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Office of Infectious Disease Services Bureau of Epidemiology and Disease Control Arizona Department of Health Services

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Executive Summary

Valley fever is an infection caused by a fungus that is found in the soil of the southwestern United States, and parts of Mexico, Central and South America. People become infected after inhaling fungal spores made airborne by disturbance of soil by natural or human activity. It is not contagious and cannot be transmitted from animals to humans. Sixty percent of infected persons experience no or mild symptoms. The remaining 40% experience a self-limited respiratory disease with symptoms such as fever, cough, fatigue, chest pain, shortness of breath, and rash. In less than 5% of people with symptoms, it can cause severe respiratory disease or disseminated disease outside of the lungs requiring treatment with antifungal medication. Treatment may need to be continued for many months or possibly for life. There is no vaccine and preventing infection is difficult.

Continued surveillance for valley fever by the Arizona Department of Health Services (ADHS) has demonstrated that:

- Nearly two-thirds of all cases reported nationwide reside in Arizona.
- Valley fever is one of the most commonly reported infectious diseases in Arizona.
- 94% of cases reported in Arizona reside in Maricopa, Pima, and Pinal Counties.
- In the last decade, the incidence of reported valley fever in Arizona has increased from 58.1 per 100,000 persons in 2005 to 84.4 per 100,000 persons in 2014.¹

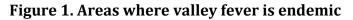
An analysis of valley fever-associated hospitalizations from hospital discharge data noted that:

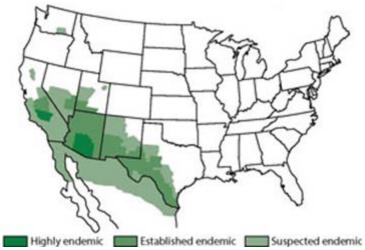
- In 2014, there were 717 hospitalizations associated with a primary diagnosis of valley fever.
- In 2014, hospitalization charges for Arizona residents with a primary diagnosis of valley fever totaled \$51 million.

¹ Changes in laboratory reporting in 2009 and 2012 have significantly impacted the number of reported cases.

Introduction

Valley fever, also known as coccidioidomycosis, is an infection caused by the fungus *Coccidioides* spp. It has affected inhabitants of the Southwestern desert of the U.S. for thousands of years.² The fungus is present in the top 2 – 8 inches of warm, dry soils at lower elevations of the American Southwest, especially Arizona and California, as well as parts of Mexico and Central and South America.





When soil is disrupted (e.g., by wind, earthquakes, or human activity), fungal spores become dispersed in the air. Susceptible individuals breathe in the spores resulting in infection. Infection causes mild or no symptoms in about 60% of cases. The remaining 40% experience a flu-like respiratory illness with symptoms

Source: CDC including cough, fever, fatigue, chest pain, shortness of breath, headaches, rash, and joint and muscle aches. Symptoms generally begin 1 – 4 weeks after exposure and may last for several weeks, causing significant disruption including lost time at work and school. Most cases recover without treatment and become immune for life. However, less than 5% of people experience severe illness in the form of severe respiratory or disseminated disease.

Dissemination is the spread of the infection outside of the lungs. Although nearly any part of the body can become infected, the skin, bones, and central nervous system are the most common sites of dissemination. Risk factors for dissemination include weakening of the immune system due to underlying health conditions (e.g., HIV/AIDS, organ transplant), immunosuppressive medication (e.g. corticosteroids, chemotherapy, biopharmaceuticals for autoimmune diseases), African American or Filipino race, male sex, and pregnancy. Disseminated disease can be deadly and requires treatment. Anti-fungal medications can

² Harrison WR, Merbs CF, Leathers CR. Evidence of coccidioidomycosis in the skeleton of an ancient Arizona Indian. J Infect Dis 1991;164:436-7.

be used to control the infection, but can have side effects. There is no cure or vaccine for valley fever.

Valley fever is a reportable communicable disease in Arizona. Arizona Administrative Code (AAC) R9-6-202, 203, 204, and 205 describe the morbidities, test results, or prescriptions required to be reported by healthcare providers, administrators of healthcare facilities, clinical laboratory directors, institutions, schools, pharmacists, and others. Healthcare providers and laboratories are required to report a case of or positive test result for valley fever to the Arizona Department of Health Services within five working days. Arizona requires reporting by both healthcare providers and clinical laboratories as a dual surveillance measure to increase the sensitivity of the surveillance system and improve the completeness of reporting. Diseases are reported via secure electronic reporting systems, fax, mail, or telephone using the communicable disease report (CDR) form. More information about the current reporting requirements can be found on the Arizona Office of the Secretary of State's website.³ Additional information on communicable disease reporting as well as reporting can be found on the Office of Infectious Disease Services (OIDS) website.⁴

Previously, ADHS received a legislative appropriation as well as funding from the Centers for Disease Control and Prevention (CDC) and the Arizona Biomedical Research Commission (ABRC) for valley fever prevention and control activities. Since 2012, ADHS has received funding through the CDC's Epidemiology and Laboratory Capacity program to continue some of these activities.

