

# **VALLEY FEVER**

## **A primer for non-medical people**

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### **INTRODUCTION**

This primer is written for non-medical people in the hope that it will be a source of useful information for those living in the arid areas of the southwestern United States and in Mexico where the valley fever fungus thrives and where valley fever infections are very common. Although many brief articles on valley fever have been published - in pamphlets, newspapers, magazines, and encyclopedia and although many articles on the subject have appeared in medical journals and other scientific magazines and texts, we are aware of no previous attempt to present a thorough discussion of this disease to the non-medical public.

This book is arranged in four parts. The first section (Section ONE) is an overview of valley fever which attempts to explain what the disease is, how the disease is caused in people and in animals, what the symptoms are, what the complications of the disease are, how the disease is detected (diagnosed), and what treatments, both medical and surgical, are available. This section is for a "quick study" so that the reader can gain a good general understanding of the disease in about one hour of reading time.

Section TWO amplifies some of the important features touched on in Section ONE - for those readers who want more detailed information. Some of the social and economic issues associated with valley fever are also discussed.

Section THREE covers the history of valley fever - how it was identified and how knowledge of the disease developed. The works of some of the many physicians and other scientists who made important contributions to the understanding, identification, and treatment of valley fever are briefly outlined.

The final section (Section FOUR) is a selected, annotated bibliography, which we hope will direct interested readers to other sources of information about valley fever.

## **SECTION ONE DEFINITIONS**

The medical name for valley fever is coccidioidomycosis - often called "cocci" (pronounced KOK-SEE) for short. The name of the fungus, which causes valley fever or "cocci", is *Coccidioides immitis*. The medical name for valley fever comes from the first word of the name of the fungus - *Coccidioides*. The ending of the name - mycosis - means a fungus infection. So the entire word coccidioidomycosis - means an infection caused by the fungus *Coccidioides*. A fungus is a member of the plant family. Molds and mushrooms are examples of other members of the fungus group of plants. Cocci's other name - valley fever - probably arose because of the prevalence of the disease in the San Joaquin valley and great Central valley of California.

### **WHY LEARN ABOUT VALLEY FEVER?**

We assume that since you have read this far you are interested in learning about valley fever. If you live in an area where the disease is prevalent there are several good reasons to study it. First of all, valley fever quite commonly affects people who live in hot dry areas with alkaline soil. These areas include the Central and San Joaquin valleys and desert areas of California, as well as the arid areas of Nevada, Utah, Arizona, West Texas, New Mexico, Mexico, Central America, and South America. Animals also develop valley fever - especially dogs, horses, cattle, and llamas. Cats are rarely infected.

The area in California where valley fever occurs most frequently is Kern County, located at the southern end of San Joaquin valley. The Phoenix and Tucson areas of Arizona also experience a large number of valley fever infections. You as an individual are quite likely to be affected by valley fever if you live in an area where the cocci fungus is prevalent. For instance, 30% or more of the residents of Bakersfield, Kern County, California have positive skin tests for valley fever. A person (or animal) with a positive skin test has had a valley fever infection and has developed immunity to the fungus and therefore will never contract valley fever again. Almost everyone who lives long in an area where the disease is prevalent has been infected themselves or knows someone who has had the disease. The social, medical, and economic impacts of the disease are considerable. These aspects are discussed in Section TWO.

## **HOW DO YOU GET VALLEY FEVER?**

The cocci fungus lives as a saprophyte - in a sort of hibernation state - in dry, alkaline soil. When weather and moisture conditions are favorable, the fungus "blooms" and forms many tiny spores which lie dormant in the soil until they are stirred up by wind, by vehicles, by excavation, etc. - and become airborne. These very light, microscopically small (2 to 4 microns) spores called arthrospores - can float invisibly in the air for long periods of time, and they can be blown by the wind over great distances - many miles. When a susceptible human (or animal) that is not immune inhales these airborne spores, they enter the lungs and cause an infection (pneumonia). In general, the greater the number of spores inhaled the larger and more severe the infection (pneumonia).

## **WHAT KINDS OF SYMPTOMS AND HEALTH PROBLEMS DOES VALLEY FEVER CAUSE?**

Symptoms usually begin about two weeks after a susceptible person or animal inhales the spores.

