66TH ANNUAL COCCIDIOIDOMYCOSIS STUDY GROUP MEETING

EPIDEMIOLOGY POSTER ABSTRACTS (SESSION 1: FRIDAY PM)

1. DIFFERENCES IN VALLEY FEVER RISK PERCEPTION AMONG RESIDENTS OF KERN COUNTY, CALIFORNIA, A HIGHLY ENDEMIC AREA OF *COCCIDIOIDES IMMITIS*

Antje Lauer

CSUB, Bakersfield, USA

INTRODUCTION: Valley Fever, also known as coccidioidomycosis, is a disease of the Americas with increasing incidence over the last 20 years. The disease has no cure and no vaccine is currently available that protects humans against this disease. This study investigated Valley fever risk perception among residents of Kern County, California, a highly endemic region of *Coccidioides immitis*.

METHODS: The participants of this study (n=824) were predominantly students enrolled at California State University Bakersfield and their friends and families. A questionnaire that focused on *i)* knowledge of the pathogen and the disease, *ii)* Valley fever risk perception compared to other infectious and non-infectious diseases, *iii)* perception of disease prevention, as well as *iv)* sources of information about the disease.

RESULTS: Evaluation of the questionnaires showed that participants of differed gender, age, ethnicity, level of education, and religious belief varied regarding knowledge and risk perception of Valley fever, perception of disease prevention, and preferred sources of information about the disease.

CONCLUSION: By addressing the observed differences in Valley fever risk perception, education on Valley fever in the highly endemic area of the pathogen in Kern County, California, could be improved when adapted to the needs of different population groups with the goal of reducing incidence of Valley fever in our study area.

2. DESCRIPTION OF THE INCREASE IN REPORTED COCCIDIOIDOMYCOSIS CASES FROM 2016-2021, MARICOPA COUNTY

Jennifer Collins

Maricopa County Department of Public Health, Phoenix, USA

INTRODUCTION: Maricopa County Department of Public Health (MCDPH) saw a steady increase in reported coccidioidomycosis cases from 2016 to 2021, with the highest increase occurring from 2019 to 2021. We conducted an analysis of coccidioidomycosis cases to identify whether specific subpopulations were accounting for more cases over time.

METHODS: We analyzed coccidioidomycosis case data from Arizona's statewide communicable disease surveillance system, MEDSIS. Annual coccidioidomycosis case rates for Maricopa County residents were calculated using population denominator estimates provided by the Arizona Department of Health Services Population Health and Vital Statistics for each year from 2016 to 2020; preliminary 2021 coccidioidomycosis data and 2020 population denominators were used to estimate 2021 case rates. Age- and gender-specific case rates were also calculated.

RESULTS: In 2016, there were 4,437 coccidioidomycosis cases reported in Maricopa County, while there were almost twice as many in 2021 (8,628). The biggest one-year increase occurred from 2018 (5,522 cases) to 2019 (7,268 cases), a 32% increase in coccidioidomycosis cases. Annual overall case rates increased from 10.7 coccidioidomycosis cases per 10,000 Maricopa County residents in 2016 to 19.4 cases per 10,000 in 2021. An increase across all age groups and genders was observed from 2016 to 2021. From 2016 to 2021, those younger than 20 years of age had the lowest increase in case rates (34%), whereas case rates in individuals 65 years of age and older increased by 95%. Cases among individuals aged 20-64 increased by 73%. Overall, no gender-specific differences in case rates were noted; however, from 2018 to 2019, females had a 1-year increase in case rates of 33%, whereas this same increase took 2 years for males (2018-2020).

Table 1. Coccidioidomycosis case counts and rates by age groups and gender

	2016		2017		2018		2019		2020		2021	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Age												
≥14Y	156	1.8	138	1.6	150	1.7	190	2.2	220	2.5	207	2.4
15-19Y	176	6.2	170	5.9	202	7.0	228	7.7	256	8.6	250	8.4
20-44Y	1,247	8.8	1,273	8.9	1,628	11.1	1,976	13.0	2,341	15.4	2,299	15.1
45-64Y	1,510	15.1	1,766	17.3	1,817	17.5	2,329	21.8	2,654	24.9	2,799	26.2
≥65Y	1,348	22.9	1,623	26.3	1,725	27.1	2,545	36.9	2,692	39.1	3,073	44.6
Total	*4,437*	*10.7*	*4,970*	*11.8*	*5,522*	*12.9*	*7,268*	*16.4*	*8,163*	*18.4*	*8,628*	*19.4*
Gender												
Female	2,222	10.6	2,364	11.1	2,916	13.4	4,022	17.9	4,078	18.2	4,242	18.8
Male	2,205	10.8	2,595	12.4	2,585	12.2	3,237	14.8	4,053	18.5	4,358	19.9
Total	*4,437*	*10.7*	*4,970*	*11.8*	*5,522*	*12.9*	*7,268*	*16.4*	*8,163*	*18.4*	*8,628*	*19.4*

Rates are per 10,000 Maricopa County residents

CONCLUSION: Coccidioidomycosis cases have increased across Maricopa County from 2016 to 2021 for all categories of age and gender; however, individuals 65 years of age and older had the highest increase in cases, even after accounting for population growth. Additional analyses to describe the increase of coccidiomycosis cases from 2016 to 2021 will include disease severity, geographical regions, and endemic exposure history.

3. COCCIDIOIDOMYCOSIS CASES AND SARS-COV-2 TESTING, 2020–2021, MARICOPA COUNTY, ARIZONA

Christopher N. Tran, Brandon J. Howard, Nicole M. Jarrett, Rebecca H. Sunenshine, Jennifer E. Collins

Maricopa County Department of Public Health, Phoenix, USA

INTRODUCTION: In 2020 and 2021, Maricopa County had 8,163 and 8,537 coccidioidomycosis cases reported to public health, respectively, an increase over the previous 5-year average of 5,509 (2021 data still preliminary). Due to the COVID-19 pandemic, there was an unprecedented number of people seeking diagnostic testing for symptoms of respiratory illness. Given similar clinical presentations between COVID-19 and coccidioidomycosis,1,2 we sought to determine whether individuals who tested positive for COVID-19 had a longer time to coccidioidomycosis diagnosis than individuals who tested negative for COVID-19.

METHODS: We used public health data from MEDSIS, a state-wide centralized surveillance system for communicable diseases, including demographic and testing data of COVID-19 cases and confirmed coccidioidomycosis cases. Cases of coccidioidomycosis are classified as “Confirmed” if there is positive coccidioidal serology (IgM or IgG reactivity by EIA or IMDF), positive culture, or positive histology. Otherwise, the record is classified as “Not a Case.” All SARS-CoV-2 laboratory results (positive and negative) are required to be reported to public health pursuant to Arizona Executive Orders 2020-37 and 2021-19 (effective as of May 21, 2020). Negative Coccidioides laboratory results are not required to be reported.

Cases of coccidioidomycosis were matched to COVID-19 cases and SARS-CoV-2 test results using unique identifiers (UID) if specimens were collected within 365 days of each other. We analyzed the timing and results of SARS-CoV-2 tests that occurred between 1 day and 90 days, 180 days, or 365 days prior to a confirmed Coccidioides spp. test. We calculated the time from an individual’s first SARS-CoV-2 test within the specified time period to their first positive Coccidioides spp. test.

RESULTS: From January 1st, 2020, to December 31st, 2021, a total of 16,700 confirmed cases of coccidioidomycosis were reported to Maricopa County Department of Public Health. After matching by UID, 9,873 persons were identified as having had at least one SARS-CoV-2 test conducted within 365 days prior to testing positive for Coccidioides spp. Of these, 8,011 (81.1%) had only tested negative for SARS-CoV-2, and 1,863 (18.9%) tested positive for SARS-CoV-2 at least once prior to testing positive for Coccidioides spp. Individuals who had at least one positive SARS-CoV-2 test had a

shorter time to coccidioidomycosis diagnosis (median 54.0 days, IQR 154 days) compared to individuals who tested negative only (median 65.0 days, IQR 179 days). The same pattern was observed when the first SARS-CoV-2 test was conducted within 180 and 90 days prior to testing positive for Coccidioides spp.

CONCLUSION: There is no evidence of increased time to coccidioidomycosis diagnosis when an individual tests positive for SARS-CoV-2 within 90, 180, and 365 days prior to coccidioidomycosis diagnosis.

Table. Confirmed coccidioidomycosis cases with preceding COVID-19 testing, Maricopa County, Arizona, January 2020–December 2021, N=9,873

			Number of days from first SARS-CoV-2 test to positive *Coccidioides* spp. test		
SARS-CoV-2 test results	Cocci cases, N	SARS-CoV-2 tests prior to cocci diagnosis, mean	Mean	Median	Interquartile range (Q1-Q3)
Within 365 days					
Negative only	8,011	2.3	111.0	**65.0**	179 (15-194)
At least one positive	1,863	3.3	97.7	**54.0**	154 (9-163)
Positive only	*672*	*1.3*	*69.9*	*21.0*	*103.5 (4-107.5)*
Both negative & positive	*1,190*	*4.4*	*188.4*	*191.5*	*188 (92-280)*
Within 180 days					
Negative only	7,509	2.0	59.2	38.0	91 (11-102)
At least one positive	1,463	2.5	49.8	28.0	80 (6-86)
Positive only	*692*	*1.3*	*38.6*	*12.0*	*61 (4-65)*
Both negative & positive	*771*	*3.6*	*97.1*	*98.0*	*96 (50-146)*
Within 90 days					
Negative only	6,806	1.7	31.5	23.0	44 (8-52)
At least one positive	1,153	2.1	25.7	14.0	39 (4-43)
Positive only	*670*	*1.3*	*21.1*	*9.0*	*26 (3-29)*
Both negative & positive	*483*	*3.2*	*50.3*	*53.0*	*46 (27-73)*

References

1.Center for Disease Control and Prevention. (2020, December). Symptoms of Valley Fever | Coccidioidomycosis | Types of Fungal Diseases | Fungal | CDC. https://www.cdc.gov/fungal/diseases/coccidioidomycosis/symptoms.html

2.Centers for Disease Control and Prevention. (2021, February 22). Coronavirus Disease 2019 (COVID-19) – Symptoms. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html

66TH ANNUAL COCCIDIOIDOMYCOSIS STUDY GROUP MEETING

BASIC SCIENCE AND ECOLOGY POSTER ABSTRACTS (SESSION 2 SATURDAY AM)

1. EXPLORING THE STATISTICAL LINKS BETWEEN COCCIDIOIDOMYCOSIS CASES AND WILDLAND FIRES

Morgan E. Gorris[1], Kimberly A. Kaufeld[1], Staci A. Hepler[2], David M. Kline[3]

[1]Los Alamos National Laboratory, Los Alamos, NM, USA. [2]Wake Forest University, Winston-Salem, NC, USA. [3]Wake Forest School of Medicine, Winston-Salem, NC, USA

INTRODUCTION: Wildland fires are a known source of dust and bioaerosol emissions and a documented cause for a localized coccidioidomycosis outbreak among wildland firefighters. We hypothesize wildland fires may also be a source for long-range transport of *Coccidioides* and that increases in coccidioidomycosis case counts may be attributable to wildland fire activity.

