Valley Fever

2012 Annual Report

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

Arizona Department of Health Services

Table of Contents

List of Figures and Tables

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 when they inhale 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. A vaccine does not exist for this disease and preventing infection is difficult.

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

- Two-thirds of all cases reported nationwide reside in Arizona.
- Valley fever is the second most commonly reported infectious disease in Arizona.
- 96% 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 quadrupled from 47.9 per 100,000 persons in 2003 to 198.8 per 100,000 persons in 2012.[1]

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

- In 2012, there were 1,070 hospitalizations associated with a primary diagnosis of valley fever.
- Between 2003 and 2012, hospitalization charges for Arizona residents with a primary or secondary diagnosis of valley fever totaled $923 million in 2012 dollars.

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

A special investigation of valley fever cases among children (< 18 years) and young adults (aged 18 – 25 years) reported in 2011 was conducted to assess the impact of the disease on this population. There is a substantial personal and economic burden due to valley fever among younger Arizonans:

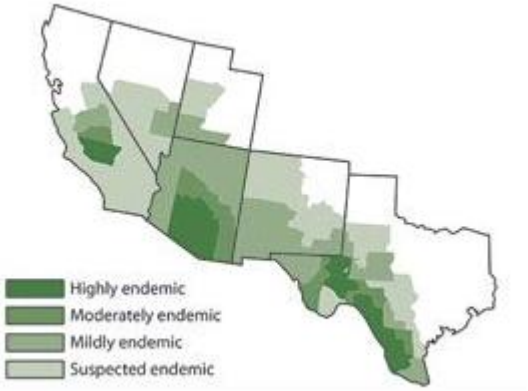
- Most patients were otherwise healthy and reported no underlying conditions.
- Symptoms lasted for a median of one month with nearly 30% continuing to experience symptoms at the time of interview.
- More than half received antibiotics during the course of their illness.
- 20% were hospitalized during their illness.
- Both children and young adults experienced significant disruption in daily life due to their illness including lost time at school and work.

Valley fever continues to have significant impact on the residents, healthcare system and economy of Arizona.

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 United States 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.

Figure 1. Areas endemic with Valley Fever



Source: CDC

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 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 health care providers, administrators of health care 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 health care 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 a secure web system, fax, mail, or telephone systems 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] http://www.azsos.gov/public_services/Title_09/9-06.htm.
[4] http://www.azdhs.gov/phs/oids/reporting/

Epidemiology in Arizona

The first reported case of valley fever in Arizona was described in 1938.[5] Arizona accounts for approximately 66% 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, greatly increasing the total number of reported cases. In 2012, a change in testing methods at Lab A took place leading to a decline in the number of cases reported in late 2012 (Table 1; Figure 2).[7]

While the above-mentioned reporting changes account for some of the increase in reported cases, the complete causes of this increase are 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, fungal spore formation and dispersal
- Increased construction or desert soil disturbance in areas where the fungus lives

In 2012, 12,920 cases of valley fever were reported to ADHS. This is a decrease of 3,552 cases (22%) in comparison to 2011.

[5] Arizona State Department of Health. Arizona Public Health News: Coccidioidomycosis in Arizona. 1959; Vol 52 No 2.
[6] Increase in Reported Coccidioidomycosis – United States, 1998 – 2011. MMWR 62(12):217-221.
[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 – 2012

