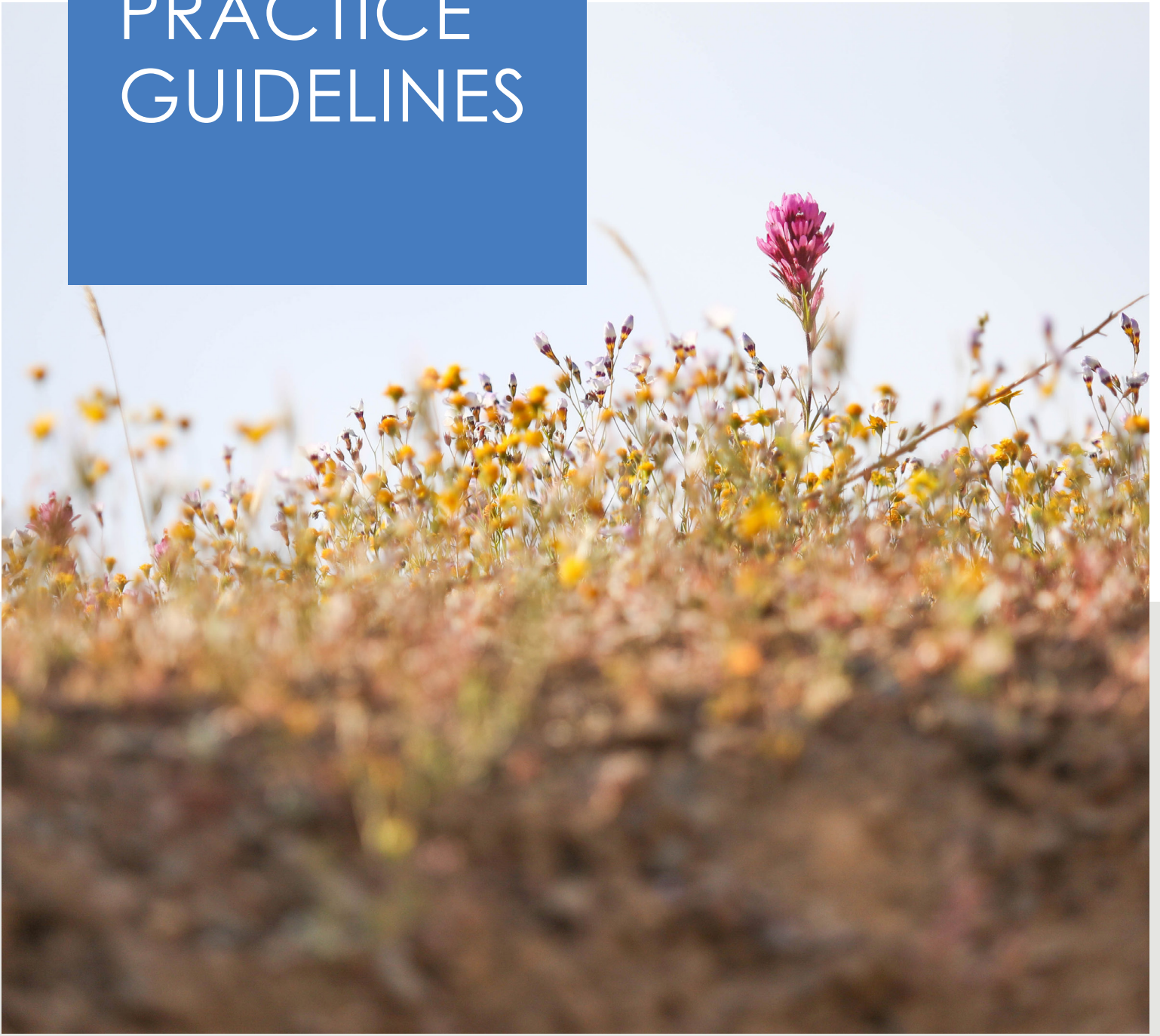


Valley Fever

CLINICAL PRACTICE GUIDELINES

 Valley Fever Institute
at Kern Medical



1700 Mount Vernon Avenue
Bakersfield, CA 93306

www.ValleyFeverInstitute.com
Research Phone Number: (661) 706-6748
Referral Phone Number: (661) 664-2200

CLINICAL MANIFESTATIONS

Commonly presents as pulmonary disease.

- Most common is persistent pneumonia
- Persistent hilar and mediastinal lymphadenopathy.
- Rare cases present as disease, which can resemble pulmonary tuberculosis.
- First symptoms occur 7-21 days after infection.
- 60% of the time infection is asymptomatic.
- 40% of infections will have symptoms.
- 1 out of the 40% are diagnosed.

RARE FINDINGS

01

Bronchial mass may be present with bronchoscopy.

02

Fibrocavitary pneumonia can occur in association with diabetes or pre-existing pulmonary fibrosis.

03

Miliary disease is 10 times more frequently seen with cocci in endemic areas than in tuberculosis.