METHODS: We explored statistical relationships between wildfire activity and changes in coccidioidomycosis case counts in California from 2000-2019. We collected fire perimeter data from the CAL FIRE Wildfire Perimeters and Prescribes burns data set, as well as wildfire emissions from the Global Fire Emissions Database (Version 4.1). We gathered coccidioidomycosis case data from the California State Department of Health.

RESULTS: So far, we have found no statistical relationship between coccidioidomycosis cases and wildfire activity alone. This is likely due to interannual climate conditions playing a stronger role in case dynamics. We are continuing our analysis and will incorporate known climate drivers.

CONCLUSION: Determining whether wildland fires are a cause for long-range transport of *Coccidioides*, or a cause for increased coccidioidomycosis cases in the surrounding region due to some other circumstance, will benefit mitigation efforts and messaging surrounding coccidioidomycosis risk.

2. RESISTANCE OF ENVIRONMENTAL FUNGI TO AZOLE DRUGS USED TO TREAT VALLEY FEVER

Jocelyne Lopez, Antje Lauer

CSUB, Bakersfield, USA

INTRODUCTION: The extent of azole drug resistance among environmental fungi in Kern County, California, a known hot spot for Valley fever, where agriculture is highly industrialized, is currently unknown.

METHODS: In a classroom exercise, Biology undergraduate students isolated 69 pure cultures of environmental fungi from airborne spores near the California State University Bakersfield (CSUB) campus and exposed them to different concentration of various azole drugs to investigate their spectrum of resistance using a solid medium-based approach. We did not include *Coccidioides* spp. isolates because of safety reasons.

RESULTS: Most fungal isolates which belonged to seven different orders, some of them known opportunistic pathogens to humans or plants, showed resistance against concentrations of azole drugs used to treat patients that suffer from candidiasis, aspergillosis or coccidioidomycosis.

CONCLUSION: This finding has implications for public health, because it shows the imminent risk of losing treatment options for fungal diseases that infects thousands of patients in the Southwestern U.S. every year.

3. BREAKING THE MOLD: APPLYING NEXT-GENERATION SEQUENCING TO THE URBAN AERO-MYCOBIOME IN PHOENIX, AZ IN SEARCH OF COCCIDIOIDES

W. Tanner Porter, Parker Montfort, Bailey Flores, Jolene Bowers, Dave Engelthaler

Translational Genomics Research Institute, Flagstaff, USA

Introduction: Coccidioidomycosis continues to be a significant public health burden within the Phoenix, AZ metropolitan area. However, very little is known about the drivers of aerosolization of Coccidioides and other fungal organisms that comprise the aero-mycobiome. To further understand the spatial and temporal dynamics of the aero-mycobiome, we utilize next-generation sequencing to take a holistic approach in monitoring the aero-mycobiome across space and time.

Methods: Portable air sampling units were used for air sampling across 24 hours across 23 sites in the Phoenix metropolitan area. Collections were conducted as part of ongoing surveillance in collaboration with the U.S. Department of Homeland Security, AZ Department of Health Services, and the Centers for Disease Control and Prevention. DNA was extracted from air filters using Qiagen DNeasy PowerLyzer PowerSoil kits, and the fungal ITS region was amplified using previously described primers. Amplicons were sequenced on an Illumina MiSeq V2 Nano kit (500 cycles). Reads were mapped and classified using Qiime2 and the UNITE database.

Results: One hundred air filters were processed with ITS sequencing across seven sites with varying temporal scales. Ascomycota and Basidiomycota encompassed most of the reads mapping to reference sequences. Additionally, several unique site-specific and seasonal patterns were observed across space and time in these data.

Conclusion: Understanding the drivers and composition of the aero-mycobiome across space and time will allow for a better understanding of the aero-mycobiome and the potential for risks associated with inhalation, and identify potential relationships between Coccidioides and other fungal species. Further understanding of the aero-mycobiome will not only have public health implications for coccidioidomycosis, but also other endemic fungal diseases or host responses (e.g., allergies) that are spread through the air.

4. CHARACTERIZATION OF SECONDARY METABOLITES RELEASED BY COMPETING SOIL MICROORGANISMS THAT ARE SHOWN TO INHIBIT THE GROWTH OF *COCCIDIOIDES* SPP.

Matthew Morales, Daniel Kollath, Bridget Barker

The Pathogen and Microbiome Institute, Northern Arizona University, Flagstaff, AZ, USA

Introduction: *Coccidioides* spp., the causative agent of coccidioidomycosis (commonly known as Valley fever), thrives in the semi-arid and alkaline soil environment. Spores are released, inhaled, and establish in the mammalian hosts' respiratory system, causing Valley fever. While little is known about the potential for microbial competition in soil, there have been preliminary observations to suggest that several soil bacterial and fungal organisms have the capability to inhibit growth of *Coccidioides* by releasing metabolites.

Methods: Chemical metabolites will be extracted from the zone of inhibition in solid growth media, using a methanol extraction. Using High Performance Liquid Chromatography (HPLC), fractions of the metabolite will be collected. These fractions will be characterized using Matrix-Assisted Laser Desorption/Ionization Mass Spectroscopy (MALDI-MS) or Hydrogen Proton Nuclear Magnetic Resonance (^{1}H NMR).

Results: Preliminary results from HPLC indicate there are clear fractions that have registered after running secondary metabolite samples through the analytical HPLC column. To further assess, these samples will be separated into fractions and analyzed using MALDI-MS.

Conclusion: The interpretation of this analytical chemistry will depict the chemical structure of metabolites associated with the inhibition of *Coccidioides* spp. growth. These techniques in a microbiological context will introduce the possibility of describing other substances that can benefit modern antimicrobial medicine, specifically within the context of Valley fever.

8. THE CHARACTERIZATION OF NOVEL ONYGENALEAN FUNGI ISOLATED FROM PRAIRIE DOGS IN THE WESTERN UNITED STATES

Kaitlyn Parra, Bridget Barker

Pathogen and Microbiome Institute, Northern Arizona University, Flagstaff, USA

INTRODUCTION: Nine novel fungal isolates were found in a quest to identify *Coccidioides* spp. as the suspected disease affecting the endangered black footed ferret in Aubrey Valley, AZ, USA. Prairie dogs were used as an indicator of disease by analyzing the mycobiome of the prairie dog lungs harvested from the region.

METHODS: The lungs were used to culture out any fungi in the lungs and genetic analysis was used to identify the species of fungi. The genetic analysis using Sanger Sequencing determined nine novel species from the fungi grown. Whole genome and phylogenetic analysis were performed on the novel isolates. The analysis revealed five isolates grouped together, while the other four were scattered throughout the Onygenalean order. To characterize isolates, the macro and micro morphology was documented, and the growth rate was calculated on two media types. The macromorphology was

studied by observing the colony patterns of the isolates on five different growth media: 2% glucose 1% yeast extract agar (2GYE), malt extract agar (MEA), oatmeal agar (OA), potato agar (PDA), and yeast extract agar (YEA) at 30°C for 6 weeks. To describe micromorphology, differential interference contrast (DIC) microscopy was utilized, and a slide culture method was developed. Growth rate was determined through radial growth experiments on two media types (2GYE and MEA) which then was used to compare the isolates growth rate through a two-way ANOVA to determine if the clustered fungi were the same genus or species.

RESULTS: Through these experiments, the seven strains (two isolates of the nine were lost) have been characterized. The three clustered fungi were determined to be the same species which has been formally named *Emmonsiellopsis cynomysii*. While the other fungal isolates were novel, they were not formally named in this work.

CONCLUSION: With the initial use of genomic analysis and current standard culturing methods, the project combines contemporary techniques with classic mycological methods to further identify the potential threat the novel isolates may pose for mammals.

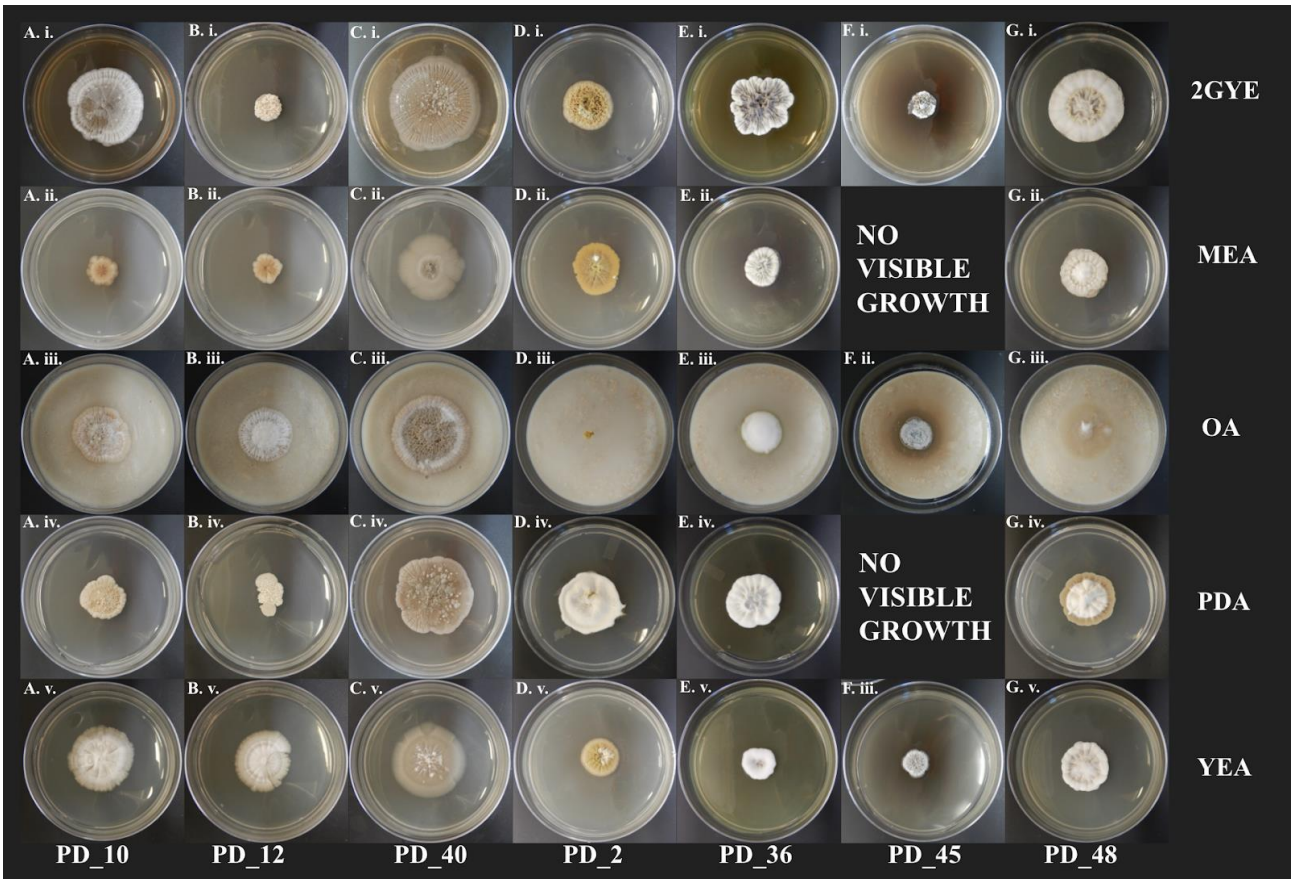

Figure 1. The novel isolates grown on 2% glucose 1% yeast extract agar (2GYE), malt extract agar (MEA), oatmeal agar (OA), potato agar (PDA), and yeast extract agar (YEA) at 30°C for 6 weeks. A.i.-A.v. represent PD_10. B.i.-B.v. represent PD_12. C.i.-C.v. represent PD_40. D.i.-D.v. represent PD_2. E.i.-E.v. represent PD_36. F.i.-F.iii. represent PD_45. G.i.-G.v. represent PD_48

