Hypophysectomy in dogs and cats

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Introduction
Transsphenoidal selective adenomectomy is the primary therapy for Cushing’s disease in humans. The most common approach in humans is by the standard microsurgical submucosal transseptal transsphenoidal procedure using a neurosurgical operating microscope. There are many virtues of the midline transsphenoidal approach. Most importantly, it is the least traumatic route of surgical access to the sella. The lack of visible scars, lower morbidity and mortality as compared with transcranial procedures, the necessity of only a brief hospital stay, the relatively brief recuperative period add to the procedure’s appeal. More and more human pituitary surgeons employ the pure endoscopic endonasal transsphenoidal surgical approach for pituitary tumor removal using rigid endoscopes. The pure endoscopic approach in humans is facilitated by the air-filled sphenoid sinus that is only separated by a thin bony floor from the pituitary fossa.

In dogs the most common method of treatment for Cushing’s disease or pituitary-dependent hypercortisolism (PDH) remains medical treatment with mitotane (o,p’-DDD) or trilostane. However, medical therapy leaves the pituitary adenoma untreated. Also, it may be hypothesised that the removal of the chronic negative feedback exerted by the glucocorticoid excess at the pituitary can actually stimulate pituitary tumor proliferation and expansion.

At the Utrecht University transsphenoidal hypophysectomy was re-started in 1993 and has become an important addition in the management of Cushing’s disease in the Netherlands (and occasionally for patients coming from other European countries). Until now 330 dogs and 30 cats have undergone pituitary surgery. Surprisingly, pituitary surgery in dogs and cats is, besides the Netherlands, only advocated in a few other institutions (Japan, Italy, UK and only very recently the USA). In dogs the indications for pituitary surgery include pituitary corticotroph adenomas (causing Cushing’s disease), debulking of clinically non-functioning pituitary macroadenomas (causing diabetes insipidus or central neurological signs by the tumor mass effect) and occasionally sellar meningiomas.

Surgical Technique
Pituitary surgical techniques include selective removal of the pituitary adenoma (adenomectomy), removal of the adenohypophysis (adenohypophysectomy), removal of a significant part of pituitary tumor mass in the case of a macroadenoma (pituitary debulking), or complete removal of the pituitary gland including the tumor (hypophysectomy). Hypophysectomy in the dog and cat is performed by the midline transoral, transnasopharyngeal, transphenoidal, microsurgical approach with the animal in sternal recumbency. Access to the pituitary fossa is obtained with a burr. An operating loupe or videoscope is used to provide magnification. Bone punches are used to enlarge the opening created in the inner cortical lamina of the sphenoid bone. Following incision of the dura mater, the pituitary adenoma is extracted through the dural opening using fine neurosurgical grasping forceps and suction. In most cases the complete adenohypophysis is usually affected by the tumor and there is no sharp definition between adenoma and normal pituitary tissue. Unlike humans with Cushing’s disease, well-defined pituitary (micro)adenomas are rare in dogs and cats. The hypophysectomy is considered complete when 1) there is an unobstructed view of the ventral hypothalamic surface and the opening to the third cranial nerve is visible and 2) the adenohypophysis is removed.
ventricle, and 2) there are no pituitary remnants upon exploration of the extensions of the hypophysial fossa. The pituitary fossa can also be inspected for pituitary tumor remnants using rigid endoscopes, e.g., and endoscope with a diameter of 2.7 mm and a 30 degree viewing angle. In dogs with giant (>2 cm) pituitary adenomas, the aim is to reduce as much of the tumor tissue as possible to reduce the mass effect (debulking).

Postoperative intensive care includes close monitoring of vital functions, plasma electrolytes (sodium and potassium), plasma osmolality, and central venous pressure. Oral water intake is encouraged as soon as possible. Postoperative medication includes antibiotics and analgesics. Hormone replacement consists of hydrocortisone (1 mg/kg IV every 6 hours) and desmopressin, a vasopressin analogue (4 μg administered as a drop into the conjunctival sac every 8 hours for 2 weeks). When the dog has resumed eating and drinking, oral replacement therapy is started: cortisone acetate (1 mg/kg every 12 hours) and thyroxine (15 μg/kg every 12 hours). Over a period of 4 weeks the dose of cortisone acetate is gradually tapered to 0.25 mg/kg every 12 hours. Desmopressin (0.01%) is administered for 2 weeks, 1 drop into the conjunctival sac every 8 hours.

Results and Complications
The efficacy of transsphenoidal hypophysectomy in the treatment of dogs with PDH has been investigated in a prospective study in 181 dogs with a median age of 9 years. The 1-, 2-, 3-, and 4-year estimated survival rates were 86%, 83%, 80%, and 79%, respectively. Treatment failures included postoperative mortalities (= death within 4 weeks after surgery irrespective of the cause of death, 14 dogs), and incomplete hypophysectomies (12 dogs). The 1-, 2-, 3-, 4-year estimated relapse-free fractions were 90%, 77%, 72%, and 62%, respectively. Survival and disease-free fractions after hypophysectomy were markedly higher in dogs with nonenlarged pituitaries than in dogs with enlarged pituitaries. The main postoperative complications after hypophysectomy are reduction in tear production (31%) and prolonged diabetes insipidus (53%). Tear production restored to normal values in 79% of the affected dogs over a median period of 9 weeks. Diabetes insipidus occurred more frequently in dogs with enlarged pituitaries than in dogs with nonenlarged pituitaries and was permanent in 22% of the dogs. The results compare favourably with those of 129 dogs treated with o,p'-DDD in the same institution in another time frame. With longer follow-up time, hypophysectomy leads to better results than o,p'-DDD treatment.

Adrenocortical Function after Hypophysectomy
Adrenocortical function after hypophysectomy can easily be measured using the basal urinary cortisol/creatinine ratio (UCCR) in samples collected at home. When the patient leaves the hospital, usually 3 days after surgery, owners receive tubes for urine collection at 2 weeks, 8 weeks, 6 months, and 1 year after surgery. Thereafter yearly assessment of adrenocortical function is advised. Urine samples are collected at home when the dog is 24 hours free of cortisone medication. The early (<8 weeks) UCCR has prognostic value when considering long term survival and disease free fractions. In dogs with early postoperative UCCR < 5 x 10⁻⁶, the survival and disease free fractions are greater than in dogs with early postoperative values between 5 and 10 x 10⁻⁶.

Pituitary Surgery in Cats
The indications for transsphenoidal hypophysectomy in cats are: Cushing’s disease caused by an ACTH-cell pituitary adenoma or acromegaly caused by a GH-cell pituitary adenoma. Both conditions in cats are usually accompanied by diabetes mellitus requiring insulin administration. Transsphenoidal hypophysectomy has a higher morbidity and mortality in cats with PDH than in dogs. In cats with acromegaly with concurrent insulin-resistant diabetes mellitus, hypophysectomy has an excellent prognosis resulting in disappearance of diabetes mellitus, discontinuation of insulin administration within 1 to 4 weeks after surgery, and normalization of GH and IGF-1 levels.

Further Reading
Figure 1  Transverse contrast-enhanced computed tomography of the skull of a dog with Cushing’s disease due to a pituitary adenoma, before (A) and 8 weeks after transsphenoidal hypophysectomy (B).