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A 62-year-old man comes to the emergency department due to 3 days of severe sore throat, difficulty swallowing, and hoarseness. He has no chronic medical conditions but has not seen a physician for many years. The patient received recommended childhood vaccinations but has had none since then. He is a farmer and has not traveled recently but has been in contact with migrant farmworkers. Temperature is 38.3 C (101 F), blood pressure is 110/60 mm Hg, and pulse is 116/min. Physical examination reveals pharyngeal erythema and edema with coalescing, gray exudate. Bilateral cervical lymph nodes are enlarged and tender. A rapid streptococcal test result is negative. Throat swab culture grows non-spore-forming, gram-positive rods. Which of the following is most helpful in preventing the systemic complications of this infection in this patient?

☐ A. Airway edema reduction with inhaled epinephrine

☐ B. Antibiotics administration to kill bacteria within the bloodstream

☐ C. Blunting the immune response with glucocorticoids

☐ D. Preformed antibody administration to bind bacterial product

☐ E. Vaccination with inactivated bacterial toxin

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A 62-year-old man comes to the emergency department due to 3 days of severe sore throat, difficulty swallowing, and hoarseness. He has no chronic medical conditions but has not seen a physician for many years. The patient received recommended childhood vaccinations but has had none since then. He is a farmer and has not traveled recently but has been in contact with migrant farmworkers. Temperature is 38.3 C (101 F), blood pressure is 110/60 mm Hg, and pulse is 116/min. Physical examination reveals pharyngeal erythema and edema with coalescing, gray exudate. Bilateral cervical lymph nodes are enlarged and tender. A rapid streptococcal test result is negative. Throat swab culture grows non-spore-forming, gram-positive rods. Which of the following is most helpful in preventing the systemic complications of this infection in this patient?

☐

A. Airway edema reduction with inhaled epinephrine [2%]

☐

B. Antibiotics administration to kill bacteria within the bloodstream [19%]

☐

C. Blunting the immune response with glucocorticoids [2%]

☒

D. Preformed antibody administration to bind bacterial product [45%]

☐

E. Vaccination with inactivated bacterial toxin [29%]

Omitted

Correct answer
D

45%

Answered correctly

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08/13/2018

Last Updated

Explanation

Diphtheria

Here is developed countries due to widespread vaccination

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Explanation

Diphtheria	
Epidemiology	- Rare in developed countries due to widespread vaccination - Risk: inadequate vaccination/10-year booster shot
Pathogenesis	Toxigenic <i>Corynebacterium diphtheriae</i> colonizes respiratory tract → secretes diphtheria toxin → inhibits host protein synthesis (ADP-ribosylation of EF-2) → local and systemic toxin-mediated effects
Manifestations	- Local: pseudomembranous pharyngitis, cervical LAD - Systemic: myocarditis/heart failure, neurologic toxicity - Pharyngeal edema/pseudomembrane spread can obstruct respiratory tract
Treatment	Diphtheria antitoxin (most important) - Antibiotics

EF-2 = elongation factor-2; LAD = lymphadenopathy.

Diphtheria is caused by infection with toxigenic strains of *Corynebacterium diphtheriae*, a non-spore-forming, gram-positive rod that is transmitted by aerosolized droplets. Cases are rare in the United States due to widespread vaccination efforts. However, infections can occur in those who received inadequate childhood vaccines or those who did not receive booster vaccination every 10 years.

The manifestations of diphtheria are due to the elaboration of **diphtheria toxin (DT)**, an exotoxin that **irreversibly inhibits host protein synthesis** by ADP-ribosylation of elongation factor-2. Local effects include pharyngitis and tonsillitis, often with thick, **grey-white pseudomembranes**. Systemic effects are caused by the absorption of DT into the bloodstream and include potentially life-threatening cardiac (eg, myocarditis) and neurologic complications.

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received inadequate childhood vaccines or those who did not receive booster vaccination every 10 years.

The manifestations of diphtheria are due to the elaboration of **diphtheria toxin (DT)**, an exotoxin that **irreversibly inhibits host protein synthesis** by ADP-ribosylation of elongation factor-2. Local effects include pharyngitis and tonsillitis, often with thick, **grey-white pseudomembranes**. Systemic effects are caused by the absorption of DT into the bloodstream and include potentially life-threatening cardiac (eg, myocarditis) and neurologic complications.

The primary treatment for diphtheria is the urgent administration of **diphtheria antitoxin**, which contains **preformed, neutralizing antibodies** that binds and inactivates circulating toxin. Because it cannot inhibit the toxin that has already entered cells, it should be administered as soon as possible. Antibiotic therapy (eg, penicillin, erythromycin) is also given to reduce continued elaboration of DT from the nasopharyngeal infection.

(Choice A) Inhaled, racemic epinephrine can be used in the treatment of croup, which usually presents with cough, inspiratory stridor, and/or hoarseness. Epinephrine could reduce airway swelling in patients with diphtheria, but it would not inhibit the local and systemic effects of the toxin.

(Choice B) *C diphtheriae* is noninvasive and does not typically enter the bloodstream. Although antibiotics are administered in acute infection, this component of therapy is less important than providing antitoxin to neutralize DT.

(Choice C) Corticosteroids are sometimes used in the treatment of epiglottitis to reduce airway inflammation and limit the risk of airway compromise. Epiglottitis manifestations typically include stridor, drooling, respiratory distress, and the assumption of the "tripod" position. Most cases are caused by infection with *Haemophilus influenzae* type B in unvaccinated individuals.

(Choice E) Active immunization with the diphtheria toxoid (given as part of the childhood DTaP vaccine) prevents diphtheria. Diphtheria toxoid can also be given as part of tetanus boosters in adults. However, the immune response to vaccination is slow; in undervaccinated patients who are acutely ill, administration of preformed antitoxin antibodies is preferred.

Educational objective:

The primary treatment for diphtheria is diphtheria antitoxin (passive immunization), which inactivates circulating toxin. Antibiotics should also be administered to reduce continued production of toxin.

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2/5/2019



A 22-year-old woman comes to the office for a routine prenatal visit. She is 16 weeks pregnant with her first child. Two months ago, she had a mononucleosis-like illness with fever, myalgia, and fatigue, and she was diagnosed with cytomegalovirus infection. The patient recovered with symptomatic treatment and is currently asymptomatic. Her other medical problems include episodic migraine headaches and benign choroidal nevus. She takes prenatal vitamins and does not use tobacco, alcohol, or illicit drugs. The patient has a family history of hypertension and glaucoma. Physical examination findings and prenatal ultrasound are unremarkable. This patient's unborn infant is at greatest risk for which of the following eye conditions?

- ☐ A. Chorioretinitis
- ☐ B. Choroidal nevus
- ☐ C. Congenital cataract
- ☐ D. Glaucoma
- ☐ E. Inclusion conjunctivitis
- ☐ F. Retinitis pigmentosa
- ☐ G. Retinoblastoma

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A 22-year-old woman comes to the office for a routine prenatal visit. She is 16 weeks pregnant with her first child. Two months ago, she had a mononucleosis-like illness with fever, myalgia, and fatigue, and she was diagnosed with cytomegalovirus infection. The patient recovered with symptomatic treatment and is currently asymptomatic. Her other medical problems include episodic migraine headaches and benign choroidal nevus. She takes prenatal vitamins and does not use tobacco, alcohol, or illicit drugs. The patient has a family history of hypertension and glaucoma. Physical examination findings and prenatal ultrasound are unremarkable. This patient's unborn infant is at greatest risk for which of the following eye conditions?

- ☒ A. Chorioretinitis [60%]
- ☐ B. Choroidal nevus [2%]
- ☐ C. Congenital cataract [18%]
- ☐ D. Glaucoma [3%]
- ☐ E. Inclusion conjunctivitis [8%]
- ☐ F. Retinitis pigmentosa [5%]
- ☐ G. Retinoblastoma [1%]

Omitted

Correct answer
A



60%
Answered correctly



6 Seconds
Time Spent

01/21/2019
Last Updated

Explanation

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Explanation

Up to 5% of women develop a **primary cytomegalovirus (CMV) infection** (typically a mononucleosis-like illness with fever and mild hepatitis) during pregnancy. Vertical transmission to the fetus occurs in approximately one-third of cases, with the highest risk of transmission occurring in the first trimester. **CMV-related complications** observed in infants exposed to the virus **in utero** include **chorioretinitis** (most common eye-related problem), sensorineural deafness, seizures, jaundice, hepatomegaly, splenomegaly, and microcephaly.

(Choice B) Choroidal nevus (eye freckle) is a nonhereditary, usually benign pigmented area underneath the retina and is not associated with in-utero CMV infection.

(Choice C) Congenital cataract can be seen with in-utero rubella infection.

(Choice D) Glaucoma can be present at birth and may be primary or secondary (eg, tumor). However, it is not a known complication of CMV infection.

(Choice E) Inclusion conjunctivitis is seen with *Chlamydia trachomatis* infection of the newborn.

(Choice F) Retinitis pigmentosa is an inherited degenerative eye disease that leads to severe vision impairment and is not a complication of in-utero CMV infection.

(Choice G) Retinoblastoma is the most common malignant eye cancer in children and is caused by a chromosomal mutation that is hereditary or sporadic. CMV infection in utero is not associated with causing retinoblastoma.

Educational objective:

The most common eye-related complication of congenital cytomegalovirus infection is chorioretinitis.

References

- Ocular abnormalities in congenital cytomegalovirus infection.

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A 54-year-old man is brought to the emergency department due to a week of progressive headaches and confusion. He was treated for viral esophagitis 6 months ago and *Pneumocystis pneumonia* 2 months ago. Temperature is 38 C (100.4 F), blood pressure is 142/86 mm Hg, and pulse is 64/min. The patient is lethargic and oriented to person and place only. CT scan of the head shows a mildly increased ventricle size but no other abnormalities. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein concentration and pleocytosis. The latex agglutination test is positive for soluble polysaccharide antigen. Light microscopy of this patient's cerebrospinal fluid is most likely to reveal which of the following?

☐

A. Budding yeast

☐

B. Germ tubes

☐

C. Nonseptate hyphae

☐

D. Spherules with endospore

☐

E. Sporangium

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A 54-year-old man is brought to the emergency department due to a week of progressive headaches and confusion. He was treated for viral esophagitis 6 months ago and *Pneumocystis pneumonia* 2 months ago. Temperature is 38 C (100.4 F), blood pressure is 142/86 mm Hg, and pulse is 64/min. The patient is lethargic and oriented to person and place only. CT scan of the head shows a mildly increased ventricle size but no other abnormalities. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein concentration and pleocytosis. The latex agglutination test is positive for soluble polysaccharide antigen. Light microscopy of this patient's cerebrospinal fluid is most likely to reveal which of the following?

- ☒ A. Budding yeast [42%]
- ☐ B. Germ tubes [7%]
- ☐ C. Nonseptate hyphae [10%]
- ☐ D. Spherules with endospore [25%]
- ☐ E. Sporangium [14%]

Omitted

Correct answer
A



42%
Answered correctly



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09/09/2018
Last Updated

Explanation

Cryptococcus neoformans

Veget with a polysaccharide capsule

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Explanation

Cryptococcus neoformans	
Morphology	• Yeast with a polysaccharide capsule • Round/oval cells with narrow-based buds
Epidemiology	• Soil and pigeon droppings • Respiratory transmission • Opportunistic infection in patients with AIDS (CD4 <100/mm³)
Infection	• Meningoencephalitis: Progressive headache, fever, confusion • Possible disseminated disease
Diagnosis	• India ink stain of cerebrospinal fluid • Latex agglutination of cerebrospinal fluid • Culture using Sabouraud agar
Treatment	• Amphotericin B and flucytosine (induction) • Fluconazole (maintenance)

This patient's opportunistic infections (viral esophagitis, *Pneumocystosis pneumonia*) raise suspicion for **untreated AIDS**. He now has headache, fever, confusion, and polysaccharide antigens in the cerebrospinal fluid (CSF) indicating likely **cryptococcal meningitis**. This opportunistic infection is caused by *Cryptococcus neoformans*, a yeast with a thick **polysaccharide capsule**. Diagnosis is often made by identifying polysaccharide (cryptococcal) antigens in the CSF using latex agglutination. Round or oval **budding yeast** can also be visualized with **India ink stain**. Most patients have **elevated opening pressures** on lumbar puncture due to increased vascular permeability secondary to inflammation and/or yeasts obstructing CSF outflow from the arachnoid villi.

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Fluconazole (maintenance)

This patient's opportunistic infections (viral esophagitis, *Pneumocystosis* pneumonia) raise suspicion for **untreated AIDS**. He now has headache, fever, confusion, and polysaccharide antigens in the cerebrospinal fluid (CSF) indicating likely **cryptococcal meningitis**. This opportunistic infection is caused by *Cryptococcus neoformans*, a yeast with a thick **polysaccharide capsule**. Diagnosis is often made by identifying polysaccharide (cryptococcal) antigens in the CSF using latex agglutination. Round or oval **budding yeast** can also be visualized with **India ink stain**. Most patients have **elevated opening pressures** on lumbar puncture due to increased vascular permeability secondary to inflammation and/or yeasts obstructing CSF outflow from the arachnoid villi.

(Choice B) *Candida albicans* forms germ tubes (true hyphae) if incubated in 37 C (98.6 F) serum for 3 hours. This test helps differentiate *C. albicans* from other *Candida* species. *C. albicans* meningitis is extremely rare (even in patients with HIV) and would not be associated with a positive polysaccharide antigen.

(Choice C) *Mucor* and *Rhizopus* species are characterized by **nonseptate hyphae** that branch at wide angles. These fungi cause severe infections of the paranasal sinuses (mucormycosis) in patients who are immunosuppressed (eg, diabetes mellitus).

(Choice D) *Coccidioides immitis* is associated with the formation of **spherules**, which then rupture to release endospores. This fungus primarily causes community-acquired pneumonia in endemic areas (eg, Arizona desert); central nervous system infection is quite rare and would not be associated with a positive polysaccharide antigen.

(Choice E) Mold fungi (eg, *Rhizopus*) form **sporangia**, which produce and contain spores. *Cryptococcus* is a yeast and does not reproduce with sporangia.

Educational objective:

Cryptococcus neoformans causes meningoencephalitis in patients with untreated AIDS. Diagnosis can be made by detecting the polysaccharide capsule in cerebrospinal fluid using the latex agglutination test. India ink staining of cerebrospinal fluid is also used for diagnosis and can demonstrate round or oval budding yeast.

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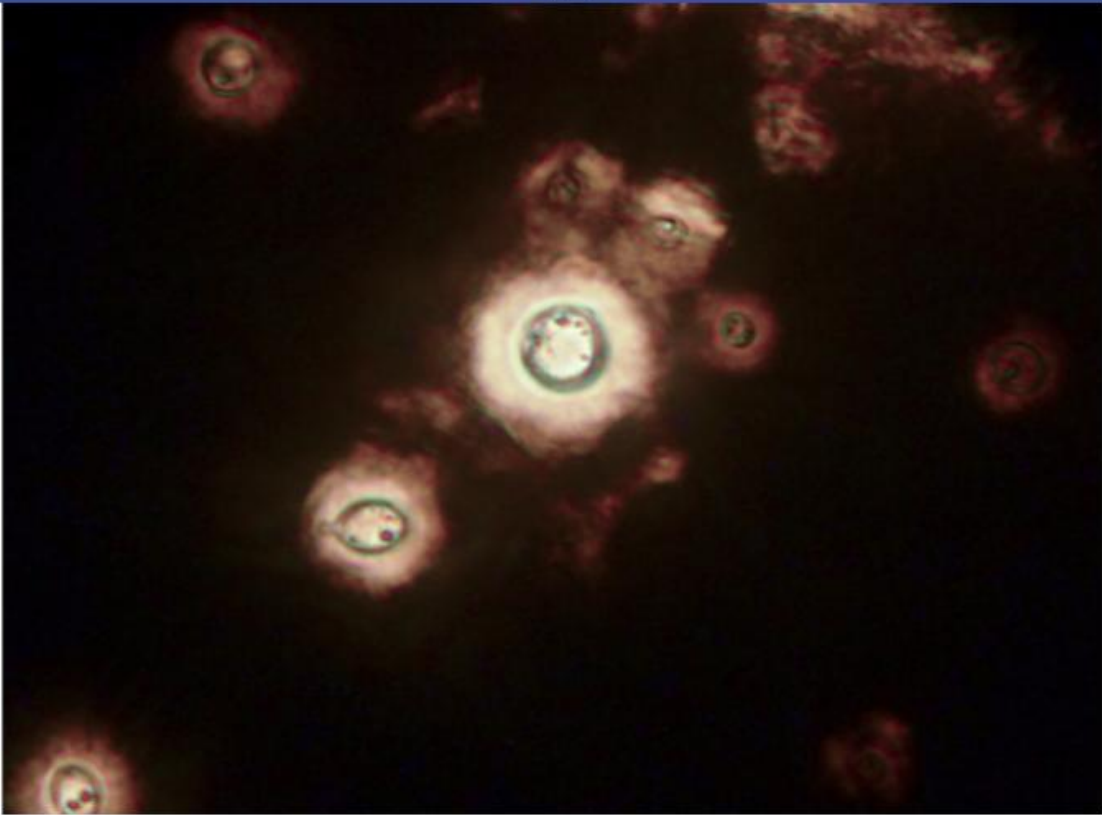
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• Fluconazole (maintenance)

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A 70-year-old man is hospitalized due to abrupt-onset, severe left thigh pain with no preceding trauma. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, pulse is 120/min, and respirations are 24/min. Left thigh examination shows diffuse swelling with dusky skin discoloration and several bullae filled with hemorrhagic fluid. There is significant tenderness and crepitus on palpation. Gram staining of the bullae fluid reveals numerous gram-positive rods, and subsequent culture grows *Clostridium septicum*. Which of the following is the greatest risk factor for this patient's current condition?

☐ A. Colonic malignancy

☐ B. Hemochromatosis

☐ C. Indwelling vascular catheter

☐ D. Multiple myeloma

☐ E. Recent antibiotic use

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2/5/2019

A 70-year-old man is hospitalized due to abrupt-onset, severe left thigh pain with no preceding trauma. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, pulse is 120/min, and respirations are 24/min. Left thigh examination shows diffuse swelling with dusky skin discoloration and several bullae filled with hemorrhagic fluid. There is significant tenderness and crepitus on palpation. Gram staining of the bullae fluid reveals numerous gram-positive rods, and subsequent culture grows *Clostridium septicum*. Which of the following is the greatest risk factor for this patient's current condition?

- ☒ A. Colonic malignancy [19%]
- ☐ B. Hemochromatosis [11%]
- ☐ C. Indwelling vascular catheter [32%]
- ☐ D. Multiple myeloma [10%]
- ☐ E. Recent antibiotic use [26%]

Omitted

Correct answer
A



19%
Answered correctly



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Time Spent



10/20/2018
Last Updated

Explanation

Clostridium septicum is a spore-forming, exotoxin-producing, gram-positive bacterium that is a normal commensal of the gastrointestinal tract in humans. Although the organism is largely nonpathogenic, breakdowns in the gastrointestinal mucosa can lead to invasion with subsequent **hematogenous dissemination** to healthy muscle tissue, resulting in **spontaneous gas gangrene** (nontraumatic). Manifestations include **rapid-onset muscle pain**, fever, **hemorrhagic bullae** with dusky surrounding skin, and tissue edema/crepitus. Urgent antibiotics and surgery are

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Correct answer

A

19%

Answered correctly

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10/20/2018

Last Updated

Explanation

Clostridium septicum is a spore-forming, exotoxin-producing, gram-positive bacterium that is a normal commensal of the gastrointestinal tract in humans. Although the organism is largely nonpathogenic, breakdowns in the gastrointestinal mucosa can lead to invasion with subsequent **hematogenous dissemination** to healthy muscle tissue, resulting in **spontaneous gas gangrene** (nontraumatic). Manifestations include **rapid-onset muscle pain**, fever, **hemorrhagic bullae** with dusky surrounding skin, and tissue edema/**crepitus**. Urgent antibiotics and surgery are required, as the infection is often fatal even with early treatment.

Most cases of spontaneous gas gangrene are triggered by an underlying **colonic malignancy**, which creates a portal of entry for the bacteria. Inflammatory bowel disease and immunosuppression are also risk factors. Unlike *C septicum* gas gangrene, *C perfringens* gas gangrene is usually associated with preceding trauma.

(Choice B) Patients with hemochromatosis are at increased risk for fulminant *Vibrio vulnificus* infections (the organism is dependent on free iron for growth). Although *V vulnificus* can cause rapid-onset sepsis and bullous skin lesions, it is a gram-negative bacterium. In addition, most infections occur due to shellfish consumption or wound contamination with seawater.

(Choice C) Indwelling vascular catheters increase the risk for candidemia, which can cause sepsis, abscesses, and pustular skin lesions on an erythematous base.

(Choice D) Multiple myeloma impairs lymphocyte function and reduces the ability of plasma cells to generate normal immunoglobulin, which increases risk of infection. Pneumonia due to *Streptococcus pneumoniae* and *Haemophilus influenzae* and urinary infections due to *Escherichia coli* are most common.

(Choice E) Recent antibiotic use increases the risk of *C difficile* infection, which usually presents with diarrhea, fever, and abdominal pain.

Educational objective:

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Clostridium septicum is a spore-forming, exotoxin-producing, gram-positive bacterium that is a normal commensal of the gastrointestinal tract in humans. Although the organism is largely nonpathogenic, breakdowns in the gastrointestinal mucosa can lead to invasion with subsequent **hematogenous dissemination** to healthy muscle tissue, resulting in **spontaneous gas gangrene** (nontraumatic). Manifestations include **rapid-onset muscle pain**, fever, **hemorrhagic bullae** with dusky surrounding skin, and tissue edema/**crepitus**. Urgent antibiotics and surgery are required, as the infection is often fatal even with early treatment.

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(Choice E) Recent antibiotic use increases the risk of *C difficile* infection, which usually presents with diarrhea, fever, and abdominal pain.

Educational objective:

Clostridium septicum is a spore-forming, exotoxin-producing, gram-positive organism that is the most common cause of spontaneous gas gangrene (eg, rapid-onset pain, hemorrhagic bullae, tissue crepitus). Underlying colonic malignancy is the greatest risk factor for infection.

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A 34-year-old man came to the office due to white plaques on his buccal mucosa that he incidentally discovered while brushing his teeth. After appropriate workup, he was found to be HIV positive, with a CD4+ T lymphocyte count of 280/mm³. He was referred to an infectious diseases specialist for follow-up but was noncompliant with appointments. The patient returns 3 years later due to several months of pain and itching in the perirectal area. He also has intermittent rectal bleeding and often sees bright red blood on the tissue after wiping. The patient did not seek medical care because he thought he had hemorrhoids. On examination, a single, hard mass with superficial ulceration measuring approximately 2x2 cm is noted in the anal canal. No hemorrhoids are present. There is no palpable regional lymphadenopathy. Which of the following pathogens is most likely responsible for this patient's current anal pathology?

☐ A. Adenovirus

☐ B. *Candida albicans*

☐ C. *Chlamydia trachomatis*

☐ D. Cytomegalovirus

☐ E. Epstein-Barr virus

☐ F. Herpes simplex virus type 2

☐ G. Human papillomavirus

Submit

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A 34-year-old man came to the office due to white plaques on his buccal mucosa that he incidentally discovered while brushing his teeth. After appropriate workup, he was found to be HIV positive, with a CD4+ T lymphocyte count of 280/mm³. He was referred to an infectious diseases specialist for follow-up but was noncompliant with appointments. The patient returns 3 years later due to several months of pain and itching in the perirectal area. He also has intermittent rectal bleeding and often sees bright red blood on the tissue after wiping. The patient did not seek medical care because he thought he had hemorrhoids. On examination, a single, hard mass with superficial ulceration measuring approximately 2x2 cm is noted in the anal canal. No hemorrhoids are present. There is no palpable regional lymphadenopathy. Which of the following pathogens is most likely responsible for this patient's current anal pathology?

☐

A. Adenovirus [0%]

☐

B. *Candida albicans* [5%]

☐

C. *Chlamydia trachomatis* [2%]

☐

D. Cytomegalovirus [7%]

☐

E. Epstein-Barr virus [4%]

☐

F. Herpes simplex virus type 2 [10%]

☒

G. Human papillomavirus [67%]

Omitted

Correct answer G

67%

Answered correctly

5 Seconds

Time Spent

11/09/2018

Last Updated

Explanation

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This patient with HIV likely has **anal squamous cell carcinoma** given the duration of pain, itching, and rectal bleeding in addition to the visible **ulcerative mass** (anal cancers are ulcerative in >50% of cases). Anogenital squamous cell carcinomas and their precursors, squamous intraepithelial lesions, have been linked to **human papillomavirus (HPV)** infection. Intraepithelial neoplasias of the cervix, vulva, penis, and anus have a well-documented association with HPV types 16 and 18. A strong correlation between HPV and invasive carcinoma has been established for cervical cancer.

Immunodeficiency states (eg, AIDS) increase host susceptibility to HPV infection and more severe infection. **HIV**-positive men who have sex with men are at increased risk of developing anal squamous cell carcinoma (anal intercourse is hypothesized to be related), and HIV-positive women are more prone to developing cervical squamous cell carcinoma.

(Choice A) Adenoviruses can cause severe upper respiratory illnesses, pneumonia, and disseminated infection in immunosuppressed patients.

(Choices B and E) HIV-positive patients often experience reactivation of latent Epstein-Barr virus (EBV) infection. EBV replication in such patients is associated with certain lymphomas and with oral hairy leukoplakia, which typically manifests as white plaques on the lateral tongue margins (this patient's white buccal plaques on initial diagnosis were more likely thrush due to *Candida*).

(Choice C) *Chlamydia trachomatis* causes lymphogranuloma venereum (LGV), characterized by an ulcerative or vesicular lesion on the external genitalia followed by significant regional lymphadenopathy. Proctitis with tenesmus and bloody discharge can be seen with both LGV and anal carcinoma; however, LGV has a less indolent clinical course, and painful lymphadenopathy is a cardinal feature.

(Choice D) HIV-positive patients with CD4+ cell counts <100/mm³ are at significantly increased risk of developing cytomegalovirus (CMV) infection, which most frequently causes retinitis in AIDS patients. CMV involvement of the gastrointestinal tract typically manifests as esophageal ulcers or colitis, not anal masses.

(Choice F) Although AIDS increases the prevalence of herpes simplex virus type 2 (HSV-2) infection and the frequency of symptomatic genital herpes recurrences, HSV-2 is not typically associated with anogenital carcinoma. A large, hard mass is not characteristic of herpetic lesions (classically painful vesicles or ulcers).

Educational objective:

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men are at increased risk of developing anal squamous cell carcinoma (anal intercourse is hypothesized to be related), and HIV-positive women are more prone to developing cervical squamous cell carcinoma.

(Choice A) Adenoviruses can cause severe upper respiratory illnesses, pneumonia, and disseminated infection in immunosuppressed patients.

(Choices B and E) HIV-positive patients often experience reactivation of latent Epstein-Barr virus (EBV) infection. EBV replication in such patients is associated with certain lymphomas and with oral hairy leukoplakia, which typically manifests as white plaques on the lateral tongue margins (this patient's white buccal plaques on initial diagnosis were more likely thrush due to *Candida*).

(Choice C) *Chlamydia trachomatis* causes lymphogranuloma venereum (LGV), characterized by an ulcerative or vesicular lesion on the external genitalia followed by significant regional lymphadenopathy. Proctitis with tenesmus and bloody discharge can be seen with both LGV and anal carcinoma; however, LGV has a less indolent clinical course, and painful lymphadenopathy is a cardinal feature.

(Choice D) HIV-positive patients with CD4+ cell counts $<100/\text{mm}^3$ are at significantly increased risk of developing cytomegalovirus (CMV) infection, which most frequently causes retinitis in AIDS patients. CMV involvement of the gastrointestinal tract typically manifests as esophageal ulcers or colitis, not anal masses.

(Choice F) Although AIDS increases the prevalence of herpes simplex virus type 2 (HSV-2) infection and the frequency of symptomatic genital herpes recurrences, HSV-2 is not typically associated with anogenital carcinoma. A large, hard mass is not characteristic of herpetic lesions (classically painful vesicles or ulcers).

Educational objective:

Human papillomavirus (HPV) types 16 and 18 are strongly associated with anal and cervical squamous cell carcinoma. HIV infection increases the prevalence of HPV infection and the risk of anal carcinoma; this risk is further augmented in men who have sex with men.