9. INVESTIGATION OF KEY PROTEASES IN THE PARASITIC PHASE OF *COCCIDIOIDES*

Christina Homer, Mark Voorhies, Anita Sil

UCSF, San Francisco, USA

INTRODUCTION: *Coccidioides* infects and kills immunocompetent individuals when they inhale arthroconidia from the soil and, despite current antifungal treatment, continues to cause unacceptably high morbidity and mortality. In the soil, arthroconidia develop into a hyphal form, but, in the host, the ability of *Coccidioides* to cause disease depends on an elaborate developmental transition to form spherules, a morphology unique to *Coccidioides*. Delineating which genes are

required for spherulation will lead to identification of therapeutic targets and accelerate discovery of new antifungals for the treatment of coccidioidomycosis.

METHODS: We are studying two families of secreted proteases, subtilases and deuterolysins, that have undergone evolutionary expansion in the *Coccidioides* lineage and appear to be linked to spherule development. We have examined the deuterolysins' and subtilases' expression profiles in published datasets. To study protease activity, we have grown *Coccidioides* on media with keratin or gelatin as the only carbon source and looked for growth as an indication of protease activity. To demonstrate the biologic significance of these protease families, we have studied spherulation in the presence of AEBSF (a serine protease inhibitor) and 1,10-phenanthroline (a metalloprotease inhibitor) and used microscopy to characterize the developmental consequences of protease inhibition.

RESULTS: Published transcriptional data indicates spherule-predominant expression for the deuterolysins and for approximately half of the subtilases. Additionally, we have demonstrated that *Coccidioides* produces both gelatinase and keratinase activity. Molecular work is ongoing to determine if these protease activities can be directly attributed to the deuterolysins and subtilases, respectively. Finally, using a class-wide serine protease inhibitor targeting the subtilases, we have inhibited the transition from arthroconidia to spherules in vitro.

CONCLUSION: By linking protease activity to the transition to spherule morphology, we have demonstrated the importance of further dissecting the role of these two expanded protease families in the parasitic phase of *Coccidioides* biology. Furthermore, these results support inhibition of the subtilase protease family as a possible therapeutic strategy for coccidioidomycosis.

10. AN OPTIMIZED ORGANIC GENOMIC DNA EXTRACTION FOR *COCCIDIOIDES SPP.*

Mitchell Bryant

Pathogen and Microbiome Institute, Flagstaff, USA

INTRODUCTION: *Coccidioides spp.* are fungal pathogens present in the arid soil of the American Southwest. This group of pathogenic fungi are responsible for coccidioidomycosis, a disease commonly known as Valley fever. Although *Coccidioides* infects thousands of people each year, the organism is rather poorly characterized, and little is known about mechanisms of infection. Currently, there is no effective vaccine or treatment against coccidioidomycosis. Molecular biology is one of the primary tools used to gain an enhanced understanding of how gene function relates to pathogenesis and virulence. Many molecular techniques including DNA sequencing and Southern blotting, require input of large quantities of in-tact genomic DNA (gDNA). However, *Coccidioides spp.* cells are notoriously hard to disrupt without vigorous mechanical force which is likely to fragment gDNA. This project details a phenol chloroform DNA extraction optimized to obtain high yields of unfragmented gDNA from *Coccidioides spp.* using liquid nitrogen grinding to disrupt the cell wall without shearing the DNA. Although conventional bead beating and homogenization methods offer a high level of workflow convenience, they are incapable of extracting a large amount of unsheared gDNA. The protocol outlined in this poster will provide a detailed workflow for extraction of unfragmented gDNA from *Coccidioides spp.* which is essential for downstream molecular genetics applications such as whole genome long read sequencing and Southern blotting.

METHODS: 50mL 2xGYEliquid culture was inoculated from *Coccidioides* spp. glycerol stock and grown at 30C for 7 days. 2xGYE plates were then inoculated with liquid culture and grown at 30C. After 7 days, plates were scraped with a sterile scalpel and mycelial material was flash frozen in liquid nitrogen. Frozen mycelia were then ground in a precooled mortar and pestle. After thorough grinding, powdered mycelia are added to 1mL fungal lysis buffer in 1.5mm bead tubes and homogenized for 15 seconds at 6m/s using a BeadBug homogenizer. Standard phenol chloroform DNA extraction protocol was then performed, and each sample was eluted in 50uL H2O. DNA was quantified using both Qubit 4.0 and gel electrophoresis.

RESULTS: By optimizing the standard phenol chloroform gDNA extraction for *Coccidioides* spp, higher yields of unsheared gDNA are obtained. Prior to optimization with liquid nitrogen grinding, typical phenol chloroform DNA extraction yields were between 1ug and 3ug per sample and highly fragmented due to bead beating. Using this optimized DNA extraction protocol with liquid nitrogen grinding, yields of 10ug to 20ug of unsheared gDNA are obtainable.

CONCLUSION: Although many methods for fungal gDNA extraction are available, existing methods often result in low yields of sheared gDNA and are not optimized for *Coccidioides* spp. Using this optimized phenol:chloroform extraction with liquid nitrogen grinding makes it possible to obtain large amounts of unsheared gDNA for use in sensitive

downstream applications such as long read whole genome sequencing and Southern blotting. By using this optimized protocol, researchers can reliably obtain large yields of unfragmented *Coccidioides* spp. gDNA for downstream analysis.

11. PROGRESS TOWARDS A VALLEY FEVER BREATH TEST: IN VIVO BIOMARKERS FROM A MURINE MODEL

Emily A. Higgins Keppler[1,2], Heather L. Mead[3], Marley C. Van Dyke[4], Douglas F. Lake[1], D. Mitchell Magee[5], Bridget M. Barker[6], Heather D. Bean[1,2]

[1]School of Life Sciences, Arizona State University, Tempe, AZ, USA. [2]Center for Fundamental and Applied Microbiomics, The Biodesign Institute, Tempe, AZ, USA. [3]The Translational Genomics Research Institute (TGen), Phoenix and Flagstaff, AZ, USA. [4]Microbiology Department, UT Southwestern, Dallas, TX, USA. [5]Center for Personalized Diagnostics, Biodesign Institute, Arizona State University, Tempe, AZ, USA. [6]The Pathogen and Microbiome Institute, Northern Arizona University, Flagstaff, AZ, USA

INTRODUCTION: The current diagnostics for Valley fever are severely lacking due to poor sensitivity and invasiveness, leading to delayed diagnosis, inappropriate treatment, lost productivity, and increased medical costs. There is a critical need for novel diagnostics for detecting and identifying Valley fever lung infections. Our long-term goal is to develop a breath-based diagnostic for coccidioidomycosis lung infections. Our current objective is to identify and validate volatile biomarkers of Coccidioides immitis and C. posadasii infections via metabolomics analyses of mouse model lung infections. Herein we present data on the volatile profiles of bronchoalveolar lavage fluid (BALF) samples from murine lung infections with C. immitis RS and C. posadasii Silveira.

METHODS: The protocol for animal infection (16-009) was approved by the Institutional Animal Care and Use Committee at Northern Arizona University, in accordance with Animal Welfare Assurance A3908-01 from the US Department of Health and Human Services. Female C57BL/6 mice were infected by intranasal inoculation with C. immitis RS (n=6), C. posadasii Silveira (n=6), or vehicle control (n = 4). A dose of 100 conidia in 30 µl sterile PBS was used for infection. The mice were allowed to develop symptoms for 10 days and then euthanized. Tracheal intubation followed by PBS washing recovered approximately 2 mL of BALF for VOCs analysis by headspace solid phase microextraction (HS-SPME) and two-dimensional gas chromatography coupled with time-of-flight mass spectrometry (GC×GC-TOFMS) and for cytokine analysis by a mouse magnetic 26-Plex ProcartaPlexTM panel. Mouse spleen and brain were homogenized in 1 mL of sterile PBS followed by culture of 10-fold dilutions of each tissue on 2X GYE agar to quantify fungal dissemination. Data analysis: Hierarchical clustering analysis (HCA), principal component analysis (PCA), and Kendall correlation were performed on cytokine and volatile data.

RESULTS: We observe that the VOCs of the BALF samples are correlated to cytokine production and classify mice based on their individual levels of infection. We did not observe any separation between the C. immitis and C. posadasii infected mice by their BALF VOCs via PCA; however, separation of these classes was observed by PCA of the cytokines.

CONCLUSIONS: Our pilot data indicate that Valley fever infections produce VOCs that may yield biomarkers for a breath test. We have collected BALF and sputum from human patients with community-acquired pneumonia, and the next steps will be to determine which Valley fever biomarkers can differentiate between bacterial and fungal etiologies of disease.

12. COCCIDIOIDOMYCOSIS *EX VIVO* CYTOKINE RELEASE ASSAY USING RECOMBINANT *COCCIDIOIDES* ANTIGENS.

Eric Holbrook[1], Ian Robey[2], Althea Campuzano[4], Nhung Nguyen[4], ChiungYu Hung[4], Kenneth Knox[3], Garrett Grischo[3], Mrinalini Kala[3], Joshua Malo[2], Heidi Erickson[2], Neil Ampel[2], Chadi Hage[5] and Joseph Wheat[1].

