The Epidemiology of Coccidioidomycosis –

15 California Counties, 2007-2011

Produced for the California Coccidioidomycosis Collaborative

January 22, 2014

Michael L. MacLean, M.D., M.S.
Health Officer, Kings County

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Prevette, Trudi	Stanislaus County
Rose, Kelly	Merced County
Slack, Erin	Ventura County
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Part One

The Collaborative

The California Coccidioidomycosis Collaborative is an informal association of individuals with a commitment to addressing the many challenges faced in defining the occurrence and the burden of coccidioidomycosis (CM) in California. While a wide range of disciplines and affiliations are represented, the majority of participants are engaged in the fields of epidemiology or the laboratory sciences. This report on the June 2012 meeting of the Collaborative in Hanford, California reflects this current emphasis on county-based epidemiology. Additional subjects addressed in this report include clinical laboratory science, field ecology of the fungus, hospitalization rates for CM in California, CM admissions to a regional pediatric specialty hospital and the recent and ongoing work of the Occupational Health Branch at the California Department of Public Health.

Fifteen California counties provided the epidemiology data used in the current report. This initiative grew out of six county meeting held in 2011. The six county meeting was less structured and was limited to the epidemiology of CM in the six counties. The reporting intervals for the counties ranged from four years to twenty years. The cumulative case count for the six counties was 14,864. All counties noted significant year to year variability but patterns varied among the counties. In the five counties with state or federal institutions, the inmate populations were observed to have a significantly increased risk for CM. The inmate cases were observed to skew the gender and age distributions in the counties with inmate cases. The risk of CM wasn't evenly distributed in any of the six counties. The participants noted that three major north/south California highways pass through highly endemic areas. The observed case counts were thought likely to be an underestimate of the CM cases due to under-diagnosis of CM in these six endemic counties. The report of this meeting is available at **www.countyofkings.com/health/cocci.**

A Brief Review of Clinical Coccidioidomycosis

Coccidioidomycosis is the disease that results from infection with a soil-growing fungus. The two related species of the fungus Coccidioides cause identical disease. The fungus is found in limited areas of the Americas. In the United States, six states are known to be endemic for the fungus: California, Arizona, Nevada, Utah, New Mexico and Texas. Even in those states the affected areas tend to be spotty. The fungus is also known to be present in Mexico and in some other areas in Central and South America.

The fungus grows under the superficial few inches of soil where it is subject to drying out. Upon drying, the fungus produces tiny spore-like structures that can readily become air borne when the soil is disturbed. Inoculation of spores into the skin causes localized disease and very rarely systemic disease but this form of infection is rare. Inhalation of the spores is the primary route of infection. The disease is not spread person to person.

Following infection, 60% of persons develop either no disease or the disease produced doesn't prompt them to seek medical attention. The other 40% of infected persons develop an influenza-like illness with some combination of fever, chills, sweats, chest pain, joint and muscle aches, headache and fatigue. The latter symptom is common and can be profound and last for months. Chest x-rays are very often abnormal. Pneumonia is perhaps the most common finding but there are many other changes that are seen frequently. The pneumonia seen is consistent with a clinical class of illness termed community-acquired pneumonia (CAP). Pending further clinical testing, these pneumonias are clinically indistinguishable. There are many causes of CAP. Antibiotics are usually and appropriately prescribed pending the results of the clinical testing. Antibiotics are not affective agents for the treatment of CM. In most cases, the pneumonia caused by coccidioidomycosis will eventually resolve without any specific treatment.

We know that most of these patients will recover without treatment because the earliest known effective treatment was often withheld. The treatment had to be given by slow intravenous infusion; patients had to be treated for weeks and would spend many hours per week getting the infusion. The treatment was very unpleasant with significant immediate side effects. Patients who had completed a previous course of treatment were often resistant to being treated again because of the side effects of the treatment. The treatment was dose dependent toxic to the kidney. We now have oral medications that are much better tolerated and much less toxic. Currently, the decision to treat is much less daunting for patients and for providers and treatment is likely now more common.

Some individuals develop more complicated CM. An unknown percent of cases develop persistent or progressive pulmonary disease. Some persons have asymptomatic residual pulmonary conditions, e.g., a cavity or a nodule. These conditions usually require additional diagnostic studies, sometimes invasive procedures. Those with progressive pulmonary disease require continued treatment.

The disease can spread beyond the lungs where it can infect any organ of the body. The most commonly involved extra pulmonary sites are lymph nodes, skin and bone. Involvement of the meninges, the lining of the central nervous system, may be the most serious form of disseminated disease. Coccidioidal meningitis requires lifetime treatment. The most commonly used medication can cause birth defects if taken early in pregnancy. Dissemination is sometimes seen in persons with no clear prior illness due to coccidioidal infection.

Although anyone can develop a complicated form of CM, there are recognized risk factors for complicated disease. Any pre-existing disease that compromises the immune system increases the risk of complicated CM. Diabetes, kidney disease, HIV, and some cancers are examples of such diseases. Some medications may increase the risk for complicated disease, e.g., immune modulators used to treat rheumatoid arthritis and other autoimmune diseases. Male gender is a moderate risk factor for dissemination. Third trimester pregnancy is another. Race is known to be a significant risk factor for disseminated disease. The risk of dissemination in African-Americans and Filipino-Americans is widely recognized. The increased risk in the black males is at least 500% that of white males. Other racial/ethnic groups may be at increased risk for dissemination. As will be discussed later, some racial groups are unrepresented in the areas endemic for coccidioidal infection making it more challenging to assess the risk in these groups. In those patients with symptomatic disease, the risk for dissemination is commonly estimated at 5-8%. These estimates tend to ignore the elevated risk of dissemination in certain populations. The stated estimates probably overestimate the risk for some individuals and underestimate the risk for others. We have very poor estimates how often people develop other, non-disseminated forms of complicated CM.

The signs and symptoms of the common clinical cases of CM are nonspecific. In most cases, the diagnosis of the typical case of CM will rely on testing serum for antibodies directed at components of the coccidioidal organism – serology studies. These can be absent early in the course of disease and repeat testing may be needed. Less frequently, the diagnosis is based on culture of the fungus. In more complicated cases the diagnosis is established by pathologic examination of tissue, e.g., following a biopsy. The pathologic findings are characteristic and diagnostic.

Under-diagnosis of a clinical illness is hard to prove. The idea that many cases of CM go undiagnosed once the affected individuals access the health care system is plausible. The nonspecific clinical presentations can be caused by many other, unrelated conditions. Perhaps the most characteristic rash, erythema nodosum, isn’t typically present and can be due to diseases other than CM. The testing needed to establish the diagnosis is unique to CM; the clinical provider has to consider CM as a diagnosis to order the necessary testing. Serology testing can be falsely negative early in the clinical illness and may need to be repeated. In the meantime, many of the other diagnostic possibilities require empiric antibiotic treatment – treatment that wouldn't benefit CM. Most CM illness will resolve without specific treatment and the search for a diagnosis stops once the illness is no longer present.

There is evidence that CM specific testing is under-utilized even in a known endemic area. In Arizona, in highly endemic Maricopa County, only 2-13% of outpatients with community- acquired pneumonia were ever tested for CM by serology. The majority of patients had symptoms for more than two weeks before they were tested. Of those tested, 15% had a positive test. In this study a positive correlation between testing and private health insurance was also found. [7]

In another study from Arizona, patients with knowledge of CM prior to the onset of their disease were twice as likely to request testing. They were also diagnosed earlier. The study also found that non-Hispanic whites were more likely to be informed about CM prior to their illness. [27]

The community acquired pneumonia practice guidelines developed by the Infectious Disease Society of American recommend consideration of coccidioidomycosis in areas that are "endemic" for the disease. [18] Endemic isn't further defined in the Guidelines. The online Center for Disease Control map indicates that the southern San Joaquin Valley is highly to moderately endemic. The central coast and all of southern California are listed as being "suspected" endemic.

The Valley Fever Center for Excellence has pointed out that there is value in making the diagnosis of CM even if specific treatment isn't always necessary. Knowing the diagnosis will allow for proper monitoring for complications, help avoid repeated courses of unnecessary antibiotic therapy, prevent unnecessary diagnostic testing and reassure those patients who experience prolonged convalescence.

Prior infection is thought to confer immunity to repeat infection. In some cases it would be useful to know if persons were previously infected. The antibodies used for diagnosis usually don't persist beyond two years after the original illness. Serology testing isn't a reliable method for assessing previous infection. For decades, a skin test for coccidioidal infection was available. The test was analogous to the skin test used to detect latent tuberculosis infection. This skin test was withdrawn from the market for commercial reasons. The FDA has recently approved a new skin test for coccidioidal infection. The availability of this preparation is presently held up for commercial reasons.

A Brief, Selective History of Coccidioidomycosis in California

Early Work in California:

Coccidioidomycosis (CM) was known to be present in California in 1894. At that time and for more than three decades, progressive, disseminated disease was the only clinically recognized disease. Coccidioidal granuloma, as it was then termed, was known to be caused by fungus. The disease was noted to be usually fatal.

"San Joaquin or desert fever" was a recognized clinical entity in Kern County before its cause was known. It was defined in Kern County as pneumonia associated with a characteristic rash known as erythema nodosum. Dr. Myrnie Gifford, Chief Assistant Health Officer in Kern County, helped to prove the association between the coccidioidal fungus and San Joaquin Fever. For the ten year period 1931 to

1939, Kern County reported 301 suspected cases; 180 proven cases and 35 deaths. Dr. Gifford noted that there were some concerns about stigmatizing the San Joaquin Valley as an unhealthy place to live. She suggested the term “San Joaquin Valley Disease” as a name for disseminated disease while “San Joaquin Fever” be used to refer to the more benign form of the disease. [14]

World War II:

World War II resulted in the creation of military installations throughout California and the southwestern United States with the introduction of many individuals naïve to coccidioides. The endemic areas of the United States were less well defined at the start of WWII. The Medical Statistics Division of the Army’s Surgeon General’s Office estimated that for the period 1942-1945 there were 3,809 CM cases in the Armed Forces and 39 deaths. [23] Not all these cases were acquired in California.

During the war, the US Army funded Dr. C.E. Smith to study CM in Armed Forces personnel at four airfields in the San Joaquin Valley. All the service men were skin tested on arrival and then periodically. Most of these recruits were young adults. All were active service people. There were relatively few women involved in the study. Over the period July 1941-December 1945, there were 1,352 infections defined as skin test conversions. Sixty percent of these never had symptoms. Erythema nodosum was noted in 24% of the white women (there were no black servicewomen) and 4.3% of the white men. None of the African-American servicemen developed erythema nodosom. Dissemination was seen in 0.25% of the infections in white servicemen. The dissemination rate in black servicemen was 3.7% of infections, i.e., the dissemination rate in blacks was ten times that of whites. [23]

In April 1943 physicians at March Field Station Hospital near the City of Riverside admitted 12 African-American servicemen with acute pulmonary CM. The servicemen had been involved in construction work at a military facility near Blythe, California, an area not then known to be endemic. Almost six hundred servicemen were tested with intradermal coccidioidin antigen at periodic intervals between April 1, 1943 and July 26, 1943. Three hundred fifty-nine, 63%, of those studied were African-American. The remaining 214 were white. One hundred thirty-five (23.6%) of these servicemen had a skin test conversion from negative to positive. Eighty-three (14.4%) of 573 servicemen were hospitalized. The conversion rate and the hospitalization rate didn’t vary significantly by race. During the follow up period only four of the cases disseminated and there was one death. All of these occurred in the black servicemen. Over the next six months an additional 17 servicemen were hospitalized. The authors felt they had identified a new endemic region in California – “we should like to report that region, roughly triangular bounded by Banning and Needles, California and Yuma, Arizona, as a new endemic area for Coccidioides immitis.” [32]

Archeology Students:

Archeology field work at Native American sites in California and elsewhere have led to outbreaks of CM. This includes three sites in California, sites not usually thought of as endemic. In the interval between 1968 and 1972 three outbreaks of coccidioidomycosis, a total of 89 cases were noted in archeology professionals and students engaged in field work in Yolo [17], Butte [31] and Tehama Counties [30]. The fungus was cultured from the soil at the archeology dig sites in two of the counties.

A Dust Storm:

A massive dust storm in south San Joaquin Valley on December 20-22, 1977 was associated with an epidemic of coccidioidomycosis throughout much of northern California. In the 12 weeks following dust storm, the U. C. Davis Coccidioidomycosis Serology Laboratory confirmed 397 new cases. Most of these cases were from traditionally non-endemic areas of northern California including seven cases in San Francisco and ten cases in Oakland. [20] The number of cases associated with the dust storm likely was much greater. Not all specimens would have been sent to the UCD laboratory; many reportable diseases in California go unreported; many cases were likely misdiagnosed in 1978, especially in the non-endemic areas of the state. During the first five months of 1978 the number of cases reported to the state by all clinical providers exceeded the number of cases reported in twelve months for each of the preceding four years.

The 1977 dust storm was associated with an increased incidence of cases in endemic counties. For example, in the four weeks following the dust storm, an outbreak was noted at Lemoore Naval Air Station in Kings County. Eighteen cases were noted, four of whom developed disseminated disease. One of the disseminated cases died of his disease. People of color were disproportionately affected. [33]

A Recent California Outbreak:

The reported cases of coccidioidomycosis in California increased dramatically in the early 1990s. After averaging 428 cases per year between 1981-1990, the number of cases doubled in 1991 and by 1992 peaked at 4,516. By 1995 the number of reported cases per year was still twice the average annual number observed in the preceding decade. [29] Most of the increase in cases was noted in Kern County. For the period 1981-1990, 52% of the cases reported in California were from Kern County. Seventy percent of the cases reported in the three years 1991-1993 were reported in Kern County. Kern, Tulare, San Luis Obispo, and Los Angeles Counties reported 84% of the cases during the three year interval. An increase in cases was seen, however, widely throughout the state. For example, the combined cases from Contra Costa, Alameda, and Santa Clara Counties for the three year interval, 1991-1993, was 24% of the average number of cases reported in California the preceding decade. This outbreak lasted four to five years. A much smaller increase in cases was noted in Arizona in the early 1990s. [15] The cause of this California outbreak remains unexplained.

Following Natural Disasters:

In the seven weeks following the Northridge earthquake of January 17, 1994, two hundred three cases were reported. (The study in the literature addressed only cases that were older than 13 years.) Fifty-five percent of the cases were hospitalized. The median length of hospital stay was a week. Within 12 weeks of the earthquake, 3.7% of the cases developed disseminated disease. There were three deaths associated with this outbreak. [22]

Following a large wildfire in October 2003, Ventura County noted a significant increase in reported CM cases. The outbreak peaked about three months after the wildfire. (See Figure 1) The wildfire occurred in the area of Ventura County where the landslides were noted following the 1994 earthquake.

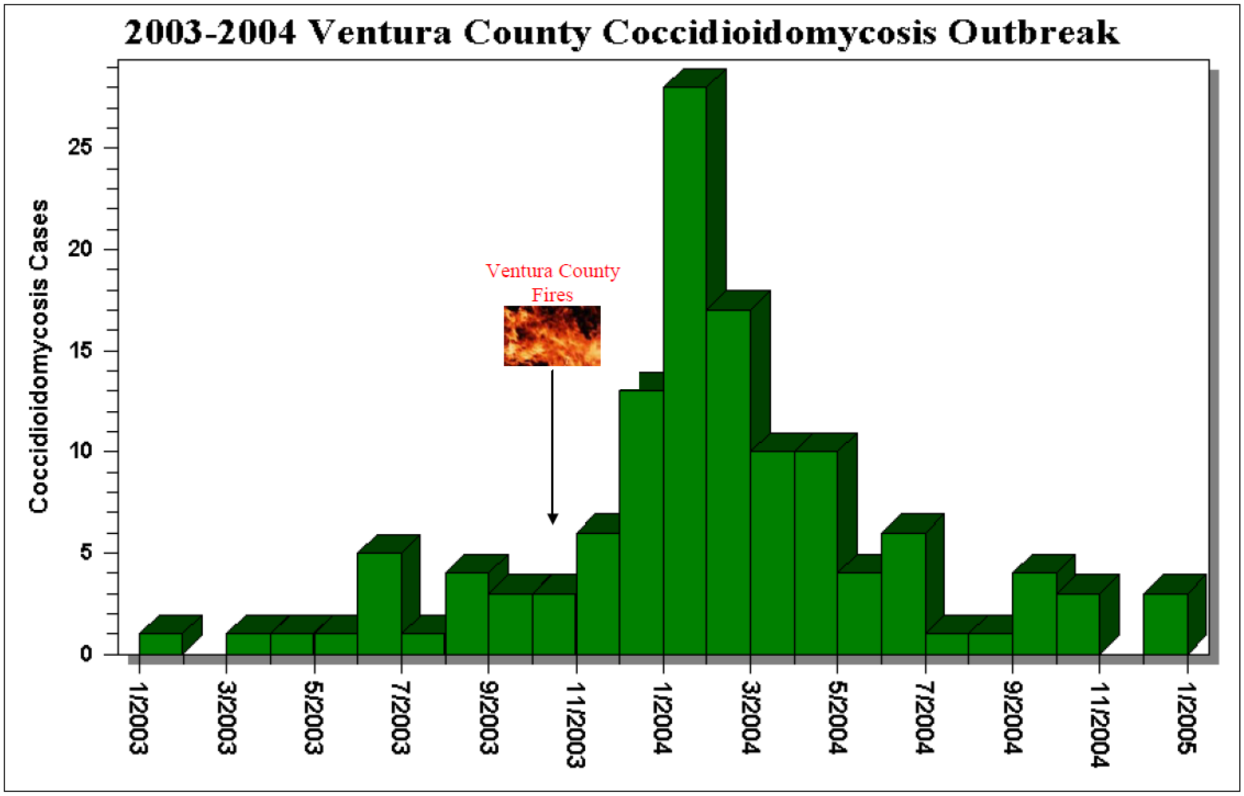

Figure 1
Data Sources: Ventura County WebCMR. Ventura County Health Statistics and Epidemiology Group.

