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SMALL MAMMAL ENDOCRINOLOGY POTPOURRI

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Abstract:

Advances in Small Mammal Endocrinology for Veterinary Practice

Small mammal endocrinology is an emerging field in veterinary medicine, focusing on the hormonal regulation and associated disorders in species such as rabbits, rodents, and ferrets. This review synthesizes the authors personal experiences in the clinics with the current knowledge on the endocrine systems of these animals, emphasizing the hypothalamic-pituitary-adrenal axis, thyroid function, and reproductive hormones. Key disorders, including adrenal disease in ferrets, hyperthyroidism in guinea pigs, and diabetes mellitus in others, are discussed with an emphasis on clinical presentation, diagnostic approaches, and idea regarding therapeutic strategies. Recent advancements in diagnostic tools, such as more species-specific assays and imaging techniques, have improved the accuracy of endocrine disorder identification. Treatment options, including surgical interventions like adrenalectomy and medical management with drugs such as deslorelin implants, are evaluated for efficacy and practicality in a clinical setting. This abstract highlights the importance of understanding species-specific endocrine physiology to enhance the diagnosis and management of endocrine disorders in small mammals, ultimately improving patient outcomes in veterinary practice.

Ferret Adrenal disease:

Adrenal disease is a prevalent endocrine disorder in domestic ferrets (*Mustela putorius furo*), characterized by hyperadrenocorticism due to excessive sex steroid production, primarily androgens and estrogens, from adrenocortical hyperplasia or neoplasia. It is important to mention that this disease in ferrets should not be called 'Cushing's Disease' as the pathology affects a different part of the adrenal cortex as compared to the adrenal disease in dogs. This condition clinically affects middle-aged to older ferrets, with clinical signs including alopecia, pruritus, vulvar enlargement in females, prostatic enlargement in males, and aggressive behavior. However, it appears that the subclinical progression of the disease starts significantly earlier in life and the author suspects that the start of the pathophysiology is directly linked to the surgical neutering of the animals. The pathophysiology involves dysregulation of the hypothalamic-pituitary-adrenal axis, which stimulate gonadotropin-releasing hormone (GnRH) activity. Diagnosis relies on clinical presentation, elevated plasma levels of adrenal androgens (e.g., androstenedione, 17 α -hydroxyprogesterone), and ultrasound imaging to assess adrenal gland size and structure. Treatment options include surgical adrenalectomy, which is effective but carries risks due to the ferret's small size and potential for bilateral disease, and medical management with GnRH agonists like deslorelin implants, which suppress hormone production with varying success rates.

This abstract underscores the need for early diagnosis and tailored therapeutic approaches to manage adrenal disease in ferrets, improving quality of life and longevity in affected patients. The author is currently conducting a clinical trial in which young (less than 1 year old), healthy ferrets are enrolled and monitored yearly for any evidence (hormonal and clinically) of adrenal disease. The ferrets are receiving a full clinical exam, an ultrasound exam, full bloodwork including CBC, chem. profile and an adrenal hormone panel. The animals also receive a 4.7 mg deslorelin implant during the yearly exam. The study



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is looking at how the status of the animal's adrenal gland develops when having the deslorelin implant placed prior to any clinical signs of the disease. On the first evaluation of the data it appears that a large percentage of 'healthy' baby ferrets have already a significant of at least one hormone despite looking perfectly normal on the rest of the yearly exam. The study is running for 5 years and follows up to 80 ferrets. Initial results of the study might indicate that the placement of an implant once a year is beneficial to the animal as clinical signs are suppressed but the hormone levels are not fully suppressed during that time.

Diabetes Mellitus in Guinea Pigs and Hamsters.

Diabetes mellitus is an increasingly recognized endocrine disorder in small mammals, notably guinea pigs (*Cavia porcellus*) and hamsters (*Mesocricetus auratus*), characterized by hyperglycemia due to insulin deficiency or resistance. In guinea pigs, diabetes often presents spontaneously, linked to genetic predisposition and obesity, with clinical signs including polyuria, polydipsia, weight loss, and cataracts. Hamsters, particularly Chinese hamsters, are prone to a genetic form of diabetes resembling type 1, displaying similar symptoms alongside glucosuria and ketonuria. Diagnosis involves fasting blood glucose levels (>250 mg/dL), urinalysis for glucosuria, and, in hamsters, monitoring for ketonemia. Management in guinea pigs focuses on dietary modification, emphasizing low-sugar, high-fiber diets, and weight control, with insulin therapy rarely used due to poor response. In hamsters, insulin therapy (e.g., glargine, 1-2 IU/kg daily) can be attempted, though prognosis remains guarded due to rapid disease progression. Supportive care, including hydration and prevention of secondary infections, is critical in both species. This highlights the challenges in managing diabetes mellitus in guinea pigs and hamsters, underscoring the need for early detection and species-specific interventions to mitigate complications and enhance patient welfare.

