Pituitary anatomy and physiology

Sara Galac, DVM, PhD

Pituitary anatomy

The pituitary gland is referred to as the "master gland" because, despite its small size, it plays a major regulatory role throughout the entire endocrine system.[1] The pituitary gland is solitary and also known as the "*hypophysis*". It sits in a depression of the sphenoid bone called the sella turcica, which places it directly beneath the hypothalamus. Its location as an appendage of the brain points to its significance as the relay between the nervous and humoral mechanisms that jointly control several functions. Specific features in pituitary topography affect both the manner of expansion due to a growing tumor and the most convenient surgical approach, which is made via the sphenoid bone in the cat. Growing masses tend to expand through the path of least resistance, which in cats is dorsally toward the hypothalamus because the sella turcica is a shallow cup that prevents downward or lateral growth.

The pituitary gland consists of two parts, which are derived from different embryological origins and have separate functions: the adenohypophysis or the anterior lobe (AL), and neurohypophysis or a posterior lobe (PL).[2] During embryogenesis, the AL develops from Rathke's pouch, which arises from the roof of the primitive mouth in contact with the base of the brain. Rathke's pouch subsequently separates by constriction from the oral cavity. The anterior wall thickens and forms the pars distalis of the AL. The posterior wall of Rathke's pouch is closely attached to the neural tissue of the PL and it forms the pars intermedia (PI), owing the name to its location between the two major parts of the pituitary gland, the pars distalis and the PL (Fig. 1.1). Simultaneously, the neurohypophysis (PL) forms as a midline evagination of neural tissue from the floor of the hypothalamus (diencephalon). At the end of the organogenesis, the neurohypophysis remains attached to the hypothalamus and, like the adenohypophysis, remains in close proximity to the hypothalamus. This close anatomical association between the hypothalamus and all three areas of the pituitary gland is a prerequisite for their functional relationship, which is collectively described as the hypothalamus-pituitary axis.[3]

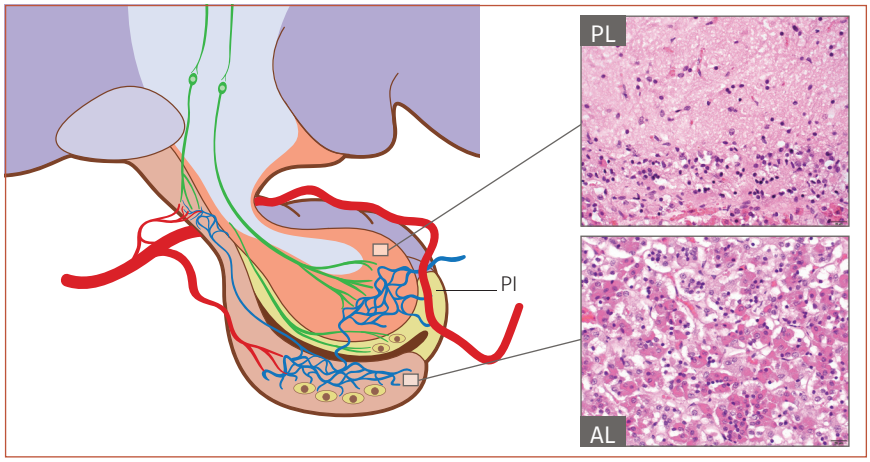

FIGURE 1.1. Histopathology and schematic illustration of a feline pituitary gland. AL: adenohypophysis or anterior lobe; PL: neurohypophysis or posterior lobe; PI: parts intermedia. Partially adapted from: Mol JA. Pituitary function. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical Biochemistry of Domestic Animals. Elsevier. 2008:561-604.

Pituitary vascularization

The adenohypophysis and neurohypophysis are separately vascularized. The rostral hypophyseal arteries form the uniquely organized capillary plexus of the median eminence that is in close proximity to nerve terminals of the hypophysiotropic neurons. The capillary plexus forms a "portal blood system" which, with the system in the liver, represent the two portal systems recognized. The blood-brain barrier is incomplete in the area of the median eminence, permitting protein and peptide hormones to move into intercapillary spaces and the nerve terminals contained therein.[2,4] These terminals respond to humoral and neuronal stimuli by synthesizing and secreting "releasing" and "inhibiting" factors into the portal system. The portal capillaries coalesce into a series of vessels that descend through the pituitary stalk and form a second capillary plexus surrounding the AL cells.

