LESSON ASSIGNMENT

LESSON 7
Systemic Mycoses

TEXT ASSIGNMENT
Paragraphs 7-1 through 7-5

TASK OBJECTIVES
After completing this lesson, you should be able to:

7-1. Select the statement that correctly describes characteristics of *Histoplasma capsulatum*.

7-2. Select the statement that correctly describes characteristics of *Blastomyces dermatitidis*.

7-3. Select the statement that correctly describes characteristics of *paracoccidioides brasiliensis*.

7-4. Select the statement that correctly describes characteristics of *Coccidioides immitis*.

SUGGESTION
After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
7-1. INTRODUCTION

a. As a group, systemic mycoses usually originate as pulmonary system infections. They may progress systemically or affect any internal organ and may show cutaneous and subcutaneous involvement. Infections may vary from mild, flu-like respiratory syndrome to severely fulminating systemic infections. Organisms causing systemic mycoses are exogenous and are acquired via inhalation of viable spores. With the exception of Cryptococcus neoformans, all are diphasic, having two different morphological forms that are temperature dependent. Clinical specimens include skin scrapings, sputum, and biopsy material. Because of their extreme pathogenicity, it is of extreme importance that any specimen likely to contain a systemic organism be handled with caution, and only within a biological safety hood!

b. The systemic mycoses are histoplasmosis, blastomycosis, paracoccidioidomycosis, coccidioidomycosis, and cryptococcosis (see Lesson 4).

7-2. HISTOPLASMOSIS

a. Histoplasmosis is a disease caused by Histoplasma capsulatum or by Histoplasma duboisii. These organisms are found in soil that is fertilized by the droppings of fowl (especially chickens and blackbirds) and bats. Histoplasma capsulatum causes North American histoplasmosis and is endemic to areas of the US such as the central Mississippi River valley, the Ohio River valley, and the Appalachian mountains. Histoplasma duboisii causes African histoplasmosis and is endemic to central and western Africa.

b. Primary infection occurs by inhalation of viable spores. In the initial infection, lesions with lymph-node enlargement occur throughout the lung. The majority of cases are asymptomatic, or present as self-limiting mild respiratory infections. Positive skin tests and calcifications in the lung may be incidental findings long after the infection has resolved. However, some infections cause a large variety of clinical manifestations because of a tendency to enter the bloodstream during the primary infection and cause progressive disease at one or more anatomic sites. If this occurs, calcified lesions are seen in the affected organs and tissue. The body attempts to clear the fungus from the bloodstream via the reticuloendothelial cells located throughout the body. These cells are always involved in a systemic infection.

c. Diagnosis of histoplasmosis depends on the stage of the mycosis. Screening for acute pulmonary histoplasmosis may be accomplished with a positive skin test using histoplasmin, a mycelial antigen. The skin test may show a positive reaction as early as two weeks after exposure and will then remain positive for years. Serological titers against yeast and mycelial antigens are performed for a positive skin test. A single
serum titer of $\geq 16$ against the yeast antigen is highly suggestive of recent infection. A rise in titer between sequentially collected sera is diagnostic of a current infection. In disseminated histoplasmosis, skin tests and the complement fixation titers are negative in more than half the cases. Organisms may be seen on direct blood smears and may be grown from routine blood cultures if incubated for 10 to 15 days. The organism may also be seen on smears from bone marrow aspirates, liver biopsy, and skin lesions. Urine cultures may be positive. All tissue obtained for fungal studies should be stained with Gomori's methenamine, silver, or periodic acid-Schiff stains.

d. Laboratory identification of Histoplasma is discussed below.

(1) Direct examination of clinical specimens shows single, budding blastoconidia. $H.\ capsulatum$ is 1 to 5 mcm in size while $H.\ duboisii$ is 7 to 15 mcm. Organisms growing intracellularly in mononuclear cells is a diagnostic feature. $H.\ capsulatum$ is oval with a vacuole and dark staining crescent body. $H.\ duboisii$ is thick-walled and oval to hourglass in shape.

