

## **Section 2**

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# **Pre-conference Program: AEMV Scientific Program**

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# Intra-arterial Blood Pressure in Ferrets Compared to Peripheral Blood Pressure

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## Session #125

Summary Style Manuscript

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## Introduction

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Aldosterone, which is produced in the zona glomerulosa, is one hormone that influences blood pressure. In ferrets, LH-receptors are present in the zona glomerulosa.<sup>3</sup> When ferrets develop adrenal gland disease, LH-receptors are activated, which consecutively may result in increased aldosterone plasma concentrations and an associated increase in blood pressure.<sup>1</sup>

Doppler ultrasound is the most widely used method to measure indirect peripheral systolic arterial pressure in ferrets, but it consistently underestimates direct systolic pressure and is imprecise.<sup>2</sup> Therefore it should be used only to detect general trends in blood pressure.<sup>2</sup>

In this study, indirect blood pressure measurements from the tail, front, and hind leg were compared to the direct arterial blood pressures in 14 male ferrets at hypotensive, normotensive, and hypertensive states. For indirect blood pressure measurements, an oscillometric sphygmomanometer and a veterinary high definition oscillometry (HDO) monitor were used.

## Results

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Overall, measurements using the tail were considered most reliable. The systolic, mean, and diastolic arterial pressures (SAP, MAP, and DAP) measured with the HDO monitor were consistently higher than the direct values during hypotensive states, whereas values during hypertension were substantially lower. The values measured at normotensive states corresponded better.

The oscillometric sphygmomanometer consistently overestimated SAP. When looking at the MAP and DAP, a change from over- to underestimation could be seen with an increase of blood pressure, similar to measurements with the HDO monitor.

## Conclusion

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There is an inconsistency between indirect and direct blood pressure measurement, regardless of the technique used.

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# A Comparison of Direct and Indirect Blood Pressure Monitoring Techniques in Rabbits

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## Session #130

Summary Style Manuscript

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Accurate techniques for evaluating blood pressures in rabbits are vital for monitoring patients under general anesthesia and evaluating the cardiovascular status of patients in an emergency situation. Indirect measures of blood pressure using the Doppler or oscillometric techniques are non-invasive, require less expensive equipment, and are easier to perform than direct measures of blood pressure requiring an arterial catheter. This project was designed to evaluate Doppler and oscillometric blood pressure monitoring techniques in comparison to the invasive direct technique in rabbits under general anesthesia with isoflurane. Indirect systolic blood pressures were measured peripherally on the thoracic limbs of 7 healthy adult New Zealand white rabbits. These values were compared to concurrent measures of direct blood pressure obtained via catheterization of the central ear artery.

In estimating systolic blood pressure, the Doppler technique consistently underestimated the pressure (median -12 mmHg [IQR -16, -5]), and the oscillometric technique greatly overestimated (median + 20 mmHg [IQR 15, 27]). Diastolic blood pressure measured using oscillometry underestimated the pressure (median -11 mmHg [IQR -17, -4]), widening the measured pulse pressure difference, but the calculated mean arterial pressure using oscillometry most accurately estimated the direct arterial pressure (median + 3 mmHg [IQR -1, 10.25]). All indirect measurements were significantly different from the direct pressure ( $P < 0.0001$ ).

This data suggests that Doppler monitoring is a better indirect technique for estimating systolic blood pressure. If oscillometry is used to measure blood pressure, the calculated mean arterial blood pressure most accurately represents the direct measure of arterial blood pressure.



# Aplastic Myeoloid Anemia in Ferrets

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## Session #135

Summary Style Manuscript

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Anemia is a common clinical finding in pet ferrets (*Mustela putorius furo*) presenting for illness. As in other species, anemia in ferrets can have multiple underlying causes. Classification of anemia response (regenerative vs regenerative) and/or by mechanism (blood loss, accelerated erythrocyte destruction, or reduced or defective erythropoiesis) is helpful in determining etiology. A number of diseases have been shown to produce anemia in ferrets and include trauma, gastrointestinal ulceration, neoplasia (including leukemia and hematopoietic neoplasia), chronic renal disease, chronic inflammation, and immune suppression.<sup>1,2</sup> Bone marrow suppression caused by excess estrogen has been suggested, but not documented.

The authors and others have identified severe anemia of unknown origin in ferrets ranging from 6 months to 3 years of age. Hematocrit ranged from 6 to 15% in affected ferrets. In these cases, exact etiology remained elusive. Bone marrow analysis revealed abnormalities classified as the following: erythroid arrest, pancellular maturation arrest, and erythroid depletion. Ancillary tests included complete blood count, chemistry panel, radiographs, adrenal sex hormone analysis, liver biopsy, and exploratory surgery. Results were variable, and all ferrets initially responded to supportive care including multiple blood transfusions. A single case was treated with immune-suppressing drugs but failed to respond. Most eventually succumbed, but a single case recovered spontaneously.

Case details will be reported in the proceedings. The purpose of this presentation is to increase awareness of severe non-regenerative anemia in ferrets. Additional cases are being actively solicited from colleagues for further study. Data will be compiled and analyzed so that consistent findings among affected ferrets, if any, can be detected. Practitioners are encouraged to collaborate in this study by providing case documentation for affected animals. Inclusion criteria for this study and standardized case documentation forms will be made available to practitioners. While underlying etiologies may be multiple, coordination may help discover commonalities in these cases.

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# Post-Surgical Hyperthermia in Ferrets

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## Session #140

Summary Style Manuscript

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The purpose of this presentation is to describe cases of post-surgical transient hyperthermia in ferrets (7 at the time of print). Hyperthermia was characterized by temperature spikes of up to 106°F (~41°C) 30–40 minutes post-anesthesia that persisted for 4–8 hours. In all patients, hyperthermia was managed with active cooling (cool IV fluids, towels, ice packs) and ferrets recovered uneventfully. The exact cause of hyperthermia is unknown; however, in most cases seen by the author, ferrets were treated with butorphanol (0.1–0.3 mg/kg IM), morphine 0.10 mg/kg administered as an epidural, isoflurane, and meloxicam (0.2 mg/kg). Some ferrets also received midazolam, lidocaine/bupivacaine administered as a line block, and butorphanol plus low-dose lidocaine administered as constant rate infusion (CRI). Some patients received fentanyl instead of butorphanol.