1. MiraVista Diagnostics Indianapolis, IN
2. University of Arizona Health Sciences, Tucson, AZ
3. Department of Medicine, University of Arizona College of Medicine, Phoenix, AZ
4. University of Texas San Antonio, TX
5. Indiana University School of Medicine Indianapolis, IN

INTRODUCTION: Within endemic regions, it is common to screen individuals prior to organ transplantation or the initiation of immunosuppressive therapy for the presence of anti-*Coccidioides* antibodies. Such assessment may indicate prior exposure and signal the need for antifungal prophylaxis. While often done, this approach has limitations as current serology measures only the short-lived arm of humoral immunity. This study seeks to establish an *ex vivo* cytokine release assay using recombinant *Coccidioides* antigens to more reliably assess past infection, with a goal of improving risk stratification, prophylaxis strategies, and future need for vaccination.

METHODS: Four recombinant, coccidioidal antigens were expressed and isolated from *E. coli* or *Uncinocarpus reesii*. Contaminating endotoxin was removed using commercially purchased resin followed by ensuring that endotoxin levels were below the detection limit using the LAL method (<0.1EU). Protein concentration was determined using the BCA method and normalized by converting concentrations to molarity using molecular weight. Whole blood was collected from individuals with clinically resolved (latent) coccidioidomycosis (IRB 2105781507) and stimulated using recombinant antigens, positive control (T27K, staphylococcal enterotoxin b [SEB] and/or phytohaemagglutinin [PHA]) or media alone for 24 hours at 37°C with 5% CO2. Individuals with illness or medications known to suppress the cellular immune response were excluded. After removing cells interferon gamma (IFN-γ) was quantified by ELISA (BioLegend). A stimulation index (SI) was calculated by dividing the IFN-γ concentration of antigen stimulated samples by the the IFN-γ concentration of the media stimulated control. A SI of ≥2 was considered positive. Additionally, whole blood was collected from individuals outside the endemic region from Indianapolis, IN with known resolved histoplasmosis infection to serve as disease specific controls and blood samples from healthy subjects in Tennessee as negative controls

RESULTS: The viability of whole blood for cytokine production was verified using several positive controls including T27K and SEB. The SI values were 4,941±11,825 (range 4 to 31,718) and 26,395±44,324 (range 1,893 to 105,193) for T27K and SEB, respectively. This demonstrates that a viable cellular immune response can be induced from the whole blood samples. The four recombinant antigens were also able to stimulate the production of IFN- γ. The four antigens ranged in SI from an average of 74±40 (range 1 to 342) to 21,552±34,442 (range 255 to 82,170).

CONCLUSIONS: These results demonstrate the feasibility of using recombinant coccidioidal antigens to induce IFN-γ from individuals with resolved coccidioidomycosis. The use of recombinant antigens allows for more reproducible antigen production and standardized responses for use in the *ex vivo* cytokine release assay.

13. IDENTIFYING GENES INVOLVED IN THE TEMPERATURE DEPENDENT MORPHOLOGICAL TRANSITION IN COCCIDIOIDES POSADASII

Keith Walcott[1], Bastian Joehnk[1], Mark Voorhies[1], Claire Dubin[2], Rachel Brem[2], Anita Sil[1]

[1]University of California, San Francisco, San Francisco, USA. [2]University of California, Berkeley, Berkeley, USA

INTRODUCTION: *Coccidioides posadasii* is a thermally dimorphic fungal pathogen and the causative agent of Valley Fever. Coccidioides is endemic to Southern California, Arizona, Central and South America. Valley Fever poses a serious health and financial burden to those afflicted with the illness; Californians alone incur costs of close to $200M/year for health-related expenses. In the soil, Coccidioides grows as mycelia, or vegetative filaments, that develop into arthroconidia which can be easily aerosolized. Upon inhalation, arthroconidia swell and undergo nuclear division and segmentation to form spherules filled with endospores. During infection, the spherules rupture, and endospores spread throughout the body and develop into more spherules.

METHODS: To identify genes involved in the morphological transition between the environmental and host phase, we are profiling the population genomics and phenotypic diversity of a collection of Coccidioides posadasii clinical isolates. Sequence analysis of these isolates revealed that a subset of them form a diverse but closely related population that is suitable for a type of forward genetic screen called a Genome Wide Association Study (GWAS). Arthroconidia from 54 clinical isolates were pooled and grown in competition under conditions replicating the host or the environment, after which genomic DNA was extracted and sequenced. GWAS analysis was used to identify alleles that are differentially abundant under each condition.

RESULTS: 9 genes were identified with statistically significant differences in allele abundance under each condition. Using CRISPR/Cas9, we are disrupting each gene in the reference Silveira strain. The growth phenotype of each knockout mutant is then determined under the environmental and host conditions. Our preliminary studies have identified one

mutant strain with a growth defect under environmental conditions. The corresponding gene encodes a protein with homology to a MRC1 checkpoint mediator.

CONCLUSION: We will expand this GWAS pipeline to interrogate other conditions related to virulence so that we can better understand Coccidioides and how it causes disease in the host.

14. HUMANIZATION OF ANTI-CTS-1 MURINE MONOCLONAL ANTIBODY INTO HUMAN IgG AND IgM REAGENTS.

Francisca Grill[1], Thomas Grys[2], Collin Jugler[1], Qiang Chen[1], Douglas Lake[1]

[1]Arizona State University, Phoenix, USA. [2]Mayo Clinic Arizona, Phoenix, USA

INTRODUCTION: Because Valley Fever (VF) mimics other viral and bacterial respiratory infections, it is difficult to diagnose using clinical symptoms alone. Laboratory diagnosis may be performed by detecting antibodies against a Coccidioidal protein called CTS-1. None of the FDA cleared kits (Immy and Meridian) include dilution controls, *yet it is a federally required aspect of every test run*. To meet the requirement, clinical microbiology laboratories must re-use previously positive patient sera, so they are forced to collect, store and re-use patient sera that reacted strongly with Coccidioides spp.-coated ELISA plates in a previous test to use as IgG and IgM antibody “dilution controls” in subsequent tests. This is not ideal and is a non-standard process.

METHODS: To address the problem of re-using patient sera as "dilution controls" in the clinical laboratory, we humanized a murine anti-CTS-1 monoclonal antibody into human IgG and IgM using molecular techniques. Then the anti-CTS-1 Mab was expressed from plants as human IgG and human IgM protein and purified.

RESULTS: Humanized anti-CTS-1 IgG and IgM demonstrated binding in both FDA-approved Immy and Meridian enzyme immunoassay (EIA) kits so that they can be used as dilution controls in any laboratory that uses these FDA-approved diagnostic EIAs for VF.

CONCLUSION: These reagents might eliminate the need for laboratory personnel to collect, store, and re-use previously positive serum samples to aid in the diagnosis of coccidioidomycosis.

66TH ANNUAL COCCIDIOIDOMYCOSIS STUDY GROUP MEETING

CLINICAL AND CASE PRESENTATION ABSTRACTS (SESSION 3, SATURDAY PM)

1. TROUGH SERUM POSACONAZOLE CONCENTRATIONS IN DOGS BEING TREATED FOR REFRACTORY COCCIDIOIDOMYCOSIS

Lisa Shubitz[1,2], Sallianne Schlacks[3], Christine Butkiewicz[1], Polina Vishkautsan[2], Kate Worthing[3]

[1]Valley Fever Center for Excellence, University of Arizona, Tucson, USA. [2]Veterinary Specialty Center of Tucson, Tucson, USA. [3]College of Veterinary Medicine, University of Arizona, Tucson, USA

Introduction: Posaconazole is a newer potent azole antifungal used for treatment of refractory coccidioidomycosis in humans. Trough serum posaconazole concentrations were measured in a series of dogs with refractory coccidioidomycosis.

Methods: A retrospective review of dogs treated with posaconazole for refractory coccidioidomycosis was performed at one veterinary hospital. Refractory coccidioidomycosis was defined as having failed at least two other antifungal medications. During treatment, the dogs had at least one trough serum posaconazole concentration measured by UPLC-MS (7 dogs) or by bioassay (1 dog). Measurements were performed approximately 28 days after starting treatment, and at least 2 weeks after a dosage change. Serum was collected from dogs before the next scheduled dose was given. Serum posaconazole concentrations and serum chemistry data collected the same day were reviewed together.

Results: Eight dogs with trough serum posaconazole concentrations being treated for refractory coccidioidomycosis were identified. Posaconazole was administered as a dry oral product in capsules or tablets or as commercial suspension (Noxafil, 40 mg/ml). One dog received 10 mg/kg q24 hrs of suspension and developed a trough serum concentration of 2.08 µg/ml. The other 7 dogs received initial dosages of dry products ranging from 4.7 - 5.5 mg/kg/day either once daily (4 dogs) or divided q.12 hr (3 dogs). Trough serum concentrations of posaconazole ranged from 1.52 µg/ml to >6 µg/ml (median 3.55 µg.ml) in these dogs. Mild to moderate, and often transient, elevations in liver enzyme activities were common; 7/8 dogs were concurrently taking glucocorticoids. In one dog (trough posaconazole concentration >6 µg/ml), ALT increased. The drug dosage was reduced to 2.5 mg/kg/day, with a reduction in ALT, and trough posaconaole concentrations were 2.06 and 2.56 µg/ml tested several months apart. At 19 months, drug was discontinued due to reactive hepatitis documented by liver biopsy. Dogs were treated for 9-21 months. Six dogs experienced remission during treatment while 2 dogs were euthanized after 18 and 21 months of treatment for worsening complications of coccidioidomycosis.

Conclusions: Dogs taking posaconazole for refractory coccidioidomycosis developed serum concentrations of posaconazole well above the accepted therapeutic threshold for this disease. Liver function should be monitored in dogs taking posaconazole. Additional studies should be performed to refine dose recommendations for therapy in dogs.

Abstracted from "Posaconazole treatment of refractory coccidioidomycosis in dogs," by L. Shubitz, S. Schlacks, C. Butkiewicz, and P. Vishkautsan. This study is published in its entirety in *Journal of Veterinary Internal Medicine* (Vol 35(6), Nov/Dec 2021, pp 2772-2777; https://doi.org/10.1111/jvim.16282)

2. CAREGIVER QUALITY OF LIFE IN PATIENTS WITH COCCIDIOIDOMYCOSIS

Hazem Aboaid[1], Helen Meng[2], Ji Il Jeon[1], Rupam Sharma[1], Rasha Kuran[1,3,4], Royce H. Johnson[1,3,4], Arash Heidari[1,3,4]

[1]Valley Fever Institute, Kern Medical Center, Bakersfield, USA. [2]Touro University California College of Osteopathic Medicine, Vallejo, USA. [3]Department of Medicine, Kern Medical Center, Bakersfield, USA. [4]Division of Infectious Disease, Kern Medical Center, Bakersfield, USA

Introduction: Quality of life (QoL) measurements have become an important way to evaluate the care provided to patients and their caregivers. QoL provides pertinent information concerning the emotional and social experience of individuals which is not available for traditional assessments. Our study focuses on the burden and QoL of caregivers of patients with coccidioidomycosis. To the best of our knowledge, this is the first study of its kind.

