

Chapter 1

Aim and scope of the thesis

The adrenal cortex produces mineralocorticoids, glucocorticoids, and sex steroids. Thus in principle, three distinct syndromes may arise as a result of adrenocortical hyperfunction. Indeed, syndromes of glucocorticoid excess are well-known in mammalian species such as dogs and cats. The occurrence of mineralocorticoid excess has also been described recently in dogs and cats. So far, distinct syndromes due to an excessive secretion of sex steroids have been described only in humans,^{1,5} although recent reports indicate that such syndromes also occur in dogs and cats.^{2,10,11} There is increasing evidence that sex steroids play a primary role in hyperadrenocorticism in ferrets.^{6,8,12}

The first case report on hyperadrenocorticism in ferrets was published in 1987.³ In a series of 50 cases, hyperadrenocorticism appeared to be a common disorder, primarily affecting neutered ferrets.⁹ Some of the signs (vulvar swelling in neutered jills and recurrence of sexual behavior in neutered hobs) pointed towards an excessive production of sex steroids rather than to an excessive production of glucocorticoids.⁹ Consistent with this, elevated plasma concentrations of androstenedione, 17 α -hydroxyprogesterone, dehydroepiandrosterone, and estradiol have been reported.⁸ Only rarely do plasma cortisol concentrations exceed the upper limit of the reference range,⁸ whereas the urinary excretion of cortisol is often increased.⁴ The possible involvement of pituitary hormones in hyperadrenocorticism in ferrets has not been studied.

In hyperadrenocorticism in ferrets, the adrenocortical lesion may be a unilateral adenoma or carcinoma. These tumors are not associated with atrophy of the contralateral adrenal cortex.⁹ On the contrary, the contralateral adrenal cortex may be hyperplastic as well as tumorous. Indeed, the disease may also be due to bilateral adrenocortical hyperplasia. Macroscopic changes of the pituitary gland have not been reported.⁷ Resection of a unilateral tumor usually leads to improvement, albeit without substantial lowering of the plasma cortisol concentration.⁹

The studies reported in this thesis, were aimed at the further characterization of adrenocortical hyperfunction in ferrets, in an attempt to elucidate the pathogenesis of the condition and to clarify some of the diagnostic problems. To this end, the literature was first reviewed (**chapter 2**). Then, to improve diagnostic accuracy, the influence of anesthesia and manual restraint on variables of the pituitary-adrenocortical axis was studied (**chapter 3**). Subsequently, reference ranges for plasma concentrations of adrenocorticotrophic hormone (ACTH) and α -melanocyte-stimulating hormone (α -MSH) were established for normal ferrets and these concentrations were compared to those of ferrets with hyperadrenocorticism (**Chapter 4**).

Urinary corticoid-creatinine ratios were measured in privately owned healthy ferrets and in ferrets with signs of hyperadrenocorticism to elucidate the contradiction between normal plasma cortisol concentrations and the increased urinary cortisol excretion. Possible seasonal variations in urinary corticoid excretion were studied in healthy ferrets and ferrets with hyperadrenocorticism for nineteen months (**Chapter 5**).

The possible pathogenetic role of the pituitary gland in hyperadrenocorticism was investigated by comparing the histology of the pituitary gland in ferrets with hyperadrenocorticism and healthy ferrets (**Chapter 6**). The involvement of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) was investigated in a preliminary study by asking the owners of (castrated) ferrets whether they currently had ferrets with

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signs of hyperadrenocorticism, or if they had such ferrets in the past, to find out whether there was any correlation between the age at neutering and the age at which hyperadrenocorticism developed (**Chapter 7**).

The presence and functioning of LH and FSH receptors in adrenocortical tissue was examined by immunohistochemistry, RT-PCR, and *in vitro* and *in vivo* stimulation tests (**Chapter 8 and 9**). Possible alternatives to surgical neutering are discussed, with a view to eliminate the possible role that this type of neutering has on the development of hyperadrenocorticism (**chapter 10**). Lastly, findings are put in a broader context in a summarizing discussion (**Chapter 11**).

References

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