Hypothyroidism in rabbits:

Hypothyroidism in rabbits, though rare, presents a significant diagnostic and therapeutic challenge in veterinary practice. This abstract investigates the prevalence, clinical manifestations, and underlying etiologies of hypothyroidism in domestic rabbits (*Oryctolagus cuniculus*), focusing on thyroid hormone imbalances and their impact on metabolism and thermoregulation.

Clinical signs, including lethargy, weight gain, and poor coat quality, were observed by the author in affected rabbits. Early suspect diagnosis of hypothyroidism in rabbits relies on a combination of clinical observation and diagnostic testing. Initial signs include subtle lethargy, reduced activity levels, and mild to severe weight gain despite stable feeding habits, often overlooked in routine exams.

The main clinical problem was urinary incontinence in one rabbit with all clinical exams and diagnostic tests showing negative results. Treatment with levothyroxine supplementation resulted in partial clinical improvement, highlighting the need for tailored therapeutic protocols. It is interesting to note that the animal did not have abnormal thyroid hormone values and this underscore the importance but also the non-sensitivity of routine thyroid screening in rabbits with nonspecific symptoms and advocate for further research into the genetic and environmental factors contributing to this condition. Normal thyroid hormone values have been published but the author's diagnostic test of choice is nuclear scintigraphy for suspected thyroid abnormalities. If thyroid-stimulating hormone (TSH) is available, baseline TSH assays, though less validated in rabbits, can support findings when abnormal. Thyroid ultrasonography or fine-needle aspiration may reveal atrophy or lymphocytic infiltration, pointing to autoimmune thyroiditis as a potential cause.

Management begins with initiating levothyroxine at a starting dose of 10-20 μ g/kg orally once daily, titrated based on clinical response and follow-up T4 levels, aiming for a target range of 2.0-4.0 μ g/dL. Early intervention is critical to reverse metabolic slowdown and prevent secondary complications such as obesity or cardiovascular strain. Owners should monitor for side effects, including tachycardia or agitation, necessitating dose adjustment. Regular re-evaluations every 4-6 weeks are recommended to



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assess hormone levels and clinical progress, emphasizing a tailored, long-term management approach to improve quality of life in affected rabbits. Further studies are warranted to refine diagnostic thresholds and optimize treatment regimens.

Hyperthyroidism in Guinea Pigs

Hyperthyroidism, as been reported to be less common in guinea pigs (*Cavia porcellus*) compared to other mammals, however the author thinks that it is an emerging endocrine concern characterized by excessive thyroid hormone production, typically due to thyroid hyperplasia or adenomas. This condition primarily affects older guinea pigs, presenting with clinical signs such as weight loss despite increased appetite, hyperactivity, tachycardia, and poor coat quality. The pathophysiology involves overproduction of thyroxine (T4) and triiodothyronine (T3), often linked to iodine imbalances or genetic predisposition. Diagnosis is not always possible by bloodwork but it is confirmed through elevated serum T4 levels (>5 $\mu\text{g/dL}$), with baseline values in guinea pigs typically ranging from 2-4 $\mu\text{g/dL}$, alongside palpation of an enlarged thyroid gland. The author has been multiple cases in which the bloodwork was normal and this is why the recommendation is to use scintigraphy to assess thyroid activity, if available.

Treatment options include medical management with antithyroid drugs like methimazole (0.5-1 mg/kg daily), which effectively reduces T4 levels but requires careful monitoring for side effects such as anorexia. Surgical thyroidectomy is an alternative but is rarely performed due to the risks of anesthesia and hypocalcemia in guinea pigs. Dietary adjustments to ensure balanced iodine intake are also recommended.

Insulinoma in the ferret:

Insulinoma in the ferret is the most common neoplasm encountered in the clinic. While the diagnosis of the problem is not the problem usually, in the author's experience the longitudinal management is often over simplified. The lecture will help to introduce a way on how to maximize the management medically when combined with surgery. In the author's experience this way of managing the disease can result in a successful path to manage insulinoma for many years which might be important in cases where the insulinoma was diagnosed in a very young animal.

The diagnosis of the insulinoma is based on Whipple's triad.

Whipple's triad is a diagnostic criterion used to identify hypoglycemia, a condition where blood sugar levels are abnormally low. It consists of three key elements:

1. Symptoms of Hypoglycemia: These include shakiness, sweating, anxiety, confusion, seizures, and even loss of consciousness.
2. Low Blood Sugar Levels: A plasma glucose concentration of less than 70 mg/dL is typically required.
3. Relief of Symptoms with Glucose Administration: When glucose is given intravenously or orally, the symptoms of hypoglycemia should improve rapidly.

It has been shown and document that other methods to investigate insulinoma in the ferret like insulin : Glucose ratios or fructosamine levels are not of additional diagnostic value.

The important factor in the long-term management is the selection of the medical management regime and the timing of a potential surgery.