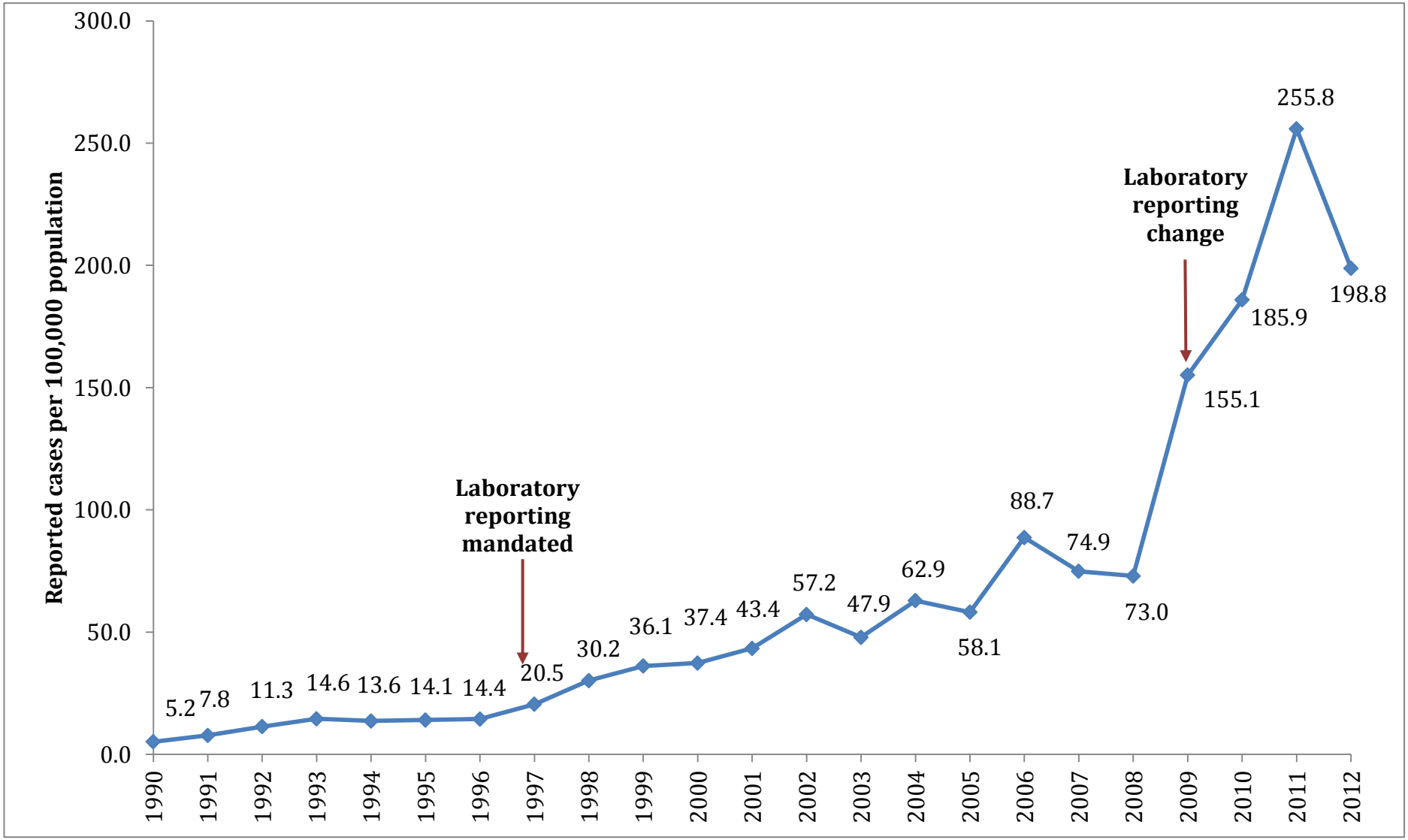


Table 1. Reported cases of valley fever, 1990 - 2012

	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

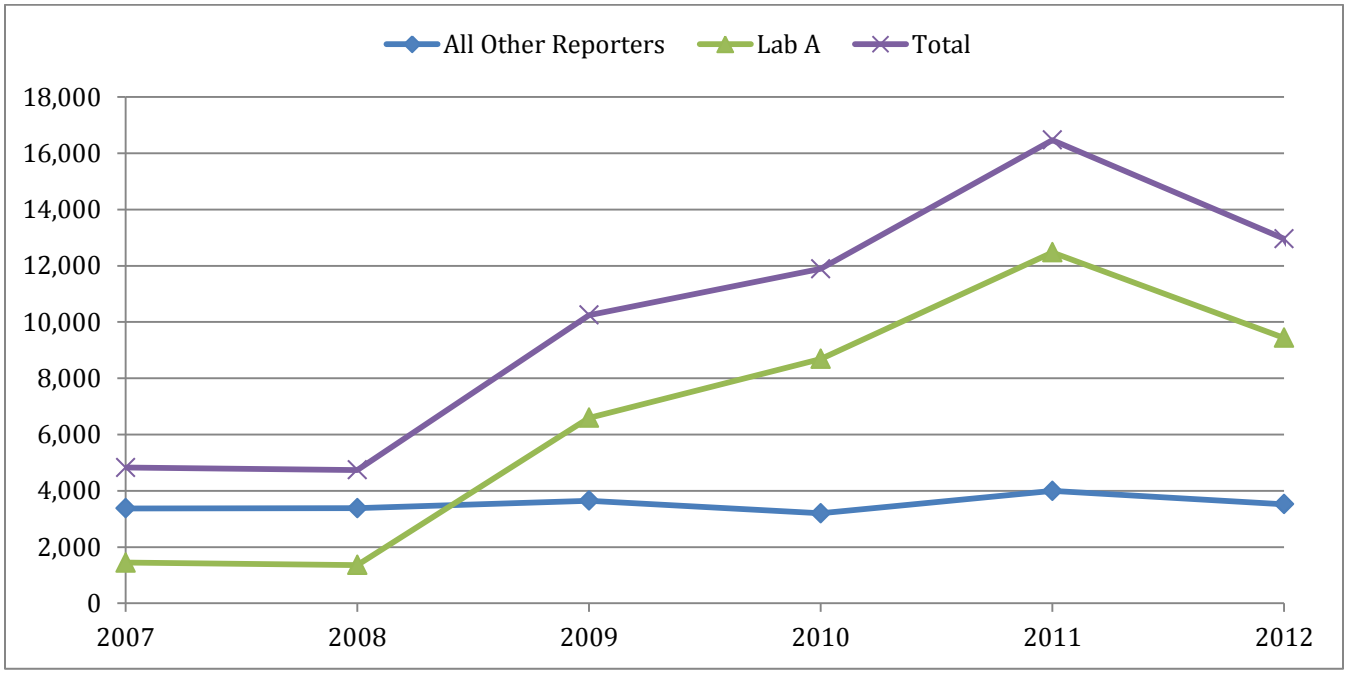
Reporting Sources and Changes in Laboratory Reporting Practices

Ninety-nine percent of cases were reported by laboratories in 2012. The proportion of cases reported by a single major commercial laboratory (Lab A) has increased in recent years. In mid-2009, Lab A altered its reporting practices for valley fever, greatly increasing the total number of reported cases (Table 2; Figure 2). Changes in reporting and testing at Lab A significantly impacted the number of reported cases from 2009 – 2012.

Table 2. Proportion of cases reported by Lab A, 2007 -2012

	2007	2008	2009	2010	2011	2012
Lab A	30.0%	28.7%	64.4%	73.1%	75.8%	72.8%
All Other Reporters	70.0%	71.3%	35.6%	26.9%	24.2%	27.2%

