

# COCCIDIOIDOMYCOSIS

## Learning objectives

To know in detail about,

- Morphology and cultural characteristics of *Coccidioides immitis*
- Coccidioidomycosis
- Diagnostic methods for coccidioidomycosis
- Sporotrichosis
- Blastomycosis

## INTRODUCTION

- Coccidioidomycosis is usually a benign, inapparent, or mildly severe upper respiratory infection that resolves naturally.
- On occasion, the disease may become an acute or chronic, disseminating, fatal mycosis.
- The etiologic agent, *Coccidioides immitis*, is the most virulent of the fungal pathogens.
- The disease is not uncommon among laboratory workers who isolate the agent.
- It is endemic in the soils of the Southwest United States and Central South America.
- Dust storms increase the incidence of disease.
- Of domestic animals, dogs are most frequently affected, although horses are occasionally affected as well.
- Infections also occur in cats, swine, sheep, cattle, human and nonhuman primates, and some 30 species of non-domestic mammals.

## MORPHOLOGY

- In the soil, *C. immitis* is a mould made up of slender septate hyphae that give rise, on thicker secondary branches, to chains of infectious arthroconidia (arthrospores, arthroaleuriospores, arthroaleurioconidia).
- These are bulging, thick-walled cells, separated by empty cells, through which breaks occur when arthroconidia are dispersed.
- In tissue, arthroconidia grow into spherical sporangia with birefringent walls, "spherules", which by internal cleavage produce several hundred "endospores".
- The walls disintegrate, allowing dissemination of endospores, each of which may repeat the cycle or, on a nonliving substrate, give rise to mycelial growth.
- Though only arthroconidia are naturally infectious, endospores can experimentally initiate disease. Sexual spores are not known.
- "Coccidioidin" in supernatants of mycelial *C. immitis* broth cultures is largely polysaccharide, but contains some amino acid nitrogen.
- It is used in cutaneous hypersensitivity and serologic tests.
- "Spherulin," a lysate of cultured spherules, is also used in skin tests. Both are leukotactic.

## CUTURAL CHARACTERISTICS AND RESISTANCE

### Cultural characteristics

- This dimorphic fungus grows more quickly than the other dimorphic pathogens (1-2 weeks), but the same cultivation media are used.
- On Sabouraud's or blood agar, at 25° C or 37° C, a moist white colony develops that later is covered with a fluffy mycelium. Bovine blood agar is hemolyzed.
- Arthroconidia are produced in 5 to 7 days. Mycelial growth should be evident within a week and is examined for presence of arthroconidia in a lactophenol cotton blue wet mount.

- Thick-walled, barrel-shaped arthroconidia alternating with empty disjunctive cells is characteristic.
- The isolate can be reconverted to the sporangial phase by animal inoculation or cultivation in a spherule medium.
- The sporangial phase is produced at 40°C in media containing casein hydrolysate, glucose, biotin, glutathione and a salt mixture.

## Resistance

- Arthroconidia resist drying and tolerate heat and salinity better than do competing soil organisms.
- In summer heat, *C. immitis* survives in soil layers nearer the surface than its competitors.
- When conditions favor growth again after rains, *C. immitis* repopulates the superficial soil layers first, ensuring its widespread dispersal.

## PATHOGENESIS

- Infection is mainly by inhalation of dust. Primary cutaneous infections are rare. Infection is initiated by inhalation of the arthrospores.
- Relevant cell products include proteases, T suppressor cell activator, and leukotactic agents. Leukocytes *in vitro* encourage arthroconidial metamorphosis to spherules.
- The agent triggers an inflammatory response in the lung, is engulfed but not killed by phagocytes and is conveyed to the lymph node, where another inflammatory focus develops.
- Inflammation is stimulated in part by a potent serine protease, which is liberated during the growth of the fungus *in vivo* (digests elastin, collagen, and immunoglobulins).
- Normally, cell-mediated immune responses arrest the process at this stage following stimulation of TH -1, lymphocytes that activate macrophages.
- With inadequate cell-mediated immunity, dissemination can occur to bones, skin, abdominal viscera, heart, genital tract, and eye (and rarely in animals to brain and meninges).

## CLINICAL SIGNS AND LESIONS

### Clinical Signs

- In all species, overt disease is the exception. Highest prevalence of canine systemic coccidioidomycosis is observed in male dogs, 4 to 7 years of age.
- Young Boxer dogs and Doberman pinschers are highly susceptible.
- Pulmonary disease may be asymptomatic, symptomatic of variable degree, benign and chronic, or progressive.
- Dissemination may occur, but only in the dog and human, and depends on host resistance and the level of exposure.
- There may be respiratory signs (including cough), fever, lameness due to bone involvement, or discharging sinuses from deep lesions.
- The disease is most common in Boxers and Doberman Pinschers.
- The disease has not been reported in cats.
- In cattle, sheep, and swine, the disease is usually asymptomatic, limited to lungs and regional lymph nodes and undiagnosed until slaughter.