Wildfire associated CM outbreaks haven't previously been reported. The removal of surface vegetation or even soil disturbance consequent to fire fighting activities could provide a plausible biologic basis for facilitating the dispersal of fungal spores. The temporal association of an outbreak of CM following the wildfire doesn't prove causation but is intriguing.

Occupational Disease:

Ten of 22 Navy SEALS developed CM following a six week training exercise in the fall of 2001 near Coalinga in western Fresno County. The training involved a great of dust exposure and no respiratory protection was used. There was a delay in the diagnosis of the first clinical cases because CM wasn't considered as a diagnosis by the treating clinicians. Only three of the SEALs reported missing any work days, 1-3 days. There was no dissemination. At the time of the study's submission one SEAL was unable to do any underwater diving because of a pulmonary cavity. [9]

Ten of twelve construction workers developed CM after installing a large underground water pipe. The exposure occurred while working at Camp Roberts, a military base that straddles San Luis Obispo and Monterey Counties. None of them were military personnel. None of the workers used any respiratory protection. The Occupational Health Branch at CDPH took the lead in investigating this outbreak. Another person working at the same site the following February also developed CM. One member of the first group developed disseminated disease.[10]

Outbreak in a Special Population:

In January 2007, the California Department of Health Services issued a report on a 2005 outbreak of CM among inmates of Pleasant Valley State Prison in Fresno County. [1] Beginning in September of that year there was a dramatic increase in the inmate cases reported. The number of cases reported at this prison was three times the average of the cases reported in the previous four years. The observed rate at the prison was 38 times that observed in the neighboring city of Coalinga. The study confirmed at least 166 cases, 18% of which were hospitalized. Twenty-seven percent of the cases had disseminated disease and there were four deaths. None of the patients with disseminated disease died. The relative risk of African-American inmates was almost twice that of non-Hispanic white inmates. Inmates with chronic pulmonary disease, diabetes and heart disease were noted to be at significantly increased risk of being diagnosed with CM. A subsequent report on deaths in California prisons noted that there were 36 CM inmate deaths during the six year interval 2006-2011. [11]

Summary of June 12, 2012 Presentations

Laboratory Science Presentations:

The recovery of the Coccidioides organism from the environment is challenging. On occasion the organism hasn't been recovered from sites where there is strong epidemiologic evidence that the fungus is highly endemic, for example in sites near Pleasant Valley State Prison or Avenal State Prison. Improved sensitivity of recovery of the organism from the soil could help us to better understand the ecology of the organism in relation to human and animal disease. Highly sensitive means of detecting the organism in the soil might be useful in preventing the disease in humans, for example, in the context of anticipated occupational or recreational exposure.

James Beebe, PhD with the San Luis Obispo County Public Health Laboratory reported on his current research: Rapid Detection of Coccidioides in Soil Samples. Dr. Beebe has initiated a research project

"With the goal of improving the laboratory detection of Coccidioides in soil samples by highly aerated liquid medium cultivation using a selective-enrichment medium, followed by PCR detection of the presence of the agent, confirmed by solid medium culture of positive samples."

Additional information about his research project is available in the Laboratory Section of the Supplement.

Antjel Lauer, Ph.D. with California State University Bakersfield reported on the work of her research team: Detection of C. immitis Growth sites with Culture Independent Methods. Her research team includes the Monterey County Public Health Laboratory.

"The focus of the team's project is to identify growth sites of the fungal pathogen *Coccidioides immitis*, the causative agent of Valley Fever, in the Southern San Joaquin Valley, by a combination of molecular biology, satellite imagery, and soil parameter characterization. Furthermore, we have isolated and identified bacterial species that are antagonists to *C. immitis* and might be of value in a bioremediation attempt to suppress the growth of the pathogen in selected areas."

Additional information about his research project is available in the Laboratory Section of the Supplement.

Demosthenes Pappagianis, M.D. with the Coccidioidomycosis Serology Laboratory at the University of California at Davis reported on the work of his team: Coccidioidomycosis in California State Correctional Institutions, January 2010-May 2012.

"We have provided information on recognition of new cases of coccidioidomycosis in California State Prisons to indicate seasonal and geographic association with infection. Some of the prisons lie outside the recognized endemic areas and cases recognized there, can be accounted for by at least two explanations: transfer of an infected individual from a prison in the endemic area to a non-endemic prison or assignment of an individual from a non-endemic prison to fight fires in an endemic area.

The graphic depiction of cases that we have detected serologically is incomplete in that the serologic testing we have conducted at the UC Davis Coccidiodomycosis Serology Laboratory does not include test results obtained by other laboratories. Additional problems associated with the picture of Coccidioidomycosis in California State Prisons are the following:

a. The annual reported cases usually refer to newly recognized coccidioidomycosis. However, the fact that this disease can be chronic means that active disease reported in a given year continues beyond that year leading to significant cumulative numbers of active cases not included in the annual reporting.
b. Employees as well as inmates are subject to infection.
c. The varying degrees of severity of coccidioidomycosis are based on factors such as ethnic derivation, underlying medical conditions (diabetes mellitus, chronic pulmonary disease).
d. There is uncertainty as to the duration of currently available treatment, and related relapses.
e. Certain forms of the disease necessitate years (and possibly a lifetime) of medical management, e.g. with meningitis or synovitis.
f. Certain forms of the disease necessitate drastic surgical procedures, e.g., in disseminated coccidioidomycosis involving the spine.
g. There is concern about the availability of appropriate follow-up and possible prolonged treatment after discharge of inmates from prison."

Other June 12, 2012 Presentations

CDPH Occupational Health Branch Work on Occupational Coccidioidomycosis

Barbara Materna, PhD, CIH, Chief, Occupational Health Branch, CDPH
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June 22, 2012

- General functions of the Occupational Health Branch, CDPH
- Perform investigations of selected occupational disease cases, including occupational infectious diseases – OHB has authority to perform onsite investigations in California workplaces.
- Conduct surveillance of selected occupational injury and illness endpoints – Currently OHB does not conduct surveillance of occupational cocci cases.
- Provide information, educational materials, and technical assistance – OHB responds to inquiries from employers, workers, health officers, other agencies, etc., on occupational health topics. Workplace Hazard Helpline: 1-866-282-5516
  Website: www.cdph.ca.gov/programs/OHB
- Interface with local health departments, Cal/OSHA, Federal OSHA, National Institute for Occupational Safety and Health (CDC), employer and worker groups, and many others on occupational health issues.

- Investigation of occupational cocci outbreak among a construction crew digging a trench at Camp Roberts military base in 2007; very high attack rate (10/12 of crew members) and 1 worker with disseminated disease; made recommendations for respiratory protection and other prevention/dust-mitigation measures.
  - Collaboration with San Luis Obispo County and CDPH Infectious Diseases Branch
  - Production of two publications: (1) Cummings KC et al. Point-source outbreak of coccidioidomycosis in construction. Epidemiology & Infection. April 2010; 138(4):507-511. (2) Das R et al. Occupational coccidioidomycosis in California. J Occup Environ Med. May 2012; 54(5):564-71.

- The Das R et al. publication cited above (distributed at the meeting) includes an analysis of California workers' compensation claims for occupational cocci, 2000-2007 (n=461). Identified occupations with the highest rates of cocci claims as agriculture, construction, and services.
  http://www.cdph.ca.gov/programs/ohb/Documents/OccCocci.pdf

- Examples of technical assistance requests
  - Advised California Dept. of Corrections on plans to apply a "soil cement" product on exposed soil areas at a prison with cocci cases as a dust mitigation measure.
  - Participated in calls related to investigation of multiple cases of cocci identified in inmates who had worked as wild land firefighters or conservation crew members in soil-disturbing activities.

- Educational materials under development – Jennifer McNary, industrial hygienist
    - Fact sheet for employers on occupational cocci – requested by Health Officers
    - Tailgate training material for wild land firefighters

Children's Hospital of Central California

Gregg Pullen, MT (ASCP) M, RM (NRCM), CIC, presented: Coccidoidomycosis – Impact on Children's Hospital of Central California. CHCC is a pediatric specialty hospital located in Madera County.

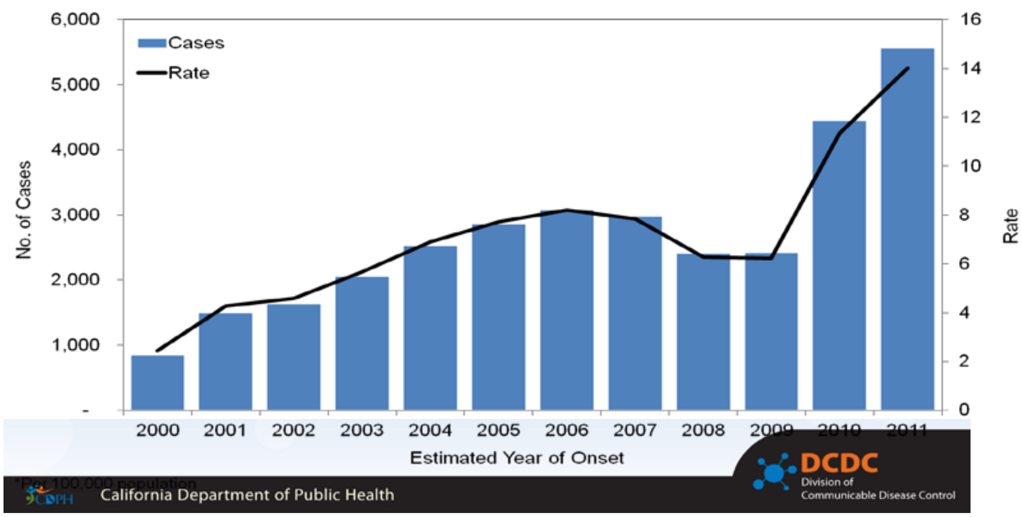
- Between 2001 and 2009 we averaged **23** admissions per year for coccidioidomycosis
- Beginning in 2009 we experienced an increase in cocci admissions, which became dramatic in 2011 (**52** admits) and 2012 (**45** admits to date)
- We observed a cluster of cocci cases from patients living in Avenal, CA, in late 2011 & early 2012
- The number of inpatients on a given day with cocci increased from 1-2 patients, to an average of **8-10** patients, and a max of **16** patients recently
- The outpatient Infectious Disease Clinic practice at Children's Hospital is now roughly **80-90%** cocci patients

California Department of Public Health Data

Gail Sondermeyer, MPH is the epidemiologist involved with the Mycotic Diseases Project at CDPH. Her report covered the 12 year interval, 2000-2011 whereas the Collaborative data covers the five year interval 2007-2011. Her incidence data was derived from the confidential morbidity reports sent to the state. The data included a caveat that the data was provisional because the de-duplication process at the state was incomplete. (The state may receive more than one report on the same case) She also wasn't able to separate readily the institutional cases from the community cases. As will be noted later, the gender and age distribution of the institutional cases skews the state gender and age distribution.

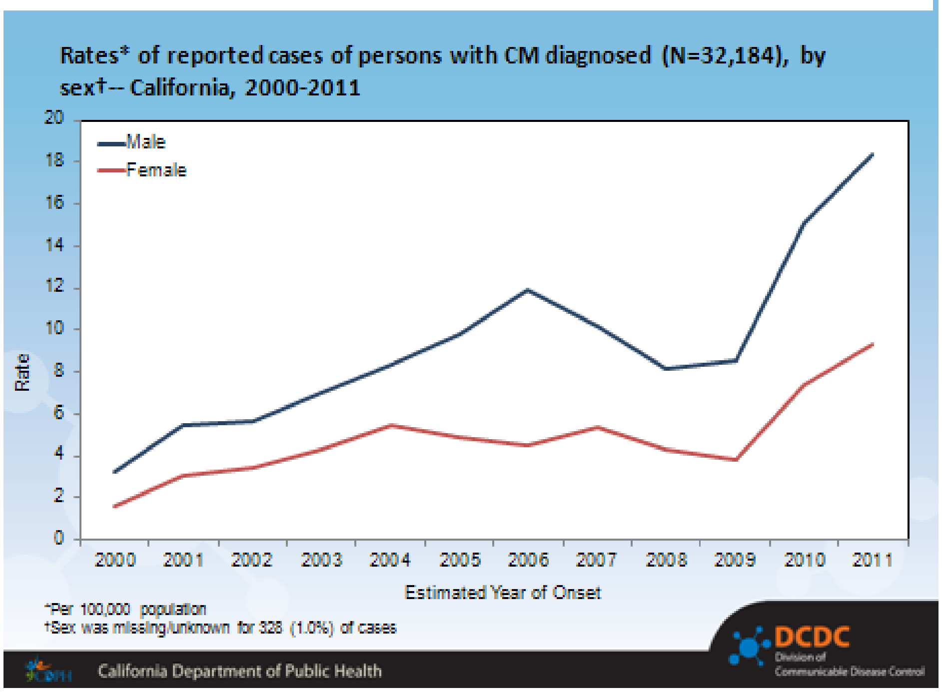
With a goal of making the CDPH data presented more accessible to those without training in epidemiology, the author has provided extensive comment on the data presented by Ms. Sondermeyer. He is solely responsible for these comments.

Numbers and rates* of reported cases of persons with CM diagnosed (N=32,184) – California



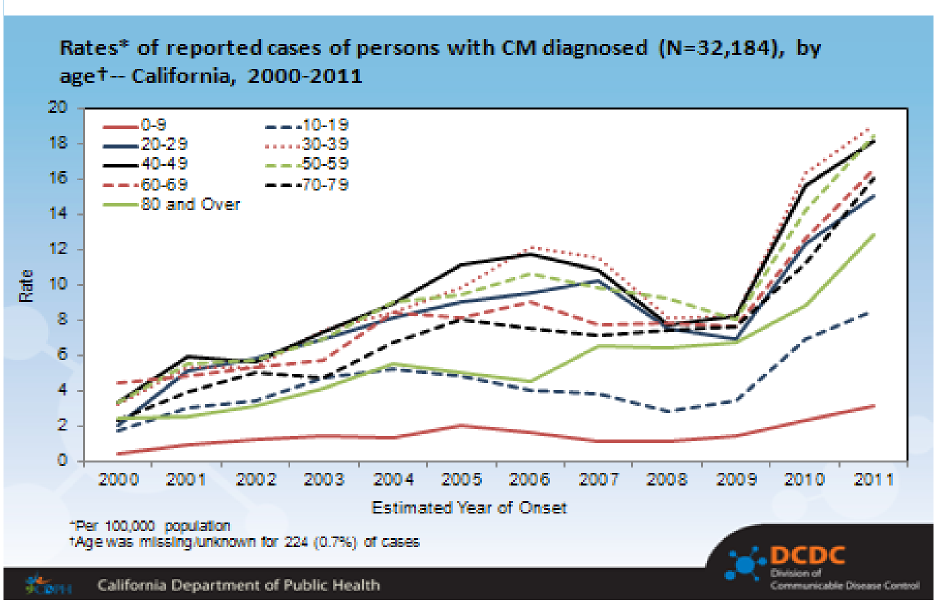
This preliminary data provides a time frame greater than twice that of the Collaborative study. The incidence rate rose steadily from 2000 through 2006. The changes in rate noted during this interval appear significant. All of the observed changes in rate over time in California remain unexplained. Beginning in 2010, laboratories were required to report positive specimens. California medical providers previously were the only mandated reporters. They may not consistently comply with this mandate. The new laboratory mandate has created some challenges for laboratories (Personal Communication: Demosthenes Pappagianis). We don't know how successful laboratories have been in reporting. Kern County has always had a large number of cases and has in effect had laboratory reporting for decades. Any significant changes seen in Kern County after 2009 would be unlikely due to the laboratory mandate. Regardless, it remains possible that the laboratory reporting mandate has contributed to the increased incidence seen after 2009. This would, of course, imply that all the rates prior to 2010 were low because of under-reporting artifact. (Provider diagnosed cases weren't counted because they weren't reported.)

