PROCEEDINGS OF THE 59th ANNUAL COCCIDIOIDOMYCOSIS STUDY GROUP MEETING

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Proceedings of the 59th Annual

Coccidioidomycosis Study Group

Meeting Number 59

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University of California

Skaggs School of Pharmacy

San Diego, California

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COCCI STUDY GROUP 59TH ANNUAL MEETING
AGENDA
San Diego, California
April 11, 2015

7:00-8:00 A.M. **Breakfast, Registration, Poster Set-up**

8:00-5:00 P.M. **Poster Visitation Available - Hosted in Foyer**
Moderator: Suzanne Johnson

List of Posters by Title and Authorship

1. **Fluconazole-associated Hypercalcemia in Patients with Coccidioidomycosis**
   Chan N, Blair J, Westphal S, Tehrani L, Seville M

2. **Uphill Both Ways: Quality of Life in Treated and Non-Treated Valley Fever**
   Garrett A, Chang Y, Blair J

3. **Sarcoid Histopathology in Coccidioidomycosis**
   Yourison I, Kuberski T

4. **What to do about Valley Fever? A critical review of options for Public Health**
   Brown, P, Cisneros R, Gaab, E, Goldman-Mellor S, Ridgway D, Sipan C

5. **Classification and Analysis of Laboratory Results for Reported Coccidioidomycosis Cases, Arizona, 2014**
   Khan M, Bhattarai B, Erhart L, Tsang Clarisse, Brady S

6. **Identification of *Coccidioides immitis* in archaeological soil samples from Madera County, California**
   Majewski T, Parise K, Rivas S, Doerry N, Martinez S, Garcia D, Dreibe E, Engelthaler D, Keim P, Lauer A, Barker B

7. **Coccidioidomycosis among California Hispanic farm workers: A CDC/NIOSH-funded study at the University of California Davis and Merced Campuses**
   Sipan C, Emery K, Bang H, Portillo-Silva C, Pinkerton K, McCurdy S

8. **Solar Panel Construction in the Mojave Desert Can Pose a Risk of Increasing Valley Fever Incidence**
   Lauer A, Colson A

9. **A Retrospective Natural History Study of Coccidioidomycosis in California**
   Tartof S, Yu K, Rieg G, Contreras R, Xie F, Benedict K, Fong K, Truong J, Higashiyama N, Jacobsen S, Mody R

10. **Establishing an antibody detection EIA to detect *Coccidioides* specific antibodies in canines**
    Holbrook E, Durkin M, Smedema M, Wheat L

11. **Natural History of *Coccidioidomycosis* Lung Nodules**
Sachdeva M, Sahota G, Rosario J, Mills P, Peterson M, Bilello K

12. **Coccidioidomycosis in Washington State, 2015: An Update on an Emerging Infection**
Oltean H, Wohrle R, McCotter O, Chow N, Litvintseva A, Chiller T, Clifford W

13. **Decrease in Coccidioidomycosis Cases Reported to the National Notifiable Diseases Surveillance System, 2011–2013**
Benedict K, Derado G, and Mody R

8:00-8:15 A.M. **Convene Meeting/Introductions/PosterLogistics/Amenities**
Antonino Catanzaro, Suzanne Johnson

8:15-10:00 A.M. **Clinical Science - Human**
Moderator: John Galgiani

- **Adjunctive Corticosteroid Therapy in the Treatment of Coccidioidal Meningitis**
Thompson III G, Wang S, Bercovitch R, Bolaris M, Van Den Akker D, Lopez R, Heidari A, Catanzaro A, Cadena J, Chin-Hong P, Spellberg B, Blair J, Johnson R

- **Wheezes and Desert Breezes: When Asthma and Valley Fever Collide**
Azadeh N, Rank M, Lewis J, Wesselius L, Cheng M, Blair J

- **Bronchoscopy Findings of Coccidioidomycosis**
Heidari A, Munoz A, Alkatib R, Sobhani N, Lankarani D, Qaqish S

- **Central Valley Lung Nodule Calculator: A Prospective Analysis of a Newly Developed Calculator in a Coccidiodomycosis Endemic Area**
Ronaghi R, Rashidian A, Mills P, Peterson M

- **Report of a Patient with Both Coccidioidomycosis and Histoplasmosis**
Hussain S, Kuberski T

- **Disseminated Coccidioidomycosis: Two Cases of Parotid Gland Involvement**
Jabbour A, Stockamp N, Libke R

- **Pediatric Coccidioidomycosis Patients: Psychosocial factors**
Gaab E

10:00-10:30 A.M. **Poster Visitation/Break**
Posters 1-7

10:30-12:00 A.M. **Laboratory and Experimental Science**
Moderator: Douglas Lake

- **Preliminary Results About Physical, Chemical and Biological Characterization of Coccidioidin for its Use in Immunosorbent Assay**
  Villegas-García S, Castañón-Olivares L, Arreguín Espinosa R, Cuevas C, Monterrubio Zavala C, Laniado Laborín R

- **Novel Potent and Selective Fungal CYP51 Inhibitors for Treatment of Coccidioidomycosis**
  Garvey E, Shubitz L, Trinh H, Lewis M, Galgiani J, Fothergill A, Wiederhold N, Hoekstra W, Yates C, Schotzinger R

- **Early Host Innate Immune Response in a Murine Model of Pulmonary Coccidioidomycosis**
  Lewis E, Doyle A, Barker B

- **Defect in the TH17- IL17 Pathway as a Cause of Severe Granulomatous Disease**
  Heidari A, Krogstad P, Yourshaw M, Ameri G, Abukamleh H, Myers S, Aguirre D, Grewal R, Johnson R

- **Whole Exome Sequencing Identification of Human Genetic Polymorphisms Associated with Extrapulmonary Dissemination of Coccidioidomycosis**
  Yourshaw M, Krogstad P, Johnson R, Ameri G, Abukamleh H, Meyer S, Aguirre D, Grewal R, Heidari A

- **Identification of Lectin-binding Coccidioidal Glycoproteins**
  Kaushal S, Chowdhury Y, Grys T, Magee D, Blair J, Colby T and Lake D

12:00-1:00 P.M. **Lunch**

1:00-1:30 P.M. **Business Meeting, Cocci Study Group**
Moderator: Antonino Catanzaro, President, CSG

Agenda: Bylaws amendment discussion and vote; **Neil Ampel assumes Presidency of CSG,** CSG #60 date, host and vote; Election for 2 Members at large; discussion and CSG recommendation for CSG #61 International Meeting date and site; discussion and vote regarding satellite meetings as regular venue; Treasurer's report by Royce Johnson

1:30-2:30 P.M. **Clinical Science - Veterinary**
Moderator: Lisa Shubitz

- **Clinicopathologic and Gross Renal Pathologic Findings in Dogs with Coccidioidomycosis**
  Mehrkens L, Mohr C, Sykes J

- **Interferon-γ Responses of Dogs to *in vitro* Stimulation with Coccidioidal Antigens Measured by Flow Cytometry**
  Shubitz L, Powell D, Frelinger J, Galgiani J

- **Risk Factors and Spatial Distribution of Canine Coccidioidomycosis in California**
  Grayzel S, Martinez Lopez B, Sykes J

- **Developing tools for veterinary surveillance in newly identified *Coccidioides* endemic areas**
  Chow N, Lindsley M, Wohrle R, Kangiser D, Durkin M, Holbrook E, Litvintseva A

2:30-3:00 P.M. **Poster Visitation/Break**
Posters 8-13

3:00-5:00 P.M. **Ecology and Epidemiology**
Moderator: Demosthenes Pappagianis

- **Coccidioidomycosis: A Possibly Underreported Cause of Death — Arizona, 2008–2013**
  Jones J, Brady S, Koski L, Khan M, Sunenshine R, Komatsu K

- **Using Hospital Discharge Data as a Source for Identifying Cocci-Associated Deaths in Maricopa County in 2012**
  Koski L, Jones J, Sylvester T, Narang J, Brady S, Kretschmer M, LaMantia N, Wells J, Sunenshine R

- **Race and Risk of Coccidioidomycosis-associated Mortality**
  Noble J, Nelson R, Fufaa G, Shafir S, Sorvillo F, Galgiani J

- **Coccidioidomycosis Skin Test Screening Results Among California State Inmates**
  Lucas K, Wheeler C, Ritter S, Tharratt S, Mohle-Boetani J

- **Phylogeography and Dispersal of *Coccidioides posadasii***
  Engelthaler D, Roe C, Driebe E, Schupp J, Gade L, Waddell V, Komatsu K, Thompson III G, Chiller T, Keim P, Litvintseva A, Barker B

- **Detecting *Coccidioides posadasii* in Soil in Southern Arizona**
  Parise K, Rivas S, Schwartzberg K, Hilsabeck R, Krohn S, Lewis E, Fisher F, Dreibe E, Caporaso G, Engelthaler D, Keim P, Barker B

- **Molecular Detection of *Coccidioides spp.* in Baja California**
  Vargas-Gastélum L, Riquelme M

- **Coccidioidomycosis Among Workers Constructing Solar Power Farms in California**
  Sondermeyer G, Wilken J, Shusterman D, McNary J, Vugia D, McDowell A, Borenstein P, Gilliss D, Ancock B, Prudhomme J, Gold D, Windham G, Lee L, Materna B

5:00 P.M. **Concluding Remarks**
Neil Ampel

7:00 P.M. **Dinner** (by reservation)
Rock Bottom Restaurant & Brewery La Jolla
8980 Villa La Jolla Drive, La Jolla, CA 92037
Antonino Catanzaro

2015 Cocci Study Group 59th Annual Meeting Host

Antonino Catanzaro / Laura Myhovich
U.C., San Diego

2015 Cocci Study Group 59th Annual Meeting Moderators

Suzanne Johnson – Poster Presentations
John Galgiani – Clinical Science, Human; Oral Presentations
Douglas Lake – Laboratory and Experimental Science; Oral Presentations
Lisa Shubitz – Clinical Science, Veterinary; Oral Presentations
Demosthenes Papagianis – Ecology and Epidemiology; Oral Presentations

Cocci Study Group Program Committee

Herbert Boro – Director
Karl Clemons
Arash Heidari
Susan Hoover
Suzanne Johnson

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Antonino Catanzaro – President
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Jessica Einstsin
Royce Johnson
Rafael Laniado-Laborin
Rebecca Sunenshine

2015 CSG Satellite Meeting: *Coccidioides* in the Environment-
Tools, Results and Future Directions
Skagg School of Pharmacy
UCSD campus
April 10, 2015

12:30-1:00	**Registration** (no added cost when registered to attend the CSG 59th Annual Meeting April 11, 2015 at U.C., San Diego)
1:00-1:15	**Opening Welcome Address**. **Bridget Barker**, Tgen North
1:15-1:45	**Suzanne Johnson**, UC Davis, *C. immitis* and *C. posadasii* at Dinosaur National Monument, Utah; Diggin' up bones and things better left alone.
1:45-2:15	**Meritxell Riquelme**, CICESE. Molecular detection of *Coccidioides spp*. in Baja California.
2:15-2:45	**Antje Lauer**, CSU Bakersfield. Detection of *Coccidioides immitis* in soils and dust of the western Mojave Desert
2:45-3:15	**Coffee Break**
3:15-3:45	**Ana Litvintseva**, CDC, Investigating the expanding geographic range of *Coccidioides*
3:45-4:15	**Dave Engelthaler**, Tgen North, Diversity of *Coccidioides posadasii* in Southern Arizona
4:15-4:45	**John Taylor**, UC Berkeley. Natural History of *Coccidioides spp*.
4:45-5:30	**Panel Discussion**: Methods (primers, sequencing, loci, DNA extraction) AND future directions (EEID, modeling needs, etc.)
	Dinner (on your own)

Fluconazole-associated Hypercalcemia in Patients with Coccidioidomycosis

Chan NH[1], Blair JE[2], Westphal SA[3], Tehrani LK[4], Seville MT[2]

[1]Division of Community Internal Medicine, Mayo Clinic in Arizona, Scottsdale, Arizona, USA
[2]Division of Infectious Disease, Mayo Clinic in Arizona, Phoenix, Arizona, USA
[3]Division of Endocrinology, Mayo Clinic in Arizona, Scottsdale, Arizona, USA
[4]Department of Pharmacy, Mayo Clinic in Arizona, Phoenix, Arizona, USA

INTRODUCTION

Fluconazole, voriconazole and itraconazole may potentiate the hypercalcemic effect of other medications, although triazoles alone have not yet been linked to hypercalcemia. We describe a case of new-onset hypercalcemia in the setting of high-dose fluconazole, resolved after the antifungal regimen was changed.

METHODS

We reviewed the Mayo Clinic database in Arizona to assess the frequency of moderate or severe hypercalcemia (calcium value of 12 mg/dL or greater) among patients with coccidioidomycosis treated with a triazole.