The inhaled spores cause an infection in the lungs. The infecting spores grow in the lung tissue and become microscopic cysts called "spherules" (little spheres). Each spherule is filled with even smaller endospores. As the infection in the lung increases, the spherules burst, allowing the endospores to be discharged into the lung tissue. Each of the numerous endospores may itself grow into a spherule. The disease will progress, that is, the pneumonia will spread until the body develops immunity to the fungus and thereby contains and suppresses the infection, or until a medication effective in destroying the fungus or in retarding the growth of the fungus is given. We will say more about that in the section on treatment.

## **SYMPTOMS**

About two weeks after a susceptible person - one who is not immune to the disease - inhales the valley fever arthrospores, the symptoms of the disease begin. These symptoms typically include fever, aching, chills, sweats, fatigue, cough, and headache symptoms, which are commonly associated with the "flu". The severity of symptoms - and the severity of the lung infection - are probably related to the number of arthrospores inhaled. The more spores inhaled, the worse the disease. The susceptibility of the "host" - the person or animal inhaling the spores - is also related to the severity of the symptoms and of the disease.

Over half of those infected have no symptoms at all and in many others symptoms can be very mild. The person may develop what amounts to a slight cold, which quickly subsides, and they will never know that the "cold" was really a mild case of valley fever unless a skin test or blood test for valley fever is performed and is positive. Others have more severe symptoms including the flu-like symptoms mentioned above. Fever and cough are prominent. Skin rashes may occur. Joint aches - especially those involving the knees - are also common. It may take six months or more for these symptoms, particularly the tiredness and joint aches, to completely subside.

Blacks, Filipinos and perhaps some other Asians are more likely to have the more severe symptoms and to have the disease spread from the lungs to other parts of the body. This spreading of the disease from the lungs to other areas - skin, bones, other organs and "soft tissues" of the body, and brain - is called "dissemination." Filipinos, blacks, native Americans, Hispanics, and Orientals are more likely to experience dissemination of valley fever than Caucasians. However, the most dangerous form of dissemination - infection of the brain lining (meninges) - called cocci meningitis - is most likely to occur in Caucasians, especially Caucasian males. Cocci meningitis is the form of dissemination most likely to end in fatality.

The most common site of dissemination is the skin. The rashes associated with valley fever are not forms of dissemination. Disseminated valley fever skin lesions usually take the form of pustules. If the pustule is pricked with a

needle and its contents looked at under a microscope, the typical cocci spherules are seen. Valley fever rashes, on the other hand, do not contain spherules.

Bones and joints are the second most common site of spread of the cocci infection. Infected bones and joints are painful. Changes in bones or joints due to cocci infection can be seen on x-ray. A bone scan will also show the areas of infection.

Meningitis - the most lethal complication of disseminated valley fever - may cause a stiff neck, severe and persistent headache, nausea, vomiting, and various other central nervous system symptoms such as disorientation, loss of balance or equilibrium, inability to think clearly, and loss of consciousness. Cocci meningitis is diagnosed by spinal tap, and by physical examination.

## **DIAGNOSIS**

Most cases of valley fever do not need to be treated. 30-60% of people in areas where the disease is highly prevalent ("endemic") - such as in the southern San Joaquin Valley of California and south-central Arizona - have positive skin tests, most of them being unaware of ever having had valley fever until they were skin-tested for the disease.

People with disseminated disease need to be treated with medicines. Dissemination - spread of the disease from the lungs to other sites in the body - happens because the individual's infection-containment system is not adequate to suppress the infection and keep it from spreading.

One measure of the infected individual's ability to deal with and contain the infection is the "complement fixation titer" of the valley fever blood test. This titer is determined as follows: a small amount of the infected person's serum - the clear part of the blood from which red and white blood cells have been removed - is diluted with an equal amount of salt solution and tested for valley fever. The serum is diluted more and more (one part serum to 2, 4, 8, 16, 32, 64, 128, 256, etc. parts of salt water) and tested at each dilution until a positive test for valley fever can no longer be detected. In general, the more dilute the serum ("higher the titer") the more severe the infection.

When the body develops immunity to the valley fever fungus, the titer falls and the valley fever skin test becomes positive. High titers (1 to 64 and higher) indicate more severe disease and lead doctors to consider prescribing anti-fungus medicine.

People with diabetes, and women who contract valley fever while they are pregnant, are particularly likely to have dissemination of the disease and, therefore, these groups of people require strong consideration for medical treatment. As we mentioned previously, Blacks, Filipinos and perhaps some other Asians are more likely to experience dissemination, as are pregnant women.

