Coccidiomycosis (Valley Fever) — Symptoms and Diagnosis

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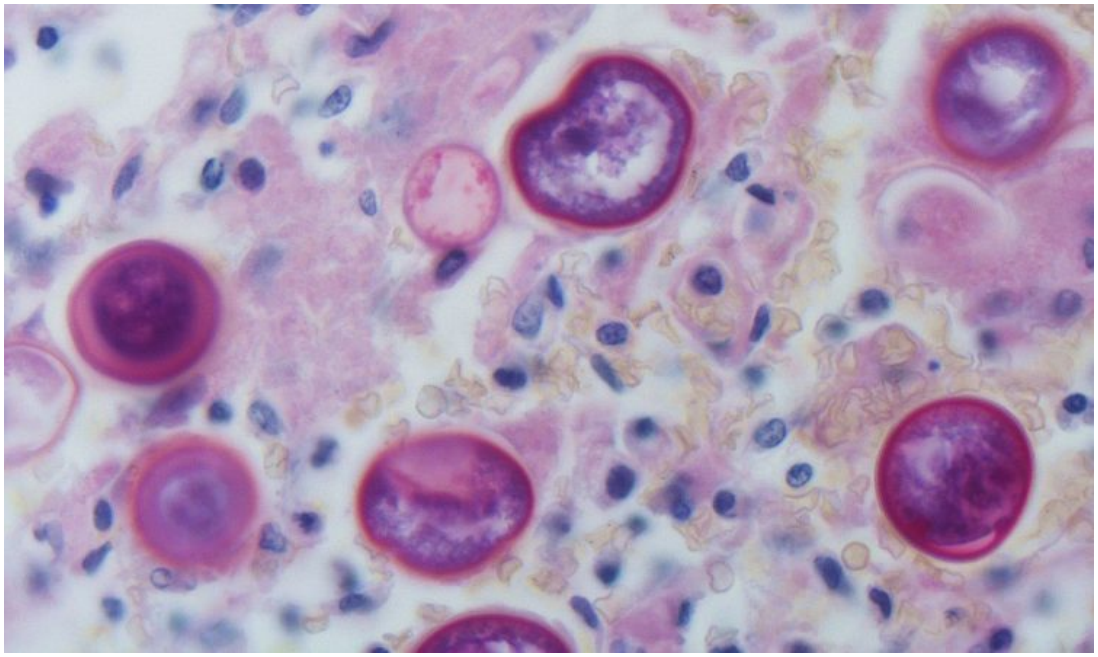
Coccidiomycosis is a fungal infection caused by Coccidioides immitis and Coccidioides posadasii. The two organisms are genetically different but phenotypically identical. The clinical symptoms produced by these two species and the immunological response of the body are similar.



Epidemiology of Coccidiomycosis

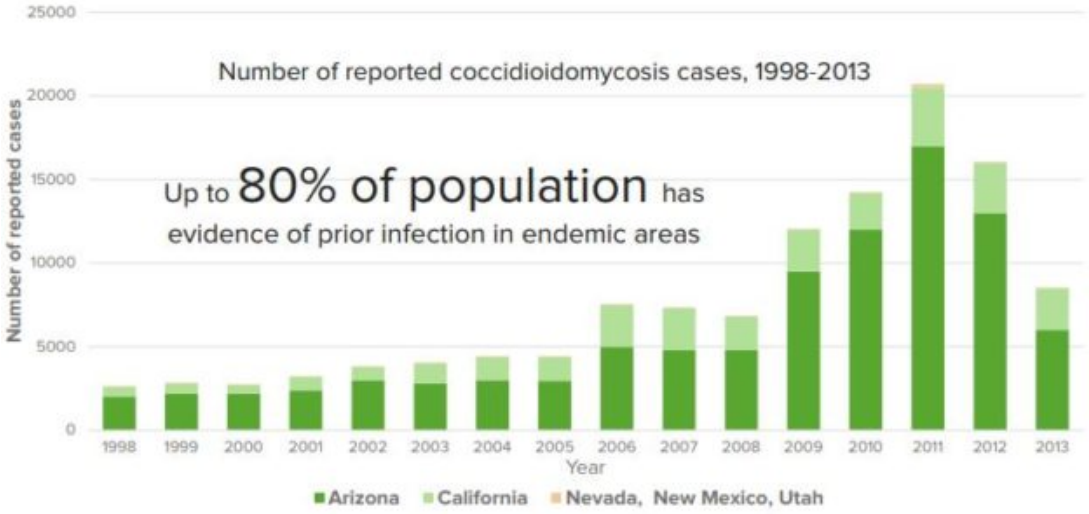
Coccidiomycosis is **endemic** in areas where the **hot summer or mild winter** prevails with an **annual rainfall of 10 – 50 cm**. The causative organism is found in **alkaline soil**, about 10 – 30cm below the surface. It remains dormant during dry spells and develops into a **mold with long filaments** during the rainy season.