NOTE: Provisional results from preliminary, partially de-duplicated CMR data



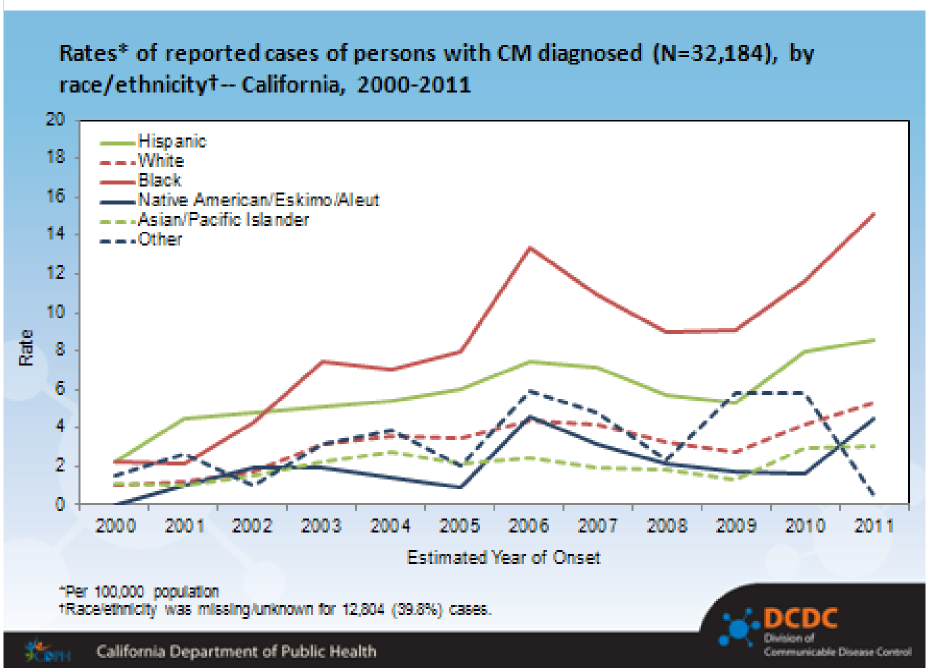
The rate of CM in males for the eleven year period consistently exceeded that of females. After remaining stable for the first four years the disparity in rates widened after 2004. This and the peak in male rates noted in 2006 are unexplained. Male prison inmates in California are over-represented in the Collaborative data. There was a very large outbreak of CM noted at Pleasant Valley State Prison in 2006. Observed changes in the rate of CM in males may be related to the high incidence of CM in California's male inmate population.

NOTE: Provisional results from preliminary, partially de-duplicated CMR data

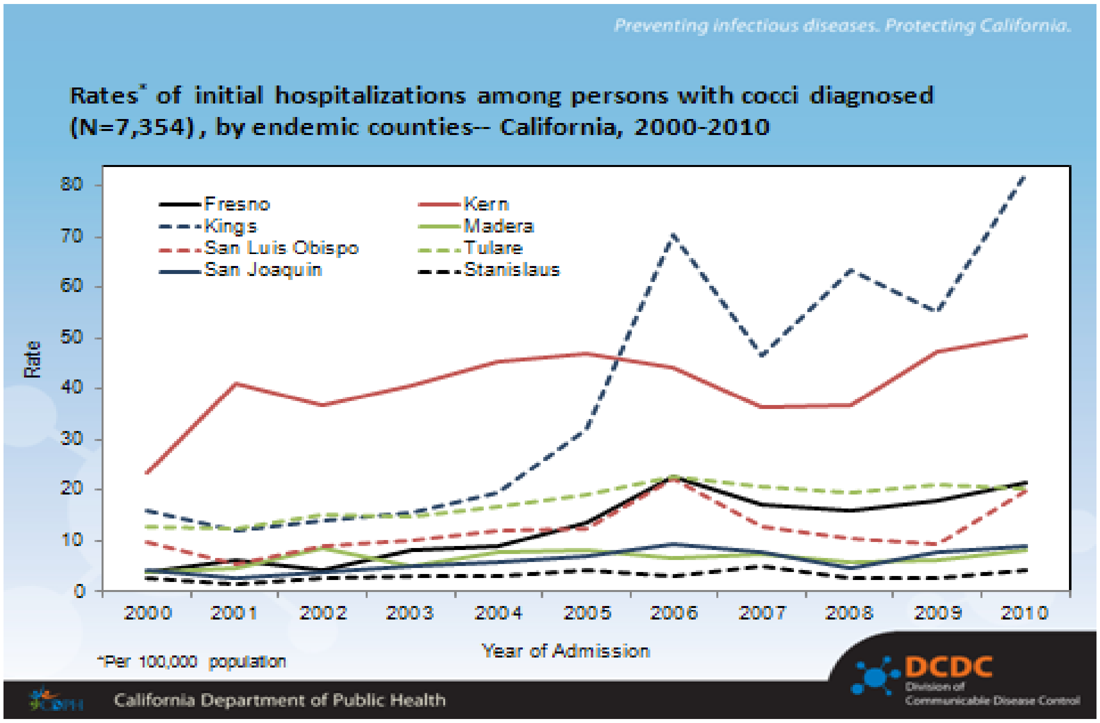


The increase in cases noted after 2009 occurred in all age groups. Those under age twenty are much less affected by CM. Those under age ten are the least affected. The age distribution of those groups little affected by institutional status didn't parallel the changes seen in other age groups. The 0-9 age group changed the least over the 12 year period and was consistently and significantly lower than the next age group 10-19. This teen to young adult group showed the most deviation from the remaining, older groups. Only this age group began falling in 2003, four to five years before the older groups. All age groups except the youngest rose rather dramatically after 2009.

NOTE: Provisional results from preliminary, partially de-duplicated CMR data

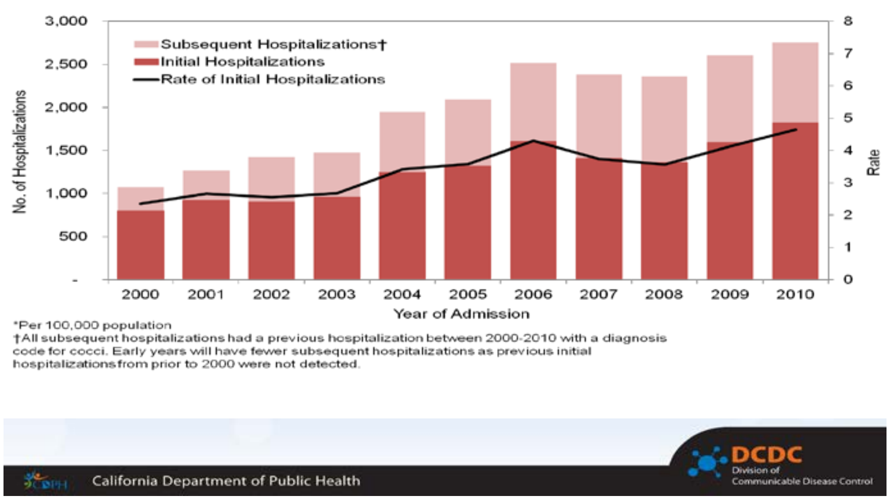


The collection of race/ethnicity data is incomplete. It is unknown if this introduces significant bias. Some observed rates in some groups, e.g. Native American/Aleut, probably are unstable because of the small numbers involved. The distribution of cases by race/ethnicity over the eleven year period appears relative stable with the exception of the rate in African-Americans. The rate rose dramatically after 2001 and for the remainder of the reporting period remained significantly about the other racial/ethnic groups. The rise in the African-American rate noted after 2001 is unexplained.



Numbers and rates* of initial and subsequent† hospitalizations among persons with cocci diagnosed (N=21,915) -- California, 2000-2010

The data covers eleven years. Seven of the counties selected are in the San Joaquin Valley. San Luis Obispo is on the central coast. Kern County is the most endemic county in the state; the high initial hospitalization rate in Kern is expected. Hospitalization rates in Kings County are somewhat unstable due to small numbers. For example, the population of Kings County is only 19% that of Kern. The high incidence of inmate cases may influence the hospitalization rate in Kings County.



Again, the data covers an eleven year interval. As was the case with hospitalizations in the endemic counties, hospitalization rates tend to trail the disease incidence rates. The incidence rate spike noted in 2010 is not reflected in the initial hospitalization rate in 2010. Noting the caveat regarding repeat hospitalization data, the proportion of hospitalizations that were not initial, remained stable over the ten year interval. The trailing of initial hospitalization rates of the incidence rates is unexplained.

Total charge for all hospitalizations of persons with cocci diagnosed (N=20,129), by expected source of payment category -- California 2000-2010

	Percent of Hospitalizations	Total Sum	Ave. Annual Sum
Government*	60.1	1,155,998,651	105,090,786†
Private Coverage	32.8	620,390,711	56,399,156
Medi-Cal*	24.0	487,613,428	44,328,493
Medicare*	23.8	470,100,789	42,736,435
Other Government*	8.0	142,200,735	12,927,340
Self-Pay	5.0	77,492,531	7,044,776
County Indigent Programs*	4.3	56,083,699	5,098,518
Workers Compensation	1.0	16,013,382	1,455,762
Other Indigent	0.5	7,251,723	659,248
Other Payer	0.5	7,780,506	707,319
Invalid/Blank	<0.1	373,238	93,310
Total		**1,885,300,742**	**171,390,977**

*Government combines charges for Medi-Cal, Medicare, Other Government, and County Indigent Programs.
†The range of the average annual sum of charges for All Government was (33,201,594-155,463,637). The minimum charge is from year 2000 and the maximum from year 2009.

California Department of Public Health

DCDC Division of Communicable Disease Control

Hospital charges do not necessarily reflect payments made. The distributions of the charges for CM by expected source of payment are probably reflective of the distribution of charges for many other clinical conditions. Even if the payment were only half of the charges, the $86,000,000 cost of hospitalization per year appears significant. This cost due to hospitalizations doesn't reflect other medically related expenses or other nonmedical costs such as lost work days due to illness.

Part Two

Collaborative Methodology

The study period was the five year interval 2007-2011. The epidemiology data used in this report was collected in a standardized format. Each of the 15 counties was asked to provide the number of cases and the incidence rates by year. The number of cases and the rates were subdivided into community and institutional cases. The institutional cases were those who were residents of a state or federal facility. The gender, age and race/ethnicity distribution of the total cases by year was provided. Finally, the distribution of cases by city or region by year was provided. With few exceptions, each of the 15 counties provided the data in the standardized format. The counties typically obtain the data from reports sent to them by clinical providers and laboratories.

Coccidioidomycosis is a reportable disease in California. Physicians and other health care providers are required to report the disease to their local health department. Since 2010 clinical laboratories have a duty to report positive tests. Health care providers report the cases through a Confidential Morbidity Report (CMR). Laboratories provide only a copy of the clinical laboratory report. The clinical and demographic data available on the CMR is much more complete than that available on the clinical laboratory report. For epidemiology purposes the state has criteria for cases, the case definition. The criteria changed during the study period. The case definition has both clinical and laboratory elements. One high incidence county uses only laboratory criteria. The other counties use both clinical and laboratory criteria but may vary in how strictly they adhere to the case definition criteria.

The date of a case may be date of CMR or laboratory report, date of diagnosis or date of onset. The latter is often missing or unreliable. The interval between illness onset and either diagnosis or date of CMR can be long due to delays in patients seeking medical care or delays in diagnosis after accessing medical care. The dates probably can't be relied on too precisely to estimate the date of infection. The delays are not necessary uniform across the counties. These differences in dates may explain some of the observed variance seen between the counties in observed incidence rates over time.

Cases are reported and counted by county of residence. Infection may have been acquired in a location outside that county. The CMR data does not include any travel history. We are unable to estimate to what extent the county of infection fails to correspond with the county of residence. For the period 2007-2011 Amador County reported eight cases of coccidioidomycosis. All were institutional cases. The Health Officer of Amador has opined that all the cases were infected outside of Amador County. (Personal Communication.) Other cases included in this report may not have been acquired in the reporting county.

Table: 1:
Rank Order of Collaborative Counties by Total Cases 2007-2011

County	5 Yr Cases	Mean #	Range #	Mean Rate	Rate Range
Kern	7,759	1,552	598-2,734	186	72-322
Fresno	2,723	545	309-726	57	33-75
Kings	1,198	240	147-350	155	97-223
Los Angeles	1,083	217	145-304	2.2	1.5-3.1
Tulare	1,003	201	175-231	44	40-51
San Diego	649	130	85-157	4.1	2.7-4.9
San Luis Obispo	633	143	87-227	47	33-84
Riverside*	334	67	48-85	3.1	2.2-3.9
Ventura	300	60	47-77	7.4	5.8-9.6
San Joaquin	285	57	27-123	7.7	3.7-16
Monterey	225	45	26-69	10	6.1-16
San Bernardino	224	45	22-75	2.1	1.0-3.4
Stanislaus	166	33	17-62	6.0	2.9-11
Merced	150	30	13-54	12	5.1-21
Santa Barbara	110	22	12-32	5.1	2.8-7.4

*Riverside County: number of cases and rate for 2011- CDPH Center for Infectious Disease: Yearly Summary of Coccidioidomycosis in California, 2011.
Rate per 100,000

The 15 participating counties include all of the San Joaquin Valley counties except Madera; all of southern California except Orange and Imperial; and all the central costal counties. These 15 counties reported 16,843 cases during the five year period, 2007-2011. Forty six percent of these were reported in Kern County. Four of the top five counties by reported number of cases are located in the San Joaquin Valley. These four counties along with San Luis Obispo are the top five counties by incidence rate. A substantial number of the remaining cases were reported in counties outside the San Joaquin Valley.

The top five counties by mean incidence rates in 1991-1993 were Kern, Tulare, Kings, San Luis Obispo and Monterey. Three of the counties had higher incidence rates observed than in the current study: Kern 384/100,000; Tulare 77/100,000; and San Luis Obispo 60/100,000. The rate in Monterey County was about the same at 11/100,000. The four year interval was chosen to bracket an outbreak so any comparisons of rates should be approached with caution. The comparison of the rates does suggest that the current rates are not historic highs.

There may be a bias in the data. Under-diagnosis and under-reporting in California may result in a falsely low estimate of the number of cases in California. If that is the case, CM may be more likely to be diagnosed and reported in the counties known to be more endemic. Correction of the diagnosis/reporting bias likely wouldn't alter the ranking significantly but would likely lessen the disproportionate number of cases in the more endemic counties. The proportion of Kern County cases in the Collaborative data is smaller than that observed in the 1990s outbreak, 46% vs.70%. In the early 1990s Kern County providers had over fifty years experience with CM. It's tempting to speculate that the decrease proportion of Kern cases is due to improved diagnosis of the disease in the other counties.

The percent of cases that are institutional/inmate varies dramatically from 63% in Kings County to 0% in Tulare County. Nineteen percent of the Collaborative cases were institutional. Inmate cases are disproportionately represented in the Collaborative data. The institutional cases skew the gender and age distribution of the Collaborative cases. Inmate cases likely also affect the race/ethnicity distribution of Collaborative cases. With some exceptions, the institutional cases will be discussed separately.

For unexplained reasons, the observed incidence of coccidioidomycosis in most of the 15 counties varied significantly over time. Tulare County and Ventura County showed the least year to year variance. Some of the variance may be random especially in those counties with relatively few cases per year. The average incident rates noted in this study should be viewed with caution. The range of the rates is provided to remind one of the variance. The observed incidence rate in California has previously been noted to fluctuate significantly over long intervals. The previously noted spike in cases noted in the early 1990s is an example. The incidence rates noted in this five year study may not be representative of rates observed over longer intervals.

As was noted previously in the eleven year California data, the total number of cases in the fifteen counties increased remarkably after 2009. Figure 2 demonstrates that the observed increase occurred primarily in the community cases. The institutional curve differs markedly from the community curve. This difference remains unexplained.

