A 32-year-old woman, gravida 2, para 1, at 20 weeks' gestation comes to the physician for a prenatal visit. She feels well. Her first pregnancy was uncomplicated and the child was delivered vaginally. Medications include folic acid and an iron supplement. Her temperature is 37°C (98.6°F), pulse is 98/min, respirations are 18/min, and blood pressure is 108/76 mm Hg. Abdominal examination shows a uterus that is consistent in size with a 20-week gestation. The second-trimester scan shows no abnormalities. The patient intends to travel to Mozambique next month to visit her grandmother. Which of the following drugs is most appropriate for pre-exposure prophylaxis against malaria in this patient?

- A- Doxycycline
- B- Mefloquine
- C- Primaquine
- D- Chloroquine

Explanation: Mefloquine is the prophylactic medication of choice for pregnant individuals traveling to areas where P. falciparum is endemic and resistance to chloroquine is likely. Other options such as doxycycline are contraindicated during pregnancy due to adverse effects on the fetus.

Malaria & travel medicine

Q10 (AMBOSS): A 10-year-old girl is brought to the physician because of high-grade fever, myalgia, and generalized fatigue for 3 days. She returned from a 2-week vacation to northern Brazil 4 days ago. She has received chemoprophylaxis with chloroquine. Immunizations are up-to-date. There is no family history of serious illness. She appears ill. Her temperature is 39.4°C (103°F), pulse is 110/min, and blood pressure is 94/54 mm Hg. Examination shows jaundice of the conjunctivae and skin. The abdomen is soft and nontender; the spleen is palpated 2 to 3 cm below the left costal margin. Laboratory studies show:

Hemoglobin 10.1 g/dL

Leukocyte count 4,650/mm³

Platelet count 200,000/mm³

Serum:

Glucose 56 mg/dL

Creatinine 0.8 mg/dL

Bilirubin, total 4.7 mg/dL

Direct 0.9 mg/dL

Lactate dehydrogenase 212 U/L

Which of the following is the most likely to confirm the diagnosis?

- A- Heterophile antibody test
- B- Direct antiglobulin test
- C- Thick and thin blood smea
- D- Enzyme testing

Explanation: Thick and thin blood smears are used to diagnose malaria. Thick blood smears are used as initial tests to detect the parasites, while thin blood smears confirm the diagnosis and determine the type of Plasmodium species. Malaria has an incubation period of a minimum of seven days and should be considered in individuals with fever and a history of recent travel to endemic areas (e.g., tropical Africa, Asia, and South America).

P. falciparum is resistant to chloroquine in most malaria-endemic regions except for some parts of Central America and the Caribbean. Alternatives to chloroquine for antimalarial prophylaxis include mefloquine, atovaquone-proguanil (in children weighing ≥ 5 kg), and doxycycline (in children ≥ 8 years of age).

General Infectious diseases

Q1 (Pretest): A 40-year-old female nurse was admitted to the hospital because of fever to 39.4°C (103°F). Despite a thorough workup in the hospital for over 3 weeks, no etiology has been found, and she continues to have temperature spikes greater than 38.9°C (102°F). Which of the following statements about diagnosis is correct?

- A. Chronic infection, malignancy, and collagen vascular disease are the most common explanations for this presentation.
- B. Influenza may also present in this manner.
- C. Lymphoma can be ruled out in the absence of palpable lymphadenopathy.
- D. SLE is an increasing cause for this syndrome.
- E. Factitious fever should be considered only in the patient with known psycho-pathology.