References

- [Risk of human papillomavirus-associated cancers among persons with AIDS.](#)
- [Anal cancer: an overview.](#)

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A 6-year-old boy is brought to the emergency department by his parents with a 2-day history of fever and headaches. The parents report that he vomited once this afternoon. All of his vaccinations are up-to-date and he has no significant past medical history. His temperature is 38.7 C (102 F). Examination shows mild pharyngeal erythema in addition to neck stiffness. Cerebrospinal fluid analysis reveals the following:

Glucose	65 mg/dL
Protein	85 mg/dL
Leukocytes	300/mm ³
Differential	
Neutrophils	15%
Lymphocytes	85%
Red blood cells	none

Which of the following infectious agents is most likely to have caused this patient's illness?

☐

A. Coronavirus

☐

B. *Cryptococcus neoformans*

☐

C. Enterovirus

☐

D. Mumps virus

☐

E. *Neisseria meningitidis*

☐

F. *Streptococcus agalactiae*

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Glucose	65 mg/dL
Protein	85 mg/dL
Leukocytes	300/mm ³
Differential	
Neutrophils	15%
Lymphocytes	85%
Red blood cells	none

Which of the following infectious agents is most likely to have caused this patient's illness?

- ☐ A. Coronavirus
- ☐ B. *Cryptococcus neoformans*
- ☐ C. Enterovirus
- ☐ D. Mumps virus
- ☐ E. *Neisseria meningitidis*
- ☐ F. *Streptococcus agalactiae*
- ☐ G. *Streptococcus pneumoniae*

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Protein	85 mg/dL
Leukocytes	300/mm ³
Differential	
Neutrophils	15%
Lymphocytes	85%
Red blood cells	none

Which of the following infectious agents is most likely to have caused this patient's illness?

☐ A. Coronavirus [13%]

☐ B. *Cryptococcus neoformans* [4%]

☒ C. Enterovirus [56%]

☐ D. Mumps virus [7%]

☐ E. *Neisseria meningitidis* [6%]

☐ F. *Streptococcus agalactiae* [1%]

☐ G. *Streptococcus pneumoniae* [8%]

Omitted

Correct answer

56%

Answered correctly

9 Seconds

Time Spent

10/05/2018

Last Updated

Block Time Remaining: 00:01:00

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This child has clinical evidence of meningitis (fever, headache, vomiting, stiff neck). Analysis of the cerebrospinal fluid (CSF) shows **normal** glucose, marginally elevated protein, and pleocytosis with a **lymphocytic** predominance. This pattern suggests **aseptic meningitis**, which is usually viral in etiology. **Enteroviruses** (eg, coxsackievirus, echovirus, poliovirus) are responsible for >90% of cases. Clinical symptoms are similar to meningitis caused by bacterial or fungal pathogens. However, aseptic meningitis is generally **less severe**, and focal neurologic signs, seizures, and alterations in mental status are absent. The presence of any of these should prompt consideration of other conditions, including bacterial meningitis, encephalitis, and intracranial hemorrhage. A negative Gram stain and **sterile culture** will further support the diagnosis of aseptic meningitis.

(Choice A) Coronavirus is a common cause of cold symptoms. It is not a common cause of viral meningitis.

(Choice B) *Cryptococcus neoformans* is a common cause of meningitis in immunocompromised patients (eg, AIDS patients). The diagnosis is made by testing for cryptococcal antigens or by identifying India ink-stained organisms in the CSF.

(Choice D) The mumps virus can cause aseptic meningitis, but this would be extremely unlikely in this fully immunized child. Meningitis caused by mumps is accompanied by parotitis in 50% of cases.

(Choices E, F, and G) *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common causes of bacterial meningitis in adults; *S agalactiae* (group B *Streptococcus*) is the most common cause of meningitis in neonates. Bacterial and viral meningitis both cause fever, nuchal rigidity, and headache. However, this patient's CSF analysis is more suggestive of aseptic meningitis.

Educational objective:

Fever; meningeal signs (eg, headache, neck stiffness); and cerebrospinal fluid that shows lymphocytic pleocytosis, a modestly elevated protein level, and normal glucose are suggestive of aseptic meningitis. Enteroviruses are the most common cause of aseptic meningitis.

References

- Viral meningitis.
- Meningitis.

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A 22-year-old woman comes to the emergency department with dysuria, vulvar pain, and itching. She has felt feverish and fatigued for the last few days. She has a new sexual partner and has been using a hormonal vaginal ring to prevent pregnancy. The patient had chlamydia 3 years ago and was treated with antibiotics. Physical examination reveals inguinal lymphadenopathy and tender vesicular lesions covering both labia majora and the perineum. This patient's infection can lead to which of the following conditions?

☐ A. Facial nerve palsy

☐ B. Locomotor ataxia

☐ C. Postherpetic neuralgia

☐ D. Recurrent genital ulcers

☐ E. Squamous cell vulvar carcinoma

Submit

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Text Zoom

A 22-year-old woman comes to the emergency department with dysuria, vulvar pain, and itching. She has felt feverish and fatigued for the last few days. She has a new sexual partner and has been using a hormonal vaginal ring to prevent pregnancy. The patient had chlamydia 3 years ago and was treated with antibiotics. Physical examination reveals inguinal lymphadenopathy and tender vesicular lesions covering both labia majora and the perineum. This patient's infection can lead to which of the following conditions?

☐

A. Facial nerve palsy [1%]

☐

B. Locomotor ataxia [2%]

☐

C. Postherpetic neuralgia [16%]

☒

D. Recurrent genital ulcers [68%]

☐

E. Squamous cell vulvar carcinoma [10%]

Omitted

Correct answer
D

68%

Answered correctly

3 Seconds

Time Spent

08/09/2018

Last Updated

Explanation

Herpes is one of the most common **sexually transmitted** diseases. This patient's systemic symptoms (eg, **fever**, myalgia); **inguinal lymphadenopathy**; and itchy, painful, vesicular genital rash are typical of **primary genital herpes**. Genital herpes is most commonly caused by **herpes virus type 2 (HSV-2)**. The characteristic rash on the genitalia or **buttocks** occurs in stages - **vesicles**, **ulcers**, and then **crusting**.

Following infection, HSV lies dormant in the sacral dorsal root ganglia and can be reactivated to cause **recurrent genital lesions**. Recurrence

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Herpes is one of the most common **sexually transmitted** diseases. This patient's systemic symptoms (eg, **fever**, myalgia); **inguinal lymphadenopathy**; and itchy, painful, vesicular genital rash are typical of **primary genital herpes**. Genital herpes is most commonly caused by **herpes virus type 2 (HSV-2)**. The characteristic rash on the genitalia or **buttocks** occurs in stages - **vesicles**, **ulcers**, and then **crusting**.

Following infection, HSV lies dormant in the sacral dorsal root ganglia and can be reactivated to cause **recurrent genital lesions**. Recurrence tends to be localized and less severe due to humoral immunity from prior infection. Patients are more contagious during a recurrence, and barrier contraception prevents spread.

(Choice A) Facial nerve palsy can be a neurological manifestation of Lyme disease (caused by the spirochete *Borrelia burgdorferi*) or HSV-1. HSV-1 typically causes oral rather than genital vesicles. Lyme disease typically causes fatigue, anorexia, headache, and occasional fever, without a vesicular rash.

(Choice B) Untreated syphilis can infect the dorsal roots of the spinal column and lead to tertiary neurosyphilis characterized by tabes dorsalis (locomotor ataxia) and general paresis. Primary syphilis typically presents with a single painless genital lesion (**chancere**) after initial infection with *Treponema pallidum* spirochete.

(Choice C) Varicella zoster virus also invades the dorsal root sensory ganglia, and reactivation from the dorsal root ganglia causes herpes zoster (eg, shingles). A complication of shingles is postherpetic neuralgia (persistent pain after resolution of lesions). Typical presentation of herpes zoster is a painful vesicular rash in a dermatomal distribution without systemic involvement, in contrast to this patient with bilateral vesicular lesions and fever.

(Choice E) Human papillomavirus is an oncogenic double-stranded DNA virus that exclusively infects the epithelial cells, predisposing to the development of cervical and vulvar carcinoma. Warts are the most common skin manifestation.

Educational objective:

Primary infection with herpes simplex virus type 2 (HSV-2) typically presents with fever and a painful vesicular genital rash. HSV-2 primarily infects the sacral dorsal root ganglia and can be reactivated to cause recurrent genital lesions.

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Question Id: 11514



A 25-year-old man with multiple injuries sustained in a motorcycle accident develops osteomyelitis while in the hospital. The organism is identified as methicillin-sensitive *Staphylococcus aureus*, and antibiotics are started. Which of the following is the most important measure to reduce the risk of transmission to other patients?

- ☐ A. Contact precautions
- ☐ B. Hand hygiene
- ☐ C. Isolation precautions
- ☐ D. Masks
- ☐ E. Restricting visitors

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Text Zoom

A 25-year-old man with multiple injuries sustained in a motorcycle accident develops osteomyelitis while in the hospital. The organism is identified as methicillin-sensitive *Staphylococcus aureus*, and antibiotics are started. Which of the following is the most important measure to reduce the risk of transmission to other patients?

A. Contact precautions [16%]

✓

B. Hand hygiene [69%]

C. Isolation precautions [6%]

D. Masks [6%]

E. Restricting visitors [0%]

Omitted

Correct answer B

69%

Answered correctly

3 Seconds

Time Spent

01/07/2019

Last Updated

Explanation

Hand hygiene by health care workers is the single most important measure to reduce the risk of transmission of microorganisms between patients. It includes handwashing with soap and water or using alcohol-based hand sanitizers that do not require water. Proper handwashing technique involves washing all surfaces of the hands and fingers with soap and water for at least 15 seconds, drying with a disposable towel, and using the towel to turn off the faucet. Alcohol-based hand sanitizer should cover all surfaces of the hands and fingers and be allowed to dry. The World Health Organization recommends handwashing before and after touching a patient, before aseptic procedures, and after contact with body fluids or patient surroundings.

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Explanation

Hand hygiene by health care workers is the single most important measure to reduce the risk of transmission of microorganisms between patients. It includes handwashing with soap and water or using alcohol-based hand sanitizers that do not require water. Proper handwashing technique involves washing all surfaces of the hands and fingers with soap and water for at least 15 seconds, drying with a disposable towel, and using the towel to turn off the faucet. Alcohol-based hand sanitizer should cover all surfaces of the hands and fingers and be allowed to dry. The World Health Organization recommends handwashing before and after touching a patient, before aseptic procedures, and after contact with body fluids or patient surroundings.

(Choice A) Contact precautions involve wearing nonsterile gloves for all patient contact and gowns during substantial contact with infective material. These precautions are indicated when caring for patients with specific multidrug-resistant bacteria (eg, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci) or with certain parasitic or viral pathogens. This patient's **methicillin-sensitive** *Staphylococcus aureus* infection does not require use of contact precautions.

(Choice C) Isolation precautions are indicated in the care of patients with infectious airborne diseases (eg, tuberculosis) and involve a private airborne infection isolation room with negative air pressure, closed doors, and the use of specialized particulate respirator masks.

(Choice D) Facemasks are used as a barrier for respiratory secretions and are not a substitute for hand-washing.

(Choice E) Restricting visitors is unnecessary, although all visitors should wash their hands before and after contact with the patient.

Educational objective:

Hand hygiene is the single most important measure to reduce the risk of transmission of hospital-acquired infections.

References

- [Update on hand hygiene.](#)

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Question Id: 116

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A 28-year-old man comes to the emergency department due to 2 weeks of headaches, fever, and episodes of inattentiveness. The patient has a history of Hodgkin lymphoma and is undergoing treatment with combination chemotherapy. Temperature is 38.2 C (100.8 F), blood pressure is 138/84 mm Hg, and pulse is 72/min. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein levels and low glucose levels. Light microscopy of the cerebrospinal fluid is shown in the image.

Which of the following should be included in initial treatment for this patient's current condition?

☐ A. Amphotericin B

☐ B. Ampicillin

☐ C. Ceftriaxone

☐ D. Ganciclovir

☐ E. Pyrimethamine

☐ F. Voriconazole

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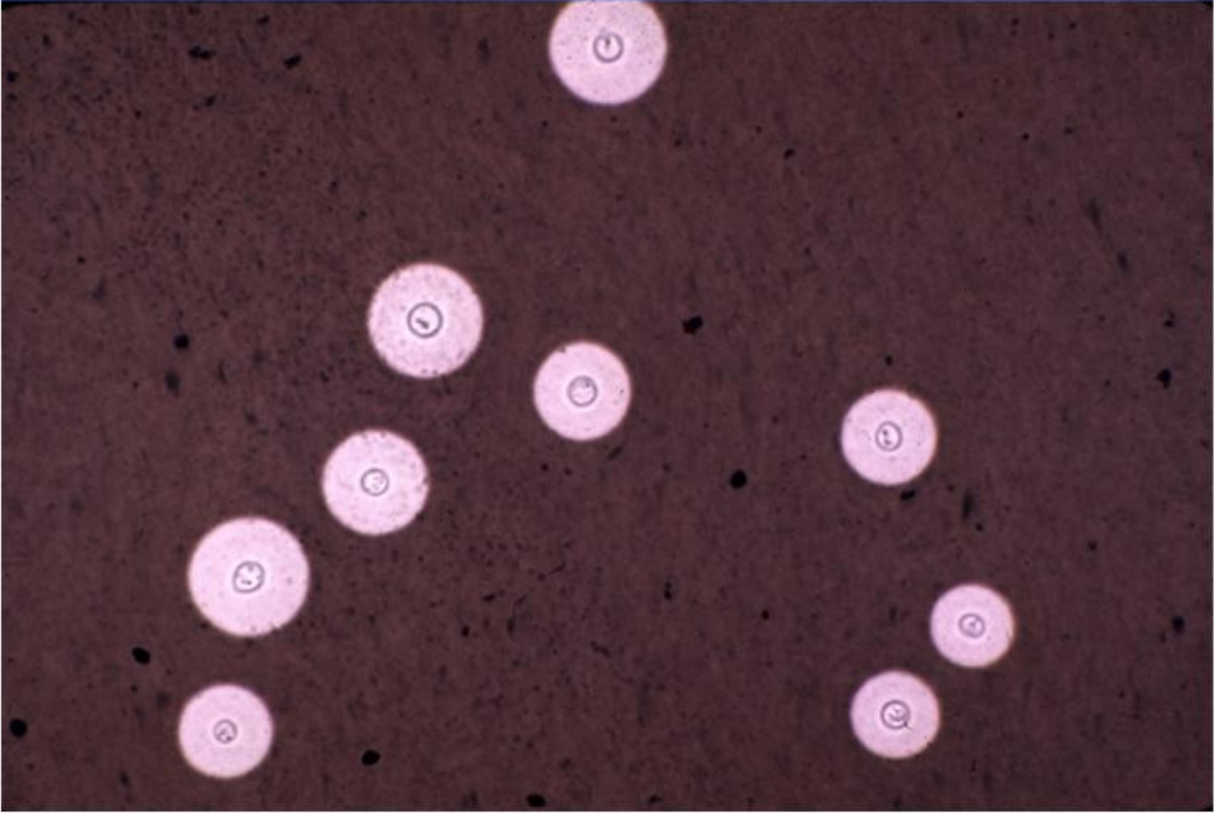
Notes

Calculator

Reverse Color

Text Zoom

Exhibit Display



Zoom In

Zoom Out

Reset

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Question Id: 116

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A 28-year-old man comes to the emergency department due to 2 weeks of headaches, fever, and episodes of inattentiveness. The patient has a history of Hodgkin lymphoma and is undergoing treatment with combination chemotherapy. Temperature is 38.2 C (100.8 F), blood pressure is 138/84 mm Hg, and pulse is 72/min. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein levels and low glucose levels. Light microscopy of the cerebrospinal fluid is shown in the image.

Which of the following should be included in initial treatment for this patient's current condition?

☐ A. Amphotericin B

☐ B. Ampicillin

☐ C. Ceftriaxone

☐ D. Ganciclovir

☐ E. Pyrimethamine

☐ F. Voriconazole

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A 28-year-old man comes to the emergency department due to 2 weeks of headaches, fever, and episodes of inattentiveness. The patient has a history of Hodgkin lymphoma and is undergoing treatment with combination chemotherapy. Temperature is 38.2 C (100.8 F), blood pressure is 138/84 mm Hg, and pulse is 72/min. Lumbar puncture reveals an elevated opening pressure, and cerebrospinal fluid analysis shows moderately increased protein levels and low glucose levels. Light microscopy of the cerebrospinal fluid is shown in the image.

Which of the following should be included in initial treatment for this patient's current condition?

✓

☒

A. Amphotericin B [82%]

☐

B. Ampicillin [1%]

☐

C. Ceftriaxone [5%]

☐

D. Ganciclovir [3%]

☐

E. Pyrimethamine [2%]

☐

F. Voriconazole [5%]

Omitted

Correct answer

A

82%

Answered correctly

3 Seconds

Time Spent

09/02/2018

Last Updated

Explanation

Clinical features of cryptococcal meningoencephalitis

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Explanation

Clinical features of cryptococcal meningoencephalitis	
Presentation	• Headache, fever & lethargy typically developing over 2 weeks, sometimes longer • Symptoms often more acute & severe in HIV patients
Diagnosis	• Lumbar puncture showing low glucose & increased protein; leukocyte count particularly low in HIV patients • Transparent capsule seen on India ink staining • Cryptococcal antigen detected in cerebrospinal fluid • Culture on Sabouraud agar
Treatment	• Initial treatment: Amphotericin B & flucytosine • Long-term maintenance therapy: Fluconazole

Cryptococcus neoformans is an opportunistic yeast that can be visualized with **India ink staining**. India ink stains the background of the slide black, which allows the **thick polysaccharide capsule** of the yeast to be visualized (clear halo between the dark background and the black center of the organism). India ink staining of the cerebrospinal fluid (CSF) is a common diagnostic modality in those with suspected cryptococcal meningitis. However, CSF cryptococcal (polysaccharide) antigen testing is more sensitive and specific, so it is also usually performed. Culture of the fungus on **Sabouraud agar** confirms the diagnosis.

Patients with cryptococcal meningitis usually develop slowly worsening headache, fever, and lethargy. Immunocompromised individuals are at greatest risk, particularly those who have AIDS or hematologic cancers or patients on chronic glucocorticoids. CSF analysis usually shows low glucose, increased protein, and mild pleocytosis with a predominance of lymphocytes. Initial treatment involves induction therapy with **amphotericin B** and flucytosine. Once patients are stabilized, they are switched to long-term maintenance therapy with fluconazole.

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Cryptococcus neoformans is an opportunistic yeast that can be visualized with **India ink staining**. India ink stains the background of the slide black, which allows the **thick polysaccharide capsule** of the yeast to be visualized (clear halo between the dark background and the black center of the organism). India ink staining of the cerebrospinal fluid (CSF) is a common diagnostic modality in those with suspected cryptococcal meningitis. However, CSF cryptococcal (polysaccharide) antigen testing is more sensitive and specific, so it is also usually performed. Culture of the fungus on **Sabouraud agar** confirms the diagnosis.

Patients with cryptococcal meningitis usually develop slowly worsening headache, fever, and lethargy. Immunocompromised individuals are at greatest risk, particularly those who have AIDS or hematologic cancers or patients on chronic glucocorticoids. CSF analysis usually shows low glucose, increased protein, and mild pleocytosis with a predominance of lymphocytes. Initial treatment involves induction therapy with **amphotericin B** and flucytosine. Once patients are stabilized, they are switched to long-term maintenance therapy with fluconazole.

(Choices B and C) Ampicillin is used to treat *Listeria meningitis*; *Listeria* is a gram-positive rod with characteristic tumbling motility on light microscopy. Ceftriaxone can treat pneumococcal and *Haemophilus influenzae* meningitis. Ampicillin and ceftriaxone are beta-lactam antibiotics that inhibit peptidoglycan cross-linking and lead to bactericidal effects. Fungi cannot be treated with beta-lactam antibiotics as their cell walls do not contain peptidoglycan.

(Choice D) Ganciclovir inhibits viral DNA synthesis and is used to treat cytomegalovirus meningoencephalitis, which is diagnosed using PCR.

(Choice E) Pyrimethamine is an antifolate agent used in the treatment of malaria and toxoplasmosis.

(Choice F) Azole drugs inhibit the synthesis of ergosterol, a crucial fungal cell membrane component. Spectrum of activity varies based on the particular agent; voriconazole is most effective against *Aspergillus*. Fluconazole is used for long-term maintenance therapy in cryptococcal meningitis, but is fungistatic at typically used doses and is less effective than amphotericin B for initial treatment.

Educational objective:

Patients with suspected cryptococcal meningitis can be diagnosed using India ink staining of the cerebrospinal fluid. Treatment with amphotericin B and flucytosine is required at first, followed by long-term fluconazole maintenance therapy.

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A 68-year-old woman comes to the emergency department due to cough and shortness of breath. She has a history of chronic obstructive pulmonary disease and often coughs up clear sputum in the mornings. However, over the past 4 days, her cough has worsened significantly, and she now is expectorating thick, yellow sputum. The patient also feels "winded" when walking short distances or doing light house work. She is a former smoker with a 40-pack-year history. Temperature is 37.2 C (99 F), blood pressure is 130/70 mm Hg, pulse is 90/min, and respirations are 22/min. The patient is breathing with pursed lips. The expiration phase is prolonged. Lung auscultation reveals vesicular breath sounds with diffuse wheezes. Chest x-ray shows hyperinflated lungs with flattened diaphragm. There are no parenchymal opacities or pleural effusion. Respiratory infection with which of the following pathogens most likely triggered this patient's worsening symptoms?

☐

A. *Bordetella pertussis*

☐

B. *Haemophilus influenzae*

☐

C. *Klebsiella pneumoniae*

☐

D. *Legionella pneumophila*

☐

E. *Staphylococcus aureus*

☐

F. *Streptococcus pyogenes*

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Text Zoom

A 68-year-old woman comes to the emergency department due to cough and shortness of breath. She has a history of chronic obstructive pulmonary disease and often coughs up clear sputum in the mornings. However, over the past 4 days, her cough has worsened significantly, and she now is expectorating thick, yellow sputum. The patient also feels "winded" when walking short distances or doing light house work. She is a former smoker with a 40-pack-year history. Temperature is 37.2 C (99 F), blood pressure is 130/70 mm Hg, pulse is 90/min, and respirations are 22/min. The patient is breathing with pursed lips. The expiration phase is prolonged. Lung auscultation reveals vesicular breath sounds with diffuse wheezes. Chest x-ray shows hyperinflated lungs with flattened diaphragm. There are no parenchymal opacities or pleural effusion. Respiratory infection with which of the following pathogens most likely triggered this patient's worsening symptoms?

☐

A. *Bordetella pertussis* [5%]

☒

B. *Haemophilus influenzae* [32%]

☐

C. *Klebsiella pneumoniae* [13%]

☐

D. *Legionella pneumophila* [20%]

☐

E. *Staphylococcus aureus* [23%]

☐

F. *Streptococcus pyogenes* [4%]

Omitted

Correct answer
B

32%

Answered correctly

3 Seconds

Time Spent

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Last Updated

Explanation

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Explanation

Chronic obstructive pulmonary disease exacerbation	
Triggers	• Viral infection: Rhinovirus, influenza, parainfluenza • Bacterial infection: <i>Haemophilus influenzae</i>, <i>Moraxella catarrhalis</i>, <i>Streptococcus pneumoniae</i> • Air pollution, pulmonary embolism
Clinical presentation	• Increased dyspnea &/or cough • Change in sputum color or quality
Physical examination	• Increased respiratory rate, wheezing • Pursed lip breathing with prolonged expiration
Diagnostic testing	• Arterial blood gas: Hypoxemia, CO₂ retention • Chest x-ray: Hyperinflation & flattened diaphragm

This patient with a history of chronic obstructive pulmonary disease (COPD) has worsened respiratory status (dyspnea, wheezes, pursed breathing) and purulent sputum production, raising strong suspicion for **COPD exacerbation**. The majority of COPD exacerbations are caused by **infections** of the upper airway. Infection results in mucus hypersecretion, damage to ciliated cells, cytokine-mediated airway inflammation, and increased respiratory capillary permeability, which can worsen existing airflow obstruction and lead to COPD exacerbation.

Most COPD exacerbations are due to common upper respiratory pathogens including ***Haemophilus influenzae***, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and rhinovirus. However, patients with severe COPD are also at risk for more opportunistic pathogens such as *Pseudomonas aeruginosa*. COPD exacerbation can also be induced by exposure to allergens (leading to eosinophilic inflammation of the airway) and environmental pollution.

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Most COPD exacerbations are due to common upper respiratory pathogens including *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and rhinovirus. However, patients with severe COPD are also at risk for more opportunistic pathogens such as *Pseudomonas aeruginosa*. COPD exacerbation can also be induced by exposure to allergens (leading to eosinophilic inflammation of the airway) and environmental pollution.

(Choice C) *Klebsiella pneumoniae* is a common cause of nosocomial pneumonia and may cause community-acquired pneumonia in patients with COPD; it is characterized by "currant-jelly" sputum and early abscess formation.

(Choice E) *Staphylococcus aureus* is a common cause of postinfluenza pneumonia. However, patients with pneumonia have an infiltrate on chest x-ray (unlike this patient).

(Choice F) *Streptococcus pyogenes* is a common cause of acute bacterial pharyngitis but does not usually cause COPD exacerbation.

Educational objective:

Most chronic obstructive pulmonary disease exacerbations are caused by infection with an upper respiratory pathogen. The leading bacterial cause is *Haemophilus influenza* and the leading viral cause is rhinovirus.

References

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A 12-year-old boy is brought to the emergency department by paramedics after being found unresponsive at home. He had 24 hours of headache, nausea, and fever, which his parents were treating with acetaminophen. His temperature is 39.6 C (103.4 F). Physical examination reveals neck stiffness. Lumbar puncture is performed. Analysis of cerebrospinal fluid shows marked pleocytosis, and Gram stain shows gram-negative cocci in pairs. The parents are concerned about their younger son, who shares a bedroom with the patient. Which of the following is the most appropriate management of this patient's household contacts?

☐ A. Immediate vaccination

☐ B. Observation only

☐ C. Prophylactic penicillin

☐ D. Prophylactic rifampin

☐ E. Prophylactic sulfamethoxazole

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Text Zoom

A 12-year-old boy is brought to the emergency department by paramedics after being found unresponsive at home. He had 24 hours of headache, nausea, and fever, which his parents were treating with acetaminophen. His temperature is 39.6 C (103.4 F). Physical examination reveals neck stiffness. Lumbar puncture is performed. Analysis of cerebrospinal fluid shows marked pleocytosis, and Gram stain shows gram-negative cocci in pairs. The parents are concerned about their younger son, who shares a bedroom with the patient. Which of the following is the most appropriate management of this patient's household contacts?

☐

A. Immediate vaccination [7%]

☐

B. Observation only [4%]

☐

C. Prophylactic penicillin [8%]

☒

D. Prophylactic rifampin [76%]

☐

E. Prophylactic sulfamethoxazole [3%]

Omitted

Correct answer D

76%

Answered correctly

3 Seconds

Time Spent

09/05/2018

Last Updated

Explanation

This patient's presentation and the finding of gram-negative diplococci highly suggest meningitis due to *Neisseria meningitidis*. *N meningitidis* is transmitted by direct contact with contaminated **respiratory secretions** or aerosolized droplets. As a result, people with **close or intimate** contact (eg, household contacts, kissing contacts, health care workers who directly contacted secretions) are at markedly increased risk of meningococcal infection. **Antibiotic** chemoprophylaxis can prevent these secondary cases if given promptly. A history of meningococcal

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Text Zoom

Explanation

This patient's presentation and the finding of gram-negative diplococci highly suggest meningitis due to ***Neisseria meningitidis***. *N meningitidis* is transmitted by direct contact with contaminated **respiratory secretions** or aerosolized droplets. As a result, people with **close or intimate** contact (eg, household contacts, kissing contacts, health care workers who directly contacted secretions) are at markedly increased risk of meningococcal infection. **Antibiotic** chemoprophylaxis can prevent these secondary cases if given promptly. A history of meningococcal vaccination does not preclude the need for antibiotic chemoprophylaxis.