RESULTS

Over an almost eight-year span, approximately 1% (23/2133) of patients with a diagnosis of coccidioidomycosis developed hypercalcemia subsequently, of which 87% (20/23) had moderate or severe hypercalcemia. Forty five percent (9/20) of the moderately or severely hypercalcemic patients were taking triazoles. The majority of these nine cases had comorbidities that predispose or contribute to hypercalcemia (four patients had tertiary hyperparathyroidism, two had multiple myeloma and one had adrenal insufficiency). Two patients developed severe hypercalcemia (calcium value of 14 mg/dL or greater) while on high dose fluconazole, with one patient on 800 mg daily in the setting of acute kidney injury and 1200 mg daily in the other patient with normal renal function. Coincident with hypercalcemia management, the antifungal regimen was changed from fluconazole to voriconazole in these two patients, with no recurrence of hypercalcemia at last follow-up

CONCLUSIONS

Moderate or severe hypercalcemia is uncommon in coccidioidomycosis and is rare in those treated with triazoles. High dose fluconazole may be associated with symptomatic hypercalcemia, especially in patients with predisposing comorbidities.

Uphill Both Ways: Quality of Life in Treated and Non-Treated Valley Fever

Garrett AL, Chang Y and Blair J

Mayo Clinic Arizona, Department of Infectious Diseases

INTRODUCTION

Primary pulmonary coccidioidomycosis is characterized by a prolonged duration of respiratory symptoms, fever, arthralgias and fatigue. We prospectively administered the fatigue severity scale (FSS) and short form 36 (SF-36) questionnaires to patients with primary pulmonary coccidioidomycosis to quantify the effect of the disease on quality of life.

METHODS

Patients with confirmed or probable primary pulmonary coccidioidomycosis were enrolled in a prospective observational 24-week study. The study did not specify whether or not antifungal treatment was to be provided, and such decisions were left to the treating clinician. Patients were asked to complete the FSS and SF-36 questionnaires at 4 week intervals throughout the duration of the study.

RESULTS

Thirty-six patients met inclusion criteria and agreed to participate in the study. Twenty patients received antifungal treatment, and 16 did not receive antifungal treatment. At the onset of coccidioidal illness, the mean FSS was higher (more fatigue) in the treatment group. However, in early illness, both groups displayed higher levels of fatigue than other disease populations such as systemic lupus erythematosis and multiple sclerosis. A gradual trend of improvement in the FSS scores were seen over the 24-week period, and scores in each group fell below the level of "severe fatigue" (<4) at weeks 12 and 16 in the non-treatment and treatment groups respectively. By week 24, the mean FSS score was at the level of the general population in the non-treatment group. The SF-36 component and profile scores were lower (more symptoms) in the treatment group at most all time points compared to the non-treatment group; both groups showed a similar pattern of improvement over the study period. Mental and emotional health scores were not as severely affected as physical scores within the SF36. The majority of patients reached a level of physical functioning similar to the general population (50) at week 12.

CONCLUSION

Pulmonary coccidioidomycosis causes severe fatigue and significantly affects patients' physical abilities. Fatigue was higher and quality of life was more affected in the treatment than non-treatment group. The course of fatigue is prolonged with a gradual improvement in quality of life measures over the 24-week period, regardless of antifungal administration.

Sarcoid Histopathology in Coccidioidomycosis

Yourison Isaac and Kuberski Tim

U of Arizona College of Medicine, Phoenix

INTRODUCTION

The cause of a sarcoid is unknown. The diagnosis of sarcoid requires consistent tissue histopathology and exclusion of agents known to cause non-caseating granulomas. A potential relationship between Coccidioides and sarcoidosis was suggested by a case report presented at the Coccidioidomycosis Study Group Meeting in 2013. That patient was diagnosed with sarcoid based on typical tissue histopathology and excluding potential causes, including coccidioidomycosis. He was followed prospectively for seven years when he developed disseminated coccidioidomycosis. We present another patient with disseminated coccidioidomycosis who was studied retrospectively because he had lung histopathology consistent with sarcoidosis.

METHODS

A 34 year old African-American male was diagnosed with disseminated coccidioidomycosis in 2008. He grew Coccidioides from an elbow culture; Coccidioides serology was positive at 1:8. In 2012 his clinical course was complicated by a hospitalization after he developed respiratory failure requiring mechanical ventilation. During that hospitalization he underwent a lung biopsy. The tissue from the lung biopsy showed non-necrotizing granulomas consistent with sarcoidosis. There was no histopathologic or culture evidence of a Coccidioides infection. His Coccidioides serology was negative. The histopathology from this patient and the patient reported in 2013 were independently reviewed by three different pathologists who were all in agreement that the histopathology of each was consistent with sarcoid with no evidence of Coccidioides.

RESULTS

The sarcoid histopathology of the two case study patients, one prospectively and one retrospectively, were both associated with a disseminated Coccidioides infection. These clinical observations suggest that the histopathology of these two patients were indistinguishable from those in the non-endemic area of Coccidioides.

CONCLUSIONS

These two unique case studies support the hypothesis that in the endemic area Coccidioides can be a cause of sarcoid histopathology and supports Coccidioides as a potential cause of sarcoidosis.

What to do about Valley Fever? A critical review of options for Public Health

Brown, Paul, Cisneros, Ricardo, Gaab, Erin, Goldman-Mellor, Sidra, Ridgway, Derry, Sipan, Carol

U.C. Merced

INTRODUCTION

Over the past eighteen months, we have engaged in a systematic analysis of the options for mitigating the impacts of Valley Fever. This included a systematic review of the literature, meetings with researchers, community members, and policy makers, and review by an expert panel of the options for addressing Valley Fever in the San Joaquin Valley. These discussions have focused on the evidence pertaining to prevention, detection, treatment, and survivorship of Valley Fever. The purpose of this session is to present the results from this review and our public health recommendations for mitigating the impacts of Valley Fever on the people in the region.

METHODS

Systematic review of published literature, grey or unpublished literature, discussions with various groups in the region, and a critical analysis of the evidence of the effectiveness of interventions aimed at preventing, detecting, treating, and supporting life after treatment for people with Valley Fever. This includes consideration of vaccines, workplace prevention, recommendations to the general public, evidence on detection of the condition by primary care providers, treatment effectiveness and likelihood of improved treatment in the future, and support and quality of life for people after contracting Valley Fever.

RESULTS

While there are a number of guidelines for preventing Valley Fever, there is limited evidence regarding the effectiveness of these efforts. Furthermore, feedback from employers and workers in the region suggest that the prevention guidelines are impractical and seldom enforced. There is little evidence that a vaccine, if ever developed, would be cost effective. Enhanced efforts to promote testing and detection of Valley Fever offer the most promising avenues. Additional efforts are also needed to support survivors of Valley Fever.

CONCLUSIONS

Public Health should place renewed emphasis on public health campaigns aimed at both at risk communities and primary healthcare providers to promote testing and early detection of Valley Fever in the region.

Classification and Analysis of Laboratory Results for Reported Coccidioidomycosis Cases, Arizona, 2014

Khan, Mohammed;[1,2] Bhattarai, Bikash;[1] Erhart, Laura;[1] Tsang, Clarisse;[1] Brady, Shane[1]

[1] Arizona Department of Health Services, Phoenix, AZ
[2] Laney Graduate School and Rollins School of Public Health, Emory University, Atlanta, GA

INTRODUCTION

The Arizona Department of Health Services (ADHS) conducts surveillance for coccidioidomycosis using reported laboratory test results. However, reference laboratories and healthcare providers report results as text which is difficult to analyze. We developed and evaluated a text-matching algorithm to classify laboratory test results for coccidioidomycosis cases reported in 2014. We then analyzed these results to determine the distribution of test types and results among confirmed cases and to assess how many cases were confirmed by a single test result.

METHODS

Coccidioidomycosis laboratory test results from the ADHS infectious disease surveillance system were analyzed using a SAS-based string-matching algorithm. Results were classified by test type (enzyme immunoassay [EIA], immunodiffusion, complement fixation, culture/histopathology, quantitative immunodiffusion, latex agglutination, PCR), interpretation (positive, negative, indeterminate), and where applicable, antibody (IgM, IgG). A 5% random sample of analyzed results was manually reviewed to determine sensitivity, specificity, and inter-rater agreement of interpretation. Descriptive and inferential statistics were calculated using SAS 9.3.

RESULTS

19,298 *Coccidioides* laboratory results for 6,108 patients were reported to ADHS in 2014. 18,620 (96.4%) could be classified by the algorithm. Manual review indicated high sensitivity (99%), specificity (96.3%), and inter-rater agreement (Kappa = 0.95). Of the classified laboratory results, frequencies of test types were as follows: 11,296 (60.7%) EIA, 3,450 (18.5%) immunodiffusion, 2,839 (15.2%) complement fixation, 719 (3.9%) culture/histopathology, 179 (0.9%) quantitative immunodiffusion, 28 (0.2%) latex agglutination, and 104 (0.6%) not coccidioidomycosis. An average of 3 labs (range: 1 – 44) were reported per patient. 70% of results were positive. 5,438 patients, encompassing 17,999 classifiable labs, met the ADHS case definition for a confirmed case. 3,013 (55.4%) cases had only one positive test result. Of these, 2,628 (87.2%) were EIA results of which 1,372 (52.2%) were IgG only and 1,256 (47.8%) were IgM only.

CONCLUSIONS

Classification and analysis of laboratory test results was feasible and proved to be accurate upon manual review. The algorithm will be used routinely to help improve data quality. It will also allow us to examine testing patterns for reported patients and may provide insight into the impact of laboratory testing on the epidemiology of coccidioidomycosis.

Identification of *Coccidioides immitis* in Archaeological Soil Samples from Madera County, California

Majewski, Teresita,[1] Parise, Katy L,[2] Rivas, Stephanie,[2] Doerry, Natasha,[2] Martinez, Suzanne,[3] Garcia, Daniel,[3] Driebe, Elizabeth M,[4] Engelthaler, David M,[4] Keim, Paul,[4] Lauer, Antje,[3] and Barker, Bridget M[4]
[1]Statistical Research, Inc., Tucson, Arizona; [2]Northern Arizona University Flagstaff, Arizona; [3]California State University Bakersfield, Bakersfield, California; [4]Tgen North, Flagstaff, Arizona

INTRODUCTION

Soil samples from archaeological sites excavated in the 1970s in the Hensley Lake area of Madera County, California, were suspected to contain arthroconidia of the fungal pathogen *Coccidioides immitis*, the causative agent of coccidioidomycosis in California. Collection rehabilitation funded by the U.S. Army Corps of Engineers, St. Louis District, made it possible to obtain samples for the current study, which aimed to investigate if these soil samples that were stored at room temperature for several decades indeed contained the pathogen and could pose a risk for archaeologists analyzing them in the future or for the collections managers who work in the facilities where these soil samples are stored.

METHODS

DNA from 176 soil samples was extracted and different culture independent polymerase chain reaction (PCR) based methods were applied to detect the *Coccidioides* spp. The methods of choice were: (1) a nested PCR approach based on the protocol developed by Baptista-Rosas et al. (2012)* with modifications using two different diagnostic primer pairs, in addition to (2) a diagnostic PCR approach followed by a real-time PCR method which targets a repeated region of the *Coccidioides* genome that identifies both endemic strains (*C. immitis* and *C. posadasii*). This approach was developed by the Translational Genomics Research Institute TGen North Facility together with The Center for Microbial Genetics and Genomics (MGGen) and is currently licensed by PathoGene (DxNA, St. George, UT) for clinical applications. The soils that tested positive for *Coccidioides* DNA were also tested for growth of fungal colonies.

RESULTS

Out of 176 soil samples, the presence of the pathogen was confirmed in 15 (8.5%). Different PCR-based methods led to different results. Fungi grew on 4 of the 15 PCR-positive soils. Definitive identification of these fungal colonies is ongoing.

CONCLUSIONS

Some of the soil samples that were stored at room temperature for several decades indeed contained the pathogen, possibly viable, and thus could pose a risk for archaeologists and collections managers that would handle or analyze these soils.

*****Baptista-Rosas, Raul C, Jovani Catalan-Dibene, Adriana L Romero-Olivares, Alejandro Hinojosa, Tereza Cavazos, and Meritxell Riquelme, 2012, Molecular detection of *Coccidioides* spp. from environmental samples in Baja California: linking Valley Fever to soil and climate conditions. *Fungal Ecology* 5(2):177–190.

Coccidioidomycosis among California Hispanic farm workers: A CDC/NIOSH-funded study at the University of California Davis and Merced campuses

Sipan, Carol[1], Emery, Kirt[2], Bang, Heejung[3], Portillo-Silva, Catherine[1], Pinkerton, Kent[3,] McCurdy, Stephen A.[3]
[1] Health Sciences Research Institute, University of California Merced, Merced, California
[2] Health Assessment and Epidemiology Program, Kern County Public Health Services Department, Bakersfield, California
[3] Western Center for Agricultural Health and Safety, University of California Davis, Davis, California

Introduction
High endemicity for *Coccidioides immitis* in California's San Joaquin Valley is of special concern because of the region's agricultural importance. Persons of Hispanic ancestry predominate among the agricultural labor force and are at increased risk for disseminated disease. Whereas agriculture has long been recognized for increased risk for coccidioidomycosis, case reporting by occupation is lacking, and studies have not addressed potential occupational risk factors such as crop and task. Moreover, there are few data characterizing knowledge and understanding of coccidioidomycosis among agricultural workers, information essential for designing educational and social marketing interventions.

