Valley fever Diagnostics Current Methods and Challenges

Fariba Donovan MD, PhD
The University of Arizona,
Valley Fever Center for Excellence

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Objectives

- Challenges involved with the early diagnosis of coccidioidomycosis.
- Current available diagnostic methods and their limitations.
- Future plans for better diagnostic methods for early detection.

Valley fever Awareness

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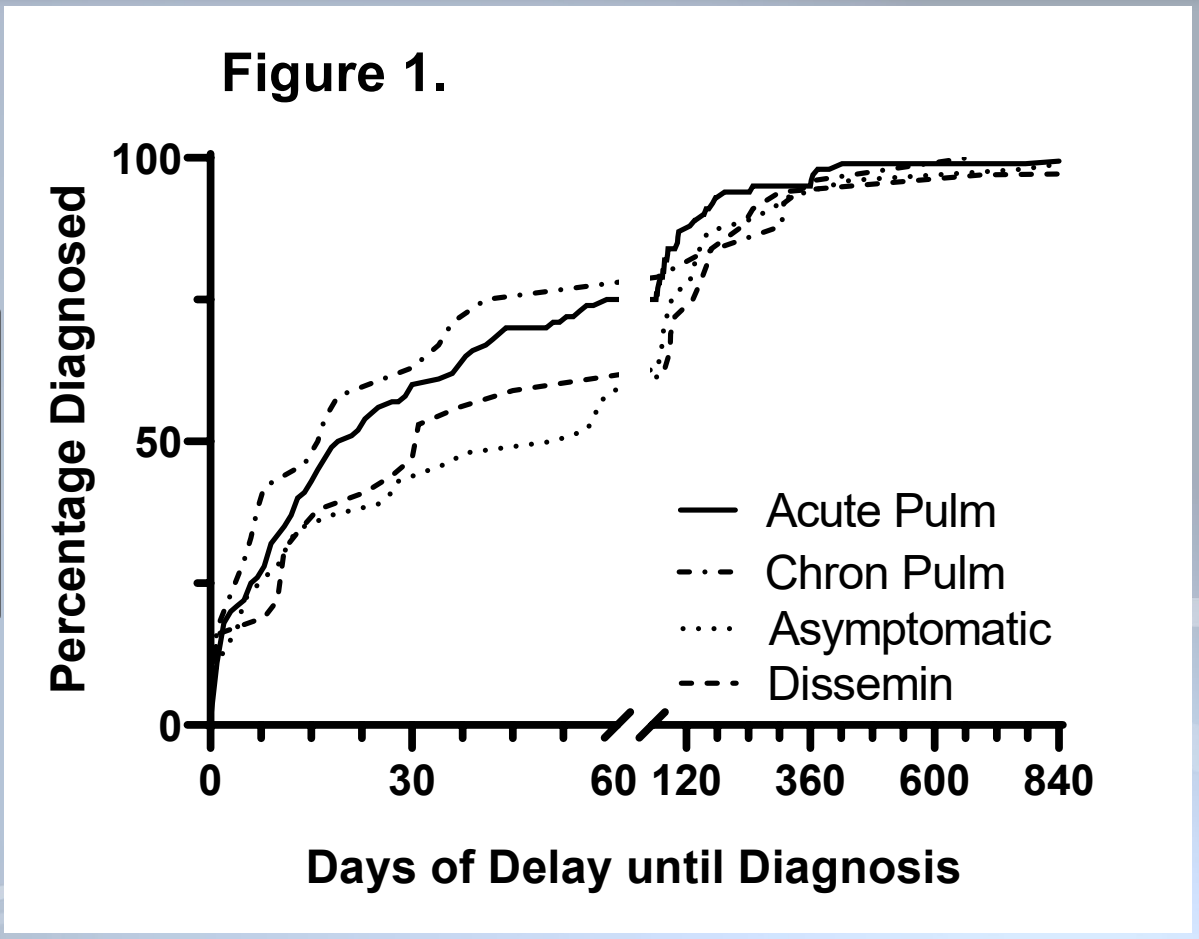
Current Clinical Practice for Valley fever

- Arizona CAP
  - ~ 25% - 30% due to Coccidioides
    BUT
  - < 15% are tested for Coccidioides
- ~ 1,000 new AZ medical licenses/year
  - 12% received MD in AZ
  - 40% no AZ GME
- 80% didn't know:
  - VF is reportable
  - Vaccine does not exist
- 40% of clinicians are not confident to treat VF