Of the listed agents, **rifampin** is the only effective choice. Rifampin penetrates well into all body compartments, including the upper respiratory tract, and will eliminate nasopharyngeal colonization. Other effective agents include ciprofloxacin (not routinely used in children due to concerns about connective tissue injury) and intramuscular ceftriaxone, which is effective but not widely used due to the painful mode of administration. Chemoprophylaxis should be given as soon as possible, preferably within 24 hours of diagnosis.

(Choice A) Vaccination is an important public health strategy for control of meningococcal disease in general, but does not play a role in post-exposure prophylaxis. Immunity following a post-exposure vaccination does not occur in time to prevent disease.

(Choice B) A person's risk for infection is 500-1,000 times greater following an exposure to a meningococcal disease patient, and disease onset can be rapid. Therefore, observation alone is not an appropriate strategy for exposed close contacts.

(Choice C) Although penicillin can be used for treatment of susceptible meningococcal infections, it has not been shown to eliminate nasal carriage or prevent secondary cases. Therefore, it should not be used for chemoprophylaxis.

(Choice E) Sulfamethoxazole was the first agent to be used as chemoprophylaxis for meningococcal disease. However, it is no longer an effective agent due to widespread resistance.

Educational objective:

Rifampin is the most frequently used agent for chemoprophylaxis of meningococcal disease. Persons with exposure to the respiratory secretions of a patient with meningococcal disease require chemoprophylaxis. Vaccination is an important public health strategy but is not useful for post-exposure prophylaxis.

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Researchers studying fungal pathogens isolated an ergosterol biosynthetic gene by polymerase chain reaction. Using homologous recombination, they then developed a new strain of *Candida* with a mutated allele for that gene. The mutant strain was cultured in the presence of several different antifungal agents. Compared to isolates from the wild-type strain, isolates from the mutant *Candida* strain exhibited enhanced growth in the presence of drug X. Further investigation revealed that the mechanism of resistance to drug X was a decrease in ergosterol incorporation into the cell membrane. Based on this data, drug X is likely to be most closely related to which of the following antifungal agents?

☐ A. Caspofungin

☐ B. Cyclosporine

☐ C. Flucytosine

☐ D. Griseofulvin

☐ E. Nystatin

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Question Id: 271

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Tutorial

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Researchers studying fungal pathogens isolated an ergosterol biosynthetic gene by polymerase chain reaction. Using homologous recombination, they then developed a new strain of *Candida* with a mutated allele for that gene. The mutant strain was cultured in the presence of several different antifungal agents. Compared to isolates from the wild-type strain, isolates from the mutant *Candida* strain exhibited enhanced growth in the presence of drug X. Further investigation revealed that the mechanism of resistance to drug X was a decrease in ergosterol incorporation into the cell membrane. Based on this data, drug X is likely to be most closely related to which of the following antifungal agents?

☐

A. Caspofungin [22%]

☐

B. Cyclosporine [2%]

☐

C. Flucytosine [8%]

☐

D. Griseofulvin [9%]

☒

E. Nystatin [57%]

Omitted

Correct answer
E

57%

Answered correctly

3 Seconds

Time Spent

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Last Updated

Explanation

The main classes of antifungal medications currently in use include:

1. **Polyenes** (eg, amphotericin B, nystatin): Bind to ergosterol molecules in fungal cell membranes, creating pores and causing cell lysis
2. **Triazoles** (eg, ketoconazole, fluconazole, itraconazole, voriconazole): Inhibit the synthesis of ergosterol

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2/5/2019

1. **Polyenes** (eg, amphotericin B, nystatin): Bind to ergosterol molecules in fungal cell membranes, creating pores and causing cell lysis
2. **Triazoles** (eg, ketoconazole, fluconazole, itraconazole, voriconazole): Inhibit the synthesis of ergosterol
3. **Echinocandins** (eg, caspofungin, micafungin): Inhibit the synthesis of glucan, a component of the fungal cell wall
4. **Pyrimidines**: Flucytosine, the only agent in this class of antifungals, is converted to 5-fluorouracil within the fungal cell and interferes with fungal RNA and protein synthesis.

(Choice A) Caspofungin is an antifungal agent that blocks synthesis of the glucan component of the fungal cell wall. It is active against *Candida* and *Aspergillus*. Caspofungin does not bind ergosterol.

(Choice C) Flucytosine is used in combination with amphotericin B primarily for the treatment of cryptococcal meningitis in patients with HIV. It is a nucleotide analog that competitively inhibits RNA synthesis in fungal cells.

(Choice D) Griseofulvin interacts with fungal cell microtubules, inhibiting mitosis. It accumulates in keratin-containing tissues and is used to treat dermatophyte infections (eg, *Microsporum*, *Epidermophyton*, *Trichophyton*).

The main groups of antifungal drugs are polyenes, azoles, echinocandins, and pyrimidines. Polyene antifungals (eg, amphotericin B, nystatin) act by binding ergosterol in the fungal cell membrane.



A 34-year-old woman comes to the physician complaining of fever, dysuria, and flank pain. Her temperature is 37.8 C (100 F), blood pressure is 122/78 mm Hg, and pulse is 84/min. Physical examination elicits suprapubic and costovertebral angle tenderness. Urine dipstick analysis reveals positive leukocyte esterase and nitrite. A subsequent urine culture grows colonies of motile Gram-negative rods demonstrating a green metallic sheen on eosin methylene blue (EMB) agar and hemolysis on blood agar. Which of the following is the most important bacterial factor responsible for this patient's condition?

- ☐ A. Capsule
- ☐ B. Heat-labile enterotoxin
- ☐ C. O antigen
- ☐ D. Fimbrial antigen
- ☐ E. Lipid A

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A 34-year-old woman comes to the physician complaining of fever, dysuria, and flank pain. Her temperature is 37.8 C (100 F), blood pressure is 122/78 mm Hg, and pulse is 84/min. Physical examination elicits suprapubic and costovertebral angle tenderness. Urine dipstick analysis reveals positive leukocyte esterase and nitrite. A subsequent urine culture grows colonies of motile Gram-negative rods demonstrating a green metallic sheen on eosin methylene blue (EMB) agar and hemolysis on blood agar. Which of the following is the most important bacterial factor responsible for this patient's condition?

☐

A. Capsule [14%]

☐

B. Heat-labile enterotoxin [6%]

☐

C. O antigen [6%]

☒

D. Fimbrial antigen [59%]

☐

E. Lipid A [12%]

Omitted

Correct answer
D

59%

Answered correctly

3 Seconds

Time Spent

01/09/2019

Last Updated

Explanation

Escherichia coli is part of the normal bacterial flora of the intestinal tract. It is a motile, Gram-negative bacillus that is facultatively anaerobic and able to ferment both lactose and glucose. *E. coli* grows well on blood, MacConkey, and eosin methylene blue (EMB) agar plates. EMB agar is a selective and differential medium used to isolate and identify enteric pathogens from contaminated clinical specimens. On EMB agar, organisms

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Escherichia coli is part of the normal bacterial flora of the intestinal tract. It is a motile, Gram-negative bacillus that is facultatively anaerobic and able to ferment both lactose and glucose. *E coli* grows well on blood, MacConkey, and eosin methylene blue (EMB) agar plates. EMB agar is a selective and differential medium used to isolate and identify enteric pathogens from contaminated clinical specimens. On EMB agar, organisms that ferment lactose, such as *E coli*, bind to dye in the agar and produce colonies that have a distinct green metallic sheen. Most strains of *E coli* also demonstrate beta-hemolysis on blood agar.

E coli is responsible for urinary tract infections (UTIs), neonatal meningitis, and several types of gastroenteritis. The virulence factors expressed by a particular strain of *E coli* will determine disease characteristics. **Fimbriae**, or **pili** (Type 1 fimbriae, P fimbriae, and S fimbriae), are one of the most important virulence factors expressed by *E coli*. They permit the adhesion of *E coli* to epithelial cells, uroepithelial cells, and enterocytes.

E coli causes approximately 80% of all UTIs. UTIs are more common in women than men due to the female urethra being significantly shorter. *E coli* originates in the feces and spreads to colonize the perineal, genital, and – most importantly – the periurethral regions. During sexual intercourse or bladder catheterization, *E coli* can be propelled into the urethra and bladder from the colonized periurethral region. P-fimbriae (pyelonephritis-associated pili) adhesion then allows uropathogenic *E coli* to colonize the bladder and ureters, causing cystitis and pyelonephritis.

(Choice A) *E coli* strains causing neonatal meningitis synthesize K1 capsular antigens. The K1 antigen is considered the major determinant of virulence among strains of *E coli* that cause meningitis.

(Choice B) Enterotoxigenic *E coli* produce heat-stable (ST) and/or heat labile (LT) enterotoxins. ST activates guanylate cyclase, causing an increase in cGMP. LT activates adenylate cyclase, increasing cAMP levels. In both structure and mode of action, LT is very similar to the cholera toxin.

(Choice C) The O antigen is a variable polysaccharide antigen found on the outer membrane that is used to classify Gram-negative bacteria. It is the most extracellular component of lipopolysaccharide (see Choice E).

(Choice E) The lipid A component of lipopolysaccharide is similar for all enterobacteria. Lipid A causes activation of macrophages, leading to widespread release of IL-1, IL-6, and TNF-alpha, which in turn causes the signs and symptoms of septic shock.

Educational objective:

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by a particular strain of *E coli* will determine disease characteristics. **Fimbriae**, or **pili** (Type 1 fimbriae, P fimbriae, and S fimbriae), are one of the most important virulence factors expressed by *E coli*. They permit the adhesion of *E coli* to epithelial cells, uroepithelial cells, and enterocytes.

E coli causes approximately 80% of all UTIs. UTIs are more common in women than men due to the female urethra being significantly shorter. *E coli* originates in the feces and spreads to colonize the perineal, genital, and – most importantly – the periurethral regions. During sexual intercourse or bladder catheterization, *E coli* can be propelled into the urethra and bladder from the colonized periurethral region. P-fimbriae (pyelonephritis-associated pili) adhesion then allows uropathogenic *E coli* to colonize the bladder and ureters, causing cystitis and pyelonephritis.

(Choice A) *E coli* strains causing neonatal meningitis synthesize K1 capsular antigens. The K1 antigen is considered the major determinant of virulence among strains of *E coli* that cause meningitis.

(Choice B) Enterotoxigenic *E coli* produce heat-stable (ST) and/or heat labile (LT) enterotoxins. ST activates guanylate cyclase, causing an increase in cGMP. LT activates adenylate cyclase, increasing cAMP levels. In both structure and mode of action, LT is very similar to the cholera toxin.

(Choice C) The O antigen is a variable polysaccharide antigen found on the outer membrane that is used to classify Gram-negative bacteria. It is the most extracellular component of lipopolysaccharide (see Choice E).

(Choice E) The lipid A component of lipopolysaccharide is similar for all enterobacteria. Lipid A causes activation of macrophages, leading to widespread release of IL-1, IL-6, and TNF-alpha, which in turn causes the signs and symptoms of septic shock.

Educational objective:

E coli is one of the dominant components of the normal flora in the intestinal tract of humans and animals. It causes approximately 80% of all urinary tract infections. P fimbriae are the most important virulence factor that uropathogenic *E coli* express. Without P fimbriae, *E coli* would not be able to bind to uroepithelial cells and infect the bladder, ureters, and kidneys. Instead, the bacteria would simply be washed away during urination.

References

- [Origins and virulence mechanisms of uropathogenic Escherichia coli.](#)

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A 32-year-old woman comes to the emergency department due to 4 weeks of worsening cough, shortness of breath, and low-grade fevers. She also has had an unintentional weight loss of 4.5 kg (10 lb) over the past 3 months. Temperature is 37.1 C (98.8 F), blood pressure is 120/70 mm Hg, pulse is 102/min, and respirations are 22/min. Pulse oximetry shows 86% on ambient air. Lung auscultation reveals bilateral crackles. There are no heart murmurs, and jugular venous pressure is normal. Chest x-ray reveals diffuse interstitial infiltrates. The patient undergoes bronchoscopy; silver staining of the bronchoalveolar lavage specimen is shown in the image.

Which of the following is the most appropriate pharmacotherapy for this patient's current condition?

☐

A. Caspofungin

☐

B. Ceftriaxone and azithromycin

☐

C. Doxycycline

☐

D. Ganciclovir

☐

E. Trimethoprim-sulfamethoxazole

☐

F. Vancomycin

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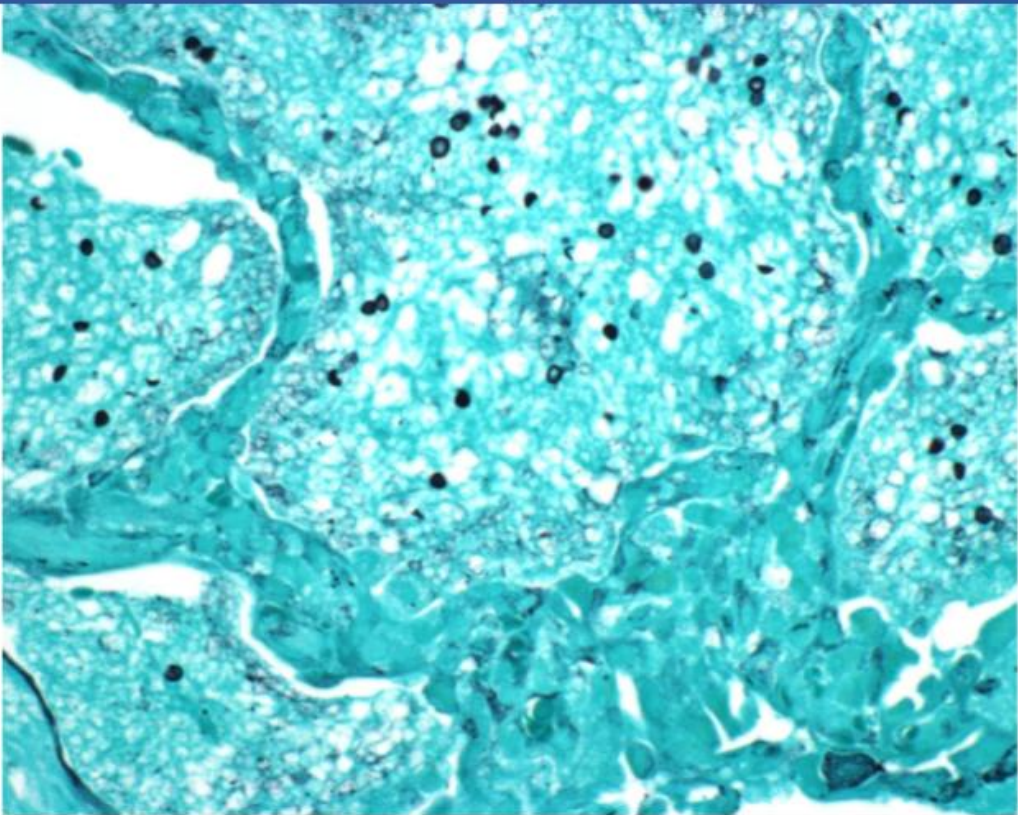
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Which of the following is the most appropriate pharmacotherapy for this patient's current condition?

☐

A. Caspofungin

☐

B. Ceftriaxone and azithromycin

☐

C. Doxycycline

☐

D. Ganciclovir

☐

E. Trimethoprim-sulfamethoxazole

☐

F. Vancomycin

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Which of the following is the most appropriate pharmacotherapy for this patient's current condition?

☐

A. Caspofungin [14%]

☐

B. Ceftriaxone and azithromycin [12%]

☐

C. Doxycycline [7%]

☐

D. Ganciclovir [1%]

☒

E. Trimethoprim-sulfamethoxazole [62%]

☐

F. Vancomycin [1%]

Omitted

Correct answer
E

62%

Answered correctly

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Explanation

Pneumocystis pneumonia is an AIDS-defining illness that is often seen in patients who were previously unaware of HIV infection. The

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Explanation

Pneumocystis pneumonia is an AIDS-defining illness that is often seen in patients who were previously unaware of HIV infection. The underlying pathogen is an atypical fungus called **Pneumocystis jirovecii**. This organism is inhaled and enters the alveolar space. Healthy patients rapidly clear the inoculation, but those with impaired cell-mediated immunity are at risk for a noninvasive infection that fills the alveoli and leads to slowly worsening pulmonary symptoms (eg, dry cough, shortness of breath), hypoxia, and a diffuse, **bilateral interstitial infiltrate**. Fever and weight loss are also usually present.

P jirovecii cannot be cultured; therefore, definitive diagnosis requires identification of the organism in respiratory secretions. **Methanamine silver stain** is frequently used to identify the cell wall of the pathogen, which often appears as a crescent, a crushed ping-pong ball, or a circular ring around a clear center. First-line treatment with **trimethoprim-sulfamethoxazole** is usually curative.

(Choice A) Invasive pulmonary aspergillosis is treated with caspofungin and is most common in patients with severe immunosuppression (eg, AIDS, neutropenia). It usually presents with fever, cough, chest pain, dyspnea, and hemoptysis. Silver stain can be used to diagnose aspergillosis, but numerous **hyphae** (not cystic organisms) will be seen.

(Choice B) Ceftriaxone and azithromycin are often used to treat community-acquired bacterial pneumonia, which usually presents with a few days of productive cough, fever, and shortness of breath. Chest x-ray typically reveals a **lobar infiltrate** rather than a diffuse interstitial infiltrate.

(Choice C) Doxycycline can be used to treat *Mycoplasma pneumoniae*, which often presents with several weeks of incessant cough and chest x-ray showing interstitial infiltrates. However, significant hypoxia is uncommon, and *M pneumoniae* is not identified on silver stain.

(Choice D) Patients with advanced AIDS are at risk for cytomegalovirus (CMV) pneumonia, which is treated with ganciclovir and can cause fever, cough, dyspnea, and diffuse pulmonary infiltrates. The presence of "owl's eye" inclusion bodies on histopathology strongly supports a CMV infection; it is not seen on silver stain.

(Choice F) Vancomycin inhibits cell wall synthesis and is primarily used for severe or drug-resistant, Gram-positive bacterial infections such as methicillin-resistant *Staphylococcus aureus*.

Educational objective:

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leads to slowly worsening pulmonary symptoms (eg, dry cough, shortness of breath), hypoxia, and a diffuse, **bilateral interstitial infiltrate**. Fever and weight loss are also usually present.

P jirovecii cannot be cultured; therefore, definitive diagnosis requires identification of the organism in respiratory secretions. **Methanamine silver stain** is frequently used to identify the cell wall of the pathogen, which often appears as a crescent, a crushed ping-pong ball, or a circular ring around a clear center. First-line treatment with **trimethoprim-sulfamethoxazole** is usually curative.

(Choice A) Invasive pulmonary aspergillosis is treated with caspofungin and is most common in patients with severe immunosuppression (eg, AIDS, neutropenia). It usually presents with fever, cough, chest pain, dyspnea, and hemoptysis. Silver stain can be used to diagnose aspergillosis, but numerous **hyphae** (not cystic organisms) will be seen.

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(Choice F) Vancomycin inhibits cell wall synthesis and is primarily used for severe or drug-resistant, Gram-positive bacterial infections such as methicillin-resistant *Staphylococcus aureus*.

Educational objective:

Pneumocystis pneumonia is common in patients with advanced HIV and usually presents with slowly worsening cough and dyspnea, hypoxia, and bilateral interstitial infiltrates. Diagnosis requires visualizing the organism in respiratory secretions using special stains (eg, silver stain). First-line treatment is trimethoprim-sulfamethoxazole.

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(Choice D) Patients with advanced AIDS are at risk for cytomegalovirus (CMV) pneumonia, which is treated with ganciclovir and can cause fever.

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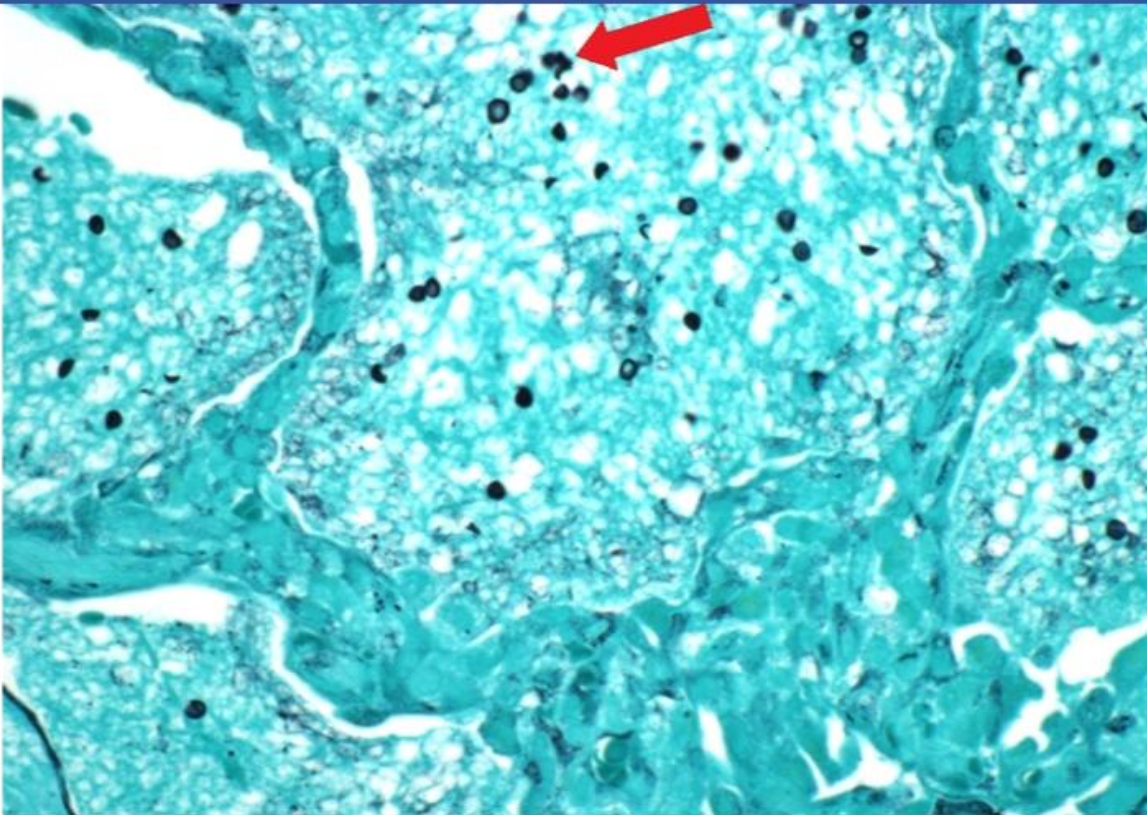
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(Choice D) Patients with advanced AIDS are at risk for cytomegalovirus (CMV) pneumonia, which is treated with ganciclovir and can cause fever

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A 23-year-old woman is evaluated due to 10 days of nonproductive cough, low-grade fever, headache, and malaise. The patient has no other medical problems and takes no medications. Lung examination reveals scattered rales. Chest x-ray reveals bilateral patchy areas of consolidation. She has mild anemia and an elevated serum lactate dehydrogenase level. The patient is treated for presumed *Mycoplasma pneumoniae* with azithromycin. Two months later, her symptoms and the anemia have resolved. Which of the following best explains the resolution of this patient's anemia?

☐ A. Elimination of bacterial cell wall antigens

☐ B. Elimination of intraerythrocytic microorganisms

☐ C. Fading of immune response against the bacteria

☐ D. Replenishment of body iron stores

☐ E. Replenishment of intracellular enzyme stores

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☐

A. Elimination of bacterial cell wall antigens [8%]

☐

B. Elimination of intraerythrocytic microorganisms [12%]

☒

C. Fading of immune response against the bacteria [59%]

☐

D. Replenishment of body iron stores [14%]

☐

E. Replenishment of intracellular enzyme stores [5%]

Omitted

Correct answer
C

59%

Answered correctly

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Explanation

Cold agglutinin disease

Infection
(eg, *Mycoplasma pneumoniae*)

Hematologic malignancies

Warm agglutinin disease

Medications

SLE, CLL

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Infection (eg, *Mycoplasma pneumoniae*)

Hematologic malignancies

Cross-reactive IgM

Areas below core body temperature

Blood vessel

Complement

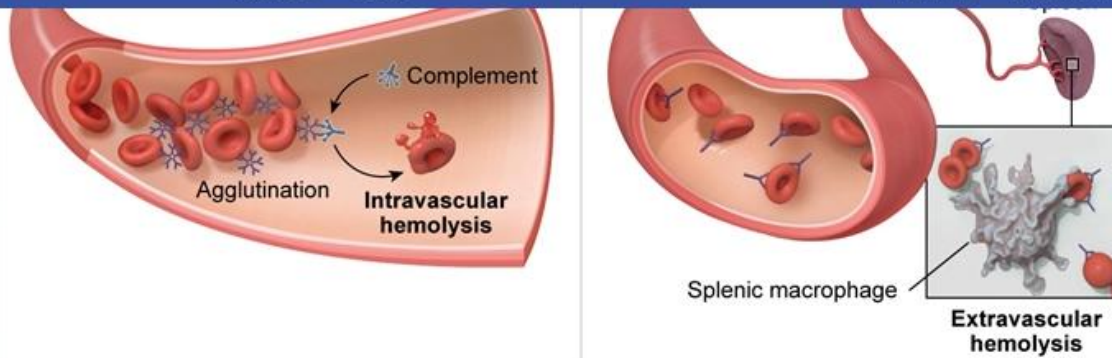
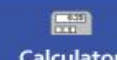
Agglutination

Intravascular hemolysis

The diagram illustrates the mechanism of drug-induced immune hemolytic anemia. At the top, 'Medications' and 'SLE, CLL' are shown with arrows pointing to a Y-shaped 'IgG' antibody. An arrow points from the IgG antibody to a human figure with a red glow on the torso, labeled 'At core body temperature'. A line extends from the human figure to a large, cross-sectioned spleen. Inside the spleen, several red blood cells are shown, some with blue Y-shaped antibodies attached to their surface. An inset shows a microscopic view of red blood cells with antibodies bound to them.

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CLL = chronic lymphocytic leukemia; SLE = systemic lupus erythematosus.

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Mycoplasma pneumoniae is a common cause of tracheobronchitis and walking pneumonia. It attacks the respiratory epithelium by binding to an oligosaccharide (**I-antigen**) that is also present on the surface of erythrocytes. This leads to the formation of **cross-reacting IgM antibodies** that attach to red blood cells, activate the complement system, and cause erythrocyte lysis.

The cross-reacting antibodies are called **cold agglutinins** because they bind to erythrocytes in areas where the blood temperature is below core body temperature (eg, distal extremities, nose). Most patients with cold agglutinins are asymptomatic, but some develop manifestations of intravascular **hemolytic anemia** such as elevated reticulocyte count and lactate dehydrogenase level. IgM titers usually begin to fall approximately 4 weeks after initial infection leading to a resolution of the hemolytic anemia (within 8 weeks).

Other extrapulmonary manifestations of *M pneumoniae* include Stevens-Johnson syndrome, joint pain, encephalitis, cardiac rhythm disturbances, and bullous myringitis.

(Choice A) *M pneumoniae* is an atypical bacterium; it has a plasma membrane composed of cholesterol (unlike most bacteria) and no cell wall. The lack of a cell wall makes this pathogen resistant to beta-lactam antibiotics.

(Choice B) Malaria and babesiosis are associated with intraerythrocytic organisms that can cause cell lysis and anemia. However, these pathogens usually cause high fever and more severe clinical syndromes. In addition, azithromycin monotherapy is not an effective cure for these

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The cross-reacting antibodies are called **cold agglutinins** because they bind to erythrocytes in areas where the blood temperature is below core body temperature (eg, distal extremities, nose). Most patients with cold agglutinins are asymptomatic, but some develop manifestations of intravascular **hemolytic anemia** such as elevated reticulocyte count and lactate dehydrogenase level. IgM titers usually begin to fall approximately 4 weeks after initial infection leading to a resolution of the hemolytic anemia (within 8 weeks).

Other extrapulmonary manifestations of *M pneumoniae* include Stevens-Johnson syndrome, joint pain, encephalitis, cardiac rhythm disturbances, and bullous myringitis.

(Choice A) *M pneumoniae* is an atypical bacterium; it has a plasma membrane composed of cholesterol (unlike most bacteria) and no cell wall. The lack of a cell wall makes this pathogen resistant to beta-lactam antibiotics.

