Adrenocorticotropic hormone (ACTH)-independent hypercortisolism in dogs is known to be the result of autonomous glucocorticoid secretion by an adrenocortical tumor. Several studies in humans have demonstrated that the aberrant expression or abnormal function of hormone receptors other than ACTH-receptors in adrenocortical tumors can be the cause of the excessive production of cortisol. In the dog, meal-induced hypercortisolism that most likely was due to aberrant expression of gastric inhibitory polypeptide (GIP) receptors has been identified so far in one dog. Here, we report on a screening of 23 surgically removed adrenocortical tumors of dogs with hypercortisolism for the presence of aberrant receptors. Normal adrenal tissue served as control tissue. The receptors of interest were those for GIP, vasopressin (V1, V2 and V3), and luteinizing hormone (LH). Amounts of mRNA for these receptors were quantified using fluorescent quantitative PCR (qPCR). mRNA of all receptors appeared to be present in both normal adrenals as adrenocortical tumors. The mRNA expression levels for GIP and V2 receptors were significantly decreased in the tumors compared with the normal adrenals. For the V1, V3 and LH receptor no difference was found between the expression in tumors and in normal adrenals. These findings indicate that, in general, overexpression of the investigated receptors is not the cause for adrenal-dependent hypercortisolism in dogs.

2. Galac S et al. Hyperadrenocorticism in a dog due to meal-induced hypercortisolism. 2006 Submitted
Effect of GnRH administration on FSH and LH concentrations in anestrous ovariectomized bitches

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The aim of this study was to determine the basal and gonadotropin releasing hormone (GnRH)-induced plasma concentrations of follicle stimulating hormone (FSH) and luteinizing hormone (LH) in four anestrous and four ovariectomized (OVX) bitches. Blood samples were obtained via jugular venipuncture 40 min before and 0, 10, 20, 30, 60, 90, and 120 min after the i.v. administration of 10 µg/kg synthetic GnRH. The basal plasma FSH and LH concentrations were significantly higher in the OVX bitches than in the anestrous bitches. In the anestrous bitches the plasma FSH concentration was significantly higher than the pretreatment level at 10, 20, and 30 min, whereas the plasma LH concentration was significantly elevated at 10 and 20 min. The maximal GnRH-induced plasma FSH concentration in the anestrous bitches did not surpass the lowest plasma FSH concentration in the OVX bitches, whereas the GnRH-induced plasma LH concentrations in the anestrous bitches overlapped with the basal plasma LH concentrations in the OVX bitches. In the OVX bitches GnRH administration did not induce a significant change in the plasma FSH concentration, whereas the plasma LH concentration increased significantly at 10 and 20 min. In conclusion, in anestrous bitches GnRH challenge results in increased plasma levels of both FSH and LH, whereas in the OVX bitches, in which the basal plasma FSH and LH concentrations are higher, only a rise in the plasma LH concentration is present. The results also suggest that a test to measure plasma concentration of FSH in single samples appears to have potential in verification of neuter status or the diagnosis of remnant ovarian tissue in the bitch.

Indoor confinement is a risk factor in the development of type 2 feline diabetes mellitus

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Introduction
The aim of this study was to evaluate the role of dietary carbohydrate content and physical activity on the development of type 2 diabetes mellitus in cats.

Materials and Methods
In a retrospective questionnaire-based study information was collected on dietary history and physical activity in 97 cats with type 2 diabetes mellitus and 194 matched control cats. Conditional logistic regression analysis was performed to determine the effect of carbohydrate content of the cat’s diet and the outdoor/indoor status on the risk of developing diabetes mellitus.

Results
The percentage of dry (carbohydrate-rich) food in a cat’s diet was not significantly related to the risk for the development of diabetes mellitus. However, outdoor/indoor status of cats was a highly significant explanatory variable for the risk of developing this disease.

Conclusion
Indoor confinement of cats increases the risk for developing type 2 diabetes mellitus, whereas the percentage of dry food in a cat’s diet is not a direct risk factor for the development of this disease.
Companion Animals: Royal Canin Resident and Research Award

Retrospective Evaluation of Canine Hepatitis

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This retrospective study was conducted to evaluate the frequency of different types of canine hepatitis, with emphasis on the efficacy of prednisone treatment in cases of chronic hepatitis with or without cirrhosis. All cases were presented between 2002-2006 at the Department of Clinical Sciences for Companion Animals (UKG), University Utrecht, and were selected based on the results of histopathologic evaluation of at least two liver biopsies.