Methods: This study was approved by the Kern Medical Institutional Review Board. Literature search was conducted on PubMed and Google scholar. This study has been designed and conducted at the Valley Fever Institute clinic in Bakersfield, California, USA. Caregivers of patients with coccidioidomycosis were included in this study. A "caregiver" was identified as an adult 18 years or older. Both the patient and their caregiver were consented to participate in this study. The health-related questionnaire QoL for caregivers of adults with traumatic brain injury (TBI-CareQOL) in two

languages English and Spanish was utilized to collect the data. Our study aim is to enroll 100 subjects to determine whether caregivers' QoL is a determinant of patients' QoL among our study population. To this date, 17 subjects have been enrolled.

Results: 64.7% (n=11) of the patients were males. 76.4% (n=13) of the caregivers were females. [RS1] 58.8% of the caregivers felt like they were the only ones who can care for their patients. 52.9% of the caregivers admitted to "having too much to do" in terms of their responsibilities as caregivers. 52.9% of the caregivers expressed frustration with their situation. 52.9% of the caregivers felt that the stress of this disease is impacting their overall health. [Table 1]

Conclusion: There is a spectrum of burdens that affect the caregivers' QoL that eventually reflect the care and wellbeing of patients. This is particularly more visible when dealing with chronic debilitating diseases such as coccidioidomycosis. Identifying these burdens will assist clinicians to better understand the care to improve the overall quality of care.

Table 1: Statistics of the study.

Patient Gender	***Number***
Male	11
Female	6
Patient Age	
18 and older	14
< 18	3
Caregiver Gender	
Male	4
Female	13
Caregiver Age Range	
18-30	3
31-50	8
+50	6
Caregiver Relationship to Patient	
Mother	5
Wife	5
Son	2
Husband	1
Father	1
Daughter	1

Sister	1
Girlfriend	1
Type of Coccidioidomycosis	
Pulmonary	14
Central Nervous System (CNS)	7
Osseous, Cutaneous, Soft tissue	9
Significant results of the study	
Caregivers being the only ones who can care for the patient	10
Caregivers having too many responsibilities as a caregiver	9
Caregivers expressing frustration with their situation	9
Caregivers with stress impacting their overall health	9

3. PEDIATRIC LARYNGEAL COCCIDIOIDOMYCOSIS: A CASE SERIES IN AN ENDEMIC REGION

Fouzia Naeem[1], James McCarty[2], Mark R Rowe[3], Kelly Kathleen Hady[3], Mary Anne Tablizo[3], Vini Vijayan[3]

[1]Valley Children's Healthcare, Madera, USA. [2]Stanford University School of Medicine, Stanford, USA. [3]Valley Childrens Healthcare, Madera, USA

Introduction: Coccidioidomycosis is an infection caused by fungi of the genus Coccidioides (C. immitis and C. posadasii) and endemic in the southwestern United States, south-central Washington, northern Mexico, and South and Central America. Acquisition of infection is mainly through inhalation. While the majority of those infected remain asymptomatic, one-third of patients develop mild, self-limited pulmonary infection. Less than 1% develop disseminated disease involving skin, bones, joints, and meninges. Published data on pediatric disseminated coccidioidomycosis is sparse and limited to case reports or case series. Primary laryngeal disease, an unusual presentation of coccidioidomycosis, is rare but has been reported both in adults and children. In this study, we review cases of pediatric laryngeal coccidioidomycosis treated at a tertiary care center located in an endemic region.

Methods: We performed a retrospective chart review of patient's ≤ 21 years of age who were treated at a tertiary care center with the diagnosis of laryngeal coccidioidomycosis from January 2010 to December 2017.

Results: Five patients with laryngeal coccidioidomycosis were identified. Median age was 1.8 years (IQR: 1-12). Four patients were previously healthy, without any comorbid conditions, and one had previously diagnosed ulcerative colitis. Common clinical features included noisy breathing, hoarse voice, sore throat, and fever. Prior to diagnosis, the median duration of illness was 24 days (IQR: 12-81), and all patients received alternate diagnoses on initial presentation. Associated pulmonary disease was found in three of the patients and three had abnormal neck imaging. All underwent laryngoscopy and bronchoscopy. Based on operative findings, coccidioidomycosis was highly suspected in all cases. Common operative findings included subglottic inflammation with narrowing. The initial coccidioidal enzyme immunoassay (EIA) was negative in one patient and the maximum coccidioidal CF titer was ≥1:16 in 4/5. However, initial coccidioidal CF titer was noted to be negative in 3/5 patients. All had positive cultures and histopathological findings consistent with coccidioidomycosis. Three of the patients required tracheostomy. The median duration of treatment was 11.7 months (IQR: 6.5-8.6), and all recovered completely.

Conclusion: While uncommon, laryngeal coccidioidomycosis is a potentially severe infection due to upper airway obstruction and the need for tracheostomy. The precise mechanism of infection, local acquisition versus hematogenous spread, remains unclear. In endemic areas, laryngeal cocci should be considered in the differential diagnosis of infants and

children presenting with subacute upper airway disease. With appropriate medical and surgical management, the prognosis remains favorable.

4. A CASE SERIES OF COINCIDENT COCCIDIOIDOMYCOSIS AND MALIGNANCY

Rupam Sharma[1,2], Jordan Slaton[2], Mehul Mistry[2], Navpreet Dhillon[2], Leila Moosavi[1], Arash Heidari[1,2,3], Royce Johnson[1,2,3], Rasha Kuran[1,2,3], Rahul Polineni[1,3], Everardo Cobos[1,4]

[1]Kern Medical, Bakersfield, USA. [2]Valley Fever Institute, Kern Medical, Bakersfield, USA. [3]David Geffen School of Medicine, UCLA, Los Angeles, USA. [4]David Geffen School of Medicine, UCLA, Bakersfield, USA

Introduction: Coccidioidomycosis (CM) is an endemic mycosis common in the Central Valley of California. In 2019, approximately 37% of CM infections in California were reported in Kern County. CM and malignancies share many common symptoms. In proved cases of coexistence, the diagnoses were usually suspected and made sequentially rather than concomitantly. This is either due to lack of response, relapse, or accidental. The purpose of this study is to study cases with concomitant CM and malignancies.

Methods: The Institutional Review Board of Kern Medical approved this study. A retrospective chart review of patients' records between 2016 and 2019 with the diagnosis of either cancer or CM was performed. 13 patients with concomitant diagnoses were identified.

Results: All 13 patients had pulmonary CM. Five cases had dissemination from which one was to lymphatic tissue. Cancer preceded the onset of CM in 8/13 patients, CM preceded the onset of cancer in 3/13 patients and one patient exhibited a simultaneous onset of CM and Cancer. 12/13 patients underwent therapeutic treatment with fluconazole. 11 patients underwent surgical resection for cancer, 1 patient had sero-reactivation of CM post fluconazole therapy. 1 patient succumbed to the disease.

Conclusions: The identified coincidence of coccidioidomycosis and malignancy is less than anticipated but still requires attention. The interaction between the two conditions is not well understood and management is formidable. A close collaboration between infectious diseases and oncology teams is paramount.

5. COCCIDIOIDOMYCOSIS AND THE FIVE RASHES

Bianca Torres[1,2], Valerie F. Civelli[1,3], Carlos D'Assumpcao[1,2], Arash Heidari[1,2], Royce H. Johnson[1,2], Rasha Kuran[1,2]

[1]Kern Medical, Bakersfield, USA. [2]Valley Fever Institute, Bakersfield, USA. [3]Clinica Sierra Vista, Bakersfield, USA

Introduction: Cutaneous eruptions are among the most common findings with primary pulmonary coccidioidal infections. Awareness of these skin manifestations will improve early diagnosis and guide appropriate clinical decision-making. The purpose of this study is to identify different types of immune-mediated cutaneous presentations associated with a primary pulmonary coccidioidal infection.

Methods: The Institutional Review Board of Kern Medical approved this study. A retrospective review of the patients' records utilizing the Valley Fever Institute Patient Database was performed. Literature search was conducted on PubMed and google scholar using the search terms: coccidioidomycosis skin manifestations, immunology of coccidioidal rashes, coccidioidomycosis immune-mediated rash.

Results: This study found five reactive or immune-mediated rash types: 1-Erythema Nodosum, 2- Erythema Multiform, 3-Morbilliform, 4-Urticarial, and 5-Erythema Sweetobullosum. All cases with one or more of above rashes reported complete recovery upon follow up visits.

Conclusion: Skin rashes associated with acute pulmonary coccidioidomycosis correspond with hypersensitivity to coccidioidal antigens and should be distinguished from cutaneous dissemination. Recognition thereof will assist clinicians in making accurate diagnosis.

6. EFFECT OF TRANSITIONING AZOLE THERAPIES ON OUTCOMES OF COCCIDIOIDOMYCOSIS

Rachael Jongsma, Jeff Jolliff, Arash Heidari, Royce Johnson, Rasha Kuran

Kern Medical, Bakersfield, USA

INTRODUCTION: Isavuconazole (isavuconazonium sulfate) is an oral azole antifungal that in recent years has been used as a treatment option for refractory coccidioidomycosis. Many patients who receive isavuconazole are eventually unable to continue isavuconazole therapy for a variety of reasons (e.g., termination of patient assistance programs, insurance coverage, etc.). This situation provides a unique opportunity to observe the effects of isavuconazole on disease burden as patients transition between azole therapy.

PURPOSE: To assess the change in disease severity when transitioning from isavuconazole to other azoles in the treatment of coccidioidomycosis due to cessation of patient assistance programs or drug exclusion policies.

METHOD: This is a retrospective observational study on patients 18 years and older who were treated with isavuconazole for coccidioidomycosis in the outpatient setting within the Kern Medical system. Institutional review board approval was obtained through Kern Medical. The patients included were transitioned from isavuconazole to an alternative azole antifungal and they were required to be on that latest therapy for at least six months. Patients were identified using the pharmacy operating system during a timeframe of October 2018 through May 2021. Clinical outcomes were measured via modified Mycosis Study Group (MSG) (Catanzaro 1983) treatment score or the MSG treatment score (Dismukes 1980) for central nervous system (CNS) infection before, during, and after isavuconazole therapy to quantify the progression or regression of coccidioidomycosis.