Postanesthetic hyperthermia is well documented in cats, and hyperthermia is defined as a rectal temperature exceeding 102.5°F (~39.2°C). Some studies document temperatures in excess of 107°F (~41.7°C).<sup>1–3</sup> Multiple studies link hyperthermia with use of hydromorphone<sup>2</sup>; however, hyperthermia is seen with lesser frequency with other combinations of drugs as well, including medetomidine/diazepam/ketamine and medetomidine/propofol.<sup>1–3</sup> In all cases, however, incidence of hyperthermia is highest in groups receiving hydromorphone as part of an anesthetic regimen.<sup>1</sup> In one study, the use of ketoprofen with hydromorphone did not affect incidence of hyperthermia.<sup>1</sup> In another study, drug regimens containing buprenorphine without hydromorphone did not produce hyperthermia.<sup>2</sup>

Morphine injected into rats produces dose-dependant hyperthermia, which peaks at 45–60 minutes post injection. Morphine increases extracellular glutamate levels and down-regulates NMDA receptors, increasing glutamatergic transmission. Glutamate induces hyperthermia. Increases in glutamatergic transmission maximize hyperthermia evoked by morphine.<sup>3</sup> It is possible the mechanism for production of hyperthermia in other species with other morphine-like drugs is similar.

The use of opioids is common in ferrets, either as analgesics, or as part of pre-surgical sedation and anesthesia.<sup>4</sup> However, the author is unaware of reports of anesthetic-related hyperthermia in the ferret in the literature. Anecdotal reports abound.

Ongoing observations will be reported at the conference. It is important for practitioners anesthetizing ferrets to carefully monitor body temperature during the recovery period, especially those receiving opioid drugs.

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# Mediastinal Masses in Rabbits: Another Therapeutic Option

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## Session #145

Summary Style Manuscript

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Mediastinal masses in rabbits present a diagnostic and therapeutic challenge. Most rabbits present with either lymphoma or thymoma, and cytologic interpretation can be challenging without a biopsy. Although surgical excision of thymomas can be curative, rabbits present a high anesthetic risk, which is even greater for a thoracotomy.

Five rabbits with mediastinal masses were treated with radiation therapy. A dose of 600 cGy was administered weekly for 6 weeks for a total dose of 3600 cGy. All patients also received a short course of prednisolone therapy at induction, lasting from 7 to 30 days. A full necropsy was performed to confirm the preliminary diagnosis and to evaluate all organs for the presence of lymphoma. Three of the 5 masses were confirmed to be thymomas; 1 mass was a lymphoma; and in the fifth patient, no mass could be identified in the thoracic cavity either grossly or histopathologically, nor was there any evidence of lymphoma in any tissue.

Measurable shrinkage of the mass occurred in all patients. Two of the 5 patients had recurrence of the mediastinal mass, at 25 months and 12 months, respectively, after the onset of treatment. Radiation was repeated in both patients, who survived 25 months and 17 months post-treatment. The remaining 3 rabbits died of unrelated causes at 23, 7, and 5 months. Based on these findings, radiation therapy is a non-surgical therapeutic option for mediastinal masses in rabbits that offers increased survival times without compromising quality of life.



# Clinical Aspects of Hyperthyroidism in the Guinea Pig

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## Session #150

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*Abstract:* Anecdotal reports suggest hyperthyroidism occurs in guinea pigs, but none are peer-reviewed. The authors have had multiple cases of hyperthyroidism that responded positively to clinical treatment. This abstract summarizes the most important clinical information about this condition to help facilitate recognition, diagnosis, and treatment in the clinical setting.

## Signalment

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It appears that hyperthyroidism can affect all ages; however, most reported cases occur in animals over 3 years of age.<sup>1</sup> Thyroid hyperplasia, adenoma, and carcinoma all have been responsible for clinical signs.

## Clinical Signs

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In reviewing over 40 cases, clinical signs varied significantly; however, some changes were consistently found and can be considered key clinical signs. These include hyperactivity and hyperesthesia; animals often are polyphagic but appear thin or to be losing weight. Other common but not consistent clinical findings included diarrhea or soft stool, polyuria/polydipsia, and a palpable mass in the neck. Progressive alopecia has been reported.<sup>1</sup> Occasionally, the guinea pig has tachycardia and should be examined for cardiovascular abnormalities.<sup>1</sup>

## Diagnosis

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The diagnosis can be difficult as results from various diagnostic tests can often be inconclusive. The  $T_4$  and  $T_3$  blood concentrations have been unreliable indicators, both to confirm disease and to monitor the response to medical treatment. It is possible to encounter an animal with severe clinical signs but the  $T_4$  and  $T_3$  levels are not significantly elevated. As a baseline for normal values, previously published material is available (Table 1). A fine needle aspirate with cytological evaluation can aid in the diagnosis of a thyroid tumor, but it can not assess endocrine activity. One author (R.W.) has found that fluid aspirated from the neck mass often reveals extremely high  $T_4$  concentrations and correlates well with systemic  $T_4$  elevation. The diagnostic option of choice is nuclear scintigraphy as it appears to be a more reliable method to detect a hyperfunction of the organ. While the infrastructure and the availability of this diagnostic test are not great, the interested clinician should try to locate a local veterinary or human medical facility, which is equipped with a gamma camera. As an alternative choice of imaging an ultrasound exam of the thyroid can be performed to detect any anatomical changes in the gland.

**Table 1.** Gender specific values for thyroid hormone in the guinea pig (n = 6).<sup>2</sup>

T <sub>4</sub> male:	2.9 ± 0.6 ug/dl	T <sub>3</sub> male:	39 ± 17 ng/dl
T <sub>4</sub> female:	3.2 ± 0.7 ug/ dl	T <sub>3</sub> female	44 ± 10 ng/dl
Free T <sub>4</sub> male:	1.26 ± 0.41 ng/dl	Free T <sub>3</sub> male:	257 ± 35 pg/dl
Free T <sub>4</sub> female:	1.33 ± 0.25 ng/dl	Free T <sub>3</sub> female:	260 ± 59 pg/dl

One of the authors (J.M.) has successfully demonstrated a hyperactive thyroid in a guinea pig with a dose of 1.2 mCi of Technetium (pertechnetate) (Tc-99m), which was given as an intravenous bolus via the cephalic vein. In this instance, diagnostic images were obtained 60–80 minutes post injection.<sup>3</sup> However if a gamma camera and ultrasound is not available, the tentative diagnosis can be made through a combined review of the history, the clinical exam/signs, and the blood work (complete blood count and chemical profile, including T<sub>4</sub> and T<sub>3</sub> levels). In suspect cases, a trial therapy of methimazole can be started, as the response to medical treatment is usually very fast and obvious.