Methods
The proposed work will contribute to the long-term goal of reducing the burden of coccidioidomycosis in agricultural workers by (1) conducting a survey to assess knowledge, attitudes, beliefs, and behaviors regarding coccidioidomycosis among 100 agricultural workers in Kern County, California, a highly endemic area; (2) conducting a case-control study involving persons undergoing coccidioidomycosis serology testing from Kern Medical Center (100 cases with positive serology, 100 controls with negative serology) to identify crops and agricultural work activities associated with coccidioidomycosis; and (3) exploratory sampling of respirable dusts for *Coccidioides* in areas of potential exposure. The potential use of the Spherusol© skin test with one or more of the above study groups will be discussed.

Results (to be determined)
Data collection for this 3-year study is pending IRB approval. The major immediate outcome from the proposed work is improved understanding regarding (1) knowledge, attitudes, beliefs, behaviors relevant to coccidioidomycosis and (2) high-risk circumstances (e.g., crops and activities) among agricultural workers.

Conclusions (to be determined)
Findings will be used to develop future prevention and detection efforts to lower the health burden of coccidioidomycosis in agricultural workers and their families.

Solar Panel Construction in the Mojave Desert Can Pose a Risk of Increasing Valley Fever Incidence

Lauer, Antje; Colson, Aaron
California State University Bakersfield, Bakersfield, California

INTRODUCTION

The Mojave Desert in California has seen ambitious photovoltaic system development in the past and more will be constructed in the near future because of a Renewable Portfolio Standard which requires that 25% of California's electricity come from renewable resources by 2016, and 33% by 2020. The Antelope Valley area, our study site, is located west of Edwards Airforce Base (EAFB) (Kern County) and is characterized by slightly alkaline, clay-rich and grey desert soils, which are low organic matter. Soils in this area are similar to soils where *Coccidioides immitis* has been detected in the past (around EAFB). We have investigated soils from 6 sites where solar panel development started in 2014/15, and investigated the presence of the pathogen using a culture independent PCR-based approach.

METHODS

DNA from 36 soil samples was extracted, and we applied a nested PCR method based on the protocol developed by Baptista-Rosas et al. (2012) with modifications using two different diagnostic primer pairs that target different areas of the intertranscribed spacer (ITS) region of the ribosomal gene (Greene et al. 2000; Johnson et al. 2014) instead of the diagnostic primer pair proposed in the original protocol. All positive PCR products were sequenced to detect false positives.

RESULTS

We were able to confirm the presence of the pathogen at 2 out of the 6 sites.

CONCLUSIONS

The ambitious plan to switch from fossil fuel to renewable energy in California is appreciated and needed. However, it should be considered that disturbance of soil in cocci endemic areas poses a high risk to construction workers and the general public living in the area. Clay rich soils that are disturbed pose a high risk to contribute to PM10 and PM2 dust development in the summer and fall when soils are dry. A screening for the presence of *Coccidioides* spp. should be included in environmental studies prior to allowing disturbance of soils in cocci endemic areas.

A Retrospective Natural History Study of Coccidioidomycosis in California

Tartof S[1], Yu K[2], Rieg G[2], Contreras R[1], Xie F[1], Benedict K[3], Fong K[2], Truong J[2], Higashiyama N[2], Steven Jacobsen[1], Mody R[3]

[1] Kaiser Permanente Southern California Department of Research & Evaluation, Pasadena, CA
[2] Southern California Permanente Medical Group, Multiple Cities, CA
[3] Centers for Disease Control and Prevention, Atlanta, GA

INTRODUCTION In endemic regions coccidioidomycosis (cocci) may be responsible for 15-30% of community-acquired pneumonia (CAP) cases, yet the disease is under-recognized. Significant knowledge gaps exist in regard to disease risk factors, diagnosis and treatment. This study creates the largest cocci cohort to date in order to better understand the natural history and other descriptive aspects of cocci disease.

METHODS This study includes two separate but complementary analyses. *Inquiry I* includes all patients diagnosed with and receiving treatment for CAP as outpatients at Kaiser Permanente Southern California (KPSC) facilities from January 1, 2011 through December 31, 2011. CAP patients are defined by all three of the following: 1) a CAP ICD-9-CM code during an outpatient visit (including emergency department and urgent care); 2) a chest radiography CPT code within 2 weeks before or 4 weeks following first use of CAP ICD-9-CM; and 3) an antibiotic prescription within 2 weeks before or 2 weeks following first use of CAP ICD-9-CM. Those with a diagnosis of cocci by ICD-9-CM before 2011 and those who were hospitalized in the 2 weeks before CAP diagnosis were excluded. Those without one year of continuous enrollment following the period from the CAP diagnosis (allowing for 30 day gaps) were also excluded. The percentage of CAP patients serologically tested for cocci (including enzyme immunoassay [EIA], complement fixation [CI], or immunodiffusion [ID]) and the percentage testing positive were evaluated. *Inquiry II* includes all patients diagnosed with cocci (any form) during outpatient or inpatient care at a KPSC facility during January 1, 2011 through December 31, 2011 by: 1) a positive cocci IgM or IgG serology test from any source (includes EIA, CI and ID tests), or 2) any culture positive for cocci, or 3) any pathology report identifying Coccidioides.

RESULTS After applying inclusion and exclusion criteria, a total of 35,567 CAP patients were identified. Of CAP patients, 1,977 (5.6%) were tested for cocci. Of these, 370 (19%) were positive for cocci upon initial testing. The cocci cohort (*Inquiry II*) includes a total of 8,485 positive cocci tests in 2,693 patients. Of these patients, 686 (25.5%) had an ICD-9 code for cocci before 2011. No distinct seasonality was observed among the 2007 cocci cases diagnosed in 2011 and the race and ethnicity composition of cocci patients was similar to that of CAP patients.

CONCLUSIONS We present preliminary data for this ongoing study. Moving forward, this study will further describe testing practices for cocci and correlates of positivity of cocci among CAP patients, where and with what symptoms cocci patients initially present for healthcare, how patients diagnosed with cocci are clinically managed and monitored, and the natural history of cocci pneumonia, including duration and sequence of symptoms, clinical outcomes (e.g. resolution, complications, dissemination, hospitalization, death), and their respective association with antifungal treatment.

Establishing an Antibody Detection EIA to Detect *Coccidioides* Specific Antibodies in Canines

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INTRODUCTION

The diagnosis of coccidioidomycosis in canines is largely based on clinical signs, histology, radiography and serology. The most commonly employed serological tool for the detection of coccidioidomycosis in dogs is immunodiffusion (ID) that screens for sample reactivity against the CF and TP antigens. IDCF titers are considered to correlate with the disease state. However, ID may be falsely-negative, especially in immunocompromised patients and in acute disease, is labor-intensive, requires several days to develop and several more days to determine the titer in positive specimens. The use of an antibody detection EIA system could improve sensitivity, throughput and turnaround times.

METHODS

Microplates were coated with *Coccidioides* antigen and used for testing serums from dogs with proven and probable coccidioidomycosis and controls in the MiraVista *Coccidioides* antibody EIA. Standards and controls containing anti-*Coccidioides* antibodies were used and the results were reported in EIA units.

RESULTS

IgG antibodies were detected in 87.9% (n=58) of dogs with coccidioidomycosis. The assay specificity was 95.4% using endemic healthy dogs (n=48) and non-endemic healthy dogs (n=17). The positive likelihood ratio (LR+) was 19.1 and the LR-was 0.13. Both tests were positive for 48 cases (82.7%), both tests were negative for 3 cases (5.2%), EIA positive and ID negative for 3 cases (5.2%) and EIA negative and ID positive for 4 cases (6.9%).

CONCLUSIONS

The MiraVista *Coccidioides* antibody EIA is sensitive and specific for use in dogs, comparing favorably to current serological methods. The use of this assay has the potential to aid in the diagnosis of coccidioidomycosis in dogs by providing increased throughput and reduced turnaround times compared to ID.

Natural History of *Coccidioidomycosis* Lung Nodules

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INTRODUCTION

Coccidioidomycosis is a fungal infection endemic to the southwestern United States commonly identified when patients present with lung nodules. Studies of small sample sizes and isolated case reports prior to the advent of computed tomography (CT) demonstrate that pulmonary nodules develop after an acute infection in 5% of cases. This study is the first to investigate the natural history of lung nodules due to Coccidioidomycosis.

METHODS

We identified 163 patients with lung nodules due to *Coccidioidomycosis* seen between November 2009 and June 2014. We reviewed clinical and radiographic characteristics (Table 1). To determine which features were risk factors for *Coccidioidomycosis* lung nodules we used the Pearson's χ^2 test.

RESULTS

Results of the descriptive analysis can be found in Table 1. The mean nodule size was 2.5 cm and most were solid with satellite nodules being a common finding. Slightly more than half of patients had positive serology. Most patients were symptomatic with time to symptom resolution averaging 4.5 months. Most patients were not treated. No clinical or radiographic characteristic significantly predicted *Coccidioidomycosis* lung nodules (diabetes, symptoms present, cavitary lesions, calcification, positive serology). Patients with diabetes were treated more frequently (39% vs 26% of patients without diabetes, p=0.69). Patients who received treatment had larger nodules than those untreated (2.95 cm versus 2.13 cm, p=0.02). However, there was no significant association between nodule size and diabetes, presence of symptoms, ethnicity, gender, tobacco use or positive serology. Nodule size decreased at a consistent rate over time (Table 2). Over the first 3 month interval, nodule size decreased at higher rate in Non-Hispanic Whites vs. Hispanics and in non-diabetics vs. diabetics. Over a 24 month period, nodule size in patients who received anti-fungal treatment decreased at a higher rate than in untreated patients.

CONCLUSIONS

The natural history of *Coccidioidomycosis* lung nodules is largely unknown. Our review of 163 pts identified after referral to a lung nodule program is a step towards improving our understanding. We found that most patients are symptomatic, almost half have negative serologic tests and most don't receive treatment. Incremental decrease in lung nodule size was seen over time.

Table 1. Characteristics of patients with *Coccidiodomycosis* lung nodules at University of California, San Francisco-Fresno between November 2009 and June 2014

Mean age (years)	53 ± 13.9
Gender	Male: 61% Female: 39%
Ethnicity	Non-Hispanic Whites: 55% Hispanic: 36% African-American: 6% Asian: 2% Unknown: 1%
History of Tobacco Smoking	Never Smoker: 54% Ex-Smoker: 25% Current Smoker: 21%
History of Diabetes Yes No	 21% 79%
Prior history of *Coccidioidomycosis:* Yes No	 10% 90%
Occupation	Field Worker: 21% Prison Exposure: 10% Construction Worker: 4% Other: 65%
Mean nodule size (cm)	2.46 ± 1.66
Nodule location	RUL: 37% RML: 6% RLL: 21% LUL: 12% LLL: 24%
Nodule Border	Lobulated: 24% Smooth: 61% Spiculated:13% Diffuse: 2%
Nodule Calcification Yes No	 11% 89%
Cavitary Lesions	30%
Number of Nodules 1 2 3 4 ≥ 5	 68% 15% 2% 0.6% 15%
Satellite Nodules	50%
Mediastinal Adenopathy	5%
Pleural Effusion	2%
Consolidation	18%
Symptomatic	70%
Immunodiffusion (serology test) Positive Negative	 58% 42%
Treatment with Anti-Fungal Yes No	 42% 58%
Time to resolution of symptoms (mean)	4.5 months ± 6.8
Duration of follow-up (mean)	13.5 months ± 12

Table 2. Average change in size of *Coccidioidomycosis* lung nodule over time.

0 to 3 months	3 to 6 months	9 to 12 months	12 to 24 months
-0.46 cm	-0.46 cm	-0.34 cm	-0.38 cm

Coccidioidomycosis in Washington State: an Update on an Emerging Infection

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INTRODUCTION Coccidioides has long been recognized as an endemic pathogen in the southwestern United States and parts of Central and South America. Washington State was previously considered far north of the endemic range of this fungus, but Coccidioides was recently identified in the soil of south-central Washington. Physicians diagnosed three unrelated cases of acute coccidioidomycosis, between June 2010 and May 2011, in south-central Washington residents who did not have recent travel to previously-defined endemic areas. Whole genome sequencing determined that a soil isolate collected from a suspected exposure site was genetically indistinguishable from the corresponding patient's clinical isolate. Environmental sampling has been identified Coccidioides from two sample sites in one Washington county. This provided direct evidence that the infection was acquired in Washington and that C. immitis exists in the state's environment. Retrospective review of coccidioidomycosis cases in animals identified two dogs and a horse, with no known out-of-state travel.

METHODS Current coccidioidomycosis surveillance strategies include passive reporting of human and animal cases to Washington State Department of Health. Reported cases are interviewed to determine clinical course, travel history, and any potential soil exposures. Clinical isolates are sent to the public health laboratory when available. Targeted environmental soil sampling is conducted around suspected exposure sites. A canine serosurvey was initiated in July 2014, which has collected approximately 1,000 serum samples for testing at CDC.