Caudal hypophyseal arteries supply the PL. From the primary plexus of the PL, blood flows into the systemic circulation but also through the AL and the hypothalamus[1]. The vascularization of the PI is closely linked to that of the PL, but while the PL has a rich blood supply, the PI is poorly vascularized (Fig. 1.2).[3]

Pituitary cell differentiation

The adenohypophyseal (AL) cells follow three main pathways of differentiation:

1. Cells expressing pro-opiomelanocortin (POMC), leading to secretion of adrenocorticotropic hormone (ACTH) and α-melanocyte-stimulating hormone (α-MSH) by corticotrophs and melanotrophs, respectively.
2. Gonadotroph cells secreting follicle-stimulating hormone (FSH) and luteinizing hormone (LH).
3. Pit1-dependent cell lines (somatotroph, lactotroph, and thyrotroph cells), leading to secretion of growth hormone (GH), prolactin (PRL), and thyroid-stimulating hormone (TSH).

Eventually, the mature AL is populated by at least five distinct types of endocrine cells responsible for the synthesis and secretion of the six trophic hormones they produce: somatotrophs (secreting GH), lactotrophs (secreting PRL), thyrotrophs (secreting TSH), corticotrophs (synthesizing the precursor molecule POMC, which gives rise to ACTH and related peptides), and gonadotrophs (secreting LH and FSH) (Fig. 1.2). The distribution of the various secretory cells of the AL is not random but has a topological and numeric organization. The AL consists of a central wedge containing thyrotrophs and corticotrophs and lateral wings containing somatotrophs and lactotrophs. The gonadotrophs are distributed diffusely throughout the gland.[5]

The PI contains two types of cells that can synthesize POMC. One is similar to the corticotrophs and in the other, ACTH is cleaved into α-MSH and corticotropin-like intermediate-lobe peptide ($ACTH_{18-39}$ or CLIP).[3,5]

The neurohypophysis consists of a set of magnocellular neurons in the supraoptic and paraventricular hypothalamic nuclei, from which axons extend through the pituitary stalk to terminate on fenestrated blood vessels in the PL.[2]

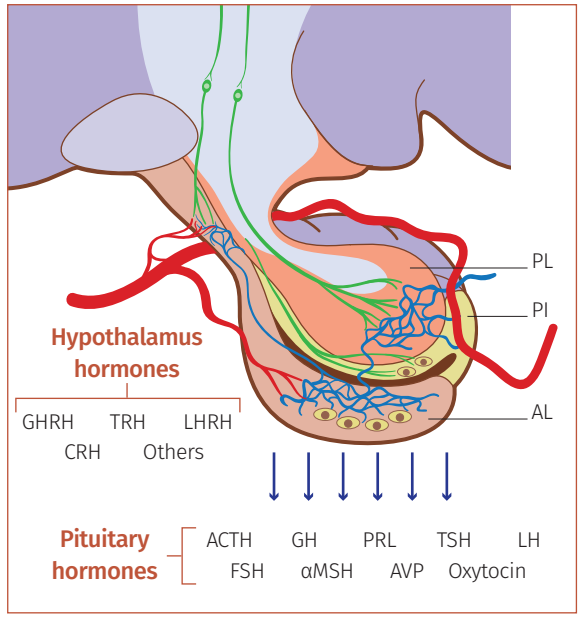

FIGURE 1.2. Schematic representation of the relationship of the hypothalamus and pituitary gland. The hypothalamus exerts control over the anterior lobe (AL) through releasing and inhibiting factors that reach the AL cells via capillaries of the pituitary-portal system. The posterior lobe (PL) of the pituitary is downward projection of the hypothalamus. The pars intermedia (PI) is under direct neurotransmitter control. Adapted from: Meij BP, Kooistra HS, Rijnberk A. Hypothalamus-pituitary system. In: Rijnberk A, Kooistra HS, eds. Clinical Endocrinology of Dogs and Cats. Schlütersche. 2010:13-54.

