

# **Aleutian Disease In Ferrets**

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## **Introduction**

We will refer to the Aleutian disease virus as ADV, the organism that causes the disease, and Aleutian disease as AD. Recently there has been quite a bit of erroneous information being passed around the Internet relating to outbreaks of this disease in various parts of the country. Ferret owners are left confused and understandably frightened. In researching this paper, journal and textbook articles were reviewed and interviews were conducted with two highly regarded veterinarians who have extensive experience with ferrets, Bruce Williams, DVM, PhD), and Karen Rosenthal, DVM, MS, Diplomate ABVP-Avian. Dr. Williams is currently a pathologist for the Dept. of Telemedicine, Armed Forces Institute of Pathology, in Washington, DC. Dr. Rosenthal is Director of Special Species Medicine at University of Pennsylvania School of Veterinary Medicine. In addition we have drawn from our own experience with this disease in over 24 years of practice. This article will address some of the questions that have been recently raised. As will be noted, there is still much unknown about this disease.

## **History**

AD is not a new disease and was first reported in ferrets in the late 1960's. [3,4] The virus was named after the Aleutian strain of the mink in which AD was first discovered in the 1940's. Historically, AD has not been a significant clinical disease in the pet ferret. In our own practice, (Midwest Bird & Exotic Animal Hospital/Westchester, IL), we diagnosed perhaps one to two cases of ferrets clinically ill with ADV per year from the mid 80's to the early 90's.[10] In recent years, the clinically evident AD has been almost nonexistent in our practice. Evidence of ADV has been found for many years upon postmortem microscopic examination of the tissues of clinically normal laboratory ferrets in various areas of the country.

## Cause

AD is caused by a parvovirus and may have strains of varying strength and varying immune response. The ADV is related to (but not the same as) the dog parvovirus, the cat parvovirus (feline panleukopenia) and the human parvovirus (Fifth's disease). ADV in ferrets may be a mutation of ADV of mink. Essentially the virus interferes with the immune system. ADV causes a huge increase in antibodies (specifically gammaglobulins) in the blood. This condition is known as hypergammaglobulinemia. These antibodies combine with the ADV particles to form compounds called antigen/antibody complexes. [4,5] These complexes are deposited within the tissues of multiple organs in the body, such as kidneys, liver, bile ducts, spinal cord, gastrointestinal tract, blood vessels and bladder, resulting in inflammation. Within the inflamed tissues two types of white blood cells predominate: plasmacytes and lymphocytes. If the inflammation is mild, the ferret may appear clinically normal. If the inflammation is severe enough, the ferret will show signs of disease relating to the organ or organs affected. For instance, if the spinal cord is affected, the ferret will exhibit signs of neurological disease. The exact mechanism by which the ADV affects the immune system is still poorly understood, but we do know that the end result is inflammation seen in multiple organs on microscopic examination. Interference with the immune system could cause the ferret to be more susceptible to viral enteritis, canine distemper virus, lymphoma and other diseases. [9]

## Transmission

Transmission of ADV can be via the air, but is usually accomplished by direct contact with infected ferrets' urine, saliva, blood, or feces. ADV can also be transmitted through contact with contaminated cages, gloves, towels, or humans. At this time it is impossible to say with any certainty how quickly or easily the disease is transmitted. Dr. Williams believes that transmission of the ADV may be difficult and that prolonged contact with the virus is necessary to spread the infection.[8] Dr. Rosenthal feels it is more easily spread and that variations in ease of transmission may be related to the virulence or strength of each strain or its geographic location. [9] Ferrets may contract the virus but never develop clinical signs of AD. We know very little about this "carrier state" including how often or under what conditions the virus is shed by the carrier, how long the infection can last and whether the ferret can ever completely rid its body of the virus. We have to assume that an ADV positive ferret, even if it appears clinically normal, has the potential to shed the virus at anytime.

## Clinical Signs

The onset of clinical signs is extremely variable. There is no accurate way of determining if or when a ferret that has been exposed to ADV will develop disease. No prediction can be made as to the severity or type of clinical signs that may be manifested. It is important to note that historically the majority of ferrets that have been exposed to ADV never developed obvious clinical signs of the disease. Some ferrets may be carriers of the virus for years before developing clinical signs. Some ferrets may even revert to a "negative" ADV status based on blood testing after a period of time. [10]

The disease has been described historically in mink and ferrets as a chronic, progressive, wasting disease. However, more recently (last 15 years up to the present time), AD most frequently presents in ferrets as an ascending (traveling from the back towards the front) paresis (weakness) of the hind quarters. [1,2,6,7,10] Other signs can include lethargy, melena (blood in the stool), twitching or seizures, anemia, or enlargement of the liver or spleen. It is important to note that a number of other much more common diseases can present with similar clinical signs as AD including foreign bodies in the stomach, eosinophilic gastroenteritis, canine distemper, kidney or liver failure and lymphosarcoma, to name a few. AD cannot be diagnosed on clinical signs alone. Hypergammaglobulinemia may be present in the end stages of the disease.

