Chapter 23

Microbial Diseases of the Cardiovascular and Lymphatic Systems
Cardiovascular and Lymphatic Systems

Learning Objective

23-1  Identify the role of the cardiovascular and lymphatic systems in spreading and eliminating infections.
Cardiovascular and Lymphatic Systems

- Plasma leaves blood to become interstitial fluid
- Lymph capillaries: transport interstitial fluid to blood
- Lymph nodes contain:
  - Fixed macrophages
  - B cells
  - T cells
Figure 23.2 The relationship between the cardiovascular and lymphatic systems.

(a) Capillary system in lung

(b) Lymph node

- Interstitial fluid
- Lymph capillaries
- Blood capillaries
- Arteriole
- Venule
- Tissue cells
- Valve to prevent backflow
- Lymphocytes and macrophages
- From lymphatic capillary system
- From heart
- To heart
- To lymphatic system
- To lymphatic system
Check Your Understanding

Why is the lymphatic system so valuable for the working of the immune system? 23-1
23-2 List the signs and symptoms of sepsis, and explain the importance of infections that develop into septic shock.

23-3 Differentiate gram-negative sepsis, gram-positive sepsis, and puerperal sepsis.

23-4 Describe the epidemiologies of endocarditis and rheumatic fever.

23-5 Discuss the epidemiology of tularemia.
Bacterial Diseases

Learning Objectives

23-6 Discuss the epidemiology of brucellosis.
23-7 Discuss the epidemiology of anthrax.
23-8 Discuss the epidemiology of gas gangrene.
23-9 List three pathogens that are transmitted by animal bites and scratches.
Sepsis and Septic Shock

- **Septicemia**
  - Persistent pathogens or their toxins in blood

- **Sepsis**
  - Systemic inflammatory response

- **Severe sepsis**
  - Sepsis and decreased blood pressure

- **Septic shock**
  - Sepsis and uncontrollable decreased blood pressure

- **Lymphangitis**
  - Inflamed lymph vessels accompanying septicemia and septic shock
Figure 23.3 Lymphangitis, one sign of sepsis.
Gram-Negative Sepsis

- **Endotoxin shock**
  - Endotoxins cause blood pressure to decrease
  - Antibiotics can worsen condition by killing bacteria
  - Possible treatment
    - Human activated protein C, an anticoagulant
Gram-Positive Sepsis

- Nosocomial infections
  - Group B streptococcus, *S. agalactiae*
  - *Enterococcus faecium* and *E. faecalis*
Puerperal Sepsis

- Childbirth fever
  - *Streptococcus pyogenes*
  - Transmitted to mother during childbirth by attending physicians and midwives
Diseases in Focus: Infections from Human Reservoirs

- A 27-year-old woman has a fever and cough for 5 days. Despite aggressive treatment with fluids and massive doses of antibiotics, she dies 5 hours after hospitalization. Catalase-negative, gram-positive cocci are isolated from her blood.

- What infections could cause these symptoms?
Gram-positive cocci.
Check Your Understanding

✓ What are two of the conditions that define the systemic inflammatory response syndrome of sepsis? 23-2

✓ Are the endotoxins that cause sepsis from gram-positive or gram-negative bacteria? 23-3
Bacterial Infections of the Heart

- **Endocarditis**
  - Inflammation of the endocardium
- **Subacute bacterial endocarditis**
  - Alpha-hemolytic streptococci from mouth
- **Acute bacterial endocarditis**
  - *Staphylococcus aureus* from mouth
- **Pericarditis**
  - Streptococci
Figure 23.4 Bacterial endocarditis.

Fibrin-platelet vegetations

Normal appearance
Figure 23.5 A nodule caused by rheumatic fever.
Rheumatic Fever

- Inflammation of heart valves
- Autoimmune complication of *Streptococcus pyogenes* infections
Check Your Understanding

✓ What medical procedures are usually the cause of endocarditis? 23-4
Tularemia

- *Francisella tularensis*
  - Gram-negative rod
- Zoonosis
- Transmitted from rabbits and deer by deer flies
- Bacteria reproduce in phagocytes
Figure 23.6 Tularemia cases in the United States (2000–2008).
Brucellosis (Undulant Fever)

- *Brucella* spp.
  - Gram-negative rods that grow in phagocytes
- *B. abortus* (elk, bison, cows)
- *B. suis* (swine)
- *B. melitensis* (goats, sheep, camels)
- Undulating fever spikes to 40°C each evening
- Transmitted via milk from infected animals or contact with infected animals
Clinical Focus: What is the cause?