(2) Mycelial forms of $H.\ capsulatum$ and $H.\ duboisii$ are indistinguishable. Colonial growth rate is slow, taking 10 to 14 days. Surface color of colonies is white to tan, with reverse being non-pigmented to orange; appearance is cottony. Microscopic examination reveals branching, septate hyphae. Small microconidia (2 to 5 mcm) are pyriform to round and borne on short conidiophores. Large microconidia (7 to 25 mcm) are tuberculate, thick-walled, round to pyriform, and borne on short conidiophores. (Figure 7-1.)

![Figure 7-1. Mycelial form of Histoplasma capsulatum.](image)

(3) Care must be taken not to confuse the mold phase of Histoplasma capsulatum with Sepedonium species. This saprophyte resides in soil and Histoplasma capsulatum may be recovered from sputum as a contaminant. In vitro conversion of the mold phase to yeast phase and back to mold phase of Histoplasma capsulatum will confirm its identification.

(4) The yeast phase of Histoplasma requires a temperature of 35ºC. The growth rate is slow, taking 5 to 10 days for colonial growth. Colony color is white to
cream with a butyrous texture. Microscopic morphology shows oval budding blastoconidia. *H. capsulatum* is small, 2 to 3 mcm in diameter. (Figure 7-2.) *H. duboisii* are large, 8 to 12 mcm in size.

![Figure 7-2. Yeast of *Histoplasma capsulatum*.](image)

### 7-3. BLASTOMYCOSIS

a. The etiological agent of blastomycosis (common name—North American blastomycosis) is *Blastomyces dermatitidis*. It occurs most often in individuals who come in close contact with soil, especially in the Mississippi and Ohio River valleys.

b. Primary infection of the lungs occurs upon inhalation of viable spores from the soil. Because of a strong, natural resistance to this organism, infections are often asymptomatic and are detected only by a positive skin test. In typical cases of progressive blastomycosis, the patient experiences symptoms similar to a persistent "chest cold" with low-grade fever, weight loss, and progressive disability. Examination reveals evidence of pneumonia that may involve any segment or lobe of the lung. Cavity formation in the lung and lymph node involvement are frequent. Pulmonary lesions may heal while lesions of skin, bone, and joints continue to develop. As these later lesions form, symptoms, that is, fever, sweats, chills, and weakness increase. Untreated patients with systemic blastomycosis may die as early as six months but more commonly in 1 to 2 years post infection.

c. Laboratory Identification of *Blastomyces dermatitidis* is discussed below.

(1) Clinical specimens include sputum, skin scrapings, pus and biopsy material. Complement fixation tests are of little value because antigens are neither specific nor sensitive. Immunodiffusion is specific with a sensitivity of 80 percent. Diagnosis is usually made by recovery of organism. During yeast phase, this organism is white to tan in color with a verrucose texture. Microscopic examination of clinical material reveals yeast form of the organism that is characterized by thick-walled blastoconidia, 8 to 15 mcm in diameter. Single buds are attached to the parent cell by a broad base. (Figure 7-3.)
Figure 7-3. Yeast form of *Blastomyces dermatitidis*.

(2) The mycelial phase of *Blastomyces dermatitidis* exhibits a slow growth rate of 7 to 14 days. Colonies are white to tan, with a cottony appearance. Microscopic examination shows branching, septate hyphae. Microconidia are 4 to 5 mcm, pyriform, and located terminally on short conidiophores. They are often referred to as "lollipops." (Figure 7-4.)