Figure 3. Cases reported annually by reporting organization, 2007 - 2012



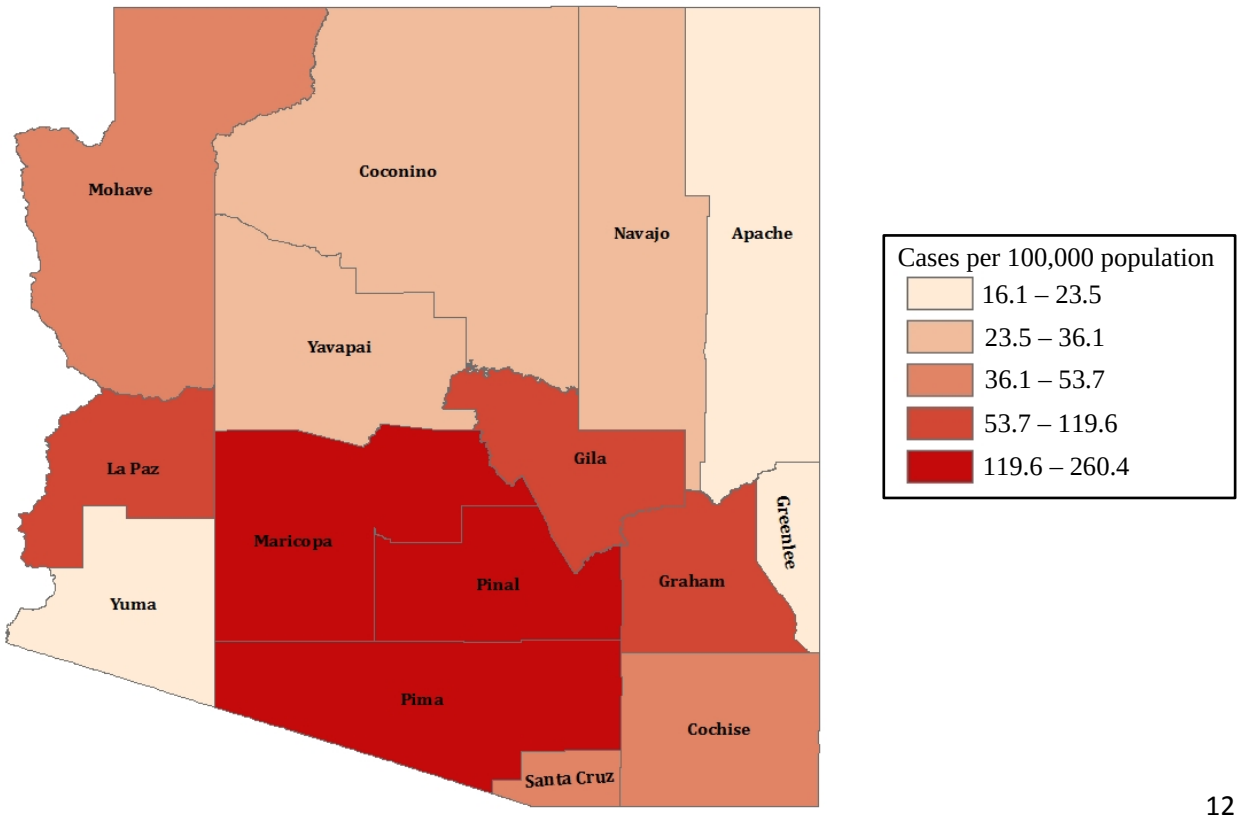
Geographic Distribution

Cases were reported from every county in Arizona in 2012. Rates of reported valley fever were highest in Maricopa, Pinal, and Pima counties. This is consistent with prior years (Table 3; Figure 4).

Table 3. Reported cases and rates by county, 2012

	Cases	Cases per 100,000 population	Average cases per 100,000 population (2007 – 2011)
Apache	17	23.5	17.7
Cochise	48	36.7	30.8
Coconino	48	35.7	21.0
Gila	49	91.4	57.2
Graham	33	88.4	57.4
Greenlee	2	23.3	16.4
La Paz	25	119.6	108.4
Maricopa	10,116	260.4	195.8
Mohave	109	53.7	43.7
Navajo	39	36.1	26.0
Pima	1,555	157.0	122.9
Pinal	774	198.9	136.8
Santa Cruz	19	39.0	25.7
Yavapai	53	25.0	18.1
Yuma	33	16.1	8.3
Arizona	12,920	198.8	149.0

Figure 4. Cases per 100,000 population by county, 2012



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 2012, valley fever was a primary or contributing cause of death in 39 deaths in Arizona (Table 4). These data may underreport causes of death and may contain errors. Thus, this is likely an underestimate of the true number of deaths attributable to valley fever.

Table 4. Deaths attributable to valley fever by county, 2012

County	Primary cause of death	Primary or secondary cause of death
Apache	0	0
Cochise	1	1
Coconino	0	0
Gila	1	1
Graham	0	0
Greenlee	0	0
La Paz	0	0
Maricopa	13	21
Mohave	0	0
Navajo	0	0
Pima	7	11
Pinal	3	5
Santa Cruz	0	0
Yavapai	0	0
Yuma	0	0
Arizona	25	39

Demographics

In 2012, the age of reported valley fever cases ranged from 11 days to 105 years old with a median age of 46 years. The highest rates of valley fever occurred among people older than 65 years; rates of reported infections among Arizonans in this age group are 47% higher than those in the general population (292.6 cases per 100,000 vs. 198.8 per 100,000 respectively) (Table 5).

Table 5. Reported cases and rates by age groups, 2012

Age Group* (Years)	Cases	Cases per 100,000
<5	59	13.3
5-14	499	54.6
15-24	1387	150.6
25-34	1,857	214.5
35-44	2,215	267.3
45-54	2,175	260.0
55-64	1,923	257.0
65-74	1,587	294.6
75-84	866	295.2
85+	299	275.7

*Age could not be ascertained for 53 cases (approximately 0.4% of all cases).

Fifty-eight percent of reported cases were female (228.2 cases per 100,000 females), while 41.3% were male (164.8 cases per 100,000 males). Gender was not reported for 141 cases (approximately 1.1% of all cases) (Table 6). Prior to 2009, the majority of reported cases were male. Reporting changes may have caused this shift.