(Choice B) Malaria and babesiosis are associated with intraerythrocytic organisms that can cause cell lysis and anemia. However, these pathogens usually cause high fever and more severe clinical syndromes. In addition, azithromycin monotherapy is not an effective cure for these infections.

(Choice D) Iron deficiency anemia, which is most commonly due to blood loss, can often be improved by replenishing body iron stores (eg, oral iron supplementation). Chronic infection or inflammatory conditions can be associated with anemia of chronic disease, which is due to impaired utilization of iron (not absolute iron deficiency).

(Choice E) Enzyme deficiencies that cause anemia include glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate kinase deficiency. Infection and medications that cause oxidative stress (eg, sulfonamides, antimalarial agents) can cause hemolysis in patients with G6PD; however, G6PD is an X-linked disorder (it is seen in men).

Educational objective:
Mycoplasma pneumoniae binds an oligosaccharide on the respiratory epithelium that is also present on erythrocytes, leading to the generation of cross-reacting IgM antibodies (cold agglutinins). Patients with *M pneumoniae* infections often develop mild, transient hemolytic anemia that resolves as IgM antibody titers decline (6-8 weeks after infection begins).

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A 29-year-old woman comes to the hospital due to fever and skin rash. She returned from a trip to Brazil 10 days ago. Her symptoms started 5 days ago with a headache, retro-orbital pain, high-grade fever, and joint and muscle pains. She has also had an episode of epistaxis. Today, she noticed a skin rash all over her body. Examination shows a diffuse maculopapular rash and scattered petechiae. Laboratory study results show thrombocytopenia. Her boyfriend traveled to Brazil with her and is asymptomatic. Which of the following diseases has a similar mode of transmission to that causing this patient's symptoms?

☐ A. Chikungunya fever

☐ B. Lymphogranuloma venereum

☐ C. Meningococcal meningitis

☐ D. Pulmonary tuberculosis

☐ E. Rocky Mountain spotted fever

☐ F. Typhoid fever

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A 29-year-old woman comes to the hospital due to fever and skin rash. She returned from a trip to Brazil 10 days ago. Her symptoms started 5 days ago with a headache, retro-orbital pain, high-grade fever, and joint and muscle pains. She has also had an episode of epistaxis. Today, she noticed a skin rash all over her body. Examination shows a diffuse maculopapular rash and scattered petechiae. Laboratory study results show thrombocytopenia. Her boyfriend traveled to Brazil with her and is asymptomatic. Which of the following diseases has a similar mode of transmission to that causing this patient's symptoms?

A. Chikungunya fever [51%]

B. Lymphogranuloma venereum [2%]

C. Meningococcal meningitis [6%]

D. Pulmonary tuberculosis [1%]

E. Rocky Mountain spotted fever [28%]

F. Typhoid fever [9%]

Omitted

Correct answer
A

51%

Answered correctly

3 Seconds

Time Spent

11/30/2018

Last Updated

Explanation

This patient's presentation after recent travel to Brazil is consistent with **dengue fever (DF)**. DF is due to a virus transmitted by the *Aedes aegypti* mosquito. It is prevalent in tropical and subtropical regions (South and Southeast Asia, Pacific Islands, Caribbean, Americas). DF

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This patient's presentation after recent travel to Brazil is consistent with **dengue fever (DF)**. DF is due to a virus transmitted by the *Aedes aegypti* mosquito. It is prevalent in tropical and subtropical regions (South and Southeast Asia, Pacific Islands, Caribbean, Americas). DF presents as an acute febrile illness with headache, retro-orbital pain, and joint and muscle pain. Other findings can include hemorrhage (eg, petechiae, purpura, epistaxis, melena), thrombocytopenia, leukopenia, and hemoconcentration.

The *Aedes* mosquito also transmits the virus causing **chikungunya**, a febrile illness with flulike symptoms, prominent polyarthralgia/arthritis (hands, wrists, ankles), and diffuse macular rash. As a result, many areas have had simultaneous outbreaks of both dengue and chikungunya. Preventive measures against both infections include protective barriers (eg, bed nets, window screens) and insect spraying.

(Choice B) Lymphogranuloma venereum can be caused by direct sexual contact with an infected individual.

(Choice C) Meningococcal meningitis is acquired by droplet contact. In a health care setting, measures to prevent transmission include wearing a face mask within 3 feet of the patient (who is typically placed in a private room).

(Choice D) Pulmonary tuberculosis is usually spread through airborne contact. Patients are placed in a negative-pressure isolation room, and specific respirator masks are worn by all contacts and visitors.

(Choice E) Rocky Mountain spotted fever is due to *Rickettsia rickettsii*, which is transmitted by ticks rather than mosquitoes.

(Choice F) Typhoid fever is caused by *Salmonella* and is usually acquired from contaminated food or water, typically in areas with poor sanitation.

Educational objective:

The *Aedes aegypti* mosquitoes can transmit the viruses that cause dengue fever and chikungunya. Classic dengue fever presents as an acute febrile illness with headache, retro-orbital pain, and joint and muscle pain. Chikungunya is a febrile illness with flulike symptoms, prominent polyarthralgias, and diffuse macular rash.

References

- Recent introduction and rapid dissemination of Chikungunya virus and Dengue virus serotype 2 associated with human and mosquito

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A 28-year-old woman is brought to the emergency department due to abrupt onset of high fever, severe headache, photophobia, and confusion. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, and pulse is 118/min. On examination, the patient is obtunded and diaphoretic. There is increased resistance to passive neck flexion. Pupillary reflexes are brisk and symmetric, and the patient moves all extremities equally to painful stimuli. Lumbar puncture is performed, and cerebrospinal fluid (CSF) analysis reveals neutrophilic pleocytosis, elevated protein, and low glucose. CSF Gram stain shows no bacteria, and fungal antigen testing is negative. Wet mount preparation of the CSF shows motile trophozoites. Which of the following most likely predisposed this patient to her current condition?

- ☐ A. Cohabitation with a person with a similar illness
- ☐ B. Hiking in wooded areas of New England
- ☐ C. Participation in recreational water activities
- ☐ D. Recent business trip to Southeast Asia
- ☐ E. Unprotected intercourse with a new partner

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A 28-year-old woman is brought to the emergency department due to abrupt onset of high fever, severe headache, photophobia, and confusion. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, and pulse is 118/min. On examination, the patient is obtunded and diaphoretic. There is increased resistance to passive neck flexion. Pupillary reflexes are brisk and symmetric, and the patient moves all extremities equally to painful stimuli. Lumbar puncture is performed, and cerebrospinal fluid (CSF) analysis reveals neutrophilic pleocytosis, elevated protein, and low glucose. CSF Gram stain shows no bacteria, and fungal antigen testing is negative. Wet mount preparation of the CSF shows motile trophozoites. Which of the following most likely predisposed this patient to her current condition?

A. Cohabitation with a person with a similar illness [3%]

B. Hiking in wooded areas of New England [6%]

C. Participation in recreational water activities [63%]

D. Recent business trip to Southeast Asia [15%]

E. Unprotected intercourse with a new partner [11%]

Omitted

Correct answer
C

63%
Answered correctly

3 Seconds
Time Spent

10/28/2018
Last Updated

Explanation

Primary amoebic encephalitis

Infection with *Naegleria fowleri* (free-living, motile protozoan)

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Primary amoebic encephalitis

Pathophysiology	• Infection with <i>Naegleria fowleri</i> (free-living, motile protozoan) • Exposure during recreational water activities (eg, boating, diving) • Mucosal invasion → penetration of cribriform plate → meningoencephalitis
Presentation	• Acute fever, confusion, headache, photophobia, CN palsies • CSF - ↑ protein, neutrophils; motile trophozoites on wet mount
Management	• Nearly all cases are fatal • Antibiotics (eg, amphotericin B) administered but usually insufficient

CN = cranial nerve; CSF = cerebrospinal fluid.

This patient has meningeal signs, confusion, and trophozoites in her cerebrospinal fluid (CSF), raising strong suspicion for **primary amebic meningoencephalitis (PAM)**. PAM is caused by ***Naegleria fowleri***, a free-living, motile, protozoan parasite that lives in warm water and soil worldwide. Exposure primarily occurs when humans inadvertently inhale the organism during **recreational water activities** such as swimming, diving, or using hot springs. Most individuals do not become ill, but a minority develop fatal meningoencephalitis after *N fowleri* penetrates the olfactory mucosa, crosses the cribriform plate, and invades the olfactory bulb.

Patients with PAM usually develop acute confusion, high fever, photophobia, and meningeal symptoms (eg, neck stiffness, headache). Lumbar puncture opening pressures are often markedly elevated, and CSF analysis typically reveals neutrophilic pleocytosis, high protein, and low glucose. Suspicion is usually raised when CSF testing is negative for bacterial, viral, or fungal pathogens. The diagnosis is confirmed when **wet mount** of the CSF reveals **motile trophozoites**. Antibiotics (eg, amphotericin B) are often administered, but PAM is almost always fatal.

(Choice A) *Neisseria meningitidis* is a gram-negative bacterium that is typically spread by close contact with a carrier or infected individual. It is a common cause of community-acquired bacterial meningitis and usually presents with rapidly progressive headache, myalgia, confusion, sepsis, and death. Patients also frequently have an ecchymotic/purpuric rash. Diagnosis is often made with blood culture and/or CSF Gram stain.

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diving, or using hot springs. Most individuals do not become ill, but a minority develop fatal meningoencephalitis after *N fowleri* penetrates the olfactory mucosa, crosses the cribriform plate, and invades the olfactory bulb.

Patients with PAM usually develop acute confusion, high fever, photophobia, and meningeal symptoms (eg, neck stiffness, headache). Lumbar puncture opening pressures are often markedly elevated, and CSF analysis typically reveals neutrophilic pleocytosis, high protein, and low glucose. Suspicion is usually raised when CSF testing is negative for bacterial, viral, or fungal pathogens. The diagnosis is confirmed when **wet mount** of the CSF reveals **motile trophozoites**. Antibiotics (eg, amphotericin B) are often administered, but PAM is almost always fatal.

(Choice A) *Neisseria meningitidis* is a gram-negative bacterium that is typically spread by close contact with a carrier or infected individual. It is a common cause of community-acquired bacterial meningitis and usually presents with rapidly progressive headache, myalgia, confusion, sepsis, and death. Patients also frequently have an ecchymotic/purpuric rash. Diagnosis is often made with blood culture and/or CSF Gram stain.

(Choice B) Lyme disease, a tick-borne illness caused by the spirochete *Borrelia burgdorferi*, is **endemic** to the wooded areas of New England. Patients with early disseminated Lyme disease can sometimes develop cranial nerve palsies or lymphocytic meningitis, but wet mount of the CSF would not show trophozoites. Diagnosis of early disseminated Lyme disease is usually made with serology.

(Choice D) Malaria is a mosquito-borne protozoal illness that is endemic to Southeast Asia. Patients with malaria can develop encephalopathy (cerebral malaria) with confusion, headache, and delirium. However, CSF analysis is usually fairly normal, and trophozoites are not typically seen in the CSF. Malaria is usually diagnosed when trophozoites are isolated on **peripheral blood smear**.

(Choice E) Syphilis is caused by the spirochete *Treponema pallidum* and is transmitted primarily by unprotected sexual intercourse. Patients with syphilis infections can occasionally develop lymphocytic meningitis early in infection. However, syphilis is usually diagnosed with serology; trophozoites would not be present in the CSF.

Educational objective:
Naegleria fowleri is a free-living, motile protozoan that lives in warm water. Exposure can result in primary amebic encephalitis, which is characterized by acute fever, headache, confusion, and neck stiffness. The diagnosis is confirmed when motile trophozoites are seen on cerebrospinal fluid wet mount. Nearly all patients die.

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Settings

A 29-year-old male is hospitalized with low-grade fever and high serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). His serum is positive for HBsAg. You should inform the patient that the most likely outcome for his infection would be:

- ☐ A. Complete resolution
- ☐ B. Fulminant hepatitis
- ☐ C. Stable chronic hepatitis
- ☐ D. Chronic hepatitis with progression to cirrhosis
- ☐ E. Chronic hepatitis with progression to hepatocellular carcinoma

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A 29-year-old male is hospitalized with low-grade fever and high serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). His serum is positive for HBsAg. You should inform the patient that the most likely outcome for his infection would be:

✔ ☒

A. Complete resolution [58%]

☐

B. Fulminant hepatitis [5%]

☐

C. Stable chronic hepatitis [19%]

☐

D. Chronic hepatitis with progression to cirrhosis [9%]

☐

E. Chronic hepatitis with progression to hepatocellular carcinoma [7%]

Omitted

Correct answer
A

58%

Answered correctly

3 Seconds

Time Spent

08/09/2018

Last Updated

Explanation

Hepatitis B virus infection can produce one of three syndromes: acute hepatitis with complete resolution; chronic hepatitis (with or without cirrhosis and the attendant increased risk of hepatocellular carcinoma); or fulminant hepatitis with massive liver necrosis. By far the most common outcome in HBV-infected adults (> 95%) is acute hepatitis with mild or subclinical symptoms that eventually completely resolve.

(Choice B) Fulminant hepatitis occurs in < 1% of patients who develop acute hepatitis.

(Choice C) Only 4-5% of patients with hepatitis B virus infection will go on to develop chronic hepatitis. Of those, 50-80% will remain stable with

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☐

D. Chronic hepatitis with progression to cirrhosis [9%]

☐

E. Chronic hepatitis with progression to hepatocellular carcinoma [7%]

Omitted

Correct answer
A

58%

Answered correctly

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08/09/2018

Last Updated

Explanation

Hepatitis B virus infection can produce one of three syndromes: acute hepatitis with complete resolution; chronic hepatitis (with or without cirrhosis and the attendant increased risk of hepatocellular carcinoma); or fulminant hepatitis with massive liver necrosis. By far the most common outcome in HBV-infected adults (> 95%) is acute hepatitis with mild or subclinical symptoms that eventually completely resolve.

(Choice B) Fulminant hepatitis occurs in < 1% of patients who develop acute hepatitis.

(Choice C) Only 4-5% of patients with hepatitis B virus infection will go on to develop chronic hepatitis. Of those, 50-80% will remain stable with no evidence of cirrhosis.

(Choice D) Approximately 20-50% of patients with chronic hepatitis B infection will also eventually develop cirrhosis.

(Choice E) Hepatocellular carcinoma arises in 10% of patients with chronic hepatitis and cirrhosis.

Educational Objective:

The most common outcome in HBV-infected adults (> 95%) is acute hepatitis with mild or subclinical symptoms that eventually completely resolve.

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A 25-year-old woman comes to the emergency department due to 2 days of abdominal pain and bloody diarrhea. A few days ago, she attended a church barbeque party. The patient lives alone and has no medical problems. She does not know if anyone else at the party developed similar symptoms. Her temperature is 37.1 C (98.8 F), blood pressure is 119/76 mm Hg, pulse is 92/min, and respirations are 16/min. There is abdominal tenderness with no rebound or guarding. Guaiac-positive bloody stools are detected on rectal examination. Stool cultures reveal an *Escherichia coli* strain that does not produce glucuronidase and does not ferment sorbitol on sorbitol-containing MacConkey agar. Which of the following best describes the mechanism of action of the toxin produced by these bacteria?

A. Activates adenylate cyclase

B. Activates guanylate cyclase

C. Disrupts the cellular cytoskeleton

D. Inactivates elongation factor-2

E. Inactivates ribosomal subunits

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Text Zoom

A 25-year-old woman comes to the emergency department due to 2 days of abdominal pain and bloody diarrhea. A few days ago, she attended a church barbeque party. The patient lives alone and has no medical problems. She does not know if anyone else at the party developed similar symptoms. Her temperature is 37.1 C (98.8 F), blood pressure is 119/76 mm Hg, pulse is 92/min, and respirations are 16/min. There is abdominal tenderness with no rebound or guarding. Guaiac-positive bloody stools are detected on rectal examination. Stool cultures reveal an *Escherichia coli* strain that does not produce glucuronidase and does not ferment sorbitol on sorbitol-containing MacConkey agar. Which of the following best describes the mechanism of action of the toxin produced by these bacteria?

☐

A. Activates adenylate cyclase [14%]

☐

B. Activates guanylate cyclase [8%]

☐

C. Disrupts the cellular cytoskeleton [12%]

☐

D. Inactivates elongation factor-2 [11%]

☒

E. Inactivates ribosomal subunits [53%]

Omitted

Correct answer
E

53%

Answered correctly

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Last Updated

Explanation

Mechanism of action of selected bacterial exotoxins		
Organism	Toxin	Mechanism & effects

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Mechanism of action of selected bacterial exotoxins

Organism	Toxin	Mechanism & effects
<i>Bacillus anthracis</i>	Anthrax exotoxin	Edema factor: Increases cyclic AMP concentration by acting as an adenylate cyclase, causing edema & phagocyte dysfunction
		Lethal factor: Zinc-dependent protease that inhibits mitogen-activated protein kinase signaling, causing apoptosis & multisystem physiologic disruption
<i>Bordetella pertussis</i>	Pertussis toxin	Disinhibits adenylate cyclase through G _i ADP-ribosylation, increasing cAMP levels; causes edema & phagocyte dysfunction
	Adenylate cyclase toxin	Functions as an adenylate cyclase, increasing cAMP levels; causes edema & phagocyte dysfunction
<i>Clostridium botulinum</i>	Botulinum toxin	Blocks presynaptic release of acetylcholine at the neuromuscular junction, resulting in flaccid paralysis
<i>Clostridium difficile</i>	Toxin A	Recruits & activates neutrophils, leading to release of cytokines that cause mucosal inflammation, fluid loss & diarrhea
	Toxin B	Induces actin depolymerization, leading to mucosal cell death, bowel wall necrosis & pseudomembrane formation
<i>Shigella dysenteriae</i>	Shiga toxin	Halts protein synthesis by disabling the 60S ribosomal subunit, leading to intestinal epithelial cell death & diarrhea
<i>Streptococcus</i>	Pyrogenic exotoxin	Acts as a superantigen, inducing fever & shock; associated with scarlet fever & streptococcal toxic shock syndrome

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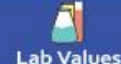
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Unlike enteroinvasive *E coli*, EHEC does not invade the intestinal mucosa. Unlike enterotoxigenic *E coli* (ETEC), EHEC does not produce heat-labile toxin (LT) or heat-stable toxin (ST).

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cooked hamburger meat. In contrast to most *E coli* strains, O157:H7 *E coli* does **not** ferment sorbitol during overnight incubation. As a result, sorbitol-containing MacConkey agar is used for isolation. Also, unlike other *E coli* strains, *E coli* O157:H7 does **not** produce glucuronidase.

EHEC elaborates a **Shiga-like toxin** virtually identical to the Shiga toxin produced by *Shigella dysenteriae*. This toxin is phage encoded, and its production is enhanced by iron deficiency. The Shiga and the Shiga-like toxins inactivate the 60s **ribosomal subunit** in human cells, leading to an inhibition of protein synthesis and eventual cell death. Infection with EHEC can also lead to hemolytic-uremic syndrome, characterized by thrombocytopenia, microangiopathic hemolytic anemia, and renal insufficiency (sometimes with uremia).

Unlike enteroinvasive *E coli*, EHEC does not invade the intestinal mucosa. Unlike enterotoxigenic *E coli* (ETEC), EHEC does not produce heat-labile toxin (LT) or heat-stable toxin (ST).

(Choice A) Toxins produced by *Bordetella pertussis* (adenylate cyclase toxin), ETEC (LT), *Campylobacter jejuni* (*C jejuni* enterotoxin), and *Vibrio cholerae* (cholera toxin) result in increased intracellular cyclic AMP in intestinal mucosal cells, which leads to decreased absorption and increased secretion of sodium, chloride, and water.

(Choice B) ETEC (ST) and *Yersinia enterocolitica* (*Y enterocolitica* enterotoxin) produce toxins that increase intracellular cyclic GMP, leading to watery diarrhea and electrolyte loss.

(Choice C) *Clostridium difficile* produces an exotoxin capable of disrupting the cytoskeleton (toxin B/cytotoxin). This toxin acts by depolymerizing actin, leading to cell death.

(Choice D) Exotoxins produced by *Corynebacterium diphtheriae* (diphtheria toxin) inhibit protein synthesis in eukaryotic cells by catalyzing ADP-ribosylation of elongation factor (EF)-2, causing EF-2 inactivation.

Educational objective:

Enterohemorrhagic *Escherichia coli* O157:H7 infection is a common cause of bloody diarrhea and can lead to hemolytic-uremic syndrome. It is associated with consumption of undercooked ground beef and elaborates a Shiga-like toxin capable of inhibiting protein synthesis in colonic mucosal cells and renal endothelial cells. This particular strain of *E coli* is unable to ferment sorbitol and does not produce a glucuronidase.

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A 57-year-old woman is hospitalized with high-grade fevers, chills, and right upper abdominal pain. Her temperature is 40 C (104 F). Physical examination of the abdomen shows rebound tenderness. Laboratory studies show elevated alkaline phosphatase. Imaging studies reveal a fluid-filled cavity within the right lobe of the liver. Which of the following microorganism/route combinations is most likely to be the cause of this patient's infection?

☐ A. *Chlamydia trachomatis* due to ascending cholangitis

☐ B. Cytomegalovirus by direct invasion from a nearby source

☐ C. *Entamoeba histolytica* due to a penetrating stab wound

☐ D. *Staphylococcus aureus* by hematogenous route

☐ E. *Streptococcus pneumoniae* by portal vein

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A 57-year-old woman is hospitalized with high-grade fevers, chills, and right upper abdominal pain. Her temperature is 40 C (104 F). Physical examination of the abdomen shows rebound tenderness. Laboratory studies show elevated alkaline phosphatase. Imaging studies reveal a fluid-filled cavity within the right lobe of the liver. Which of the following microorganism/route combinations is most likely to be the cause of this patient's infection?

☐

A. *Chlamydia trachomatis* due to ascending cholangitis [15%]

☐

B. Cytomegalovirus by direct invasion from a nearby source [4%]

☐

C. *Entamoeba histolytica* due to a penetrating stab wound [28%]

☒

D. *Staphylococcus aureus* by hematogenous route [46%]

☐

E. *Streptococcus pneumoniae* by portal vein [5%]

Omitted

Correct answer
D

46%

Answered correctly

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01/17/2019

Last Updated

Explanation

The presence of a **fluid-filled cavity** in the liver in conjunction with fevers, chills, and right upper abdominal pain is suggestive of a **hepatic abscess**. In underdeveloped countries, hepatic abscesses have a relatively high incidence and are usually caused by **parasitic infections** (eg, *Entamoeba histolytica*, echinococcal). In contrast, hepatic abscesses are uncommon in developed countries and are caused by **bacterial infection** in about 80% of cases.

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The presence of a **fluid-filled cavity** in the liver in conjunction with fevers, chills, and right upper abdominal pain is suggestive of a **hepatic abscess**. In underdeveloped countries, hepatic abscesses have a relatively high incidence and are usually caused by **parasitic infections** (eg, *Entamoeba histolytica*, echinococcal). In contrast, hepatic abscesses are uncommon in developed countries and are caused by **bacterial infection** in about 80% of cases.

Pyogenic bacteria can gain access to the liver through the following routes:

- **Biliary tract infection** (eg, ascending cholangitis)
- **Portal vein pyemia** (bowel or peritoneal sources)
- Hepatic artery (systemic hematogenous seeding)
- Direct invasion from an adjacent source (eg, peritonitis, cholecystitis)
- Penetrating trauma or injury

The types of organisms causing a hepatic abscess depend on the route of hepatic access. Systemic hematogenous seeding of the liver secondary to *Staphylococcus aureus* infection at a distant site is the most plausible choice of all the answer options.

(Choice A) Ascending cholangitis is usually caused by enteric gram-negative bacilli (eg, *Escherichia coli*, *Klebsiella*) and enterococci. *Chlamydia trachomatis* is transmitted sexually and is not found in the enteric environment.

(Choice B) Hepatic abscesses that arise by direct invasion from a nearby source are usually enteric gram-negative bacilli and enterococci. Cytomegalovirus can cause hepatitis in the immunosuppressed patient, but it is not associated with the development of a hepatic abscess.

(Choice C) Traumatic penetrating injuries to the abdomen (eg, stab wound) typically result in abscesses that contain mixed aerobic and anaerobic flora. *Entamoeba histolytica* is most often transmitted through foodborne exposure and in areas with poor sanitation. It can cause a hepatic abscess by ascending from the colon through the portal venous system.

(Choice E) *Streptococcus pneumoniae* colonizes the nasopharynx and typically causes disease within the respiratory tract region (eg, pneumonia, otitis media, sinusitis) and meningitis. However, hepatic abscesses due to portal vein seeding typically arise from abdominal infectious processes (eg, appendicitis, diverticulitis) and *S pneumoniae* is not an enteric pathogen.

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• Biliary tract infection (eg, ascending cholangitis)

• Portal vein pyemia (bowel or peritoneal sources)

• Hepatic artery (systemic hematogenous seeding)

• Direct invasion from an adjacent source (eg, peritonitis, cholecystitis)

• Penetrating trauma or injury

The types of organisms causing a hepatic abscess depend on the route of hepatic access. Systemic hematogenous seeding of the liver secondary to *Staphylococcus aureus* infection at a distant site is the most plausible choice of all the answer options.

(Choice A) Ascending cholangitis is usually caused by enteric gram-negative bacilli (eg, *Escherichia coli*, *Klebsiella*) and enterococci. *Chlamydia trachomatis* is transmitted sexually and is not found in the enteric environment.

(Choice B) Hepatic abscesses that arise by direct invasion from a nearby source are usually enteric gram-negative bacilli and enterococci. Cytomegalovirus can cause hepatitis in the immunosuppressed patient, but it is not associated with the development of a hepatic abscess.

(Choice C) Traumatic penetrating injuries to the abdomen (eg, stab wound) typically result in abscesses that contain mixed aerobic and anaerobic flora. *Entamoeba histolytica* is most often transmitted through foodborne exposure and in areas with poor sanitation. It can cause a hepatic abscess by ascending from the colon through the portal venous system.

(Choice E) *Streptococcus pneumoniae* colonizes the nasopharynx and typically causes disease within the respiratory tract region (eg, pneumonia, otitis media, sinusitis) and meningitis. However, hepatic abscesses due to portal vein seeding typically arise from abdominal infectious processes (eg, appendicitis, diverticulitis) and *S pneumoniae* is not an enteric pathogen.

Educational objective:

Staphylococcus aureus can cause hepatic abscesses via hematogenous seeding of the liver. Enteric bacteria (eg, *Escherichia coli*, *Klebsiella*, and enterococci) can cause hepatic abscesses by ascending the biliary tract (ie, ascending cholangitis), portal vein pyemia, or direct invasion from an adjacent area (eg, cholecystitis).

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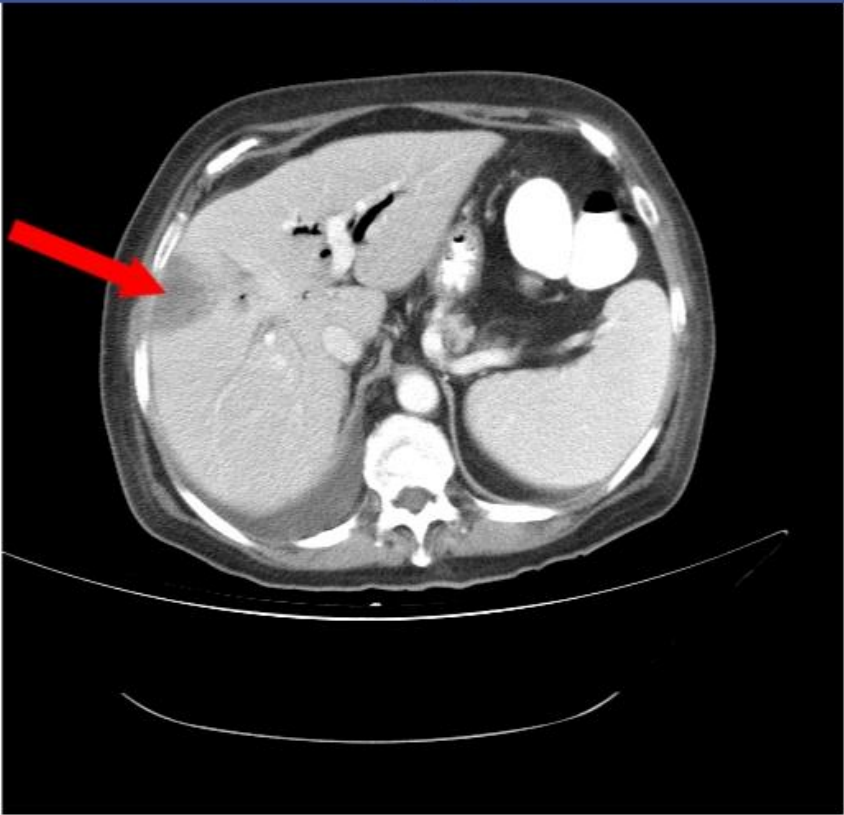
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A 34-year-old woman comes to the office for evaluation of recurrent transient pulmonary infiltrates. The patient has a history of bronchial asthma and has had several exacerbations over the past few years, particularly during the winter months. She is currently asymptomatic. She has no other medical problems and has never traveled outside the United States. Her medications include albuterol as needed and medium-dose inhaled glucocorticoids. Temperature is 37.1 C (98.8 F). Physical examination is unremarkable. Complete blood count shows eosinophilia. A chest CT scan reveals proximal bronchiectasis. This patient's condition is most likely related to colonization with which of the following?