## Therapy

Multiple different treatment modalities for hyperthyroidism exist, once the clinical diagnosis has been established. Each treatment has its distinct advantages and disadvantages; the owner should be made aware of all these factors when deciding which treatment option to choose.

### Medical treatment

The drug of choice is methimazole, which has been used in cats with the same problem. Drug dosages have been extrapolated from cat dosages and range from 0.5 to 2 mg/kg PO q24h.

*Advantage:* This is the least invasive option to treat patients. A clinical response is usually seen within 48 hours and the drug is not very expensive. It is administered only once daily.

*Disadvantage:* Medication needs to be given for life. It can be difficult to monitor the effect based on hormone levels, and the veterinarian needs to go by clinical response. In other species (eg, cats), the drug has some minor side effects, with vomiting, anorexia, and depression being the most frequent. Hematologic effects of eosinophilia, leukopenia, and lymphocytosis are usually transient and generally do not require drug withdrawal. In rare but serious cases, the following may occur: self-induced excoriations, bleeding, hepatopathy, thrombocytopenia, agranulocytosis, and acquired myasthenia gravis. In case of toxicity (overdose), agranulocytosis, hepatopathy, and thrombocytopenias are perhaps the most serious effects that may be seen (all reported in other species).<sup>4</sup>

It is unclear to what extent these side effects apply to the guinea pig. To date, no side effects have been reported in the guinea pig.<sup>1</sup>

### Surgical excision

*Advantage:* Surgical excision can be curative if the pathological tissue is removed completely. With this method, there is no need to medicate for the animal's lifetime.

*Disadvantage:* Surgical excision can be a complicated due to the anatomical location of the thyroid gland. Several thyroid carcinomas (3 guinea pig patients) in one clinic (R.W.) could not be surgically excised due to extensive vascular and other vital tissue involvement. Surgery should ideally not be attempted before the animal is medically stabilized in order to avoid post surgical complications (C. Orcutt, oral communication, 2008). It is interesting to note that hyperthyroid human patients (and those receiving exogenous thyroid replacement) may be susceptible to developing severe hypertension and tachycardia when given ketamine. However, the veterinary significance of this potential problem is unknown.<sup>4</sup>

### **Percutaneous ethanol injection**

Alcohol ablation was attempted 2 times on the same guinea pig with only transient improvement; eventually the guinea pig died 1 month after last OH injection (R.W.).

### **Radioactive treatment with I-131**

One of the authors (R.W.) treated 1 patient with I-131, resulting in a good quality of life. A 6-year-old pig (~650 g) was administered 1 mCi subcutaneously once. The patient's hormone level was rechecked 3 weeks later ( $T_4 = 2.5 \mu\text{g/dl}$ ) before discharge from the hospital ( $T_4$  was  $14 \mu\text{g/dl}$  before I-131 treatment). The patient lived for 14 months after the treatment, then died of chronic renal failure. There was no indication of azotemia at the time of treatment; none of the guinea pigs ( $n = 5$ ) diagnosed with hyperthyroidism by the clinician (R.W.) had elevated blood urea nitrate levels at the time of hyperthyroid diagnosis. This feature appears to be different from cats with hyperthyroidism, which often display elevated BUN concentrations.

*Advantage:* The authors consider this as the best treatment option for long-term control and possible cure of hyperthyroidism. Treatment renders all hyper functional thyroid tissue, including ectopic tissue, nonfunctional. This treatment is less invasive than surgery, has a higher success rate, and can be administered IV or SC.

*Disadvantage:* Animals receiving treatment need to be brought to a special clinic that can perform the procedure. Further, the infrastructure of such clinics is not well established, and limited clinical data is available on the use of this treatment is available. Further, relapse is possible. Post-therapy isolation for several days to weeks is required because the animal will be radioactive after the treatment. Proper doses need to be determined.

## **Recommended Monitoring**

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### **Medical therapy**

Recommended monitoring includes a physical exam (including recording of body weight), complete blood work,  $T_4$  at 2 weeks; if normal, reassess q6 months or if adverse effect or recurrent signs of hyperthyroidism occur.

### **Thyroidectomy**

Recommended monitoring includes a physical exam (including recording of body weight), complete blood work with postoperative monitoring of serum calcium (including ionized calcium) if bilateral thyroidectomy,  $T_4$  at 2 weeks, then monitoring of  $T_4$  q3–6 months.

### **Radioactive iodine therapy**

Recommended monitoring includes a physical exam (including recording of body weight), complete blood work, and  $T_4$  2 weeks after treatment, then monitoring of  $T_4$  q3–6 months.

## Prognosis

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The prognosis can be good in cases where the problem was diagnosed in early states of the disease and response to the treatment is good. In severe cases and in cases where the animal is debilitated, the prognosis is less favorable. Sometimes secondary complications can occur, such as secondary pneumonia or aspiration of food when eating.