Figure 7-4. Mycelial form of *Blastomyces dermatitidis*

7-4. **PARACOCCIDIOIDOMYCOSIS**

a. Paracoccidioidomycosis, commonly called South American blastomycosis) is a disease process caused by paracoccidioides brasiliensis. Primary inoculation is by inhalation of viable spores into the lungs. The disease rarely progresses, disseminates, or causes severe infection if immunity is normal. There is a marked loss of pulmonary function, however, when it does occur. The primary lesions usually heal and remain latent but may be reactivated years later. Reactivation may occur for no apparent reason or may be secondary to immunosuppressive disease or therapy. Upon reactivation, lesions progress and disseminate to other organs. Mucocutaneous ulcers are the most common disseminated manifestation. These ulcers originate as papules, develop into vesicles, and later become encrusted, granulomatous ulcers. Deeper destruction, with spreading to adjacent tissue, follows. Regional lymph nodes ulcerate and develop draining sinuses. Dissemination continues in the lymphatic system, spleen, intestine, and liver.
b. Diagnosis is based on the demonstration of *Paracoccidioides brasiliensis* in specimens taken from lesions. Clinical specimens include scraping of mucocutaneous lesions, exudate, pus, sputum, bronchial washings, feces, and tissue taken by biopsy. Direct examination of clinical specimens demonstrates the yeast phase of this diphasic organism that is identified by thick-walled globose blastoconidia, ranging in size from 12 to 14 mcm. It has multiple buds attached to the parent cell by thin necks. Buds are 2 to 5 mcm in size. This form is often referred to as the "pilot's wheel." (Figure 7-5.)

![Figure 7-5. Yeast form of *Paracoccidioides brasiliensis*.](image)

c. Laboratory Identification of *Paracoccidioides brasiliensis* is discussed below.

(1) The mycelial phase of *Paracoccidioides brasiliensis* is slow growing, taking 14 to 21 days for visible growth. Colonies are white to tan, with a texture that is downy to heaped. Microscopic examination shows fine, branching, septate and usually sterile hyphae, but will occasionally show sessile microconidia on the hyphae. (Figure 7-5.)

(2) During the yeast phase of this organism, colonies are white to tan with a verrucose texture. Macroscopic colony morphology resembles *Blastomyces dermatitidis*.

7.5. COCCIDIOIDOMYCOSIS

a. The etiological agent for coccidioidomycosis, commonly called Valley Fever or San Joaquin Valley Fever, is *Coccidioides immitis*. Geographic distribution is the lower Sonoran life zone of the US, the desert region of Mexico, and Central and South America, where soil is dry, arid, and alkaline. The organism does not survive in moist climates because of competing fungal flora.

b. *Coccidioides* immitis is diphasic, but instead of having the usual yeast and mold phase, it has a mold phase at room temperature and a tissue phase in *vivo*. Therefore, because it has two morphologically different phases that are temperature dependent, it qualifies as a diphasic or dimorphic organism. It resides in the soil as mycelia composed of hyphae that are 2 to 4 mcm in diameter. Hyphae fragment into highly resistant arthroconidia. Arthroconidia become airborne whenever soil is
disturbed. Arthroconidia are inhaled by humans, thereby initiating the infection. Each arthroconidium develops into a spherule (tissue phase) in vivo. Each spherule, 36 to 60 mcm in diameter, contains numerous endospores that are 2 to 5 mcm in diameter. Endospores are released when the spherules rupture, spreading the infection within the host.

c. Coccidioidomycosis may present as an acute to subacute pneumonia that may become complicated by chronic pulmonary infection, or disseminate to other body organs. 60 percent of reported infections are asymptomatic, whereas 40 percent demonstrate fever, a mild cough and a small amount of white sputum. Caucasians may develop a rash due to allergic reaction. When primary the pulmonary infection fails to heal, dissemination occurs via the bloodstream. In untreated patients, mortality rate is 100 percent if the central nervous system becomes involved. Other infective sites are lung, liver, bone, spine, joints, and subcutaneous tissue. Only a small percentage of infections progress past the primary pulmonary stage.

d. Laboratory identification of *Coccidioides immitis* is discussed below.