- A 3-year-old boy is seen by his pediatrician for fever, malaise, painful left underarm lymph node, and skin sloughing off his left ring finger.
Clinical Focus: What is the cause?

Gram-stained bacteria cultured from lymph node.
Clinical Focus: What Is the Cause?

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Antibody Titer</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bartonella</em></td>
<td>0</td>
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<tr>
<td><em>Ehrlichia</em></td>
<td>0</td>
</tr>
<tr>
<td><em>Francisella</em></td>
<td>4096</td>
</tr>
<tr>
<td>CMV</td>
<td>0</td>
</tr>
<tr>
<td><em>T. gondii</em></td>
<td>0</td>
</tr>
</tbody>
</table>
Anthrax

- *Bacillus anthracis*
  - Gram-positive, endospore-forming aerobic rod
- Found in soil
- Cattle are routinely vaccinated
- Treated with ciprofloxacin or doxycycline
Anthrax

- **Cutaneous anthrax**
  - Endospores enter through minor cut
  - 20% mortality

- **Gastrointestinal anthrax**
  - Ingestion of undercooked, contaminated food
  - 50% mortality

- **Inhalational (pulmonary) anthrax**
  - Inhalation of endospores
  - 100% mortality
Biological Weapons

- **1346**: plague-ridden bodies used by Tartar army against Kaffa
- **1937**: plague-carrying flea bombs used in the Sino-Japanese War
- **1979**: explosion of *Bacillus anthracis* weapons plant in the Soviet Union
- **1984**: *Salmonella enterica* used against the people of The Dalles, Oregon
- **1996**: *Shigella dysenteriae* used to contaminate food
- **2001**: *B. anthracis* distributed in the United States
# Biological Weapons

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus anthracis</em></td>
<td>“Eradicated” polio and measles</td>
</tr>
<tr>
<td><em>Brucella</em> spp.</td>
<td>Encephalitis viruses</td>
</tr>
<tr>
<td><em>Chlamydompha psittaci</em></td>
<td>Hermorrhagic fever viruses</td>
</tr>
<tr>
<td><em>Clostridium botulinum</em> toxin</td>
<td>Influenza A (1918 strain)</td>
</tr>
<tr>
<td><em>Coxiella burnetii</em></td>
<td>Monkeypox</td>
</tr>
<tr>
<td><em>Francisella tularensis</em></td>
<td>Nipah virus</td>
</tr>
<tr>
<td><em>Rickettsia prowazekii</em></td>
<td>Smallpox</td>
</tr>
<tr>
<td><em>Shigella</em> spp.</td>
<td>Yellow fever</td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td></td>
</tr>
<tr>
<td><em>Yersinia pestis</em></td>
<td></td>
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</tbody>
</table>
Gangrene

- **Ischemia**: loss of blood supply to tissue
- **Necrosis**: death of tissue
- **Gangrene**: death of soft tissue
- **Gas gangrene**
  - *Clostridium perfringens*, gram-positive, endospore-forming anaerobic rod, grows in necrotic tissue
  - Treatment includes surgical removal of necrotic tissue and/or use of hyperbaric chamber
Systemic Diseases Caused by Bites and Scratches

- *Pasteurella multocida*
- *Clostridium*
- *Bacteroides*
- *Fusobacterium*
- *Bartonella henselae*: cat-scratch disease
Figure 23.10 Electron micrograph showing the location of *Bartonella henselae* within a red blood cell.
Diseases in Focus: Infections Transmitted by Soil or Water

- A 65-year-old man with poor circulation in his legs develops an infection following injury to a toe. Dead tissue further reduces circulation, requiring amputation of two toes.
- What infection could cause these symptoms?
Gram-stained bacteria from the patient's toe.
A 10-year-old girl is admitted to a local hospital after having fever (40° C) for 12 days and back pain for 8 days. Bacteria cannot be cultured from tissues. She has a recent history of dog and cat scratches. She recovers without treatment.