## **MEDICAL TREATMENT**

At the time of this writing, three medicines taken orally and two medicines given intravenously are approved by the United States Food and Drug Administration (FDA) for use against valley fever.

The drug with the generic name ketoconazole (sold under the trade name Nizoral) is the oldest of the three approved oral anti-fungal medications. Ketoconazole can cause liver enzyme elevation and even hepatitis with jaundice in some people. Patients taking ketoconazole therefore need to be examined by a physician periodically (about once a month) and they need to have a liver function blood test about once a month. If liver enzyme levels determined by the blood test rise, ketoconazole therapy is discontinued immediately. It is also important not to use alcohol or to take certain other drugs, which may affect the liver while taking ketoconazole.

The generic name of a second, and newer, FDA-approved oral anti-fungal medication is fluconazole - trade name Diflucan. Periodic liver function testing is required while taking this medication. Fluconazole may also be given intravenously. This drug has proved to be very useful in treating disseminated disease, particularly in meningitis.

The third oral anti-fungal drug approved for use against valley fever has the generic name itraconazole - trade name Sporanox.

Because ketoconazole has been prescribed longer and more extensively than the other two drugs, more is known about its effects and side effects. It is not used in severe cases of valley fever because it is not as effective in the suppression of the fungus *Coccidioides immitis* as is the intravenous medication amphotericin-B. The same is true of the other two oral anti-fungal agents mentioned above.

The most effective medication for the treatment of valley fever infections is amphotericin-B - a drug which has been in use against fungus infections since the 1950's. However, there are drawbacks and side effects with use of amphotericin-B. This drug is not effective when taken orally. It must be given intravenously or into the spinal fluid or into valley fever abscess cavities. When receiving amphotericin, most patients experience side effects that are quite bothersome. These include a feeling of being weak and ill ("malaise"), along with the development of fever, chills, sweats, nausea, vomiting, joint pains, and muscle cramps. Medications such as steroids, antihistamines, antiemetics (drugs to treat nausea), and tranquilizers are often given at the same time as the amphotericin to decrease the intensity of side-effects and allow patients to be more comfortable while receiving intravenous amphotericin.

The most serious side effect of amphotericin administration is decreased kidney function. Amphotericin causes damage to kidney cells and this decreases the kidney's ability to filter waste chemicals from the blood. It is very important to perform frequent blood tests to check kidney function during amphotericin therapy. The dose of amphotericin given may need to be reduced, or the frequency of giving the amphotericin may need to be decreased until the kidneys have recovered sufficiently to show adequate function on blood testing. Amphotericin is also given by "spinal tap" into the spinal fluid at the base of the brain of patients who develop valley fever meningitis, and it is used to irrigate valley fever abscesses in bone and "soft tissues".

## SURGICAL TREATMENT

Probably the most commonly performed surgical procedure for the treatment of valley fever is the insertion of a venous access device ("Groshong" catheter, "Broviac" catheter or subcutaneous reservoir - "Porta-cath"). These devices allow amphotericin-B to be given into a large central vein - usually the superior vena cava, the large vein which drains into the top of the heart instead of giving the amphotericin into a vein of the arm or the hand. Amphotericin is often given three times a week, and arm and hand veins are quickly inflamed and "used up" so that they no longer carry blood. The venous access devices mentioned above allow amphotericin to be given much more easily and painlessly.

The drainage of valley fever abscesses in soft tissues and in bones and joints, or the removal of bone infections (osteomyelitis) is also performed fairly commonly in areas where valley fever is prevalent. Valley fever can form nodules in the lung which are seen on chest x-ray. These are often biopsied with a needle under local anesthesia or through a bronchoscope - an instrument that looks down through the windpipe into the air passages of the lung. Valley fever also can produce cavities in the lung - areas where the lung tissue has been completely destroyed by the valley fever infection - leaving a rounded hole in the lung that may be partly filled with fluid. Chest x-rays can also detect these lung cavities. If lung cavities grow, if they cause the patient to cough up blood, or if they burst and cause the lung to collapse then surgical treatment by opening the chest and removing the infected portion of lung is often necessary. Intravenous amphotericin-B therapy is given in conjunction with lung removal procedures in the treatment of valley fever lung cavities.