RESULTS: A total of 17 patients were identified who lost patient assistance eligibility for isavuconazole. Two had prior authorizations approved, while the rest were denied. Of those with denied prior authorizations, 10 were excluded due to lack of data while on isavuconazole, nonadherence or becoming lost to follow-up, not transitioning therapy immediately after isavuconazole, or have pending follow-up data. Four patients remained eligible to be included. Given the low number of patients included in this study, statistical analysis was not performed. Of the four patients included in this study, one with coccidioidomycosis meningitis was transitioned from intravenous liposomal amphotericin B to isavuconazole to for patient convenience in order to ensure adherence. The other two with pulmonary coccidioidomycosis and the one with coccidioidomycosis meningitis were transitioned to isavuconazole due to either failure or intolerance to fluconazole. All four patients experienced a decrease in their MSG score when they transitioned to isavuconazole. One patient with coccidioidomycosis meningitis saw an increase in their MSG score when they transitioned to itraconazole, while the other saw no change when they transitioned to itraconazole. The patient with pulmonary coccidioidomycosis saw an improvement in their MSG score when they transitioned to itraconazole, while the other patient with pulmonary coccidioidomycosis experience no change in MSG score when they transitioned to voriconazole.

CONCLUSION: In a cohort of four patients, one patient (25%) experienced worsening coccidioidomycosis meningitis and one patient (25%) experienced improvement on pulmonary coccidioidomycosis, while two patients (50%) experienced no change in their disease control. Given the low participant number, further study is warranted to determine long term disease control in patients with coccidioidomycosis who have been subjected to drug exclusion policies by their medical insurance company.

7. THE UNEXPECTED INCREASE OF CD57+ CD8+ T CELLS IN DISSEMINATED COCCIDIOIDOMYCOSIS

Alexis V Stephens[1], Terrie S Ahn[1], Timothy Thauland[2], Arash Heidari[3], Royce H. Johnson[3], Maria Garcia-Lloret[1], Manish J Butte[1,2]

[1]Division of Immunology, Allergy, and Rheumatology, Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, 90095, USA
[2]Department of Microbiology, Immunology, and Molecular Genetics, University of California Los Angeles, Los Angeles, CA, 90095, USA
[3]Valley Fever Institute, Kern Medical Center, Bakersfield, CA

INTRODUCTION
$CD8^+$ T-cells appear to be necessary for vaccine immunity in murine *Coccidioides* models. However, the role for $CD8^+$ T-cell responses in human *Coccidioides* infection (and in other fungal infections in general) has not been well described.

In Disseminated Coccidioidomycosis (DCM), the pathogen may never be fully cleared. Our immunology dogma tells us that chronic antigen exposure drives T cells to an "exhausted" state, with lower effector function and cytokine output. We sought to investigate if patterns of CD8+T-cell dysregulation could identify patients with DCM.

METHODS
We conducted flow cytometric analysis to assess T-cell phenotypes and cytokine production from 97 patients with uncomplicated Valley Fever (UVF), chronic pulmonary disease or DCM. These patients were consented on an IRB-approved protocol. We focused primarily on the CD8+ T-cell compartment whose role in coccidioidomycosis is less understood.

RESULTS
Patients with disseminated disease had higher PD-1(exhaustive phenotype) and higher CD-57("senescence") in CD8 T cells. Further review of CD8 T cell subsets also showed that those with disseminated disease have fewer naïve CD8 than other categories. Fever Naïve T Cells indicates a decrease potential to respond to new antigens. Patients with disseminated disease have more CD8+ T-cell effector memory RA(TEMRA). An accumulation of TEMRA could indicate the severity of initial disease. Patients with disseminated disease have higher HLA-DR expression. The Increased HLA-DR expression may indicate ongoing antigen exposure in patients with DCM.

DISCUSSION
The unexpected excess of "senescent" (CD8+CD57+) and exhausted (CD8+PD-1+) T cells in DCM further prompted an exploration of CD8 T cell subgroups.
The role and function of $CD8^+$ T-cell subsets expressing the CD57 carbohydrate antigen is incompletely understood. Some prior studies have shown CD57 expression on exhausted, terminally differentiated, and "senescent" T-cells with poor proliferative potential. In this light, $CD57^+$ T-cells may embody the refractoriness to restimulation that is well established in DCM. This is further supported by the finding of high levels of PD-1+ T-cells showing an exhausted phenotype.
Taken together, these results suggest that ongoing antigen exposure and T-cell exhaustion is a characteristic of DCM that is distinct from other CM categories. In future work, we will ascertain the proliferative and effector potential of $CD57^+$ and PD-1 cells upon restimulation with *Coccidioides* antigen, and compare the transcriptional programs run by these T-cells to canonical "exhaustion" programs. Another future direction is to look at medications that reverse the exhaustive phenotype(PD-1 Inhibitors) already used in cancer which may be applicable as a treatment for DCM.

8. ASSESSMENT OF T-HELPER CELL PHENOTYPES IN DISSEMINATED AND UNCOMPLICATED COCCIDOIDOMYCOSIS

Terrie S. Ahn[1], Timothy J. Thauland[2], Alexis V. Stephens[1], Dana Brucker[3], Arash Heidari[3], Royce H. Johnson[3], Maria I. Garcia-Lloret[1], Manish J. Butte[1,2]

[1]Division of Immunology, Allergy, and Rheumatology, Department of Pediatrics, University of California, Los Angeles, USA. [2]Department of Microbiology, Immunology, and Molecular Genetics, University of California Los Angeles, Los Angeles, USA. [3]Valley Fever Institute, Bakersfield, USA

INTRODUCTION

Type-1 immunity, featuring the key effector cytokine interferon-gamma (IFN-γ), is critical for immunity to coccidioidomycosis in humans. Humans with inborn, genetic imbalances in type-1 versus type-2 immunity show heightened susceptibility to disseminated coccidioidomycosis (DCM). Here, we sought to identify how generalizable this finding is by analyzing CD4+ T-helper cell phenotypes by chemokine receptor patterns and by cytokine production in many patients with DCM as compared to those with uncomplicated Valley Fever (UVF),

chronic pulmonary coccidioidomycosis, and healthy controls. In addition, as we have previously published, excessive Th2 activity may be therapeutically actionable through medications like dupilumab, a monoclonal antibody that blocks the IL-4 and IL-13 receptors and downregulates Type-2 responses. We sought to evaluate whether Th2/Th1 skewing by cytokine could predict those with greater response to dupilumab *in vitro*.

METHODS

Blood samples from 97 subjects with a history of coccidioidomycosis followed at the Valley Fever Institute (18 UVF, 19 Chronic Pulmonary, 60 DCM) and 29 healthy controls were collected after informed consent and according to IRB-approved protocols. T cells were analyzed by flow cytometry after staining for chemokine receptors Th1 (CCR6-CCR4-CXCR3+), Th2 (CCR6-CCR4+CXCR3-), and Th17 (CCR6+CCR4+CXCR3-) and for their production of intracellular cytokines (IFN-γ, IL-4, IL-17A, respectively) upon stimulation under neutral conditions. *In vitro* incubation of T cells with dupilumab was followed by flow cytometric analysis of IL-4+ and IFN-γ production pre- and post-treatment.

RESULTS

We identified a subset of patients with coccidioidomycosis who demonstrated elevated Th2 to Th1 ratios by their T-cell chemokine receptor patterns as compared to healthy controls. It appeared that the degree of Th2 to Th1 skewing worsens with severity of disease category (Fig. 1). We found that 25% of patients with DCM had an elevated IL-4 to IFN-γ ratio (Fig. 2). The subtype of DCM (severe pulmonary, cutaneous, skeletal or meningitis) had no influence on T-helper cell phenotype. The patients with high Th2/Th1 ratios identified by their chemokine receptor patterns differed from those identified by their cytokine production after stimulation (Fig. 3). Both higher Th2/Th1 ratio cytokine (IL-2/IFN-γ) (Fig 4.) and lower IFN-γ production (not shown) pre-dupilumab were predictive of greater IFN-γ increase post-dupilumab treatment *in vitro* when studied in our DCM patients.

DISCUSSION

These findings show that dysregulated T-helper cell responses may be compromised in coccidioidomycosis, especially in patients with DCM. It is as yet unclear whether dysregulated T cell immunity is a cause of worsened disease or an effect. Th2 to Th1 ratios by chemokine versus by cytokine were non-correlative suggesting that chemokine markers are not a good surrogate measure of cytokine production after T-cell stimulation. In prior pilot studies, we found that T27K, a coccidioidal antigen preparation, failed to consistently induce human cellular responses *in vitro*; thus, we used neutral CD3/CD28 stimulation for T-cell activation here. This is one limitation of this study as these *in vitro* polyclonal stimulating conditions may not reflect *in vivo* T-helper cell responses specific to *Coccidioides*. These data indicate that dysregulated T-cell responses, as indicated by higher Th2 to Th1 ratios by cytokine, may be reprogrammed by cytokine blockade.

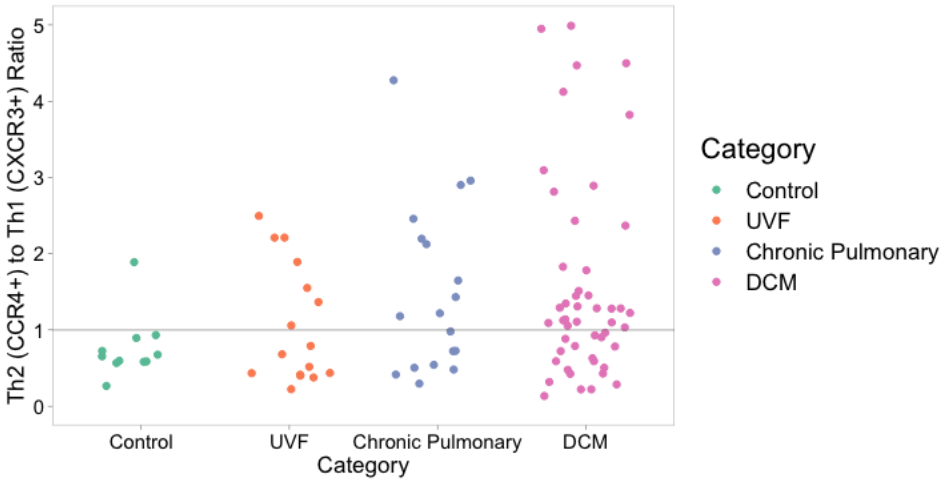

Figure 1. A subset of patients with coccidioidomycosis demonstrate abnormal T-helper cell phenotypes by chemokine with Th2/Th1 imbalance (CCR4+/CXCR3+); an increasingly skewed ratio appears to correlate with disease severity.