Pituitary physiology

Overview

The hypothalamic-pituitary axis constitutes the main axis of the neuroendocrine system. The pituitary integrates signals from the periphery and brain to control vital functions such as growth, reproduction, lactation, basal metabolism and stress response.[3] The hypothalamic-pituitary axis consists of three major components: a neuroendocrine system connected to an endocrine system by the portal circulation, a neurosecretory pathway, and the direct neural regulation of PI.[4]

All hypophysiotropic hormones secreted from AL are peptides, except dopamine. In addition to its major role as a neurotransmitter, dopamine is the most important inhibitor of PRL secretion. All hypophysiotropic hormones are secreted in a pulsatile pattern.[6,8]

The neuroendocrine system

The neuroendocrine system connects clusters of peptide- and monoamine-secreting cells in the ventral hypothalamus to the AL. Their products are "*releasing hormones*" and "*inhibiting factors*", such as GH-releasing hormone (GHRH), thyrotropin-releasing hormone (TRH), corticotropin-releasing hormone (CRH), gonadotropin-releasing hormone (GnRH), somatostatin and dopamine (Fig. 1.2). These products are stored in nerve terminals within the median eminence at concentrations 10-100 times greater than elsewhere in the hypothalamus. From the median eminence, these factors are released into capillaries of the hypothalamic-hypophyseal portal system and then transported to the AL, where they regulate hormone production and secretion. Because the portal blood flow to the pituitary is not compartmentalized, the hypothalamic releasing hormones gain access to all the endocrine cells in the AL. Action specificity is achieved by the presence of unique receptors on each individual type of AL cell.

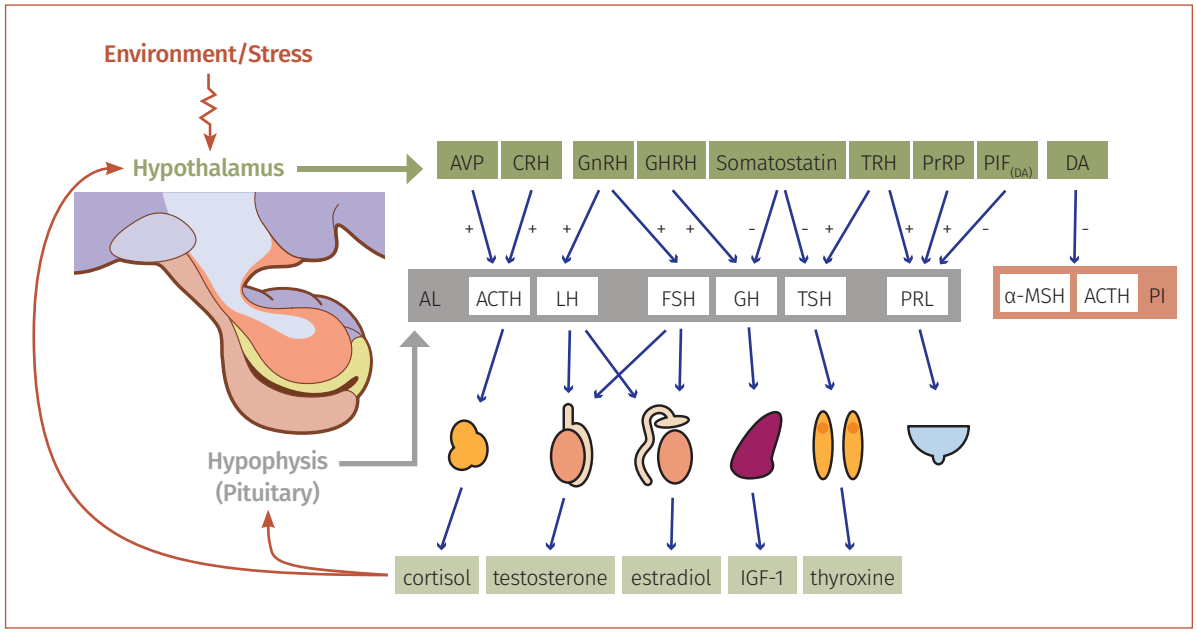

FIGURE 1.3. Simplified diagram of the hypophysiotropic regulation of the secretion of hormones in the adenohypophysis. ACTH: adrenocorticotropic hormone; AL: anterior lobe, AVP: arginine-vasopressin; CRH: corticotropin-releasing hormone; DA: dopamine; FSH: follicle-stimulating hormone; GH: growth hormone; GHRH: growth-hormone releasing hormone; IGF-1: insulin-like growth factor; LH: luteinizing hormone; α-MSH: α-melanocyte-stimulating hormone; PI: pars intermedia; PIF: prolactin-inhibitory factor; PRH: prolactin-releasing hormone; PRL: prolactin; TRH: thyrotropin-releasing hormone; TSH: thyroid-stimulating hormone; +: stimulation; –: inhibition. Adapted from: Meij BP, Kooistra HS, Rijnberk A. Hypothalamus-pituitary system. In: Rijnberk A, Kooistra HS, eds. Clinical Endocrinology of Dogs and Cats. Schlütersche. 2010:13-54.