What infections could cause these symptoms?
Check Your Understanding

✓ What animals are the most common reservoir for tularemia? 23-5

✓ What ethnic group in the United States is most commonly affected by brucellosis, and why? 23-6

✓ How do animals such as cattle become victims of anthrax? 23-7

✓ Why are hyperbaric chambers effective in treating gas gangrene? 23-8

✓ *Bartonella henselae*, the pathogen of cat-scratch disease, is capable of growth in what insect? 23-9
Vector-Transmitted Bacterial Diseases

Learning Objectives

23-10 Compare and contrast the causative agents, vectors, reservoirs, symptoms, treatments, and preventive measures for plague, Lyme disease, and Rocky Mountain spotted fever.

23-11 Identify the vector, etiology, and symptoms of five diseases transmitted by ticks.

23-12 Describe the epidemiologies of epidemic typhus, endemic murine typhus, and spotted fevers.
Plague

- **Causative agent**: *Yersinia pestis*, gram-negative rod
- **Reservoir**: rats, ground squirrels, and prairie dogs
- **Vector**: *Xenopsylla cheopis*
- **Bubonic plague**: bacterial growth in blood and lymph
- **Septicemia plague**: septic shock
- **Pneumonic plague**: bacteria in the lungs
Figure 23.11 A case of bubonic plague.
Figure 23.12 The U.S. geographic distribution of human plague, 1970–2004.
Relapsing Fever

- **Causative agent**: *Borrelia* spp., spirochete
- **Reservoir**: rodents
- **Vector**: ticks
- Successive relapses are less severe
Lyme Disease

- **Causative agent**: *Borrelia burgdorferi*
- **Reservoir**: deer
- **Vector**: ticks
- **First symptom**: bull’s-eye rash
- **Second phase**: irregular heartbeat, encephalitis
- **Third phase**: arthritis
Figure 23.15 The common bull’s-eye rash of Lyme disease.
Figure 23.13 Lyme disease in the United States, reported cases by county, 2008.

KEY

Cases per 100,000 population

- 1.01–10.00
- 10.01–100.00
- ≥100.01
Figure 23.14a The life cycle of the tick vector of Lyme disease.

(a) The tick, *Ixodes scapularis*, has a 2-year life cycle in which it requires three blood meals. The tick is infected by its first blood meal and can pass on the infection to a human in its second.
Figure 23.14b-c The life cycle of the tick vector of Lyme disease.

(b) Comparison of actual tick sizes.

(c) The cause of Lyme disease, *Borrelia burgdorferi*.

Ehrlichiosis and Anaplasmosis

- **Human monocytotropic ehrlichiosis (HME)**
  - **Causative agent:** *Ehrlichia chaffeensis*
    - Gram-negative, obligately intracellular (in white blood cells)
  - **Reservoir:** white-tailed deer
  - **Vector:** Lone Star tick

- **Human granulocytic anaplasmosis (HGA)**
  - **Causative agent:** *Anaplasma phagocytophilum*
  - **Reservoir:** deer
  - **Vector:** ticks
Typhus

- *Rickettsia* spp.
  - Obligate intracellular parasites
  - In endothelial cells of the vascular system
  - Arthropod vectors
Typhus

- **Epidemic typhus**
  - **Causative agent**: *Rickettsia prowazekii*
  - **Reservoir**: rodents
  - **Vector**: *Pediculus humanus corporis*
  - Transmitted when louse feces are rubbed into bite wound
Typhus

- Endemic murine typhus
  - Causative agent: *Rickettsia typhi*
  - Reservoir: rodents
  - Vector: *Xenopsylla cheopis*
Spotted Fevers

- **Rocky Mountain spotted fever** (tickborne typhus)
- Caused by *Rickettsia rickettsii*
- Measles-like rash, except that the rash also appears on palms and soles
Figure 23.16 The U.S. geographic distribution of Rocky Mountain spotted fever (tickborne typhus) 2008.