RESULTS As of January 2015, a total of eight confirmed human cases with suspected or confirmed local acquisition have now been identified, all from south-central Washington. These case patients include a case of disseminated meningitis, a cutaneous infection, and six primary pulmonary infections. The suspected exposure sites for these cases now span 3 counties. Continued environmental sampling efforts are ongoing in these endemic areas. Among 261 canine serum samples tested by EIA, there have been seven (2.7%) positive results. Whole-genome sequencing (WGS) revealed that the Washington C. immitis isolates represent a phylogenetic clade distinct from California.

CONCLUSIONS Geographic ranges for Coccidioides sp. and the prevalence of coccidioidomycosis are still not fully understood; continued efforts in Washington and surrounding states are necessary to increase our understanding of the distribution of this pathogen and the risk to human and animal inhabitants. A project to model environmental conditions, including soil variables, could help direct surveillance efforts to high-risk areas. Efforts to increase clinical awareness of the disease are likely to identify other cases of coccidioidomycosis. Other projects to determine estimated prevalence of infection in animals and people are currently under consideration.

Decrease in Coccidioidomycosis Cases Reported to the National Notifiable Diseases Surveillance System, 2011–2013

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INTRODUCTION CDC receives data on nationally notifiable diseases such as coccidioidomycosis from state and territorial public health agencies through the National Notifiable Diseases Surveillance System (NNDSS). Coccidioidomycosis cases reported to NNDSS increased dramatically during 1998–2011; a trend that may have been partially related to a change in the Council of State and Territorial Epidemiologists case definition in 2008. We provide an update on the national epidemiology of coccidioidomycosis by describing the trends in cases reported during 2011–2013.

METHODS We calculated crude, age-specific, and age-adjusted annual incidence rates (AIR) for Arizona, California, and other states where coccidioidomycosis is endemic and reportable (Nevada, New Mexico, and Utah) by dividing the number of confirmed cases in NDNSS by U.S. Census Bureau population estimates. Rates were age-adjusted using the 2000 U.S. standard population. We used a negative binomial regression model, which accounts for changes in population size and age and sex distribution, to assess statistical significance of incidence trends. We also examined trends in the number of cases reported from non-endemic states.

RESULTS From 2011 to 2013, age-adjusted incidence decreased from 42.6 per 100,000 to 17.1 per 100,000 in all endemic areas combined ($p=0.007$), from 247.7 to 84.1 in Arizona ($p<0.001$), from 14.9 to 8.3 in California ($p<0.001$), and from 3.2 to 2.1 ($p=0.084$) in other endemic states. The decrease was similar among all age groups. In all endemic areas combined, the percent change in age-adjusted incidence was -23% from 2011 to 2012 and -48% from 2012 to 2013. In non-endemic states, the number of reported cases was the same in 2011 and 2012 (240 cases each year) but decreased to 143 in 2013. Preliminary data suggest a smaller overall decrease in endemic areas from 2013 to 2014.

CONCLUSIONS Although we document a decrease in reported cocci cases from 2011 through 2013, the reasons for this decrease are unknown. Possible contributing factors may include environmental factors, changes in land usage, a reduction in the number of susceptible non-immune persons, or changes in testing or reporting practices. The decrease in Arizona may be partially related to changes in testing at a major commercial laboratory in late 2012; however, similar changes are not known to have occurred in California or other states, suggesting that other factors also contributed to the decrease. Future work is needed to assess whether these trends are real or artifactual. Despite this decrease, the number of reported cases remains substantial. Furthermore, NNDSS underestimates the true number of cases because it is a passive surveillance system and because coccidioidomycosis is not reportable in every state. Coccidioidomycosis is also likely under-diagnosed, even in highly endemic areas; increased clinician awareness and increased testing are needed to reduce delayed and missed diagnoses and to obtain a more accurate estimate of the burden of disease.

Adjunctive Corticosteroid Therapy in the Treatment of Coccidioidal Meningitis

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Background Coccidioidal meningitis is a morbid condition with severe consequences including stroke or the development of hydrocephalus. Adjunctive corticosteroid therapy has been examined in the treatment of other CNS infections and has shown a survival benefit in the treatment of tuberculous meningitis. We sought to determine if any benefit was observed in those given corticosteroid therapy during treatment of coccidioidomycosis associated cerebrovascular accident (CVA).
Methods As part of a multicenter retrospective study all patients with coccidioidal meningitis were identified and underwent chart review. Clinical variables including demographic data, patient symptoms and exam findings, serum coccidioidal CF antibody titers, CSF results, and the onset of a CVA attributed to their diagnosis of coccidioidomycosis were abstracted. The use of corticosteroids as adjunctive therapy was included for dose, duration, and the presence of additional CVA symptoms after starting corticosteroids.
Results One-hundred five patients with coccidioidal meningitis were identified and all were included for analysis. A CVA occurred in 18/105 (17%) patients. Fifteen patients received corticosteroids as adjunctive therapy, while three received only standard antifungal treatment. Dexamethasone was the most commonly prescribed corticosteroid and the majority of patients received 10mg followed by 4mg four times daily (9/15). All three patients without adjunctive therapy experienced a second CVA, while only 1/15 (7%) receiving adjunctive treatment experienced a second CVA. This difference was highly significant (P=0.0049). There was no difference in time to discharge, AEs, or patient mortality at 90 days.
Conclusion Adjunctive corticosteroid therapy reduced the rate of recurrent CVA in patients with coccidioidal meningitis and was well tolerated with few adverse events. Those with coccidioidomycosis associated CVA may benefit from a corticosteroid taper.

Wheezes and Desert Breezes: When Asthma and Valley Fever Collide

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INTRODUCTION

Asthma is a common condition with a population adjusted prevalence of 8%. Coccidioidomycosis is a common pulmonary infection in the southwestern US. The interaction between coccidioidomycosis and asthma is not well understood and the implications on management are potentially important in endemic areas.

METHODS

This study evaluated the effects of pulmonary coccidioidomycosis and asthma on the other's clinical course by examining predetermined endpoints of asthma and coccidioidomycosis. We identified 33 patients with diagnoses of both asthma and coccidioidomycosis (group 1), 33 age and gender matched patients with a diagnosis of asthma only (group 2), and 33 age and gender matched patients with a diagnosis of pulmonary coccidioidomycosis only (group 3). We evaluated predetermined endpoints of asthma and coccidioidomycosis including rate of disseminated cocci, duration of symptoms and of antifungal therapy, hospitalization, death, rates of asthma exacerbations, and escalation of asthma therapies.

RESULTS

Baseline characteristics were similar amongst all three groups. Compared with the pre-coccidioidomycosis findings, patients in group 1 had worsening of all asthma outcomes, except for FEV1. After the diagnosis of coccidioidomycosis: Patients were on more asthma medications (median 0.0 vs 2.0, p=0.0001), including more courses of systemic steroids [mean (SD) 0.3 (0.6) vs 0.9 (4.2), p<0.001]. Additionally, patients reached a higher "STEP" level after the diagnosis of coccidioidomycosis (median 0.0 vs. 1.0, p<0.0001). They also required more visits to healthcare practitioners per year, [mean (SD) 0.1 (0.3) vs 0.2 (0.4), p=0.0342].
When comparing coccidioidomycosis endpoints for patients in group 1 vs group 3 we found no significant difference in coccidioidal outcomes in patients with asthma, including rates of dissemination in (group 1 (3.1%) vs 0 (0%) in group 3 p=1.0000), median duration of coccidioidal symptoms(6 weeks for both groups p=0.2352), requirement for antifungal medication [21(65.6%) patients in group 1 vs 24 (72.7%) in group 3, p= 0.5977], and duration of antifungal treatment [26.5 vs 11 weeks respectively, p= 0.0889. Ten (30.3%) patients in group 1 vs. 0 in group 3 required systemic corticosteroids for manifestations of coccidioidomycosis, p=0.0009.

CONCLUSION

Active pulmonary coccidioidomycosis appears to significantly worsen asthma outcomes. However asthma did not appear to worsen coccidioidal outcomes, despite patients being more likely to receive systemic corticosteroids.

Bronchoscopy Findings of Coccidioidomycosis

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Background

Coccidioidomycosis is an endemic fungal infection found predominantly in the Southwestern United States. Majority of cases present with pulmonary symptoms. During early states of disease making diagnosis is difficult and mostly delayed. Fibro optic bronchoscopy has been successfully utilized in prompt and definitive identification of coccidioidomycosis. This study analyzes data from patients with pulmonary coccidioidomycosis who underwent bronchoscopy.

Methods

Retrospective IRB approved chart review. Kern Medical Center's data base of 1541 patients from 2003 to 2014 was used. Cases were defined as patients who underwent bronchoscopy and had either positive serology {Immunodiffusion IgM (IDIgM) or IgG (IDIgG) with Complement Fixation titers (CF) at Kern County Public Health Lab.} or had microbiological or histopathological evidence of coccidioidomycosis. Epi Info 7 was utilized for statistical analysis.

Results

98 cases met the criteria. 71 (72%) cases were male. 37 (38%) had diabetes. Most common presenting symptoms were cough 64% (n=63) followed by fever 39% (n=38). Chest x-ray showed evidence of cavitary lesions in 19% of patients (n=19). Female sex was a risk factor for positive cavitary lesions in chest x-ray; {OR: 5.2(1.8-16) P=0.002}.
Spherules were found only in 7% of sputum samples (3/40) compare to 17% from bronchoscopy samples (16/91); P=0.2. Cultures were positive in 21% of sputum samples (10/47) compare to 74% of samples from bronchoscopy (47/63) P<0.001. In 22 cases (22%) initial serology was only positive for IDIgG and in 7 (7%) cases all initial serology markers were negative. Patients with positive cultures from any source had higher chance of CF titers of 8 or above {OR: 3.3 (1.1-10), P=0.03}.
Direct visualization during bronchoscopy showed 65% presence of mild or moderate bronchitis; 22% presence of mucosal or sub mucosal nodule or lesions. Bronchoscopy samples were positive for presence of endosporulating spherules in 22 cases (22%).

Conclusion

Bronchoscopy is a valuable diagnostic tool in the diagnosis of pulmonary coccidioido

Central Valley Lung Nodule Calculator: A Prospective Analysis of a Newly Developed Calculator in a Coccidiodomycosis Endemic Area

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Introduction

Lung nodules are common, and differentiating malignant from benign disease can be challenging. Several on-line calculators are available to assist clinicians but were not developed in Coccidiodomycosis endemic areas. We have evaluated the accuracy of these calculators in our patient population and found them to have very poor predictive value for Coccidioidomycosis. While there are clinical and radiographic differences between the two diseases in our population, each individually lacks discrimination.

Methods

We identified 302 patients with lung cancer (n=192) or Coccidioidomycosis (n=110) seen between December 2009 and May 2013. We identified radiographic and clinical characteristics that differed between the two groups and calculated an odds ratio for each. Using the odds ratio, we developed a scoring system to assist the clinician in calculating the probability of lung cancer. We subsequently tested the scoring system in 61 patients who were not used in defining the scores (28 Coccidioidomycosis patients and 33 lung cancer patients). Using these patients we calculated sensitivity, specificity, PPV and NPV compared to the available on-line calculators.

Results

Using the initial 302 patients, the new calculator computed a mean score for patients with Cocci of 9.6 (95%CI: 6.1-13.2) and a mean score for patients with lung cancer of 15.8 (95%CI: 11.4-20.1) ($p=10^{-6}$). Using the 95% CI we assigned a value of <11 points as identifying patients with Cocci, 11-14 as indeterminant, and >14 as predicting lung cancer. We then applied the calculator to 61 newly diagnosed patients. The average score for patients with Coccidioidomycosis or lung cancer in this population was 8.21 (95%CI: 5.4-10.9) and 19.98 (95%CI: 15.9-24.5). Using our predetermined cut points for Coccidioidomycosis, the sensitivity for this calculator was 93%, specificity was 97%, PPV was 96% and NPV was 94%.

Conclusion

Coccidioidomycosis can present as lung nodules and be difficult to differentiate from lung cancer. Currently available decision support calculators perform poorly in discriminating nodules due to the two diseases. Using radiographic and clinical parameters we have developed a calculator that very accurately identifies those patients likely to have lung nodules due to Coccidioidomycosis. Future studies will be done to refine and test this calculator in these populations.

Table 1: Calculator showing variables studied, and points given to each variable to differentiate between Coccidioidomycosis lung nodules and lung cancer.