The neurosecretory pathway

The neurosecretory pathway is involved in osmoregulation through production and release of vasopressin (VP). A similar pathway is involved in parturition and nursing through secretion of oxytocin and prolactin. The three hormones are synthesized by the populations of magnocellular neurons and stored in secretory vesicles within the nerve terminals on the PL. Here they are secreted into the systemic circulation in response to an appropriate stimulus.

Direct neural regulation

The PI is under the dopaminergic tonic inhibitory influence and β-adrenergic stimulation.[6] The main hormones synthesized in PI are ACTH and α-MSH, other POMC-related proteins include β-endorphin and β-lipotopin.[7] Dopamine secreted from the hypothalamic arcuate nucleus inhibits PI secretion, while mild stress, such as handling and physical restraint, causes impressive increases in the plasma concentrations of ACTH and α-MSH.

Hormones of the adenohypophysis (AL)

Under physiologic and most pathologic conditions the basal plasma concentration of each of the six major AL hormone systems (ACTH, LH and FSH, TSH, GH, and PRL) is regulated via a feedback (closed-loop) system.[3,8] Secretion of hypophysiotropic hormones is, in turn, suppressed by the products of target endocrine glands such as the thyroid, adrenals, and gonads. Apart from this long-loop feedback system, some hormones secreted into the general circulation, such as PRL and GH, regulate their own secretion by directly acting on the hypothalamus (short-loop feedback). Additionally, there is evidence of an ultra-short loop, by which the hormone acts within the hypophysis through autocrine and paracrine communication. Superimposed on these regulatory mechanisms there are other signals, mediated by neurotransmitters and hypophysiotropic hormones that represent the influence of the environment (temperature, light, dark), stress (pain, fear), as well as intrinsic rhythmicity. These regulatory factors influence peptide synthesis and/or release in AL cells, where each of the steps in hormone synthesis and ultimate secretion represents a potential control point in the regulation of circulating hormone concentrations. Modulation of the amount of mRNA, the efficiency of transcription and translation, the processing from pre-pro-hormone to pro-hormone to hormone, and intracellular degradation of stored hormone determine, separately or jointly, determine the amount of hormone available for release.

Growth Hormone (GH)

The secretion of GH is under inhibitory (somatostatin) and stimulatory (GHRH) hypothalamic control and under direct influence of ghrelin at the level of the pituitary gland. The GHRH is released in response to physiological stimuli, such as physical exercise, fasting, lactation, and hypoglycemia.[8] Ghrelin stimulates GH release in a dose-dependent manner. The main GH-target cells are hepatocytes, skeletal myocytes, adipocytes, and growth plate chondrocytes. The effects of GH can be divided into rapid metabolic actions and the more chronically developing anabolic effects. The acute metabolic responses result in lipolysis and restricted glucose transport across the cell membrane. The long lasting effects of GH are mainly mediated via insulin-like growth factor 1 (IGF-1), which is synthesized in the liver. GH causes its own downregulation (negative feedback, short-loop) by stimulating somatostatin-producing neurons in the hypothalamus. The GH-secretion is also modulated by a long-loop feedback control by IGF-1.[9]

Prolactin (PRL)

Secretion of PRL is principally regulated by tonic inhibition provided by dopamine from the hypothalamus. Dopamine binds to its membrane receptor on lactotrophs and inhibits PRL release. Neurogenic stress and sensory stimuli of suckling can override dopamine inhibition. Besides the inhibitory dopaminergic tone, several substances are known to have PRL-release promoting activity, such as TRH, VP, and angiotensin II. PRL binds to its own receptors on dopaminergic neurons of the hypothalamus, increasing dopamine synthesis and release, thus inhibiting its own release. The most familiar role of PRL is stimulation of mammary gland and lactation.[3,8]

TSH

Pituitary TSH secretion is controlled by the stimulatory action of hypothalamic TRH and thyroid hormones. TRH interacts with its receptor on thyrotropes but binds also on lactotrophs to release PRL. TSH is a glycoprotein that is transported in blood to thyroid epithelial cells where it stimulates cellular proliferation and the synthesis and storage of thyroglobulin and release of thyroid hormones, triiodothyronine (T_3) or tetraiodothyronine (T_4). TSH secretion is inhibited primarily by T_3, produced locally by deiodination of T_4, and also by T_3 derived from the systemic pool of free T_3. Negative feedback, which occurs at the level of the hypothalamus and hypophysis, regulates the production of TRH and TSH, respectively.[8]