## Summary

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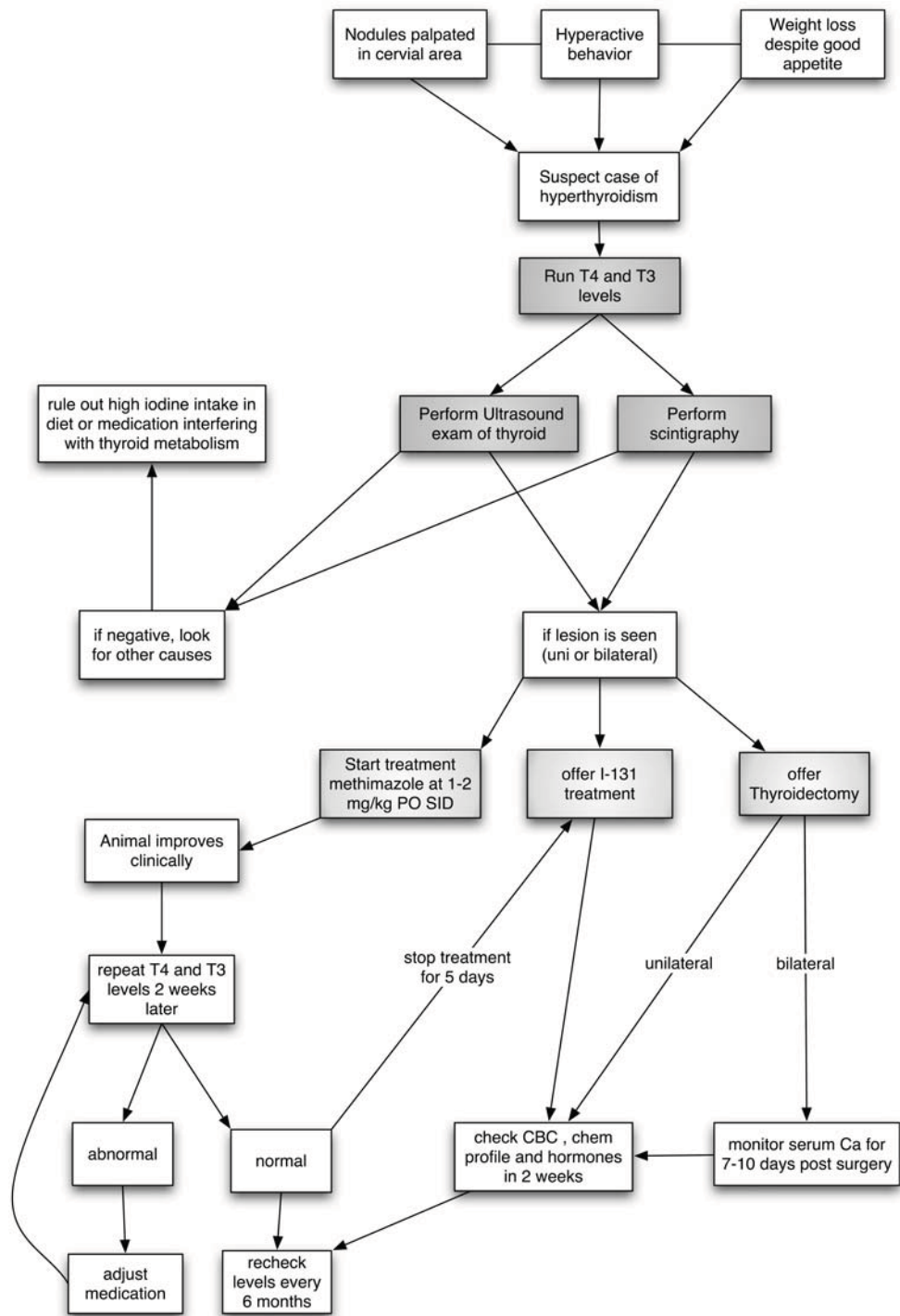
Without a doubt, it appears that functional (clinical) hyperthyroidism truly exists in the guinea pig population; it is surprising that no peer-reviewed article exists in the literature describing the clinical aspects of this pathology. Primary pathology of the thyroid gland in the guinea pig was described over 40 years ago,<sup>5,6</sup> showing that this pathology clearly exists, even if it is not common.

While no clear pattern about the sex predilection can be seen in the cases examined here, it is interesting to note that in human medicine it is known that differences exist between the activity of the thyroid gland between males and females and that the tendency for thyroid hypertrophy is greater in the female.<sup>7</sup> It is interesting to note that a parallelism has been found between the proliferative and other structural characteristics of the thyroid gland and the intensity of its metabolic activities and production of hormone. In the female guinea pig during the sexual cycle, the number of mitoses is therefore about 3 times higher than in the male. In human medicine, this would correspond to the tendency towards hyperthyroidism in females.<sup>7</sup> In addition, it is mentioned that there is a female sex-linkage of mixed thyroid tumors in man and dog.<sup>6</sup> One can speculate whether this also applies to the guinea pig.

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**Figure 1.** Algorithm used as a guide for the diagnosis and treatment of hyperthyroidism in an exotic small mammal patient.



# Aleutian Disease in Ferrets: Diagnostics and Controversies

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## Session #155

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*Abstract:* Aleutian Disease Virus (ADV) infection in ferrets has been the subject of much controversy in the UK. Difficulties in antemortem diagnosis have assisted in this controversy. This paper will outline the history of the disease in UK ferrets and summarize data on the available diagnostic tests and the likely occurrence of ADV infection in ferrets.

## Introduction

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Aleutian Disease Virus (ADV) infection was originally described in mink in the 1940s.<sup>1</sup> In mink, it appears particularly linked to an altered immune reaction to the virus linked with the Aleutian pelt color. The disease was first reported in ferrets in the 1960s.<sup>1</sup> ADV is a parvovirus occurring as various strains, some associated with ferrets and some with mink. Ferret-associated strains appear to cause less severe disease in mink than mink-derived strains, while mink-derived strains cause less severe reaction in ferrets than ferret-derived strains.<sup>2</sup> However, a range of mustelid species can harbor each of the strains.<sup>1</sup> Overall, ferrets appear much less susceptible to disease than mink.<sup>2</sup>

Disease is caused by deposition of immune complexes in a variety of organs.<sup>3,4</sup> Signs may therefore be variable, ranging from neurological (paresis/ paralysis of the hindquarters, head tremors) to chronic wasting syndromes.<sup>1,3,4</sup> The latter may be linked to deposition of immune complexes leading to glomerulonephritis or bile duct proliferation or a more generalized arteritis.<sup>1,3,4</sup> In mink, an immunosuppressive syndrome has been linked to ADV infection.<sup>1</sup> While suspected in ferrets, this has not been proven. It is also shown that adult ferrets may not develop clinical signs but may either remain as asymptomatic carriers<sup>5</sup> or may clear the virus after a period of up to 180 days.<sup>2</sup> However, the classic sign of active infection is hypergammaglobulinaemia (HGG)<sup>1-6</sup>