PREVALENT SYMPTOMS

Fever (76%)

Cough (73%)

Chest pain (44%)

Fatigue (38%)

Erythema nodosum (26%)

Myalgias (23%)

Shortness of breath (22%)

Sputum production (22%)

Chills (21%)

Headache (21%)

Night sweats (21%)

Other rashes (14%)

RADIOGRAPHIC FINDINGS

10%

have negative chest radiograph at diagnosis.

70%

will have Infiltrate only.

10%

will have Infiltrate with hilar adenopathy.

10%

will have Infiltrate with effusion.

DISSEMINATED DISEASE

Rate of dissemination depends on the infected host.

Majority of disseminated disease occurs in those that have pre-existent pulmonary infections.

Minority of patients present without obvious primary pulmonary infection.

Risk Factors for dissemination

Extremes of age

Males

African American descent

Filipino descent

Immunodeficiency associated with

- Advanced HIV infection
- High dose corticosteroid therapy
- Hodgkin's Lymphoma
- Solid organ or bone marrow transplantation
- Pregnancy



Most common sites for dissemination

- Meninges (most severe) - CSF has elevated WBC, protein, & depressed glucose.
- Skin - verrucous lesions.
- Subcutaneous tissue (presents as abscess).
- Bones of the axial skeleton, pelvis, tibia, and femur.
- Joint infections of knees, elbows, wrists, and ankles.
- There are cases in virtually every body site.

DIAGNOSIS

- Based upon compatible clinical illness and the following:
- Biopsy specimen that demonstrates endo sporulations.
- Culture positive for coccidiomycosis.
- Serology that is positive for organism.
- Sensitivity and specificity of serologic testing make it helpful in:
 - » Diagnosis
 - » Assessing progression or improvement

SEROLOGIC TESTING TYPES



IgM and/or **IgG** antibodies develop in response to Coccidioidal infection.

Early immune response to infection - characterized by presence of IgM.

IgM can be detected by

- Immunodiffusion
- Enzyme Immunoassay Associated (EIA), associated with false-positive and false negative results

Compliment Fixation (CF)

CF titer provides important prognostic information.

- CF titer of 1:2 - 1:4 (usually associated with good outcome)
- CF titer of 1:16 or greater is often associated with disseminated disease.
- CF titers are not as reliable in immunocompromised patients.
- The results from some laboratories may vary from above.

Skin Testing

- Skin testing detects delayed hypersensitivity reaction to Coccidioides.
- Commonly remain positive for life.
- A positive test result may not be related to current illness (similar to tuberculin).
- A negative test result cannot exclude a diagnosis of current or past infection.
- Limited as a screening procedure for recent infection.

OTHER LABORATORY FINDINGS

- CBC and Chemistry tests may offer clues to Cocci infections.
- Community Acquired Pneumonia (in an endemic areas) associated with eosinophilia ≥ 350 cells/u probably has Cocci.



X-RAY & OTHER IMAGING

Mandatory in evaluation of primary disease.

- Plain radiograph is always performed
- CT of chest may be helpful in selected cases and cavitary disease.
- Bone Scan is used for osteomyelitis.
- MRI of bone and joint may help define problematic cases.
- MRI of brain and spinal cord will reveal meningeal enhancement, hydrocephalus, or vasculitic infarction.

TREATMENT

Patients with minimal infection may improve without therapy.

- Nodules due to cocci, have most often benign course.
 - » Do not require therapy in absence of evidence of coccidioidal infection at other sites.
 - » If cocci organisms identified in a single nodule no specific therapy usually needed.
- Cavity
 - » Simple cavities may resolve with no therapy.
 - » Limited data that therapy helps closure
 - » If cavity is near pleural surface it can, rupture into pleural space and cause hydropneumothorax requiring chest tube placement.



TREATMENT
SHOULD BE
INITIATED WITH

Moderate symptomatic pneumonic disease

All disseminated disease

Patients with CF titer $\geq 1:16$

**** The Valley Fever Institute has all tests performed at either the Kern County Public Health Department or UC Davis**



Antifungal Agents

AZOLES

- Fluconazole
 - » Usual dose 400 - 1200 mg per day
 - » At Valley Fever Institute 800-1200mg per day, treatment failures seen at 400mg per day
- Itraconazole (requires an acidic gastric pH and fat for absorption)
 - » Usual dose 400 mg per day (100mg 2 PO 2 times per day)
 - » Absorption impaired by PPI
- Voriconazole 4 mg/kg
 - » No food (2hr) pre and post dose
- Posaconazole 100 mg 3-4 per day
- Isavuconazole 186 mg 2 per day

AMPHOTERICIN B

- Used when patients are rapidly progressing in clinical course
 - Severe pneumonia with respiratory failure
 - Critical osteomyelitis
 - Other severe coccidioidal disease
- Several weeks of amphotericin B are often required for improvement
- Amphotericin is given intravenously and intrathecal for cocci meningitis

Duration of Treatment for Acute Pulmonary Disease

- For those indicated treatment can be:
 - » Initiated with azole or amphotericin.
 - » Followed by Prolonged azole therapy.
 - » Course ranges from 3-6 months or longer in high-risk patients.
- If no improvement occurs after several months:
 - » Change of azole drug or to ampho B is indicated.