These filaments break off into tiny pieces leading to **spore formation**. The spores are swept away during construction, farming and natural disasters, such as earthquakes and windstorms.

Coccidiomycosis is **endemic in the Southwestern United States, northern Mexico, parts of Central and South America**.

The population working in an **agriculture setup or at construction sites** is at higher risk of developing the disease. **Pregnant females**, especially those in their last trimester, are more prone to get the disseminated infection. Similarly, **tourists** traveling to the endemic areas may also contract the disease.

Immunocompromised patients, such as those on immunosuppressants, steroids or have HIV, are always at risk of getting the infection. **Diabetics** and individuals who underwent **thymectomy** are also included in the high-risk group.



"Epidemiology of Coccidiomycosis" Image created by Lecturio

Life Cycle of Coccidioides

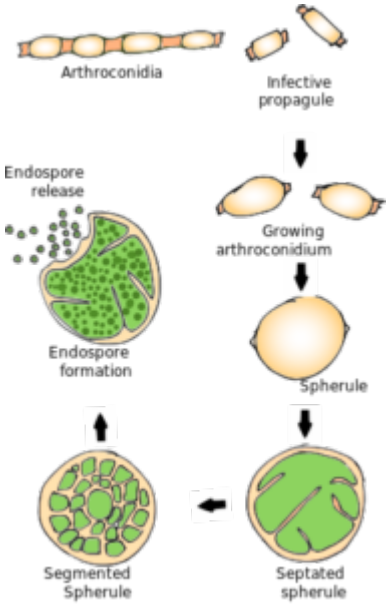


Image: "Life Cycle of Coccidioides." by Saurabh Patil – Own Work. License: CC0 1.0

The life cycle of the Coccidioides begins with dormant barrel-shaped cells known as **arthroconidia** measuring 8 – 30µm. These are the degenerative form of hyphae during prolonged dry spells. These arthroconidia form **spores** which are lightweight structures, swept away during farming, construction or during natural calamities.

These spores are inhaled, thus land in the alveoli. Inside the alveoli, they develop into **spherules**, which are doubled walled structures measuring 20 – 200µm. Within the next 48 – 72 hours, these spherules result in the formation of **septa** and **endospores**.

When these spherules rupture, the endospores are released, which infect other body tissues causing dissemination of the disease. The endospores again mature into **spherules** and the parasitic life cycle is completed.

In certain cases, **nodules** are formed around the spherules which, when burst into alveoli, cause characteristic **chest pain**, **cough,** and **hemoptysis**. Immuno-compromised people are more prone to get blood spread infection.