FSH and LH

Unlike the other hormones of the pituitary AL, each secreted by a specific cell type, FSH and LH are secreted by the same type of cell (gonadotroph). Their primary stimulator, GnRH, is released from neurons diffusely scattered in the hypothalamus. It might be expected that both FSH and LH would be secreted in equal concentrations by gonadotrophs, but whether their regulation is concurrent or differential is still poorly understood.[8] In the female, FSH binds to receptors on the follicular epithelial cells; in the male, FSH binds to receptor on testicular sustentacular cells (Sertoli cells). In both genders, production of estrogen is stimulated by FSH. In the female, LH binds to its receptor on internal thecal cells, stimulating production of testosterone. LH also binds to follicular and thecal cells of the postovulatory follicle, stimulating synthesis and secretion of progesterone. Cells of the ovarian interstitial stroma also produce testosterone. In the male, LH binds to its receptor on the interstitial cells (Leydig cells), stimulating synthesis and secretion of testosterone. Secretion of gonadotropins is under a gonadal feedback loop. The gonadal steroids bind to cells of the hypothalamus, down regulating production of GnRH and gonadotropins.[2,8]

ACTH

Secretion of ACTH by the AL is regulated by hypothalamus and central nervous system via neurotransmitters that release CRH and VP. CRH is released from small neurons in the paraventricular nucleus in response to neural signaling. The VP in pituitary portal blood is derived primarily from CRH-containing neurons, thereby being separated from the VP involved in water homeostasis.[3] In this neuroendocrine control, four mechanisms can be distinguished:[4]

1. Episodic secretion: ACTH secretion is pulsatile and cortisol secretion is independent of circadian rhythm.
2. Stress response: ACTH and cortisol are secreted rapidly following stress as a result of CRH and VP release from the central nervous system. In cats, even mild stress such as handling can induce a severe stress response.
3. Feedback inhibition by cortisol: ACTH binds to its receptor on adrenocortical cells and activates transcription of the enzymes involved in steroidogenesis. The inhibitory actions of glucocorticoids are exerted on CRH and VP production in the hypothalamus and on the corticotroph cells of the AL. The POMC-producing cells of PI are resistant to glucocorticoid suppression due to the absence of glucocorticoid receptor.
4. Immunological factors: proinflammatory cytokines invariably activate hypothalamic-pituitary axis by stimulating CRH.

α-MSH

Circulating α-MSH, synthesized from the precursor molecule POMC, mainly originates from the PI. Its release is under dopaminergic inhibition, but in cats, α-MSH response occurs also after neurogenic stress and β-adrenergic stimulation. In contrast to other tropic hormones, in about ⅓ of cats, circadian secretion of α-MSH has been documented.[10] The biological effects of α-MSH are related to pigment regulation, but may also include control of body weight and anti-inflammatory effects.

Hormones of the neurohypophysis

Oxytocin and VP are synthesized as part of a large precursor molecule composed of a signal peptide, the hormone, and a carrier protein called neurophysin and for VP also a glycopeptide.[3]

Oxytocin

The release of oxytocin by exocytosis of the secretory granules is via a calcium-mediated mechanism, initiated by a neural synapse from sensory networks in the brainstem. When released, oxytocin binds to its receptor on myoepithelial cells of the mammary alveoli and ducts, causing myofilament-driven cell contraction, thereby resulting in lactation. In addition, oxytocin binds to its receptor on smooth myocytes of the myometrium, causing uterine contraction and parturition.[1,8]

VP

The major determinant of VP release is increased plasma osmolality. Specific neurons called osmoreceptors are concentrated in the anterior hypothalamus, close to supraoptic nuclei.[2] Next to osmoregulation, significant changes in circulating blood volume and blood pressure may also influence VP release.[8] The effects of VP are mediated by three receptor subtypes: V_{1a} receptors in blood vessels, V_2 receptors on renal collecting duct epithelial cells and V_3 (also called V_{1b}) in the adenohypophysis. In the kidney, binding of VP to the V_2 receptor activates water channels (aquaporin 2) in the apical membrane of the collecting tubule cells and exhibits an antidiuretic effect. Binding of VP to V_{1a} receptor causes increased myocyte tone, vascular constriction, and elevated blood pressure. In the pituitary gland, V_3 receptor mediates ACTH-secretion.[3]

Key facts

- Pituitary gland plays a major role in the entire endocrine system.
- The pituitary gland consists of adenohypophysis and neurohypophysis, separated with pars intermedia, which anatomically belongs to adenohypophysis.
- The six major hypophysiotropic hormones secreted from adenohypophysis are ACTH, LH and FSH, TSH, GH, and PRL.
- Hormones of the neurohypophysis are oxytocin and vasopressin.
- In the pars intermedia, ACTH and α-MSH are synthesized and secreted.