Table 6. Cases by gender, 2012

	Cases	Percent of total	Cases per 100,000 population
Female	7,452	57.7%	228.2
Male	5,327	41.2%	164.8
Unknown	141	1.1%	--

Only 18.7% of cases reported to ADHS contained information about race or ethnicity. Thus, it is not possible to analyze incidence rates by race or ethnicity.

Table 7. Race or ethnicity of reported cases, 2012

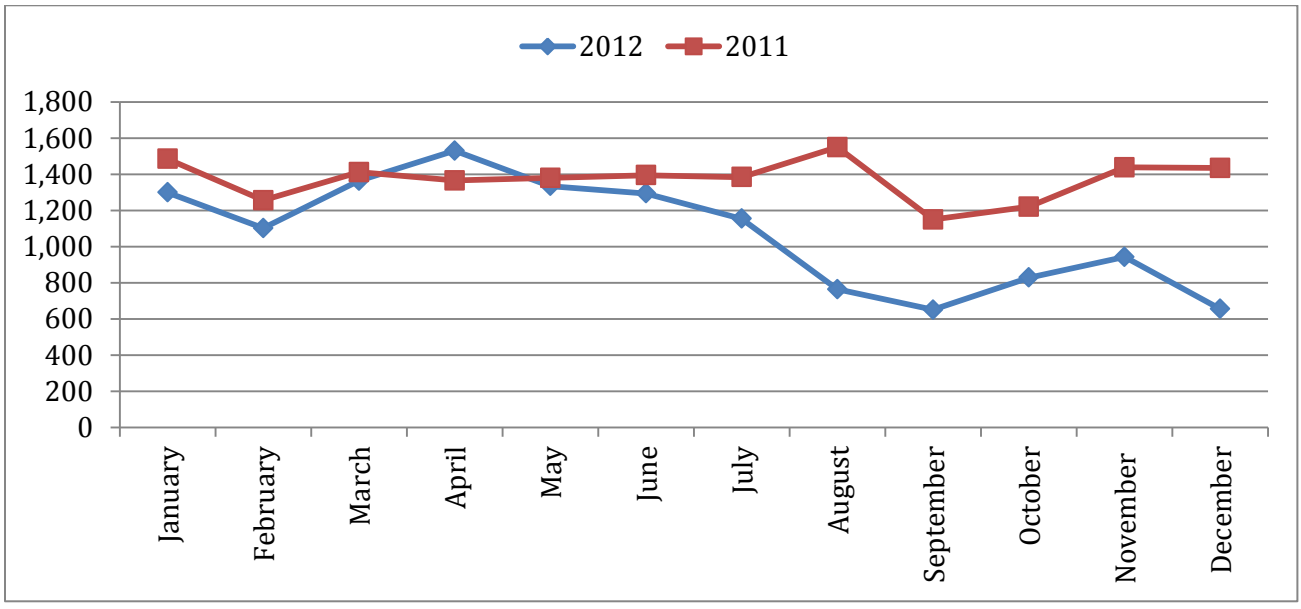
Race or ethnicity	Cases	Percent of total	Percent of cases with known race or ethnicity
Asian or Pacific Islander	58	0.5%	2.4%
Black	161	1.3%	6.7%
Hispanic or Latino	354	2.7%	14.6%
Native American	152	1.2%	6.3%

White	1,663	12.6%	67.5%
Other	60	0.5%	2.5%
Unknown	10,502	81.3%	--

Seasonality

Seasonal variation in valley fever reports has been consistently noted in past years: numbers of reported cases would 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 in 2011 and 2012. 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 health care 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 demonstrated that the median time between symptom onset to diagnosis was 55 days.[8] It is unclear why the temporal distribution of reported cases differed in 2012 from that observed in 2011.

Figure 5. Cases reported by month, 2011 and 2012



[8] 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.

Hospitalizations

A previous ADHS investigation noted that 40% of reported valley fever cases require hospitalization.[5] In 2012, there were 1,070 hospitalizations with a primary diagnosis of valley fever. The rate of hospitalizations with a primary diagnosis of valley fever has increased over time from 13.2 hospitalizations per 100,000 persons in 2003 to a high of 22.6 hospitalizations per 100,000 persons in 2011, falling again to 16.5 hospitalizations per 100,000 persons in 2012. The causes behind this increase are unclear, but may reflect improved diagnosis and recognition by healthcare providers and an increase in the incidence of disease. Pinal County continues to have the highest rate of hospitalizations (Figure 6; Table 8).