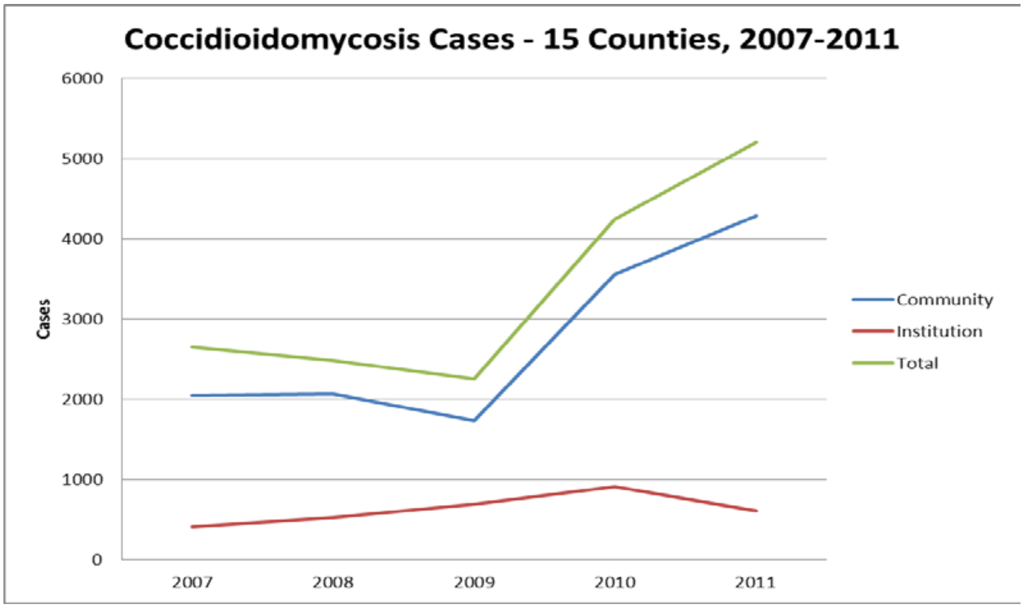


Figure 2

The increase in rates was fairly uniformly distributed in Kern County but not so in San Joaquin, Fresno, Kings or Los Angeles counties. In the three San Joaquin Valley counties the increase in cases was predominately on the western sides of the counties. In Los Angeles, most of increase was observed in the Antelope Valley.

Ten of the fifteen counties have cities or regions with consistently higher rates of CM. In Ventura County there are no clear hot spots although there is a tendency toward an increased rate in Simi Valley. Santa Barbara, San Bernardino and Riverside show no clear increase by city or region. Stanislaus provided no data by city or region. With the exception of Stanislaus and Tulare, all the San Joaquin Valley counties are significantly more endemic on the western side of the county. In Tulare, the south eastern portion of the county is more endemic. In Los Angeles County, the Antelope Valley is the most endemic area of the county. The San Fernando Valley is also more endemic but significantly less so than the Antelope Valley. Both San Luis Obispo and Monterey Counties are more endemic on the inland, eastern sides of the counties. In San Diego, there is a relatively small enclave in the south western corner adjacent to Mexico that appears to be more endemic.

In the majority of the fifteen counties, the risk for CM appears to be spotty within the county. The absolute risk of an area tends to be relative. The risk in the highly endemic area of Merced County remains less than the risk in a relatively low risk area of Kern County. For all the counties north of Kern County, the risk of CM decreases with more northern location.

Summaries of the data by county are available in the Supplement section of this report.

Gender Distribution 15 Counties, 2007-2011

The gender distribution of the cases is 66% male and 34% female. In some counties the high proportion of male inmate cases markedly affects the gender distribution. In Fresno County 84% of the cases were male. In Tulare County with no institutional cases, 58% of the cases were male. When the gender distribution for the cases is adjusted by the removal of all inmate cases the adjusted gender distribution for the 15 counties is 59% male and 41% female. (93% of the prison population of California is male.)

In four of the counties males represented 70% or more of the cases after adjusting for inmate cases. This could be a random event in the two counties with relatively few total cases over the five years: Stanislaus (n=73) and San Bernardino (n=130). The higher number of total cases in Riverside (n=261) and San Joaquin (n=285) argue against randomness as an explanation. (Riverside reported cases only for 2007-2010. Although there are two state prisons in Riverside Co., they reported no institutional cases.) If the disproportionate number of male cases in these four counties isn't random, the observation remains unexplained.

The disproportionate number of male cases in the 15 counties is inconsistent with the more recent gender distribution noted in Arizona. In 2011 only 42% of the Arizona cases were male. Prior to 2009 in Arizona the cases were disproportionately male.

The literature has previously and consistently noted that males are disproportionately reported with CM. It is not known if this is due to increased exposure, either vocational or recreational or to innate gender-dependent increased risk. It is known, given all patients diagnosed with CM, male gender is a recognized risk factor for disseminated disease.[21] [25] The gender distribution of the cases following the earthquake-related outbreak in Ventura County was 57% male and 43% female. The dust exposure due to the earthquake's landslides could be viewed as a natural experiment with a point source exposure.

Age Distribution 15 Counties, 2007-2011

The cases in the fifteen counties aren't evenly distributed by age groups. (See Table 2 and Table 3.) The 25-64 year old cohort is over-represented in the cases. They had 70% of the cases but represented only 53% of the population. Those less than 25 years old were under-represented as cases. They were 35% of population but had only 19% of the cases. The finding of less reported disease in the younger population is consistent with the consistently lower rate of disease in the under-twenty population noted in California for the eleven year period 2000-2011.

Younger persons may be at less risk of disease because of less exposure time due to age or their activities. They may also be at less risk of developing clinical disease after their exposure. That is, they may better tolerate infection and be disproportionately represented in the infected but asymptomatic outcome group. The under-representation of younger persons remains unexplained.

Table 2:

Percent and Number of Cases by Age Distribution, 15 Counties 2007-2011

Age Group	<15	15-24	25-44	45-64	65+
Number	1040	2176	6259	5228	1817
Percent	6%	13%	38%	32%	11%

Number of cases by age distribution < Total cases reported due to missing age data,

No age distribution data for Riverside Co. available for 2011.

Table 3:

Age Distribution of 15 Collaborative Counties, US Census 2010

Age Group	Percent of the Population
<15	22%
15-24	16%
25-44	28%
45-64	24%
65+	11%

Population of 15 Collaborative Counties= 22.7 million

Due to the high number of inmate cases, the age distribution of cases in the 15 counties should be influenced by the age distribution of inmates. The age distribution of inmates differs significantly from that of the general population. None of the institutions in the 15 Counties is a youth facility. In the 15 county data few if any of the inmates are under age 18. Eighty-six percent of the CDCR population is under the age of 50 years. (See California Institutional Population Estimates in the Supplement Section.)

In table 4 the age distribution of the eight counties with few inmate cases is noted. When compared with the age distribution in Table 2 the age distribution shifts toward the right, i.e., into the older age groups. The percent of cases noted in the oldest age group almost doubled.

Table 4:

Percent and Number of Cases by Age Distribution, 8 Counties with Few Institutional Cases

Age Group	<15	15-24	25-44	45-64	65+
Number	164	339	1035	1337	755
Percent	5%	9%	29%	37%	21%

Eight Counties: Los Angeles; Merced; San Diego; Santa Barbara; Stanislaus; Tulare; Riverside; Ventura.
Number of cases by age distribution < Total cases reported due to missing data.
No age distribution data available for Riverside for 2011.
3% of San Diego cases were institutional. One case in Ventura was institutional.

Only 22% of the cases reported occurred in the eight counties with few institutional cases. The age distribution observed could be somewhat more random because of the relatively smaller number of cases in the individual cells. In Table 5 the influence of inmate cases is again noted in the seven counties with the largest number of cases.

Table 5:
Mean Incidence Rates by Age Groups, Selected Counties, 2007-2011.

Age Group	<15	15-24	25-44	45-64	65+
Kern	71.4	168.8	251.0	234.5	158.6
Fresno	15.4	41.4	87.0	75.6	32.8
Kings	47.4	87.5	213.1	278.1	72.8
Los Angeles	0.2	1.2	2.0	3.8	9,5
Tulare	15.6	28.5	55.7	67.9	67.7
San Diego	N/M	2.3	3.9	5.8	9.5
San Luis Obispo	N/M	26.2	53.9	71.6	52.9

Counties with > 500 cases reported 2007-2011
Rate per 100,000
N/M – Nonmeaningful, the estimated rates are unreliable.

Although Kings is known to be less endemic than Kern, the mean incidence rate for the 45-64 year old age group in Kings County exceeded that of Kern County. The mean incidence rate for the next youngest age group closely approximated that of Kern. In Kings County where the inmate cases represented 63% of the cases for the period 2007-2011, the age distribution of the inmates affected the observed age group specific incidence rate of the county. Fresno County had higher mean incident rates than Tulare County only in the three middle age groups. There were no institutional cases in Tulare County while 56% of the Fresno cases were institutional. This suggests that the institutional cases in Fresno County influence the observed age group incidence rates in Fresno. Inmate cases could have some influence on the age-group specific incidence rates in Kern and San Luis Obispo Counties. The percent of inmate cases in both counties was much lower, 9% and 14% respectively, than seen in Kings and Fresno Counties and any effect would be harder to detect with the Collaborative data.

The three counties in Table 5 where institutional cases weren't a factor, Los Angeles, Tulare and San Diego, may best indicate the role of age in the acquisition of CM in California. Age specific incidence increases with age up to around 65 years of age. This is similar to what was observed in Arizona in 2010. It has been suggested that Arizona has a larger population of older adults at risk for CM. Large populations of older adults without prior CM exposure retire and move to Arizona, the so-called snow birds. This could explain any differences between the two states in the observed risk in retirement age individuals.

Race/Ethnicity Distribution 15 Counties, 2007-2011

Race is known to be a risk factor in coccidioidomycosis outcomes. The risk of dissemination in people of African or Filipino decent is accepted. The estimates of excess risk vary but for both groups are almost certainly increased by a factor greater than five. In a 1997-2002 hospitalization study, race was found to be an important variable in hospitalizations for CM. When looking at all of California, relative to non-

Hispanic whites, African-Americans had two and a half times the risk of being hospitalized. Asians/Pacific Islanders in California had only 80% of the risk of being hospitalized compared to non-Hispanic whites. The risk of hospitalization of Asians/Pacific Islanders was 1.62 times that of the reference whites when only the residents of Kern, Tulare, Kings and San Luis Obispo were studied.[12]

Whether race/ethnicity is a risk factor for the acquisition for any form of CM is less clear. The Collaborative data doesn't provide any new information on disease severity or risk of acquisition by race/ethnicity. The severity of disease of any of the reported cases wasn't part of the methodology adopted by the Collaborative. As many as 8% of all cases will disseminate [13], many of them will be reported before they disseminate. A significant number of cases in California are reported without clinical data available.

Race and ethnicity data for the fifteen counties were frequently missing or unknown. Fourteen counties provided race/ethnicity data. One of these suppressed three or more R/E categories. Of the fourteen counties who provided any R/E data, of the 15,965 cases reported, 37% were reported with missing or unknown data. The mean percent of missing R/E data by county was 25%. The range was 2% to 63%. Kern County had the highest rate of missing or unknown R/E data. Thirteen counties with less than three suppressed R/E categories reported 9,908 cases with known race/ethnicity. African-American cases represented 13% (n=1296) of these case. Of the African-American cases 53% were reported out of Fresno and Kings Counties where institutional cases were high. Fresno, Kings, Kern and Los Angeles Counties accounted for 85% of the African-American cases in the Collaborative data. Five percent (n=503) of the cases were Asian/Pacific Islanders. Kern, Los Angeles and San Diego Counties together accounted for 56% of these cases. Fifty percent (4908) of the cases where R/E was known were Hispanic. Thirty-three percent (n=3301) were White. Six percent (n=588) of the cases were Other/Multi-race. Native American numbers were frequently suppressed in the data because of small numbers. There were only 21 cases in Native Americans reported in this data. Two-thirds of these were reported out of Kings and Kern Counties.

In this report, the assessment of the risk of acquisition of disease is complicated by several other issues besides missing race/ethnicity data. Some racial groups are under-represented in the most endemic areas of the state. The observed lower risk of hospitalization among California's Asian/Pacific Islanders noted above likely reflects their under-representation in the most endemic areas. In highly endemic counties their risk of hospitalization is higher than non-Hispanic whites. The risk of acquiring disease within counties often isn't geographically evenly distributed and the racial/ethnic composition of some towns in a county may not reflect that of the county. The race/ethnicity of the population of highly endemic towns would be a preferred reference population when estimating risk by race/ethnicity of acquiring disease. In some counties, the inmates' high incidence rates may distort the observed racial/ethnic distribution of cases in the county. As has been noted with the gender and age distribution, inmate cases may not reflect the race/ethnic composition of the community cases.

The experience of the United States Armed Services may provide a perspective free of some of the previously noted challenges. The study design involved only active duty service personnel captured in the routinely maintained Defense Medical Surveillance System. Four hundred eighty-three incident cases during the period 1999-2011 were included. With white, non-Hispanics as the reference population both African-Americans and Hispanics had a relative risk of approximately 1.70. (Their risk of acquiring disease is 1.7 times that of the reference population.) The relative risk for the Asian/Pacific Islander service personnel was 3.53. This data would suggest that both Hispanics and African-Americans are at modestly higher risk of acquiring any coccidioidal infection compared with white, non-Hispanics. The risk for Asian/Pacific Islanders is twice that of the African-Americans and Hispanics.[19] Race/ethnicity challenges is further discussed later in this report in the context of four populations in Kings County.

Nonparticipating Counties

California has 58 counties. While the 15 counties in the Collaborative represented most of the more endemic counties, other California counties with either moderate rates or number of cases didn't participate. Eight of these counties are listed in Table 6. The counties are ranked by total cases for the period 2007-2011.

Table 6:
Coccidioidomycosis Cases and Rates, 2007-2011
Selected Nonparticipating Counties Ranked by Number of Cases

County	5 Yr. Total Cases	5 Yr. Mean Rate
Orange	276 cases	1.8
Madera	158 cases	20.4
Santa Clara	155 cases	1.7
Alameda	108 cases	1.5
Contra Costa	98 cases	2.4
Sacramento	97 cases	1.3
Solano	47 cases	2.2
Imperial	37 cases	4.1

Rate per 100,000
Data Sources - CDPH Center for Infectious Diseases:
Coccidioidomycosis Cases and Rates by Health Jurisdiction, California 2006-2010.
Yearly Summary of Coccidioidomycosis in California, 2011.

These eight counties reported 976 cases in the five year period, 2007-2011. Madera County, located in the San Joaquin Valley between Merced and Fresno Counties, had the sixth highest mean incidence rate. Orange County in southern California would have had the eleventh highest number of cases for the five year period. The observed mean incidence rates of the eight counties are similar to many of the lesser endemic Collaborative counties.

Imperial County in California and neighboring Yuma, Arizona share a similar desert climate. Both areas have much lower observed incidence rates than those observed in Phoenix and Tucson. The putative missing cases remain unexplained. Somewhat incidentally, at the Collaborative meeting Imperial County reported on a survey of providers in Imperial County. They noted that Imperial County considers itself an endemic county with an observed incidence rate of 1.8-6.3/100,000 for the period 2006-2010. Because of a concern that the low incidence rate could be due to under-testing, under-diagnosis or under-reporting, in 2011 Imperial County conducted a study of provider attitudes about CM. One hundred two local providers were surveyed. Only 23% of the providers believed CM was a problem in California. Only 43% of the surveyed providers considered CM as a potential diagnosis in patients with respiratory symptoms.

A substantial number of cases of CM were seen in the five years period in residents of counties not typically thought of as endemic. It is unknown if all or most of the infections were acquired in the county of residence. Clinical providers in these counties may be more likely to miss the diagnosis than providers in the more recognized endemic areas of the state. Clinical providers in these counties may believe that CM is rare in their county and that they needn't consider CM as a cause of their patients' clinical illnesses.

Cases and Rates

Endemic counties are typically considered those counties with relative high rates of CM, cases per population. With the exception of San Luis Obispo the highly endemic California counties are clustered in the San Joaquin Valley. As was noted in the outbreak of the early 90's and in the present study, a number of less endemic counties have more cases than the endemic counties. Most of these counties have large populations. As noted previously, in the more endemic counties there may be a diagnosis bias present. Reports are by county of residence and some cases may not have been acquired in the reporting county. Some of the explanation likely is due to the larger population of people at risk in the large population counties.

