Seroincidence and Risk of Coccidioidomycosis Infection Among Active Duty Personnel Stationed at Naval Air Station Lemoore in the San Joaquin Valley of California

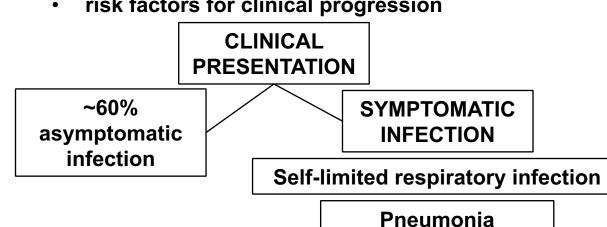
Graham C. Ellis, MD^{1,2}, Charlotte A. Lanteri, PhD³, Hsing-Chuan Hsieh, MPH^{3,4}, Paul C. F. Graf, PhD^{5,6}, Terrel Sanders, MD^{2,7}, Ryan C. Maves, MD^{2,3}, Robert G. Deiss, MD^{2,3,4,8}



¹EOD Expeditionary Support Unit TWO, Virginia Beach, VA, USA, ²Division of Infectious Diseases, Naval Medical Center San Diego, San Diego, CA, USA, ³Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, 4The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, USA, ⁵U.S. Naval Medical Research Unit No. 6, Lima, Peru, ⁶U.S. Naval Health Research Center, San Diego, CA, ⁷U.S. Naval Medical Research Unit No. 3, Accra, Ghana, ⁸Division of Infectious Diseases and Global Public Health, University of California, San Diego, San Diego, CA, USA

Background

- Coccidioidomycosis is an endemic mycosis native to SW United States (CA, AZ), Central/South America
- Dimorphic fungus Coccidioides (spp. immitis and posadasii) is causative agent via inhalation of soil containing arthroconidia spores
- Epidemiology is poorly understood, based largely on skin testing and observational studies from mid-20th century:
 - geographic distribution
 - seasonal incidence
 - risk factors for exposure/infection
- Pathogenicity determined from limited case studies/series. Gaps in the literature include:
 - clinical course
 - prognosis
 - risk factors for clinical progression



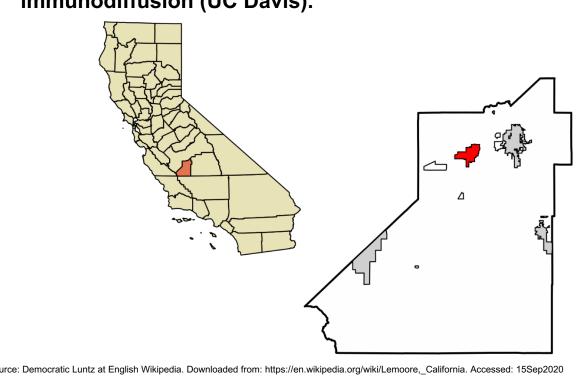
Pneumonia + erythema nodosum/multiform ("Valley Fever")

<1% multi-organ dissemination (tissues, meninges, bone)

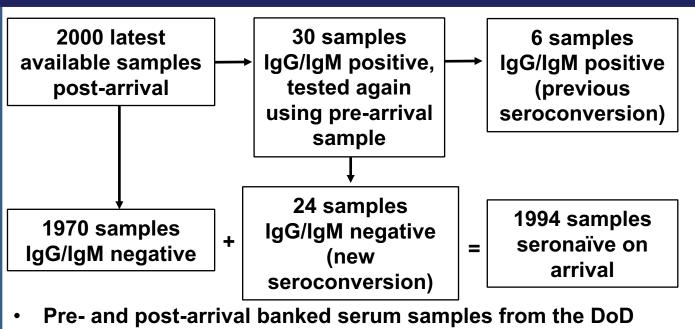
Limited Coccidioides seroincidence data support these assumptions

Methods

- Retrospective cohort study of exposure to Coccidioides spp.
- 2000 U.S. military personnel transferred to Naval Air Station Lemoore in Kings County, California between 2011 and 2017
- IgG and IgM anti-Coccidioides antibodies detected by ELISA (IMMY, Norman, OK) before and after arrival to this endemic area. Positives and equivocal results confirmed by immunodiffusion (UC Davis).



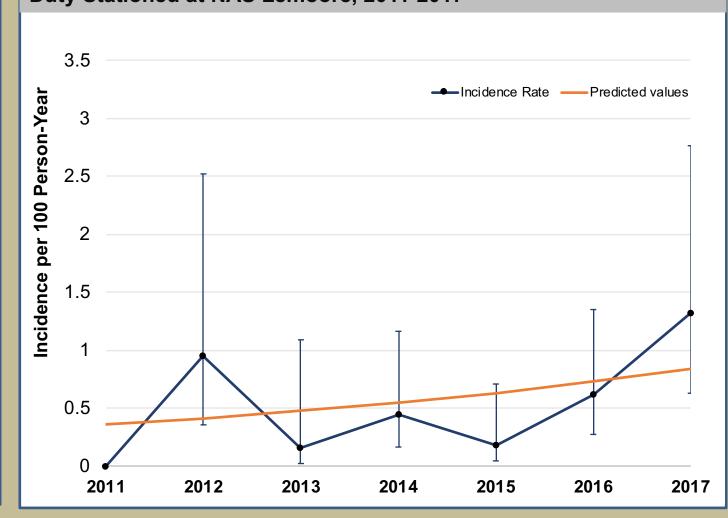
Methods (cont.)