Figure 6. Hospitalizations with a primary diagnosis of valley fever, 2003 -2012

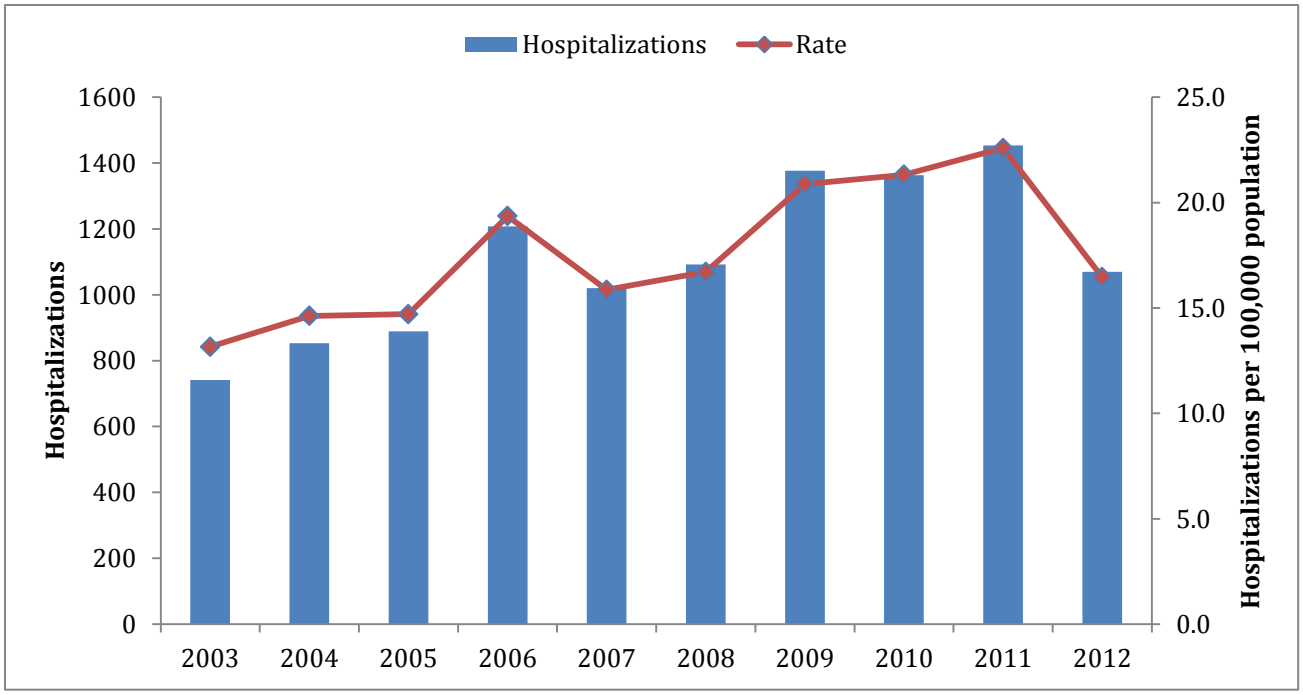


Table 7. Hospitalizations with a primary diagnosis of valley fever per 100,000 population by county, 2012

County	Hospitalizations per 100,000 population (2012)	Median hospitalizations per 100,000 population, per year (2007 – 2011)
Apache	2.8	2.8
Cochise	3.8	3.8
Coconino	1.5	2.9
Gila	13.1	5.4
Graham	5.4	13.4
Greenlee	0.0	0.0
La Paz	9.6	9.6
Maricopa	18.7	24.4
Mohave	11.3	10.3
Navajo	6.5	2.6
Pima	14.1	15.1
Pinal	29.5	34.4
Santa Cruz	2.1	2.1
Yavapai	3.3	4.7
Yuma	0.0	2.0
Arizona	16.5	20.9

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.[5] Between 2003 and 2012, hospitalization charges for Arizona residents with a primary or secondary diagnosis totaled $923 million with a median of $30,765 in total charges per hospitalization in 2012 dollars. Total annual charges also increased from $56 million in 2003 to $103 million in 2012 (Table 9). Medicare was the most frequently listed expected source of payment (34%), followed by an HMO or PPO (30.8%), the Arizona Healthcare Cost Containment System [AHCCCS] (22.3%), self pay (4.8%), and other sources (8.2%). Total charges associated with hospitalizations for which Medicare and AHCCCS were listed as sources of payment were $314 million and $205

million, respectively. The total healthcare costs attributable to valley fever are greater due to the exclusion of the cost of outpatient care and non-acute inpatient care in these figures.