DURATION OF TREATMENT

COCCI FINDINGS AND TREATMENT

Pulmonary Cavity

- Asymptomatic cavitary disease does not usually require intervention.
- Symptomatic solitary cavity cocci may benefit from azole.
- Course of azole with varying duration is appropriate until symptoms are resolved and decrease in CF titers can be used to guide therapy.
- ½ of Cavities smaller than 3cm will resolve in 6-12 months.
- If cavity persists and symptoms abate a trial of azole withdraw may be undertaken.
- If symptoms re-appear a reinstatement of therapy for a longer period is suggested.
- Indications for surgical resection of cavity include:
 - » Recurrent bacterial superinfections
 - » Recurrent or life threatening hemoptysis.
 - » Rupture of Cavity into the pleural space, with development of empyema.

Chronic Progressive Fibrocavitary Pneumonia with Cocci

Subacute illness that often results in respiratory failure and pulmonary hypertension.

- In pre-azole era often resulted in death.
- Since the advent of azoles, death is less common.
- Fluconazole or Itraconazole 400 mg or more per day is common therapy.

Coccidioidomycosis in Pregnancy

Mild disease with low CF titers are followed closely (often weekly) without treatment.

Those with greater extent of disease and high CF titers are treated.

- Amphotericin is drug of choice for those requiring therapy.
- Azole compounds demonstrate concerns, Per FDA regulations can disturb the development of the embryo or fetus causing birth defects.



DISSEMINATED DISEASE (EXTRA-PULMONARY)

- Requires more expertise and judgement than uncomplicated pulmonary disease.
- Disseminated disease of skin, soft tissue, joints and bones that is limited and not life threatening is usually treated with Azoles.

BONY DISSEMINATED DISEASE

- In multifocal bone disease that affects the axial skeleton of major long bone, Azoles may be used but many experts prefer to start with Amphotericin and finish with protracted periods of Azole treatment.
- High dose greater than (FDA may) azole therapy is often used in protracted therapies.
- Duration of therapy substantially longer than 1 year is recommended frequently. (Some experts treat for up to 3 years.)
- Doses higher than 800 mg of Fluconazole or Itraconazole are frequently administered.
- If bony disease is amenable to surgical debridement, it may be a valuable adjunct.

COCCIDIOIDAL MENINGITIS (always requires consultation)

- Fluconazole is the preferred drug.
 - » Doses of 800-1200 mg daily are given as a single dose.
- In patients failing high dose Fluconazole:
 - » Intrathecal Amphotericin B is used primarily now for those failing initial and secondary therapies.
- Treatment is usually life-long.
- Intrathecal Amphotericin Therapy
 - » Was the primary therapy for CNS Cocci until supplanted by azole therapy.
 - » Can be given by:
 - Direct cisternal injection.
 - Cisternal or Ventricular reservoir
 - Intrathecal Lumbar or reservoir injection.
- Complications of Cocci Meningitis
 - » Hydrocephalus treated with Ventriculoperitoneal shunt.



MONITORING THERAPY

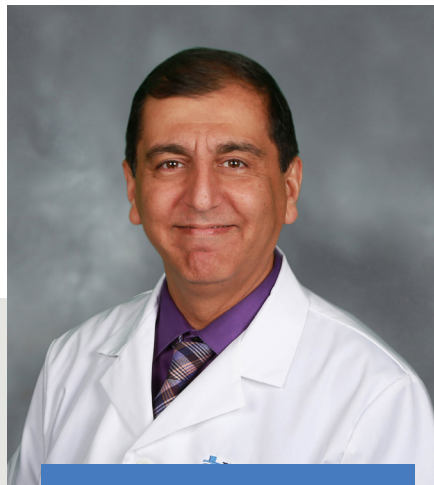
PRIMARY COCCIDIOIDOMYCOSIS

- Monitoring required at 1-3 month intervals with both laboratory and radiology studies.
- If there is suspicion for dissemination by history or on exam, biopsy and culture of suspected sites should be done.
- Lumbar puncture may be required in patients who develop headache or other neuro symptoms after the initial infection.
- Bone scan may be indicated to evaluate bony or joint involvement.
- Follow-up is a minimum of 2 years post treatment.

VALLEY FEVER INSTITUTE TEAM



Royce H. Johnson, MD



Arash Heidari, MD



Rasha Kuran, MD



Dana Brucker, RN



Augustine Muñoz, MD

A series of 28 horizontal lines for writing, arranged in pairs across the page.



1700 Mount Vernon Avenue
Bakersfield, CA 93306

www.ValleyFeverInstitute.com
Research Phone Number: (661) 706-6748
Referral Phone Number: (661) 664-2200