- ☐ A. Adenovirus
- ☐ B. *Aspergillus fumigatus*
- ☐ C. *Legionella pneumophila*
- ☐ D. *Pseudomonas aeruginosa*
- ☐ E. *Streptococcus pneumoniae*
- ☐ F. *Strongyloides stercoralis*

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A 34-year-old woman comes to the office for evaluation of recurrent transient pulmonary infiltrates. The patient has a history of bronchial asthma and has had several exacerbations over the past few years, particularly during the winter months. She is currently asymptomatic. She has no other medical problems and has never traveled outside the United States. Her medications include albuterol as needed and medium-dose inhaled glucocorticoids. Temperature is 37.1 C (98.8 F). Physical examination is unremarkable. Complete blood count shows eosinophilia. A chest CT scan reveals proximal bronchiectasis. This patient's condition is most likely related to colonization with which of the following?

☐ A. Adenovirus [5%]

☒ B. *Aspergillus fumigatus* [53%]

☐ C. *Legionella pneumophila* [4%]

☐ D. *Pseudomonas aeruginosa* [9%]

☐ E. *Streptococcus pneumoniae* [6%]

☐ F. *Strongyloides stercoralis* [20%]

Omitted

Correct answer B

53%

Answered correctly

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Explanation

Allergic bronchopulmonary aspergillosis

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Allergic bronchopulmonary aspergillosis	
History	- Asthma - Cystic fibrosis
Chest imaging	- Recurrent fleeting infiltrates - Bronchiectasis (on CT scan)
Diagnosis	- Eosinophilia - Positive skin test for <i>Aspergillus</i> - Positive <i>Aspergillus</i>-specific IgG - Elevated <i>Aspergillus</i>-specific & total IgE

Aspergillus fumigatus is a low virulence fungus that generally does not cause significant infections except in immunocompromised or debilitated patients. It may, however, colonize the bronchial mucosa. Patients with asthma or cystic fibrosis in particular may develop an allergic hypersensitivity reaction to the fungus. The result is **allergic bronchopulmonary aspergillosis (ABPA)**, which occurs in 5%-10% of corticosteroid-dependent **asthmatics**. Patients with ABPA have very high serum IgE levels, **eosinophilia**, and IgE plus IgG serum antibodies to *Aspergillus*. There is intense airway inflammation and mucus plugging with exacerbations and remissions. Repeated exacerbations may produce transient pulmonary infiltrates and proximal **bronchiectasis**.

(Choice A) Although viral respiratory infections can cause asthma exacerbations and adenovirus colonization of the lung may be associated with asthma chronicity, pure viral pneumonias do not progress to bronchiectasis.

(Choice C) Asthmatics do not have a predisposition to lung colonization with *Legionella*.

(Choice D) *Pseudomonas aeruginosa* is an opportunistic, aerobic gram-negative rod that is a frequent, and sometimes deadly, pulmonary pathogen in patients with cystic fibrosis or neutropenia.

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Elevated Aspergillus-specific & total IgE

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Aspergillus fumigatus is a low virulence fungus that generally does not cause significant infections except in immunocompromised or debilitated patients. It may, however, colonize the bronchial mucosa. Patients with asthma or cystic fibrosis in particular may develop an allergic **hypersensitivity** reaction to the fungus. The result is **allergic bronchopulmonary aspergillosis (ABPA)**, which occurs in 5%-10% of corticosteroid-dependent **asthmatics**. Patients with ABPA have very high serum IgE levels, **eosinophilia**, and IgE plus IgG serum antibodies to *Aspergillus*. There is intense airway inflammation and mucus plugging with exacerbations and remissions. Repeated exacerbations may produce transient pulmonary infiltrates and proximal **bronchiectasis**.

(Choice A) Although viral respiratory infections can cause asthma exacerbations and adenovirus colonization of the lung may be associated with asthma chronicity, pure viral pneumonias do not progress to bronchiectasis.

(Choice C) Asthmatics do not have a predisposition to lung colonization with *Legionella*.

(Choice D) *Pseudomonas aeruginosa* is an opportunistic, aerobic gram-negative rod that is a frequent, and sometimes deadly, pulmonary pathogen in patients with cystic fibrosis or neutropenia.

(Choice E) Although asthma may be a risk factor for the development of pneumococcal lung colonization and pneumonia, pneumococcal disease generally results in resolution with preservation of lung lobular architecture. Potential complications of pneumococcal bronchopneumonia or lobar pneumonia include lung abscess, empyema, and lung fibrosis. Bronchiectasis is not a common outcome of pneumococcal pulmonary disease.

(Choice F) Strongyloidiasis is typically asymptomatic but can sometimes cause pulmonary symptoms (eg, cough, asthma-like bronchospasm, hemoptysis) or a transient pneumonia as the larvae migrate through the lungs on their way to the laryngopharynx. However, progression to bronchiectasis is not commonly reported.

Educational objective:

Allergic bronchopulmonary aspergillosis (ABPA) due to *Aspergillus fumigatus* may complicate asthma. ABPA can result in transient recurrent pulmonary infiltrates and eventual proximal bronchiectasis.

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A novel antimicrobial agent that inhibits bacterial glycosyltransferase enzyme is developed. Bacteria grown in a medium containing this antibiotic become spherical, cease to grow, and subsequently lyse. So that the activity of this antibiotic against various bacteria can be determined, disks enriched with the drug are placed on agar plates containing bacterial colonies. The plates are incubated alongside control plates with the same organisms but no antimicrobial disks. The control plates all show organism growth. In the plates with the diffusion disks, resistance to the drug is determined by measuring the zone of complete growth inhibition around the disk. Which of the following bacteria is most likely to be resistant to this drug?

☐

A. *Actinomyces israelii*

☐

B. *Borrelia burgdorferi*

☐

C. *Helicobacter pylori*

☐

D. *Mycoplasma hominis*

☐

E. *Pasteurella multocida*

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A novel antimicrobial agent that inhibits bacterial glycosyltransferase enzyme is developed. Bacteria grown in a medium containing this antibiotic become spherical, cease to grow, and subsequently lyse. So that the activity of this antibiotic against various bacteria can be determined, disks enriched with the drug are placed on agar plates containing bacterial colonies. The plates are incubated alongside control plates with the same organisms but no antimicrobial disks. The control plates all show organism growth. In the plates with the diffusion disks, resistance to the drug is determined by measuring the zone of complete growth inhibition around the disk. Which of the following bacteria is most likely to be resistant to this drug?

- ☐ A. *Actinomyces israelii* [12%]
- ☐ B. *Borrelia burgdorferi* [7%]
- ☐ C. *Helicobacter pylori* [10%]
- ☒ D. *Mycoplasma hominis* [63%]
- ☐ E. *Pasteurella multocida* [6%]

Omitted

Correct answer
D63%
Answered correctly3 Seconds
Time Spent09/18/2018
Last Updated

Explanation

Peptidoglycan is the main component of the bacterial wall in both gram-positive and gram-negative organisms. It is composed of a linear glycan chain of 2 alternating sugars, N-acetylglucosamine and N-acetylmuramic acid, that are cross-linked by short peptides, thereby forming a rigid matrix. The enzyme **glycosyltransferase** is a crucial component of peptidoglycan synthesis: it adds glycan molecules to the growing

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Peptidoglycan is the main component of the bacterial wall in both gram-positive and gram-negative organisms. It is composed of a linear glycan chain of 2 alternating sugars, N-acetylglucosamine and N-acetylmuramic acid, that are cross-linked by short peptides, thereby forming a rigid matrix. The enzyme **glycosyltransferase** is a crucial component of peptidoglycan synthesis; it adds glycan molecules to the growing peptidoglycan chain. Inhibition of this enzyme would result in gaps in the bacterial cell wall, with subsequent loss of bacterial shape and cell lysis from osmotic stress.

Although most bacteria have a cell wall composed of peptidoglycan, organisms from the **Mycoplasma** genus (eg, *Ureaplasma urealyticum*, *M. hominis*) completely **lack a cell wall**. These pathogens are separated from the environment by a single phospholipid bilayer membrane composed primarily of cholesterol (similar to human cells). Therefore, antibacterial agents that target the cell wall, including penicillins, cephalosporins, carbapenems, vancomycin, and the drug described in this study, would be ineffective. *Mycoplasma* is treated primarily by medications that **inhibit bacterial ribosomal function** such as macrolides and tetracyclines.

(Choice A) *Actinomyces israelii* is a gram-positive, fungus-like bacterium that has a thick peptidoglycan cell wall. Therefore, it is likely to be inhibited by the drug described in this study. It can be effectively treated with penicillin.

(Choices B and E) *Borrelia burgdorferi* is the spirochete that causes Lyme disease. *Pasteurella multocida* is a gram-negative organism that is well-known for causing wound infections following cat bites. Because these organisms have peptidoglycan cell walls, they would likely be inhibited by a drug that blocks glycosyltransferase.

(Choice C) *Helicobacter pylori*, a gram-negative helical organism with a cell wall, is closely related to the *Campylobacter* genus. The recommended treatment regimen includes a proton pump inhibitor (eg, omeprazole) combined with clarithromycin and amoxicillin, with or without bismuth (triple or quadruple therapy).

Educational objective:

All organisms in the *Mycoplasma* genus, including *Ureaplasma urealyticum*, lack peptidoglycan cell walls and are therefore resistant to agents that target the cell wall such as penicillins, cephalosporins, carbapenems, and vancomycin. *Mycoplasma* infections can be treated with antiribosomal agents (eg, tetracyclines, macrolides).

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A 24-year-old man develops mild, nonexudative pharyngitis shortly after travel to Eastern Europe. Throat swab culture in tellurite-containing, selective media yields black, iridescent colonies. Microscopy shows club-shaped, gram-positive bacilli in a palisade arrangement, which are identified as nonpathogenic *Corynebacterium diphtheriae*. These bacteria can acquire virulence to become pathogenic through which of the following mechanisms?

☐ A. Bacterial conjugation permitting pili expression

☐ B. Chromosomal mutation permitting endotoxin production

☐ C. Environmental influences permitting toxin synthesis

☐ D. Phage conversion permitting exotoxin production

☐ E. Transformation permitting capsule formation

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A 24-year-old man develops mild, nonexudative pharyngitis shortly after travel to Eastern Europe. Throat swab culture in tellurite-containing, selective media yields black, iridescent colonies. Microscopy shows club-shaped, gram-positive bacilli in a palisade arrangement, which are identified as nonpathogenic *Corynebacterium diphtheriae*. These bacteria can acquire virulence to become pathogenic through which of the following mechanisms?

- ☐ A. Bacterial conjugation permitting pili expression [9%]
- ☐ B. Chromosomal mutation permitting endotoxin production [6%]
- ☐ C. Environmental influences permitting toxin synthesis [10%]
- ☒ D. Phage conversion permitting exotoxin production [70%]
- ☐ E. Transformation permitting capsule formation [3%]

Omitted

Correct answer
D70%
Answered correctly6 Seconds
Time Spent08/13/2018
Last Updated

Explanation

Corynebacterium diphtheriae is a non-spore-forming, gram-positive bacillus that is transmitted primarily via aerosolized droplets. Nontoxigenic strains are minimally infectious; toxigenic strains are virulent and cause the clinical syndrome of **diphtheria**. Conversion from nontoxigenic to toxigenic *C diphtheriae* occurs due to infection with a **lysogenic bacteriophage** called Corynephage beta. This phage inserts the *tox* gene into the *C diphtheriae* genome, which results in the bacterial expression of the **diphtheria AB toxin**. Diphtheria toxin irreversibly halts protein synthesis due to ADP-ribosylation of elongation factor-2 and causes severe local (eg, pseudomembranous pharyngitis) and systemic (eg,

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Explanation

Corynebacterium diphtheriae is a non-spore-forming, gram-positive bacillus that is transmitted primarily via aerosolized droplets. Nontoxigenic strains are minimally infectious; toxigenic strains are virulent and cause the clinical syndrome of **diphtheria**. Conversion from nontoxigenic to toxigenic *C diphtheriae* occurs due to infection with a **lysogenic bacteriophage** called Corynephage beta. This phage inserts the *tox* gene into the *C diphtheriae* genome, which results in the bacterial expression of the **diphtheria AB toxin**. Diphtheria toxin irreversibly halts protein synthesis due to ADP-ribosylation of elongation factor-2 and causes severe local (eg, pseudomembranous pharyngitis) and systemic (eg, myocarditis, neuritis) effects.

(Choice A) Conjugation is the direct transfer of plasmids from one bacterium to another through a pilus. Genes for antibiotic resistance are often transmitted in this manner.

(Choice B) Chromosomal mutations can theoretically lead to endotoxin production, but mutations more commonly lead to bacterial antibiotic resistance.

(Choice C) The gram-positive, spore-forming rods *Bacillus* and *Clostridium* generate toxins under environmental influences. The *B anthracis* spore, the causative agent in anthrax, survives in soil for extended periods in a state of dormancy. Only upon warming to 37° C in the presence of appropriate concentrations of CO₂ and protein do the spores germinate and begin to synthesize toxin. The case is similar for *C tetani* spores, which germinate and produce toxin only in anaerobic environments, such as necrotic wounds.

(Choice E) Transformation involves the direct uptake of genetic material from the environment with subsequent incorporation into the bacterial genome. *Streptococcus pneumoniae* acquires the ability to produce capsules via transformation. The capsule is the major virulence factor for *S pneumoniae*; strains without the capsule are not pathogenic.

Educational objective:

Lysogenic bacteriophages are responsible for converting nonpathogenic *Corynebacterium* into toxigenic *Corynebacterium*. Toxigenic strains elaborate the diphtheria exotoxin, which causes pseudomembranous pharyngitis and potentially life-threatening systemic effects (eg, myocarditis, neuritis).

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A 44-year-old man is brought to the emergency department by his wife because of confusion that began a few hours ago. Earlier in the day, he complained of a severe headache and nausea. On physical examination, his temperature is 38.3 C (101 F) and nuchal rigidity is present. Lumbar puncture and cerebrospinal fluid (CSF) examination show:

Opening pressure	300 mm H ₂ O
Glucose	20 mg/dL
Protein	200 mg/dL
RBCs	4 cells/ μ L
Leukocytes	760 cells/ μ L
Neutrophils	90%
Lymphocytes	10%

Gram stain of the CSF would most likely reveal which of the following?

- ☐ A. Bean-shaped, Gram-negative cocci in pairs
- ☐ B. Lancet-shaped, Gram-positive cocci in pairs
- ☐ C. Gram-positive cocci in clusters
- ☐ D. Non-motile Gram-negative coccobacilli
- ☐ E. Motile Gram-positive rods

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complained of a severe headache and nausea. On physical examination, his temperature is 38.5°C (101°F) and nuchal rigidity is present. Lumbar puncture and cerebrospinal fluid (CSF) examination show:

Opening pressure	300 mm H ₂ O
Glucose	20 mg/dL
Protein	200 mg/dL
RBCs	4 cells/ μ L
Leukocytes	760 cells/ μ L
Neutrophils	90%
Lymphocytes	10%

Gram stain of the CSF would most likely reveal which of the following?

- ☐ A. Bean-shaped, Gram-negative cocci in pairs [29%]
- ☒ B. Lancet-shaped, Gram-positive cocci in pairs [57%]
- ☐ C. Gram-positive cocci in clusters [5%]
- ☐ D. Non-motile Gram-negative coccobacilli [5%]
- ☐ E. Motile Gram-positive rods [1%]

Omitted

Correct answer

57%
Answered correctly5 Seconds
Time Spent08/22/2018
Last Updated

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A patient presenting with confusion, headache, fever, and nuchal rigidity should immediately raise suspicion for meningitis. In **bacterial meningitis**, cerebrospinal fluid (CSF) analysis typically shows elevated opening pressure, increased neutrophils, decreased glucose, and elevated protein. The morphology of any observed bacteria on CSF Gram stain provides an excellent preliminary identification of the pathogen (whereas cultures take time to grow).

***Streptococcus pneumoniae* is the most common cause of bacterial meningitis in adults of all ages** (see reference). On CSF Gram stain, lancet-shaped Gram-positive cocci are found in pairs. *S pneumoniae* meningitis often follows a pulmonary infection or mild upper respiratory infection. Alcoholics, sickle cell anemia patients, asplenic individuals, and those in generally poor health are at greater risk for *S pneumoniae* meningitis.

(Choice A) Bean-shaped Gram-negative cocci in pairs indicate *Neisseria meningitidis*. *N meningitidis* is the second most common cause of meningitis in patients < 60 years of age. *N meningitidis* tends to occur in outbreaks where many individuals live in close quarters (eg, army barracks and college dormitories).

(Choice C) Gram-positive cocci in clusters indicate *Staphylococcus* species. *Staphylococcus* is an unusual cause of community-acquired meningitis but is common in neurosurgical patients. It is thought that bacteria gain access to the meninges by direct inoculation during the procedure or postoperatively through the wound.

(Choice D) *Haemophilus influenzae* is a Gram-negative coccobacillus. *H influenzae* infection is becoming less common now that vaccination with the Hib capsule vaccine, a protein-capsule polysaccharide conjugate vaccine, has become widespread.

(Choice E) *Listeria monocytogenes* is a facultatively intracellular, motile, Gram-positive rod. It is the third most common cause of meningitis in neonates, after group B *Streptococci* and *Escherichia coli*. *Listeria* also causes meningitis in immunosuppressed patients and the elderly.

Educational objective:

Bacterial meningitis causes an increase in cerebrospinal fluid (CSF) neutrophil count and protein concentration as well as a decrease in CSF glucose. *Streptococcus pneumoniae* is a leading cause of community-acquired pneumonia, otitis media, and meningitis in adults. *S pneumoniae* appears on Gram stain as lancet-shaped, Gram-positive cocci in pairs.

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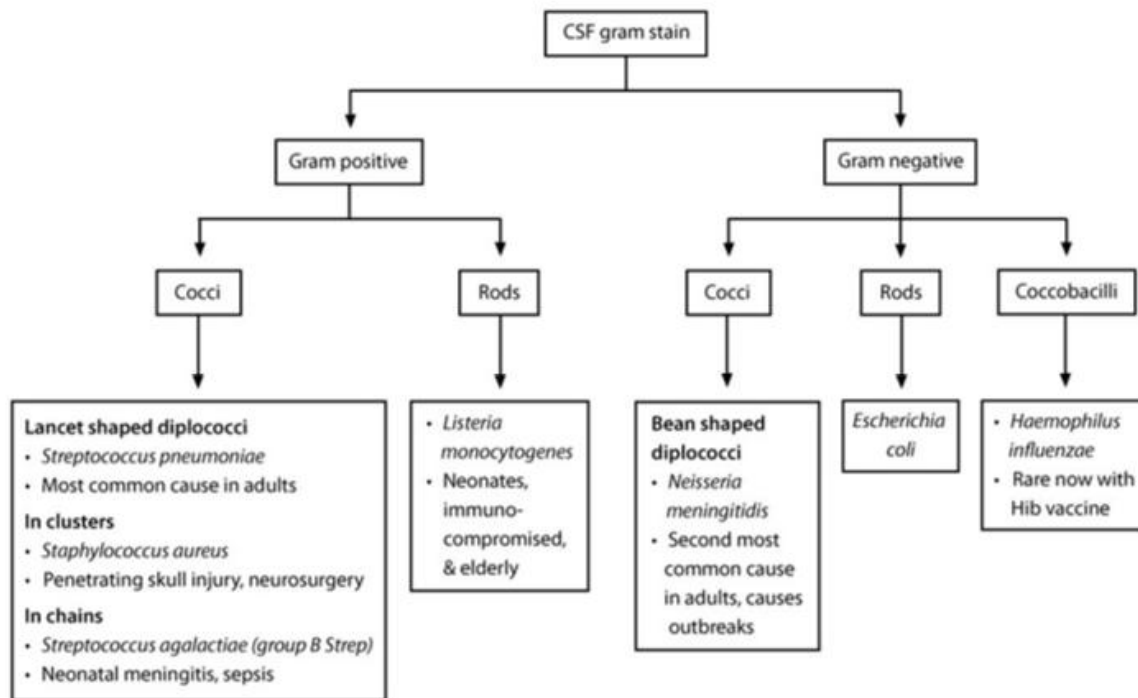
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Common causes of bacterial meningitis



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A 38-year-old man is undergoing treatment for acute myelogenous leukemia. Initially, he complained of fevers and being lethargic and fatigued all the time. However, of late, he has noted increasingly severe right-sided headaches. He describes the pain to be throbbing in nature and located behind his right eye, which is also associated with nasal stuffiness. The patient denies any previous history of allergies. Physical examination reveals right-sided proptosis and periorbital tenderness. Biopsy of the right maxillary sinus mucosa reveals the following:

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

☐ A. *Malassezia furfur*

☐ B. *Microsporum canis*

☐ C. *Rhizopus species*

☐ D. *Aspergillus fumigatus*

☐ E. *Candida albicans*

☐ F. *Cryptococcus neoformans*

☐ G. *Blastomyces dermatitidis*

☐ H. *Histoplasma capsulatum*

☐ I. *Coccidioides immitis*

☐ J. *Sporothrix schenckii*

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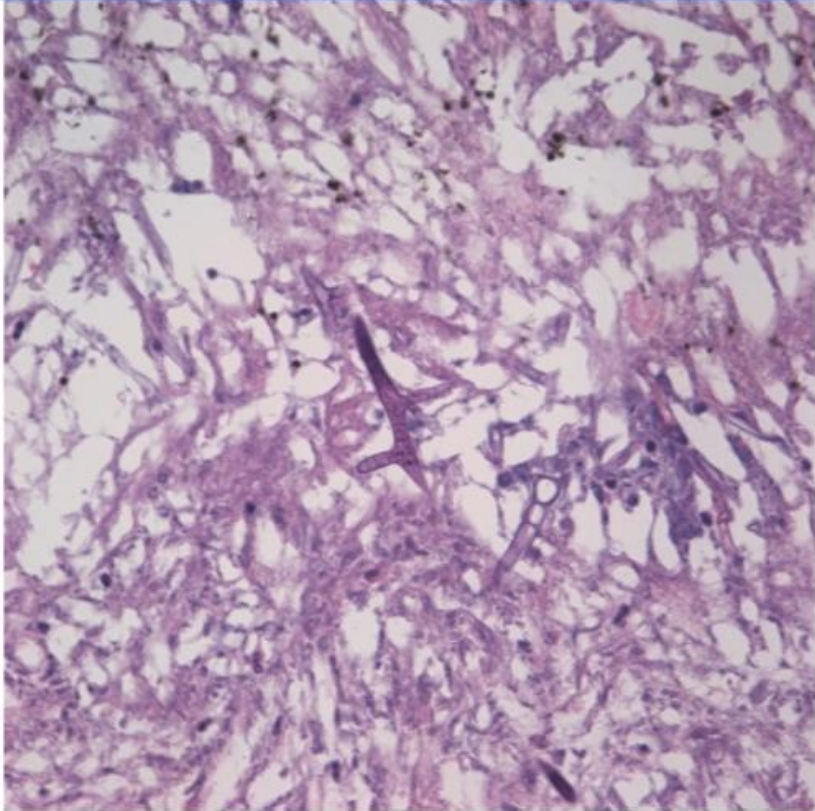
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Question Id: 106

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A 38-year-old man is undergoing treatment for acute myelogenous leukemia. Initially, he complained of fevers and being lethargic and fatigued all the time. However, of late, he has noted increasingly severe right-sided headaches. He describes the pain to be throbbing in nature and located behind his right eye, which is also associated with nasal stuffiness. The patient denies any previous history of allergies. Physical examination reveals right-sided proptosis and periorbital tenderness. Biopsy of the right maxillary sinus mucosa reveals the following:

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

☐

A. *Malassezia furfur*

☐

B. *Microsporum canis*

☐

C. *Rhizopus* species

☐

D. *Aspergillus fumigatus*

☐

E. *Candida albicans*

☐

F. *Cryptococcus neoformans*

☐

G. *Blastomyces dermatitidis*

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H. *Histoplasma capsulatum*

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I. *Coccidioides immitis*

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J. *Sporothrix schenckii*

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A 38-year-old man is undergoing treatment for acute myelogenous leukemia. Initially, he complained of fevers and being lethargic and fatigued all the time. However, of late, he has noted increasingly severe right-sided headaches. He describes the pain to be throbbing in nature and located behind his right eye, which is also associated with nasal stuffiness. The patient denies any previous history of allergies. Physical examination reveals right-sided proptosis and periorbital tenderness. Biopsy of the right maxillary sinus mucosa reveals the following:

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

- ☐ A. *Malassezia furfur* [2%]
- ☐ B. *Microsporum canis* [0%]
- ☒ C. *Rhizopus* species [73%]
- ☐ D. *Aspergillus fumigatus* [13%]
- ☐ E. *Candida albicans* [2%]
- ☐ F. *Cryptococcus neoformans* [2%]
- ☐ G. *Blastomyces dermatitidis* [1%]
- ☐ H. *Histoplasma capsulatum* [0%]
- ☐ I. *Coccidioides immitis* [0%]
- ☐ J. *Sporothrix schenckii* [0%]

Omitted

Correct answer



73%
Answered correctly



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TUTOR

Mucormycosis is an opportunistic infection caused by *Rhizopus*, *Mucor*, and *Absidia* species. The classic clinical picture is paranasal sinus involvement in a diabetic or immunosuppressed patient. The fungi form broad nonseptate hyphae that branch at right angles.

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A 4-year-old boy is brought to the physician by his mother with decreased appetite, abdominal cramps, and diarrhea over the last 3 days. The stools were initially watery but have now become bloody. On physical examination, his temperature is 100.4 F (38 C). There are signs of dehydration and he has a mildly distended abdomen with diffuse pain elicited on palpation. Stool studies are positive for fecal leukocytes and occult blood. Fecal cultures grow non-lactose fermenting, gram-negative rods on MacConkey agar. The bacteria ferment glucose without gas production, do not generate hydrogen sulfide when grown on triple sugar iron agar, and cannot replicate at refrigeration temperatures. Which of the following bacterial factors is the most important during the pathogenesis of this patient's disease?

☐ A. Exotoxin production

☐ B. Intestinal colonization

☐ C. Mucosal invasion

☐ D. Proliferation in lymph nodes

☐ E. Survival in the circulation

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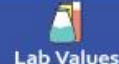
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A 4-year-old boy is brought to the physician by his mother with decreased appetite, abdominal cramps, and diarrhea over the last 3 days. The stools were initially watery but have now become bloody. On physical examination, his temperature is 100.4 F (38 C). There are signs of dehydration and he has a mildly distended abdomen with diffuse pain elicited on palpation. Stool studies are positive for fecal leukocytes and occult blood. Fecal cultures grow non-lactose fermenting, gram-negative rods on MacConkey agar. The bacteria ferment glucose without gas production, do not generate hydrogen sulfide when grown on triple sugar iron agar, and cannot replicate at refrigeration temperatures. Which of the following bacterial factors is the most important during the pathogenesis of this patient's disease?