When hospitalizations are counted instead of cases, the less endemic counties are again over -represented. The burden of hospitalizations for CM in California by county is not proportional to the reported cases by county. Sondermeyer, et al defined six counties as endemic: Kern, Tulare, Kings, Fresno, Madera and San Luis Obispo. For the period 2000-2011, these counties were the county of residence for 48.8% of the initial hospitalizations in California. [26] For the same period these six counties accounted for 76% of the reported cases in California.[2,4,5] Flaherman, et. al., reported on California CM hospitalizations by place of residence for the period 1997-2002.[12] Six counties outside the San Joaquin Valley accounted for 39% of the hospitalizations: Los Angeles; San Diego; Riverside; San Bernardino; Ventura; Orange. The six counties reported only 18% of the cases in California for the same period. [2,3,4] Neither study addressed this mismatch between hospitalizations and reported cases by county of residence. If hospitalization were positively correlated with improved diagnosis, under-diagnosis of CM would appear to be more of a problem in the less endemic areas of California. There may be other explanations for the apparent mismatch between hospitalizations and reported cases in the two time intervals noted.

Institutional Cases

Thirteen of the fifteen Collaborative Counties have one or more state or federal institutions. Two counties provided no institutional data. For the five year period 3,119 or 19% of the cases reported were inmates of state or federal institutions. The estimated state and federal institutional population in 2010 was 156,179. (See Institutional Population Estimates in the Supplement.) The remaining 81% of the cases were distributed among the 22.7 million community members in the 15 counties. In Fresno and Kings Counties the inmate cases represented over half the cases reported for the period 2007-2011. No other state has reported a disproportionate number of cases in institutional residents. For the purposes of this study, relatively few of the institutional cases were mental health inpatients with no criminal justice connection. (See Institutional Population Estimates.)

The Collaborate data allows a comparison of the observed rate of disease of the inmate cases vs. the noninstitutional cases in the county. The comparison of these rates for the six counties with more than twenty-five inmate cases is noted in Table 7.

Table 7:
Institutional Mean Incidence Rate Compared with Community Rate, Selected Counties*, 2007-2011

County	Institutional Mean Rate	Range	Community Mean Rate	Range
Fresno	4,017	2724 - 4500	25	11 - 38
Kings	805	442 – 1,370	66	44 - 114
Kern	411	138 - 678	177	69 -308
San Luis Obispo	149.1	65-210	41.2	28-68
Monterey	126.9	51-210	7.1	5-11
San Bernardino	80.9	10-250	1.7	0.9-2.5

Rate per 100,000
*Counties with > 25 institutional cases 2007-2011.

The collaborative methodology involved the reporting of cases as either community or institutional. Only cases residing in state and federal institutions were to be considered institutional cases. All rates were referenced to 2010 US Census population estimates, regardless of the year of the case. Although moderate variance is noted year to year and county by county, the observed institutional rates consistently and significantly exceed each county's observed community rate. In Kern County, where due to their number of cases the observed rates are the most stable, the ratio of the institutional rate to the community rate was 2.3 for the five year study period. The methodology used by the Collaborative may not have been used the best estimates for the inmate population.

Under a federal court over-crowding mandate, the state inmate population declined significantly during the five year interval, 2007-2011. The total CDCR population of all prisoners declined 12 %. The decline wasn't uniform across years or prisons. Over the five year study period, the inmate population of the prisons in Kings County declined by 17%. One of the three prisons, Avenal State Prison, declined by 25%. Over the five year interval the population of Pleasant Valley State Prison in Fresno County declined by 14%. The use of the 2010 U.S. Census data to estimate the average prison population may underestimate the prison population. This may have resulted in a somewhat higher estimate of institutional incidence rates.

The methodology used by the Collaborative readily permits the comparison of institutional incidence rate with the county's community incidence rate. This may not be the most meaningful comparison and may tend to exaggerate the estimate of the risk for CM attributable to inmate status. The risk of acquiring CM in most counties is not evenly distributed within the county; some areas of the county are more endemic than others. Comparing the observed incidence rate in the communities adjacent to the institutions should permit a better estimate of the attributable risk of inmate status.

Table 8:

Comparison of Selected Institutional Incident Rates with Adjacent Communities – 2007-2011

Community/Institution	Mean Incidence Rate	Total Cases
City of Delano	359	543
NKSP	610	168
KVSP	84	26
City of Wasco	356	249
WSP-Wasco	980	295
City of Taft	320	229
Taft FP	1,070	107
City of Avenal	411	188
ASP	2,195	648
City of Coalinga	513	349
PVSP/CSH	4,017	1519

Rate per 100,000

Table 8 lists the average incidence rates and the five year total number of cases in five cities in three counties. Each city is followed in the list is followed by one or more institutions located near the city. In the case of Coalinga, separate rates for the two adjacent institutions aren't available and the average rate represents that of the two institutions combined. In every case but one, the average institutional rates exceed the city rate. In the three Kern County cities: Delano, Wasco and Taft, the average rate was approximately twice the average rate of Kern County. In three of the four institutions, the institutional rate was two to three times that of the city. In highly endemic Kern County the choice of comparison community appears to make relatively modest difference.

There are three prisons in moderately endemic Kings County. One is located in a highly endemic area of the county. The incidence rates in both the City of Corcoran and the two prisons in Corcoran are much lower than that observed in Avenal. The average rate at Avenal State Prison was six times that of the City of Avenal. When the institutional rate in Kings County was compared with the county community rate the institutional rate was twelve times that of the community rate.

In lesser endemic Fresno County, the choice of comparison community makes a major difference. The average institutional incidence rate in the two institutions is almost eight times that of the adjacent city of Coalinga. When the comparison community is the non-institutionalized population of Fresno County, the institutional rate is 160 times that of the community. Inmate status in California is a significant risk factor for being reported with CM. The selection of an appropriate comparison community should improve the estimate of the degree of excess risk due to inmate status. The low rate noted at Kern Valley State Prison (KVSP) is unexplained.

KVSP had a five year average population of 4,760. The anomaly isn't due to small population size. The CDCR reception center, where the average length of stay is expected to be less than 90 days, is located at North Kern State Prison. The two state prisons are very close; they are located on the same street. This is the only known instance where inmate status appears protective. The observation could be a reporting artifact. The low rate of CM observed at KVSP probably deserves further study.

Diagnosis and Reporting Bias

Some of the excess observed rate in inmates may be the result of diagnosis or reporting artifact. There likely is no current means of exploring this supposition. There is reason to speculate that inmates with CM may be more likely to have the diagnosis established and reported.

It's likely that both clinical providers in the prisons and inmates are better informed about CM. The 2007 study of CM at Pleasant Valley State Prison recommended that inmates and staff be "frequently and repeatedly" educated about CM. This study was released on January 11, 2007. In June 2007 the Statewide Medical Director, Dwight Winslow, M.D. released a report titled: "Recommendations for Coccidioidomycosis Mitigation in Prisons in Hyperendemic Areas of California". Among many recommendations, the reports were specific about the utilization of high quality diagnostic laboratories and complete reporting of the cases diagnosed. There were many recommendations in the two reports. The CDCR hasn't issued any formal reports of any action taken to comply with the recommendations.

While neither report addressed provider education, it seems reasonable to assume that the medical providers within the prisons are aware that they are practicing in an endemic area and are skilled in the use of coccidioidal diagnostics. Educating inmates about CM may prompt them to access medical services. They may do so at a higher rate than would be seen in the general community where there may be more barriers to accessing care, e.g. financial. In most cases, CM is a self-limited disease. Community members may be more inclined to "tough it out" and not be diagnosed because they didn't seek care. Well informed inmates would be expected to be more likely to request CM testing than the general community. The author is aware of testing done on "inmate request." CM is thought to be commonly under-diagnosed in the general community. The prisons may be on the other side of the diagnosis bias. The issue of whether some of the excess observed incidence rate could be due to the higher likelihood of diagnosis in the prisons can not be resolved with the data available and will have to await studies involving the CDCR population. In the meantime it seems reasonable to assume that some of the excess observed rate likely is due to improved diagnosis within CDCR.

It is possible that the provider reporting of CM out of the prisons is more complete when compared with community providers. Dr. Winslow did include reporting in his recommendations. Laboratory reporting was mandated in California beginning in 2010. While prior to 2010 better reporting could have affected the observed rate difference, this is less likely after 2009. The hypothesis of improved reporting out of the prisons can't be tested with the data available.

Because of the observed inmate rates are so much larger than the community rates, even after adjustment for the best comparison population; it is unlikely that diagnosis or reporting bias would account for most of the excess rate seen in inmates. Inmates in the endemic areas may actually be at higher risk of acquiring CM. The 2007 report on CM in PVSP noted that only 19% of the inmates were residents of Fresno, Tulare, Kings or Kern Counties prior to incarceration. Twenty-nine percent were residents of Los Angeles prior to incarceration.

Introduction of CM Naïve Individuals

With some exceptions, the prison population in any facility or county may be significantly more transient than the surrounding community populations. The denominator in the calculated institutional rates may remain stable while the individuals making up the population in the denominator change. If the incoming populations are coccidioidal naïve, we would expect to see a higher rate than in the surrounding community, many in the community would be at low risk for disease because of prior infection. There may be more renewal of the CM naïve pool in the prisons than occurs in the adjacent communities. No data on this issue was presented at the Collaborative meeting.

Inmates as Innately at Higher Risk for Infection

Not withstanding the more recent experience in Arizona, males have traditionally been viewed as being at higher risk for CM. Essentially, all of the excess incidence rate has been seen in male inmates. Male gender could account for some, but probably not much of the excess observed rate in prisoners. This effect could even be offset by the younger age of inmates. The race/ethnicity of inmate population differs significantly from that of the comparison communities. African-Americans are over-represented in the prison population and there is data that suggests that African-Americans are at higher risk of acquiring CM. Again, this increased risk by race alone probably wouldn't account for the size of the excess risk. Inmates could be at increased risk because of the presence of other co-morbid diseases. The 2007 PVSP study noted that 23% of the inmate cases were hepatitis C affected and 16% had asthma. We have no comparison data on co-morbid conditions of inmates and the communities. Inmates very likely are disproportionately affected by hepatitis C but this condition is not known to be a risk factor for CM.

Estimated Incidence Rates in Four Populations in Kings County by Race/Ethnicity

A look at the observed incidence rates of four Kings County populations may illustrate the challenges involved in estimating the incidence of CM in various racial/ethnic groups in California. Two variables independent of race/ethnicity are known to affect the risk of acquiring CM. Within most counties there are areas that are more highly endemic than others. State and federal inmates are known to have an increased risk of acquiring CM in California. There are three state prisons in Kings County. One is located in a highly endemic area. The other two are located in a less endemic area. The recent US Census was conducted within the five year study period. The estimates of race/ethnicity now available are relatively recent. Inmate data can be broken out from the demographic data on both cities. When reviewed without including any inmate data, both cities are predominately Hispanic by ethnicity and the various non-Hispanic racial groups in the cities are small.

Table 9:
Populations of the Cities of Avenal and Corcoran by Race/Ethnicity – 2010

Race/Ethnicity	Avenal, n=9,142	Corcoran, n= 13,766
Hispanic	8,328 (91.1%)	10,938 (79.5%)
White- NH	633 (07.0%)	1,991 (14.5%)
Black- NH	48 (0.6%)	466 (03.4%)
Native Am.- NH	21 (0.3%)	61 (0.4%)
Asian- NH	52 (0.6%)	145 (01.1%)
HPI – NH	1 (<0.1%)	3 (<0.1%)
Other – NH	4 (<0.1%)	21 (0.15%)
2 or More - NH	55 (0.6%)	141 (01.0%)

NH – Non-Hispanic
HPI – Hawaiian/Pacific Islander
US Census Data

For the five year interval, 2007-2011, there were 188 community cases reported out of the City of Avenal. During the same interval only 53 community cases were reported out of the City of Corcoran. The mean annual incidence rate in the City of Avenal, 411/100,000, was more than four times that of the mean annual incidence rate of the City of Corcoran, 97/100,000. In Avenal, 137 of the cases reported were Hispanic; 51 of the cases were non-Hispanic. The mean annual incidence rate in Hispanics in Avenal was 329/100,000. The mean annual rate in Avenal non-Hispanics was 1,252/100,000. The rate observed in the non-Hispanics is likely unstable because of the small number of cases and the relatively small population of non-Hispanics in Avenal. Any rate estimates of the subgroups within the non-Hispanic population would be unreliable. In the City of Corcoran thirty-three cases were Hispanic while twenty were non-Hispanic. Because of the small number of cases observed, rates by ethnicity in the City of Corcoran would be unreliable and comparison of rates by ethnicity would be inappropriate. The rates generated would be unstable and unreliable, i.e., any observed difference could easily occur by chance alone.

Because the inmate population decreased significantly during the five year study interval, the use of the 2010 US Census would tend to underestimate the size of the prison population. The observed rates may be somewhat high because the 2010 census estimate of the population likely is low. This should affect all race/ethnic groups equally. The actual count of under-represented individuals is preserved in the census data.

Table 10:
Race/Ethnicity of the Prison Population of Kings County- 2010

Race/Ethnicity	ASP – n=6,423	CSP-Cor & SATF – n=12,118
Hispanic	2,844 (44.3%)	5,451 (45%)
White-NH	1,770 (27.6%)	2,976 (24.6%)
Black-NH	1,492 (23.3%)	3,197 (26.4%)
Native Am.-NH	61 (0.1%)	81 (0.7%)
Asian –NH	50 (0.8%)	42 (0.3%)
HPI – NH	3 (<0.1%)	8 (0.1%)
Other-NH	197 (3.0%)	337(3.0%)
2 or More-NH	10 (0.1%)	26(0.2%)

NH – Non-Hispanic
HPI- Hawaiian/Pacific Islander
UC Census Data

The race/ethnicity distributions of the two inmate populations in the prisons are similar but differ significantly with that of the communities where the prisons are located. The prison populations are much less Hispanic than the adjacent communities. During the interval 2007-2011 there were 648 cases reported out of Avenal State Prison and 106 cases reported out of the CSP-Corcoran combined with those out of the Substance Abuse Treatment Facility in Corcoran. The mean annual incidence rate at ASP was 2,018/100,000. The mean annual incidence rate for the two Corcoran prisons combined was 175/100,000.

One hundred six cases were reported out of the two Corcoran prisons during the five year study period. Forty-five of the cases were Hispanic; 61 were non-Hispanic. The mean annual incidence rate in Hispanics was 165/100,000. The rate in the non-Hispanics was 183/100,000. As noted above, rates for any subgroup within the non-Hispanic group would likely be unstable due to small number of cases. It is noted, however, that 54% of the non-Hispanic cases were African-American, i.e., about twice what would be expected if the cases were evenly distributed in the non-Hispanic subgroup.

Six hundred forty-eight cases were reported out of Avenal State Prison during the study period. Two hundred forty-four of these were Hispanic; 404 were non-Hispanic. The mean annual incidence rate in the Hispanic inmates was 1,716/100,000. One hundred nineteen cases were reported in non-Hispanic white inmates. The mean annual incidence rate for them was 1,345/100,000. One hundred eighty-nine cases were reported in non-Hispanic African-Americans. The mean annual incidence rate for them was 2,534/100,000. Rates for the remaining non-Hispanic subgroups aren't reliable because of both small number of cases and small at risk populations. It is noted, however, that 27% of the 50 Asians and 11% of the 61 Native Americans were cases. The percent Hawaiian/Pacific Islanders cases was 100%.

The four population data suggest that inmate status and the location of the prison in Kings County are the major risk factors for acquiring CM. At Avenal State Prison, the observed rates in all three of the race/ethnic groups where rates were available are remarkably high. The data support the notion that

African-American inmates are at higher risk for acquiring CM. The risk status of Hispanics is less clear. Both the City of Avenal and the City of Corcoran are predominately Hispanic and have a mix of races in the non-Hispanic subgroup. The small size of these populations and small number of cases doesn't permit the calculation of reliable incidence rates by race/ethnicity. The observed incidence in Hispanic inmates in ASP may be somewhat elevated but the increased risk appears to be modest. Some racial groups are under-represented in the four populations. The observed attack rate ASP Asians, Native Americans and HPI may be a random occurrence but remains worrisome.

Improved estimates of burden of disease by race/ethnicity are needed, especially within the Asian/Pacific Islander group. The recognized increased burden in Filipino-Americans may be shared with others within the highly diverse group termed Asian/Pacific Islanders. Historically, Filipino-Americans have been the largest population of Asian/Pacific Islanders in the endemic regions. The population of Pacific Islanders is small everywhere. The burden of disease in Asian/Pacific Islanders besides Filipino-Americans likely is unknown because the small size of the populations at risk doesn't produce reliable rate estimates.

