

Notes from Presentation by Lisa Shubitz DVM re: Valley Fever

## Valley Fever Vaccine for Dogs

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### Basics:

Valley Fever is a fungal infection caused by spores in the environment. Seventy % of all cases are in Pima, Pinal and Maricopa County. It affects mammals and reptiles, zoo animals and marine mammals. Six to ten percent of dogs will contract Valley Fever. That results in 60,000 dogs every year. They see the infection in dogs in CA, NM, TX and NV as dogs travel for visits and dog shows. Some dogs are at greater risk as they are unresponsive to fluconazole. This results in pneumonia and dissemination of the disease into the bones. Treatment for these dogs will last for month or years depending on the severity of the disease and recurrence.

### Vaccine:

The vaccine is created from a live mutant strain of valley fever. The gene required by the valley fever fungus to cause disease is removed. They do not know why the gene does this. There is a large DNA chain so it is hard for the strain to revert to one that would cause the disease.

### Δ CPS1 in Mice:

Tests were performed on C57BL/6 mice which are black and BALB/C mice which are white. These are special mice that cost about \$35 per mouse. Mice are very susceptible to Valley Fever. They also used NSG mice which are missing almost all immune systems especially portion essential to resolve a regular Valley Fever infection.

These mice cost about \$300 each. The black and white mice were exposed to ten to one hundred times the lethal dose and they did not become sick. Upon examination under a microscope, the infection was degrading within days. The NSG mice were exposed to a fifty fold lethal dose and they did not become ill. This is an important implication for dogs or humans.

The mice were vaccinated and then infected with a virulent strain of Valley Fever. They inhaled the spore directly from a pipette. There were two studies. The short term study was for two weeks. The mice were then euthanized and then their lungs were cultured. The others were allowed to survive for four weeks and then their lungs were cultured as well. Nineteen of the twenty mice survived to 4 weeks. Under examination, there was no valley fever disease growth in the mice except for one.

#### Working with Mice versus Dogs:

- Trying a longer trial with mice—6 Months—this is in process and there are three studies this year
- Studies to be able to determine if dogs are responding to the vaccine without waiting for them to be infected. This is underway with funds in Companion Animal Fund
- Draw samples from vaccinated dogs. Separate white blood cells and see if they produce an immune response—this study is in progress
- Formulation of vaccine---this is incorporating the strain plus a stabilizer liquid to ensure good shelf life for at least 12 to 18 months.
- Manufacture vaccine with USDA licensing. This will involve licensing the production plant; licensing the vaccine; performing a safety study; performing and efficacy study whereby the vaccinated dogs will be monitored for one year.

There would be two groups—a control group and vaccinated group. They would utilize 500 dogs total—half will benefit immediately. They will not use research dogs—all will be volunteers.

#### Cost:

The mouse studies and vaccination---\$100,000 to \$130,000—this would take place on the UofA campus

Manufacturing and licensing—up to \$2 million

Safety and Efficacy Trials--\$100,000 to \$150,000 and will require some participating vets to work gratis.

#### Summary:

Based on mouse studies, this vaccine will work! The cost of development is the biggest obstacle. A state grant was applied for but it was not funded. The vaccine will take three to five years to license. It is anticipated that the dogs in the study will benefit. In the long run, this could save lives and millions of dollars in vet care.

#### The T Cell study

T Cells are very important! They are one of two parts of the immune system.

Antibodies are a diagnostic tool as they are measurable. That is what is measured with the titer. Antibodies do NOT help dogs fight Valley Fever, but they are critical for fighting bacterial and viral diseases.

T Cells have a helper and killer function and are critical to get over Valley Fever. They are difficult to measure. They secrete interferon-gamma when they encounter something they remember—memory t-cell response.

The T cell study would involve collecting 20 to 40 ml blood and then pulling out the white blood cells. Then infect with VF and measure the interferon gamma.

The T cell study would have two possible outcomes:

- The surrogate test whether a dog made an immune response to vaccine resulting in protection
- Learn more about immunological responses of dogs to VF fungus. This might let us know which dogs need long term or life time treatment and which are controlling the infection.

It is unknown at this time how often the vaccine would need to be administered.

Interesting facts:

When we put our dogs on Fluconazole (Azole drugs are the only drugs used to treat VF and Fluconazole has the fewest side effects) we are only curbing the fungal growth in the lungs; we are NOT treating the disease.

Brand Name vs Generic vs Compounded Fluconazole:

Let's talk about a dog that requires 200 mg twice per day.

FDA requires that Diflucan (brand name Fluconazole) would actually have to be within 2%--so the drug would consistently be between 196 to 204 mg by law

FDA requires that Generic Fluconazole would actually have to be within 10%--so the drug would be consistently between 190 to 210 mg by law

There is no restriction on compounding pharmacies so the actual percentages of Fluconazole will typically run from 50 to 80%.

Brand name and generic fluconazole are now out of range of most adopters because of price. Compounded Fluconazole now costs about \$160 for a 3 month supply.