## SUMMARY

To summarize the information presented in Section ONE:

Valley fever = *Coccidioidomycosis* = "cocci".

Caused by a fungus - a member of the plant family.

Scientific name: *Coccidioides immitis*.

The "cocci" fungus lives in hot, dry, alkaline soil. Proper amounts of rain cause the fungus to grow ("bloom"). Many microscopic arthrospores are produced. These become air-borne, are inhaled into the lungs of a "host" (person or animal) who is not immune, and a lung infection develops.

The lung infection may be minor - about 80% of people - or more serious. In general, the more arthrospores inhaled, the larger and more serious the infection.

Almost all valley fever infections remain in the lung. Spread to other parts of the body (dissemination) occurs in about 0.5% of people infected.

Symptoms and signs of valley fever include fever, fatigue, cough, skin rashes, sweats, chills joint aches, and malaise.

Severe disseminated valley fever is more likely to occur in darker-skinned people.

The most serious form of dissemination is meningitis. It is responsible for most of the deaths caused by valley fever. Caucasian males are most susceptible to cocci meningitis.

Most cases of valley fever need no treatment

Treatment (medication) usually is necessary in patients with diabetes, in pregnant women, in patients with high complement fixation titers (1:64 and above), and in patients with dissemination – spread of the infection beyond the lungs.

Treatment medications include:

Amphotericin-B, the most effective medicine. Must be given into the blood or into the spinal fluid or into joint or abscess cavities. Not effective when given orally. Medicine is not very expensive. Giving the medicine is expensive (see Section TWO).

Ketoconazole - Nizoral. Given orally. Can cause liver-cell damage. Is expensive.

Fluconazole - Diflucan. Can be given both orally and intravenously. Penetrates well into most body fluids. Few side effects. Expensive.

Itraconazole – Sporanox. Given orally only. Does not get into spinal fluid. Fewer side effects than the other antifungal agents. Expensive.

Once you have developed a positive valley fever skin test you are immune and will not get the disease again.

Valley fever is NOT a communicable disease - meaning it does NOT spread from one person to another.

## **AVOIDANCE**

To avoid contracting valley When in endemic areas, DON'T INHALE.\* (unless your valley fever skin-test is positive. Avoid digging, plowing, driving vehicles through the soil of endemic areas where you are likely to inhale a large number of arthrospores (unless your valley fever skin test is positive).

Apply oil, asphalt, water, sod, crops, etc. to fungus-bearing soils to prevent wind-dispersion of arthrospores.

Avoid outside exercise such as tennis, jogging, etc. during dust storms (unless your you-know-what is positive). There are likely to be large numbers of arthrospores in and near endemic areas during dust storms.

\* Poor medical joke. Authors apologize.

## **SECTION TWO INTRODUCTION**

This section gives more detailed information about valley fever - what a valley fever patient might expect in the way of medical evaluation, x-ray and laboratory testing, and treatment both medical and surgical. The costs of evaluation of patients with suspected cocci and of testing for valley fever are estimated. as are treatment costs. The overall economic impact of coccidioidomycosis on one particular endemic area following a cocci "epidemic" of 1992 is discussed. The need for the development of an effective vaccine for the prevention of valley fever becomes apparent.

## SURGERY

One of the most commonly performed surgical procedures in patients with valley fever is biopsy.

Biopsy is performed to prove that the site biopsied contains valley fever organisms. This can be proven either by seeing the infecting spherules under a microscope, or by growing the *Coccidioides immitis* fungus in the bacteriology laboratory from the biopsy sample. Either one of these methods - identifying the valley fever spherules under the microscope, or growing valley fever fungus from the biopsy material - gives absolute proof that the biopsied site ("lesion") is a valley fever infection site.

Commonly biopsied valley fever infection sites are those in the lung - where "nodules" or "infiltrates" are the usual biopsy targets - and those on the skin which usually look like pustules or small blisters ("Vesicles"). Skin lesions can usually be shave-biopsied. The lesion is shaved off - using local anesthesia if necessary. Skin lesions can also be biopsied by placing a sterile needle in them, then pulling back on the plunger of a syringe attached to the biopsy needle so that the resulting vacuum in the syringe pulls tissue cells and/or fluid out of the lesion. The needle biopsy sample can then be looked at under a microscope, or sent to the bacteriology lab for "culture" - to see if valley fever fungus can be grown from the needle biopsy sample. Usually, both microscopic evaluation and bacteriology culture are performed on needle biopsy material.