- ☐ A. Exotoxin production [31%]
- ☐ B. Intestinal colonization [8%]
- ☒ C. Mucosal invasion [55%]
- ☐ D. Proliferation in lymph nodes [2%]
- ☐ E. Survival in the circulation [1%]

Omitted

Correct answer
C55%
Answered correctly3 Seconds
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Explanation

Characteristics of gram-negative bacteria

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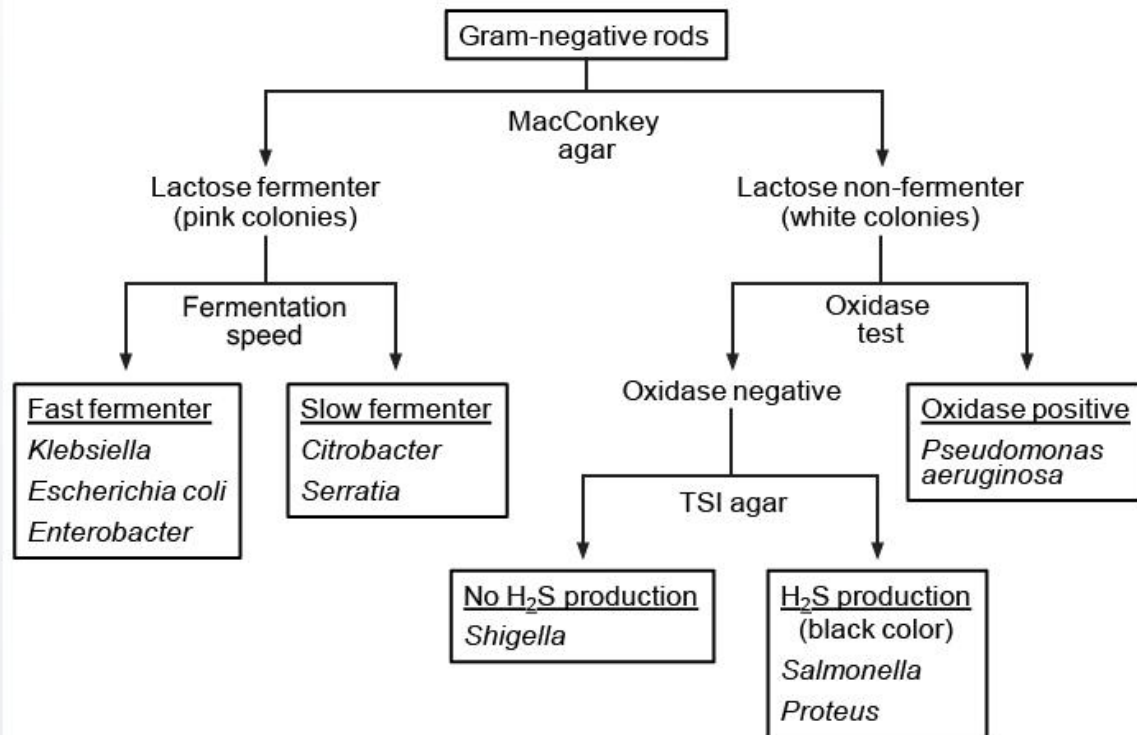
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Characteristics of gram-negative bacteria



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This patient's fever, abdominal cramps, and bloody diarrhea (**dysentery**) are consistent with bacterial enteritis. His stool culture results are most specific for a *Shigella* species (*Shigella sonnei* being most common in the United States). **Shigella** is transmitted via the fecal-oral route and is



never a component of the normal bacterial gut flora. Shigellosis is primarily a pediatric disease but also shows a predilection for men who have sex with men and adults in skilled nursing facilities. *Shigella* species are non-lactose fermenting organisms that produce acid (not gas) during glucose fermentation (in contrast to *Escherichia coli*). Furthermore, *Shigella* species are non-motile and do not produce H_2S (in contrast to *Salmonella*).

Mucosal invasion is the essential pathogenic mechanism for *Shigella* infection. *Shigella* invades the gastrointestinal mucosa, particularly via the M cells that overlie Peyer's patches. After cell entry, *Shigella* is able to lyse its containment vacuole and enter the cytosolic compartment. It then can induce apoptosis of the host cell and spread to adjacent cells via protrusions created through host-cell **actin polymerization**. *Shigella* invasion triggers a robust host inflammatory response that is largely mediated by neutrophils.

(Choice A) Some strains of *Shigella* produce shiga toxin, which damages the intestinal mucosa by inactivating the 60S ribosomal subunit, halting cellular protein synthesis. However, shiga toxin plays a minor, nonessential role in the disease process, as nontoxic strains also cause shigellosis.

(Choice B) Intestinal colonization with *Shigella* does not occur as the bacterium is highly pathogenic; transmission of as few as 10-100 organisms is sufficient to cause disease. If *Shigella* is isolated from a stool culture, an active infection is taking place.

(Choice D) Proliferation in lymph nodes is not a characteristic of *Shigella*. In contrast, both *Salmonella typhi* and *Yersinia enterocolitica* (grows at low temperatures like *Listeria*) can gain access to the lymphatics and proliferate in the mesenteric lymph nodes. *Y enterocolitica* can cause inflammation and enlargement of the lymphoid tissue around the appendix and terminal ileum ("pseudoappendicitis"), leading to right lower quadrant pain that can be confused with acute appendicitis.

(Choice E) *Shigella* infections rarely cause bacteremia, as the bacterium is readily phagocytosed and destroyed after entering the bloodstream. Enteric bacteremia is more likely to be caused by *E coli*, *S typhi* (typhoid fever), *Klebsiella*, and *Proteus*.

Educational objective:

Shigella is a non-motile, non-lactose fermenting organism that does not produce H_2S when grown on triple sugar iron agar. Mucosal invasion of the M cells that overlie Peyer's patches is an essential pathogenic mechanism for *Shigella* infection. *Shigella* then escapes the phagosome and spreads laterally to other epithelial cells via actin polymerization.

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A previously healthy 2-year-old boy is brought to the clinic with fever and mouth pain that began yesterday. He has consumed an adequate amount of fluids but refuses to eat due to the pain. The patient has no medical problems and takes no medications. Physical examination reveals swollen gums and vesicular, inflamed lesions on his hard palate and lips. He has enlarged and tender cervical lymph nodes. Which of the following is most likely responsible for this patient's condition?

☐ A. DNA virus, double-stranded, enveloped

☐ B. DNA virus, double-stranded, non-enveloped

☐ C. DNA virus, single-stranded, non-enveloped

☐ D. RNA virus, double-stranded, positive-sense

☐ E. RNA virus, single-stranded, negative-sense

☐ F. RNA virus, single-stranded, positive-sense

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☒ A. DNA virus, double-stranded, enveloped [56%]

☐ B. DNA virus, double-stranded, non-enveloped [12%]

☐ C. DNA virus, single-stranded, non-enveloped [5%]

☐ D. RNA virus, double-stranded, positive-sense [3%]

☐ E. RNA virus, single-stranded, negative-sense [9%]

☐ F. RNA virus, single-stranded, positive-sense [12%]

Correct answer
A



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Explanation

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Explanation

Primary **herpes simplex virus type 1** (HSV-1) infection is characterized by the **gingivostomatitis** (vesicles on the lips and hard palate, fever, lymphadenopathy) seen in this young patient. Recurrent HSV-1 infection causes **lip lesions** that are typically less severe due to existing cellular and humoral immunity from prior infection.

HSV-1 and other herpesviruses are **enveloped** and possess **double-stranded DNA** genomes. Transmission is usually by direct contact with infected oral secretions or lesions. Inoculation occurs on mucosa or skin where the virus replicates rapidly in the host cell nucleus and causes abnormal cell division, resulting in intranuclear inclusion bodies and **multinucleated giant cells** visible on Tzanck smear. The vesicular lesions result from cell lysis and necrosis as well as tissue destruction, inflammation, and fluid accumulation between the dermis and epidermis.

(Choice B) Most DNA viruses are double-stranded. They are enveloped (ie, surrounded by a lipid layer) or non-enveloped (ie, lacking a surrounding lipid layer). Adenovirus is a non-enveloped, double-stranded DNA virus that typically causes self-limited upper respiratory infection or gastroenteritis.

(Choice C) Parvovirus is a single-stranded, non-enveloped DNA virus that causes erythema infectiosum, or fifth disease. Patients classically present with fever, cough, and rhinorrhea followed by a "slapped-cheek" and lacy, reticular truncal rash.

(Choice D) Rotavirus, a type of reovirus, is a double-stranded, positive-sense, non-enveloped RNA virus. Rotavirus infection is a vaccine-preventable disease characterized by profuse, watery diarrhea in children.

(Choices E and F) Most **RNA viruses** are single-stranded and can be classified as negative- or positive-sense viruses. Positive-sense viruses can be directly translated into proteins, but negative-sense stranded viruses must first have their RNA converted into positive-sense strands before translation. Coxsackievirus, a single-stranded, positive-sense RNA virus of the enterovirus family, causes **hand, foot, and mouth disease**, which presents with vesicular lesions on the buccal mucosa, tongue, and soft palate. The gums and hard palate are usually involved in HSV gingivostomatitis, not hand-foot-mouth disease.

Educational objective:

Primary herpes simplex virus type 1 (HSV-1) infection in children causes gingivostomatitis (vesicular lesions on the lips and hard palate). HSV-1

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infected oral secretions or lesions. Inoculation occurs on mucosa or skin where the virus replicates rapidly in the host cell nucleus and causes abnormal cell division, resulting in intranuclear inclusion bodies and **multinucleated giant cells** visible on Tzanck smear. The vesicular lesions result from cell lysis and necrosis as well as tissue destruction, inflammation, and fluid accumulation between the dermis and epidermis.

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(Choices E and F) Most **RNA viruses** are single-stranded and can be classified as negative- or positive-sense viruses. Positive-sense viruses can be directly translated into proteins, but negative-sense stranded viruses must first have their RNA converted into positive-sense strands before translation. Coxsackievirus, a single-stranded, positive-sense RNA virus of the enterovirus family, causes **hand, foot, and mouth disease**, which presents with vesicular lesions on the buccal mucosa, tongue, and soft palate. The gums and hard palate are usually involved in HSV gingivostomatitis, not hand-foot-mouth disease.

Educational objective:

Primary herpes simplex virus type 1 (HSV-1) infection in children causes gingivostomatitis (vesicular lesions on the lips and hard palate). HSV-1 and other herpesviruses are double-stranded, enveloped DNA viruses.

References

- The RNA synthesis machinery of negative-stranded RNA viruses.
- Ultrastructure of the replication site of positive-stranded RNA viruses.

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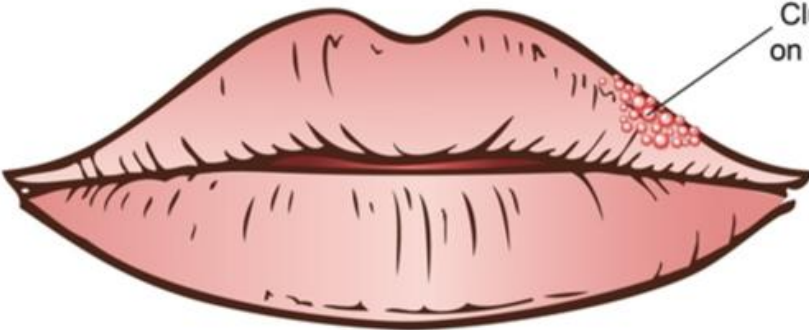
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Text Zoom

Exhibit Display

Herpes simplex virus ("cold sore")



Cluster of vesicles on vermilion border

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- ☐ A. Complete absence of memory T cells
- ☐ B. Decreased antibody production due to malnutrition
- ☐ C. High variability of microbial antigenic structure
- ☐ D. Poor antigen recognition due to antigenic mimicry
- ☐ E. Resistance to antimicrobial agents

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A 35-year-old homeless man comes to the emergency department due to urinary urgency, burning sensation on urination, and urethral discharge. The patient had similar symptoms 3 months ago, and urethral swab microscopy revealed numerous neutrophils and gram-negative diplococci. The symptoms resolved after treatment with ceftriaxone and azithromycin but recurred 4 days ago. The patient was advised to use condoms but has had many unprotected sexual encounters recently. He has no other medical problems. The patient occasionally drinks alcohol and smokes cigarettes. Temperature is 37.1 C (98.8 F). BMI is 18.8 kg/m². No suprapubic or flank tenderness is present on examination. Mild erythema is noted at the urethral meatus. Nucleic acid amplification testing of a clean catch urine specimen is positive for *Neisseria gonorrhoeae*. Which of the following is the most likely reason for the recurrence of infection in this patient?

☐

A. Complete absence of memory T cells [2%]

☐

B. Decreased antibody production due to malnutrition [6%]

☒

C. High variability of microbial antigenic structure [80%]

☐

D. Poor antigen recognition due to antigenic mimicry [3%]

☐

E. Resistance to antimicrobial agents [6%]

Omitted

Correct answer
C

80%

Answered correctly

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Explanation

This patient's symptoms of **gonococcal urethritis** (dysuria, urinary discharge) resolved with ceftriaxone and then recurred several months later

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This patient's symptoms of **gonococcal urethritis** (dysuria, urinary discharge) resolved with ceftriaxone and then recurred several months later after unprotected sexual encounters, raising suspicion for reinfection. Although infection with *Neisseria gonorrhoeae* does lead to the formation of IgA and IgG antibodies, the **high variability of gonococcal surface antigens** (eg, porins, Opa proteins, lipooligosaccharide) limits the effectiveness of the antibody response. As such, previous infection with *N gonorrhoeae* results in almost **no protective immunity** against future infections.

(Choice A) Memory T cells form in response to gonococcal infection but are not effective at preventing reinfection due to high antigenic variation (which prevents recognition of the organism).

(Choice B) The humoral antibody response can be impaired by severe malnutrition; however, the high rate of antigenic variability in gonococcal infection would already preclude development of an effective antibody response.

(Choice D) Antigenic mimicry occurs when an organism displays similar antigens to the host, preventing the host's immune system from recognizing the organism as foreign.

(Choice E) Gonorrhea is largely susceptible to third-generation cephalosporins (eg, ceftriaxone) but may be resistant to penicillins, macrolides, and fluoroquinolones. Antibiotic resistance should be suspected when initial symptoms do not improve with treatment. Because this patient's initial symptoms resolved after being treated with ceftriaxone and then recurred several months later, reinfection is far more likely than drug resistance. Patients with gonorrhea infection are also treated with azithromycin or doxycycline for potential *Chlamydia trachomatis* coinfection (which occurs in ~30% of patients).

Educational objective:

Neisseria gonorrhoeae has high antigenic variability of its surface molecules (eg, porins, Opa proteins), which prevents the formation of protective immunity and leads to susceptibility to repeat infection.

References

- New concepts in immunity to *Neisseria Gonorrhoeae*: innate responses and suppression of adaptive immunity favor the pathogen, not the

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A 22-year-old woman comes to the emergency department due to intermittent fevers and chills over the past few days. Last week, she underwent routine dental cleaning with no complications. The patient has a history of mitral valve prolapse. Temperature is 38.2 C (100.8 F). Physical examination reveals a non-ejection mid-systolic click followed by a late-systolic murmur best heard at the cardiac apex. Blood cultures are drawn and grow gram-positive bacteria that synthesize dextran from sucrose. Which of the following would be the most likely adherence site for these bacteria?

- ☐ A. Circulating heparins
- ☐ B. Endothelial surface glycoproteins
- ☐ C. Fibrin-platelet aggregates
- ☐ D. Subendothelial collagen
- ☐ E. Subendothelial glycosaminoglycans

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A 22-year-old woman comes to the emergency department due to intermittent fevers and chills over the past few days. Last week, she underwent routine dental cleaning with no complications. The patient has a history of mitral valve prolapse. Temperature is 38.2 C (100.8 F). Physical examination reveals a non-ejection mid-systolic click followed by a late-systolic murmur best heard at the cardiac apex. Blood cultures are drawn and grow gram-positive bacteria that synthesize dextrans from sucrose. Which of the following would be the most likely adherence site for these bacteria?

- ☐ A. Circulating heparins [0%]
- ☐ B. Endothelial surface glycoproteins [24%]
- ☒ C. Fibrin-platelet aggregates [53%]
- ☐ D. Subendothelial collagen [10%]
- ☐ E. Subendothelial glycosaminoglycans [11%]

Omitted

Correct answer
C

53%
Answered correctly

3 Seconds
Time Spent

11/22/2018
Last Updated

Explanation

This patient with mitral valve prolapse (as suggested by the auscultated systolic click and murmur) now has bacteremia following dental cleaning. **Viridans streptococci** are normal inhabitants of the oral cavity and cause **transient bacteremia** after **dental** procedures. These gram-positive organisms are capable of producing extracellular polysaccharides (**dextrans**) using sucrose as a substrate.

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Question Id: 1003

Explanation

This patient with mitral valve prolapse (as suggested by the auscultated systolic click and murmur) now has bacteremia following dental cleaning. **Viridans streptococci** are normal inhabitants of the oral cavity and cause **transient bacteremia** after **dental** procedures. These gram-positive organisms are capable of producing extracellular polysaccharides (**dextrans**) using sucrose as a substrate.

Dextrans facilitate streptococcal adherence to fibrin. **Fibrin and platelets** are deposited at sites of endothelial trauma, providing a site for bacterial adherence and colonization during bacteremia. In patients with pre-existing valvular lesions, viridans streptococci can adhere to the affected valve and establish infection leading to endocarditis. Other factors that facilitate pathogenesis may also be involved. *Staphylococcus aureus* is more aggressive and can adhere to intact valves. The risk of endocarditis following dental procedures is low with mitral valve prolapse, and antibiotic prophylaxis is not recommended; however, cases can still occur.

(Choice A) Circulating heparins prolong the partial thromboplastin time by activating antithrombin III, thereby decreasing thrombin activity and ultimately preventing fibrinogen conversion to fibrin, thereby preventing clot formation. Circulating heparins would not provide a binding site for bacteria.

(Choice B) Endothelial surface glycoproteins mediate binding of immune cells to endothelium, facilitated by the expression of cell adhesion molecules on the surface of inflamed endothelium. Neutrophils are then able to bind and migrate between the endothelial cells, followed by monocytes and lymphocytes.

(Choices D and E) Subendothelial collagen and glycosaminoglycans form the subendothelial fibrous cap over the central core of an atherosclerotic plaque and are potent platelet activators. When exposed (eg, denuded endothelium in atherosclerotic plaque), they contribute to rapid thrombus formation that can lead to myocardial infarction in a coronary artery.

Educational objective:

Viridans streptococci are normal inhabitants of the oral cavity and are a cause of transient bacteremia after dental procedures in healthy and diseased individuals. In patients with pre-existing valvular lesions, viridans streptococci can adhere to fibrin-platelet aggregates and establish infection that leads to endocarditis.

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A 29-year-old man is evaluated for 2 weeks of skin rash involving his hands, feet, and scalp. The rash is mildly pruritic and has progressively worsened. The patient has a history of HIV and is not adherent with antiretroviral therapy. Skin examination shows erythematous patches with scales and crusting. Biopsy of the rash shows organisms burrowed in the epidermis, as shown below:

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

A. Systemic acyclovir

B. Systemic terbinafine

C. Topical glucocorticoid

D. Topical mupirocin

E. Topical permethrin

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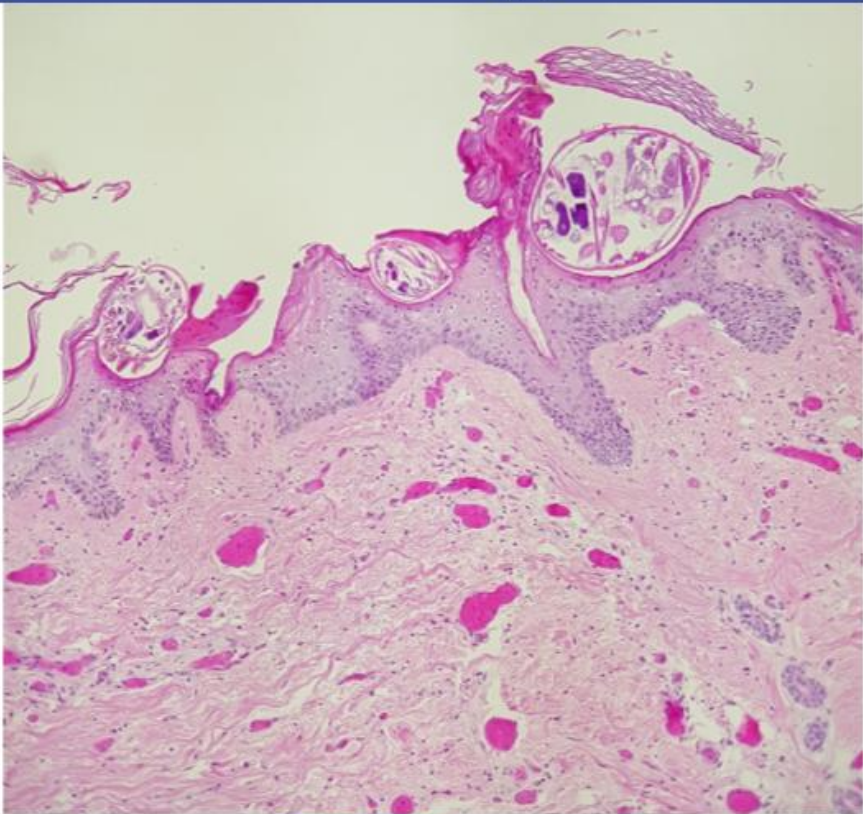
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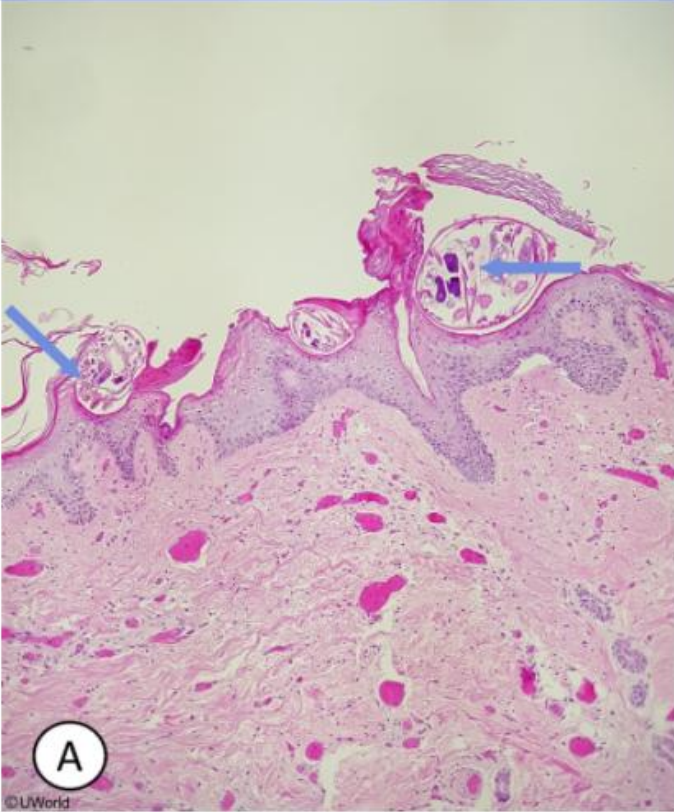
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epidermis and evoke a delayed-type hypersensitivity reaction to mite feces and eggs, which leads to an intensely pruritic rash. The mites

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

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B. Systemic terbinafine

C. Topical glucocorticoid

D. Topical mupirocin

E. Topical permethrin

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A 29-year-old man is evaluated for 2 weeks of skin rash involving his hands, feet, and scalp. The rash is mildly pruritic and has progressively worsened. The patient has a history of HIV and is not adherent with antiretroviral therapy. Skin examination shows erythematous patches with scales and crusting. Biopsy of the rash shows organisms burrowed in the epidermis, as shown below:

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

☐

A. Systemic acyclovir [5%]

☐

B. Systemic terbinafine [19%]

☐

C. Topical glucocorticoid [3%]

☐

D. Topical mupirocin [6%]

☒

E. Topical permethrin [64%]

Omitted

Correct answer
E

64%
Answered correctly

3 Seconds
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01/31/2019
Last Updated

Explanation

Scabies is a skin infection caused by the human mite *Sarcoptes scabiei*. Transmission occurs from prolonged skin-to-skin contact with an infected individual but may occasionally occur due to contact with contaminated fomites (eg, bedsheets, clothing). Mites burrow under the epidermis and evoke a delayed-type hypersensitivity reaction to mite feces and eggs, which leads to an intensely **pruritic rash**. The mite's **internal organs**, eggs, and spine can often be seen on histopathology.

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Classic scabies is associated with a mild mite burden (10-15 mites). Patients usually have several small erythematous papules on the sides/webs of the fingers, wrists, elbows, axillae, waist, and genitalia. Excoriations and **burrows** (thin, serpiginous red tracks) may be seen. In contrast, patients with impaired cell-mediated immunity (eg, **HIV**) are unable to contain the infection and usually develop **crusted scabies**, which is associated with thousands or **millions** of mites. These patients often have mild pruritis (because the inflammatory response is muted) and several erythematous patches with scaling and crusting.

Treatment is required to prevent discomfort, transmission, and potential complications (eg, secondary bacterial infection). First-line therapy includes **topical permethrin**, which blocks mite neurotransmission by impairing voltage-gated sodium channels. Permethrin cream is applied from the neck to the soles of the feet and left on for 8-14 hours. Oral **ivermectin**, an antiparasitic agent that binds chloride ion channels in invertebrate nerve and muscle cells, is an alternate medication for classic scabies and is used with permethrin for crusted scabies.

(Choice A) Oral acyclovir is used for human herpes simplex virus outbreaks, which are usually characterized by vesicular lesions on an erythematous base. The orolabial mucosa and genital area are affected most commonly. Histopathology would show an epidermal blister with acantholysis and **multinucleated cells**.

(Choice B) Oral terbinafine can be used for patients with dermatophytic infections of the skin. Dermatophytes often cause an erythematous scaly rash and erosions. Histopathology typically reveals fungal spores and/or hyphae.

(Choice C) Psoriasis is a chronic inflammatory skin condition that can be treated with topical glucocorticoids. It is usually associated with symmetric, **sharply defined skin plaques** with overlying scales on the extensor elbows, knees, and scalp. Histopathology generally shows uniform epidermal hyperplasia, **hyperkeratosis**, and perivascular lymphocytes.

(Choice D) Topical mupirocin can treat *Staphylococcus aureus*, the most common cause of purulent cellulitis. Patients usually have a focal, painful area of nodular fluctuance and surrounding erythema.

Educational objective:

Scabies is a human mite infection associated with a pruritic papular rash with excoriations and burrows. Patients with impaired cell-mediated

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(Choice D) Topical mupirocin can treat *Staphylococcus aureus*, the most common cause of purulent cellulitis. Patients usually have a focal, painful area of nodular fluctuance and surrounding erythema.

Educational objective:

Scabies is a human mite infection associated with a pruritic papular rash with excoriations and burrows. Patients with impaired cell-mediated immunity (eg, HIV) often develop a very high mite burden. Treatment with topical permethrin and/or ivermectin is generally curative.

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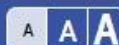
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Settings

A microbiologist is studying the structure and function of bacterial cell walls. In an experiment, group A streptococci are treated with chemicals to solubilize the cell wall. Various cell wall-associated proteins are subsequently extracted. Electron microscopic evaluation of a specific protein shows structural homology with mammalian tropomyosin and myosin. This protein acts as a virulence factor for certain species of the organism. Which of the following is the most likely function of this bacterial cell wall-associated protein?

- ☐ A. Excrete antibiotics
- ☐ B. Protect from osmotic lysis
- ☐ C. Provide mechanical cell support
- ☐ D. Resist phagocytosis
- ☐ E. Transport nutrients into the cell

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A microbiologist is studying the structure and function of bacterial cell walls. In an experiment, group A streptococci are treated with chemicals to solubilize the cell wall. Various cell wall-associated proteins are subsequently extracted. Electron microscopic evaluation of a specific protein shows structural homology with mammalian tropomyosin and myosin. This protein acts as a virulence factor for certain species of the organism. Which of the following is the most likely function of this bacterial cell wall-associated protein?

A. Excrete antibiotics [5%]

B. Protect from osmotic lysis [7%]

C. Provide mechanical cell support [31%]

D. Resist phagocytosis [46%]

E. Transport nutrients into the cell [8%]

Omitted

Correct answer
D

46%

Answered correctly

3 Seconds

Time Spent

09/11/2018

Last Updated

Explanation

Gram-positive organisms have cell walls composed primarily of a thick peptidoglycan layer and teichoic acid. However, additional cell wall components are often present that contribute to virulence, motility, or the ability to adhere to epithelial surfaces. For instance, the cell wall of **group A streptococcus** (also known as *Streptococcus pyogenes*) is studded with **M protein**, a virulence factor that **inhibits phagocytosis**, prevents complement binding, and aids in epithelial attachment.