Improved estimates of risk by both race/ethnicity and by pre-morbid conditions are needed. When linked to improved risk communication with the general population, those individuals at risk for complicated CM may have better outcomes either through primary or secondary prevention.

Only well designed, population-based future studies will answer questions about the risk of CM acquisition based on race/ethnicity. While efforts to improve collection of race/ethnicity data on reported cases should continue, this alone likely will not resolve remaining questions about race/ethnic risk for acquisition of CM.

A National Perspective

National Death Surveillance

Coccidioidomycosis doesn't typically result in a fatal outcome. A recent report on mortality associated with CM in the United States noted 3,089 deaths for the period 1990-2008. [16] The study noted that the age adjusted mortality rate peaked around 1992-1994 but otherwise has remained fairly stable over time. California and Arizona combined accounted for 80% of the deaths. California had 30% more deaths than Arizona. Nevada, Utah, New Mexico and Texas are the other recognized endemic states. These four states combined accounted for 8% of the deaths in this study. The remaining 12% of the deaths due to CM were noted in non-endemic states. Every state had at least one death or more.

The number of cases in California exceeded that seen in Arizona consistently until 1997 following Arizona's adopting of laboratory reporting. Since 1997 the reported number of cases in Arizona has consistently exceeded that of California. For the period 2007-2011, Arizona cases represented 60% of the cases reported in the United States. Unlike California, Arizona did not experience a spike in cases in the early 1990s. There was an increase in Arizona but the number of increased cases was much more modest. This increase in reported cases in California corresponds with the 1992-1994 peak mortality rate noted above and may at least in part explain the apparent excess number of California deaths. The 12% of deaths in the non-endemic states seems unexpected.

National Surveillance Challenges

Beginning in 1995 CM became a nationally notifiable disease. Various surveillance systems provide surveillance data to the CDC. CM wasn't included in this system in 2010. The CSTE case definition includes both clinical and laboratory criteria. The laboratory component of the case definition changed in 2008. Because of the large number of cases in their jurisdictions and limited resources, the state of Arizona and Kern County in California, have adopted reporting that doesn't require any clinical component. In 2009 one of the two major clinical laboratories in Arizona changed their laboratory procedure. Following this change in an Arizona laboratory, there was a significant increase in the reported incidence rate of cases and the long-standing observation of a higher incidence rate in males was reversed. For the first time in Arizona, and only in Arizona, the observed incidence in females exceeds that seen in males. [28]

When cases are defined differently over time any comments about changes in true incidence of the disease should be qualified. When different case definitions are used by the various jurisdictions comparisons between jurisdictions become problematic. Sole reliance on laboratory reports may inflate the incidence rate estimate. Strict adherence to the case definition may result in an under-estimate of the true incidence, for example, when cases aren't counted because of the challenges involved in obtaining clinical information. In both Kern County and Arizona reliance on laboratory reporting has resulted in a low rate of collection of race/ethnicity data. This data usually is not available on the laboratory report. These two jurisdictions account for a super-majority of the cases reported in the United States.

CM isn't a reportable condition in Texas, a state known to be endemic. Six percent of the deaths noted in the 1990-2008 mortality study occurred in Texas. Arizona and to a lesser extent California have taken steps to raise awareness about CM among the general population and clinical providers. This increased awareness may have resulted in more complete identification and reporting of CM cases. It's unclear if any of the other endemic states have taken similar measures. The incidence of CM in the other four endemic states may be higher than historically observed.

Population-based CM morbidity, degree of illness, data is poor. With a large number of cases reported by laboratory only, the clinical illness at the time of the report is missing on many cases. Regardless of the clinical illness at the time of the initial report some people will go on to develop more complicated disease such chronic progressive pulmonary disease or various forms of dissemination. For example, many people with coccidioidal meningitis may not be reported a second time if they've previously been reported with primary pulmonary CM. We lack a population-based estimate of the burden of disease due to complicated CM.

Central Coastal Mountain Range

The central costal mountain range of California is an area of inadequately defined risk for CM acquisition. For the current purposes, the range spans a large area extending north-south from Los Angeles County to Monterey County, if not further north. The population density of the area is quite low. Because cases are reported by residence, any observed rates would be highly unstable due to small numbers and the reports would be submitted to multiple counties. The science of reliable identification of the organism in the soil is evolving and currently is labor intensive. Again, the area of concern is large. Outbreaks in occupational groups have been observed, e.g., the construction workers at Camp Roberts and the Navy Seals were noted previously. The Occupation Health Branch of the CDPH is currently investigating another occupational outbreak in San Luis Obispo County. The outbreak in Ventura County following the Northridge earthquake was associated with landslides in the costal mountains. This area of California likely represents a poorly recognized risk for several groups. Besides the residents and some occupational groups, it may also represent a risk for people engaging in recreational activities. Multiple highways traverse the range. Travel on these highways could expose many coccioides naïve individuals.

There may be other sparsely populated, possibly remote areas of California with poorly defined high risk for CM. The fungus tends to be spotty in distribution even in the more endemic counties and hyper-endemic areas in other counties may remain unrecognized.

Coccidioides Exposure During Travel

An African-American Pullman porter normally working a route in the mid-west was assigned to fill in on a train traveling through the San Joaquin Valley on one occasion. He subsequently developed fatal disseminated CM. The story may be apocryphal but does raise a significant issue. What is the risk in travelers of acquiring CM through travel exposure in the endemic areas of California? Many highways in California traverse endemic areas. The north/south highways 101, 5 and 99 are the major north/south highways. Highways 33, 41, 58, 152 and 198 are the east/west routes through the central costal mountains. Many of the people traveling through the endemic areas would be cocci naïve. There may be limited information on this issue because the most of the cases acquired through travel would likely go undiagnosed. The Pullman porter would have eventually been diagnosed because of his disseminated disease. The much more common clinical disease probably wouldn't be diagnosed. These cases would resolve without diagnosis or specific treatment. As noted earlier, we have evidence that CM is under-diagnosed even in highly endemic areas of Arizona.

Coccidioidomycosis as a result of laboratory exposure is well established. Harold Chope, M.D. had an illustrious career in public health. He's remembered in CM circles for developing what today would be called primary pulmonary CM after an accidental exposure to a coccidioidal fungal culture while he was a medical student at Stanford in 1929. The culture was taken from a patient with coccidoidal granuloma. His laboratory-derived illness demonstrated that typically fatal coccidioidal granuloma didn't always follow exposure. A single exposure is sufficient to cause disease. Laboratory acquisition of coccidiodes may be a special case because of the size of the innoculum.

The infectious dose of coccidioides is unknown (Personal Communication: Demo Pappagianis). Neither residence in an endemic area nor repeated exposure likely is necessary to produce infection. C.E. Smith, a CM pioneer, noted cases of CM after very limited exposure. A San Francisco housewife developed CM after spending a single night in a "Valley town". Smith later commented on other travel-related cases:

> "The author has records of three persons who were infected merely as tourists on trains and of 13 others who were exposed only in riding through endemic areas by automobile or bus." [24]

In 2001 approximately three hundred people participated in a four day international model airplane competition at Lost Hills in Kern County. Despite the measures taken to control dust at the event, at least fifteen participants from eight countries were subsequently diagnosed with coccidioidomycosis. [8]

In 1996 another travel related outbreak of CM occurred. Twenty-one of 126 member church groups had clinical illness and positive coccidioides serology compatible with CM after returning from Tecate, Baja California, Mexico to Washington State. The fungus was subsequently recovered from the soil in Tecate Mexico. The duration of the stay in Mexico was six days.[6]

While the risk of infection for travelers is presently unknown, an assumption of minimal risk seems unwarranted. Considering that most infected people will develop no disease or a limited illness of weeks' to months' duration, travel through endemic areas for most people would be an acceptable risk. Travelers routinely accept other travel risks such as injury or death due to a motor vehicle accident. For some people travel through an endemic area could be an unacceptable risk. Persons at risk for complicated disease due to immune-compromising medical conditions, third trimester pregnancy or race ideally would be informed of the travel related risk.

Travel related infection and illness would be an occupational illness for certain persons, for example a tour bus driver. The worker's medical expenses and lost work time should be compensable under worker compensation provisions. Neither the workers nor the treating physicians may be adequately informed about this work-related means of acquiring CM.

Summary Remarks

1. The incidence of coccidioidomycosis varies in California over time. The cause of this variation is unknown.

2. The occurrence of CM outside the San Joaquin Valley may be more frequent than may be generally thought. The CDC's designation of the known endemic areas of California should be revised.

3. Kern County has the highest observed incidence in the state. Some of the disproportionate rate may be due to less undiagnosed and to reporting artifact.

4. Inmates in 15 Collaborative counties are disproportionately affected. Their increased risk for acquiring CM is poorly understood.

5. The collection and reporting of race/ethnicity data is incomplete. Even with complete collection of race/ethnicity data the risk for CM acquisition for some under-represented racial/ethnic groups may remain elusive. The methodology used by the Collaborative wouldn't capture the expected excess burden of disease expected for some racial groups.

6. The risk of CM within the counties wasn't evenly distributed in most of the 15 Collaborative counties. There likely are areas of California where the risk of CM is poorly defined.

7. A number of major highways in California traverse highly endemic areas of the state. The risk for travelers of acquiring CM is undefined.

8. It is likely that CM is under-diagnosed in California. This may be more of a problem in the less recognized endemic areas of the state.

9. The Collaborative identified a need for a uniform set of recommendations to prevent occupational exposure to CM. On June 13, 2013 the Occupational Health Branch at CDPH released the recommendations. These can be accessed at:
   http://www.cdph.ca.gov/programs/hesis/Pages/Publications.aspx

10. California counties probably lack the necessary resources to address adequately the epidemiologic challenges of CM in California.

11. California has no known effective strategy for either primary or secondary prevention on CM in the general population.

The Epidemiology of Coccidioidomycosis –

15 California Counties, 2007-2011

Produced for the California Coccidioidomycosis Collaborative

Supplement

County Summaries

15 Counties, 2007-2011

Fresno County:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
2,723	545	309-726	57/100,000	33-75/100,000

Fresno County reported the second highest number of cases and had the third highest observed mean incidence rate. Fifty-six percent of the cases were institutional. All the institutional cases were male. Eighty-four percent of the reported cases were male. If the institutional cases are excluded, 63% of the community cases in Fresno were male. Overall, 6% of the cases were missing race/ethnicity data. In 2011, 19% of the cases were missing race/ethnicity data. The observed number of cases increased significantly in 2010 and 2011 compared with the three preceding years, approximately 170%. Almost all the increase was observed in the community cases.

The incidence of CM in Fresno County varies significantly by location within the county. The East side/ Mountain region of Fresno County had no cases. Urban Fresno County, including the cities of Fresno and Clovis had 693 cases with a mean incidence rate of 14.6/100,000. Southwest Fresno County, including Pleasant Valley State Prison and the City of Coalinga, had 2,032 cases with a mean incidence rate of 2,138/100,000. Eighty-three percent of these cases were institutional. In the five years of the study period, the City of Coalinga noted 349 cases. The mean incidence rate in the City of Coalinga was 513/100,000 (range of 140 – 1265). The observed incidence rate in the City of Coalinga in 2011 was 900% that of 2007.

Kern County:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
7,759	1,552	598-2,734	186/100,000	72-322/100,000

Kern County reported the highest number of cases and had the highest mean incidence rate for the five years. Nine percent of the cases were institutional. The mean institutional incidence rate in Kern County was 411/100,000 (range 138-678) compared with the mean community rate of 177/100,000 (range 69-308). Ninety-seven percent of the institutional cases were male. Fifty-nine percent of the cases in Kern County were male. When the institutional cases are excluded, the 55% of the community cases were male. Sixty-three percent of the cases are missing race/ethnicity data.

Because of the relative large number of cases observed in Kern County, the incidence rates are more reliable. The observed rates show a lot of variation over time and by area of the county. The county rate in 2011 was 212% that of 2007. The lowest rate occurred in 2009 when it was 47% of the rate noted in 2007. This reduction was seen in both community and institutional cases and across all age groups.

The Desert and Mountain Regions in Kern County had the lowest mean rates in the county for the five year period, 64/100,00 and 53/100,00 respectively. If Fresno and Kings Counties with their high incidence of inmate cases are excluded, only Tulare County and San Luis Obispo County had comparable mean incidence rates, 44/100,000 and 47/100,000 respectively.

Valley North (Delano/Wasco) and Valley West (Taft) had the highest mean rates in the county for the five year period, 258/100,000 and 303/100,000 respectively. By comparison the mean rate in Valley Central (Bakersfield) was 183/100,000. The three cities with the highest mean incidence rates were Wasco, Taft and Delano. Although each of these cities has a large inmate population, the mean incidence rates remained elevated even after exclusion of the inmate cases. The mean incidence rates absent inmate cases were: Wasco 356/100,000; Taft 320/100,000 and Delano 359/100,000.

Kings County:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
1,198	**240**	**147-350**	**155/100,000**	**97-223/100,000**

Kings County reported the third highest number of cases and had the second highest mean incidence rate. Sixty-three percent of the cases were institutional; all of them male. The high number of male inmate cases skewed the gender distribution in Kings County. Eighty-five percent of the cases reported in the five year study period were male. When the inmate cases are excluded, 59% of the cases in Kings County were male. Kings County reported missing race/ethnicity data on 17% of the cases.

The incidence rate in 2011 was 213% that of 2007. During the five year study period there were 451 community cases and 747 institutional cases. The mean community rate was 66.4/100,000 (range 44-114). The mean institutional rate was 805.4/100,000 (range 442-1370). The highest community incidence rate was noted in 2010; the community rate in 2011 was 53% that of 2010. The observed institutional rate has risen each year from 2007-2011.

The western side of Kings County is more endemic than the rest of the county. This part of the county differs from the rest of the county in its topography. The foothills of the costal mountain range intrude into western Kings County.

Mean Incidence Rates Two Kings Co. Regions, 2007-2011

Region	Mean Rate	Range	Total Cases
Westside*	966.9/100,000	488-1495/100,000	834
All Other	53.3/100,000	46-72/100,000	364

* Westside includes City of Avenal, Kettleman City and Avenal State Prison

If the inmate cases are excluded, the observed incidence rate remains significantly higher than the rest of the county, 365.5/100,000.

Los Angeles County:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
1,083	**217**	**145-304**	**2.2/100,000**	**1.5-3.1/100,000**

Los Angeles had the fourth highest number of cases and ranked 14th in observed mean incidence rate. None of the cases reported were institutional. Sixty-three percent of the cases reported in Los Angeles were male. Los Angeles reported race/ethnicity data on 95% of their cases.

Between 2007 and 2011 the incidence rate in Los Angeles County doubled from 1.5/100,000 to 3.1/100,000. The rate in 2011 was 130% that of 2010.

The observed incidence was much higher in the Antelope Valley. It was elevated also but less so in the San Fernando Valley.

Mean Incidence Rates in Four L.A. Co. Regions, 2007-2011

Region	Mean Rate	Range	Total Cases
Antelope Valley	17.8/100,000	14.2-24.9	328
S. Fernando Valley	2.7/100,000	2.2-3.9	301
SW, South, Compton	1.6/100,000	0-2.7	87
Costal Cities	1.4/100,000	0.2-2.7	45

The incidence rates in the Antelope Valley and in the San Fernando Valley regions were approximate 175% higher in 2011 than in 2007. The rate observed in the Antelope Valley is similar to that noted in the City of Fresno. There is a state prison in the Antelope Valley with no reported cases.

Los Angeles County strictly complies with the state's case definition for reporting purposes. The case definition includes both clinical and laboratory elements. Los Angeles has noted significantly more success in getting clinical records from hospitals than from other medical providers. More than 55% of the cases reported were on hospitalized patients. Those laboratory cases without clinical confirmation were not reported. This strict adherence to reporting only those cases meeting the fully case definition may result in an under-estimate of cases in Los Angeles County compared with Kern County where laboratory cases are reported.

Merced:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
150	**30**	**13-54**	**12/100,000**	**5.1-21**

Merced County is ranked 14th in the number of reported cases and 6th by mean incidence rate. None of the cases reported were institutional. Sixty-five percent of the cases were male. Forty-four percent of the cases were missing race/ethnicity data.

The rate in 2010 and 2011 was 373% higher than the preceding three years. Although the small numbers involved make observed rates less stable, the west side of Merced County appears to be more endemic than the remainder of the county.