## Diagnosis

A presumptive diagnosis of AD in ferrets is based on clinical signs as described above along with a positive counter-electrophoresis (CEP) blood test, (which will be discussed shortly), and a rule out of other potential disease (done through a variety of diagnostic testing procedures). Some ferrets may also exhibit hypergammaglobulinemia which can be demonstrated on a blood test called protein electrophoresis. The gamma globulins can comprise up to 20% of the serum total protein value. [1] It is difficult to definitively diagnose AD as the primary cause of clinical disease in the live ferret. The most definitive diagnosis of AD is made by histopathologic (microscopic) examination of the tissues of multiple organs. On a post mortem examination there is very little to be seen with the naked eye that would conclusively point to a diagnosis of AD. An enlarged liver or spleen, enlarged lymph nodes or mottled kidneys may be noted, but are not specific to AD. Histopathology of an AD ferret's tissues, however, consistently reveals inflammation with clumps of lymphocytes and plasmacytes infiltrating multiple organs such as liver, bile ducts, kidneys, central nervous system (brain and spinal cord), blood vessels, gastrointestinal tract, and bladder. [1,2,6,8,9] Lymphocytic-plasmacytic infiltrates in multiple organs have historically been classic pathologic signs of AD, particularly when accompanied by glomerulonephritis (a type of kidney inflammation). In the most recent outbreaks dealt with by Dr. Williams, spinal cord inflammation is being seen without the hypergammaglobulinemia and prior to the onset of glomerulonephritis. [8]

It is important to note that if a diagnosis of ADV is to be made on a ferret that has died, it is imperative that tissues from multiple organs be submitted for histopathological examination in order to obtain an accurate diagnosis. As a minimum, the organs submitted should include: kidney, liver with bile ducts, intestine, spinal cord and bladder.

## **Blood Tests for ADV**

Currently the only available blood test for detection of ADV is the CEP test produced by United Vaccines (Madison, WI). The test is fairly inexpensive and has been used for years in both mink and ferrets. Historically it has proven to be a useful test when used to screen breeding populations of ferret and mink for ADV. However, there is currently a controversy among veterinary clinical pathologists as to the efficacy of this test. It is not considered 100% reliable by some clinical pathologists' because it can be contaminated by various proteins which can give false positive and false negative results [9]. In addition the United Vaccines CEP test can't be reproduced by other labs at this time because no scientific paper has ever been written explaining the test methodology and substantiating its validity. [9]

It should be noted that some laboratories are also offering to check ferrets for AD using tests that were designed to detect canine parvovirus antibodies. Since ADV and canine parvovirus are related, the supposition is that the canine test can be used in ferrets. However, great caution should be exercised when interpreting such a test as valid as there is no data to suggest that canine parvovirus tests can accurately assess the ADV status of a ferret. Other blood tests included the immunofluorescent antibody test (IFA) and the polymerase chain reaction test (PCR). For several years the Massachusetts Institute of Technology (MIT) Department of Comparative Pathology performed an IFA test. This test was thought to be more accurate than the CEP test, but it was more expensive. In the past if the CEP test was positive, then blood could be sent to MIT to confirm the results. Unfortunately MIT has since discontinued the test and it is no longer available to the public.

The PCR test looks at the DNA sequence of each virus. Unfortunately due to the antigenic diversity of the ADV, this test isn't practical at this time in ferrets. An early casual study done in the 1980's by the author (Brown) tested over 500 shelter ferrets using the United Vaccines CEP test. Approximately 10% tested positive for ADV, however only two of those ferrets went on to develop clinical signs consistent with ADV. There are two points to be gained from this study. One is that ADV is not uncommon in the general ferret population, and two that many if not the majority of clinically normal ferrets that test positive on the CEP test for ADV will not develop clinically evident signs of AD.

At the time of this writing, the CEP test is the only ADV blood test available that is specific for ADV, but caution should be exercised when interpreting results. One should consider repeating the test after a period of time to confirm the results in cases where AD is suspected. A positive CEP test only indicates that ADV is in the ferret's body, it does not tell you if ADV is actually causing the clinical disease being manifested. Suspected cases of AD in ferrets with overt clinical signs cannot be diagnosed strictly on the basis of a positive CEP test.