Needle biopsy of "nodules", "infiltrates", and "effusions" in the chest are also commonly performed.

A "nodule" is a rounded clump of dense tissue in the lung. It can be seen on a chest x-ray and on computed tomography ("C-T" or "CAT") scan of the chest. An "infiltrate" is an area of pneumonia in the lung. It can also be seen on chest x-ray and on C-T scan. An "effusion" is a collection of fluid OUTSIDE the lung itself, but INSIDE the chest cavity. In other words, the effusion fluid lies between the outer coating membrane of the lung (called the "pleura") and the inside of the chest wall.

Needle biopsy samples of nodules, infiltrates and effusions can be taken by injecting a local anesthetic beneath the skin and into the muscle and other "soft tissues" of the chest wall to make the area numb. The needle is then directed through the numbed chest wall into the target (nodule, infiltrate or effusion) to be biopsied. The C-T scanner or the fluoroscope are often used to guide the needle into the target. The patient would therefore often be in the C-T scanner or under the fluoroscope during the biopsy process. A sample of the target material is removed by pulling back the plunger of the syringe attached to the biopsy needle so that tissue and fluid are vacuumed into the syringe.

Other ways to obtain biopsies of chest lesions are through a bronchoscope, or a mediastinoscope, or through a thoracoscope. A bronchoscope is a long, thin, flexible tube with fiberoptic light bundles running through it. The bronchoscope can be inserted through the windpipe into the air passages in the lung. (Air passage = "bronchus"). Light is shined into the lung through the bronchoscope and small biopsies are taken through the bronchoscope under direct vision.

The mediastinoscope is a larger hollow metal tube that is inserted through a small incision in the front of the neck along the windpipe ("trachea") and down beneath the breastbone into the chest. Light is shown through the mediastinoscope into the chest, and lymph nodes - which might contain valley fever infection - are biopsied under direct vision. (Mediastinum = partition between right and left lungs).

A thoracoscope ("thorax" = chest) is an instrument which is inserted through the skin and chest wall, between the ribs into the space between the outer surface of the lung and the inner surface of the chest wall. With the patient under general anesthesia, the lung is allowed to collapse and the thoracoscope is used to examine and biopsy lesions on the outer surface of the lung or on the inner surface of the chest wall. The usual way to perform thoracoscopy is by a video-assisted technique.

A video camera on the thoracoscope images the inside of the chest cavity and the picture is watched by the surgical team on a TV screen. Instruments are inserted through small incisions in the chest wall and surgical procedures on the lung or chest wall lining (pleura) are performed by using the TV images to direct the grasping, stapling, cutting, and suctioning instruments. These TV-guided operations are referred to as video-assisted thoracic surgery or VATS procedures.

Needle biopsies of abscesses – collections of pus in soft tissues or bones - are also performed.

Needle "biopsy" of spinal fluid ("spinal tap") is performed by inserting a needle between the backbones ("vertebrae") and through the tough fibrous sac ("dura") which surrounds the spinal cord and extracting spinal fluid to analyze for evidence of valley fever meningitis.

One more frequently performed surgical procedure involves the placement of a small plastic tube ("catheter") through a large vein – usually the large "subclavian" vein which is located beneath the collar bone - into the even larger vein which drains into the upper part of the heart - the "superior vena cava". The part of the catheter outside the veins is either attached to a small plastic reservoir ("Porta-cath") from which blood can be drawn or amphotericin antifungal solution injected, or by bringing the external part of the catheter (the part not in the veins) out through the skin on the chest wall ("Groshong" or Broviac" catheter) so that blood can be drawn or amphotericin or other liquids can be injected into the bloodstream.

As mentioned in Section ONE, amphotericin is often given three times a week for many weeks and veins on the arms or hands are rapidly "used up" during amphotericin therapy. The use of a subcutaneous reservoir with attached intravenous catheter ("Porta- cath") or of an external intravenous catheter ("Groshong" or Broviac") makes frequent drawing of blood and giving of intravenous medicines much simpler and more comfortable.

## ECONOMICS

The annual cost of valley fever is considerable – but difficult to estimate. The very light cases of the disease may not even cause the patient ("victim", if you will) to miss a day's work. The more symptomatic cases - those which produce "flu" symptoms and fatigue - often cause the patient to miss several weeks of work.