In the UK, cases were reported in Southern England and a serologic survey of ferrets undertaken.<sup>7</sup> Signs were similar to those classically described. Some 8.5% of tested screened ferrets proved positive by counterimmunoelectrophoresis.<sup>7</sup> Six animals were investigated (the majority of seropositives were culled), revealing lesions in all animals, even in one that was apparently asymptomatic. Lesions consisted of mononuclear cell infiltration and perivascular cuffing in a variety of organs. Hindquarter paresis appeared linked to lesions in the spinal cord. Culling of seropositives is extremely controversial even in the UK where there has been extreme concern regarding the entry of the virus into the ferret population. Many ferrets are used for working and there is contact with wild mustelids, including released farmed mink, and subsequent spread at shows. Diagnosis does not appear straightforward with nebulous clinical signs and difficulty in demonstrating viral lesions in situ in the living animal, meaning that incidence of this disease has been both over- and under-reported. Difficulty in detecting asymptomatic carriers means that screening programmes are often ineffective. This paper will look at the various diagnostic methods available both in clinical cases and for screening.

## Diagnostic Methods

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### Clinical signs

Clinical signs, as described above, are usually generalized and non-specific. Certainly there is no single pathogenic sign for Aleutian disease, and clinical features are shared with many other diseases/ syndromes including estrogen-induced anemia, lymphoma, eosinophilic gastroenteritis, gastric ulceration, proliferative bowel disease, salmonellosis, and ferret coronavirus infection.<sup>1,8</sup> ADV infection is often cited as a primary differential diagnosis in hind limb paresis/ paralysis. A small-scale study undertaken by this author and cited by Lewington (2007)<sup>4</sup> described lesions found on dissection of the spinal cord in 7 ferrets euthanized due to hind limb paresis/ paralysis. Six showed spinal abscesses, while one showed hemorrhage in the spinal canal. None showed lesions of ADV infection on histopathology.

### Clinical pathology

With nebulous clinical signs, it is appropriate to look for suggestive changes on blood chemistry values. With the exception of hypergammaglobulinaemia (HGG), there appear to be none.<sup>7</sup> It is important for clinicians to remember when submitting samples that accurate identification of HGG relies on measurement by electrophoresis. Lowering of the albumin:globulin ratio assessed by other means does not necessarily indicate HGG. It is also important to assess the electrophoretogram—the HGG of ADV infection will show a monoclonal gammopathy as opposed to the polyclonal gammopathy of more generalized inflammatory processes.<sup>9</sup> While this change shows very well the overproduction of antibody in response to virus, and therefore should be a feature in clinical cases, it is also shown to occur in ferrets that do not develop signs (though the rise in gammaglobulins may be less in these cases),<sup>1</sup> clinical signs may develop before HGG is apparent,<sup>10</sup> and, of course, failure to show monoclonal HGG is not indicative of an uninfected ferret (ie, serum electrophoresis is not suitable as a screening test).

### Serology

Serology is used to detect exposure to virus. The main disadvantage of using serology in the diagnostic setting is that it only indicates exposure, not active infection. In this disease, it is also the case that none of the methods can determine the strain of ADV to which the ferret has been exposed. Given the differences in disease produced by different strains, this could be a major disadvantage. It is also true that not all antibody-positive ferrets will develop disease nor will they, necessarily, shed virus for extended periods. Several methods have been in use, though only enzyme-linked immunosorbent assay (ELISA) is available currently.

### Counterimmunoelectrophoresis

The “classic” test is counterimmunoelectrophoresis (CEP) and has been available from United Vaccines (US) and Harlan Olac (UK), though it appears to no longer be available. Some UK commercial laboratories still list this in their pricelist, though it is likely this is an historical reference only. This appears to be a very specific test and does appear to be useful in ferrets.<sup>7</sup> However, it is a test designed for screening mink and so is not particularly sensitive. The main reason ferrets are not as prone to developing clinical signs of disease is that they do not produce the huge antibody response (and therefore not the immune complex deposition).<sup>2</sup> The test, therefore, is very likely to produce false negatives. This may explain why ferrets having previously tested positive will subsequently often re-test negative.<sup>7</sup> In the UK, this test was used extensively for screening healthy ferrets. This was for 2 reasons: the test is very cheap if samples are batched and only small volumes of blood are required. Blood could, therefore, be collected by toenail clip. This procedure was, however, condemned by the UK National Ferret Welfare Society as “cruel.” It also resulted in “testing evenings” where large groups of ferrets were

brought together for testing. Given the transmissibility of the virus and the insensitivity of the screening test, it is likely that these testing evenings were more responsible for spread of infection than for eradication of virus from the population!

### **Immunofluorescent antibody**

Immunofluorescent (IFA) antibody tests have been shown to be more sensitive than CEP and have, previously, been used to confirm CEP results. The test appears not to be currently available. However, given that disease is linked to high antibody levels, it is hard to see why a more sensitive test would help in the clinical setting. However, it may be more useful in screening

### **Enzyme-linked immunosorbent assay**

An ELISA test is available currently (ADV Antibody ELISA, Avecon Dagnostics Inc, Mannheim, Germany). This test is advertised as a highly sensitive test capable of detecting only ferret strains of ADV. It is available for use on blood or saliva, the latter being especially used in a point-of-care kit. While a sensitive serology test could be useful in screening, caution is required with this test. There appear to be no data regarding its sensitivity and specificity in ferrets and there is no data comparing this test with the CEP method.<sup>3,6</sup> This author performed a small-scale study comparing tests reported in Lewington (2007).<sup>4</sup> The saliva testing kit was used and sample collection proved very difficult—the recommendation is that a sponge is placed in the mouth for 60 seconds to allow saliva collection. The study was abandoned after 9 animals for fear of foreign body ingestion! Of the 9 animals sampled, each was tested using saliva ELISA and blood CEP. Six ferrets were negative by both methods, 1 was positive by both methods, and 2 were positive by CEP and negative by ELISA. The latter 2 results were felt to be due to difficulties in sample collection

### **Polymerase chain reaction**

Polymerase chain reaction (PCR) tests for viral antigen are currently available, both as screening tests for blood and body fluids or as in situ hybridization (ISH) tests for suspect clinical cases/ postmortem specimens. On speaking to various laboratories, it is clear that there are differences between these tests—some do appear to be specific to the ferret ADV strains,<sup>5</sup> while others are not sure. In terms of screening tests, PCR would appear to require animals to be persistently shedding or viremic, which may not be the case. Liver biopsy for ISH would be the most accurate method but is very invasive for screening tests