## Treatment

There is no effective treatment for either the clinical disease or carrier state of AD in ferrets. Supportive care with syringe feeding, fluid therapy, anti-inflammatory drugs, and various other medications are used to treat the clinical signs. Treatment may be helpful in mildly affected AD ferrets, but will rarely reverse the disease in severely affected cases. There is no vaccine for AD and it would be contraindicated because of the way ADV interacts with the immune system. [1] Where exposure is suspected, cleaning with appropriate agents will kill the virus. The virus is susceptible to formalin, sodium hydroxide, and phenol compounds.[1] Some of the products that are active against parvoviruses in general include Synphenol-3, Roccal-D, and ParvoGuard. If poor sanitation is practiced, ADV can remain active in the environment for up to two years. Quarantine in pet households is not practical because of the long incubation period of the virus and its probable prevalence in the ferret population. Complete prevention would include strict sanitation with isolation and culling of the ADV seropositive ferrets. Culling (terminating) of clinically normal ADV positive ferrets is only recommended by the authors for breeding facilities and not for pet households.

## Discussion

ADV has been recognized in ferrets for more than thirty years and the mortality rate has been low. Dr. Williams commented that he's diagnosed about 3-4 cases per year over the last three years, based on histopathologic signs. The authors commented earlier that cases of AD are uncommon in their practice whereas diseases such as enteritis, lymphoma, insulinoma, adrenal disease and others are encountered on a daily basis. AD has been reported for years in the US and Europe with the occasional "outbreak". In an "outbreak" in Texas in a ferret shelter two years ago, an ascending paresis (weakness) and paralysis was observed without wasting or glomerulonephritis. In that case, 4 ferrets died in a group of 65 ferrets, 61 of which were seropositive on the CEP test for ADV. Since then nine more ferrets have died but their deaths haven't been definitely confirmed as being caused by ADV. There have been other reported "outbreaks" in Michigan, Pennsylvania, Alabama, and the East Coast. Information on the clinical illness or mortality in those cases was unavailable to us at this time, but ADV positive ferrets were in the group. [9]

## Recommendations

Any clinically ill ferret suspected of having AD should have a complete diagnostic workup performed to rule out other more common diseases. A diagnosis of AD cannot be made on a positive CEP test alone. Strict sanitation and quarantine should be observed whenever ANY infectious disease is suspected in an ill ferret. Good sanitation practices should always be first and foremost in any pet owners' daily regime to prevent as well as treat disease in any pet.

**Pets:** Clinically normal pets do not need to be routinely tested for ADV at this time. If a clinically normal pet ferret is tested and found positive for CEP we do not recommend euthanasia as the pet may or may not develop clinical disease in the future. In addition we do not recommend quarantining a CEP positive, clinically normal ferret because it is highly likely that all ferrets in the household are already exposed at the time of the positive finding.

**Breeding facilities:** There is concern that very young ferrets may be highly susceptible to ADV, so breeding facilities may have special risks that are not present in pet households. Neonatal mink that were infected with some strains of ADV developed fatal pneumonia. (1) In addition, some breeding facilities may be attempting to raise ADV free ferrets. In these cases it is advised to test for ADV and quarantine all ferrets coming into a breeding facility. The quarantine should continue for a minimum of one month and then be retested prior to entering the breeding population. Ferrets that test positive for ADV should be permanently removed from the breeding population. Clinically normal ADV positive ferrets may be perfectly suitable for pets and it is not necessary to euthanize them if they can be placed in a appropriate homes.

**Boarding facilities:** Boarding facilities may wish to require a negative ADV test within four to six weeks prior to boarding. Because of the uncertain nature of the test, it may even be useful to require two negative tests one month apart. However, if strict sanitary measures are used and if boarding ferrets' are kept in their own cages and not mixed in with the rest of the boarding population the chances of ADV transmission is probably minimal and testing is probably not necessary.

**Shows:** As discussed, ADV has been in the general ferret population for years and it would be nearly impossible to prevent all ADV positive ferrets from entering a show area. The problem with requiring ADV testing prior to the show is that it still does not ensure that ADV will not enter the show, due to the possibility of false negatives and the possibility of ferrets being exposed to the virus after being tested and before coming to the show.

The best prevention is that owners that attend ferret shows use good sanitation practices. Owners should clean their hands after handling other ferrets, not hold other people's ferrets against their clothing (which could become contaminated) and not allow their ferrets to intermingle with other ferrets at the show. Ferrets under 6 weeks of age are at a higher risk of contracting many infectious diseases and should not be present at a show. This is more for their protection than the concern that they will be the source of disease. It is the authors' opinion that ADV is not a reason to shut down ferret shows.

## **The Bottom Line**

**1.** Most if not the majority of ADV positive ferrets will never develop clinical signs, nor die from this disease.

**2.** The CEP test is probably not 100% accurate and may produce false positives and negatives. A definitive diagnosis of AD in a clinically ill animal cannot be based on the CEP blood test alone.

**3.** Other, more common diseases can have similar signs as AD. Always rule out other disease with a thorough diagnostic workup.

**4.** The best prevention for the spread of ADV or any other infectious disease is to use good sanitation methods at all times, even when all the ferrets are healthy.

**5. THERE IS NO REASON TO PANIC!**

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