KEY

<table>
<thead>
<tr>
<th>Cases per 1,000,000 population</th>
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<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1–14</td>
</tr>
<tr>
<td>≥15</td>
</tr>
</tbody>
</table>
Figure 23.17 The life cycle of the tick vector (*Dermacentor* spp.) of Rocky Mountain spotted fever.

1. An infected adult female tick (*Dermacentor* spp.) lays eggs.

2. Eggs hatch, and six-legged larvae develop.

3. Six-legged larva takes blood meal from small mammal, infecting it, and develops into eight-legged nymph.

4. Nymph takes blood meal from human, infecting him or her, and then develops into an adult tick.

5. Adult tick takes another blood meal and mates.
Check Your Understanding

✓ Why is the plague-infected flea so eager to feed on a mammal? 23-10
✓ What animal does the infecting tick feed on just before it transmits Lyme disease to a human? 23-11
✓ Which disease is tickborne: epidemic typhus, endemic typhus, or Rocky Mountain spotted fever? 23-12
Viral Diseases

Learning Objectives

23-13 Describe the epidemiologies of Burkitt’s lymphoma, infectious mononucleosis, and CMV inclusion disease.

23-14 Compare and contrast the causative agents, vectors, reservoirs, and symptoms of yellow fever, dengue, dengue hemorrhagic fever, and chikungunya fever.

23-15 Compare and contrast the causative agents, reservoirs, and symptoms of Ebola hemorrhagic fever and Hantavirus pulmonary syndrome.
Infectious Mononucleosis

- Epstein-Barr virus (HHV-4)
- Childhood infections are asymptomatic
- Transmitted via saliva
- Characterized by proliferation of monocytes
Burkitt’s Lymphoma

- Epstein-Barr virus (HHV-4)
- Nasopharyngeal carcinoma
- Cancer in immunosuppressed individuals and in malaria and AIDS patients
Figure 23.19 A child with Burkitt’s lymphoma.
Cytomegalovirus Infections

- Cytomegalovirus (HHV-5)
- Infected cells swell (cyto-, mega-)
- Latent in white blood cells
- May be asymptomatic or mild
- Transmitted across the placenta; may cause mental retardation
- Transmitted sexually, by blood, or by transplanted tissue
Figure 23.20 The typical U.S. prevalence of antibodies against Epstein-Barr virus (EB virus), cytomegalovirus (CMV), and *Toxoplasma gondii* (TOXO) by age.
## Viral Fevers

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Portal of Entry</th>
<th>Reservoir</th>
<th>Method of Transmission</th>
</tr>
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<tbody>
<tr>
<td>Yellow fever</td>
<td>Arbovirus</td>
<td>Skin</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Dengue</td>
<td>Arbovirus</td>
<td>Skin</td>
<td>Humans</td>
</tr>
<tr>
<td>Chikungunya</td>
<td>Arbovirus</td>
<td>Skin</td>
<td>Unknown</td>
</tr>
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</table>
# Viral Fevers

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Portal of Entry</th>
<th>Reservoir</th>
<th>Method of Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhagic fevers</td>
<td>Filovirus, arenavirus</td>
<td>Mucous membranes</td>
<td>Contact with blood</td>
</tr>
<tr>
<td><em>Hantavirus</em> pulmonary syndrome</td>
<td>Bunyavirus</td>
<td>Respiratory tract</td>
<td>Field mice</td>
</tr>
</tbody>
</table>
Figure 23.22 Ebola hemorrhagic virus.
Diseases in Focus: Viral Hemorrhagic Fevers

- What microbe could cause rash and severe joint pain in a 20-year-old woman?
Diseases in Focus: Viral Hemorrhagic Fevers
Check Your Understanding

✓ Although not a disease with an insect vector, why is Burkitt’s lymphoma most commonly a disease found in malarial areas? 23-13

✓ Why is the mosquito *Aedes albopictus* a special concern to the populations of temperate climates? 23-14

✓ Which disease does Ebola hemorrhagic fever more closely resemble, Lassa fever or *Hantavirus* pulmonary syndrome? 23-15
Protozoan Diseases

Learning Objectives

23-16 Compare and contrast the causative agents, modes of transmission, reservoirs, symptoms, and treatments for Chagas’ disease, toxoplasmosis, malaria, leishmaniasis, and babesiosis.