Variable	0 Points	1 Point	2 Points	3 Points	4 Points	Total
Age Dx	< 50	50-55	55-59	60-64	65+	
Gender	Male	Female				
Smoking Hx	Never			Past	Current	
Occup.-Ag	Agricul.	Construct.	Field Work	Mechanic	Military	
Chronic Lung Disease	None	Asthma	Bronchitis	COPD	COPD+Asthma	
Nodule Location	RML	LLL	RLL	RUL	LUL	
Nodule Border-	Diffuse	Smooth	Lobulated	Spiculated		
Family Hx	None		Asthma/COPD		Lung ca	
Nodule Size	< 2cm				>2 cm	
Total						

Report of a Patient with Both Coccidioidomycosis and Histoplasmosis

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INTRODUCTION

A 29 year old Guatemalan man presented with fever, abdominal pain and weight loss evolving over a month prior to admission. Work up revealed an abnormal CT scan of the chest with consolidation of the posterior segment of the left upper lobe and a CT scan of the abdomen which demonstrated retroperitoneal lymphadenopathy and hepatosplenomegaly. Initial laboratory testing revealed a positive HIV test (CD4=7). The Coccidioides IgG and IgM tests were both positive. Both Histoplasma
(5.29 mg/ml) and Coccidioides (2.29 mg/ml) antigenuria were detected. A lymph node biopsy was consistent with histoplasmosis and grew Histoplasma capsulatum from cultures. The bronchoalveolar lavage specimen grew Coccidioides immitis, confirmed by PCR.

METHODS

Urine specimens from 20 patients with histoplasmosis were tested in the coccidioidomycosis urinary antigen test. Twenty patients with coccidioidomycosis were tested in the histoplasma urinary antigen test. These urines were tested for cross- reactivity in the quantitative urinary antigen assays. The results are given in Table 1.

RESULTS

TABLE 1:

	Coccidioidomycosis patients		Histoplasmosis patients	
	Coccy antigen	Histo antigen	Histo antigen	Coccy antigen
Patient 1	8.1 ng	2.87 ng	>19 ng	0.12 ng
Patient 2	>8.2 ng	<0.4 ng	>19 ng	0.15 ng
Patients 3-20	0.07 - 5.15 ng	0 ng	0.48 - >19 ng	0 ng

Cross-reactions were restricted to those with very high urinary antigen concentrations (Patients 1 and 2).

CONCLUSIONS

This immunosuppressed patient illustrates that both histoplasmosis and coccidioidomycosis can occur in the same individual and can exhibit Histoplasma and Coccidioides antigenuria. The urinary antigen tests were both positive in this patient. The analysis of 20 patients with Coccidioides antigenuria and 20 patients with Histoplasma antigenuria showed that cross reaction was restricted to those with very high antigen levels. A correct diagnosis can be determined by comparison of the antigen levels in the two assays.

Disseminated Coccidioidomycosis: Two Cases of Parotid Gland Involvement

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INTRODUCTION

We have recently identified two cases of non-immunosuppressed patients who developed *Coccidioides immitis* infection within the parotid gland. Upon presentation and prior to detailed evaluation, each patient was initially suspected of having underlying malignancy. The diagnosis of coccidioidomycosis in each case was established initially with invasive diagnostic testing and later confirmed microbiologically, histologically and serologically.

CASE PRESENTATIONS

Case 1: A 28 year old male with left facial mass preceded by a community acquired pneumonia was seen in consultation. His pulmonary infection was complicated and slow to resolve with empiric antibiotics. He was later found to have left facial swelling. Initial imaging showed two lobulated enhancing masses within the left parotid gland. He underwent fine needle aspiration, and a biopsy showed acute inflammation and granulomatous inflammation with aggregates of histiocytes. The tissue culture grew *Coccidioides immitis.* Following needle diagnosis, serologic studies showed a complement fixation titer of 1:1024. He was treated with Fluconazole 600 mg orally daily with clinical improvement within one year.

Case 2: A 67 year old Hispanic male with diabetes and hypertension presented with left facial mass at his parotid area. CT imaging of his neck showed a left anterolateral parotid large irregular mass, with regions of necrosis and degeneration. Fine needle aspiration was inconclusive. PET scan showed left hyper-metabolic parotid soft tissue. Total left parotidectomy postsurgical frozen section biopsy showed necrotizing granuloma, and spherules were detected on tissue culture. His initial serology showed complement fixation titer of 1:64. He was started on Fluconazole 600 mg daily for 3 months then the dose was decreased to 400 mg daily with clinical improvement.

DISCUSSION

Coccidioidomycosis is known to disseminate following initial pulmonary infection. Commonly, this includes the skin, meninges, and bone/joint areas. However, *C. immitis* can disseminate throughout the body. Dissemination to glandular tissue is uncommon, but has been reported in the pancreas, thyroid, prostate, adrenal glands, and even the intrasellar space. Further, dissemination involving the human parotid gland has been reported twice in the literature. Diagnosis was initially achieved via invasive testing in most cases. The differential diagnosis of parotid lesions is broad including malignancy as well as infection (i.e. *Staphylococcus*, mycobacteria, Epstein-Barr virus, Coxsackie virus, cytomegalovirus, Cryptococcus, and Histoplasma). Even in endemic areas, the diagnosis of disseminated coccidioidomycosis may be missed due to unusual presentations. Whether non-invasive testing and treatment can confirm the diagnosis remains to be determined.

Pediatric Coccidioidomycosis Patients: Psychosocial factors

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INTRODUCTION

Little has been written about the psychosocial effects of coccidioidomycosis on children and families. Anecdotally, doctors report that in many cases, disseminated pediatric coccidioidomycosis patients experience fatigue and other symptoms that limit them from age-typical childhood activities and behaviors. However, research is needed to characterize the profile, effects and implications of coccidioidomycosis on children and their families.

METHODS

This mixed-methods study documents the psychological functioning, quality of life, and illness perceptions of a sample of pediatric coccioidomycosis patients and their families. Primary caregivers of pediatric patients and patients from a major hospital in the San Joaquin Valley of California were interviewed regarding their perceptions of coccidioidomycosis detection, access to care and the patient/family experience. Children with coccidioidomycosis (age 6 and up) were asked to rate their overall health and give measures of quality of life (KIDSCREEN-27), illness perceptions (a drawing task and CIPQ), and coping skills (KidCope). All qualitative and quantitative data was triangulated and salient results presented.

RESULTS

Children and their families expressed many concerns that might be addressed by researchers, caregivers, and healthcare providers. Primary caregivers first main symptoms noted ranged widely (from severe shortness of breath to mild rashes to an absence of symptoms). Their rating of their children's overall health status at that time also ranged widely (from poor to good at the time the first symptom was noticed). Most primary caregivers indicated that they had received most of the information they needed, but still had some unanswered questions. Some children did not understand why they were hospitalized and even went so far as to express resentment at their hospitalizations which kept them from their friends. About half of the children indicated that they believed that their illness "strongly affects the way others think about" them and how they think of themselves.

CONCLUSIONS

Science and medical providers may benefit from an improved understanding of well-being in children diagnosed with coccidioidomycosis who are receiving hospital services.

Preliminary Results About Physical, Chemical and Biological Characterization of Coccidioidin for its Use in Inmmunosorbent Assay

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INTRODUCTION The Pharmacopoeia of the United States of Mexico, has established that coccidioidin (Coccidioides spp. antigen) for skin test and serology, is made from the aqueous phase obtained from the culture of Coccidioides spp., however, the information about the biological, physical and chemical properties of this "crude extract" is scarce. Coccidiodin is a glycoprotein which can give positive reactions with antibodies raised against other fungi in highly sensitive techniques such as immunoassays. Therefore, for efficient diagnosis of coccidioidomycosis and to conduct epidemiological studies of sero-prevalence, it is necessary to have an antigen with high sensitivity plus good specificity. The aim of this work is to purify the coccidioidin to identify a specific antigen that can be used in the Enzyme-linked Immunosorbent Assay (ELISA).

METHODS Three lots of Coccidioidin (A, B and C), from the Instituto de Diagnóstico y Referencia Epidemiológico (INDRE) were analyzed by: a) Protein quantification by the bicinchoninic acid method; b) Electrophoretic pattern in sodium dodecyl sulfate polyacrylamide gel; c) Separation of proteins by ion exchange chromatography (high performance liquid chromatography or HPLC), d) Ouchterlony double immuno diffusion test (DID) and e) ELISA.

RESULTS

	Antigen A	Antigen B	Antigen C
DID	negative vs. anti-Coccidioides antibodies	negative vs. anti-Coccidioides antibodies	negative vs. anti-Coccidioides antibodies
ELISA	positive vs. anti-Coccidioides and anti-Histoplasma antibodies	positive vs. anti-Coccidioides and anti-Histoplasma antibodies	positive vs. anti-Coccidioides and anti-Histoplasma antibodies
Protein concentration (µg/ml)	4,526	4,392	7,627
Number and size of protein fractions (KDa)	146, 96, 85.5 y 79	146, 89, 79, 73 y 10	146, 89, 79, 70.5 y 37
Number of fractions separated by HPLC	2	5	0

CONCLUSIONS Tests carried out show that the biological results were the same in the three kinds of antigen; however, each lot has different physicochemical properties. With the different protein fractions purified, more study is needed to continue standardization for ELISA technique against homologous and heterologous antisera of Coccidioides spp.

Novel Potent and Selective Fungal CYP51 Inhibitors for Treatment of Coccidioidomycosis

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Background

Dissemination of primary pulmonary coccidioidomycosis can lead to chronic and even lethal disease (e.g., meningitis). Treatment options particularly for chronic disease are limited by safety issues and poor efficacy. Viamet's lead clinical agent VT-1161 is efficacious in models of pulmonary and CNS coccidioidomycosis. The objective of the current study was to identify molecules with even greater anti-*Coccidioides* potency than VT-1161.

Methods

Viamet's fungal CYP51 inhibitor library was screened against *Coccidioides posadasii* strain Silveira using the CLSI M38-A2 protocol. Formal MICs were determined against 5 isolates each from California (*C. immitis*) and non-California (*C. posadasii*), and selectivity versus key human CYP enzymes was measured biochemically. For in vivo studies, Swiss-Webster mice (N=10/dose group) received 70-90 spores of strain Silveira intracerebrally, and were treated orally once-daily starting 48 h post-infection for 7 d and sacrificed 2 d after treatment. Fungal burdens from brain samples were compared by ANOVA.

Results

Forty-two compounds completely inhibited growth at 1 μg/ml (vs. VT-1161's complete inhibition at 4 μg/ml). Eight compounds were tested against 10 *Coccidioides* isolates, with the MIC geometric means of 0.08 to 0.22 μg/ml (historical VT-1161 value was 1.6 μg/ml). Each of the 8 compounds weakly inhibited human CYPs 2C9, 2C19, 3A4, and 19 (IC_{50}'s from 23 to >200 μM). VT-1598 and VT-1694 were dosed orally at 4 and 20 mg/kg daily and directly compared with 20 mg/kg VT-1161 in the murine model of CNS coccidioidomycosis. The mean fungal burden for each treatment group was significantly lower than the vehicle control group ($P < 0.001$). VT-1694 was superior to VT-1161 at the same dose ($P < 0.001$). Most impressively, 4 mg/kg VT-1598 was superior to 20 mg/kg VT-1161 ($P < 0.001$). Additionally, in the 20 mg/kg VT-1598 group, 4/10 mice had negative brain cultures, with the highest burden being 18 colony-forming units (CFU)/gm (compared to mean values of 267,900 and 11,000 CFU/gm for the vehicle control and 20 mg/kg VT-1161 groups, respectively).

Conclusions

VT-1598 and VT-1694 have been identified as advanced lead compounds for the treatment of coccidioidomycosis, with a pre-clinical candidate to be progressed into pre-clinical development for the treatment of this serious fungal infection.

Early Host Innate Immune Response in a Murine Model of Pulmonary Coccidioidomycosis

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Introduction

Coccidioidomycosis, also known as Valley Fever, is a mycosis endemic to many desert areas in the United States, Mexico, Central and South America. This mycosis is caused by soil-dwelling Coccidioides species. The route of infection for human and other vertebrate host species is inhalation of aerosolized arthroconidia, which leads to the Coccidioides parasitic life cycle. An influenza-like illness is the most common symptomatic manifestation that can result from an acute pulmonary infection. The host innate immune response after the initial inhalation of arthroconidia is not well understood. To gain a better understanding of the initial stages of coccidioidomycosis, the host cytokine expression profiles of select cytokines were assessed in a murine model of early pulmonary coccidioidomycosis.

Methods

Eight-week-old inbred BALB/c female mice were each inoculated intranasally with 10_5 arthroconidia of either C. immitis strain RMSCC2006, C. immitis strain RS, or C. posadasii strain Silveira. Lungs were harvested, processed for RNA, and complementary DNA was synthesized from the mRNA between days 1-5 of infection. A real-time reverse transcription polymerase chain reaction assay was used to evaluate the expression profile of selected pro-inflammatory and anti-inflammatory cytokine genes. Bronchoalveolar lavage fluids (BALF) were also collected from the mice during these time points. A multiplex bead array assay was used to detect and quantify selected cytokines present in the BALF samples.

Results

The expression of some cytokines, including interferon gamma, changed gradually during the time course of the infection, whereas the expression of other cytokines, including tumor necrosis factor alpha, rapidly increased on specific days of infection. The data also suggest that the mice had a specific and differential response to different strains that were used in this study.

Conclusions

The innate immune response to additional Coccidioides species strains should be assessed in future. Gaining a better understanding of the host immune response to the initial stages of coccidioidomycosis could provide new, or improve existing diagnostics and therapeutics for this disease.

Defect in the TH17- IL17 pathway as a cause of severe granulomatous disease

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Find out the cause of this effect,
or rather say, the cause of this defect,
for this effect defective comes by cause.