Results
The various types of hepatitis are distributed as follows: acute hepatitis 9/119 (7.6%), subacute hepatitis (SAH) 26/119 (21.8%), chronic hepatitis with or without cirrhosis (CH±CIRR) 60/119 (50.4%), granulomatous hepatitis 6/119 (5%), lobular dissecting hepatitis 4/119 (3.4%), and with an unclear form of hepatitis 14/119 (11.8%).

Of the CH±CRR patients, 10/60 (16.6%) had primary copper accumulation, of which 7/10 clinically recovered after D-penicillamin therapy. Of the remaining idiopathic CH±CIRR cases 43/50 (86%) patients were treated with prednisone (1 mg/kg/day, flr 6 weeks); 12/43 (27.9%) patients died during or shortly after therapy, of which 5 progressed to cirrhosis; 15/43 (34.9%) recovered clinically; however, 4/15 histopathologically progressed to cirrhosis; 16/43 (37.2%) had an unknown clinical outcome, of which 11/16 developed cirrhosis before or at the time of referral. Of all SAH patients, 3/26 patients died, 4/26 progressed to CH±CIRR, and 12/26 clinically recovered after therapy. A breed predisposition in English Cocker Spaniels is suggested (5/26, 19.2%).

Conclusion
In a UKG referral population CH±CIRR occurs most frequently, with a moderate prognosis towards clinical recovery. SAH forms a considerable fraction with a fair prognosis towards clinical recovery.

Is “T-wave-peculiarity” on Chihuahua-ECGs a myth?

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In 1965 Detweiler and Patterson described that in normal dogs the T-waves in lead V10 were negative, except the Chihuahua. Positive T-waves in all the other breeds indicate right ventricle hypertrophy. (1) Veterinary textbooks keep on describing this phenomenon. (2)

The ECGs made on Chihuahuas in the authors’ clinic from 2004 to 2006 were retrospectively reviewed. During these 3 years 4 ECGs were made on Chihuahuas. All the 4 Chihuahuas had negative T-waves in lead V10. The underlying heart disease in 2 dogs was patent ductus arteriosus and mitral valve endocardiosis in the other 2. Echocardiography was used to confirm the underlying heart disease. None of the 4 dogs had right ventricular hypertrophy.

Based on these 4 patients we can conclude that the T-wave in lead V10 is negative in left ventricular volume overloaded Chihuahua-hearts. Whether negative T-wave is also present in echocardiographically normal Chihuahua-hearts requires examination of healthy adult Chihuahuas. Because 40 years ago echocardiography was not available, it is possible that the presence of an underlying heart disease that caused positive T-waves in those Chihuahuas was missed.

In eight beagle dogs, effects of continuous rate infusion (CRI) of dexmedetomidine on auditory and pain-related evoked potentials were investigated. Auditory and pain-related evoked potentials were recorded before, during and after CRI of dexmedetomidine in doses of 0.0, 1.0, 3.0 and 5.0 µg/kg/h. Evoked potentials were evaluated using the Rate-Dispersion-Factor. Data were analyzed using a two-way repeated-measurements ANOVA followed by post-hoc analysis when appropriate. Significant effects on the auditory evoked potentials were found at doses 1.0, 3.0 and 5.0 µg/kg/h. Significant effects on the pain-related evoked potentials were found at doses 3.0 and 5.0 µg/kg/h. In conclusion, CRI of low doses of dexmedetomidine provides both sedation and analgesia in dogs. Significant analgesia is accompanied by significant sedation. Therefore, precautions for the sedative effects must be taken at all times when using infusion protocols aimed at providing analgesia.

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Companion Animals: Royal Canin Resident and Research Award

Lingual Abscess in a Dog

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Lingual abscesses are common in ruminants but have rarely been described in companion animals. Without appropriate care, lingual abscesses can turn into serious emergencies. A 4 year-old mixed-breed dog was presented with clinical signs associated with an acute severe swelling of the tongue. Upon inspection, a small laceration was found at the ventral surface of the tongue base. A fluid-filled cavity of 2 x 3 cm with a fistulous tract leading to the laceration was observed using contrast radiography. Purulent material could be aspirated with a subdermal needle under ultrasonographic guidance. Drainage was established using a Penrose drain and systemic broad-spectrum antibiotics were administered. The dog was discharged after drain-removal and recovered completely. Histological examination of biopsy specimens obtained during surgery confirmed the clinical diagnosis. 