References

1. Konig HE, Liebich HG. Endocrine glands. In: Konig HE, Liebich HG, eds. Veterinary Anatomy of Domestic Animals. Schattauer 2004:537-546.
2. Dyce K, Sack W, Wensing C. The endocrine glands. In: Dyce K, Wensing C, eds. Textbook of Veterinary Anatomy. Saunders 2010:216-222.
3. Meij BP, Kooistra HS, Rijnberk A. Hypothalamus-pituitary system. In: Rijnberk A, Kooistra HS, eds. Clinical Endocrinology of Dogs and Cats. Schlütersche 2010:13-54.
4. Galac S, Reusch C, Kooistra HS RA. Adrenals. In: Rijnberk A, Kooistra HS, eds. Clinical Endocrinology of Dogs and Cats. Schlütersche 2010:93-154.
5. Capen C. Endocrine glands. In: Maxie M, ed. Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. 5th ed. St Louis: Saunders 2007:505-525.
6. Kemppainen RJ, Peterson ME. Regulation of alpha-melanocyte-stimulating hormone secretion from the pars intermedia of domestic cats. *Am J Vet Res* 1999;60:245-249.
7. Peterson ME, Kemppainen RJ, Orth DN. Plasma concentrations of immunoreactive proopiomelanocortin peptides and cortisol in clinically normal cats. *Am J Vet Res* 1994;55:295-300.
8. Goff JP. The Endocrine system. In: Erickson HH, ed. Duke's Physiology of Domestic Animals. John Wiley & Sons 2015:617-725.
9. Reusch CE. Disorders of Growth hormone. In: Feldman EC, Nelson RW, Reusch CE, Scott-Moncrieff JC, Behrend EN, eds. Canine and Feline Endocrinology. Elsevier 2015:37-76.
10. Kemppainen RJ, Peterson ME. Domestic cats show episodic variation in plasma concentrations of adrenocorticotropin, alpha-melanocyte-stimulating hormone (alpha-MSH), cortisol and thyroxine with circadian variation in plasma alpha-MSH concentrations. *Eur J Endocrinol* 1996;134:602-609.

GH excess: acromegaly (hypersomatotropism)

Stijn J.M. Niessen, DVM, PhD, DECVIM, PGCertVetEd, FHEA, MRCVS
Christopher J. Scudder, BVSc, PhD, DACVIM, MRCVS

Background and history

Acromegaly is the clinical syndrome that results from growth hormone (GH) excess. Since an individual with "acromegaly" has typical clinical signs, purists may argue that the term hypersomatotropism (HST) is preferred, since it includes those with clinical signs and those with excess GH but yet to develop signs. While this might sound semantic, research has shown that, as in humans, GH excess in cats probably develops over a considerable period of time prior to the appearance of external acromegalic features (see Clinical features and diagnosis).

In humans, HST was once considered rare. However, hypersomatotropism/acromegaly is being recognized more commonly and with a variety of presentations. A similar situation seems to be the case in cats. Until a decade ago, only a handful of cats with GH excess had been described and the condition was thought to be rare; "one would be lucky to encounter a single such cat in one's veterinary career". As a consequence, many veterinary schools did not provide much or any information on this disorder. Descriptions of the condition, when and if provided, also focused on its presentation in a diabetic cat with pronounced external acromegalic features.

These perceptions regarding feline acromegaly changed when a study began in which all diabetic cats in the United Kingdom were screened for the disease, regardless of level of insulin resistance and regardless of the presence or absence of classic external acromegalic features (Fig. 2.1).[1,2] At that time, 2003, the disease was "re-discovered" and focused research ensued, uncovering many new insights on this old disease, including that it is not always associated with acromegalic external features, difficult to control diabetes mellitus or diabetes mellitus at all (Fig. 2.1).