- **Serum Repository**
- Time in endemic area calculated by subtracting sample collection date from station arrival date
- Medical histories and participant demographics such as military occupational specialty codes collected from electronic medical record
- Participants stratified by history of Coccidioides-specific or general respiratory illness ICD9/ICD10 codes

Results (cont.)

Figure 1. Incidence of *Coccidioides* Seroconversion Among Active **Duty Stationed at NAS Lemoore, 2011-2017**



Results

Table 1. Demographics of Active Duty at NAS Lemoore by Seroconversion Status and Cocci/Pneumonia Diagnosis

		Seroconversion		*מ	Cocci/Pneumonia Diagnosis		n *	Total
		No	Yes	ρ	No	Yes	p*	TOLAI
Age		23.0[20.0-27.0]	22.5[19.0-26.5]	0.5358	24.0[20.0-27.0]	21.0[19.5-25.0]	0.0572	23.0[20.0-27.0]
Gender	Male	1657(83.86)	20(83.33)	>0.999	1644(84.05)	33(75.00)	0.1067	1677(83.85)
	Female	319(16.14)	4(16.67)		312(15.95)	11(25.00)		323(16.15)
Race/Ethnicity	Caucasian	910(46.05)	6(25.00)	0.1098	892(45.60)	24(54.55)	0.5885	916(45.80)
	African American	298(15.08)	5(20.83)		299(15.29)	4(9.09)		303(15.15)
	Asian/Pacific Islander	120(6.07)	2(8.33)		118(6.03)	4(9.09)		122(6.10)
	Hispanic	338(17.11)	4(16.67)		335(17.13)	7(15.91)		342(17.10)
Grade	Enlisted	1791(90.64)	24(100.00)	0.1999	1772(90.59)	43(97.73)	0.1799	1815(90.75)
	Warrant	4(0.20)	0		184(9.41)	1(2.27)		4(0.20)
	Officer	181(9.05)	0					181(9.05)
Total		1976(98.80)	24(1.20)		1956(97.80)	44(2.20)	•	2000

Values are presented as n(%) *For continuous variables, p-values were calculated with Mann-Whitney U/Wilcoxon Rank Test. For categorical variables, p-values were calculated with Chi-Square/fisher exact.

Table 2. Seroconversion Status of Active Duty at NAS Lemoore by Cocci/Pneumonia Diagnosis

Table 2. Deloconversion diatus of Active Buty at NAO Lemoore by Occent neumonia Biagnosis										
	Cocci/Pne									
Seroconversion	No		Total							
Selocoliversion		Pneumonia		Cocci & Pneumonia		iolai				
		Pre-arrival	Post-arrival	Pre-/Post-arrival*	Pre-arrival					
No, or unknown	1929(97.92)	21(1.07)	18(0.91)	1(0.05)	1(0.05)	1970(98.50)				
Previous exposure	6(100.00)	0	0	0	0	6(0.30)				
Yes, or possible	21(87.50)	0	1(4.17)	0	2(8.33)	24(1.20)				
Total	1956(97.80)	21(1.05)	19(0.95)	1(0.05)	3(0.15)	2000				
/alues are presented as n(%) *One subject has two pneumonia-related diagnosis before arrival and one Cocci-related diagnosis after arrival										

Results (cont.)

- 24 of 1994 (1.2%) seronaïve participants tested newly positive for anti-Coccidioides antibodies after at least 12 months on station
- Annual seroconversion incidence 0.0-1.32 from 2011-2017
- Overall seroconversion incidence 0.5 per 100 person years
- Seropositive participants more frequently diagnosed with coccidioidomycosis/pneumonia than seronegative (p=0.027)
- No statistically significant association between demographic characteristics (age, gender, race, education, military service, military rank) and seroconversion or disease on both adjusted and unadjusted models
- Majority of seroconversion and disease seen in Electrical/Mechanical Equipment Repairers (63.33% and 45.45% respectively) followed by Electronic Equipment Repairers (13.33%, 20.45%) although no statistically significant differences among the occupational specialty codes
- Clinical disease detected in three seroconverters (10%)

Conclusions

- Coccidioides seroincidence similar to that observed in the literature, adding longitudinal evidence to epidemiologic assumptions about coccidioidomycosis
- A trend toward increasing incidence over this six year study is consistent with the classification of coccidioidomycosis as an emerging infectious disease
- **Despite assumptions of environmental transmission patterns** based on disease ecology and limited observational studies, we did not detect a difference in transmission based on military occupational specialty codes or other demographics thought to increase risk
- Rates of diagnosed disease in our cohort were lower than the historically-assumed 40% symptomatic rate
- Our study is limited by its retrospective nature, coccidioidomycosis is likely underreported
- Further clinical and epidemiologic coccidioidomycosis research, particularly in broader endemic regions, is warranted

Acknowledgments

This project has been funded by the National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), under Inter-Agency Agreement Y1-AI-5072, the Defense Health Program, U.S. DoD, under award HU0001190002, the Armed Forces Health Services Branch's Global Emerging Infectious Surveillance program, Infectious Disease Clinical Research Program, and the Henry M. Jackson Foundation.

Disclaimer. The views expressed are those of the authors and do not necessarily reflect the official policy or position of the Uniformed Services University of the Health Sciences, Henry M. Jackson Foundation, National Institutes of Health and Department of Health and Human Services, Department of the Navy, Army, Department of Defense, nor the U.S. Government. This research has been approved by USUHS ID IRB.





Correspondence

Correspondence may be directed to: LT Graham Ellis at graham.ellis@navy.mil