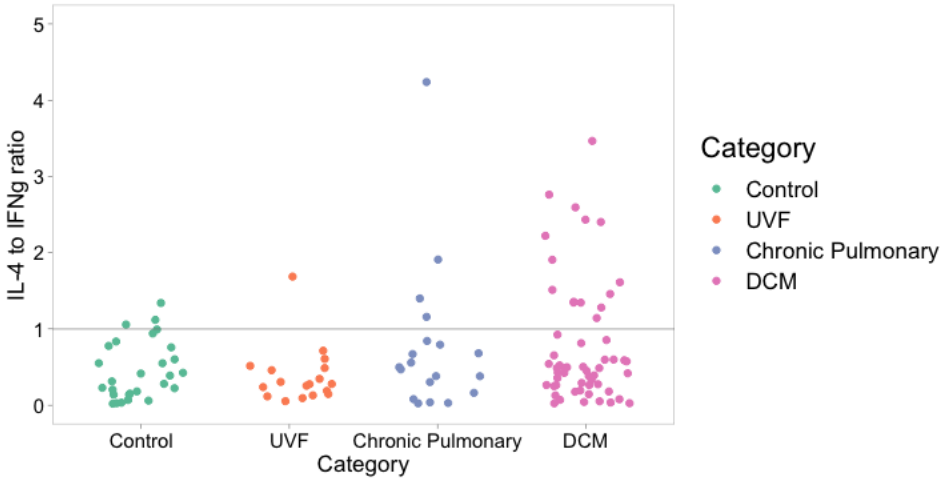

Figure 2. A subset of patients with coccidioidomycosis, particularly those with DCM, demonstrate abnormal T-helper cell phenotypes by cytokine with Th2/Th1 imbalance (IL-4/IFNγ).

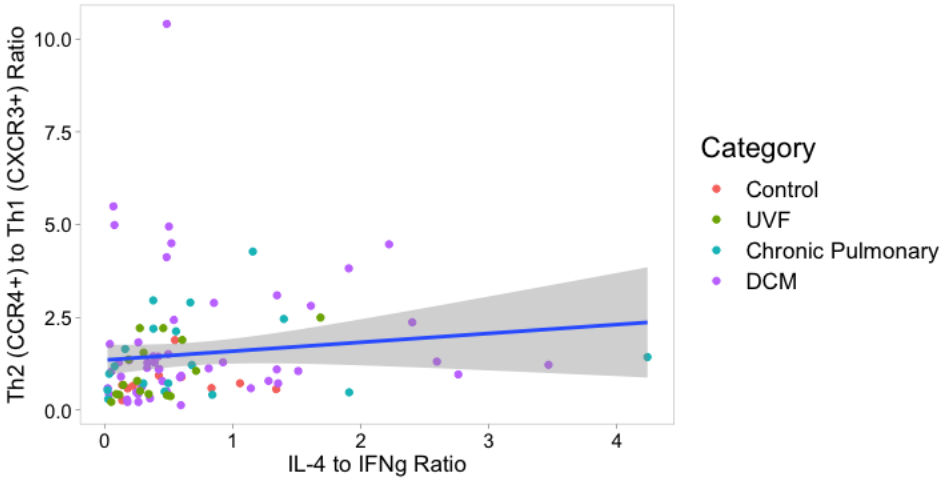

Figure 3. Th2/Th1 ratios by chemokine receptors do not correlate with Th2/Th1 ratios by cytokine production.

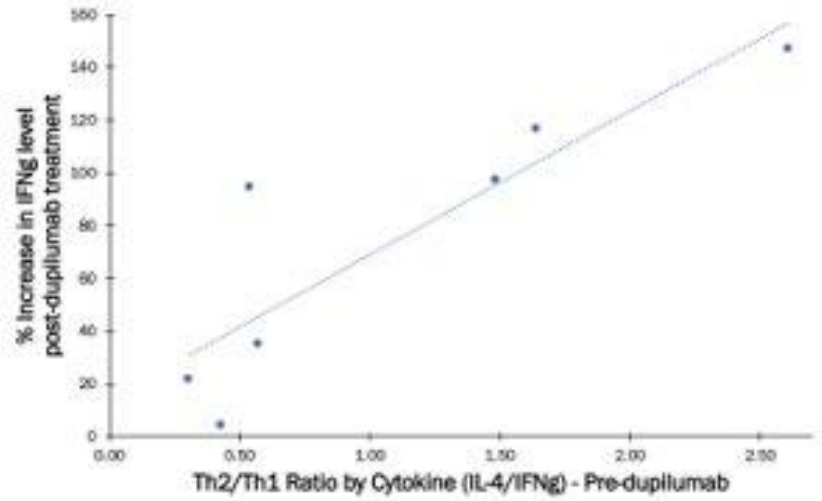

Figure 4. Higher pre-dupilumab Th2/Th1 ratios by cytokine (IL-4/ IFN-γ) correlate with greater IFN-γ increase post-dupilumab treatment *in vitro.*

9. PULMONARY GIANT CAVITARY COCCIDIOIDES WITH FUNGAL BALL AND HEMOPTYSIS

Vishal Narang, Kevin Dao, Sara Jaratanian, Carlos D'assumpcao, Augustine Munoz, Arash Heidari

Kern Medical-UCLA, Bakersfield, USA

Introduction: The risk of severe and cavitary CM is increased in diabetic individuals. The cavitary disease may progress, leading to erosion of vasculature and pulmonary parenchyma as well as further complications. Here we present a case of cavitary CM in an uncontrolled diabetic nonadherent to treatment presenting with giant fungal ball and hemoptysis.

Methods: Approval was obtained from the Institutionalized Review Board (IRB) at Kern Medical. A single patient case report was conducted.

Results: The patient is a 48-year-old Hispanic male with diabetes mellitus and untreated pulmonary CM, who presented with hemoptysis for 1 day, night sweats, and a 45-lb weight loss. On arrival, he was found to have a giant cavity measuring 10 x 8 x 7 cm predominantly in the left lower lobe with a central filling mass within the cavity. During his hospitalization, he continued to experience up to ~300mL hemoptysis daily. He underwent bronchoscopy which confirmed CM mycetoma with direct stain and fungal cultures. Interventional radiology was consulted who performed successful arterial embolization of the right tracheobronchial and intercostal bronchial artery to control his hemoptysis. He was placed back on fluconazole and discharged home. One week later he returned in respiratory distress with fever, shortness of breath, and hypoxemia. Imaging revealed new left lower lobe and lingular consolidations. His workup was consistent with aspiration of cavitary material to the left lung. His oxygen requirements increased significantly, and he was placed on steroids and liposomal amphotericin b with rapid improvement of symptoms. He transitioned to Posaconazole and his condition continued to improve. He was discharged home on oral Posaconazole and outpatient follow up.

Conclusion: This case describes one giant cavitary lesion from possibly two separate lesions. Poorly controlled diabetic individuals are already at increased risk for cavitary lesions. The management of giant pulmonary cavitary CM with mycetoma and bleeding remains a challenge. In a patient presenting with hemoptysis and a cavitary lesion, a multidisciplinary team consisting of pulmonary, thoracic surgery, and interventional radiology is essential.

CASE PRESENTATIONS

1. A CASE OF COCCIDIOIDAL MENINGITIS WITH BIOFILM OBSTRUCTING VP SHUNT DUE TO CUTIBACTERIUM ACNES

66TH ANNUAL COCCIDIOIDOMYCOSIS STUDY GROUP MEETING

Rupam Sharma[1,2], Royce Johnson[1,2,3], Gerard David[4], Majid Rahimifar[5], Arash Heidari[1,2,3]

[1]Kern Medical, Bakersfield, USA. [2]Valley Fever Institute, Kern Medical, Bakersfield, USA. [3]David Geffen School of Medicine, Los Angeles, USA. [4]Kaiser Permanante, Bakersfield, USA. [5]Memorial Hospital, Bakersfield, USA

Introduction: Coccidioidomycosis is a fungal infection that causes more than 150,000 infections in the US each year, predominantly in the southwestern states. While typically this is a mild to moderate respiratory illness, approximately 1% of the patients develop disseminated disease. Roughly half of these disseminated cases result in meningitis. Between 15 – 40% of those cases develop hydrocephalus either early or late in the course of their disease requiring a ventriculoperitoneal (VP) shunt. One of the major problems with VP shunts is superimposed bacterial infection. The most commonly recognized infecting organisms are: Staphylococcus epidermidis, Staphylococcus aureus, Escherichia coli, Klebsiella, Proteus and Pseudomonas. In recent years an increasing prevalence of Cutibacterium acnes has been found in CSF shunt infections. Valley Fever Institute encountered a patient with a VP shunt infection caused by Cutibacterium acnes and evaluation of the literature did not reveal any previously reported cases.

Methods: Institutional Review Board of Kern Medical approved this study. A retrospective review of the patient's record was performed. Literature search was conducted on PubMed and google scholar using the search terms were: Cutibacterium, Propionibacterium, coccidioidomycosis meningitis complications.

Results: A 32-year-old woman with coccidioidal meningitis onset 10 years prior subsequently required bilateral VP shunts for non-communicating hydrocephalus. She had multiple VP shunt revisions: 4 years prior, 3 years prior, two revisions within one year prior. All aerobic cultures from the VP shunt revisions were negative for any growth. Anaerobic cultures were not performed.

A year after her last shunt revision, she developed recrudescent headaches and was subsequently diagnosed to have bilateral VP shunt failure requiring another complete shunt replacement. During distal externalization, a biofilm material within shunts was noticed. Cultures remained negative. A collective decision was made to collect anaerobic cultures from the ventricular catheters before completion of the revision and she was discharged in stable condition. After discharge, intraoperative anaerobic cultures grew *Cutibacterium acnes*. Almost exactly a month later, the patient again presented with worsening headaches, blurred vision and vomiting due to both VP shunts failure and subsequently underwent removal of shunts along with an antibiotic course for *Cutibacterium acnes* which grew from the intraoperative cultures. Following revision and hospital discharge patient did not have any further recurrence of shunt failures and her meningitis has remained stable to date.

Conclusions: *Cutibacterium acnes* could infect and obstruct cerebral shunts due to the production of biofilm, however, diagnosis is usually missed by routine aerobic cultures. Obtaining anaerobic cultures could prevent a missed diagnosis of this pathogen. As far as we were able to discern this is the first reported case of Cutibacteirum VP shunt infection in a coccidioidal meningitis patients. We believe that this occurs more frequently but is unrecognized due to the subtle signs and symptoms and delays in the growth of Cutibacterium.

2. A CASE OF CONCURRENT DISSEMINATED COCCIDIOIDOMYCOSIS AND EMBRYONAL CARCINOMA WHEN LICE AND FLEAS COEXIST

Michael Ke[1,2], Arash Heidari[1,2], Michael Valdez[1,2], Allen Tsiyer[1], Rasha Kuran[1,2], Royce Johnson[1,2]

[1]Kern Medical, Department of Medicine, Division of Infectious Diseases, Bakersfield, USA. [2]Valley Fever Institute, Bakersfield, USA

Introduction

Coccidioidomycosis (CM) is a fungal infection endemic to the southwestern United Stated with a wide range of clinical presentations depending on the infected organ systems. CM causes a primary pulmonary infection. One percent of cases disseminate, via hematogenous or lymphatic spread. It is in these cases, that more severe symptoms may present and potentially overlap the characteristics of other systemic illnesses. Herein is a case of CM disseminated to lymph nodes in a 24-year-old man with concomitant metastatic embryonal carcinoma. It is difficult to identify the primary etiology for many components of this patient's presentation and the relationship between these two concurrent disease processes is not entirely clear. Factors that may contribute include the phenomenon of locus minoris resistentiae, comorbidity, or a shared immune response between infectious organisms and malignant cells.