23-17 Discuss the worldwide effects of these diseases on human health.
Chagas’ Disease

- Also called **American trypanosomiasis**
- **Causative agent:** *Trypanosoma cruzi*
- **Reservoir:** rodents, opossums, armadillos
- **Vector:** reduviid bug
Figure 23.23 *Trypanosoma cruzi*, the cause of Chagas’ disease (American trypanosomiasis).
Figure 12.33d Arthropod vectors.

(d) Kissing bug
Toxoplasmosis

- Caused by *Toxoplasma gondii*

- Transmission:
  - Ingesting undercooked meat
  - Contact with cat feces

- Congenital infection
  - Stillbirth
  - Neurological damage
Figure 23.24 The life cycle of *Toxoplasma gondii*, the cause of toxoplasmosis.

1. Immature oocyst is shed in cat feces.
2. Mature oocysts develop by sporogony and contain two sporocysts, each with four infective sporozoites.
3. Oocysts can infect many hosts, including mice, domestic animals, and humans, via ingestion.
4. Sporozoites from ingested oocysts invade animal tissue and develop into bradyzoites within tissue cysts or into tissue-invading tachyzoites.
5. Cat ingests bradyzoites in tissue cysts of animals, usually mice.

If a pregnant woman accidentally ingests oocysts (contacted when changing a cat litter box), prenatal infection of the fetus may occur.

If humans eat undercooked meat containing tissue cysts, they may become infected.

Immature cyst

Definitive host

Intermediate hosts

Sporogony

Mature oocyst (10–13 μm x 9–11 μm)

Sporozoites

Sporocysts

Bradyzoites

Tachyzoites

Immature oocyst

Sporozoite

Cat ingests bradyzoites in tissue cysts of animals, usually mice.

If humans eat undercooked meat containing tissue cysts, they may become infected.

If a pregnant woman accidentally ingests oocysts (contacted when changing a cat litter box), prenatal infection of the fetus may occur.
Malaria

- **Four major forms:**
  - *Plasmodium vivax*
  - *P. ovale*
  - *P. malariae*
  - *P. falciparum*

- **Vector:** *Anopheles* mosquito

- **Definitive host:** *Anopheles* mosquito
Figure 23.26 Malaria.

(a) Merozoites being released from lysed RBCs

(b) Malarial blood smear; note the ring forms.
Figure 23.25 Malaria in the United States.

KEY

Malarial areas in 1912
Figure 12.20 The life cycle of *Plasmodium vivax*, the apicomplexan that causes malaria.

1. Infected mosquito bites human; sporozoites migrate through bloodstream to liver of human.
2. Sporozoites undergo schizogony in liver cell; merozoites are produced.
3. Merozoites released into bloodstream from liver may infect new red blood cells.
4. Merozoite develops into ring stage in red blood cell.
5. Ring stage grows and divides, producing merozoites.
6. Merozoites are released when red blood cell ruptures; some merozoites infect new red blood cells, and some develop into male and female gametocytes.
7. Another mosquito bites infected human and ingests gametocytes.
8. In mosquito’s digestive tract, gametocytes unite to form zygote.
9. Resulting sporozoites migrate to salivary glands of mosquito.