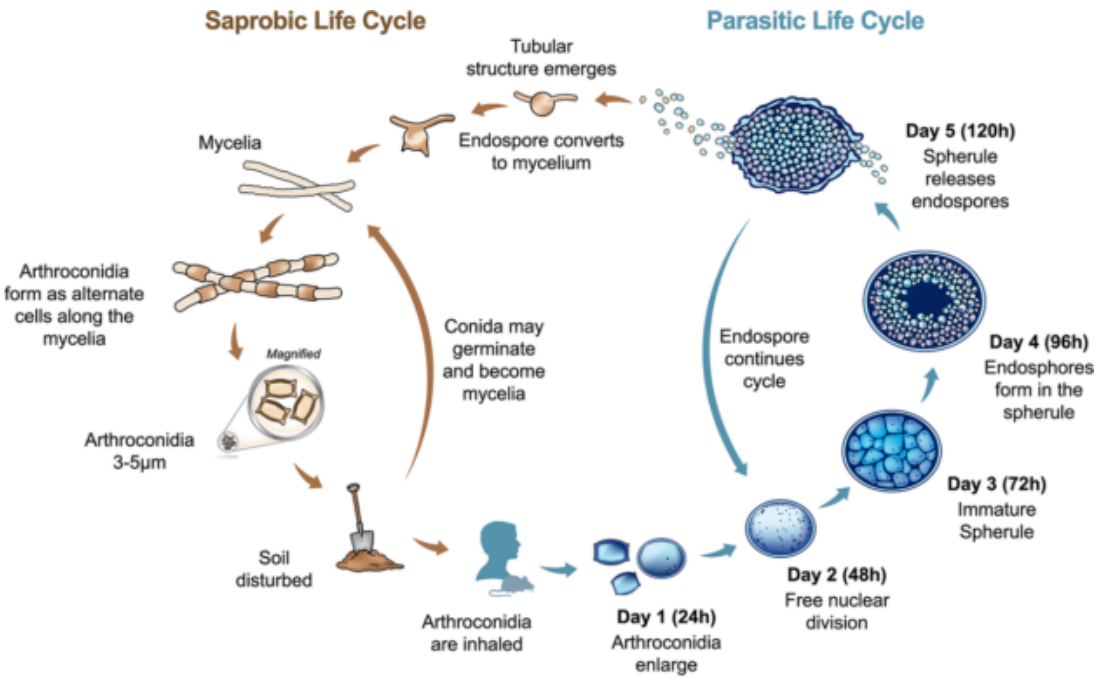


Image: "Both Coccidioides species share the same asexual life cycle, switching between saprobic (on the left) and parasitic (on the right) life stages. The saprobic cycle is found in the environment and produces the infectious arthroconidia. The conidia may be inhaled by a susceptible host, or may return to the environment to continue the saprobic life cycle. The parasitic life cycle is initiated when arthroconidia enlarge and transform into immature spherules, either in vivo or under specific in vitro conditions. From 24 to 72 hours, spherules undergo free nuclear division and begin developing endospores. From 72 to 120 hours, the mature spherules rupture to release endospores. Each endospore can initiate a new spherule, or, under particular atmospheric conditions, nutrient changes, and/or lower temperature, the endospore can convert to a mycelium and initiate the saprobic phase. This occurs in rare circumstances in the living host, but is found most commonly in the environment." by Lewis ERG, et al. – http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1004762. License: CC BY 4.0

Pathogenesis of Coccidiomycosis

The **innate immune cells** are particularly involved in the defense against the organism. This activates the T lymphocytes. The inflammatory cytokines, specifically the gamma interferon, are released causing the destruction of the organism.

Any **impairment in the cell-mediated immunity** results in incomplete evacuation of the organism from the body. The **phagocytized arthroconidia,** if drained into lymph vessels, may cause **lymphangitis**.

In addition to the activation of cell-mediated immunity, these organisms also activate the **complement pathway**, which promotes the **chemotaxis of the eosinophils and the neutrophils**. The pathogenicity of the organism is particularly related to its ability to **bypass phagocytosis**.

The **non-respiratory transmission** involves direct invasion into the skin causing **local lymph nodes infection**. This is, however, a self-limiting condition, which resolves spontaneously.

Signs and Symptoms of Coccidiomycosis

Image: "The right side of this patient's neck displayed a chronic lesion that had been determined to be due to a Coccidioides sp. fungal infection." by CDC/ Dr. Lucille K. Georg – This media comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #15740. License: Public Domain

The **incubation period** of Coccidioides is **10 – 16 days**. While more than half of the infected people remain asymptomatic, others develop signs and symptoms. The primary infection most of the time starts with respiratory symptoms of **a cough** and **breathlessness**. The organism causes **bronchitis** and **pneumonia** which resolves in a few weeks.

In endemic areas, however, Coccidioides result in **community-acquired pneumonia** in 20% of the individuals. Other notable symptoms include **lethargy muscle and joint ache**, **fever**, **rash,** and **headaches**. The **classic triad** of the disease comprise of **fever**, **erythema nodosum** and **joint pain** also termed as '**desert rheumatism'.**

The acute infection is also known as **Valley fever**. Around 5% of the infected individuals do not recover from the acute infection and go into a chronic state. The morbidity and mortality rate increases in the chronic state.

Typical features of **chronic disease** include **a cough**, **fever**, **night sweats**, **weight loss**, **osteomyelitis,** and **meningitis**. The disseminated form of the disease is more severe resulting in **multiple skin lesions**, **inflammation of the vital organs,** leading to death. The figure shows the skin lesion in disseminated infection.

Management of Coccidiomycosis

Diagnosis

Coccidiomycosis is diagnosed with the help of clinical history and investigations. It is important to **differentiate coccidiomycosis from bacterial infections** such as bacterial pneumonia or bacterial meningitis.

The initial investigations which can be performed include **culture and staining of body fluids and exudates** with **Papanicolaou** or **Grocott's methenamine silver stains** which demonstrate the presence of spherules.

Tube precipitin (TP) assay, **complement fixation assays** and **enzyme-linked immunosorbent assay** (ELISA) are also used. TP assay is very specific for coccidiomycosis, while ELISA is more sensitive and is therefore used as a screening tool.

CSF findings help in the diagnosis of meningitis. Similarly, a **chest x-ray** may point towards the underlying lung disease. The gold standard is DNA detection of coccidioides through **polymerase chain reaction** (PCR).

Treatment

The treatment plan of coccidiomycosis involves **azoles** as the first line of therapy. However, due to its **teratogenicity**, it is **not recommended in pregnancy or to lactating females**. **Amphotericin B** is reserved for severe worsening cases which involve the vital organs.

Follow-up

Follow-up visits on a regular basis are required. These are to **monitor the adverse effects of antifungal treatment** and the **response to therapy** after every 1 – 3 months, to be continued for a period of 1 – 2 years, or until the resolution of the disease.

References

Coccidioidomycosis via medscape.com

Valley Fever (Coccidioidomycosis) via cdc.gov

Notes