³ <u>http://apps.azsos.gov/public_services/Title_09/9-06.pdf</u>

⁴ <u>http://www.azdhs.gov/phs/oids/reporting/</u>

Epidemiology in Arizona

The first reported case of valley fever in Arizona was described in 1938.⁵ Arizona accounts for approximately 65% of all valley fever cases reported nationwide.⁶ Thousands of cases of valley fever are reported to ADHS each year. However, public health surveillance only captures a fraction of infections. Most infected persons do not seek care or may not receive diagnostic testing when they do. Thus, the total number of infections in Arizona is likely several times higher than the number reported to ADHS.

Cases of valley fever have been reported to ADHS for decades. Laboratory reporting of valley fever was mandated in 1997. Since then, reports of valley fever have increased dramatically. In 2009, a major commercial laboratory (Lab A) altered its reporting practices for valley fever, after consultation with ADHS, to include reporting of enzyme immunoassay (EIA) results, greatly increasing the total number of reported cases. In 2012, a change in testing methods at Lab A contributed to a substantial decline in the number of cases reported in late 2012 and 2013 (Table 1; Figure 2).⁷

In 2014, 5,624 cases of valley fever were reported to ADHS. This is a decrease of 237 cases (4%) compared to 2014. A decrease in case counts was also noted by other states in 2014. The causes of variability in reported case counts remains poorly understood. Contributing factors may include:

- Migration of susceptible people to the highly endemic counties in Arizona
- Increased recognition and testing by healthcare providers
- Increased awareness and care-seeking among the general public
- An increase in the number of people with weakened immune systems due to aging, immunosuppressive medications, or underlying health conditions
- Changes in precipitation, dust storms, and other climate-related phenomena that may affect fungal growth, spore formation and dispersal
- Increased construction or desert soil disturbance in areas where the fungus lives

 ⁵ Arizona State Department of Health. Arizona Public Health News: Coccidioidomycosis in Arizona. 1959; Vol 52 No 2.
⁶ <u>http://www.cdc.gov/fungal/diseases/coccidioidomycosis/statistics.html</u>

⁷ All incidence rate calculations included in this report are based on population denominators estimated by the ADHS Health Status and Vital Statistics Section using population projections obtained from the Arizona Department of Administration.

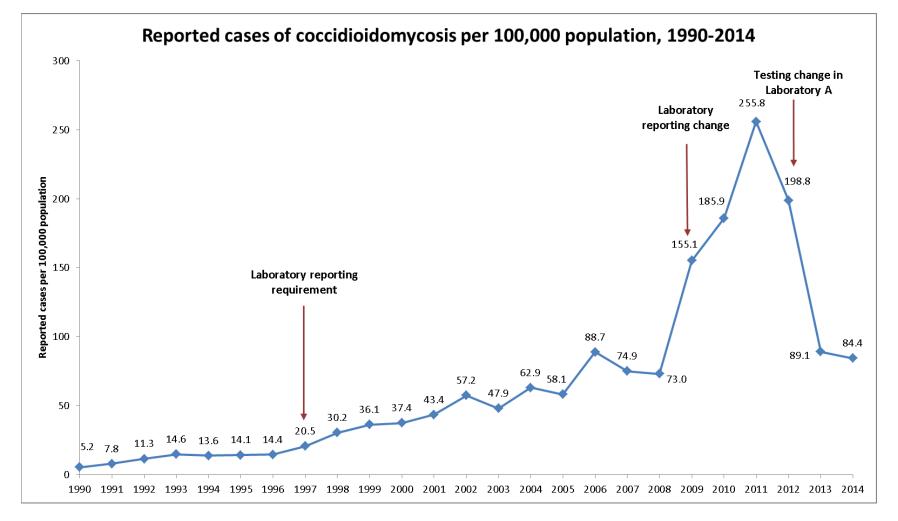


Figure 2. Reported cases of valley fever per 100,000 population, Arizona 1990 - 2014