Delays in Valley fever Diagnosis

BUMC-T
43% of Diagnoses
Delayed > 1 month



Donovan et al. EID, 2019

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Summary of Patients with CAP BMG and BUMG, total 2017-2019

Measure Year	Patients With Initial Diagnosis of Pneumonia	25 % Of Patients With Initial Diagnosis of Pneumonia	Patients With Diagnosis Of Cocci	Patients With Cocci Tests	Patients With Positive Cocci Test Results
2017	837	209	26	26	23
2018	851	213	19	19	13
2019	629	157	12	12	7
Grand Total	2,268	567	57	57	43

Delays in Diagnosis

- Delays in coccidioidomycosis diagnosis is > 30 days in 43% of cases.
- Substantial cost/healthcare utilization is related to the diagnosis delay.
- Unnecessary antibacterial usage is directly related to this delay.

Improving Awareness

- Banner Health and the UA Valley Fever Center for Excellence are changing the way Arizona clinicians recognize and manage patients with Valley fever.
- Central to this change will be the expanded role of primary care clinicians in earlier diagnosis and management of uncomplicated Valley fever.

The Valley Fever Tool Kit

www.vfce.arizona.edu

Support Resources

- Process Flow pocket guide.
- Wall posters and patient educational brochures
- Nurse practitioner referral support? (proposed)
- EMR alerts? (only if wanted by the clinicians)

Training Resources

- Webinar Overview
- Primary Care Tutorial
- PowerPoint presentation online
- CME presentations at individual clinical practices.

Coccidioidomycosis Commonly Used Diagnostic Modalities

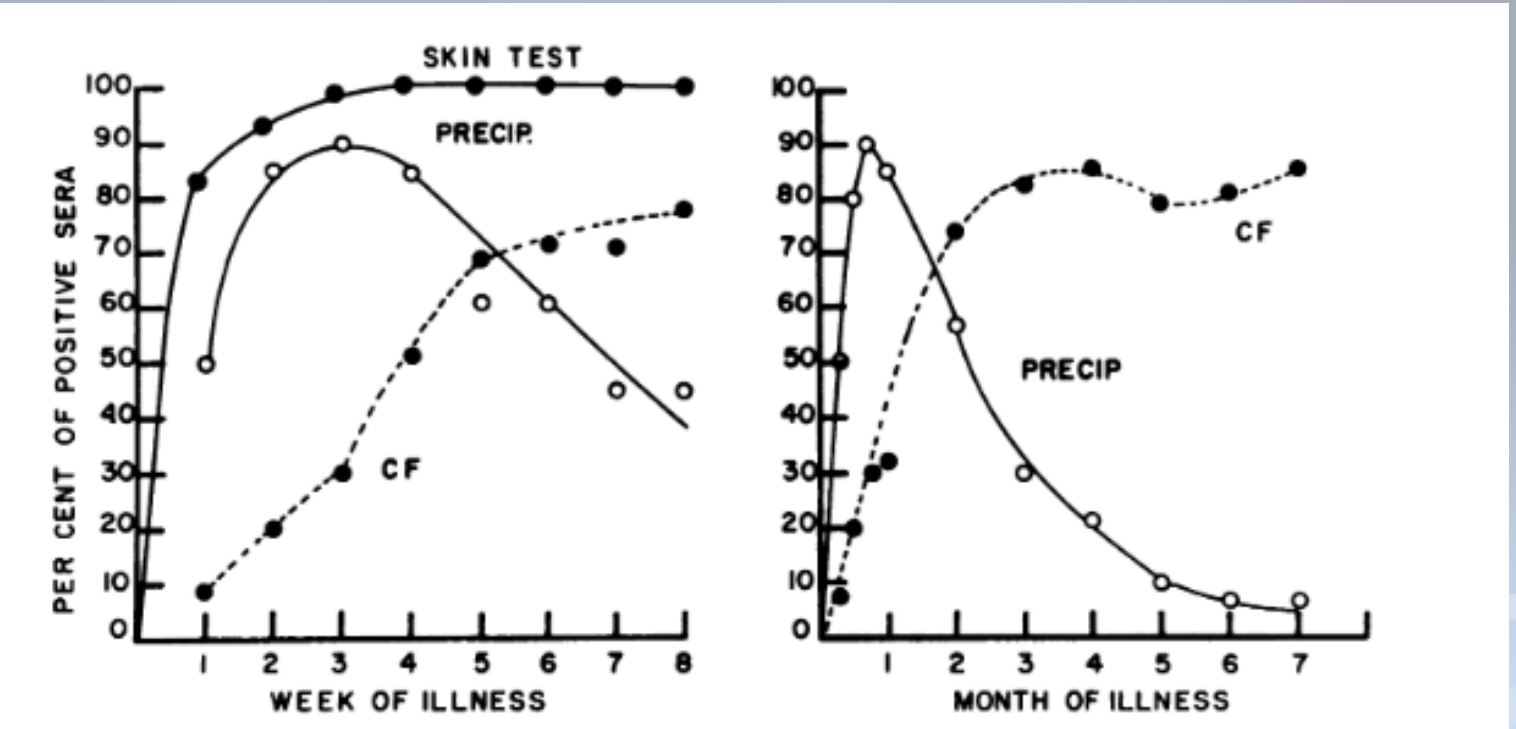
- Serology
- Culture
- Pathology
- Imaging (CXR, CT)
- Skin test (adaptive immunity)