Mean Incidence Rates in Two Merced County Regions, 2007-2011

Region	Mean Rate	Range	Total Cases
Westside*	39.3/100,000	15-75/100,000	91
All Other	5.7/100,000	2.4-11	59

*Westside includes Gustine, Dos Palos and Los Banos

Monterey:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
225	45	26-69	10/100,000	6.1-16/100,000

Monterey ranked 11th by number of cases reported and 7th by mean incidence rate. Thirty percent of the cases were institutional; all the institutional cases were male. Seventy-nine percent of the cases reported were male. After excluding the inmate cases, 71% of the community cases were male. Thirty-two percent of the cases were missing race/ethnicity data.

The rate in 2010 and 2011 was 180% that of the preceding three years. Thirty percent of the cases were institutional with a higher, if somewhat unstable, observed incidence rate. The mean institutional rate was 126.9/100,000 (range 51-210) compared with the mean community rate of 7.7/100,000 (range 4.6-11.9).

Excluding the inmate cases there were 159 community cases. Eighty-five percent of these cases were noted in the eastern side of the county, two areas termed Salinas and South County. The North County and Peninsula/Big Sur regions had only 25 cases in the five year interval. There are no prisons in the Salinas region. The mean rate for Salinas was 11.1/100,000. The mean rate for South County was 35/100,000. There are two prisons in the South County region. If inmate cases are excluded the mean rate for South County was 16/100,000.

Riverside:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
334	67	48-85	3.1/100,000	2.2-3.9/100,000

Riverside County ranked 8th in the number of cases and 13th in the observed mean incidence rate. Riverside County reported data on the four year interval 2007-2010. The number of cases and the observed incidence rate in 2011 was obtained from the CDPH's "Yearly Summary of Coccidioidomycosis in California, 2011".

There are two state prisons in Riverside County both in Blythe but no institutional cases were reported. Seventy-three percent of the cases for the period 2007-2010, n=261, were male. Race/ethnicity data was missing on 21% of the cases reported in the four year reporting interval.

The incidence rate in Riverside County increased about 50% in 2009 then stayed at about the same rate for the next two years. The data doesn't support any regional concentration of CM risk in Riverside Co. for the four years reported.

Distribution by Region in Riverside County, 2007-2010

Region	Cases	Mean Rate
West	128	4.5/100,000
South	20	1.9/100,000
Mid	39	4.4/100,000
East	74	5.7/100,000

Forty-nine percent of the cases were reported in the West region. Two of the regions have small number of cases. These should be expected to result in unreliable rates. The observed rates in the West and East regions are not clearly different.

San Bernardino:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
224	45	22-75	2.1/100,000	1.0-3.4/100,000

San Bernardino County ranked 12th in the number of cases reported and 15th by mean observed incidence rate. Eighteen percent of the cases were institutional. The state prison in Chino has only male inmates. The federal prison in Victorville is 91% male. Seventy six percent of the cases in San Bernardino Co. were male. If it's assumed that all the institutional cases were male, after excluding inmate cases, the percent of the cases that were male is 70%. Twenty-nine percent of cases in San Bernardino were missing race/ethnicity data.

The number of cases increased each year beginning in 2009. The rate in 2011 was 262% that of 2007. There is no observed clustering of cases in San Bernardino by location with the exception of Chino in 2011. The observed incidence rate in Chino in 2011 was 35.4/100,000. The 28 cases in Chino that year accounted for 13% of all the cases observed in five years in San Bernardino. The California Institute for Men is located in Chino. The observed institutional rate in 2011 was 248.7/100,000. In 2011 32% of the cases were institutionalized

San Diego:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
649	130	85-157	4.1/100,000	2.7-4.9/100,000

San Diego County ranked 6th by cases reported and 12th by mean incidence rate. Three percent of the cases were institutional. The cases were 62% male. Thirty-six percent of the cases were missing race/ethnicity data. The mean of the incidence rates for 2008-2011 is 165% that of 2007. The observed rate after 2007 was level.

A region designated as the South Region is small in area, bordering on Mexico. The five year mean incidence rate in the South Region was 8.7/100,000, range 5.1 to 10. It occupies the south-western corner of San Diego County. Chula Vista, located in the South Region accounted for 89 cases in the five year interval with a mean incidence rate of 7.5/100,000 compared with a mean incidence rate of 4.5/100,000, n=116, in the City of San Diego, located in an adjacent Region to the north. Somewhat surprisingly two large Regions, designated East and North Inland, would appear to be more suitable habitat for the fungus but had relatively low incidence rates compared with South Region.

San Joaquin:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
285	**57**	**27-123**	**7.7/100,000**	**3.7-16/100,000**

San Joaquin County ranked 10th in the number of cases reported and 8th by mean observed incidence rate. Eight percent of the cases reported were institutional. All the institutional cases were male. Seventy-two percent of the reported cases were male. The proportion of cases that were male was consistent for each of the five years. After correcting for male institutional cases, seventy percent of the cases were male. Seventeen percent of the cases were missing race/ethnicity data.

The incidence rate began to increase in 2010 and then rose sharply in 2011. The rate in 2011 was 440% that of 2009. Almost all of the increase was noted in the City of Tracy on the western side of the county. Over the five year study period 65% of the cases occurred in Tracy residents. Nineteen of the twenty institutional cases occurred in 2010 and 2011. Seventy percent of the inmate cases were noted in Tracy in 2011.

Mean Incidence Rate in Two San Joaquin Cities, 2007-2011

City	Mean Rate	Range	Cases
Tracy	44.5/100,000	22-118	183
Stockton	3.9/100,000	2.4-5.8/100,000	57

San Luis Obispo:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
633	**143**	**87-227**	**47/100,000**	**33-84/100,000**

San Luis Obispo County ranked 7th in the number of cases reported and 4th in the mean incidence rate. Fourteen percent of the cases were institutional. All the institutional cases were male. For the five year study period 70% of the cases in San Luis Obispo were male. If the institutional cases are removed, 62% of the community cases were male. Only 4% of the cases were missing race/ethnicity data.

There was a marked increase in the number of cases observed in 2011. The number observed in 2011 was 224% that of the mean of the preceding four years. The increase was proportionately increased in both the community and the institutional populations. The incidence rate in 2011 was 83.8/100,000.

The observed institutional rate is somewhat unstable because of small numbers. The mean four year rate, 2010 was unreliable, was 305/100,000. The mean five year rate for the community cases was 41.2/100,000.

The map provided by San Luis Obispo showed an increasing incidence rate going in a northeastern direction from the City of San Luis Obispo, through Atascadero and Templeton to Paso Robles.

Santa Barbara:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
110	22	12-32	5.0/100,000	2.8-7.4/100,000

Santa Barbara County ranked 15th in the number of cases reported and 11th by mean observed incidence rate. Four of the cases were institutional. All the institutional cases were male. Sixty-four percent of the cases in Santa Barbara were male. Thirty-three percent of the cases were missing race/ethnicity data.

Despite the relative small numbers there appears to be an increase in cases after 2008. The average of the years 2008-2011 is 178% larger than the average of 2007 and 2008.

There was no clear clustering of cases in Santa Barbara by city.

Stanislaus:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
166	33	17-62	6.0/100,000	2.9-11/100,000

Stanislaus County ranked 13th in the number of cases reported and 10th by mean observed incidence rate. None of the cases reported were institutional. Sixty-eight percent of the cases in Stanislaus were male. Data on race/ethnicity provided was incomplete.

The rate in 2010 was 325% higher than in 2009. The rate in 2011 was 120% the rate in 2010. Stanislaus provided no data on rates by regions or cities.

Tulare:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
1,003	201	175-231	44/100,000	40-51/100,000

Tulare County ranked 5th in both the number of cases reported and in mean incidence rate observed. There were no institutional cases. Fifty-eight percent of the cases were male. Sixteen percent of the cases were missing race/ethnicity. The observed incidence rate showed very little variation over time; the rate in 2011 was 108% of that of 2007.

Mean Incidence Rate Four Tulare County Cities, 2007-2011

City	Mean Rate	Range	Cases
Porterville	86.8/100,000	71-106	260
Tulare	74.7/100,000	57-86	215
Lindsey	76.2/100,000	60-128	44
Visalia	28.3/100,000	23-33	172

Visalia is the largest city in the county and is located in the north-western part of the county. In 1991 a clustering of cases was seen in the southeastern part of Tulare County including Porterville and other smaller communities. The rate in Visalia at that time was relatively low. The high rate in the City of Tulare wasn't noted in 1991.

Drurry, E.: Coccidioidomycosis in Tulare county, California, 1991: reemergence of an endemic disease. Journal of Medical and Veterinarian Mycology. 35, 1997:321-326.

Ventura:

Total Cases	Mean/Yr.	Range #/Yr.	Mean Rate/Yr.	Rate Range
300	**60**	**47-77**	**7.4/100,000**	**5.8-9.6**

Ventura County ranked ninth in the total number or cases reported and in the mean incidence rate for the five year study period. Only one of the cases was institutional. There was no observed tendency of the number of cases to increase over time. The highest observed number of cases was noted in 2007. Sixty-three percent of the cases were male. Twenty-eight percent of the cases were missing race/ethnicity data.

The comparison of incidence rates by city in Ventura County is complicated by the relative small number of incident cases. The data suggest that there may be a modest increased risk of CM in Semi Valley.

Mean Incidence Rates in Five Ventura County Cities, 2007-2011

City	5 Yr Number	Mean Rate 5 Yrs	Range
Oxnard	65	6.7/100,000	4.1-11
Thousand Oaks	26	4.2/100,000	0-8.1
Semi Valley	64	10.4/100,000	7.3-11
Ventura	32	6.1/100,000	4.8-8.6
Camarillo	21	6.5/100,000	1.5-12.5

June 12, 2012 Presentations

Rapid Detection of Coccidioides in Soil Samples

San Luis Obispo County Public Health Laboratory

James L. Beebe, PhD

Background:

Coccidoides immitis and ***Coccidioides posadasii*** are agents of Valley fever, and currently classified as select agents. Coccidioides species grow as filamentous fungi in soils of the lower Sonoran life zone, producing abundant filamentous growth in times of rainfall, then form arthrospores as a protective life stage in the dry season or under drought conditions.

Inhalation of aerosolized arthrospores can result in a pneumonitis in human—clinical or subclinical—called Valley fever, a significant public health problem in California. Disseminated disease occurs rarely, but more commonly in dark-skinned peoples, with life-threatening progression at times.

Coccidioides is difficult to grow from soils, but relatively easy to grow, but time-consuming, from human specimens such as sputum with general solid mycologic media.

Research premise

- Fungi are highly aerobic micro-organisms, growing rapidly under aerobic conditions, ie high aeration.
- Most microorganisms grow faster in liquid medium than solid medium.
- In solid medium culture, Coccidioides species grow as colonies slowly, while in liquid medium, an individual spore germinates and grows into a spherical propagule or fungus ball.
- Combination of liquid medium culture with PCR detection has not heretofore been evaluated for detection of Coccidoides in soil samples.

Research Goal

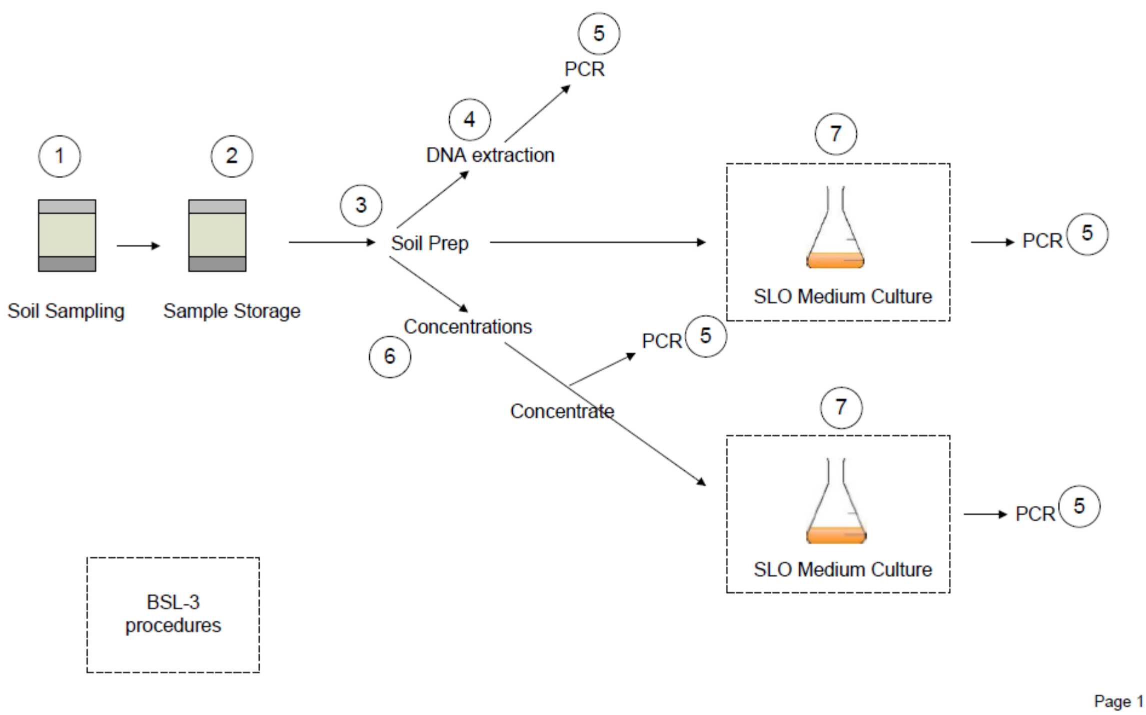
Improve the laboratory detection of Coccidioides in soil samples by highly aerated liquid medium cultivation using a selective-enrichment medium, followed by PCR detection of the presence of the agent, confirmed by solid medium culture of positive samples.

General Strategy

Develops safe methods using a surrogate non-pathogen (Malbranchea sp) including inoculum standardization, liquid culture, growth measurements to determine optimal medium and growth conditions, then application of PCR to actually detect Coccidioides vegetative elements.

See Figure 1 for the general strategy

Figure 1 Coccidioides Detection in Soil



Research Objectives

A. **Standardize arthrospore inoculum** using an arthrospore-producing non-pathogen Malbranchea sp. then Coccidioides

Figure 1 #7

Progress: 1

1. Ryan Henderson learned to grow Malbranchea, verify purity of cultures, producing arthrospores and using a hemocytometric method, measure spore counts and production of arthrospores by Malbranchea over time.

2. Initial test of Coccioides inoculums produced by J Beebe and Shannon Kilbert .Cultivation of C1 and D1 strains in 1%Yeast Extract (YE) successful in producing propagules in ca 5 days.

3. Revise arthrospore inoculum harvest procedure to add a glass wool column concentration step.

B. Develop a **liquid culture method.**

Figure 1 #7

Progress:

-An incubator shaker that can be used in a biosafety cabinet has been obtained on loan from Hardy Diagnostics. Eight 125mL flasks can be accommodated.

- Baffle flasks have been obtained from Bellco glass; choices of flask closure include cotton rolled in gauze, stainless steel caps, biomembranes and others

- A variety of liquid culture media are described in the literature.

- Possible selective agents include boric acid, cycloheximide, low pH and various combinations of the above.

- Enrichment supplement candidates include yeast extract and common microbiologic supplements.

1. Colin Khoshabian established a procedure using 1% Yeast Extract liquid medium.

2. Matthew Appelbaum developed soil sampling procedure; compounded SLO medium

C. Develop a method for **measurement of liquid culture fungus growth**.

Figure 1 #7

Progress: Literature search and colleague inquiry shows that ATP can be a reliable measurement of growth. ATP measurement device and supplies obtained on loan from Hardy Diagnostics.

1. Colin Khoshabian established a procedure using Malbranchea.

2. J Beebe and S Kilbert validated a BSL3 ATP-based growth measurement procedure using Malbranchea cultures as a surrogate for Cxy.

D. Develop a **PCR method**

Figure 1 #5

Progress: a method for use of Roche LightCycler has been obtained—method is successfully in use at Monterey County PHL for human specimen testing.

1. Jacque Moskowitz established a procedure using ITS target.

2. Use PCR method to detect Cxy growth in SLO medium

E. Develop a **soil sample extraction method**

Figure 1 #3

Progress:

1. Matthew Appelbaum performed SLO area sample collection, established a prototype soil extraction procedure, performed SLO medium culture of the six samples collected. No visible fungal growth observed. PCR of the sediments performed by Jacque Moskowitz were negative.
2. PCR negative and positive soil samples from Bakersfield, CA area and Sharks Tooth hill (Oildale, CA) provided by Dr Antje Lauer. Stored at -70C.