Sexual reproduction:
- Female gametocyte
- Male gametocyte
- Zygote

Asexual reproduction:
- Gametocytes
- Female
- Male
- Merozoites

Intermediate host: Mosquito
Malaria

- **Prophylaxis**
  - Chloroquine
  - Malarone: atovaquone and proguanil
  - Mefloquine

- **Treatment**
  - Artemisinin: artesunate and artemether

- **Control**
  - Bed nets
Figure 23.27 Cutaneous leishmaniasis.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Visceral Leishmaniasis</th>
<th>Cutaneous Leishmaniasis</th>
<th>Mucocutaneous Leishmaniasis</th>
<th>Babesiosis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Fatal if untreated</td>
<td>Papule</td>
<td>Disfiguring</td>
<td>Replicates in RBCs</td>
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<tr>
<td><strong>Causative Agent</strong></td>
<td><em>Leishmania donovani</em></td>
<td><em>L. tropica</em></td>
<td><em>L. braziliensis</em></td>
<td><em>Babesia microti</em></td>
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<tr>
<td><strong>Vector</strong></td>
<td>Sandflies</td>
<td>Sandflies</td>
<td>Sandflies</td>
<td><em>Ixodes ticks</em></td>
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<td><strong>Reservoir</strong></td>
<td>Small mammals</td>
<td>Small mammals</td>
<td>Small mammals</td>
<td>Rodents</td>
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<td><strong>Treatment</strong></td>
<td>Amphotericin B or miltefosine</td>
<td>Amphotericin B or miltefosine</td>
<td>Antimony compounds</td>
<td>Atovaquone and azithromycin</td>
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<td><strong>Geographic Distribution</strong></td>
<td>South Asia, Sudan, Brazil</td>
<td>Asia, Africa, Mediterranean, Central America, South America</td>
<td>Yucatán, South America</td>
<td>United States</td>
</tr>
</tbody>
</table>

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Check Your Understanding

✓ What tickborne disease in the United States is sometimes mistaken for malaria when blood smears are inspected? 23-16

✓ Eliminating which of these diseases, malaria or Chagas’ disease, would have the greater effect on the well-being of the population of Africa? 23-17
Learning Objective

23-18 Diagram the life cycle of *Schistosoma*, and show where the cycle can be interrupted to prevent human disease.
Schistosomiasis

- Tissue damage (granulomas) in response to eggs lodging in tissues
Figure 23.29 A granuloma from a patient with schistosomes.
## Types of Schistosomiasis

<table>
<thead>
<tr>
<th>Schistosome</th>
<th>Location</th>
<th>Signs/Treatment</th>
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</thead>
<tbody>
<tr>
<td><em>S. haematobium</em></td>
<td>Granulomas in urinary bladder wall</td>
<td>Africa, Middle East</td>
</tr>
<tr>
<td><em>S. japonicum</em></td>
<td>Granulomas in intestinal wall</td>
<td>East Asia</td>
</tr>
<tr>
<td><em>S. mansoni</em></td>
<td>Granulomas in intestinal wall</td>
<td>African, Middle East, South America, Caribbean</td>
</tr>
<tr>
<td>Swimmer’s itch</td>
<td>Cutaneous allergic reaction to cercariae</td>
<td>U.S. parasite of wildfowl</td>
</tr>
</tbody>
</table>
(b) Life cycle of Schistosoma, cause of schistosomiasis.

1. Adult female flukes lay eggs.
2. Eggs reach body of water after being excreted in human feces or urine.
3. Eggs hatch into free-swimming larvae (miracidia).
5. Miracidium reproduces in snail, forming several cercariae.
6. Cercariae are released from the snail.
7. Free-swimming cercariae penetrate human skin, losing tail.
8. Cercariae travel through circulatory system to intestinal blood vessels, where they mature into adults.

(a) Male and female schistosomes. The female lives in a groove on the ventral (lower) surface of the male schistosome (“split-body”), is continuously fertilized, and continuously lays eggs. The sucker is used by the male to attach to the host.
Check Your Understanding

✓ What freshwater creature is essential to the life cycle of the pathogen causing schistosomiasis?

23-18
A 22-year-old soldier returning from a tour of duty in Iraq has three painless skin ulcers. She reports being bitten by insects every night. Ovoid, protozoa-like bodies are observed within her macrophages by examination with a light microscope.

What infections could cause these symptoms?
Diseases in Focus: Infections Transmitted by Vectors

[Image of a microscopic view of a biological sample, labeled LM 5 µm]

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