## **Discussion**

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This remains a difficult diagnosis and the importance of ADV to the ferret population is still not clear. It is, however, clear that there is no one definitive test and that the uncertain progress (coupled with an insensitive screening test) of the disease means that UK policy (still practiced in some areas) of culling antibody-positive ferrets is unacceptable

For diagnosis of suspect clinical cases, suggestive signs with a monoclonal gammopathy would be suggestive. Antemortem confirmation may be possible (depending on organ affected) by organ biopsy and in situ hybridization (ISH). ELISA serology may also help, but until this test is evaluated in ferrets this should not be recommended

For screening, the picture is much less clear now that there is no easy-to-use serology test available. If accurate in ferrets, the ELISA test could be of use where ADV-free colonies are required to be maintained. However, the importance of this in the general pet ferret population is unclear as disease is rare and antibody-positive ferrets

are more likely not to develop signs. In another small study by this author reported in Lewington (2007),<sup>4</sup> a small group of persistently antibody-positive ferrets was maintained for several years in which time none developed HGG or signs attributable to ADV infection. All were followed to death—the most common causes being cardiomyopathy and lymphoma. Lesions attributable to ADV infection were not found in any of these animals

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# Inguinal Herniation of the Urinary Bladder in a Female Rabbit

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## Session #160

Summary Style Manuscript

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A 4-month-old intact female Flemish giant cross rabbit was presented to The University of Tennessee Veterinary Teaching Hospital with a recent onset of lethargy, anorexia, foul-smelling red urine, diarrhea, and a large soft tissue swelling in the right ventral pelvic region. Physical examination, whole body radiographs, fine needle aspiration and cytology of the swelling, and an excretory urogram were performed in this case. Tests indicated that the swelling was due to a herniation of the urinary bladder through the right caudoventral abdominal wall. The results of a complete blood count were within normal limits. Abnormalities on a biochemical profile included an increase in blood urea nitrogen (53 mg/dl; reference range, 15–30 mg/dl), hyperglycemia (256 mg/dl; reference range, 75–150 mg/dl), hyperphosphatemia (7.6 mg/dl; reference range, 2.3–6.9 mg/dl), increased alkaline phosphatase (70 IU/L; reference range, 4–16 IU/L), and elevated creatine kinase concentration (3175 IU/L; reference range, 58.6–175.0 IU/L).<sup>1,2</sup> The rabbit was hospitalized with supportive therapy and successful surgical correction of the hernia was performed 3 days after the initial presentation. At the time of surgery, it was evident that the grossly thickened urinary bladder was present within a fluid-filled inguinal hernia sac. The bladder was incarcerated by a complete hernial ring formed by the right inguinal musculature. The etiology of the herniation could not be definitively determined, but it was likely congenital or non-traumatically acquired. This presentation includes a review of the anatomy, pathophysiology, classifications, and surgical repair of inguinal hernias.

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# Pathological Aspects of Thyroid Tumors in Guinea Pigs (*Cavia porcellus*)

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## Session #165

Summary Style Manuscript

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This report describes 20 cases of thyroid tumors in guinea pigs submitted between 1998 and 2008. Median age was 4.3 years (range, 2.5–6 years). Submissions were from 7 males and 10 females; sex was not reported in 3 cases. Four submitted tumors were from excisional biopsy samples, and 16 were collected at necropsy. Eight tumors were benign thyroid adenomas, 11 were adenocarcinomas, and 1 was too autolyzed to determine malignancy. One adenocarcinoma metastasized to heart and lungs. Osseous metaplasia was present in 3 adenomas and 4 adenocarcinomas; radiographic mineral opacity was detected in one of these cases.

Patients with thyroid adenoma also had myocardial disease or atrophy of fat (n = 7 for each condition), chronic renal disease (n = 4), and metastatic mineralization or marked weight loss (n = 3 for each). Acute myocardial degeneration, chronic renal disease, hepatitis, biliary cysts, ovarian cysts, and hepatocellular necrosis were also found in patients with thyroid adenoma (n = 2 for each), as were metastatic mineralization, urinary bladder transitional cell carcinoma, pulmonary adenoma, pulmonary adenocarcinoma, splenic hematoma secondary to torsion, lymphoid thyroiditis in the contralateral gland, bilateral ovarian cysts, lymph node thrombosis, urolithiasis with cystitis, hepatic lipidosis, pancreatic islet cell carcinoma, chronic pleuritis, uterine leiomyoma, pituitary adenomatous hyperplasia, aspiration pneumonia, pulmonary adenoma, peritonitis, cystic endometrial hyperplasia, duodenal leiomyosarcoma, uterine leiomyoma, gliosis with spongiform encephalopathy, and gastric perforation (n = 1 for each).

Guinea pig thyroid tumors are typically rare and benign<sup>1</sup>; however, 11/20 thyroid tumor submissions demonstrated adenocarcinomas.

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# Mammary Gland Tumors in Guinea Pigs (*Cavia porcellus*)

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## Session #170

Summary Style Manuscript

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This report describes 38 mammary tumors in guinea pigs submitted between 2001 and 2008. Median patient age was 4 years (range, 1.5–7.5 years). Submissions included those from males (21/38), females (14/38), and unknown sex (3/38). Tumors were unilateral in 34 cases and bilateral in 2 cases; side was not reported in 2 cases. Two males and no females had been neutered before the mass was identified, and reproductive organs were submitted together with the mammary tumor from 1 male and 2 females.

Samples were submitted for histopathology by excisional biopsy (n = 35) or cytological examination of a needle aspirate (n = 3). Five females and 11 males had adenocarcinoma; 6 females and 7 males had adenoma; 3 females had lipoma; and 1 male had a cyst. Evidence of metastasis was present in 2 males with adenocarcinoma. Neoplasia was diagnosed in all 3 cytological samples (2 males and 1 sex not reported). In 2 remaining guinea pigs where sex was not reported, 1 had an adenoma and 1 had an adenocarcinoma. Mammary gland hyperplasia was not found in males, but did occur in 8 females with concurrent tumors, 5 with adenocarcinoma, and 3 with lipoma. Mammary cancer is uncommon in male mammals, but a greater proportion of male guinea pigs in the submitted cases had adenocarcinoma (11/21) than did females (5/14).