Methods Ethical approval for this single patient case report was obtained from the Kern Medical Institutional Review Board (IRB # 21085). After which, a chart review was conducted.

Results A 24-year-old man from the central valley of California presented with a new rash. Examination showed periorbital edema and diffuse raised and hyperpigmented skin lesions. Differentials included psoriasis and CM. CM serology showed nonreactive IgM immunodiffusion (ID), very weakly reactive IgG ID, and complement fixation (CF) titer <1:2. The patient was lost to follow-up but returned 6 weeks later with a 17-pound weight loss, progression of the rash, and proximal muscle weakness. The examination was consistent with a heliotrope rash and CK was elevated. He was prescribed prednisone 60 mg daily for presumed dermatomyositis. 2 weeks later, he developed fevers and CM CF titer increased to 1:16. He was started on fluconazole 800 mg daily. 5 weeks later, he developed diffuse lymphadenopathy and imaging showed multiple pulmonary nodules, a destructive lesion in the iliac bone, and retroperitoneal and pelvic lymphadenopathy. Repeat CM CF titers increased to 1:64 and the patient was started on liposomal amphotericin B infusions. Shortly thereafter, new retroperitoneal and right testicular masses were identified. Histopathology from both orchiectomy and retroperitoneal mass biopsy revealed embryonal carcinoma while right inguinal lymph node excisional biopsy showed granulomatous inflammation with endosporulating spherules diagnostic of CM. The patient completed 9 weeks of amphotericin and subsequent bone scan showed no definite foci of increased uptake. He also completed 3 cycles of Etoposide, Ifosfamide, and Cisplatin. On subsequent clinic visits, weight was up-trending and improvement in rash and lymphadenopathy were noted.

Conclusion This case demonstrates a correlation between the administration of steroids and increase in CF titer. As coccidioidomycosis and several types of malignancies may have overlapping clinical presentations, a thorough physical examination and tissue sampling are necessary to distinguish. In rare cases, coexistence may occur. “Läuse und Flöhe haben.” A German phrase, which translates to “Having lice and fleas,” refers to having two reasons for a problem. Understanding the underlying etiology or identifying the relationship between concomitant conditions is essential to formulate the most appropriate treatment plan. This patient responded well to separate treatment regimens for both disseminated coccidioidomycosis and embryonal carcinoma.

3. A CASE OF COCCIDIOIDAL MENINGITIS WITH LOW-PRESSURE HYDROCEPHALUS

Michael Valdez[1,2], Shikha Mishra[1,2], Rasha Kuran[1,2], Arash Heidari[1,2]

[1]Kern Medical, Department of Medicine, Division of Infectious Diseases, Bakersfield, USA. [2]Valley Fever Institute, Bakersfield, USA

Introduction Meningitis is the most devastating complication of coccidioidal (Cocci) infections and has a predilection for the basilar portion of the brain. Hydrocephalus, typically communicating, with elevated intracranial pressure (ICP) is the most common complication of cocci meningitis. Treatment with azoles or serial lumbar punctures (LP) are generally not adequate and patients often require cerebrospinal fluid (CSF) shunting. Despite shunting, mortality is still 10%. Shunt malfunctions are well documented and typically associated with elevated ICP. The syndrome of inappropriately low-pressure hydrocephalus (SILPAH) is an extremely rare phenomenon characterized by low ICP. In SILPAH, CSF drains to the spinal subarachnoid space, however, not via the ventricular system or CSF shunt. There is a resultant outward expansion of brain parenchyma and hydrocephalus with increased brain compliance. It is this increased brain compliance that is responsible for low ICP. Herein is a case of a 67-year-old male with cocci meningitis complicated by ventriculoperitoneal (VP) shunt failure with low-pressure hydrocephalus and abdominal pseudocyst.

Methods Ethical approval for this single patient case report was obtained from the Kern Medical Institutional Review Board (IRB # 22010) and a retrospective chart review was conducted.

Results A 67-year-old male with cocci meningitis and hydrocephalus post VP shunt placement presented with altered mental status. Shuntogram was negative and opening pressure (OP) on LP was 24 cmH2O. Cocci complement fixation (CF) titer was 1:8 in the CSF and 1:16 in the serum. The patient became obtunded and required intubation. Mentation improved after shunt revision and the patient was discharged on Fluconazole 1200 mg daily. CSF obtained from the shunt later grew *Coccidioides immitis*. He returned to the hospital 5 months later with encephalopathy, ataxia, and urinary incontinence. Shuntogram showed no kink or discontinuity and CT brain showed stable hydrocephalus with new small subdural fluid collections. No surgical intervention was recommended by neurosurgery at this time. CF titer increased to 1:32 in CSF and 1:252 in serum. CT abdomen showed the distal VP shunt within a ventral hernia communicating with a large abdominal pseudocyst. MRI brain 4 days later showed worsening hydrocephalus and OP was 16 cmH2O. Patient again

became obtunded and required intubation for airway protection. Neurosurgery placed an external ventricular drain (EVD) set to subzero pressure and mentation subsequently improved slowly over the course of 1-2 weeks. Patient was eventually extubated and transferred to a higher level of care where a ventriculopleural shunt was placed after which he was discharged and lost to follow-up.

Conclusion Although rare, low-pressure hydrocephalus is critically important to recognize as a complication of patients with coccidioidal meningitis who require shunt placement. Recurrent episodes of acute hydrocephalus superimposed on baseline chronic hydrocephalus likely contribute to loss of brain plasticity, or increased compliance, which may account for inappropriately low pressure. The approach is unique and requires urgent neurosurgical evaluation and close interdisciplinary interaction between clinicians.

4. NEUROPARENCHYMA COCCIDIOIDOMAS COMPLICATED WITH PREGNANCY DURING THERAPY

Carlos D'Assumpcao[1,2,3], Rupam Sharma[1,2], Royce Johnson[1,2,3], Rasha Kuran[1,2,3]

[1]Kern Medical, Bakersfield, USA. [2]Valley Fever Institute, Kern Medical, Bakersfield, USA. [3]David Geffen School of Medicine, UCLA, Los Angeles, USA

Introduction: Coccidioidomycosis disseminated to the central nervous system (CNS), if left untreated, is generally fatal. Meningeal and intraparenchymal involvement can create treatment challenges due to unknown antifungal CNS pharmacokinetics and pharmacodynamics. CNS coccidioidomycosis treatment is lifelong and must be tailored to patient's life events. Presented here is a young female with multiple intraparenchymal coccidioidomas who became pregnant. Treatment management challenges are discussed.

Methods: The Institutional Review Board of Kern Medical approved this study. A retrospective chart review of patient's electronic health record was performed. Literature search was conducted on Google Scholar and PubMed.

Results: A 31-year-old Hispanic female developed a dry cough and fever three months prior to presentation. Serum coccidioidomycosis immunodiffusion IgM and IgG were reactive and complement fixation was 1:512 (Kern County Public Health Department). Imaging at the time found miliary dissemination of pulmonary coccidioidomycosis. She was prescribed fluconazole 400 mg daily for two months before presentation to our center. She subsequently developed headaches, dyspnea and bilateral thigh soreness. Neuroimaging found multiple enhancing nodules scattered throughout brain parenchyma, the largest lesion at the posterior margin of left pons, as well as cervical, thoracic and lumbar spinal cord. However, lumbar puncture found no evidence of meningitis. Liposomal Amphotericin B was considered but due to lack of access to care, fluconazole was increased to 1000mg daily in the meantime. Her serum fluconazole levels ranged between 37 to 89 mg/L.

Four months after initial symptoms, she developed open draining left sub clavicular abscess. Left clavicular abscess grew Coccidioides immitis. Repeat neuroimaging found a decrease in the number and size of enhancing lesions in brain parenchyma and cervical, thoracic, and lumbar spinal cord.

Seven months after the initial symptoms, the patient was found to have an unexpected pregnancy. Due to azole teratogenicity, she was switched to intravenous liposomal Amphotericin B for the duration of her pregnancy.

Conclusions: Disseminated coccidioidomycosis to central nervous system with intraparenchymal involvement without meningitis is unusual. The considered opinion of the VFI is that Liposomal Amphotericin B may well be preferred therapy. Patient access to care, preferences, and the risk of teratogenicity of high dose azoles, factor into therapeutic options.

5. MILIARY COCCIDIOIDOMYCOSIS WITH HEPATIC AND CUTANEOUS DISSEMINATION

Jani Kim, Erik Jensen, Geetha Sivasubramanian

University of California San Francisco, Fresno Campus, Fresno, USA

INTRODUCTION: Coccidioides sp. are dimorphic fungi that are endemic to the southwest United States. Pulmonary disease is the most common presentation and often self-limited. Miliary coccidioidomycosis is rare but associated with high fungal burden, lymphatic and hematogenous dissemination. We present a case of miliary coccidioidal pneumonia with dissemination to liver and skin.

66TH ANNUAL COCCIDIOIDOMYCOSIS STUDY GROUP MEETING

CASE PRESENTATION: A 61-year-old male with end-stage renal disease on hemodialysis and diabetes mellitus was admitted with worsening abdominal distension, failure to thrive and confusion. He was diagnosed with pulmonary coccidioidomycosis two months prior and was on oral fluconazole. Examination showed a cachectic man, with bilateral rales, abdominal distension, and a skin lesion over left knee. CT chest revealed diffuse miliary pattern of infiltrates. Coccidioides complement fixation titer of the serum was 1:128. Bronchoalveolar lavage fluid was negative for tuberculosis. Disproportionately elevated alkaline phosphatase with ongoing symptoms raised concern for disseminated disease to liver and skin. Liver biopsy revealed non-necrotizing granulomatous inflammation suggestive of disseminated coccidioidomycosis. Punch biopsy of the skin lesion showed granulomatous dermatosis with fungal spherules consistent with coccidioidomycosis. Spinal fluid and ascitic fluid analysis were unremarkable. He remains hospitalized on intravenous amphotericin.

CONCLUSION: Miliary coccidioidomycosis is a rare presentation and usually happens in patients with underlying immunosuppressive conditions. It is usually associated with a high fungal inoculum and dissemination via lymphatic and hematogenous route to distant organs. Diagnosis requires a high index of suspicion. Treatment requires several weeks of amphotericin B followed by maintenance azole therapy.