Explanation: Patients may develop fever as a result of infectious or noninfectious diseases. The term fever of unknown origin (FUO) is applied when significant fever (usually defined as $> 38.3^{\circ}\text{C}$ or $> 101^{\circ}\text{F}$) persists without a known cause after an adequate evaluation. Several studies have found the leading causes of FUO to include infections, malignancies, collagen vascular diseases, and granulomatous diseases. As the ability to more rapidly diagnose some of these diseases increases, their likelihood of causing undiagnosed persistent fever lessens. Infections such as intra-abdominal abscesses, tuberculosis, hepatobiliary disease, endocarditis (especially if the patient had previously taken antibiotics), and osteomyelitis may cause FUO. In immunocompromised patients, such as those infected with HIV, a number of opportunistic infections or lymphomas may cause fever and escape early diagnosis. Self-limited infections such as influenza should not cause fever that persists for many weeks. Neoplastic diseases such as lymphomas and some solid tumors (eg, hypernephroma and primary or metastatic disease of the liver) are associated with FUO. A number of collagen vascular diseases may cause FUO. Since conditions such as systemic lupus erythematosus are more easily diagnosed today, they are less frequent causes of this syndrome. Adult Still disease, however, is often difficult to diagnose. Other causes of FUO include granulomatous diseases (ie, giant cell arteritis, regional enteritis, sarcoidosis, and granulomatous hepatitis), drug fever, and peripheral pulmonary emboli. Factitious fever is most common among young adults employed in health-related positions. A prior psychiatric history or multiple hospitalizations at other institutions may be difficult to obtain, since these patients often skirt around the truth. Such patients may induce infections by self-injection of nonsterile material, with resultant multiple abscesses or polymicrobial infections. Alternatively, some patients may manipulate their thermometers. In these cases, a discrepancy between temperature and pulse or between oral temperature and witnessed rectal temperature will be observed.

Q2 (MKSAP): A 19-year-old female college freshman is evaluated for possible meningitis. Cerebrospinal fluid analysis shows a leukocyte count of 13,259/uL ($13,259 \times 10\%L$) with 85% neutrophils, a glucose concentration of 40 mg/dL (2.2 mmol/L) and a protein level of 230 mg/dL (2300 mg/L). Gram stain shows many neutrophils and gram-negative diplococci. The patient is placed in a private room and intravenous antibiotics are initiated.

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

- A- Face mask
- B- High-filter mask
- C- Nonsterile gloves and gown
- D- Sterile gloves and gown

Explanation: The most appropriate next step is the use of a face mask. This patient has *Neisseria meningitidis* meningitis. Droplet precautions should be initiated when this diagnosis is suspected and require that healthcare workers within 6 to 10 feet of the index patient wear a face mask. Appropriate infection control measures for all patients include hand hygiene and standard precautions.

The human nasopharynx is the only known reservoir for meningococcal meningitis. Meningococci are spread from person to person by respiratory droplets of infected nasopharyngeal secretions. Persons with significant exposure to the index patient (same household, day-care center, or anyone with direct contact with a patient's oral secretions) should receive chemoprophylaxis with appropriate antibiotics. Significant health care exposure includes personnel with potential for intimate contact (within feet) of the patient's respiratory secretions. For infection spread by direct contact with the patient (for example, vancomycin-resistant enterococci), additional infection control measures include patient placement into a private room or with those who have a similar infection and the use of nonsterile gloves and gowns for direct contact with the patient or any infective material. Airborne infection precautions are appropriate for illnesses transmitted by airborne droplet nuclei (for example, tuberculosis, measles, and varicella). Additional infection control measures include placement into a private room, typically in a pressure-negative room, and special masks with a filtering capacity of 95% of particulates (N-95 respirator or a powered air purifying respirator [PAPRI])

General Infectious diseases

Q3 (500Best): A 33-year-old man travels to South Africa to take part in a safari. On arriving, the patient takes his antimalarial tablets. A few days into his course he becomes ill complaining of shortness of breath, pallor and bloody urine. Blood tests reveal anaemia and reduced haematocrit, while a blood smear shows the presence of Heinz bodies. The most likely diagnosis is:

- A- Hereditary elliptocytosis
- B- Glucose-6-phosphate dehydrogenase deficiency
- C- Hereditary spherocytosis
- D- Autoimmune haemolytic anaemia