The typical patient with flu-like valley fever will go to a doctor to find out what is wrong. In areas where cocci is common, valley fever infections usually occur in the hot, dry summer and fall months - particularly after a period of windy weather or after an outright dust storm. A doctor who has practiced for any length of time in "cocci country" will have a high index of suspicion. When a patient presents with a cough and "flu" symptoms and fever and fatigue in the hot months of the year, the doctor is going to ask questions about dust exposure especially about occupational and recreational exposure.

Agricultural workers, construction workers, oil-field workers, telephone linemen, geologists - people who work outdoors and who are exposed to wind and dust - are somewhat more likely to contract valley fever. So are people whose hobbies or sports activities expose them to wind and dust: runners, joggers, bikers, off-road vehicle enthusiasts, tennis players, rock hounds, amateur (and professional) archeologists, etc. However, valley fever does not only infect adults who work and play outside. Infants and children quite regularly are infected. The authors have also occasionally seen valley fever infections in nursing home patients, and in others who rarely or never go outside. An open window, an open door, a gust of wind – – – presumably these are all that is required for the beginning of a new case of valley fever.

When a patient presents with the classic symptoms and a convincing exposure history, the diagnosis of valley fever suggests itself. It should be understood, however, that the symptoms of valley fever are not specific for, nor diagnostic of, valley fever. Fever, cough, tiredness, joint and muscle aches, malaise can be due to viral infections, bacterial infections, infections by a fungus other than *Coccidioides immitis*, etc. But - - - in "cocci country", especially in the summer and fall, the "classic" symptoms just mentioned suggest valley fever as the most likely diagnosis. As stated in Section ONE, the diagnosis of valley fever is proven by the valley fever blood test and/or by seeing under the microscope valley fever spherules collected from the infected patient.

The doctor will usually begin with a thorough physical examination, checking for a stiff neck, enlarged lymph nodes, lung noises suggesting bronchitis or pneumonia, skin eruptions (valley fever may cause two typical kinds of rash) as well as pustular eruptions from disseminated cocci – as described in Section ONE. Then chest x- rays, a skin test and a blood test for valley fever will probably be advised.

In uncomplicated, non-disseminated valley fever, symptoms usually subside in a few weeks or months. An area of pneumonia typically will be seen on chest x-rays and this will gradually clear, perhaps leaving a rounded "nodule" in the lung where the cocci pneumonia was. The valley fever blood test will need to be tracked to make sure the complement-fixing antibody titer falls to non-worrisome levels. If the skin test is negative initially, it will probably be repeated until a positive reaction is recorded. A positive skin test reassures the doctor that his patient has developed immunity to the fungus, and will not again contract valley fever if he or she inhales cocci arthrospores.

What might the cost be for an "uncomplicated" case of valley fever like the one outlined above?

A new-patient evaluation in a doctor's office will probably average \$100 (at the time of this writing) - with three or four follow-up visits in the \$30 to \$50 range – about \$250. Lung specialists - doctors with extra training in lung diseases - often charge more.

Three or four sets of chest x-rays (front and side view) with an x-ray specialist's reading -probably average about \$100 a set. That's about \$400.

Skin tests are \$16 to \$20 each. Figure two tests – the first is often negative – \$40. Three or four valley fever blood tests ("serologies") are often needed - at about \$50 per test – \$200.

The average, uncomplicated cocci case causes the loss of about two weeks work. Factor in that cost – and multiply by the number of uncomplicated cases of valley fever per year.

In Kern County, California in 1992 (an epidemic year for valley fever) there were 3,500 new cases documented by cocci blood tests. Most of those cases fell into the uncomplicated category similar to the case outlined above. The total cost of uncomplicated valley fever in Kern County, California in 1992, therefore, would have been about \$890 x 3,500 = \$3,115,000. To this must be added the lost time and productivity due to illness - estimated at two weeks per case. Two weeks per case x 3,500 cases = 7,000 lost workweeks. The economic impact of uncomplicated valley fever is considerable.

Even more considerable is the economic impact of complicated and disseminated cases. Patients with spread of the valley fever fungus infection from the lungs to other parts of the body (dissemination) require much more extensive (and therefore much more expensive) treatment – often over much longer periods of time (months or even years). Most patients in this group require at least one hospitalization. Many will require intravenous antifungal therapy, and many will require at least one surgical procedure. Fortunately, only about 1 to 2% of patients who contract valley fever will develop dissemination. The great majority of those who do develop disseminated disease will ultimately recover and will be able to return to work and to full activity.