	Reported cases	Incidence of reported cases per 100,000 population
1990	191	5.2
1991	287	7.8
1992	437	11.3
1993	592	14.6
1994	580	13.6
1995	626	14.1
1996	655	14.4
1997	869	20.5
1998	1,556	30.2
1999	1,813	36.1
2000	1,922	37.4
2001	2,302	43.4
2002	3,118	57.2
2003	2,695	47.9
2004	3,665	62.9
2005	3,515	58.1
2006	5,535	88.7
2007	4,832	74.9
2008	4,768	73.0
2009	10,233	155.1
2010	11,888	185.9
2011	16,472	255.8
2012	12,920	198.8
2013	5,861	90.2
2014	5,624	84.4

Reporting Sources and Changes in Laboratory Reporting Practices

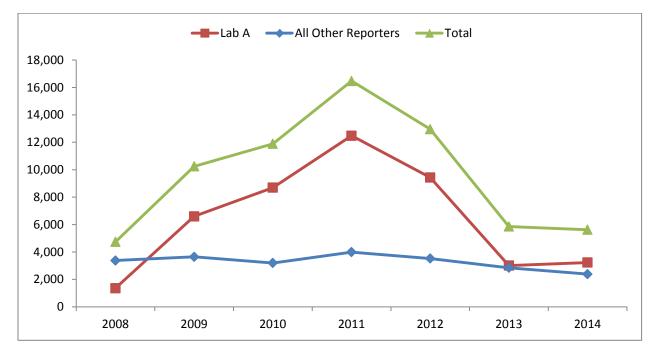
Ninety-eight percent of cases were reported by laboratories in 2014. The proportion of cases reported by a single major commercial laboratory (Lab A) increased from 2009-2011. In mid-2009, Lab A altered its reporting practices for valley fever after consultation with ADHS, to include reporting of enzyme immunoassay (EIA) results, greatly increasing the total number of reported cases (Table 2; Figure 2). The same laboratory changed the

testing platform used for EIAs, and in 2013 the number of cases reported statewide declined 55% compared to 2012.

	2008	2009	2010	2011	2012	2013	2014
Lab A	28.7%	64.4%	73.1%	75.8%	72.8%	51.4%	57.5%
All Other Reporters	71.3%	35.6%	26.9%	24.2%	27.2%	48.6%	42.5%

Table 1. Prop	portion of cases re	eported by Lab A	A, 2008 - 2014
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Figure 2. Cases	s reported annu	ally by reporting o	organization,	2008 - 2014



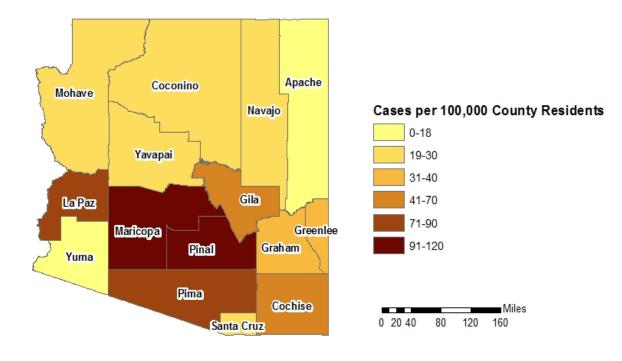
Geographic Distribution

Cases were reported from every county in Arizona in 2014. Rates of reported valley fever were highest in Maricopa, Pima, and Pinal Counties. This is consistent with prior years, with the exception of Pinal County having the highest rates in 2014 (Table 3; Figure 4).

	Cases	Cases per 100,000 population	Average cases per 100,000 population (2008 - 2014)
Apache	12	16.7	20.2
Cochise	63	48.6	37.5
Coconino	30	21.5	24.0
Gila	34	62.7	69.4
Graham	14	36.5	55.8
Greenlee	4	38.2	18.4
La Paz	17	80.2	105.0
Maricopa	3,937	98.2	193.3
Mohave	54	26.5	43.6
Navajo	29	26.6	30.9
Pima	890	88.4	124.3
Pinal	461	116.3	145.0
Santa Cruz	14	28.3	31.3
Yavapai	40	18.6	20.5
Yuma	25	11.8	10.7
Arizona	5,624	84.4	148.9

Table 3. Reported cases and rates by county, 2014

Figure 3. Cases per 100,000 population by county, 2014



Mortality

Valley fever is rarely lethal. However, infection in persons who are severely immunosuppressed, for example due to HIV/AIDS, may lead or contribute to death. Based on causes of death listed on death certificates from 2014, valley fever was a primary or contributing cause of death in 42 deaths in Arizona (Table 4). A recent public health investigation found that death certificates might underreport valley fever as a cause of death. Deaths attributable to valley fever from 2008-2013 were underreported seven fold compared to estimates of the total number of deaths attributable to valley fever.⁸ Thus, these data are likely an underestimate of the true number of deaths attributable to valley fever.