Respiratory Cryptosporidiosis in Falcons

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Three mixed-bred raptors (Falco rusticolus, Falco cherrug) from a German falcon breeder were presented with a history of respiratory distress. In one bird a laryngeal stridor was noted, and oral examination revealed an epiglottal swelling. Biopsies were taken and histologically examined, indicating presence of Cryptosporidium spp. In the other two birds, nasal discharge and sneezing were the main clinical symptoms. Diagnostic work-up included nasal flushing and culture of the materials collected. Results confirmed a cryptosporidial infection. PCR identified the causative agent to be Cryptosporidium baileyi. No cryptosporidia were found in faecal samples, suggesting the infection was confined to the respiratory system. Analysis of drink water samples and prey (pigeons, quail) failed to identify the source of infection. In two birds treatment was initiated with paromomycin and azithromycin, respectively. No clinical improvement was seen after several weeks of treatment, and the birds were euthanized. Cryptosporidia are small coccidian parasites, causing widespread disease in humans and many other vertebrates. In birds, both C. meleagridis and C. baileyi have been implicated in causing respiratory or gastrointestinal disease in over 30 different species. This is the first report describing disease due to cryptosporidial infection in the order of Falconiformes. As the infection is usually transmitted by shedding of sporulated oocysts via excreta (faeces or aerosols) into the environment, the prime source for infection appears to be ingestion of contaminated drinking water, soil or food. In our case, several attempts were made to identify the source of infection, but unfortunately without success.
Pyogranulomatous skin nodules in a cat associated with Mycobacterium abscessus.

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A 3-year-old male castrated domestic shorthair cat was presented with recurrent firm nodules in the abdominal skin. Previously, resected nodule material had revealed histopathological features consistent with atypical mycobacteriosis and shown intra-lesional Ziehl-Neelsen positive acid-fast bacteria. The nodules had recurred after one week. At physical examination the cat showed no signs of systemic disease. On the skin of the abdominal wall several nodules with linear extension patterns and central excoriation were found. No draining tracts were seen. Clinical differential diagnosis included actinomycosis, nocardiosis, deep fungal infections as cryptococcosis or phaeohyphomycosis, dermatophytic pseudomycetoma, botryomycosis and mycobacterial granuloma. A presumptive diagnosis of mycobacterial granuloma was made on the basis of the earlier Ziehl-Neelsen stain. The owners elected euthanasia because of a possible health risk.

The histopathological findings in the skin biopsies were compatible with atypical mycobacteriosis. Direct PCR for M.tuberculosis-complex was negative. Culturing revealed a rapidly-growing mycobacterium which was identified as M. abscessus by spoligotyping.

Mycobacterial infections in cats do occur, albeit infrequently, and mostly involve the (sub)cutaneous tissues. Penetration of the skin apparently occurs with skin trauma or bites; lesions consist of a typical granulomatous or pyogranulomatous reaction.

M. abscessus was considered a saprophyte, but recent reports of infections in humans suggest that it should be regarded as an emerging pathogen. To our knowledge, this is the first report of pyogranulomatous skin nodules in a cat associated with a M. abscessus infection in Europe.

Cataract in the Dutch Labrador Retriever population

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In the Dutch Labrador population different types of (cortical) cataracts exist, most of which are assumed to be phenotypic variations of the same genetic disorder. If affected, animals are excluded from breeding.

The aims of this study were to determine whether selective breeding has decreased the prevalence of cataracts in the Dutch Labrador population and if posterior polar triangular cataract is genetically related to other types of cortical cataracts.

Retrospective (re-)evaluation was performed of 18,283 ophthalmic examinations on 9,017 Labradors between 1977 and 2006 by ECVO-registered veterinary ophthalmologists. The results of these were combined with data on more than 110,000 Labradors in a database (GCS-Datamanager). For evaluation purposes, the presumed hereditary, mostly cortical, cataracts were divided into posterior polar triangular cataract (type I) and three other types. From 1980 to 2000, the prevalence of cataract (PRA affected animals excluded) in the population has been stable at 8%.

If one of the parents was affected by cataract type I, all types of cataract occurred in the offspring (type I: 59% and other types: 41%). If one of the parents was affected by any other type of cataract, the offspring also showed type I cataracts (50%), among others.