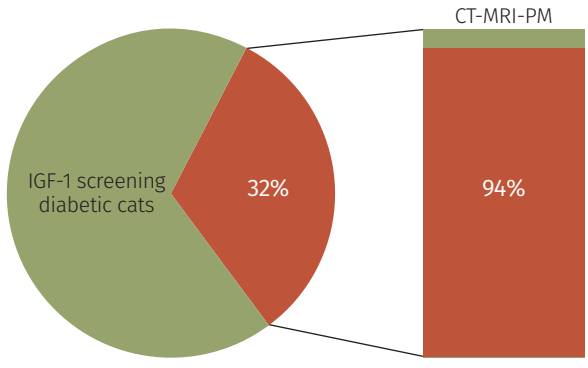

FIGURE 2.1. The importance of acromegaly among diabetic cats was demonstrated in a study on a randomized group of UK diabetic cats which revealed that 32% had a serum IGF-1 concentration >1000 ng/ml; a subpopulation was assessed through brain imaging (CT or MRI) or post mortem (PM) and revealed 94% of cases with an IGF-1 >1000 ng/ml to indeed have a pituitary mass.

Incidence and pathogenesis

Acromegaly in cats is, perhaps, 10 times more prevalent than in humans, affecting an estimated 1 in 800 diabetic and non-diabetic cats.[2,3,4,5]

Screening studies

As mentioned, although HST was thought to be rare, when preconceived ideas about its presentation where set aside, screening studies showed a different picture. The largest screening study to date evaluated 1,221 diabetic cats; 319 (26.1%) had serum IGF-1 concentrations >1000 ng/ml (95% confidence interval: 23.6-28.6%).[2] Of these 319 cats, 63 (20%) underwent pituitary imaging and/or necropsy and 60 of the 63 cats (95%) were found to have a pituitary mass. 56 masses were identified on computed tomography (CT), 3 with magnetic resonance imaging (MRI), and 1 on necropsy. These data project a positive predictive value for assaying serum IGF-1 for HST of 95% (95% confidence interval: 90-100%), which suggests that about 25% of all UK diabetic cats have acromegaly. However, only 24% of clinicians indicated a strong pre-test suspicion that their patient had acromegaly because most did not display typical phenotypical acromegaly signs.[2] Studies conducted in the Netherlands and Switzerland demonstrated a similar prevalence: approximately 1 in 5 diabetic cats had HST.[3]

Should we be screening diabetic cats in practice?

The scientific debate about the prevalence of feline HST/acromegaly among diabetic cats is ongoing. Differences in results might relate to the use of differing IGF-1 assays, recruitment methods, geographical influences, and even differences in toxin exposure (see below). Nevertheless, from a clinical point of view, the outcome of these debates will not change the overall message coming from studies conducted in the last decade: feline HST/acromegaly should be ruled out in any cat as a possible cause of its diabetes mellitus. The argument has been made that since it is generally accepted to screen for urinary tract infections (UTI) in feline diabetics (prevalence estimate 12%) it seems only logical to also recommend screening newly diagnosed diabetic cats for the presence of HST/acromegaly (prevalence estimate 18-32%). Given the tremendous implications on optimal treatment method, potential for diabetic remission, and prognosis, each new diabetic cat should be assessed for this underlying condition.

Is diabetes mellitus always present?

Diabetes mellitus is more difficult to control in cats when secondary to HST. The literature supports this concept by reporting higher doses of insulin required in the management of diabetic HST cats as compared to those with uncomplicated (non-HST associated) diabetes mellitus.[1,2] However, this might not be obvious in the early phases of HST-associated diabetes. Some of those cats will appear like any other diabetic cat; in fact, diabetes mellitus might not even be present in some cats with HST. The prevalence of diabetes mellitus in HST cats appears higher than in humans, where the prevalence of diabetes mellitus varies between 9 and 52%.[4] Risk of developing diabetes mellitus is higher in humans who have chronic untreated acromegaly and those with higher IGF-1 concentrations.[5,6] Therefore, this clinical difference might be due to the diagnosis of HST in cats occurring later in the disease process.

Non-diabetic cats with hypersomatotropism

When the screening net is thrown wider and the disorder actively considered in non-diabetic cat populations, various clinical scenarios appear. These conditions, in which HST may be the underlying trigger, include hypertrophic cardiomyopathy-like (HCM-like) disease (including incidentally encountered myocardial thickening during routine or pre-anesthetic screening), later life-onset snoring or stertor, and central nervous system abnormalities that include seizures and other signs associated with an enlarging pituitary mass. As the index of suspicion expands, it is likely that concurrent diabetes mellitus will not be as common at the time of presentation as it is currently. Although exact figures of the prevalence of HST/acromegaly in these latter non-diabetic populations are not known, it is expected that correctly identifying and treating the cats with acromegaly will improve outcomes. Unpublished data suggest that 5 to 7% of cats with myocardial thickening diagnosed as HCM actually have HST.

This is especially important since HCM is not curable whereas HST can be treated.