Explanation: This patient is most likely suffering from glucose-6-phosphate dehydrogenase deficiency (G6PD) (B). This is an important enzyme which maintains levels of glutathione, an important protective factor against oxidative stress. Exposure to drugs such as dapson or antimalarials such as primaquine can denature haemoglobin which produces Heinz bodies with precipitant haemoglobin. Hereditary elliptocytosis (A) is usually associated with iron deficiency anaemia and is not greatly impacted by an additional stressor such as oxidant influences. Hereditary spherocytosis (C) occurs due to a defect in the cell membrane protein spectrin which predisposes such cells to become accumulated within the spleen and more fragile. Autoimmune haemolytic anaemia (D) is due to autoimmune mediated attacks upon RBCs, usually through the action of autoantibodies or complement. Microangiopathic haemolytic anaemia (E) is characterized by anaemia and schistocytes on blood smear produced from the shearing of RBCs upon fibrin meshes formed in the small vasculature, which most often forms due to increased activation of the coagulatory system.

Q4(500Best): A 69-year-old man, who is recovering from an emergency laparotomy for a ruptured duodenal ulcer, develops profuse offensive diarrhoea. His postoperative course has been complicated by chest infections and he has just been stepped down onto the main wards from the intensive care unit. Stool cultures have revealed *C. difficile* toxin. What is the most appropriate treatment?

- A- Oral metronidazole
- B- Intravenous fluids
- C- Intravenous hydrocortisone
- D- Oral aciclovir

Explanation: Clostridium difficile colitis is a hospital-acquired infection that is caused by the use of broad-spectrum antibiotics. The use of these antibiotics causes eradication of normal gut flora and subsequent colonization of the gut by *C. difficile*. Patients may present with profuse, offensive diarrhoea. This is treated with a course of oral metronidazole (A). Intravenous fluids (B) may be required if the diarrhoea has resulted in significant dehydration. However, management with fluids alone does not eradicate the bacteria. Intravenous hydrocortisone (C) is not a treatment for *C. difficile* colitis. Oral acyclovir (D) is an anti-viral agent that is not useful in the treatment of *C. difficile* colitis. Oral co-amoxiclav (E) is a broad-spectrum antibiotic that may result in *C. difficile* colitis. Therefore, this is the incorrect answer.

Q5 (500Best): A 66-year-old woman presents to your clinic with a 1-week history of haemoptysis. Which of the following from the list of answers below is not a cause of haemoptysis?

- A. Pulmonary tuberculosis
- B. Bronchiectasis
- C. Aspergilloma
- D. Wegener's granulomatosis
- E. Asthma

Explanation: Pulmonary tuberculosis (A), Bronchiectasis (B), Aspergilloma (C) and Wegener's granulomatosis (D) cause haemoptysis. Other causes include:

- bronchogenic carcinoma;
- pulmonary abscess;
- farmer's lung;
- pulmonary embolus;
- Goodpasture's syndrome.

Asthma (E) does not result in patients presenting with haemoptysis.

Q6 (AMBOSS):

- A-
- B-
- C-
- D-

Explanation:

General Infectious diseases

Q6 (AMBOSS): A previously healthy 25-year-old man comes to the physician because of a 4-day history of fever, joint and body pain, diffuse headache, and pain behind the eyes. This morning he noticed that his gums bled when he brushed his teeth. He returned from a backpacking trip to the Philippines 4 days ago. His temperature is 39.4°C (103.0°F). Physical examination shows a diffuse maculopapular rash. His leukocyte count is 3,200/mm³ and platelet count is 89,000/mm³. Further evaluation shows increased serum levels of a flavivirus. Which of the following is the most likely causal pathogen?

- A- Chikungunya virus
- B- Ebola virus
- C- Hepatitis C virus
- D- Dengue virus

Explanation: This patient's symptoms are highly suspicious for dengue hemorrhagic fever, which is caused by the dengue virus, a flavivirus transmitted by the arthropod vector *Aedes aegypti*. This diagnosis is supported by the laboratory findings of Flaviviridae in the patient's serum. Diagnosis can be confirmed with nucleic acid testing, serologies, or viral culture. Treatment consists of supportive therapy, including close monitoring for possible bleeding, because dengue can be a hemorrhagic infection, especially after repeated infections involving multiple serotypes.