F. Develop a **Flurocarbon Concentration of Arthrospores** from soil extracts.

Figure 1 #6

1. Locate source of fluorocarbon fluid – purchased

G. Determine **Optimal combination of SLO medium cultivation and PCR testing**

Figure #7

1. Observe growth characteristics of known Cxy isolates in 1%YE Beebe and Kilbert
2. Observe growth characteristics of known Cxy isolates in SLO medium
3. Test PCR-positive and negative soil samples in SLO medium; observe for growth of typical fungal propagules and PCR ID

H. Conduct large **sampling and testing** of SLO County sites

- compare recoveries at multiple labs with split soil samples

<u>Detection of *C. immitis* growth sites with culture independent methods</u>

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The focus of our collaborative project is to identify growth sites of the fungal pathogen *Coccidioides immitis*, the causative agent of Valley Fever, in the Southern San Joaquin Valley, by a combination of molecular biology, satellite imagery, and soil parameter characterization. Furthermore, we have isolated and identified bacterial species that are antagonists to *C. immitis* and might be of value in a bioremediation attempt to suppress the growth of the pathogen in selected areas.

First results obtained in 2008 and 2009 to detect *C. immitis* by multiplex PCR (Greene et al., 2000; Lauer et al., 2022) in different non-agricultural areas around Bakersfield California, indicated the presence of the fungus in soils that have about equal parts of sand, clay, and silt (clay loam), a pH between 7.8 and 8.5, an available water capacity of about 0.15 – 0.2 cm/cm, a water content of about 30 (1/3 bar), an available water supply (0-25 cm) of 4-5, and a Cation Exchange Capacity (CEC7) of over 20 (Lauer et al., 2011). Those soils belonged to the Garces, Chanac, and Pleito soil series which are characterized by mixed mineralogy, superactive CEC activity, fine loamy particle size, and thermic soil temperature. Additional sites investigated in 2011 (unpublished data) confirmed these early findings. Based on these observations, predictions can be made about potential growth sites of the pathogen. All information about soil parameters to characterize our sampling sites was obtained from the USDA websoilsurvey database and the soil series extent mapping tool from the Center for Environmental Informatics at Pennsylvania State University (see references).

We also use examined Landsat-5 Thematic Mapper multispectral images of Kern County by using training pixels at a 750 m × 750 m section of Shark Tooth Hill (STH), a site confirmed to be a *C. immitis* growth site, to implement a Maximum Likelihood Classification scheme to map out the locations within the ROI where the fungus might be found. With this tool, we could predict environments that might be suitable habitats for *C. immitis*. We found that about 70% of the sites (23 sites investigated altogether) that were indicated by satellite imagery as potentially positive for the pathogen were also positive when investigated by multiplex PCR.

In addition to multiplex PCR to detect the pathogen, we also used a combination of PCR and Denaturing Gradient Gel Electrophoresis (DGGE) to detect *C. immitis* with a primer pair that detects all fungi based on the 18S rRNA gene (Hoshino and Morimoto, 2008), followed by sequencing of 18S rDNA fragments that were found in the melting area of *C. immitis*. By using DNA extracts from soil samples from different parts of the Southwestern US, we were able to detect the pathogen more often than with multiplex PCR, indicating a higher sensitivity of the PCR/DGGE method compared to the multiplex PCR. DNA from a *C. immitis* isolate was used as a control (isolate M39).

Our research also focused on the isolation and identification of bacterial species that can inhibit the growth of *C. immitis*. We were able to identify about 20 mostly *Streptomyces* spp. and *Bacillus* spp. that were strong anti-*C. immitis* in challenge assays on nutrient media in the lab. In a future field study, a subset of these bacterial species will be tested for their ability to suppress the growth of the pathogen in its natural environment. The isolates were obtained from a site that was close to a *C. immitis* growth site, but did not contain the pathogen based on multiplex PCR.

Our results indicated that the combination of satellite imagery, soil type information, multiplex PCR, and PCR/DGGE are powerful tools to predict and confirm the presence of *C. immitis*. These methods can also be used to further investigate the ecological niche occupied by this pathogen in other areas where the fungus is suspected to persist, as well as providing an advisory public health tool which might be useful in coccidioidomycosis prevention. As long as no vaccine is available to prevent outbreaks of coccidioidomycosis, investing in disease prevention is the best strategy to reduce incidence. A bioremediation attempt might be of use in areas that are planned for construction or are near schools and recreation areas.

Greene, D. R., Koenig, G., Fisher, M. C., & Taylor, G. W. (2000). Soil isolation and molecular identification of *Coccidioides immitis*. *Mycologia*, **92** : 406–410.

Hoshino, Y.T. and Morimoto, S. (2008) comparison of 18S rDNA primers for estimating fungal diversity in agriculture soils using polymerase chain reaction-denaturing gradient gel electrophoresis. *Japanese Society of Soil Science and Plant Nutrition*. 54:701-710.

Lauer, A., Baal J. C. H., Baal J. D. H., Verma M., Chen J. M. (2011). Detection of *Coccidioides immitis* in Kern County, California, by multiplex PCR. *Mycologia*, doi:10.3852/11-127.

United States Department of Agriculture accessible at: (http://websoilsurvey.nrcs.usda.gov/)

Soil series extent mapping tool from the Center of Environmental Informatics (CEI) accessible at: (http://www.cei.psu.edu/cei_wp/).

Coccidioidomycosis in California State Correctional Institutions

Demosthenes Pappapianis, Daniel Davis, Jessica Einstein
UD Davis Coccidioidomycosis Serology Laboratory

Coccidioides Infections 2010

Abbr	Institution*		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total Cases	Average Population	Infections/ 100,000
ASP	Avenal SP	Avenal	5	3	3	4	7	10	9	41	49	52	27	6	216	6,347	3,403
CCC	Cal Correctional Ctr	Susanville				1				1	3	1	1		7	5,487	128
CCI	Cal Correctional Inst	Tehachapi	2								1		3	1	7	5,874	119
CIM	Cal Institution for Men	Chino														5,008	
CMF	Cal Medical Facility	Vacaville	1		1										2	2,625	76
CMC	Cal Men's Colony	San Luis Obispo	1		2	1		2			4	6	5	2	23	6,329	363
CRC	Cal Rehab Ctr, Men	Norco				2			1				1		4	4,325	92
CAL	Cal SP, Calipatria	Calipatria										1			1	4,156	24
CEN	Cal SP, Centinela	Imperial														4,310	
COR	Cal SP, Corcoran	Corcoran	4	2	1	1		2	1	1	4	5	4	3	28	5,220	536
LAC	Cal SP, Los Angeles Co	Lancaster	3		1		3	5	3		2	2	3		22	4,530	486
SAC	Cal SP, Sacramento	Folsom														2,938	
SQ	Cal SP, San Quentin	San Quentin											1		1	4,993	20
SOL	Cal SP, Solano	Vacaville		1											1	5,058	20
SATF	Cal SATF and SP	Corcoran		1	1		1				1	1	2		7	6,560	107
CVSP	Chuckawalla Valley SP	Blythe									1				1	3,407	29
CTF	Correctional Training Facility	Soledad	1	2					2	1					6	6,367	94
DVI	Deuel Vocational Institution	Tracy			1							2			3	3,837	78
FSP	Folsom SP	Folsom														3,599	
HDP	High Desert SP	Susanville			1									1	2	4,403	45
IRON	Ironwood SP	Blythe														3,986	
KVSP	Kern Valley SP	Delano		3	1	1	1		1	4	3	4	1		19	4,682	406
MCSP	Mule Creek SP	Ione	2					2		1				1	6	3,715	161
NKSP	North Kern SP	Delano														5,373	
PBSP	Pelican Bay SP	Crescent City														3,290	
PVSP	Pleasant Valley SP	Coalinga	18	6	8	13	6	18	33	44	62	71	41	37	357	4,669	7,646
RJD	RJ Donovan Corr Facility	San Diego	2							2					4	4,535	88
SVSP	Salinas Valley SP	Soledad														3,747	
SCC	Sierra Conserv Ctr	Jamestown							1	1		2			4	5,403	74
WSP	Wasco SP	Wasco														5,893	
CIW	Cal Inst for Women	Corona														2,402	
CCWF	Central Cal Women's Facility	Chowchilla														3,732	
VSP	Valley SP	Chowchilla														3,479	
	Totals:		39	18	20	23	18	39	51	96	130	147	89	51	721	160,279	13,997

UC Davis Coccidioidomycosis Serology Laboratory

Coccidioides Infections 2011

Abbr	Institution*		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total Cases	Average Population	Infections/ 100,000
ASP	Avenal SP	Avenal	24	15	21	9	13	13	16	18	45	42	20	30	266	5,728	4,644
CCC	Cal Correctional Ctr	Susanville												1	1	5,415	18
CCI	Cal Correctional Inst	Tehachapi													0	5,538	0
CIM	Cal Institution for Men	Chino													0	5,827	0
CMF	Cal Medical Facility	Vacaville		1											1	2,804	36
CMC	Cal Men's Colony	San Luis Obispo		1	1						3	2		3	10	6,147	163
CRC	Cal Rehab Ctr, Men	Norco				1				1					2	4,109	49
CAL	Cal SP, Calipatria	Calipatria	1						1				1		3	4,230	71
CEN	Cal SP, Centinela	Imperial													0	4,133	0
COR	Cal SP, Corcoran	Corcoran	4	4	1	3	1	2	1	4	1	3	6	3	33	4,811	686
LAC	Cal SP, Los Angeles Co	Lancaster				1		1					1		3	4,258	70
SAC	Cal SP, Sacramento	Folsom									1				1	2,834	35
SQ	Cal SP, San Quentin	San Quentin								1	1	1	1	1	5	4,691	107
SOL	Cal SP, Solano	Vacaville		1	1										2	4,936	41
SATF	Cal SATF and SP	Corcoran	3					2	2	1	2	3	1		14	6,234	225
CVSP	Chuckawalla Valley SP	Blythe													0	3,161	0
CTF	Correctional Training Facility	Soledad					1	1		1	2	2		1	8	6,546	122
DVI	Deuel Vocational Institution	Tracy			1	1		1					1	1	5	3,694	135
FSP	Folsom SP	Folsom									1				1	3,640	27
HDP	High Desert SP	Susanville	1		1			1		1		1	1		6	4,177	144
IRON	Ironwood SP	Blythe													0	4,004	0
KVSP	Kern Valley SP	Delano								1		1			2	4,610	43
MCSP	Mule Creek SP	Ione													0	3,558	0
NKSP	North Kern SP	Delano													0	4,976	0
PBSP	Pelican Bay SP	Crescent City													0	3,192	0
PVSP	Pleasant Valley SP	Coalinga	38	19	22	23	21	20	16	36	39	53	47	28	362	4,483	8,074
RJD	RJ Donovan Corr Facility	San Diego			1										1	4,267	23
SVSP	Salinas Valley SP	Soledad													0	3,872	0
SCC	Sierra Conserv Ctr	Jamestown	1	1	1					1	2	2	1		9	5,237	172
WSP	Wasco SP	Wasco													0	5,578	0
CIW	Cal Inst for Women	Corona													0	2,032	0
CCWF	Central Cal Women's Facility	Chowchilla													0	3,646	0
VSP	Valley SP	Chowchilla	1				1	1							3	3,278	92
	Totals:		73	42	50	38	37	42	36	65	97	110	80	68	738	145,843	14,977

UC Davis Coccidioidomycosis Serology Laboratory

Coccidioides Infections 2012

Abbr	Institution*		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total Cases	Average Population	Infections/ 100,000
ASP	Avenal SP	Avenal	23	19	11	9	10								72	5,173	1,392
CCC	Cal Correctional Ctr	Susanville				1									1	4,860	21
CCI	Cal Correctional Inst	Tehachapi													0	4,636	0
CIM	Cal Institution for Men	Chino													0	5,192	0
CMF	Cal Medical Facility	Vacaville					1								1	2,395	42
CMC	Cal Men's Colony	San Luis Obispo													0	5,548	0
CRC	Cal Rehab Ctr, Men	Norco													0	3,884	0
CAL	Cal SP, Calipatria	Calipatria													0	4,059	0
CEN	Cal SP, Centinela	Imperial													0	3,715	0
COR	Cal SP, Corcoran	Corcoran	1	3	4	2	1								11	4,529	243
LAC	Cal SP, Los Angeles Co	Lancaster													0	3,812	0
SAC	Cal SP, Sacramento	Folsom													0	2,778	0
SQ	Cal SP, San Quentin	San Quentin			1	1									2	3,883	52
SOL	Cal SP, Solano	Vacaville													0	4,408	0
SATF	Cal SATF and SP	Corcoran	2	2		2									6	5,744	104
CVSP	Chuckawalla Valley SP	Blythe													0	2,723	0
CTF	Correctional Training Facility	Soledad	3	2	4		1								10	5,841	171
DVI	Deuel Vocational Institution	Tracy				1									1	2,613	38
FSP	Folsom SP	Folsom													0	3,030	0
HDP	High Desert SP	Susanville					2								2	3,817	52
IRON	Ironwood SP	Blythe													0	3,564	0
KVSP	Kern Valley SP	Delano													0	4,210	0
MCSP	Mule Creek SP	Ione													0	3,106	0
NKSP	North Kern SP	Delano													0	4,701	0
PBSP	Pelican Bay SP	Crescent City													0	3,089	0
PVSP	Pleasant Valley SP	Coalinga	37	28	24	14	15								118	3,750	3,147
RJD	RJ Donovan Corr Facility	San Diego					1								1	3,643	27
SVSP	Salinas Valley SP	Soledad				1									1	3,638	27
SCC	Sierra Conserv Ctr	Jamestown			1										1	4,712	21
WSP	Wasco SP	Wasco													0	5,113	0
CIW	Cal Inst for Women	Corona													0	1,651	0
CCWF	Central Cal Women's Facility	Chowchilla													0	2,884	0
VSP	Valley SP	Chowchilla													0	2,427	0
	Totals:		66	54	45	31	31	0	0	0	0	0	0	0	227	128,128	5,338

UC Davis Coccidioidomycosis Serology Laboratory

California Institutional Population Estimates

Instate CDCR Prison Population by Gender, 2007-2011 as of June 30

Year	Total Pop	Male #	Male %	Female #	Female %
2007	172,231	160,229	93 %	11,607	07 %
2008	165,790	154,620	93 %	11,170	07 %
2009	159,084	148,295	93 %	10,789	07 %
2010	156,179	146,281	94 %	9,898	06 %
2011	152,199	142,765	94 %	9,434	06 %

CDCR Data Analysis Unit: Monthly Report of Population as of Midnight.

Instate CDCR Prison Population June 30, 2007 – June 30, 2011:

Total Population decreased by 12%
Male Population decreased by 11%
Female Population decreased by 19%

Mean Percent of CDCR Instate Population by Gender June 30, 2007-June 30, 2011:

Male 93.4%
Female 06.6%

Age Distribution of Adult Offenders Incarcerated in California State Prisons, 2009

Age Group	Percent
18-29	**31%**
30-39	**29%**
40-49	**26%**
50+	**14%**

Corrections: Year at a Glance, CDCR, Fall, 2011

Federal Inmates in California Prisons as of March 21, 2013

Name	County	Population
Atwater USP	Merced	1,572
Dublin FCI	Alameda	1,420
Herlong FCI	Lassen	1,567
Mendota FCI*	Fresno	692
San Diego MCC	San Diego	998
Terminal Island FCI	Los Angeles	1,154
CI Taft	Kern	2,337
Lompoc FCC	Santa Barbara	3,315
Victorville FCC	San Bernardino	3,638

*Mendota FCI opened in 2011.
93% of the inmates in all US Bureau of Prisons Facilities are Male.
US Bureau of Prisons Weekly Summary on March 31, 2013.

California State Hospitals

For the period 2005-2011 the average daily census for all California hospital services was 5,096 with little variance year to year. This data included Coalinga State Hospital, Salinas Valley Psychiatric Program and Vacaville Psychiatric Program. Four major hospitals accounted for 86% of the inpatient days. Seventy five percent of the inpatient days resulted in few if any cases in the Collaborative study. Napa County did not participate in the study. Metropolitan State Hospital is in Los Angeles where no institutional cases were reported. Very few cases if any were likely reported out of Patton State Hospital in San Bernardino County. Twenty three percent of the inpatient days were at Atascadero State Hospital. All of the admissions at Atascadero are involved with some criminal justice proceedings. Two of the counties, Kern and Kings, with a large number of inmate cases have no mental health hospitals. Coalinga State Hospital is located in Fresno County near Pleasant Valley State Prison. At the Collaborative meeting Dr. Pappagianis reported on serology results in 2010 and 2011 consistent with incident disease. He noted 774 cases at PVSP for the two years. It seems likely that few of the institutional cases reported at Collaborative meeting involved mental health patients not involved in the criminal justice system.

Data Source: Department of Mental Health – Historical Population Data

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