Hamlet II 101
William Shakespeare

Background For many years investigators and clinicians familiar with Coccidioidomycosis have suspected a genetic basis for clinical severity of disease and most particularly disseminated disease. Surrogates for immunogenic defects have been suggested.
One of these, African American race has been demonstrated with statistical significance. Additional work showed African Americans with severe disease had a different distribution of HLA subgroups than African Americans with lesser disease.
Filipinos have anecdotal data suggesting increased severity / increased disseminated disease.
Recently techniques for genetic sequencing have become available to investigate potential loci of immunogenic variations.
Methods After approval by the institutional review boards of Kern Medical Center and UCLA, twenty patients with disseminated Coccidioidomycosis were selected from the Coccidioidomycosis clinic of Kern Medical Center.
Specimens of saliva and whole blood were collected, expeditiously shipped, and processed. DNA was extracted from peripheral bloom mononuclear cells and submitted for whole exome sequence analysis by the UCLA Core Microarray Laboratory on an Illumina HiSeq 2500 instrument. We filtered the resulting data for variants in genes known or suspected to be in pathways relating to responses to fungal infections that had higher allele frequencies in South East Asians than in persons of European descent.

Result A potentially significant abnormality found in one patient was an IL17R defect. This individual suffered Lepromatous Leprosy as a preadolescent, pulmonary Tuberculosis as a teenager and disseminated meningeal Coccidioidomycosis as a young adult.
This patient was found to have a mutation in an intracellular domain of the IL17 receptor involved in activation of phagocytes and endothelial cells. Natural Killer cell deficiency has been described in IL17R k.o. mice.

Conclusion Exome analysis allows the investigation of the host genome protein abnormalities that can affect host defense against systemic fungal infections.
It is our contention that the Coccidioidomycosis disease seen in this patient is the direct result of IL17R deficiency. The other granulomatous disease entities probably are mediated by this deficiency as well.

Whole Exome Sequencing Identification of Human Genetic Polymorphisms Associated with Extrapulmonary Dissemination of Coccidioidomycosis

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INTRODUCTION

Both prospective and retrospective studies have indicated that extrapulmonary dissemination of coccidioidomycosis occurs at an elevated rate among otherwise healthy African Americans and Filipinos, suggesting genetic predisposing factors may be present.

METHODS

With approval from the Office for Protection of Research subjects, peripheral blood was obtained from a group of 20 ethnically diverse adults with extrapulmonary dissemination of coccidioidomycosis. DNA was extracted from peripheral blood mononuclear cells and submitted for whole exome sequence analysis by the UCLA Core Microarray Laboratory on an Illumina HiSeq 2500 instrument. We filtered the resulting data for variants in genes known or suspected to be in pathways relating to responses to fungal infections.

RESULTS

We identified a mean of 246,708 variants from the human reference genome per sample, of which a mean of 6336 per sample passed quality controls, affected protein sequence or splicing, and had a frequency of 10% or less in an exome database of ~60,706 un-phenotyped individuals. We identified 3 African American individuals with polymorphisms in the gene (*CHIT1*) encoding human chitinase that are known to reduce enzymatic activity. One of these individuals also possessed a missense change in the coding sequence of Dectin-1, a C-type lectin–like receptor involved in the recognition of cell wall components by macrophages and other antigen presenting cells.

CONCLUSIONS

Using whole exome analysis, we have identified two genetic polymorphisms that may contribute to macrophage dysfunction, enhancing the risk of dissemination of coccidioidomycosis.

Identification of Lectin-binding Coccidioidal Glycoproteins

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INTRODUCTION

Lectins are proteins that bind carbohydrates (or glycans on glycoproteins). Since fungi possess different glycosylation enzymes than mammalian cells, many of their glycan structures are different from mammalian glycans. We previously showed that certain lectins bind to spherules and endospores in infected human lung tissue.. To advance our findings, we employed lectin-based affinity chromatography and mass spectrometry to identify the Coccidioidal glycoproteins that bind to lectins.

METHODS

Lectin-based affinity chromatography was performed using GlcNAc-binding Griffonia simplificonia lectin II (GSL II) and succinylated wheat germ agglutinin (sWGA)-agarose beads from Vector Labs. Elutions from the lectin-bead columns were subjected to SDS-PAGE followed by in-gel trypsin digestion. Glycoproteins from gel slices were then subjected to high performance liquid chromatography and electrospray ionization tandem mass spectrometry. Spectra obtained from mass spectrometer were searched and analyzed using the *Cocciodioides posadasii* (Silviera strain) database using Mascot and X! Tandem.

RESULTS

SDS-PAGE of elutions from lectin affinity columns demonstrated the presence of glycoproteins with GlcNAc moieties. Analysis of spectra from trypsin-digested lectin column elutions revealed a list of over 40 Coccidiodal glycoproteins from spherulin, a laboratory-grown fungal lysate. De-glycosylation of spherulin using PNGase abrogated binding to the two lectins. A competition ELISA between GSL II and sWGA suggests that both lectins bind the same glycan structure in spherulin, but sWGA demonstrates stronger binding.

CONCLUSIONS

This is the first report of the GSLII- and sWGA-binding glycoproteome from in vitro grown *Coccidioides* spherules. The mass spec-based identities of Coccidioidal glycoproteins are enzymes involved in metabolism and growth, perhaps not surprisingly because spherulin is prepared from laboratory-grown spherules in the absence of host attack. Since many parent proteins were identified from GSL II and sWGA lectin affinity chromatography, it appears that GlcNAc is not an uncommon glycan structure on coccidioidal proteins.

Clinicopathologic and Gross Renal Pathologic Findings in Dogs with Coccidioidomycosis

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INTRODUCTION

We have observed evidence of protein-losing nephropathy in some dogs with coccidioidomycosis, suggestive of immune-complex glomerulonephritis. The goal of this study was to improve our understanding of the prevalence of proteinuria in dogs with coccidioidomycosis and to describe the renal histopathologic lesions in these dogs.

METHODS

Diagnostic test results for dogs with coccidioidomycosis were retrieved from the electronic medical record system of the University of California-Davis Veterinary Medical Teaching Hospital from 1990 to 2013. Paraffin-embedded renal tissue procured from dogs that were necropsied was examined using light microscopy by a board-certified veterinary pathologist.

RESULTS

156 with coccidioidomycosis were identified; 87 dogs had both serum biochemistry and a urinalysis performed, 16 had urine protein:creatinine ratios (UPCRs), and 24 had renal tissue available for histopathology. Eleven (13%) of the 87 dogs were azotemic, 55 (63%) were proteinuric (23 [26%] had ≥ 3+ proteinuria or ≥25 mg/dL), and 11 dogs had a UPCR > 1.0 (range, 1.4 to 21.5, median 4.7). Thirteen (54%) of 24 dogs had renal histopathologic lesions suggestive of immune complex glomerulonephritis. Seven of these dogs had a urinalysis performed; 6 (86%) had proteinuria as described above. Two dogs (33%) with normal glomeruli had granulomatous nephritis, one of which had intralesional *Coccidioides* spherules.

CONCLUSIONS

Coccidioidomycosis should be considered as a possible contributor to glomerular disease in dogs. Whether similar lesions occur in other mammalian hosts, including humans, warrants further investigation.

Interferon-γ Responses of Dogs to in vitro Stimulation with Coccidioidal Antigens Measured by Flow Cytometry

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Introduction

Coccidioidomycosis in dogs ranges from asymptomatic to fulminating and fatal. Standard of care is to treat all clinically ill animals with antifungal medication because of a high rate of complicated disease. As a means of in vitro assessment of a live, avirulent vaccine in dogs, we explored the memory T-cell response in dogs with current or previous coccidioidomycosis or no clinical history.

Methods

Dogs with no clinical history of illness (n=3) and dogs with coccidioidomycosis (n=3) had 40-50 mls of whole blood collected into EDTA tubes. For a negative control, pooled beagle blood (PBB) was purchased outside the endemic area. White blood cells were separated on Ficoll Hypaque and incubated overnight with dilutions of complex and recombinant coccidioidal Ags, PMA controls, or left untreated. Cells were stained for CD3, CD4, and IFN-γ and %CD4 cells producing IFN-γ was calculated.

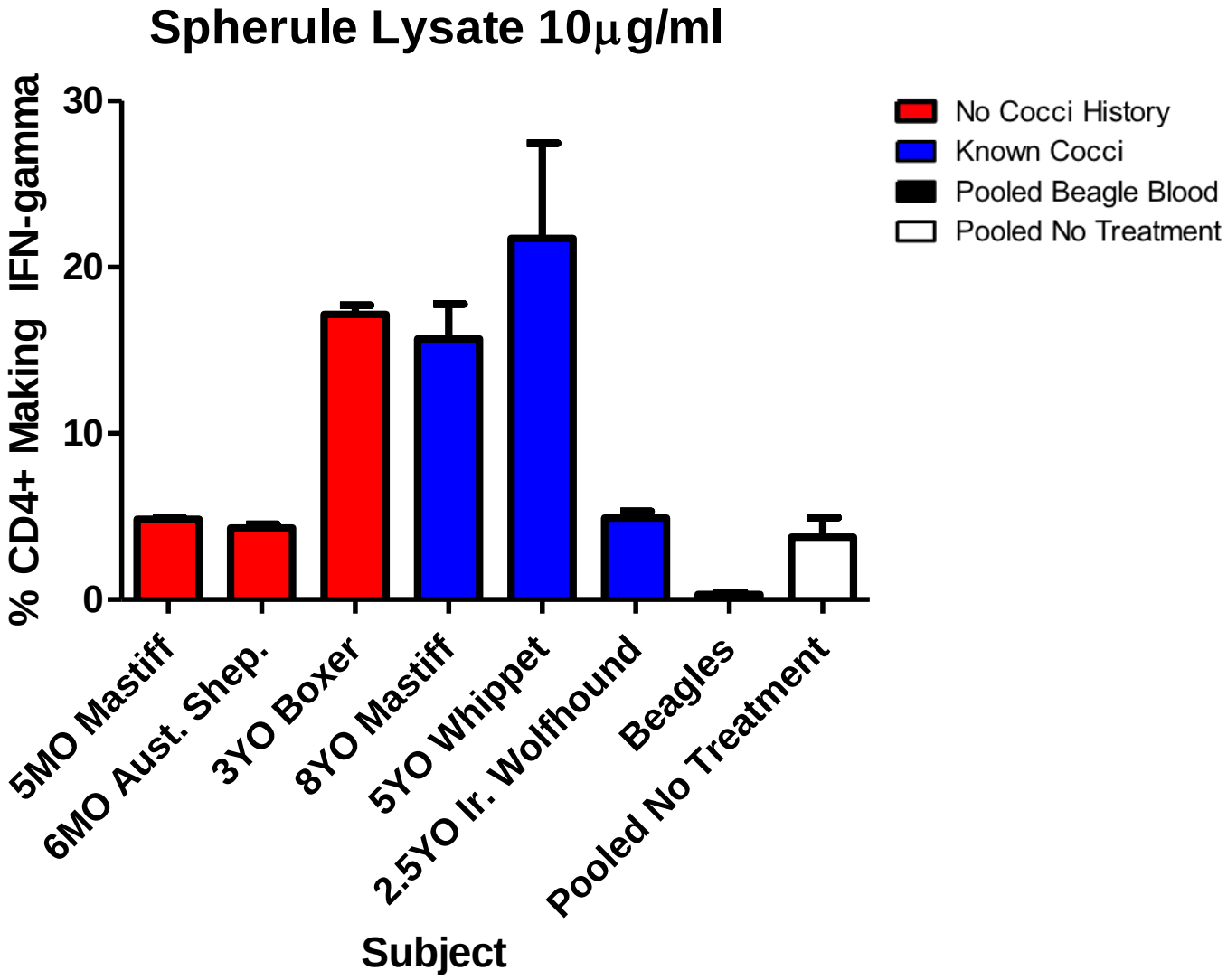
Results

Three dogs with no history of coccidioidomycosis, 2 recovered dogs, and 1 dog with active infection were tested. The PBB cells had a background fluorescence of 1-3%. Two puppies had 3-5% of CD4 cells respond, similar to the assays' negative controls. In two dogs with prior coccidioidal infection, 14-20% of total CD4 cells responded. One adult dog with no history had 20% of CD4 cells secreting IFN-γ, similar to the two recovered adult dogs, suggesting this animal had been infected, though asymptomatic. One dog with active disease showed a response indistinguishable from the negative controls, suggesting a failed immune response. This dog had progressed from respiratory to disseminated disease prior to treatment.

Conclusions

Memory T-cell responses measured by flow cytometry detected differences between known previously infected dogs and healthy puppies that have probably not been infected with Coccidioides based on age. These limited data suggest that we should be able to detect a response that would predict protection when we vaccinate dogs with a live spore vaccine. In addition, we detected a dog with no clinical history that has been infected sometime in the past and probably has durable immunity. The dog with progressive disease had essentially no T-cell response to coccidioidal antigens. With additional testing in a prospective manner, we may be able to determine if this assay has prognostic value for determining which dogs are developing durable immunity and which will need long term to lifetime treatment to maintain disease control. A systematic evaluation of dogs with good and poor clinical responses is planned for the future, in addition to testing responses of dogs post-vaccination.