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components are often present that contribute to virulence, motility, or the ability to adhere to epithelial surfaces. For instance, the cell wall of **group A streptococcus** (also known as *Streptococcus pyogenes*) is studded with **M protein**, a virulence factor that **inhibits phagocytosis**, prevents complement binding, and aids in epithelial attachment.

M protein is an alpha-helical coiled-coil protein that shares epitopes and **structural homology** with other alpha-helical coiled-coil proteins such as **tropomyosin and myosin**. In some patients, the protective antibodies against M protein that develop in *S pyogenes* acute infection may **cross-react** with myosin epitopes in the heart and cause **rheumatic carditis**.

(Choice A) Efflux pumps are generally globular proteins with multiple domains. They reside in the bacterial cell membrane and excrete toxic substances from the interior of the cell. Bacteria can use efflux pumps to generate antibiotic resistance to drugs that operate in the interior of the cell, such as fluoroquinolones and aminoglycosides.

(Choices B and C) The bacterial cell wall of *S pyogenes* provides mechanical support and protects it from osmotic lysis. It is composed primarily of peptidoglycan, which forms a mesh-like, **cross-linked polymer** of peptides and sugars.

(Choice E) Porins in the cell membrane aid in the movement of nutrients into bacterial cells. They are composed of protein strands that group together to form a barrel (beta-barrel).

Educational objective:

The major virulence factor of *Streptococcus pyogenes* is M protein, an alpha-helical coiled-coil protein that shares structural homology with tropomyosin and myosin. It extends from the cell wall and prevents phagocytosis, inhibits complement binding, and mediates bacterial adherence. Antibodies against M protein form shortly after acute infection and may cross-react with epitopes on myosin, leading to rheumatic carditis.

References

- M protein and other surface proteins on streptococci.

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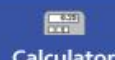
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TUTOR



A 24-year-old woman comes to the emergency department due to joint pain. A week ago, the patient had a flu-like illness with fever, malaise, and fleeting joint aches in her wrists, ankles, and knees. Over the past 2 days, the joint pain worsened, and she developed new swelling of the right knee. The patient has no chronic medical problems and has had no similar symptoms in the past. She does not use tobacco, alcohol, or injection drugs. She is sexually active, uses an oral contraceptive for birth control, and her last menstrual period was a week ago. Temperature is 38 C (100.4 F). On examination, there is no scleral icterus, facial rash, or oral ulcers but a few scattered painless vesicopustular lesions are present on the upper extremities. The right knee is warm, swollen, and tender with decreased range of motion. Both ankles and the left wrist are mildly tender to palpation but not swollen or erythematous. Arthrocentesis of the right knee joint yields 20 mL of cloudy fluid with a leukocyte count of 50,000/mm³ (90% neutrophils). Additional evaluation of the joint fluid is most likely to show which of the following in this patient?

- ☐ A. Gram-negative intracellular diplococci
- ☐ B. Gram-negative oxidase-negative curved rods
- ☐ C. Gram-positive alpha-hemolytic cocci in chains
- ☐ D. Gram-positive catalase-positive cocci in clusters
- ☐ E. Needle-shaped negatively birefringent crystals
- ☐ F. Rhomboid-shaped positively birefringent crystals

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☒ A. Gram-negative intracellular diplococci [69%]

☐ B. Gram-negative oxidase-negative curved rods [3%]

☐ C. Gram-positive alpha-hemolytic cocci in chains [4%]

☐ D. Gram-positive catalase-positive cocci in clusters [19%]

☐ E. Needle-shaped negatively birefringent crystals [1%]

☐ F. Rhomboid-shaped positively birefringent crystals [1%]

08/29/2018
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This patient has purulent arthritis of the knee, oligoarticular joint pain, and a few vesiculopustular lesions on the extremities, raising suspicion for **disseminated gonococcal infection (DGI)**. DGI is one of the most common causes of **septic arthritis** in young, sexually active individuals. It is due to the spread of ***Neisseria gonorrhoeae*** from a (usually asymptomatic) genitourinary infection into the systemic circulation. Patients typically present with either purulent arthritis or the triad of polyarthralgia, dermatitis, and tenosynovitis; however, some overlap in these 2 syndromes can occur (as in this patient). The diagnosis is made when blood, urine, or joint fluid microscopy and culture reveal **gram-negative intracellular diplococci**.

(Choice B) Salmonella appears as a gram-negative oxidase-negative curved rod. Patients with sickle cell disease are at increased risk of septic arthritis due to salmonella. However, salmonella is an uncommon cause of septic arthritis in patients who do not have sickle cell disease.

(Choice C) Viridans streptococci, a gram-positive alpha-hemolytic cocci in chains, is a common cause of infective endocarditis and can lead to septic arthritis (due to septic emboli). Patients with infective endocarditis can have flu-like symptoms and skin findings (eg, Osler nodes, Janeway lesions). However, vesiculopustular lesions on the arms are much more characteristic of DGI.

(Choice D) *Staphylococcus aureus*, a catalase-positive **gram-positive cocci in clusters**, is the most common cause of septic arthritis. However, most cases in young adults are linked to injection drug use. In addition, the presence of vesiculopustular lesions and oligoarticular arthralgias make gonococcal arthritis more likely.

(Choices E and F) Gout is caused by monosodium urate crystals that appear as **needle-shaped negatively birefringent crystals**. Pseudogout is caused by calcium pyrophosphate dihydrate crystals that appear as **rhomboid-shaped positively birefringent crystals**. Both gout and pseudogout cause inflammatory arthritis (eg, redness, warmth, pain, disability) with elevated leukocyte counts on joint fluid aspiration. However, migrating arthralgias and vesiculopustular lesions would be atypical.

Educational objective:

Septic arthritis in a young, sexually active adult should raise suspicion for disseminated *Neisseria gonorrhoeae* infection. Patients may also have the triad of polyarthritits, a vesiculopustular skin rash, and tenosynovitis. *N gonorrhoeae* is a gram-negative diplococci that is usually identified by microscopy, culture, or nucleic acid amplification.

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A 24-year-old female presents to your office with burning during urination, urine clouding and urinary frequency. She denies fever, chills and flank pain. She had a similar episode before that was treated with antibiotics. She has no other medical problems and does not use tobacco, alcohol or drugs. Her vital signs are stable. Physical examination shows suprapubic tenderness. Which of the following bacteria is most likely to be isolated from this patient's urine?

- ☐ A. *Klebsiella pneumoniae*
- ☐ B. *Salmonella typhi*
- ☐ C. *Salmonella enteritidis*
- ☐ D. *Campylobacter jejuni*
- ☐ E. *Shigella dysenteriae*
- ☐ F. *Proteus mirabilis*
- ☐ G. *Yersinia enterocolitica*
- ☐ H. *Haemophilus influenzae*
- ☐ I. *Vibrio cholerae*
- ☐ J. *Streptococcus pyogenes*
- ☐ K. *Streptococcus pneumoniae*
- ☐ L. *Entamoeba histolytica*
- ☐ M. *Escherichia coli*

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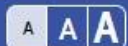
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drugs. Her vital signs are stable. Physical examination shows suprapubic tenderness. Which of the following bacteria is most likely to be isolated from this patient's urine?

- ☐ A. *Klebsiella pneumoniae* [1%]
- ☐ B. *Salmonella typhi* [0%]
- ☐ C. *Salmonella enteritidis* [0%]
- ☐ D. *Campylobacter jejuni* [0%]
- ☐ E. *Shigella dysenteriae* [0%]
- ☐ F. *Proteus mirabilis* [4%]
- ☐ G. *Yersinia enterocolitica* [0%]
- ☐ H. *Haemophilus influenzae* [0%]
- ☐ I. *Vibrio cholerae* [0%]
- ☐ J. *Streptococcus pyogenes* [0%]
- ☐ K. *Streptococcus pneumoniae* [0%]
- ☐ L. *Entamoeba histolytica* [0%]
- ☒ M. *Escherichia coli* [92%]

Omitted

Correct answer



92%

Answered correctly



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08/09/2018

Last Updated

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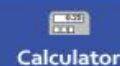
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TUTOR



Explanation

Usually, the urinary tract and urine are sterile. The presence of microorganisms in the urine is due to either a urinary tract infection (UTI), contamination or both. Contamination is highly suspected if the urine is polymicrobial or atypical of the microbial flora commonly seen in UTIs. A UTI can be symptomatic (cystitis, pyelonephritis) or asymptomatic (asymptomatic bacteriuria). It affects an estimated 20% of women at some time during their lifetimes. Most often, the infection is due to invasion by enteric coliform bacteria that inhabit the periurethral vaginal introitus and ascend into the bladder via the urethra. The most common causative organism is *Escherichia coli*, which accounts for 80% or more of cases. Most of the remainder of cases in sexually active women are caused by *Staphylococcus saprophyticus*; other gram-negative enterics such as *Proteus* account for a smaller percentage.

Normally, symptomatic UTIs are treated with a three-day course of a fluoroquinolone or TMP-SMX (trimethoprim-sulfamethoxazole). Symptoms of fever, chills and flank pain should alert the physician to the possibility of pyelonephritis.

Clinical entity	Common Organisms	Symptoms	Laboratory
Urethritis	N. gonorrhoeae C. trachomatis	Pain or burning sensation during urination, urgency or frequent urination.	UA: +WBC
Cystitis	E. coli S. saprophyticus P. mirabilis Klebsiella Enterococci	May be asymptomatic or symptomatic. Suprapubic pain and tenderness, frequent urination.	UA & Micro: +Leukocyte Esterase, +Nitrites, +bacteria, +WBC, +RBC occasionally
			UA & Micro: Same findings as in cystitis, but also

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TUTOR



Normally, symptomatic UTIs are treated with a three-day course of a fluoroquinolone or TMP-SMX (trimethoprim-sulfamethoxazole). Symptoms of fever, chills and flank pain should alert the physician to the possibility of pyelonephritis.

Clinical entity	Common Organisms	Symptoms	Laboratory
Urethritis	N. gonorrhoeae C. trachomatis	Pain or burning sensation during urination, urgency or frequent urination.	UA: +WBC
Cystitis	E. coli S. saprophyticus P. mirabilis Klebsiella Enterococci	May be asymptomatic or symptomatic. Suprapubic pain and tenderness, frequent urination.	UA & Micro: +Leukocyte Esterase, +Nitrites, +bacteria, +WBC, +RBC occasionally
Pyelonephritis	Same as cystitis	Flank pain, costovertebral angle tenderness, fever, chills, hematuria with casts	UA & Micro: Same findings as in cystitis, but also may see WBC casts indicating renal-based pyuria CBC: Elevated WBC

Educational Objective:

E. coli is the most common pathogen causing cystitis and acute pyelonephritis. The second most common cause of UTI in sexually active women is *Staphylococcus saprophyticus*. UTIs most commonly affect women because of their very short urethra; recurrent UTIs in boys or men require investigation for urinary tract obstruction or reflux.

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A 68-year-old woman comes to the office for evaluation of a skin rash. The patient says that red, painful papules erupted on her right chest 5 days ago and quickly turned into vesicles containing clear fluid. The lesions are now beginning to crust and are less painful. She has never had similar lesions and does not recall coming into contact with a person having a similar illness. Medical history is significant only for well-controlled hypertension. Physical examination shows a grouped vesicular rash involving the right T4 dermatome that is beginning to heal with crusting. The rash does not cross the midline. Lightly touching the skin elicits sharp pain. The remainder of the examination shows no abnormalities. This patient is at greatest risk of developing which of the following complications as a result of her current condition?

☐

A. Dissemination of rash to other body areas

☐

B. Painful swelling of the large joints

☐

C. Persistent pain in the affected region

☐

D. Recurrent episodes of gross hematuria

☐

E. Sensory loss in "glove and stocking" pattern

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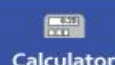
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2/5/2019



A 68-year-old woman comes to the office for evaluation of a skin rash. The patient says that red, painful papules erupted on her right chest 5 days ago and quickly turned into vesicles containing clear fluid. The lesions are now beginning to crust and are less painful. She has never had similar lesions and does not recall coming into contact with a person having a similar illness. Medical history is significant only for well-controlled hypertension. Physical examination shows a grouped vesicular rash involving the right T4 dermatome that is beginning to heal with crusting. The rash does not cross the midline. Lightly touching the skin elicits sharp pain. The remainder of the examination shows no abnormalities. This patient is at greatest risk of developing which of the following complications as a result of her current condition?

- ☐ A. Dissemination of rash to other body areas [3%]
- ☐ B. Painful swelling of the large joints [3%]
- ☒ C. Persistent pain in the affected region [85%]
- ☐ D. Recurrent episodes of gross hematuria [1%]
- ☐ E. Sensory loss in "glove and stocking" pattern [6%]

Omitted

Correct answer
C



85%
Answered correctly



3 Seconds
Time Spent



09/27/2018
Last Updated

Explanation

This patient has a vesicular rash consistent with **herpes zoster** (shingles), which is caused by **reactivation** of latent varicella-zoster virus (VZV) infection. Following the primary infection (**chickenpox**), VZV remains dormant in the **dorsal root ganglia** until emerging decades later. Decreased cell-mediated immunity (eg, older age, immunosuppressive medications, HIV infection) increases the risk of reactivation.

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Explanation

This patient has a vesicular rash consistent with **herpes zoster** (shingles), which is caused by **reactivation** of latent varicella-zoster virus (VZV) infection. Following the primary infection (**chickenpox**), VZV remains dormant in the **dorsal root ganglia** until emerging decades later. Decreased cell-mediated immunity (eg, older age, immunosuppressive medications, HIV infection) increases the risk of reactivation.

Reactivation of VZV causes hemorrhagic inflammation of the dorsal root ganglion and peripheral nerve. The resulting hypersensitive nerve function presents with **neuropathic pain** in the affected region (herpetic neuralgia), typically described as stabbing, tingling, or burning. Herpetic neuralgia can begin even before the appearance of skin lesions and may persist for up to several months. A minority of patients experience **long-term residual pain**, termed **postherpetic neuralgia**; the risk is greater in older patients (age >70) and those with more severe shingles.

(Choice A) Primary VZV infection is characterized by a diffuse vesicular rash (chickenpox), but reactivation is dermatomal. Generalized reactivation or spread to other body areas can occur in immune-compromised patients but is extremely rare in healthy individuals.

(Choice B) Reactive arthritis presents with an asymmetric peripheral oligoarthritis, often with extraarticular symptoms (eg, uveitis, conjunctivitis, urethritis). It typically follows bacterial gastrointestinal (eg, *Salmonella*, *Shigella*, *Campylobacter*) or genitourinary (eg, *Chlamydia*) infection.

(Choice D) IgA nephropathy produces recurrent glomerulonephritis and typically presents with episodic hematuria. Common triggers include upper respiratory illness, but shingles does not typically exacerbate the condition.

(Choice E) Toxic or metabolic nerve injury (eg, diabetic peripheral neuropathy) is typically proportionate to the length of the sensory nerve fibers. Symptoms appear first in the longest nerves, such as those to the feet and hands, causing a "glove and stocking" distribution. However, because reactivation of VZV occurs only in specific sensory ganglia, symptoms have a dermatomal distribution.

Educational objective:

A unilateral vesicular rash localized on a single dermatome in an older patient is most likely herpes zoster. Postherpetic neuralgia is the most common neurologic complication of varicella zoster virus infection.

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Explanation

Exhibit Display

Varicella-zoster virus (VZV) infection

The diagram illustrates the lifecycle of the Varicella-zoster virus (VZV). It features two human figures: a child on the left and an adult on the right. The child is shown with a widespread rash, representing the primary infection. A green virus particle is shown entering the child's skin. An arrow labeled 'Migration to sensory ganglion' points from the skin to a cross-section of a spinal cord, where the virus is shown entering a sensory ganglion. A long arrow labeled 'Years later' points from the child to the adult. The adult is shown with a localized rash, representing reactivation. An arrow labeled 'Migration to dermatome' points from the sensory ganglion to the adult's skin. Text labels include 'Latency (dormant VZV)' pointing to the virus in the ganglion, 'Reactivation of VZV by aging, immunosuppression' pointing to the adult's rash, and 'VZV' pointing to the virus particle. At the bottom of the exhibit are buttons: 'Zoom In', 'Zoom Out', 'Reset', and 'Add To Flash Card'.

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Explanation

Exhibit Display

Migration to dermatome

Migration to sensory ganglion

Varicella (chickenpox)
Generalized vesicular rash

Herpes zoster (shingles)
Unilateral, linear vesicular rash

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Zoom In

Zoom Out

Reset

Add To Flash Card

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Settings

An outbreak of infection with a seasonal influenza A strain is reported in a small community. The strain is similar to the one that circulated in the preceding year. Approximately 70% of the adult population in that community remains uninfected, despite prolonged and repeated exposure to ill contacts. Which of the following is the most important host factor in preventing influenza infection in these subjects?

- ☐ A. Antibodies against hemagglutinin
- ☐ B. Antibodies against neuraminidase
- ☐ C. Antibodies against RNA polymerase
- ☐ D. Antigen-nonspecific macrophage response
- ☐ E. T-cell response against nucleocapsid proteins

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TUTOR





An outbreak of infection with a seasonal influenza A strain is reported in a small community. The strain is similar to the one that circulated in the preceding year. Approximately 70% of the adult population in that community remains uninfected, despite prolonged and repeated exposure to ill contacts. Which of the following is the most important host factor in preventing influenza infection in these subjects?

- ☒ A. Antibodies against hemagglutinin [54%]
- ☐ B. Antibodies against neuraminidase [23%]
- ☐ C. Antibodies against RNA polymerase [3%]
- ☐ D. Antigen-nonspecific macrophage response [2%]
- ☐ E. T-cell response against nucleocapsid proteins [15%]

Omitted

Correct answer
A54%
Answered correctly3 Seconds
Time Spent09/20/2018
Last Updated

Explanation

In this question, 70% of the adult population in a small community with an influenza A outbreak are uninfected, because they are protected either through vaccination or from prior influenza A infection (with a similar strain). A **humoral** response with antibodies directed against **hemagglutinin** is generally the most important source of protection. These antibodies can neutralize the virus and primarily block its binding to the host cells. Antibodies to neuraminidase are not the main source of protection against reinfection although they have some protective effect (decrease extent of viral invasion and shedding) (**Choice B**).

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Omitted

Correct answer
A

54%
Answered correctly

3 Seconds
Time Spent

09/20/2018
Last Updated

Explanation

In this question, 70% of the adult population in a small community with an influenza A outbreak are uninfected, because they are protected either through vaccination or from prior influenza A infection (with a similar strain). A **humoral** response with antibodies directed against **hemagglutinin** is generally the most important source of protection. These antibodies can neutralize the virus and primarily block its binding to the host cells. Antibodies to neuraminidase are not the main source of protection against reinfection although they have some protective effect (decrease extent of viral invasion and shedding) (**Choice B**).

(Choices C and D) Circulating antibodies to internal influenza virus proteins (including the viral RNA-dependent RNA polymerase) do not confer immunity. Innate immunity (eg, antigen-nonspecific macrophage responses) does not appear to prevent primary influenza infection or reinfection. Reinfection is best prevented by adaptive immune mechanisms, which are by definition antigen-specific.

(Choice E) Cytotoxic CD8+ T cells specific for the major histocompatibility complex (MHC) class I-associated peptides derived from nucleocapsid proteins can kill infected cells and limit disease severity but are not thought to prevent infection. Expression of nucleocapsid proteins on MHC class II stimulates a CD4+ Th1-type T cell response (which stimulates CD8+ cell production through cytokines) and a CD4+ Th2-type T cell response. The Th2-type T cell response generates anti-nucleocapsid antibodies that do not appear to play a role in protective immunity.

Educational objective:

Major adaptive immune mechanisms that prevent reinfection with the influenza virus include anti-hemagglutinin antibodies.

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A 23-year-old woman participates in a research study evaluating the effect of monoclonal antibodies on viral infection. The patient has no past medical history and takes no medications. She has not been ill recently. During the study, a peripheral blood specimen is obtained. CD19 positive cells are isolated, purified, and exposed to monoclonal antibodies against cell surface complement receptor CD21. The cells are subsequently incubated along with several viruses being studied. Initial exposure to monoclonal antibodies against CD21 is most likely to prevent cell infection with which of the following viruses?

☐ A. Adenovirus

☐ B. Cytomegalovirus

☐ C. Epstein-Barr virus

☐ D. Human immunodeficiency virus

☐ E. Parvovirus B19

Submit

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2/5/2019



A 23-year-old woman participates in a research study evaluating the effect of monoclonal antibodies on viral infection. The patient has no past medical history and takes no medications. She has not been ill recently. During the study, a peripheral blood specimen is obtained. CD19 positive cells are isolated, purified, and exposed to monoclonal antibodies against cell surface complement receptor CD21. The cells are subsequently incubated along with several viruses being studied. Initial exposure to monoclonal antibodies against CD21 is most likely to prevent cell infection with which of the following viruses?

- ☐ A. Adenovirus [1%]
- ☐ B. Cytomegalovirus [4%]
- ☒ C. Epstein-Barr virus [84%]
- ☐ D. Human immunodeficiency virus [5%]
- ☐ E. Parvovirus B19 [4%]

Omitted

Correct answer
C

 84%
Answered correctly

 3 Seconds
Time Spent

 11/24/2018
Last Updated

Explanation

The initial attachment of the virion envelope or capsid surface proteins to the complementary host cell surface receptors is essential to viral tropism for specific tissues and invasion of cells. Many viruses bind to normal host cell plasma membrane receptors to enter host cells.

Epstein-Barr virus (EBV) is a herpesvirus responsible for acute infectious mononucleosis, nasopharyngeal carcinoma, and certain lymphomas

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The initial attachment of the virion envelope or capsid surface proteins to the complementary host cell surface receptors is essential to viral tropism for specific tissues and invasion of cells. Many viruses bind to normal host cell plasma membrane receptors to enter host cells.

Epstein-Barr virus (EBV) is a herpesvirus responsible for acute infectious mononucleosis, nasopharyngeal carcinoma, and certain lymphomas (eg, Burkitt lymphoma). More than 90% of the normal adult population is seropositive for EBV, which is primarily transmitted through contact with oropharyngeal secretions. The EBV envelope glycoprotein gp350 binds to **CD21** (also known as CR2), the cellular receptor for the C3d complement component. CD21 is normally present on the surface of **B cells** (CD19-positive cells) and nasopharyngeal epithelial cells. Therefore, exposure to a monoclonal anti-CD21 antibody could interfere with EBV attachment to B cells.

(Choice A) Adenovirus has hexon and penton capsomeres on its surface. Rodlike structures ("fibers") that project from the penton base capsomeres are responsible for mediating adsorption to host cells. The cell receptor for most adenovirus fibers is a transmembrane protein member of the immunoglobulin superfamily.

(Choice B) Like other herpesviruses, cytomegalovirus requires initial contact with glycosaminoglycan chains on host cell surface proteoglycans for entry into the host cell. It does not require contact with CD21.

(Choice D) HIV viruses attach to their major target host cells (CD4⁺ T cells) primarily via the binding of viral envelope glycoprotein **gp120** to the cellular CD4 transmembrane glycoprotein and the coreceptor (CCR5 or CXCR4). The HIV envelope then undergoes a conformational change that activates gp41 and initiates membrane fusion.

(Choice E) Parvovirus B19 is thought to attach to human erythroid cells via the blood group P antigen (globoside), which is expressed by mature erythrocytes, erythroid progenitors, megakaryocytes, placenta, and the fetal liver and heart. Immature cells of the erythroid family (eg, adult bone marrow, fetal liver) are most vulnerable to parvovirus B19 infection.

Educational objective:

The initial attachment of the virion envelope or capsid surface proteins to the complementary host cell surface receptors is essential to viral tropism for specific tissues and invasion of cells. Many viruses bind to normal host cell plasma membrane receptors to enter host cells. Known host cell receptor and virion/virion protein binding specificities include: CD4 with HIV gp120, CD21 with Epstein-Barr virus gp350, and erythrocyte P antigen with parvovirus B19.

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A 54-year-old man comes to the emergency department due to fever, chills, and malaise over the past day. His other medical problems include recently diagnosed Hodgkin disease. Temperature is 39.4 C (103 F), blood pressure is 102/61 mm Hg, and pulse is 114/min. The patient appears ill. Blood cultures grow motile gram-positive rods that produce a very narrow zone of beta hemolysis on blood agar. The bacteria are also found to grow well at refrigerated temperature. Which of the following processes is most important for eliminating these bacteria from the body?

A. Cell-mediated immunity

B. Eosinophil action

C. Immunoglobulin secretion

D. Mast cell activation

E. Terminal complement cascade

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2/5/2019



A 54-year-old man comes to the emergency department due to fever, chills, and malaise over the past day. His other medical problems include recently diagnosed Hodgkin disease. Temperature is 39.4 C (103 F), blood pressure is 102/61 mm Hg, and pulse is 114/min. The patient appears ill. Blood cultures grow motile gram-positive rods that produce a very narrow zone of beta hemolysis on blood agar. The bacteria are also found to grow well at refrigerated temperature. Which of the following processes is most important for eliminating these bacteria from the body?

- ☒ A. Cell-mediated immunity [59%]
- ☐ B. Eosinophil action [0%]
- ☐ C. Immunoglobulin secretion [25%]
- ☐ D. Mast cell activation [1%]
- ☐ E. Terminal complement cascade [13%]

Omitted

Correct answer
A



59%
Answered correctly



3 Seconds
Time Spent



09/18/2018
Last Updated

Explanation

Common intracellular pathogens*

Chlamydia
Francisella tularensis
Legionella

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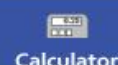


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Common intracellular pathogens*

Bacteria	<i>Chlamydia</i>
	<i>Francisella tularensis</i>
	<i>Legionella</i>
	<i>Listeria monocytogenes</i>
	<i>Mycobacterium</i>
	<i>Neisseria gonorrhoeae</i>
	<i>Nocardia</i>
	<i>Rickettsia</i>
	<i>Salmonella typhi</i>
Fungi	<i>Cryptococcus neoformans</i>
	<i>Histoplasma capsulatum</i>
Protozoa	<i>Cryptosporidium parvum</i>
	<i>Leishmania</i>
	<i>Plasmodium</i>
	<i>Toxoplasma gondii</i>
	<i>Trypanosoma</i>

*Facultative intracellular pathogens are also included.

Listeria monocytogenes is a facultative intracellular, gram-positive rod that produces a **very narrow zone of beta hemolysis** on blood agar (similar to group B *Streptococcus* [*Streptococcus agalactiae*]). *Listeria* is immotile at body temperature but demonstrates **tumbling motility at room temperature**. The pathogen is also distinguished by an ability to multiply at refrigerated temperatures (**cold enrichment**), which is one reason *Listeria* is an important cause of foodborne illness (eg, refrigerated soft cheese, meats, unpasteurized milk).

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room temperature. The pathogen is also distinguished by an ability to multiply at refrigerated temperatures (**cold enrichment**), which is one reason *Listeria* is an important cause of foodborne illness (eg, refrigerated soft cheese, meats, unpasteurized milk).

The elimination of intracellular pathogens is largely reliant on the **cell-mediated immune response** as bacteria within cells are protected from circulating immune factors (eg, antibodies, complement). Cells infected by intracellular bacteria display bacterial protein fragments on their surface, which triggers cell lysis by **cytotoxic T cells**. This releases the organism from the protected intracellular space and exposes it to phagocytosis by macrophages. Although intracellular pathogens can often replicate within inactivated macrophages due to virulence factors that prevent phagolysosome destruction, cytotoxic T-cells release **interferon gamma** to **activate macrophages** leading to the formation of fully mature (acidified) phagolysosomes capable of destroying the bacteria.

As the elimination of *Listeria* is reliant on the cell mediated immune response, patients with **impaired cell-mediated** immunity are at greatest risk for invasive *Listeria* infections (eg, sepsis, meningitis), particularly those at the extremes of age (ie, neonates, elderly) or patients who are immunosuppressed (eg, Hodgkin disease, AIDS) or pregnant.

(Choice B) Eosinophils are a component of the innate immune system and are tasked primarily with the eradication of parasitic infections (eg, helminths). Eosinophils play a minor role in the phagocytosis and destruction of intracellular bacteria.