# Giant Cell Sarcomas in Pet Rabbits

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## Session #175

Summary Style Manuscript

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Mesenchymal tumors that have many large multinucleated cells are sometimes referred to as giant cell sarcomas, but the term does not imply cell of origin. Human giant cell tumors are considered primary bone tumors (osteoclastomas).<sup>1</sup> In the veterinary literature, the best described are giant cell tumors of soft parts in horses.<sup>2</sup> In a recent study of cutaneous tumors of rabbits, a rhabdomyosarcoma and anaplastic sarcomas had multinucleated cell components.<sup>3</sup> A retrospective study identified 13 giant cell tumors in pet rabbits submitted to Northwest ZooPath from 1995–2008. Breeds included Netherlands dwarf (n = 1), giant lop (n = 1), minilop (n = 1), Dutch (n = 1), “domestic” (n = 1), and not given (n = 8). The average age was 7 years, and ages ranged from 3 to 10 years, with age not stated for 2 rabbits. Five were males, 3 were females, and age was not stated for 5 rabbits. Locations included the leg (n = 5), inguinal (n = 2), axilla (n = 1), flank (n = 1), thoracic wall (n = 1), eyelid (n = 1), thoracic cavity (n = 1), and abdominal cavity (n = 1). No metastatic lesions were identified. Time between diagnosis and euthanasia ranged from 3 days to 8 months but was not known for 10 of the rabbits. The rabbit with the intrathoracic tumor was found dead with no prior signs of illness. Histologically tumors were comprised of haphazard sheets and streams of spindloid, epithelioid, and multinucleated cells, generally with considerable anaplasia and frequent mitoses. The tumors stained positive for vimentin and most were positive for smooth muscle actin. All tumors stained negative for S-100 and for desmin. The immunohistochemical findings and morphologic features indicate that these tumors most likely were leiomyosarcomas. In rabbits, leiomyosarcomas should be considered invasive malignancies that require aggressive surgical intervention.

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# Rabbit Cutaneous Basal Cell Tumors

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## Session #180

Summary Style Manuscript

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Basal cell tumors historically were a common skin tumor diagnosis of dogs and cats. Recently, most cases of basal cell tumors previously diagnosed in domestic animals have been reclassified as trichoblastomas, based on the World Health Organization classification system.<sup>1</sup> Basal cell tumors are thought to arise from small pluripotential epithelial cells within the basal cell layers of the epidermis and adnexa. Trichoblastomas are derived from or are reduplicating the primitive hair germ of embryonic follicular development and are divided into several sub-types. The rabbit cases we examined appear to conform very closely to the biologic behavior and histopathologic patterns of trichoblastomas as described in dogs, cats, and man.

These tumors are a relatively common skin tumor of rabbits based on our submissions; however, they are infrequently reported in the literature and there, they are described as basal cell tumors.<sup>2-4</sup> From a database of 1966 rabbit submissions, 433 skin tumors (benign and malignant) were identified. Of these skin tumors, 28% (n = 122) were diagnosed as basal cell tumors. There was no sex predilection (female = 64 and male = 56). The ages ranged from 2 to 13 years, with an average of 5.8 years. The head and neck seemed to be the most common location at 20% (25/122). The limbs were involved at 17% (21/122). Although they may become very large and ulcerated, complete surgical removal is curative for this benign tumor.

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# Use of Cabergoline in the Treatment of a Pituitary Macroadenoma in a Rat

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## Session #185

### Summary Style Manuscript

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A 650-g, 2-year-old male pet rat presented due to a 3-week history of decreased thirst, apparent blindness, and sudden personality change. On physical examination, he was in good body condition and able to move around his cage without difficulty. However, he appeared unaware of his surroundings, was visually unresponsive, and seemed aggressive. Based on the history, the physical examination findings and the animal's age, our primary differential diagnosis was a pituitary tumor. The owner consented to an MRI scan of the rat's brain. Six days after the initial presentation, the imaging study was performed and showed a large mass measuring 11 x 8 x 8 mm, in the area of the pituitary gland; the brain measured 20 mm in length from olfactory bulb to cerebellum. The rat was immediately placed on cabergoline (0.6 mg/kg PO q72h). Eight weeks later, the rat returned for a follow-up imaging study. The owner reported significant improvement at home including loss of aggressive behavior and increase in activity. The physical examination was unremarkable. The second MRI showed the pituitary tumor had decreased in size. The macroadenoma measured 6 x 6 x 6 mm. Five months post-initiation of the treatment, the rat continues on the same dose of cabergoline and shows no clinical abnormalities or unusual behavior. Cabergoline, a dopamine agonist, had a marked and sustained prolactin-lowering effect. This is the first reported case of the use of cabergoline to treat successfully an MRI-documented pituitary tumor in a rat.



# Hypothyroidism in an Obese Pet Ferret

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## Session #190

Summary Style Manuscript

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The purpose of this presentation is to describe a case of presumed hypothyroidism in an obese ferret with concurrent insulinoma and adrenal neoplasia.

A 5-year-old female spayed ferret was presented for insulinoma and inability to regulate blood glucose. The referring veterinarian had treated the ferret for an insulinoma based on a classic clinical presentation (pelvic limb weakness, depression) and blood glucose of 38 mg/dl measured with an in-house chemistry analyzer. Frequent feedings, plus the addition of prednisone and diazoxide did not produce clinical improvement. On physical examination, the ferret was obese at 1628 g, with excessive subcutaneous and abdominal fat, particularly associated with the pelvic limbs, perineum, and both lateral aspects of the neck. There was slight increased respiratory effort, especially after exertion. No other abnormalities were noted. Attempts to modify drug and dietary therapy were unrewarding, and the ferret was not considered a surgical candidate due to extreme obesity. Over the course of several weeks, weight continued to increase to a maximum of 1750 g at the time of death. Blood was collected for baseline thyroid testing, and a thyroid stimulation test was performed. Results were highly suggestive of hypothyroidism. Thyroxin supplementation was begun, but the ferret died of complications related to hypoglycemic crisis. Tissues were submitted for pathology. Both thyroid glands were abnormal, with follicles containing cellular debris.