Selective breeding over nearly thirty years has not significantly decreased the prevalence of cataract in this population. Posterior polar triangular cataract in the Labrador may be regarded as a phenotypic variation of the same genetic disorder as the other types of cataract.
Companion Animals: Royal Canin Resident and Research Award

Gallbladder rupture due to mucocele in a dog
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Gallbladder mucoceles occur when the gallbladder distends abnormally from excessive accumulation of mucus within the lumen. The clinical presentation is variable, and signs may even be absent. In this report a case of gallbladder rupture by a mucocele and successful treatment is described. A 9-year-old male Shetland Sheepdog was referred to the Department of Clinical Sciences of Companion Animals of Utrecht University with lethargy, anorexia and vomiting. The dog was very painful at abdominal palpation. Abdominal ultrasound showed some free abdominal fluid and a small gallbladder with a discontinuous wall. In the abdominal cavity a free and mobile hypoechoic mass with an echogenic stellate and kiwifruit-like pattern was present. Ultrasound-guided abdominocentesis yielded a green-brown fluid, that contained macrophages and granulocytes. Explorative laparotomy revealed a ruptured gallbladder and a free gallbladder mucocele. The mucocele was removed and cholecystectomy was performed. The metronidazol, amoxicillin-clavulanic acid and carprofen postoperatively and was still alive 10 months after surgery. Gallbladder mucoceles occur most frequently in small to medium-sized and older dogs. The pathogenesis is still unknown. In this patient chronic overdistension of the gallbladder lumen with bile and mucus promoted pressure and ischemic necrosis of the wall, this together with secondary inflammation ultimately resulted in gallbladder rupture. In case of gallbladder rupture emergency surgery is necessary because of bile leakage and bile peritonitis.


Tritrichomonas foetus infection in cats in the Netherlands, a case-report
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A breeding colony of Norwegian forest cats suffered from recurrent episodes of diarrhea which predominantly affected the kittens (past 3 litters) and a recently imported breeding male. The diarrhea started at the age of 4-6 weeks and was best characterized as chronic large bowel diarrhea (semi-formed, malodorous feces). The kittens were not sick, but their growth halted temporarily. The diarrhea generally stopped after a couple of days, but would return after 2-3 weeks. Despite extensive hygienic measures, treatment with various antiparasitic drugs, antibiotics and dietary measures, no (permanent) improvement was achieved. Physical examination of 3 affected kittens showed no abnormalities other than a swollen and painful anus (1 kitten). A stained fecal smear showed no abnormalities, but a direct wet mount showed motile flagellates (2 kittens). Parasitological examination of the feces was negative in all 3 kittens. A presumptive diagnosis of Tritrichomonas foetus infection was made. All 3 kittens were successfully treated with ronidazole1 and a temporary stop with breeding was advised. In conjunction with the VMDC a PCR was developed and feces from all 16 cats was tested. All 3 kittens tested positive prior to therapy and were negative thereafter. None of the adult cats were infected. After 1 year, breeding was reinitiated and the diarrhea has not returned.

**FoxM1 expression in canine insulinoma**

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FoxM1 regulates the transcription of genes that play a crucial role in cell cycle progression. FoxM1 is expressed in various proliferating cell types and overexpressed in many human carcinomas. (1) In the mouse pancreas, FoxM1 is essential for maintaining postnatal β-cell mass. (2) Canine FoxM1 has 4 splice variants and their protein function and gene expression may differ between species and cell types. Therefore it was hypothesized that all splice variants of FoxM1 are expressed in canine pancreatic tissue and some may be overexpressed in canine insulinoma.

The hypothesis was tested by PCR with primers designed for the different splice regions, followed by sequencing of the PCR products. A pool of 6 primary insulinomas and 4 metastases was compared to a normal pancreas sample. Both in insulinomas, metastases and normal tissue only splice variant 1 was observed. Expression was much higher in the insulinoma pool than in normal tissue and this finding will be confirmed with real time PCR for each single sample. No mutations were found in the PCR products.

The difference between insulinoma and normal pancreas tissue, concerning FoxM1, lies in the overexpression of FoxM1 in insulinoma, and not in expression of other splice variants or mutations.

**References**


**Hypotonic versus isotonic water as adjuvant therapy for mastocytoma in 30 dogs: a double-blind, placebo-controlled study**

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**Introduction**

Recommended therapy for canine cutaneous mastocytoma (MCT) is wide surgical excision but location or size of the tumour may limit the success. After incomplete excision, adjuvant therapy is advised. Although adjunctive radiation therapy remains first choice, decreased recurrence has been reported after intraregional use of hypotonic water. Hypothesis of this study was that hypotonic water would improve local and distant disease free intervals compared to isotonic water.