Table 9. Total charges associated with valley fever hospitalizations in non-federal facilities in Arizona, 2003 - 2013

	Total (2012 dollars)	
	Primary	**Primary or Secondary**
2003	$35,841,244	$56,077,190
2004	$44,356,120	$68,142,341
2005	$47,775,374	$67,684,950
2006	$76,173,631	$108,673,079
2007	$63,368,983	$93,172,625
2008	$64,947,432	$90,337,944
2009	$81,650,772	$111,962,812
2010	$78,916,128	$112,143,360
2011	$75,015,531	$112,578,548
2012	$68,627,476	$102,686,897
Total	$636,672,691	$923,459,746

Additional analysis was performed for hospitalizations with a primary diagnosis of valley fever in 2012. In contrast to the gender distribution observed in reported cases, 58% of hospitalizations in 2012 involved a male patient. The age distribution of hospitalized patients was as follows: 12.0% <25 years old, 25.5% 25 –44 years old, 30.1% 45 – 64 years old, 27.4% 65 – 84 years old, and 5% 85 years or older. The median age was 52 years. Approximately 40% of these hospitalizations involved an intensive care unit (ICU) admission. Median length of stay was 4 days. Approximately 68% of these hospitalizations were associated with primary pulmonary coccidioidomycosis; 6.0% were associated with coccidioidal meningitis. Eighteen percent of patients were readmitted to the hospital; 5.6% were readmitted more than three times. Twenty-one (2.0%) patients died during a hospitalization.

Enhanced Surveillance for Valley Fever among Children and Young Adults

Approximately 8.0% and 9.0% of valley fever cases reported to ADHS in 2012 were <18 years of age and aged 18 – 25, respectively. Previous studies of pediatric valley fever have mostly consisted of case reports and retrospective case series. These studies have noted that pediatric valley fever can require lengthy hospitalization, intensive care, and in rare cases, surgery. Misdiagnosis or delays in diagnosis are also common.[9,10,11] Studies of military personnel and college students have also noted a substantial burden of disease in otherwise healthy young adults.[12,13] To better understand the impact of valley fever on these population subgroups, ADHS conducted enhanced surveillance for valley fever among cases reported in 2011 who were 25 years old or younger at the time of reporting. A total of 2,666 cases that were 25 years old or younger, including 1,266 <18 years old, were reported in 2011 and 435 patients (16.3% of all reported cases ≤25 years old) were interviewed.

A preliminary analysis indicates that the burden of valley fever in children and young adults in Arizona is substantial. While these age groups represent a small proportion of all reported cases, disease in this population can be severe and result in repeated visits to a health care provider or emergency room and hospitalization, even in otherwise healthy individuals. Both children and young adults reported median symptom duration of one month with nearly 30% continuing to experience symptoms at the time of interview. As in adults, fatigue, fever, and cough were the dominant reported symptoms. The frequency of reported symptoms was slightly higher in young adults than in children, although this may reflect a severity bias in terms of who among all infected symptomatic young adults sought care and were tested for valley fever. Approximately half of patients in either age group were prescribed antibiotics. A higher proportion of young adults were prescribed

[9] McCarty JM, Demetral LC, Dabrowski L, et al. Pediatric coccidioidomycosis in Central California: A retrospective case series. Clinical Infectious Diseases. 2013; 56(11):1579-85.

[10] Fisher BT, Chiller TM, Prasad PA, et al. Hospitalizations for coccidioidomycosis at forty-one children's hospitals in the United States. Pediatr Infect Dis J 2010; 29:243-7.

[11] Connelly MB, Zerella JT. Surgical management of coccidioidomycosis in children. J Ped Surg 2000; 35:1633-4.

[12] Stern NG, Galgiani JN. Coccidioidomycosis among scholarship athletes and other college students, Arizona, USA. Emerging Infectious Diseases. 2010; 16(2) 321-3.

[13] Crum-Cianflone NF. Coccidioidomycosis in the U.S. military: A review. Annals of the New York Academy of Sciences 2007; 1111:11-121.

antifungals. Eighty eight (20.2%) patients were hospitalized during their illness. Both age groups experienced significant disruption in daily life due to their illness including lost time at school and work. Complete findings from this investigation will be published at a later date.

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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