(1) Diagnosis is made by spherule demonstration in the direct examination of clinical specimens. Culturing can be accomplished; however, arthroconidia seen in culture are highly infective and should be handled only in biological safety hoods. (Figure 7-6.)

![Figure 7-6. Spherule of *Coccidioides immitis* in tissue.](image)

(2) Mycelial phase of *c. immitis* exhibits a moderate growth rate of 5 to 14 days. Colonies are white to tan with a brown to black reverse. Appearance is cottony. Microscopic examination shows branching septate hyphae. Rectangular to barrel shaped arthroconidia range in size from 3 to 5 mcm. Alternating light and dark staining cells are present. (Figure 7-7.) No yeast phase occurs.
Figure 7-7. Mycelial form of *Coccidioides immitis*.
EXERCISES, LESSON 7

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. What is the usual mode of infection for the systemic fungi?

2. Which of the following systemic fungus is not diphasic?
   a. Cryptococcus neoformans.
   b. Histoplasma capsulatum.
   c. Blastomyces dermatitidis.
   d. Coccidioides immitis.

3. Name the two organisms that cause histoplasmosis.

4. Histoplasmosis is a disease characterized by persistent respiratory symptoms.
   a. True.
   b. False.
5. Direct examination of a clinical specimen is diagnostic of *Histoplasma*, if:
   a. Branched chains of blastoconidia are seen.
   b. Brown sclerotic bodies are seen.
   c. The yeast form of the organism is seen.
   d. Blastoconidia are seen within mononuclear cells.

6. *Histoplasma capsulatum* can be distinguished from the contaminant *Sepedonium* by:
   a. Microscopic examination of microconidia.
   b. Characteristics of colonial morphology.
   c. Demonstration of diphasic nature of *Histoplasma capsulatum*.
   d. Origin of the clinical specimen.

7. Diagnosis of infection by *Blastomyces dermatitidis* is usually made by:
   a. Clinical symptoms of the disease.
   b. Recovery of the organism.
   c. A positive complement-fixation test.
   d. Presence of nodules in the lung.

8. Microconidia resembling "lollipops" are characteristic of which of the following organisms?
   a. *Histoplasma capsulatum*.
   b. *Sepedonium* spp
   c. *Blastomyces dermatitidis*
   d. *Coccidioides immitis*
9. If direct examination of a clinical specimen reveals thick-walled globose blastoconidia with buds arranged as a "pilot's wheel", the organism is likely to be:
   a. *Paracoccidioides brasiliensis*.
   b. *Blastomyces dermatitidis*.
   c. *Histoplasma duboisii*.
   d. None of the above.

10. Macroscopic colony morphology of *Blastomyces dermatitidis* and *Paracoccidioides brasiliensis* during their yeast phases are useful in differentiating the organisms.
   a. True.
   b. False.

11. *Coccidioides immitis* differs from other systemic fungi because it:
   a. Is monophasic.
   b. Has 2 distinct yeast phases.
   c. Is nonpathogenic.
   d. Has distinct mold and tissue phases.

12. *Coccidioides immitis* is spread within a host by:
   a. Release of endospores from a ruptured spherule.
   b. Ulcerated nodules in the lymphatic system.
   c. Reinfection due to improper hygiene.
   d. Transportation of organism within the RE cells.

13. Which systemic organism has barrel-shaped arthroconidia showing alternating light and dark staining cells?

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 7

1. Inhalation of viable spores (para 7-1a)

2. a (para 7-1a)

3. *Histoplasma capsulatum*  
   *Histoplasma duboisii*  (para 7-2a)

4. b (para 7-2b)

5. d (para 7-2d(1))

6. c (para 7-2d(3))

7. b (para 7-3c(1))

8. c (para 7-3c(2))

9. a (para 7-4b)

10. b (para 7-4c(2))

11. d (para 7-5b)

12. a (para 7-5a)

13. *Coccidioides immitis*  (para 7-5d(2))

End of Lesson 7