**Materials & methods**

In 30 dogs with marginal excised solitary MCT either hypotonic (distilled) or isotonic (Ringer’s lactate) water was injected intraoperatively. Dogs were randomized into one of the groups and the study was performed in a double-blinded way. During four consecutive weeks water was injected once weekly, after which the wound site was checked at monthly intervals.

**Results**

Histological grading revealed three grade I (two hypotonic, one isotonic), 25 grade II (10 hypotonic, 15 isotonic), two grade III (both isotonic). Three dogs died caused by the disease (two hypotonic grade II, one isotonic grade III) and three dogs had local recurrence and metastasis (two hypotonic, one isotonic). Twenty two dogs had neither signs of local recurrence nor distant metastasis after a 12 month period (12 isotonic, nine hypotonic, one lost to follow up).

**Discussion**

No significant efficacy of hypotonic water could be proven for the use in dogs with MCTs after marginal surgical excision. The striking low recurrence rate may be caused by, either intralesional pressure during injection or the use of intrallesional water in general.
High volume perioperative fluid therapy may have adverse effects. Investigating the effect of perioperative fluid therapy may improve postoperative outcome in sick patients.

Two groups were studied. Control group (C-group) included ASA I-II dogs (n=12) for elective sterilization or stifle surgery. Experimental group (E-group) included ASA III-IV dogs (n=11) that underwent abdominal surgery. Both groups received identical anaesthetic protocol. After premedication, lactated Ringer’s infusion (10 ml.kg. hour^-1) was started. Blood samples were withdrawn prior to premedication (T0), one hour afterwards (T1h), at the end of surgery (TSx) and 24 hours after surgery (T24h). Blood was analysed for packed cell volume (PCV), total proteins (TP), albumin (Alb), and creatinine (Cre). Blood parameters were compared over time and between groups using a linear mixed model.

Both groups had lower PCV, TP, Alb and Cre at T1h and TSx than at T0. E-group had lower PCV, TP and Alb at T24h, than C-group. Additionally, E-group had lower PCV, TP, Alb and Cre at T24h, than at T0. Also C-group had lower TP and Alb at T24h, than at T0. Dogs heavier than 10kg had lower PCV, TP and Alb at T24h than at T0. Also dogs lighter than 10kg had lower TP and Alb at T24h than at T0. High volume perioperative fluid administration has hemodiluting capacity that is more severe and persistent in sick dogs. Large dogs might be more affected. Perioperative fluid therapy should be carefully administered in debilitated patients.


Use of rhTSH-stimulation test in dogs.
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This study aimed to retrospectively determine the reasons why reconstituted rhTSH (recombinant human thyrotropin)-stimulation tests were performed in practice, to describe potential adverse reactions, and to evaluate whether the rhTSH-stimulation test seemed helpful to practitioners in diagnosing hypothyroidism.

A retrospective study of 323 dogs, which underwent an rhTSH-stimulation test was performed. In all dogs TSH-stimulation tests were performed using 91µg rhTSH (Thyrogen®) IV. Blood samples for determination of TT4 were collected prior to, and between 4 and 6 hours after stimulation. Following criteria were arbitrary established by the laboratory to classify dogs as euthyroid: pre-TSH TT4 >17 nmol/l and post-TSH TT4 >37 nmol/l. Dogs were considered hypothyroid if pre-TSH TT4 was <17 nmol/l and post-TSH TT4 was <20 nmol/l. No adverse reactions after rhTSH administration were observed. The rhTSH-stimulation test was performed for the following reasons: low baseline-TT4 and normal TSH concentration (39%), screening (35%), low baseline-TT4 (18%), high TSH only (4%), CBC/chemistry suggestive of hypothyroidism (4%). 30% of the dogs were considered euthyroid. 18% were considered hypothyroid, from which 80% responded well to thyroxine. 52% were considered intermediate, 44% of these dogs received medication, compared to 38% of the hypothyroid group and 60% of the euthyroid group. 36% of the intermediate stimulators had a non-thyroidal disease, compared to 32% of the hypothyroid group and 47% of the euthyroid group. 82% of the veterinarians considered the test helpful in establishing or excluding the diagnosis of hypothyroidism. Further studies to establish optimal criteria for interpreting the rhTSH-stimulation test are necessary.