Figure: CD4 interferon-γ responses of dogs to spherule lysate at 10 µg/ml. Responses to additional doses of spherule lysate and to recombinant Ag2/PRA$_{1\text{-}106}$ –CSA chimeric antigen were similar.



Risk Factors and Spatial Distribution of Canine Coccidioidomycosis in California

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INTRODUCTION
Risk factors for coccidioidomycosis in dogs are poorly understood. Since dogs may be sentinels for human coccidioidomycosis due to their closer interaction with soil, identification of high-risk regions for coccidioidomycosis in dogs may improve early recognition of emerging human disease. We sought to identify risk factors for coccidioidomycosis in dogs in California and to produce a risk map for coccidioidomycosis occurrence.

METHODS
Dogs seen at the Veterinary Medical Teaching Hospital at the University of California-Davis between 2006 and 2013 with coccidioidomycosis were identified and included in the study if their owner agreed to participate in a survey. Two controls were chosen for each case. The owner survey included questions about their dog's travel, current and previous residences, time spent outdoors, and outdoor activities. Risk factors were determined using logistic regression analysis and model outcomes were used to generate a risk map for coccidioidomycosis occurrence in California.

RESULTS
There were 41 cases and 79 controls. Risk factors were younger age, digging behavior, and travel to Arizona or the California central valley. Vizslas, Dalmatians, weimaraners, greyhounds, English pointers, bull terriers, Brittany spaniels and boxers were over-represented among the hospital population. There was a significant correlation between the reported rate of coccidioidomycosis in humans and our risk map for canine coccidioidomycosis.

CONCLUSION
Coccidioidomycosis should be highly suspected in sick young adult dogs that exhibit digging behavior and that reside in, or have a history of travel to, endemic areas. Surveillance efforts in dogs may aid in recognition of emerging geographic areas for coccidioidomycosis in humans.

Developing tools for veterinary surveillance in newly identified *Coccidioides* endemic areas

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INTRODUCTION

Knowing that coccidioidomycosis affects a wide range of wild and domesticated animals, veterinary surveillance is an important tool for expanding current knowledge of *Coccidioides* endemicity in the United States, particularly the Pacific Northwest.

METHODS

We are developing a test to investigate the prevalence of positive *Coccidioides* IgG titers in dogs from southeastern Washington. We adapted the OMEGA *Coccidioides* Antibody human enzyme immunoassay (EIA, IMMY Diagnostics, Norman, OK) for detection of IgG in a broad range of species, including dogs, by substituting secondary antibody with horseradish peroxidase conjugate of protein A/G. We compared this assay to agar gel immunodiffusion (AGID), the typical method of diagnosing coccidioidomycosis in dogs. Dog sera provided for validation purposes by MiraVista Diagnostics had also been tested in a *Coccidioides* antibody EIA developed at MiraVista Diagnostics for detection of IgG antibodies in dogs.

RESULTS

To validate a novel protein A/G EIA, we tested 22 sera from confirmed canine cases of coccidioidomycosis and 5 negative control samples: 19 of the 22 (86.5%) were positive for IgG, 2 (9%) were negative, and 1 (4.5%) was indeterminate. Of the 5 negative control samples, 4 (80%) generated negative EIA results and 1 (20%) was indeterminate. With AGID, 15 (68%) sera demonstrated IgG and 7 (32%) were negative for IgG. All 5 negative control samples generated negative AGID results. We found 6 specimens contradictory in EIA and AGID results; specifically, 5 specimens were AGID-negative and EIA positive, and 1 specimen was positive with AGID and indeterminate by EIA. Compared to the Mira Vista Diagnostic results, 15 specimens (60%) were positive in both EIAs, two (8%) were positive in the new protein A/G EIA but negative in the MiraVista EIA, two (8%) were positive in the MiraVista EIA but negative in the A/G EIA, and one (4%) was intermediate in the MiraVista EIA and negative in the protein A/G EIA.

CONCLUSIONS

We conclude that detection of anti-*Coccidioides* IgG with a new protein A/G assay is a sensitive method for determining immune status in dogs and thereby a useful tool for veterinary public health surveillance.

Coccidioidomycosis: A Possibly Underreported Cause of Death — Arizona, 2008–2013

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INTRODUCTION
Coccidioidomycosis is a respiratory disease caused by inhalation of *Coccidioides* species spores from soil. In Arizona, despite increased incidence of reported coccidioidomycosis during 1990–2012 (from 5.2 to 198.8/100,000 persons), the age-adjusted mortality rate was unchanged at ~10.6 deaths/1,000,000 persons. We compared coccidioidomycosis-attributable deaths (CADs) derived from death certificates with hospital discharge data to validate mortality surveillance.

METHODS
Arizona death certificate CADs were defined as any coccidioidomycosis-related *International Classification of Disease* (10^{th} rev.) (ICD-10) codes/text that included "coccidioidomycosis" or "valley fever" listed in causes or conditions contributing to death. Hospital discharge data CADs were defined as deceased at the hospital with a coccidioidomycosis ICD-9 diagnostic code; if no matching death certificate CAD, a death certificate and laboratory-confirmed reported coccidioidomycosis were required. We estimated total CADs for 2008–2013 among Arizona residents by capture-recapture analysis. Hospital discharge data CADs with a matching death certificate were compared with those without a death certificate match.

RESULTS
During 2008–2013, a total of 530 reported death certificate CADs (incidence: 13.6 deaths/1,000,000 persons) were reported compared with 580 hospital discharge data CADs (incidence 14.9 deaths/1,000,000 persons). Of these 580 hospital discharge data CADs, 251 (43%) were identified in death certificates. Capture-recapture estimated CADs at 1223 (incidence 31.4 deaths/1,000,000). Among the 329 hospital discharge data CADs without matching death certificate, median age was 64 (range: 4–92) years; 205 (65%) were male; 215 (65%) were white non-Hispanic; 29 (9%) were black non-Hispanic, and 21 (6%) were American Indian; 50 (15%) were Hispanic; 152 (46%) were immunocompromised; and 64 (19%) had disseminated coccidioidomycosis. There were no significant differences compared with hospital discharge data CADs with a matching death certificate.

CONCLUSIONS
CADs are underreported two-fold on Arizona death certificates, demonstrating a need for education of death certifiers to document coccidioidomycosis mortality.

Using Hospital Discharge Data as a Source for Identifying Cocci-Associated Deaths in Maricopa County in 2012

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BACKGROUND: Accurate mortality data for coccidioidomycosis (cocci) is critical to determining disease burden in a population. Jones and colleagues have identified that coccidioidomycosis associated deaths are underreported two-fold using Arizona death certificates when compared with using hospital discharge data (HDD) and death certificate data combined. The aim of this study was to determine if deaths identified solely through hospital discharge data meet the definition for coccidioidomycosis associated deaths.

METHODS: Coccidioidomycosis deaths were identified in both Maricopa County mortality data and hospital discharge data for the year 2012. Coccidioidomycosis-associated deaths were identified in mortality data as any coccidioidomycosis-related ICD-10 codes or text including "coccidioidomycosis," or "valley fever," listed in the causes or other significant conditions contributing to death. Coccidioidomycosis-associated deaths were identified in hospital discharge data as any coccidioidomycosis-related ICD-9 code in any of the 25 diagnosis fields. Of the deaths solely identified in the HDD, only those with medical records readily available through the health department's electronic medical record system were evaluated and the cause of death at discharge was determined by two independent reviewers. In addition, the statewide electronic infectious disease surveillance system was reviewed to determine if a positive laboratory test was reported to public health for same individuals.

RESULTS: Of the 78 total coccidioidomycosis deaths identified in the HDD, 36 (46.2%) were identified in both sources and 42 (53.8%) were identified solely in HDD and did not have a corresponding death record. Of the 42 deaths identified only in HDD, medical records were readily available for 22 (52.3%). Of those reviewed, 16 (72%) were determined to be a cocci-caused or cocci-contributing death and 6 were determined to not be cocci-associated. Of the 16 coccidioidomycosis-associated deaths, 10 (62.5%) had a clear diagnosis in the discharge summary, and 6 (37.5%) had clear physician notes or laboratory confirmations that indicated complications due to coccidioidomycosis. Of the total 22 reviewed deaths identified in HDD, 22 (100%) had a diagnostic test confirming coccidioidomycosis in the state electronic disease surveillance system.

CONCLUSIONS: Identification of coccidioidomycosis associated deaths from hospital discharge data in addition to death certificate data is a valid strategy to identify missed deaths associated with this disease. This strategy should be incorporated into Arizona's annual coccidioidomycosis surveillance system and should be considered for other coccidioidomycosis endemic areas.

Race and Risk of Coccidioidomycosis-associated Mortality

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INTRODUCTION
Persons of African or Filipino ancestry appear to be at increased risk of severe coccidioidal infection relative to those of European descent, but whether risk of Native Americans also differs is unknown. Huang et al. found that in the United States between 1990 and 2008 coccidioidomycosis-related deaths were increased in persons of color, including Native Americans. Here we restrict this analysis to Arizona and California to exclude US populations that have little endemic exposure.

METHODS
We analyzed de-identified, publicly available mortality data from the National Center for Health Statistics for 1990 to 2008, as did Huang et al. We also identified all deaths in which the underlying cause was attributable to coccidioidomycosis in Native Americans from the Gila River Indian Community between 1965 and 2007. Results are directly age-sex-adjusted to the US, Arizona, or California 2000 census populations.

RESULTS
Using equivalent methods, we confirmed the analysis reported by Huang et al. for the United States. However, when analysis was limited to Arizona or California, mortality rates and ratios differed from what was reported by Huang et al. (Table 1). Non-Whites in Arizona and California have higher rates than Whites, but the ratios relative to Whites are dramatically diminished for Hispanics and Native Americans and increased for Blacks.
There were 17 coccidioidomycosis-related deaths in the Gila River Indian Community between 1965-2007 (Table 2). Deaths in this group are associated with a high prevalence of immunosuppressive co-morbidities, especially type 2 diabetes. The age-sex-adjusted death rate from coccidioidomycosis was 5.6 times (95% CI 1.2-25.9) as high in the Native Americans with diabetes than in those without.

CONCLUSIONS
When analysis is restricted to states most endemic for coccidioidomycosis, mortality rates of Hispanics, Asians and Native Americans relative to Whites are attenuated. Non-White race is associated with increased mortality, and this study finds that African ancestry is associated with the highest risk of *Coccidioides*-attributable death. Confining analysis to Arizona and California gives a more precise measure of coccidioidomycosis mortality because it only considers those at risk of infection. This is especially true for Arizona, where the majority of inhabitants live within the highly endemic areas. Our findings highlight the importance of computing mortality rates for endemic diseases within the endemic regions. The relationship between type 2 diabetes and deaths from coccidioidomycosis in the Native American population deserves further investigation. The prevalence of co-morbidities within certain ethnic groups may help explain the observed increase in *Coccidioides*-attributable deaths.

Coccidioidomycosis Skin Test Screening Results Among California State Inmates

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INTRODUCTION

To reduce morbidity and mortality from coccidioidomycosis (cocci) among inmates in two prisons with very high rates of cocci (5,247/100,000), we offered the Sperusol® skin test to California state prison inmates. Inmates with negative test results are medically restricted from residing in the two prisons.

METHODS

In November and December we conducted education campaigns regarding the new cocci skin test. To facilitate offering of the voluntary test statewide, custody halted movement between prisons. Healthcare staff entered information on testing and adverse reactions in real time into a web-based application.

FINDINGS

Of 98,348 (83.2%) eligible inmates, 96,987 (98.6%) were offered the skin test. Of those offered, 37,089 (38.2%) accepted. Acceptance was substantially lower among African American (24.6%; $p<0.0001$) and Filipino (34.6%; $p=0.001$) inmates compared with white inmates (45.8%). Among those who accepted, 36,805 (99.2%) had the test administered and read. Of those tested, six (0.016%) had an immediate adverse reaction. At the time of reading 1,715 (4.7%) had any adverse reaction; itching (3.2%) or rash at the site of administration (1.2%) were the most common adverse reactions. Of those tested, 8.6% had positive tests (n=3,169). The positive rate increased with age from 4.9% among those 30 years old or under to 11.1% among those over 45 ($p<0.0001$). Inmates in the two prisons with the highest rates of cocci disease had a higher rate of positive tests than those who resided in non-endemic prisons (16.2% vs. 7.6%, $p=0.01$).

CONCLUSIONS

The acceptance rate was in the expected range for a new test with a complex educational message. The lower acceptance among African American and Filipino inmates may be due to the fact that, without testing, these groups are medically restricted from the highly-endemic prisons. The adverse reaction rate was substantially lower than reported in the Sperusol® product insert. The positive test rate is close to the rate predicted by the Centers for Disease Control and Prevention for this population.

Phylogeography and Dispersal of *Coccidioides posadasii*

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INTRODUCTION
While *Coccidioides immitis* and *C. posadasii* primarily cause disease in the desert Southwest of the United States, scattered endemic foci exist throughout the Western Hemisphere. The implementation of whole genome analysis has greatly improved our ability to conduct molecular epidemiology and phylogeographic analysis at both the regional and local levels.