Serology

- Tube precipitin (TP): Heat stable 120 KDa β-glucosidase.
- TP & Immunodiffusion TP (IDTP) detect IgM, positive **early** in illness.
- CF (complement fixation): Heat-labile chitinase.
- CF & IDCF positive **after 2-3 weeks**, IgG reaction.
- IDTP and IDCF require immunodiffusion in agar, **Specific** and **relatively sensitive**.
- CF titers have prognostic values.

Pappagianis et al, CMR, 1990,
Ampel, Medicine Reports 2010

Temporal Sequence of Immunological Changes in Non-Complicated Coccidioidomycosis



Smith et al, Public Health Rep. 1957.
Pappagianis et al, CMR, 1990.

EIA Screen for Coccidioidal Antibodies

Enzyme Immunoassay (EIA) test

- **A positive test** is very specific and usually is diagnostic.
- **A negative test** never rules out Valley fever. Repeated testing improves diagnostic sensitivity.

Which Test is The Best?

Current commercially available diagnostic tests have variable accuracy.

	EIA	MiraVista	Meridian	IMMY
Sensitivity	IgG	87%	71%	45%
	IgM	61%	29%	22%
Specificity	IgG	90%	96%	94%
	IgM	95%	99%	98%

Malo et al, Medical Mycology 2020, doi: 10.1093/mmy/myz125

Comparison of a Novel Rapid Lateral Flow Assay to EIA for Early Diagnosis of Coccidioidomycosis

- Prospective enrollment of 392 patients with suspected CM, compared the LFA with standard EIA.
- Acute pulmonary disease (74%) the most common clinical syndrome.
- Hospitalized patients constituted 75% of subjects.
- Patients frequently had ≥3 previous healthcare facility visits ($P = .05$).
- Received >3 antibacterial courses ($P < .01$).
- Procalcitonin (PCT) was <0.25 ng/mL in 52 (83%) EIA-positive patients, suggesting infection was not bacterial.

Donovan et al, CID 2021, doi: 10.1093/cid/ciaa1205

Novel LFA Agreement with EIA and Immunodiffusion

	EIA, %		IMDF, %	
	Value	**95% CI**	**Value**	**95% CI**
Sensitivity, %	**30.8**	19.9–43.5	**40.7**	22.4–61.2
Specificity, %	**92.0**	88.1–94.6	**95.2**	88.3–98.7
PPV, %	44.4	32.2–57.5	73.3	48.8–88.8
NPV, %	86.2	84.1–88.0	83.3	78.5–87.3

Donovan et al, CID 2021, doi: 10.1093/cid/ciaa1205

LFA Testing for Early Diagnosis of Coccidioidomycosis

- It is fast (takes only 30 minutes)
- High Specificity.
- Needs improvement in sensitivity for a point-of-care test.

Summary

- Raising Valley fever awareness is the key to early diagnosis.
- Expanding the role of primary care clinicians is crucial in the earlier diagnosis and management of uncomplicated Valley fever.
- Development of a rapid point-of-care testing with high sensitivity and specificity is extremely important in early diagnosis.

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Thank-You

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