(Choice C) The humoral immune system secretes immunoglobulins and is largely tasked with eliminating extracellular infections such as *Streptococci* and *Staphylococci*. This system is not able to effectively target intracellular bacteria as immunoglobulins cannot access the intracellular space.

(Choice D) Mast cells contribute to defense against parasites and play an important role in allergic responses, particularly immediate hypersensitivity reactions; they do not confer immunity to intracellular pathogens.

(Choice E) The complement system is part of the innate immune system and aids in the opsonization and destruction of bacteria. The terminal complement components (eg, C5b-C9) create a membrane attack complex to lyse bacteria and are particularly important against *Neisseria* infections.

Educational objective:

Listeria monocytogenes is a facultative, intracellular, gram-positive rod that produces a very narrow zone of beta hemolysis on blood agar, shows

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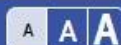
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As the elimination of *Listeria* is reliant on the cell-mediated immune response, patients with **impaired cell-mediated immunity** are at greatest risk for invasive *Listeria* infections (eg, sepsis, meningitis), particularly those at the extremes of age (ie, neonates, elderly) or patients who are immunosuppressed (eg, Hodgkin disease, AIDS) or pregnant.

(Choice B) Eosinophils are a component of the innate immune system and are tasked primarily with the eradication of parasitic infections (eg, helminths). Eosinophils play a minor role in the phagocytosis and destruction of intracellular bacteria.

(Choice C) The humoral immune system secretes immunoglobulins and is largely tasked with eliminating extracellular infections such as *Streptococci* and *Staphylococci*. This system is not able to effectively target intracellular bacteria as immunoglobulins cannot access the intracellular space.

(Choice D) Mast cells contribute to defense against parasites and play an important role in allergic responses, particularly immediate hypersensitivity reactions; they do not confer immunity to intracellular pathogens.

(Choice E) The complement system is part of the innate immune system and aids in the opsonization and destruction of bacteria. The terminal complement components (eg, C5b-C9) create a membrane attack complex to lyse bacteria and are particularly important against *Neisseria* infections.

Educational objective:

Listeria monocytogenes is a facultative, intracellular, gram-positive rod that produces a very narrow zone of beta hemolysis on blood agar, shows tumbling motility at room temperature, and can grow at refrigerated temperatures. Intracellular pathogens such as *Listeria* are largely eliminated by the cell-mediated immune response (eg, T-cells, macrophages, cytokines). Patients with impaired cell-mediated immunity are at risk for invasive *Listeria* infections.

References

- Innate and adaptive immune responses to *Listeria monocytogenes*: a short overview. Page(s): PMC2042024

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Question Id: 1005



A pharmaceutical researcher is developing a novel agent to prevent meningococcal disease in people exposed to the bacteria. Pili antigens from *Neisseria meningitidis* are extracted and used to generate monoclonal antibodies that impair normal pili function. The antibodies are administered to experimental animals with no prior exposure to *N meningitidis*. These animals, along with control animals that had not received the antibodies, are subsequently exposed to the bacteria. Compared to the control animals, a significantly greater proportion of the animals that received the antibodies remain healthy and develop no symptoms. The efficacy of these antibodies in preventing meningococcal disease is most likely due to direct interference with which of the following microbial processes?

- ☐ A. Adhesion to vascular endothelial cells
- ☐ B. Attachment to nasopharyngeal epithelial cells
- ☐ C. Hematogenous dissemination
- ☐ D. Invasion of the meninges
- ☐ E. Survival inside phagocytes

Submit

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TUTOR





A pharmaceutical researcher is developing a novel agent to prevent meningococcal disease in people exposed to the bacteria. Pili antigens from *Neisseria meningitidis* are extracted and used to generate monoclonal antibodies that impair normal pili function. The antibodies are administered to experimental animals with no prior exposure to *N meningitidis*. These animals, along with control animals that had not received the antibodies, are subsequently exposed to the bacteria. Compared to the control animals, a significantly greater proportion of the animals that received the antibodies remain healthy and develop no symptoms. The efficacy of these antibodies in preventing meningococcal disease is most likely due to direct interference with which of the following microbial processes?

- ☐ A. Adhesion to vascular endothelial cells [20%]
- ☒ B. Attachment to nasopharyngeal epithelial cells [64%]
- ☐ C. Hematogenous dissemination [4%]
- ☐ D. Invasion of the meninges [6%]
- ☐ E. Survival inside phagocytes [3%]

Omitted

Correct answer
B64%
Answered correctly3 Seconds
Time Spent10/02/2018
Last Updated

Explanation

Neisseria meningitidis is commonly isolated from the oropharynx and nasopharynx of asymptomatic carriers. Colonization rates are variable but highest in close contact populations (eg, military recruits, university students). Transmission of meningococci usually occurs through exposure to respiratory droplets or direct contact with respiratory secretions. The **pili** on the capsular surface of *N meningitidis* are primarily responsible for

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Explanation

Neisseria meningitidis is commonly isolated from the oropharynx and nasopharynx of asymptomatic carriers. Colonization rates are variable but highest in close contact populations (eg, military recruits, university students). Transmission of meningococci usually occurs through exposure to respiratory droplets or direct contact with respiratory secretions. The **pili** on the capsular surface of *N meningitidis* are primarily responsible for attachment to and **colonization of the nasopharyngeal epithelium**. Pili also play a role in bacterial movement and epithelial penetration during invasion.

Pili undergo high rates of **antigenic variation** (due to on-off gene switching and horizontal gene transfer), which limits the effectiveness of vaccines against this target. Other prominent *N meningitidis* virulence factors include IgA protease (destroys mucosal antibodies that would otherwise inhibit epithelial colonization), capsular polysaccharides (prevent phagocytosis and phagolysosome destruction), lipo-oligosaccharide (an endotoxin that is the major source of toxicity), and Opa-proteins (aid in endothelial attachment and invasion).

(Choices A and D) *N meningitidis* penetration into the central nervous system is thought to occur at the cerebral capillary endothelial surface and, potentially, at the choroid plexus (the site of the blood–cerebrospinal fluid barrier). Vaccines that target endothelial or meningeal invasion would act too late in the disease process to prevent significant illness; once *N meningitidis* enters the circulatory system, increased levels of endotoxin put patients at high risk for sepsis, circulatory collapse, and death.

(Choices C and E) Most existing meningococcal vaccines target capsular polysaccharides. Capsular polysaccharides prevent phagocytosis and allow the pathogen to replicate and disseminate within the bloodstream. They also promote bacterial survival within phagocytes by inhibiting phagolysosome destruction.

Educational objective:

Pili are the primary virulence factor that allow *Neisseria meningitidis* to initially attach to and colonize the nasopharyngeal epithelial surface. Pili undergo significant antigenic variation, which makes them a difficult vaccination target.

References

- [Neisseria meningitidis: biology, microbiology, and epidemiology.](#)

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A 2-day-old newborn develops lethargy and respiratory distress. Blood cultures grow beta-hemolytic Gram-positive cocci in chains that are bacitracin-resistant. Which of the following measures could have prevented this patient's condition most effectively?

☐

A. Penicillin at 30 weeks gestation

☐

B. Maternal vaccination

☐

C. Intrapartum ampicillin

☐

D. Postnatal immunoglobulin

☐

E. Breast feeding restriction

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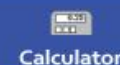
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A 2-day-old newborn develops lethargy and respiratory distress. Blood cultures grow beta-hemolytic Gram-positive cocci in chains that are bacitracin-resistant. Which of the following measures could have prevented this patient's condition most effectively?

- ☐ A. Penicillin at 30 weeks gestation [27%]
- ☐ B. Maternal vaccination [12%]
- ☒ C. Intrapartum ampicillin [50%]
- ☐ D. Postnatal immunoglobulin [6%]
- ☐ E. Breast feeding restriction [2%]

Omitted

Correct answer
C



50%
Answered correctly



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08/09/2018
Last Updated

Explanation

The finding of Gram-positive cocci in chains indicates Streptococcus as Staphylococci classically form clusters. Group A Streptococci and Group B Streptococci are beta-hemolytic, but bacitracin resistance excludes *S. pyogenes* (GAS) and indicates *S. agalactiae* (GBS).

The 2002 guidelines for perinatal group B strep prevention recommend universal prenatal screening for group B streptococcal colonization by maternal vaginal and rectal culture at 35-37 weeks gestation. In women who culture positive for GBS or in women who have had an infant affected by GBS in the past, intrapartum antibiotic prophylaxis is indicated to prevent neonatal GBS sepsis, pneumonia and meningitis. The incidence of group B streptococcal disease in babies less than a week old is declining due to these recommendations.

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The 2002 guidelines for perinatal group B strep prevention recommend universal prenatal screening for group B streptococcal colonization by maternal vaginal and rectal culture at 35-37 weeks gestation. In women who culture positive for GBS or in women who have had an infant affected by GBS in the past, intrapartum antibiotic prophylaxis is indicated to prevent neonatal GBS sepsis, pneumonia and meningitis. The incidence of group B streptococcal disease in babies less than a week old is declining due to these recommendations.

Penicillin remains the first line agent for intrapartum antibiotic prophylaxis, with ampicillin an acceptable alternative.

(Choice A) Use of penicillin G at 30 weeks gestation would serve to eliminate GBS at that time and likely for the next few weeks in the expecting mother. However, after approximately 4 weeks depending on the dose administered, she is again vulnerable to colonization with GBS. Treatment with antibiotics this early in pregnancy is ineffective for GBS prophylaxis.

(Choice B) Theoretically, immunization of women during or before pregnancy could prevent peripartum maternal disease and protect infants from perinatally acquired infection by transplacental transfer of protective IgG antibodies. This would eliminate the need for prenatal GBS screening and intrapartum antimicrobial prophylaxis in women with a clear vaccination history. Serotype-specific antibodies to GBS capsular polysaccharide have been shown to protect against disease, but as yet a vaccine is not available against GBS, so this can not be the correct answer. Vaccines are currently being developed against the capsular polysaccharide of GBS.

(Choice D) Administration of postnatal immunoglobulin in newborns suffering from GBS infections has been studied with no true demonstration of efficacy. It is not widely used in clinical practice.

(Choice E) Breast feeding should not be restricted under normal circumstances because the human milk, especially the colostrum, provides some mucosal immune protection to the newborn. Additionally, breast feeding is recommended by the American Academy of Pediatrics as the sole source of nutrition for all infants for the first six months due to its superior nutritional content, its ability to promote the proper development of the infant GI tract, and the immune protection afforded by agents such as IgA in human breast milk.

Educational Objective:

Universal prenatal screening for group B strep colonization by vaginal-rectal culture at 35-37 weeks gestation is recommended to identify colonized women who require INTRAPARTUM antibiotics, most frequently with penicillin or ampicillin, to prevent neonatal GBS sepsis, pneumonia and meningitis.

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A 46-year-old man comes to the physician due to 3 days of fever, shortness of breath, pleuritic chest pain, and cough productive of green sputum. He has smoked a pack of cigarettes daily for 20 years. On examination, there are crackles at the base of the left lung. Chest x-ray reveals a left lower-lobe consolidation. Microscopic analysis of a sputum sample shows gram-positive, lancet-shaped cocci in pairs. Which of the following characteristics are these bacteria likely to demonstrate?

- ☐ A. Bacitracin sensitivity
- ☐ B. Bile solubility
- ☐ C. Catalase positivity
- ☐ D. Complete hemolysis on agar
- ☐ E. Growth in hypertonic saline
- ☐ F. Optochin resistance

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- ☐ A. Bacitracin sensitivity [10%]
- ☒ B. Bile solubility [58%]
- ☐ C. Catalase positivity [6%]
- ☐ D. Complete hemolysis on agar [10%]
- ☐ E. Growth in hypertonic saline [4%]
- ☐ F. Optochin resistance [10%]

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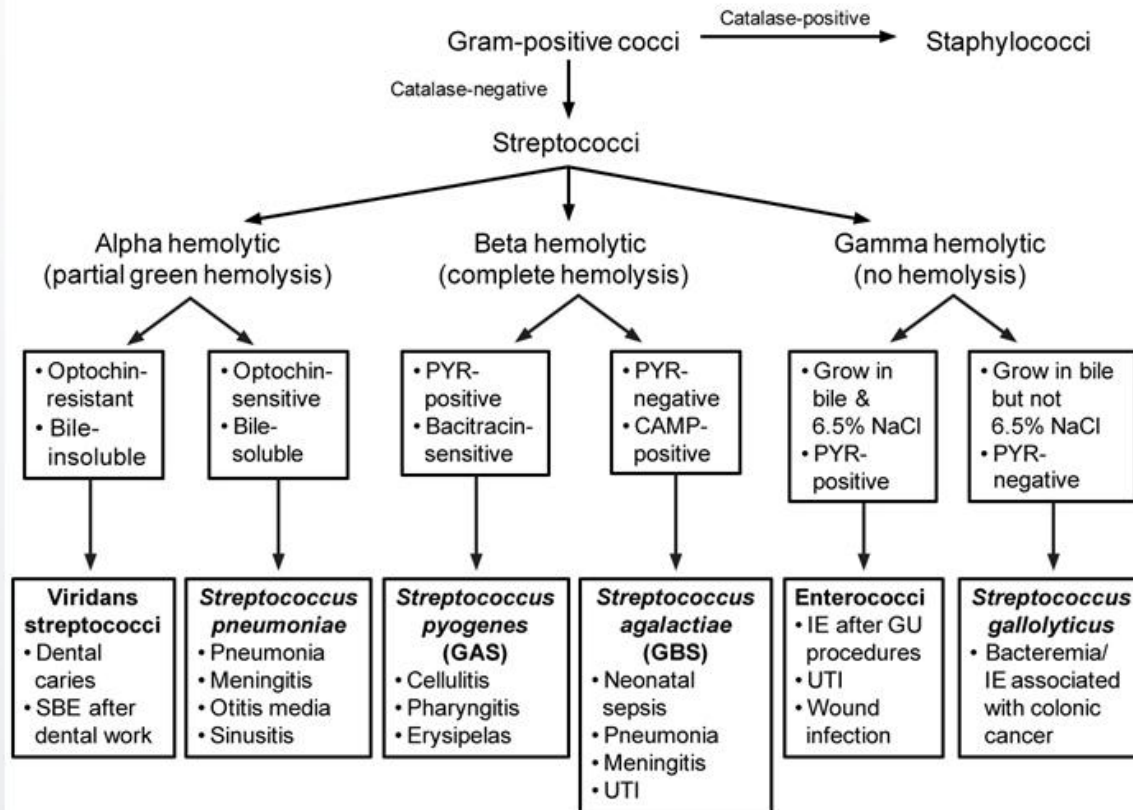
Gram-positive cocci $\xrightarrow{\text{Catalase-positive}}$ Staphylococci

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Microbiological laboratory identification of streptococci



A number of species were formally reclassified from the genus *Streptococcus* to the genus *Enterococcus*, but enterococci are included here under streptococci for simplicity.

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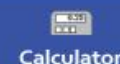
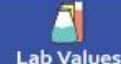
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Viridans streptococci

- Dental caries
- SBE after dental work

Streptococcus pneumoniae

- Pneumonia
- Meningitis
- Otitis media
- Sinusitis

***Streptococcus pyogenes* (GAS)**

- Cellulitis
- Pharyngitis
- Erysipelas

***Streptococcus agalactiae* (GBS)**

- Neonatal sepsis
- Pneumonia
- Meningitis
- UTI

Enterococci

- IE after GU procedures
- UTI
- Wound infection

Streptococcus gallolyticus

- Bacteremia/IE associated with colonic cancer

A number of species were formally reclassified from the genus *Streptococcus* to the genus *Enterococcus*, but enterococci are included here under streptococci for simplicity.

CAMP = Christie, Atkins, and Munch-Petersen test; **GAS** = group A streptococci; **GBS** = group B streptococci; **GU** = genitourinary; **IE** = infective endocarditis; **NaCl** = sodium chloride; **PYR** = pyrrolidonyl arylamidase; **SBE** = subacute bacterial endocarditis; **UTI** = urinary tract infection.

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The presence of lancet-shaped, gram-positive **diplococci** in the sputum sample of a patient with fever and cough is suggestive of infection with ***Streptococcus pneumoniae***. All streptococci are **catalase-negative**. The degree of hemolysis on blood agar distinguishes hemolytic (partial or complete) from nonhemolytic streptococci. The bile solubility and optochin tests are used to differentiate between **partial (green) hemolytic species (α -hemolysis)**, namely *S pneumoniae* and viridans streptococci group. Autolysin produced by *S pneumoniae* is activated by bile, resulting in cell lysis. Therefore, addition of bile salts into a tube with *S pneumoniae* growth (turbid) leads to cell lysis (clearing of turbidity); this is known as **bile solubility**. *S pneumoniae* is bile-soluble and **optochin-sensitive**; viridans group streptococci are bile-insoluble and optochin-resistant (**Choice F**).

(**Choice A**) Bacitracin susceptibility testing is used to differentiate *Streptococcus pyogenes* (bacitracin-susceptible) from other β -hemolytic streptococci. Many laboratories have replaced this test (which is not specific to *S pyogenes*) with the pyrrolidonyl arylamidase (PYR) test. Both *S pyogenes* and enterococci are PYR-positive. *Streptococcus agalactiae* is PYR-negative and enhances the area of *Staphylococcus aureus* hemolysis when grown in the same plate, resulting in a positive CAMP test (named after Christie, Atkins, and Munch-Petersen).

(**Choice C**) Staphylococci are catalase-positive; streptococci are catalase-negative.

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The presence of lancet-shaped, gram-positive **diplococci** in the sputum sample of a patient with fever and cough is suggestive of infection with ***Streptococcus pneumoniae***. All streptococci are **catalase-negative**. The degree of hemolysis on blood agar distinguishes hemolytic (partial or complete) from nonhemolytic streptococci. The bile solubility and optochin tests are used to differentiate between **partial (green) hemolytic species (α -hemolysis)**, namely *S pneumoniae* and viridans streptococci group. Autolysin produced by *S pneumoniae* is activated by bile, resulting in cell lysis. Therefore, addition of bile salts into a tube with *S pneumoniae* growth (turbid) leads to cell lysis (clearing of turbidity); this is known as **bile solubility**. *S pneumoniae* is bile-soluble and **optochin-sensitive**; viridans group streptococci are bile-insoluble and optochin-resistant (**Choice F**).

(Choice A) Bacitracin susceptibility testing is used to differentiate *Streptococcus pyogenes* (bacitracin- susceptible) from other β -hemolytic streptococci. Many laboratories have replaced this test (which is not specific to *S pyogenes*) with the pyrrolidonyl arylamidase (PYR) test. Both *S pyogenes* and enterococci are PYR-positive. *Streptococcus agalactiae* is PYR-negative and enhances the area of *Staphylococcus aureus* hemolysis when grown in the same plate, resulting in a positive CAMP test (named after Christie, Atkins, and Munch-Petersen).

(Choice C) Staphylococci are catalase-positive; streptococci are catalase-negative.

(Choice D) Complete (or β) hemolysis is characteristic of Group A streptococcus (*S pyogenes*) and Group B streptococcus (*S agalactiae*). *S aureus* (catalase-positive) also demonstrates complete hemolysis, as noted by the **arrows**.

(Choice E) γ -hemolytic (no hemolysis) catalase-negative organisms include enterococci and non-enterococci (*S bovis*). Enterococci are able to grow in hypertonic saline (6.5% NaCl) and bile. *S bovis* can grow in the presence of bile but not 6.5% NaCl. *S bovis* bacteremia is associated with colon cancer.

Educational objective:

Streptococcus pneumoniae are gram-positive, α -hemolytic, optochin-sensitive, bile-soluble diplococci. Viridans group streptococci are also α -hemolytic, but they are optochin-resistant and bile insoluble. *Streptococcus pyogenes* (Group A *Streptococcus*) appear as gram-positive cocci in chains with bacitracin susceptibility.

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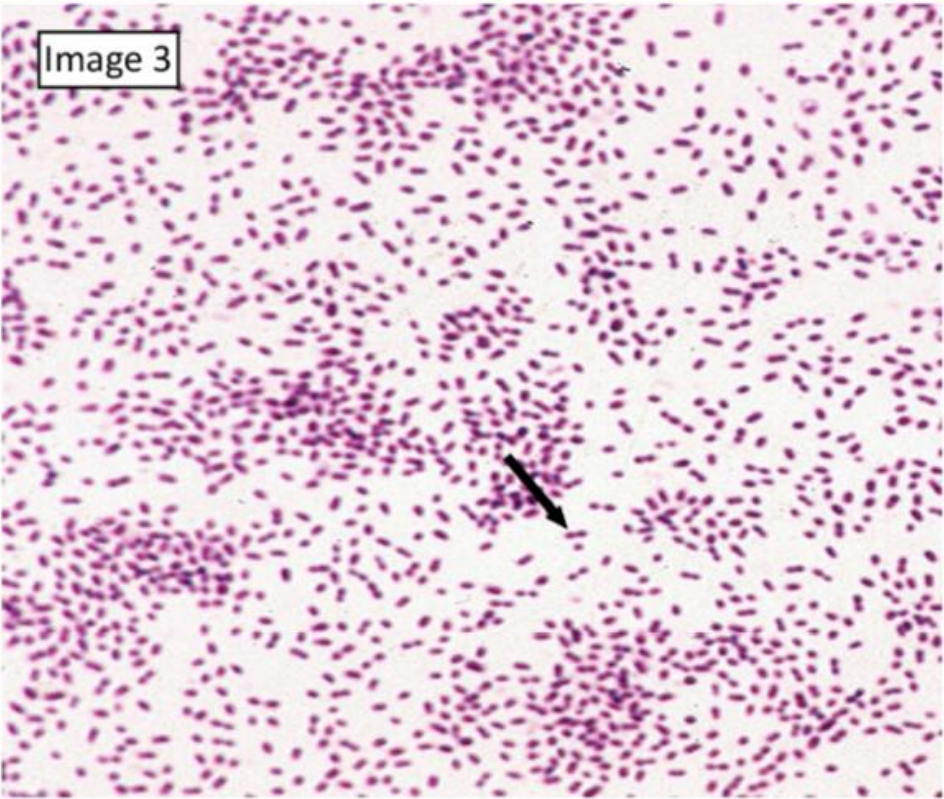
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(Choice C) Staphylococci are catalase-positive; streptococci are catalase-negative.

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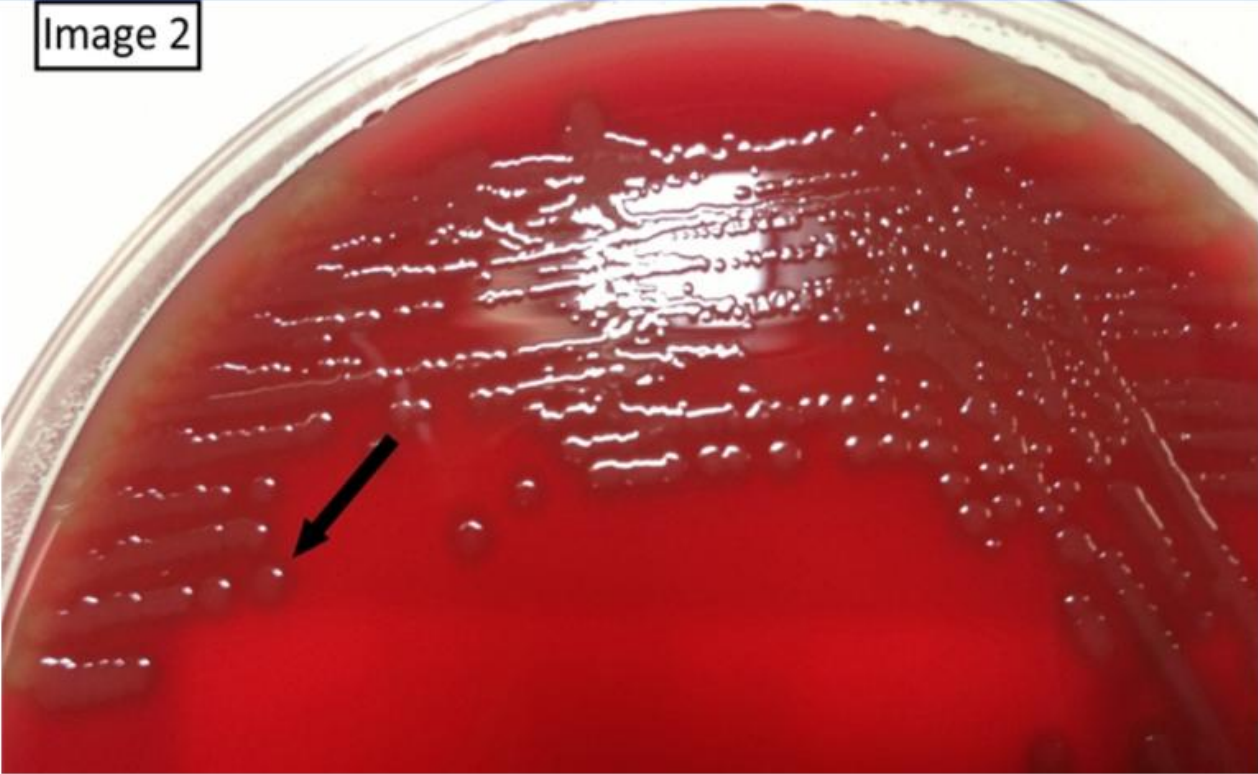
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(Choice C) Staphylococci are catalase-positive; streptococci are catalase-negative.

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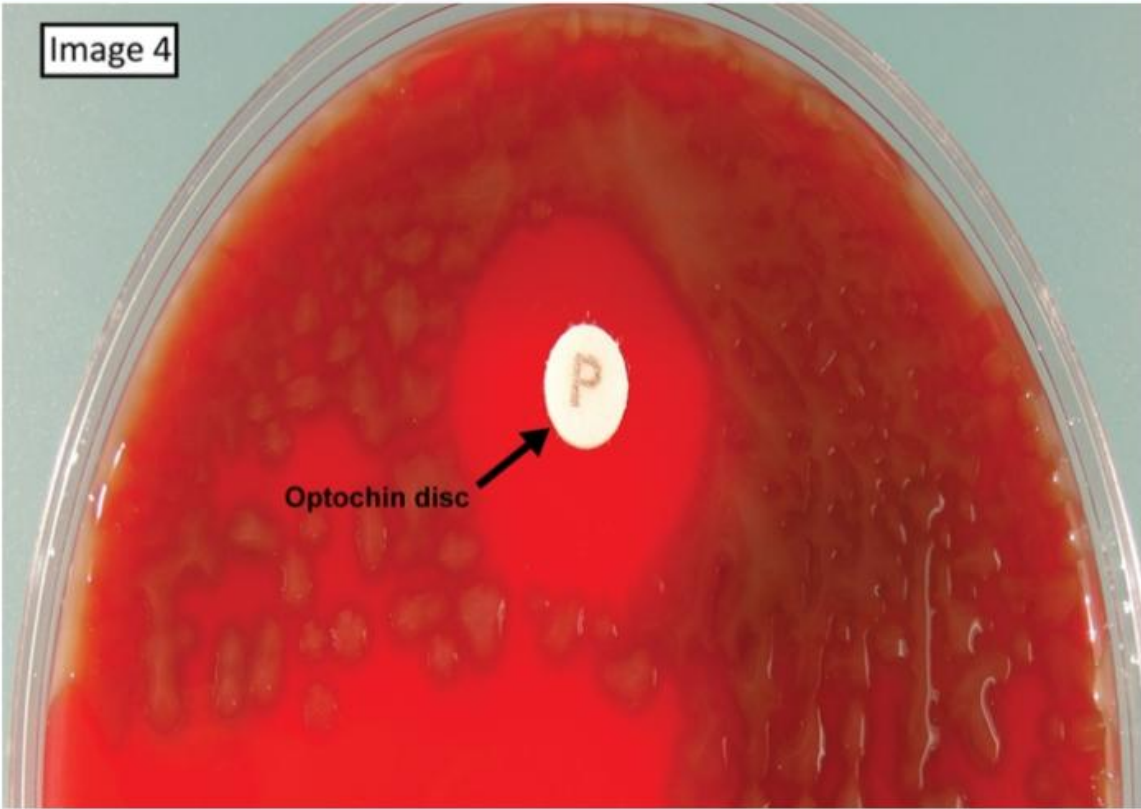
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(Choice C) Staphylococci are catalase-positive; streptococci are catalase-negative.

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