METHODS
We performed whole genome sequence analyses of 64 new and 18 previously published genomes to ascertain the population structure of *Coccidioides*, particularly within local subpopulations of *C. posadasii*. Multiple published genomes were of insufficient quality for inclusion in the final analyses.

RESULTS
Excellent coverage was obtained (avg. 67X) for the newly sequenced 48 *C. posadasii* and 18 *C. immitis* genomes. The population analysis results provide phylogenetic evidence of distinct geographically defined populations in the Phoenix and Tucson regions as well as dispersed populations in Texas, Mexico and South America along with an independently arrived population in Central America.

CONCLUSIONS
Phylogenetic analyses indicate that *C. posadasii* is the more ancient of the two species, and Southern Arizona contains the most diverse subpopulations. The results provide for a better understanding of likely dispersal routes, and a model for distribution of *C. posadasii* out of the Southern Arizona-Northern Mexico region is proposed.

Detecting *Coccidioides posadasii* in Soil in Southern Arizona

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INTRODUCTION

In Arizona, coccidioidomycosis is caused by *Coccidioides posadasii*, a soil fungus endemic to areas of the desert southwest. Previous studies showed that the distribution of *Coccidioides* in soils is sporadic and cannot be explained by soil characteristics alone, suggesting a key and previously unexplored role of other microbes, plant species, or possibly desert mammals. Previous established locations of *C. posadasii* in the soil in Arizona were resampled, and we identified new sites that contain *C. posadasii* in desert areas between Tucson and Florence, AZ. We predicted that certain organisms are positively or negatively correlated with the presence of *Coccidioides*. Previous work has indicated that *Coccidioides* is a poor competitor with other microbial organisms, yet in laboratory conditions grows on a number of different media. Based on this observation, it is possible that *Coccidioides* thrives only in a specific milieu of organisms, and/or in low microbial-burden soil.

METHODS

Soil sampling occurred in October 2013, April 2014, June 2014, and October/November 2014. Soil DNA was extracted using commercial kit-based extraction methods. Soil DNA extractions were screened using a molecular detection method originally designed for use in clinical diagnostics. This test is a real-time polymerase chain reaction, performed in triplicate technical replicates on duplicate DNA extractions. We then applied the barcoded PCR technique to amplify the bacterial 16S and fungal ITS sequences from the complex communities on a per-sample basis. We pooled all barcoded samples and sequenced on the Illumina MiSeq instrument. We analyzed these sequences with QIIME, which provides the mechanisms for quality filtering and demultiplexing samples, OTU clustering, taxonomic assignment and phylogenetic reconstruction, and statistical and visual analysis of the results. In parallel analyses for the bacterial and fungal communities we tested community compositional differences associated with the presence and absence of *C. posadasii*.

RESULTS

The real time PCR method showed greater sensitivity and specificity over standard PCR using previously published primers from Greene *et al*. The successful detection of *C. posadasii* DNA was used as a screening method for sequencing analysis. Preliminary results show that our real time PCR assay is sensitive and specific, amplifying *Coccidioides* DNA from soil samples, while not amplifying closely related fungi (less that 90% ITS identity). Community DNA sequence analysis indicated a greater number of Onygenales fungi in soil samples positive for *Coccidioides.*

DISCUSSION

The ability to test a large number of soils for the presence of *Coccidioides* is a much-needed tool in the understanding of the ecology and epidemiology of the organism. We have developed a test that shows promise in detecting *Coccidioides* in soil. Certain microbial species are more frequently associated with *Coccidioides* in the environment, suggesting that specific microbial interactions may define the growth areas for *Coccidioides*.

Molecular Detection of *Coccidioides spp.* in Baja California

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INTRODUCTION

The detection of *Coccidioides* spp. in environmental samples of areas endemic for Coccidioidomycosis has had low effectiveness. Via culture-independent molecular methods, we set out to detect this pathogen in an area of Valle de las Palmas (VDP), Baja California, Mexico, previously predicted as a putative endemic "hotspot".

METHODS

Two different microhabitats, burrows (influenced by rodent activity) and topsoil (10-15 cm below surface), were sampled in winter and summer. Total genomic DNA was extracted from the soil samples and used as template in two different approaches: first, a nested PCR designed to amplify the complete internal transcribed spacer (ITS) region of Dikarya followed by a diagnostic PCR designed to amplify the ITS2 region of *Coccidioides* spp. were carried out; next, new primers were designed to amplify the ITS1 region of *Coccidioides* spp. and reduce non-specific amplifications. In addition, soil fungal diversity was characterized by pyrosequencing.

RESULTS

From the amplification of ITS2 region, a high number of the recovered amplicons (69%) were confirmed to belong to *Coccidioides* spp.; however, other non-specific sequences belonging to *Aphanoascus canadensis, Penicillium cyclopium and P. dipodomyicola* were also amplified. With the new primers, all the putatively positive ITS1 amplicons were identified as *Coccidioides* spp. In all cases a higher prevalence of *Coccidioides* spp. was observed for burrow (82%) than for topsoil samples (18%). Furthermore, it was found that the fungal community structure (dominated by Ascomycota and Basidiomycota) was less variable between seasons (winter and summer) in burrow than in topsoil samples.

CONCLUSIONS

- The ITS1 primers in conjunction with a nested PCR, proved to be a better strategy for the detection of *Coccidioides* spp. from soil samples and to differentiate between species. This approach revealed a higher prevalence of *Coccidioides* spp. in burrows.
- The fungal community of the different microhabitats (burrows and topsoil) is influenced by changes in soil physicochemical characteristics distinctive of different seasons (winter and summer).
- Even though *Coccidioides* spp. went undetected by pyrosequencing, this strategy provides a thorough characterization of the fungal community in VDP and represents a step forward toward the characterization of the ecological niche of this pathogen.

Coccidioidomycosis Among Workers Constructing Solar Power Farms in California

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INTRODUCTION
Coccidioidomycosis has previously been associated with soil-disruptive work. During December 2012–February 2013, the California Department of Public Health (CDPH) received reports of coccidioidomycosis cases among workers constructing two solar power farms in San Luis Obispo (SLO) County, California. CDPH, SLO County Public Health Department, and the Division of Occupational Safety and Health investigated to determine the extent of the outbreak and recommend preventive measures.

METHODS
We conducted case finding via review of state occupational and disease surveillance records, a site visit to the solar farms and review of employer records, provider reports, and letters sent to current and former solar farm employees. A case was defined as laboratory-confirmed coccidioidomycosis in an employee with illness onset any time after beginning work but ≤1 month after the last workday at either solar farm. We interviewed case-patients by using a standardized questionnaire and assessed demographic and clinical characteristics, missed work days, work activities, and protective practices.

RESULTS
During October 2011–April 2014, we identified 44 cases among 3,572 workers (attack rate, 1.2/100 workers). Only 14 resided in SLO; 20 were from other CA counties and 10 were from other states. Of 41 patients interviewed, ≥80% reported fatigue, night sweats, weakness, difficulty breathing, and fever. Two had disseminated disease. Seventeen patients visited an emergency department, 9 were hospitalized, and 83% missed work a median of 22 (range, 1–547) days. The most common occupations were electrician and heavy equipment operator. Twenty-five patients reported performing frequent soil-disruptive work; of these, only 6 reported using respiratory protection frequently. Thirty-nine reported frequent dusty conditions before illness onset.

CONCLUSIONS
This outbreak occurred among construction workers in the growing solar power industry, many of whom were recruited from non *Coccidioides*-endemic areas where medical providers may not be familiar with coccidioidomycosis. With additional construction planned in *Coccidioides*-endemic areas, more workers might be exposed and infected unless effective prevention measures for construction work are implemented. We made preliminary recommendations that dust generation and exposure should be limited, worker training and access to respiratory protection should be provided, and medical provider awareness reinforced, including in non *Coccidioides*-endemic areas.

Annual Meetings of the Coccidioidomycosis Study Group

No.	Date	Location	Held in Conjunction with
1	July 18, 1956	San Francisco, CA	-
2	December 5-6, 1957	Los Angeles, CA	-
3	December 4-5, 1958	Los Angeles, CA	-
4	December 3-4, 1959	Los Angeles, CA	-
5	December 8-9, 1960	Los Angeles, CA	-
6	November 30-December 1, 1961	Los Angeles, CA	-
7	November 29-30, 1962	Los Angeles, CA	-
8	December 5-6, 1963	Los Angeles, CA	-
9	December 10-11, 1964	Los Angeles, CA	CA Thoracic Society
10	December 7, 1965	Phoenix, AZ	2nd Cocci Centennial Conference
11	April 19, 1967	Palm Springs, CA	CA Thoracic Society
12	May 1, 1968	Fresno, CA	CA Thoracic Society
13	April 15, 1969	San Diego, CA	CA Thoracic Society
14	April 1, 1970	San Francisco, CA	CA Thoracic Society
15	April 6, 1973	Newport Beach, CA	CA Thoracic Society
16	April 5, 1974	Sacramento, CA	CA Thoracic Society
17	September 30, 1974	San Francisco, CA	Cocci Cooperative Treatment Group
18	April 2, 1975	San Diego, CA	CA Thoracic Society
19	July 31, 1975	San Diego, CA	Cocci Cooperative Treatment Group
20	January 14-15, 1976	San Diego, CA	Cocci Cooperative Treatment Group
21	April 7, 1976	Palo Alto, CA	CA Thoracic Society
22	May 18, 1977	San Francisco, CA	Am Lung Association
23	April 5, 1978	Beverly Hills, CA	CA Thoracic Society
24	May 15, 1979	Las Vegas, NV	Am Lung Association

No.	Date	Location	Held in Conjunction with
25	April 11, 1980	Sacramento, CA	CA Thoracic Society
26	March 28, 1981	San Francisco, CA	CA Thoracic Society
27	May 15, 1982	Los Angeles, CA	AM Lung Association
28	March 20, 1983	La Jolla, CA	CA Thoracic Society
29	March 14-17, 1984	San Diego, CA	4th Cocci Centennial Conference
30	March 8, 1986	Santa Barbara, CA	-
31	April 4, 1987	Los Angeles, CA	-
32	April 9, 1988	Los Angeles, CA	-
33	April 8, 1989	San Jose, CA	-
34	April 7, 1990	Berkeley, CA	-
35	April 6, 1991	Tucson, AZ	-
36	April 4, 1992	Fresno, CA	-
37	April 3, 1993	Tucson, AZ	-
38	August 24-27, 1994	Stanford, CA	5th Cocci Centennial Conference
39	April 1, 1995	Bakersfield, CA	-
40	March 30, 1996	Scottsdale, AZ	-
41	March 5, 1997	San Diego, CA	-
42	April 4, 1998	Visalia, CA	-
43	March 20, 1999	Tijuana, BC, Mexico	-
44	April 1, 2000	Berkeley, CA	-
45	March 31, 2001	Tucson, AZ	-
46	April 6, 2002	Davis, CA	-
47	April 3, 2003	Scottsdale, AZ	-
48	April 31, 2004	Rosarito Beach, Mexico	-
49	April 2, 2005	Bass Lake, CA	-
50	April 23-26, 2006	Stanford, CA	6th International Symposium on Cocci
51	March 29, 2007	Tempe, AZ	-

No.	Date	Location	Held in Conjunction with
52	April 5, 2008	San Diego, CA	-
53	April 4, 2009	Bakersfield, CA	-
54	March 27, 2010	Surprise, AZ	-
55	April 2, 2011	Davis, CA	-
56	March 24, 2012	Tucson, AZ	-
57	April 6, 2013	Pasadena, CA	-
58	April 5, 2014	Phoenix, AZ	-
59	April 11, 2015	San Diego, CA	-

Supportive Web Sites

- **The Cocci Study Group – sponsor of the annual valley fever scientific meeting memorialized in these abstract proceedings**

The Coccidioidomycosis Study Group was created in San Francisco, California on July 18, 1956. This group oversees conferences, annual meetings and research studies. Much of the documented knowledge of the pathogenesis, mycology and clinical aspects of Coccidioidomycosis originated from studies performed by this research group.

www.coccistudygroup.com

- **The Valley Fever Center for Excellence**

The Valley Fever Center for Excellence, located at the University of Arizona in Tucson, was established to address the problems caused by the fungus, Coccidioides, the cause of coccidioidomycosis (Valley Fever). Two-thirds of all coccidioides infections in the United States occur in Arizona, mostly in the urban areas surrounding Phoenix and Tucson. The Center's mission is to mobilize resources for the eradication of Valley Fever (Coccidioidomycosis) through: 1) the development of public awareness and education about Valley Fever, 2) the promotion of high quality care for patients with Valley Fever, and 3) the pursuit and encouragement of research into all aspects of Coccidioides sp. and the diseases that it causes.

www.vfce.arizona.edu

- **Valley Fever Americas Foundation**

The Valley Fever Americas Foundation (VFAF) was founded by Rotary Clubs in 1995 to promote research for the cure for Valley Fever.

www.valleyfever.com