Although "acromegaly" is a general medical term used to describe any disorder in humans caused by chronic excessive GH secretion, most have a pituitary somatotroph adenoma. Other causes include somatotroph carcinomas or extra-pituitary disease (e.g. lung tumors) releasing excessive GH-releasing hormone.[6] In people, acromegaly can result in gigantism if the condition precedes epiphyseal fusion, although more commonly the condition begins in individuals who are middle-aged and older. Some people with gigantism are quite large, reaching heights of greater than 8 feet (2.4 metres). In cats, thus far, the only forms of HST/acromegaly reported have been secondary to a pituitary abnormality and all reported cases seem to be adult onset: no cat with gigantism has been reported in peer-reviewed literature.

Pituitary pathology

Most cats with acromegaly have had a pituitary somatotroph adenoma (Figs. 2.2 and 2.3). Other histologic diagnoses include pituitary hyperplasia and "carcinomatous changes". Although recent data identified the cause of HST in cats to be a somatotroph adenoma in most, 10 of 17 "adenomatous" pituitary glands also demonstrated concurrent pituitary acinar hyperplasia. This suggests the possibility of hyperplasia preceding adenomatous changes and might provide hints about the etiology of the disease (i.e. overstimulation leading to hyperplasia, eventually leading to an adenoma (Fig. 2.2).

When the pituitary becomes neoplastic, the normal pulsatile GH secretion patterns increase in both frequency and amplitude. Since pulsatile secretion patterns are occasionally associated with low GH concentrations, high doses of exogenous insulin may be periodically dangerous (Fig. 2.4). Giving insulin when the GH concentrations are increased may have quite different results as compared with administering the same dose of insulin to the same cat when the GH concentrations have fluctuated down.

In humans, adenomas secreting both GH and prolactin are common (up to 30%). Prolactin co-secretion was not a feature in a cohort of cats with HST recently evaluated. In that study, somatotroph adenomas varied in size from tiny to involving almost the entire anterior pituitary with gross anterior pituitary enlargement.

The gene expression profiles of cats with and without HST did not identify differences in any of the major anterior pituitary hormones, but did identify correlations

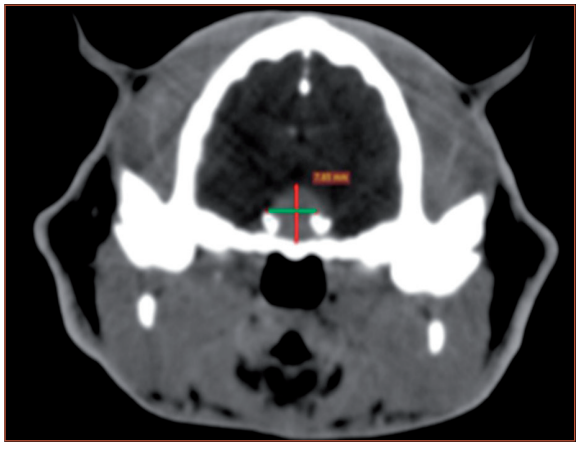

FIGURE 2.2. Transverse CT view of the brain of a cat with hypersomatotropism. An enlargement of the pituitary is clearly visible extruding from the sella turcica at the base of the brain. Maximum width is indicated by green horizontal line; maximal height by vertical red line.

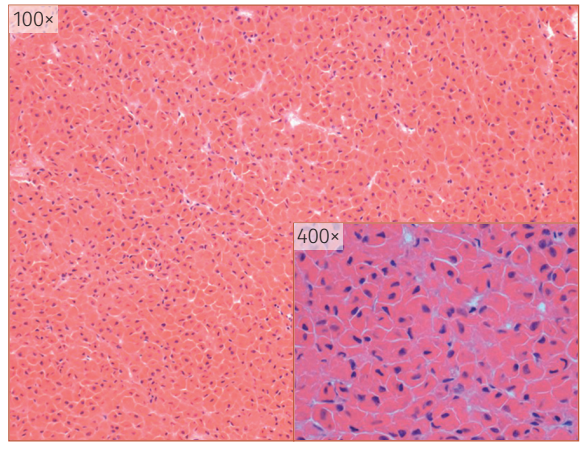

FIGURE 2.3. Histopathology (H&E staining; 100× and 400 ×) of a tumorous pars distalis of an acromegalic cat's pituitary. Normally, a balanced mixture of basophilic and acidophilic cells are seen; this tissue, from a cat with somatotrophinoma, reveals a predominance of acidophils (red staining).