Clinical findings, laboratory tests, and necropsy plus histopathology support hypothyroidism in this ferret. This disease should be considered in ferrets, especially in obese ferrets.

*Acknowledgments:* The author thanks Dr. Cheryl Greenacre and Dr. Nico Schoemaker for their assistance with this case.



# Autoimmune Myasthenia Gravis in a Ferret

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Summary Style Manuscript

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*This abstract has been presented at the 21<sup>st</sup> Annual Symposium of the European Society of Veterinary Neurology in Rhodes (2008).*

A 7-month-old male neutered ferret was evaluated for episodic pelvic limb paresis of 2-weeks' duration. On neurological examination, non-ambulatory flaccid tetraparesis with decreased spinal reflexes suggested neuromuscular disease. An electromyographic study showed subtle spontaneous activity in palmar interosseous muscles of the hind limbs (grade 1+, reference range 0 to 4+). On electroneurography, motor nerve conduction velocities were normal and compound muscle action potential amplitude was slightly decreased in the tibial nerve (3.4 mV, reference range 6 mV $\pm$ 1 mV). A severe decremental response of the compound muscle action potential was found on repetitive nerve stimulation (45.5% at the 3<sup>rd</sup> ulnar nerve stimulation). Neostigmine methylsulfate (0.04 mg/kg) injected intravenously slowly led to immediate remission. Cross-reacting acetylcholine receptor (AChR) antibodies were detected in the serum (0.35 nmol/L) using a canine and feline specific muscle extract (reference range <0.3 nmol). Although a reference range has not been established yet for ferrets in this assay system, the AChR antibody titers by immunoprecipitation radioimmunoassay measured in 5 clinically normal ferrets were less than 0.06 nmol/L. Treatment with oral pyridostigmine bromide (1 mg/kg q8h) compounded in 1-mg pills resulted in complete remission. However, the ferret was euthanized 1 month later because of recurrence of weakness.

Myasthenia gravis is a disorder of neuromuscular transmission resulting from genetic abnormalities of acetylcholine receptors (congenital form) or an autoimmune reaction against acetylcholine receptors (acquired form). To the authors' knowledge, this is the first report of acquired myasthenia gravis in ferrets and the first identification of AChR antibodies in this species.



# Osteoma of the Zygomatic Arch in a Ferret

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## Session #196

Summary Style Manuscript

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A 5-year-old male ferret was presented for a mass under the left orbit of 2 months' duration with progressive impairment of the visual field. A skull radiograph showed a 3-cm radiopaque mass diameter adherent to the left zygomatic arch. Thoracic radiographs were taken to rule out potential metastasis. Surgical removal was elected. Anesthesia was achieved with intravenous propofol (4 mg/kg) followed by intubation and isoflurane 2%–3%. A lateral approach of the mass under the left orbit was undertaken. The mass was isolated from the underlying tissue and then removed with a rongeur. Once the temporo-mandibular articulation and the frontal processes of the zygomatic bone were palpated, the ostectomy was performed between those 2 landmarks. The muscular fascia of the masseter muscles attached to the zygomatic arch is elevated. Care was taken to spare the dorsal buccal branch of the facial nerve running dorsally along the zygomatic arch. Routine closure of the muscular, dermal, and skin layer was performed. Recovery from anesthesia was uneventful. Postoperative care was provided with carprofen (4 mg/kg) every 24 hours for 7 days and morphine (0.2 mg/kg) every 6 hours for 2 days. After surgery, the ferret showed a mild defect in closing the eyelids, which was treated with artificial tears. Histology of the mass showed an advanced osteoma with high cellularity. Follow-up at 6 months showed no reoccurrence or metastasis.



# Two Cases of Rabbit Respiratory Mycobacteriosis

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## Session #198

Summary Style Manuscript

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## Case 1

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A 3-year-old male neutered rabbit was referred for an 18-month history of respiratory disease (violent sneezing, nasal discharge, and increased respiratory noise) and a recent history of anorexia. The rabbit had been treated previously with ciprofloxacin (10 mg/kg PO q12h) after the results of a biopsy from a mass in the right nasal cavity indicated mixed inflammation. Improvement had been seen during treatment, but the clinical signs returned when the antibiotic treatment was discontinued. An endoscopic evaluation revealed destruction of the nasal septum, with substitution of the surrounding epithelium and its underlying turbinates with granulomatous tissue. These findings were confirmed by a computed tomography scan. The abnormal tissue was debrided and biopsies taken. Results for the granulomatous material demonstrated acid-fast bacteria, and the rabbit was started on azythromycin (50 mg/kg PO q24h), rifampin (75 mg/kg PO q12h), and ciprofloxacin (10 mg/kg PO q12h) for 2 years. Clinical signs resolved, but 2 months after stopping the treatment the rabbit became lethargic and dyspneic again, and a *Mycobacterium avium* resistant to ciprofloxacin and rifampin was cultured; the treatment was changed to clarithromycin (50 mg/kg PO q24h), rifabutin (25 mg/kg PO q12h), and ethambutol (45 mg/kg PO q12h). This treatment resolved the clinical signs and the rabbit died at the age of 8 from an unrelated condition.

## Case 2

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A 5-year-old male neutered rabbit was referred for respiratory distress, lethargy, and anorexia. The clinical signs started 1 week previously and treatment with penicillin G procaine (40,000 IU/kg IM q24h), itraconazole (40 mg/kg PO q24h), and amikacin (10 mg/kg SC q12h) resulted in no improvement. Physical examination revealed tachypnea, increased lower respiratory tract noises, and the liver was firm on palpation. A bronchoalveolar lavage revealed vacuolated macrophages containing numerous non-staining intracellular rods. The rabbit died later on the same day of presentation. Necropsy revealed pale and firm lungs, an enlarged and mottled liver, and few capsular scars on the kidney. The histologic diagnosis was disseminated mycobacteriosis (affecting lungs, spleen, liver, kidney, brain, and heart) and encephalitozoonosis in the kidney. A real-time polymerase chain reaction method using lung tissue was positive for *Mycobacterium* species, but multiple attempts to culture the organism yielded negative results.



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