A small fraction of those with disseminated disease will never completely recover and will be left with residual problems (primarily in the brain, lungs, bones and joints) which will render them incapable of returning to their previous jobs. Some will not be able to work at all and about 30 to 40 people per year in the state of California die of disseminated coccidioidomycosis. The average cost of caring for a patient with disseminated valley fever is probably conservatively estimated at \$50,000 at the time of this writing. Patients with disseminated valley fever almost always require some form of treatment with an antifungal medicine. At the time of this writing the average cost of giving one patient 1,000 milligrams of amphotericin intravenously over a period of four weeks is \$5,240. The cost of treating one patient with 400 mgs. of fluconazole per day is \$44. per day - just for the medicine.

Many patients will need to take the antifungal medicine for 3 to 6 months - \$5,260. - just for the medicine. The current cost of amphotericin-B is about \$40. for a 50 mg. dose. To these medication costs must perhaps be added hospitalization costs, doctor visits, x-rays, laboratory tests, surgical procedures and the costs of lost productivity of the patient.

The Workers' Compensation Board of the state of California recognizes that certain cases of valley fever are job-related and are, therefore, compensable. Workers who contract valley fever whose duties frequently include wind and dust exposure may be awarded state compensation for the treatment of their disease and for lost work income.

Why would anyone choose to live in an area where valley fever is endemic? Among the roughly half of long term residents who do get valley fever, most will have light cases and will not even need to see a doctor. In fact many will never know they had the disease unless they get a valley fever skin test or blood test. Only a small fraction of the 0.5% who develop dissemination will eventually end with residual disabilities or with a fatal outcome. As demographic data demonstrate, many people enjoy living and working and vacationing in dry, sunny areas. Economic opportunities in the agriculture, petroleum, ranching, mining, aerospace and resort industries continue to attract people to these areas. The risks from tornadoes, hurricanes, floods and traffic in many other places being greater, for most the benefits outweigh our relatively small risk.

Obviously, an effective vaccine against the *Coccidioides immitis* fungus is very desirable. It would protect people (and probably also animals) from developing valley fever. A vaccine actually was developed in the early 1980's but the side-effects of the vaccine as it was then produced made it unacceptable for use in humans. It needed to be purified to reduce the severity of fever, malaise, pain and inflammation at the injection site caused by the vaccine. In 1982, AIDS was identified, and research and grant money were removed from all other projects and concentrated on AIDS research. The large number of new cases of valley fever recorded in California in the epidemic years 1991-1994 stimulated renewed interest in the production and testing of a valley fever vaccine. Currently (1999) the Valley Fever Vaccine Project is bringing us the prospect of having an effective vaccine within a very few years.

## **SUMMARY**

To summarize the information presented in Section TWO:

Methods of diagnosing, evaluating and treating valley fever are outlined.

Costs of treating valley fever - both medically and surgically - are estimated.

The overall economic impact of valley fever on an endemic area in an epidemic year is estimated.

The desirability of developing an effective vaccine for the prevention of valley fever is underscored by the sometimes-serious medical problems associated with the disease, as well as by its economic impact.

## **SECTION III HISTORY OF VALLEY FEVER**

The first case of the disease was seen in 1892 in an Argentinean soldier. The pathologists thought that this was a cancerous disease. Two years later two cases were reported from San Francisco as being caused by a parasite. It was not until the early part of this century that the disease was properly identified and named as being of fungal origin. It was described in cattle in 1929 and isolated from the soil in 1932. In the late '30's workers at the Kern County Health Department found the same organism in the sputum of people with what was then called San Joaquin Valley Fever that had been reported previously as being the cause of the fatal cases. This closed the circle of the origin of the disease when this organism was also found in the soil.

The influx of troops for flight training during World War II caused thousands of days lost due to Valley Fever by the trainees. This brought forth a crash program by the War Department that led to many important discoveries and produced the diagnostic testing described in Section II. No major advancements in treatment occurred until 1954 when work with an antibiotic called amphotericin B began, followed much later by the introduction of the oral agents described in Section I.

## **Section IV Sources of Further Information**

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