County	Primary or contributing
County	cause of death
Apache	0
Cochise	0
Coconino	0
Gila	3
Graham	1
Greenlee	0
La Paz	0
Maricopa	22
Mohave	0
Navajo	0
Pima	13
Pinal	3
Santa Cruz	0
Yavapai	0
Yuma	0
Arizona	42

Table 4. Deaths attributable to valley fever by county, 2014
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⁸ Jones J, Brady S, Koski L, Khan M, Sunenshine R, Komatsu K. Coccidioidomycosis: A possibly underreported cause of death – Arizona, 2008-2013. Coccidioidomycosis Study Group. April 2015 San Diego, CA

Demographics

In 2014, the age of reported valley fever cases ranged from six months to 102 years old with a median age of 52 years. Age could not be determined for nine cases (approximately 0.002% of all cases). The highest rates of valley fever occurred among people 75 – 84 years old; rates of reported infections among Arizonans in this age group are more than twice those in the general population (183.3 cases per 100,000 vs. 84.4 per 100,000 respectively) (Table 5).

Age Group* (Years)	Cases	Cases per 100,000
<5	22	5.1
5-14	174	18.9
15-24	512	54.4
25-34	637	71.8
35-44	764	91.5
45-54	891	105.9
55-64	940	120.3
65-74	902	151.9
75-84	571	183.3
85+	202	168.4

Table 5. Reported cases and rates by age groups, 2014

*Age could not be ascertained for 9 cases (approximately 0.002% of all cases).

Fifty-three percent of reported cases were female (88.5 cases per 100,000 females), while 47% were male (80.1 cases per 100,000 males). Gender was not reported for two cases (approximately 0.04 % of all cases) (Table 6). Prior to 2009, the majority of reported cases were male. Reporting and testing changes may have caused this shift.

Table 6. Cases by gender, 2014

	Cases	Percent of total	Cases per 100,000 population
Female	2,965	52.7%	88.5
Male	2,657	47.2%	80.1
Unknown	2	0.04%	

Only 20.3% of cases reported to ADHS contained information about race or ethnicity. Thus, it was not possible to analyze incidence rates by race or ethnicity.

Race or ethnicity	Cases	Percent of total	Percent of cases with known race or ethnicity
Asian or Pacific Islander	34	0.6%	3.0%
Black	90	1.6%	7.9%
Hispanic or Latino	195	3.5%	17.1%
Native American	104	1.9%	9.1%
White	668	11.9%	58.6%
Other	49	0.9%	4.3%
Unknown	4,484	79.7%	

Table 7. Race or ethnicity of reported cases, 2014

Seasonality

Seasonal variation in valley fever reports has been consistently noted in past years: numbers of reported cases increase from June through August and November through December. Figure 5 reflects the month in which cases were first reported to a local health department or ADHS from 2007 through 2014. This does not correspond to month of exposure to fungal spores or onset of symptoms. Possible causes of delay between exposure and reporting include the 1 - 4 week incubation period between exposure and symptom onset, delays before seeing a healthcare provider for the illness, delays in being tested for valley fever, time associated with processing and testing laboratory specimens, and time associated with reporting by a laboratory or healthcare provider to the health department. A previous ADHS study found that the median time between symptom onset to diagnosis was 55 days.⁹

⁹ Tsang CA, Anderson SM, Imholte SB, Erhart LM, Chen S, Park BJ. Enhanced surveillance of coccidioidomycosis, Arizona, USA, 2007–2008. Emerg Infect Dis. 2010;16:1738–44.

