

Coccidioidomycosis

Definition - benign, inapparent or mildly severe upper respiratory infection, which usually resolves spontaneously, but can become an acute or chronic or severe disseminated mycosis.

Causative agent **-

*Coccidioides immitis**
a hyphomycete of Fungi Imperfecti

**Recovery → protective immunity
from I⁰ pulmonary form (generally life-long)**

*18S rDNA sequencing suggests Plectomycetes (Onygenales) phylogenetic affinities.

**Sequencing suggests two species:

C. immitis, mostly the San Joaquin Valley isolets
C. posadasii, mostly the Texas, Arizona and non-US isolates

Disease Synonyms

Posadas' Disease
Valley Fever
San Joaquin Valley Fever
Valley Bumps
Desert Rhumatism
Etc.

1st so-called "fatal mycosis" to be discovered to have mild and inapparent form → protective immunity - 1920's

History

1891 - Posadas* - Argentina

1st case, live patient. Thought to have protozoan infection caused by "Coccidia-like organisms." Studied case for 7 years (duration, 11 years)

*worked with Werneck

Pickled remains still exist

1896 - Rixford & Gilchrist - 1st & 2nd**

U.S. cases (2nd and 3rd cases)

** Portugese patient from Azores who immigrated to San Joaquin Valley

- cutaneous lesions

Named organism *Coccidioides immitis*

"protozoan"- "oides"- "im"- "mitis"

Coccidia - like - not - mild

Culture attempts always → "contaminating mold"

1900 - Ophuls - Portugese from Azores; culture → mold; therefore concluded that was agent of disease

1905 - Ophuls published *C. immitis* life cycle.

1915 - Dickson begins recognition that coccidioidomycosis is associated most frequently with Southern California

(only 40 known cases by 1915)

- pulmonary origin⁺

-dissemination⁺

1920's - Chope - one of Ophul's students - infects himself → coccidioidal granuloma. Surprise! He lives!

1932 - Stewart & Meyer isolate *C. immitis* from soil in San Joaquin Valley of California

1938 - Myrnier Gifford

Valley Fever*, Valley Bumps, Valley Rhumatism-- were early forms of coccidioidomycosis***

⁺ healed lesions on lungs of autopsy patients suggested there might also be a mild form of disease

^{*} fever, pleurisy, pneumonia (mild form of disease in endemic area)

^{**} erythema nodosum (allergic response in endemic area)

^{***} proof provided by:

- 1) careful observations of patients with various types of clinical disease
- 2) isolation of fungus from sputum of many patients with above
- 3) noting that many, but not all, patients developed coccidioidal granuloma (fatal form).

~1935 - 1945 - C. E. Smith*

1. developed first precipitin test for *Coccidioides* antibody
2. standardized first coccidioidin skin test antigen - helped to define endemic area
3. gathered much data on incidence, severity, and epidemiology
4. defined and clarified clinical forms
5. formulated dust control measures to reduce disease incidence, particularly among military pilot trainees.
 - a) paving or oiling roads, air strips
 - b) planting grass
 - c) encouraging swimming as alternative outdoor sport

*reduced infection rates among air force personnel and others 65% in 1940s.

Skin-Test Impressions

1. **No sex differences prepuberty**
-with regard to infection
-with regard to dissemination
2. **4:1 male:female dissemination distribution in adults***
265/100,000 vs 74/100,000
3. **Race distribution apparent with dark skin individuals being more affected***
4. **Only 0.5% of all primary infections (conversion of skin-test to +) develop into serious disease. Of these, 10X more serious disease among blacks than caucasians.***

*not all attributable to occupational activities

Many AIDS patients test + for coccidioidomycosis (skin test). However, rate of coccidioidomycosis in AIDS patients in endemic areas is relatively low.

CA State Health Lab Recommendations to University Concerning Coccidioidomycosis*

* result of Chico epidemic (1970)

1. **No required field trips in endemic area**
2. **Information must be provided to dept heads, etc. about this mycosis**
3. **Skin test should be done to ID individuals at risk**
4. **Non-reactors should be advised (or prohibited from) not to participate**
5. **Dust control measures should be emphasized (even masks used)**
6. **Specimens should be sterilized (gas/UV)**

Also to employers of outdoor workers

Most Common Antigen(s)

Coccidioidin

obtained by extraction of polyvalent antigens from numerous strains

Antigen 1 = involved in LPA and TP tests

Antigen 2 = involved in CF and ID test

Antigens 3&4 = significance not well established

Spherulins = extracts of formalin killed spherules

Treatment: Drug of choice = Amphotericin B

AIDS Cocc - Amphi B → Itra -- indefinite s

AIDS/Cocci Amphotericin B + Itra = indefinite suppression with Itra; good results with fluconazole with primary forms

Abbreviated/Traditional Clinical Types of Coccidioidomycosis

I. Primary coccidioidomycosis

A. Pulmonary

- 1. Asymptomatic
 - 2. Symptomatic

B. Cutaneous (rare)

secondary coccidioidomycosis

- ## **Pulmonary**

1. Benign chronic III (cavitary)

2. Progressive

- Single or multisystem dissemination**

 1. Meningeal (1/3 to 1/2 of cases)
 2. Chronic cutaneous
 3. Generalized - including hematogenous spread

*Phoenix - up to 25% of AIDS patients develop coccidioidomycosis

(see handout for better, expanded version!)

REVIEW
Immunological Response after Primary Exposure to *Coccidioides immitis*
(normal patients)

1. Conidia or small spherules are phagocytized, degraded and processed by aveolar macrophage (MΦ)
2. The MΦ display the *C. immitis* antigens so that T-lymphocytes are sensitized
3. The T-lymphocyte sensitization results in the development of cell-mediated immunity and delayed-type hypersensitivity* to the fungus
4. Also to enhanced activation of more MΦ resulting in enhanced micro-biolocidal activity (killing)
5. B-lymphocytes are stimulated to produce antibodies in the sequence IgM** followed by IgG***
6. The immune response is influenced by the activity of T-lymphocytes with cytotoxic helper or suppressor function

* DTH detected by skin test with coccidioidin[^] or spherulin[^]

** IgM antibody detected by tube precipitin/immunodiffusion test - early primary or exacerbation[^]

*** IgG antibody by compliment fixation test dissemination and poor prognosis if remains high[^]
^ traditional serology