### Lesions

- Gross lesions are white granulomas varying from miliary nodules to irregular masses. Peritoneal, pleural, and pericardial effusions occur.
- The initial lesions are found in the lungs. Systemic disease may involve the meninges, bones, joints, and subcutaneous and cutaneous tissues.

- Lesions may also occur in the lung, brain, liver, spleen, and kidney.
- In acute cases, burrowing abscesses are common.
- In chronic and slowly advancing cases, focal and suppurative granulomatous lesions are common without caseation or calcification.
- Severe, disseminated disease is usually seen only in dogs and humans.
- Cattle and swine are often infected, but the disease is restricted to a few tuberculous-like lesions in the lymph nodes and sometimes the lung.

## DIAGNOSIS, TREATMENT AND CONTROL

### Diagnosis

- **Based on Direct Examination of Specimens**
  - Animal fluids and tissues are examined for spherules by wet mount in saline containing 10% KOH.
  - Spherules are 10 to 80 µm in diameter, have a thick wall, and contain endospores.
  - When the spherule bursts, it releases endospores (2-5 µm) and leaves a ghost spherule and the endospores are stained by a fungal stains such as hematoxylin and eosin and Gomori methanamine silver.
- **Based on Culture**
  - Blood agar and Sabouraud's agar with antibiotics are inoculated, tape-sealed, and incubated at 37°C and 25°C, respectively.
  - Mycelial growth should be evident within a week and is examined for presence of arthroconidia in a lactophenol cotton blue wet mount, the isolate can be reconverted to the sporangial phase by animal inoculation or cultivation in a spherule medium.
- **Based on serological test**
  - Serologic tests include the coccidioidin skin test (which is useful for prognostic purposes), immunodiffusion test, complement fixation test, latex agglutination test, and tube precipitin test.
  - Serological tests may be more useful than culture. A negative skin test is a poor prognostic sign.
  - For the immunodiffusion test, multiple lines are associated with progressive infection, whereas a single band usually indicates a stable, chronic infection.

### Treatment and control

- As for the other fungal pathogens, amphotericin B is the drug of choice.
- Nystatin is also effective, but is more toxic. Ketoconazole may be effective. Vaccines are not available.

## SPOROTRICHOSIS

- Sporotrichosis is caused by the dimorphic fungus *Sporothrix schenckii*.
- The disease is characterized by nodular lesions that suppurate, ulcerate, drain, and involve the cutaneous and subcutaneous tissues and the adjacent lymphatics.
- The fungus is widespread in nature, found in soil, on wood, and on other vegetation.
- The organism gains entrance to the skin through wounds or by traumatic implantation.
- Occasionally (especially in dogs), the infection may spread to involve bone, muscle, the central nervous system, lungs, or the genitourinary tract.
- Infections are common, particularly in horses and dogs. In dogs, the disease is more likely to disseminate and result in a fatal infection.
- In horses, the disease must be differentiated from epizootic lymphangitis (caused by *Histoplasma farciminosum*).
- The lymphocutaneous form may be nonsuppurative, or may result in ulcerations and pus that discharge at several sites along the lymphatic channel, which serves as a means of transmission for the organism within the animal.

- Laboratory rodents are highly susceptible to experimental infection, indicating the virulence of this organism is greater than that of the opportunistic fungi.
- The disease is infectious, but not contagious, and is chronic.
- This dimorphic fungus can be isolated from lesions on brain heart infusion agar, blood agar, or Sabouraud agar with cycloheximide and chloramphenicol.
- The mold is white when young, then turns brown to black.
- The hyphae are septate and fine, and the microconidia form in clusters at the hyphal tips or as sessile forms at the sides of the hyphae.
- Differentiation from similar looking fungi is by conversion of the mold to the yeast phase.
- Single-celled, cigar-shaped yeasts may or may not be seen in pus from lesions.
- Fluorescent antibody enhances visualization and confirmation of the disease.
- Serological diagnosis can be made by demonstration of a rise in complement-fixing antibody.
- Potassium iodide, Amphotericin B, ketoconazole and miconazole are effective for treatment.

## BLASTOMYCOSIS

- **Etiologic agent:** *Blastomyces dermatitidis*
- **Source:** soil enriched with decaying organic materials
- **Epidemiology:** Primarily North America with sporadic cases reported from India, Africa and the Middle East.
- **Clinical Signs**
  - Cutaneous lesions (Pustules, verrucous or ulcerated lesions) or subcutaneous abscesses.
  - Acute pulmonary disease with cough, pleuritic pain, chills, and low-grade fever.
  - Chronic pulmonary disease with productive cough, fever, weight loss, dyspnoea, and fatigue.
  - Dissemination to skin, bone and genitourinary tract may also occur.
- **Lesions:** Tissue responses suppurative and granulomatous
- **Treatment:** Amphotericin B or Ketoconazole