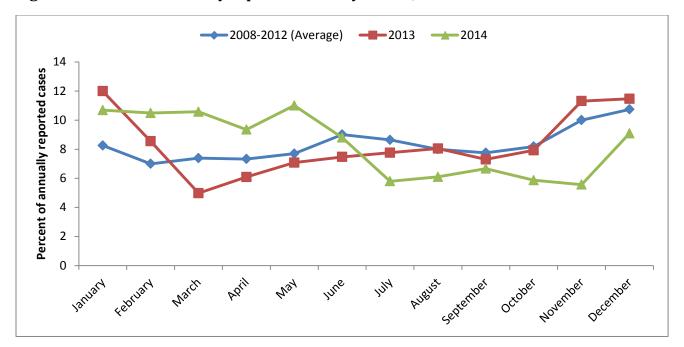


Figure 4. Percent of annually reported cases by month, 2008 - 2014

Hospitalizations

A previous ADHS investigation noted that 40% of reported valley fever cases required hospitalization.⁹ In 2014, there were 717 hospitalizations with a primary diagnosis of valley fever. The rate of hospitalizations with a primary diagnosis of valley fever increased from 14.7 hospitalizations per 100,000 persons in 2005 to a high of 22.6 hospitalizations per 100,000 persons in 2011, falling to 10.8 hospitalizations per 100,000 persons in 2014. The causes of this variability are unclear, but may reflect improved diagnosis and recognition by healthcare providers and changes in the incidence of disease. Pinal County continues to have the highest rate of hospitalizations (Figure 6; Table 8).

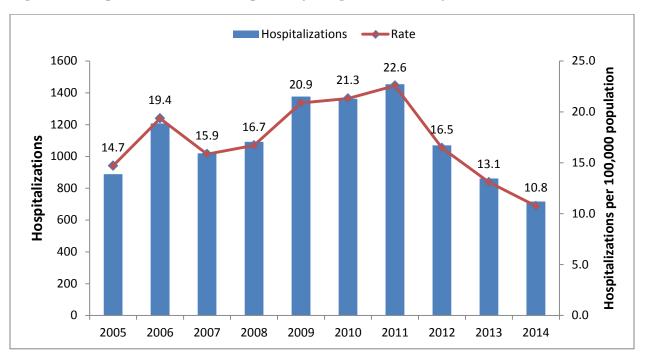


Figure 5. Hospitalizations with a primary diagnosis of valley fever, 2005 – 2014

Table 8. Rates of hospitalization with a primary diagnosis of valley fever per 100,000population by county, 2014

County	Hospitalizations per 100,000 population (2014)
Apache	2.8
Cochise	1.5
Coconino	5.0
Gila	11.1
Graham	13.0
Greenlee	0.0
La Paz	4.7
Maricopa	11.7
Mohave	2.9
Navajo	4.6
Pima	11.8
Pinal	21.7
Santa Cruz	8.1
Yavapai	1.4
Yuma	0.9
Arizona	10.8

Valley fever continues to be a costly disease. A previous investigation noted that total charges, which do not necessarily reflect actual payments, for Arizona residents hospitalized with a primary or secondary diagnosis of valley fever at non-federal facilities in Arizona were \$86 million in 2007.⁹ In 2014, hospitalization charges for Arizona residents with a primary diagnosis totaled \$51 million with a median of \$44,749 in total charges per hospitalization. The Arizona Health Care Cost Containment System (AHCCCS) was the most frequently listed expected source of payment (27.3%), followed by Medicare (25.9%), Health Maintenance Organizations (HMO) (19.7%), Medicare Risk (7.4%), PPO (6.4%), and self-pay (4.5%). Total charges associated with hospitalizations for which Medicare and AHCCCS were listed as sources of payment were \$13.4 million and \$16.7 million, respectively. The total healthcare costs attributable to valley fever are greater due to the exclusion of the cost of outpatient care and other forms of inpatient care in these figures.

Additional analysis was performed for hospitalizations with a primary diagnosis of valley fever in 2014. In contrast to the gender distribution observed in reported cases, 59.4% of hospitalizations in 2014 involved a male patient. The age distribution of hospitalized patients was as follows: 10.5% <25 years old, 26.1% 25 – 44 years old, 34.6% 45 – 64 years old, 24.7% 65 – 84 years old, and 4.2% 85 years or older. The median age was 52 years. Approximately 41.7% of these hospitalizations involved an intensive care unit (ICU) admission. Median length of stay was 5 days. Eight percent of patients were readmitted to the hospital with a primary diagnosis of valley fever. Thirteen patients (1.8%) died during a hospitalization.

Acknowledgements

Case reporting by providers and laboratories is the key to Arizona's infectious disease surveillance system. All staff within the ADHS Office of Infectious Disease Services and local health departments are acknowledged for their contributions to data collection, data entry and data analysis. Funds and technical assistance from the Arizona Biomedical Research Commission (ABRC), the Centers for Disease Control and Prevention (CDC), and the University of Arizona Valley Fever Center for Excellence (VFCE) supported this work. The contents of this report are solely the responsibility of the authors and do not represent the official views of the ABRC, the CDC, or the VFCE.

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