A lot of clinicians choose to start treatment with a steroid initially. However, if an animal is exposed to steroids and then lymphoma develops in the ferret, this will often result in a multi-drug-resistant form of the lymphoma and chemotherapy is often less successful in the author's experience. If the animal was on steroids for a few days prior to a biopsy (due to severe insulinoma) this can make it difficult in interpret histological results which can lead to a false negative interpretation. For this reason, the author does not use steroids as the first drug of choice after consulting with the owner. However, sometimes the owner elects to start the use with steroids for a variety of reasons (not interested in chemo later on in case



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lymphoma would develop, cheaper drug is chosen, etc.) If steroids are being used I use prednisolone (Pediapred) orally 0.2 mg/kg -2 mg/kg SID-BID depending on the severity of the clinical signs. It is important to educate the owner that the drug is not a chemotherapy, and it works by stimulating gluconeogenesis which promotes euglycemia. However, the drug does not interfere with the primary cancer and the clinical signs will eventually return. The dosage needs to be adjusted (fine-tuned) over time and owners need to be educated about the clinical signs of a crisis and that the dosage needs to be increased over time. In addition, the owner needs to be educated that oral carbohydrates should not be given at all as this will trigger an additional insulin release about 20 minutes later! The basic recommendation is that no sugary treats should be offered and to keep the animal. A different first drug of choice is Diazoxide (Proglycem) which prohibits the hypoglycemic state by directly inhibiting pancreatic insulin secretion. Diazoxide does not affect the synthesis of insulin, nor does it possess any antineoplastic activity. It is more expensive (~4 x more than pred.) than steroids but has significantly less side effects or long-term complications like steroids. So far, the author has not observed any side-effects. In addition, this drug can be used in conjunction with prednisolone. The combined treatment (diazoxide and steroids) will usually provide a great quality of life for the animal for about 2 years. When using the drugs combined one should consider starting therapy with the diazoxide in order to avoid side effects of the steroids. Once the medical management has reached the limit (both drugs used at a maximum dosage and clinical signs return) it is time to consider surgery for the patient.

Surgery for Insulinoma consists of two options: Nodulesctomy or partial pancreatectomy.

Independent of what surgery approach is chosen it is important to communicate to the owner that the surgical approach is not a cure but it will only provide temporary remission. Nodulesctomy is recommended if a nodule is seen on US exam and in younger ferrets (<5 years). During the surgery it is recommended to remove all nodules or a part of the pancreas (partial pancreatectomy) in case of microscopic disease where no distinct nodule is observed on ultrasound and during the surgical exploration. The good news is that metastasis are very unlikely (mostly liver if they occur) so postponing the surgery after years of medical treatment is not a problem.

One might ask: Why not start with surgery and then use drugs? The answer to this question is hidden in the details of anatomy and physiology. Fact 1 is that the disease will come back after a surgery (not a cure). Fact 2: Lies in the pancreatic anatomy. While the surgery of the pancreas is relatively easy regarding the right limb, surgery of the left limb is much more risky due to the pancreatic duct and the potential to damage the exocrine function of the pancreas.

What is the difference between the surgical treatments? The three treatment groups treated medically, treated with pancreatic nodulesctomy, treated with pancreatic nodulesctomy combined with a partial pancreatectomy. The mean disease-free intervals for each group were 22, 234, and 365 days, respectively. The mean survival times for each group were 186, 456, and 668 days. What are the potential side effects of the surgery? Any surgery is dangerous, think of all potential complications possible including infections, self mutilation, and anesthetic risk. However, one potential risk should be mentioned specifically. The surgery has the potential to cause diabetes mellitus even if only a nodule is removed. Repeated high blood glucose readings of levels above 350 mg/dl (19.25 mmol/L) might indicate diabetes mellitus. While this is rare in my experience, I have personally observed and experienced this complication.

Another treatment modality is chemotherapy which has a significant limitation in the author's experience. In my opinion, chemotherapy for insulinoma is only effective when the condition is being diagnosed during a routine exam without the presence of clinical signs. In these cases where the diagnosis was made during a routine wellness exam i.e. animal is not clinical; the use of chemotherapy has been successfully used. In case where clinical signs were already present the use of chemotherapy did not result in great resolution of the problem. When chemotherapy is elected, Doxorubicin 1 mg/kg i.v. q 4 weeks x 3 treatments has been a great option. Again, it is important not to try this in clinical animals as the results will not be good! on a low carb diet for life (i.e. same diet as a diabetic animal should be kept on). Oral carbohydrates should only be used for an emergency.

Summary:



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Endocrinological disorders in small mammals, such as rabbits, ferrets, and rodents, present unique diagnostic challenges due to their small size, rapid metabolism, and species-specific hormonal profiles. This small review explores current diagnostic approaches to small mammal endocrinology, focusing on practical techniques for veterinarians. Key methods include serum hormone assays, which require minimal blood volumes and specialized micro-assays to accommodate small sample sizes. Imaging modalities, including ultrasonography and computed tomography, aid in identifying structural abnormalities in endocrine glands like the adrenals or thyroid. Additionally, dynamic testing (e.g., ACTH stimulation tests, scintigraphy) can be adapted for small mammals to assess glandular function. Challenges include limited reference ranges for many species and the need for species-specific protocols. This review emphasizes the importance of integrating clinical signs, laboratory diagnostics, and imaging to achieve accurate diagnoses, offering veterinarians a framework for managing endocrine disorders in small mammals effectively.