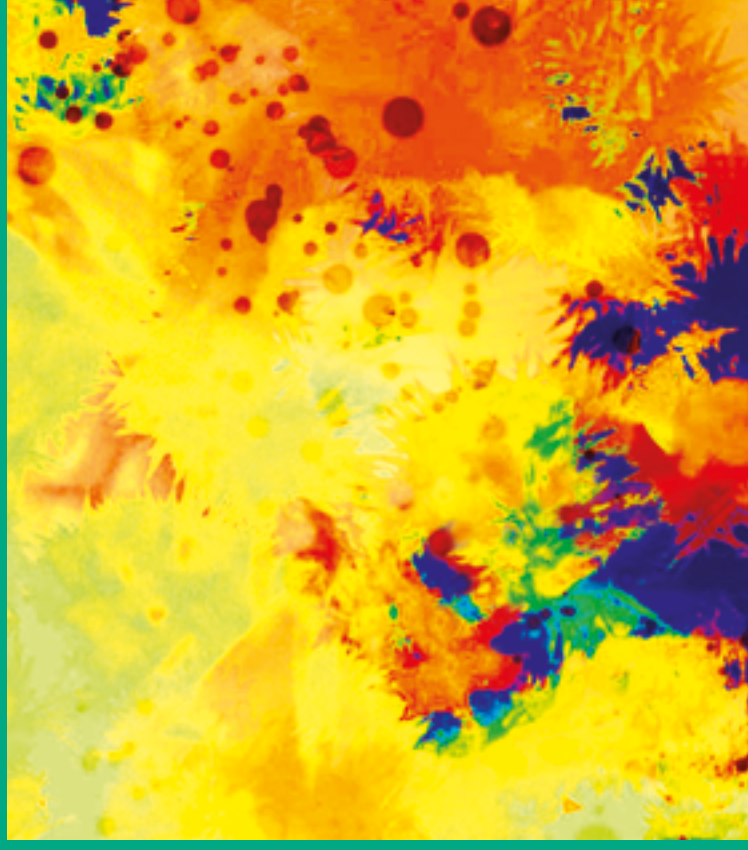

Jana Brunová
Josef Bruna

CLINICAL ENDOCRINOLOGY AND DIAGNOSTIC IMAGING

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Preface

Over the past few years, endocrinology has belonged among the most dynamically developing clinical disciplines. At the same time, we are witnessing the rapid development of new diagnostic and therapeutic procedures which are increasingly dependent on the results of imaging methods. Currently there are many monographs and textbooks available which generally examine the clinical subjects only from the viewpoint of an expert in the given field. This monograph is unique in that it excludes this one-sidedness; by combining the experience of a diagnostic radiologist with a clinical endocrinologist, this publication achieves an entirely different dimension.

This monograph is the work of leading Czech specialists in the areas of radiology and endocrinology who have extensive clinical experience with the described endocrinopathies. What makes this comprehensible publication exceptional is the fact that it not only presents the clinical view of the endocrinologist on the various covered subjects, but the reader is also given the opportunity to learn about current diagnostic trends using imaging methods. This interdisciplinary view offers the reader a comprehensive insight into the field and the necessary knowledge for their clinical practice.

I am convinced that this book provides valuable information not only for medical students, endocrinologists and radiologists, but also physicians in other medical specialties. It will certainly become a useful aid in the everyday care of patients with endocrine gland diseases.

In Prague, July 20, 2012 *Prof. MUDr. Petr Vlček, CSc.*

Introduction

This manuscript, Clinical Endocrinology and Diagnostic Imaging, is based on our extended experience and pedagogical activity in the field of clinical endocrinology and imaging methods, as well as on our clinical research, literature, and published news. We have focused mainly on the information that could be relevant for the management of endocrine patient in day-to-day practice at endocrine and imaging clinics and departments. Diagnostic imaging and intervention methods as well as endocrinology have become multidisciplinary medical specialties with accelerated progress in recent years. About thirty years ago, we took part in introducing some new imaging methods (duplex Doppler ultrasonography, computed tomography, magnetic resonance imaging) in clinical practice in the Czech Republic as well as abroad, and the developments made by new technologies since then are substantial. To our knowledge, this is the first published monograph on the subject of imaging in endocrinology.

The diagnostic and differential diagnostic data of various endocrinopathies, both clinical and imaging methods are summarized in tables to facilitate their evaluation. We present laboratory results and reference values and their ranges in conventional units (weight per volume) used in the USA and also in SI units (mole per liter) widely used in Europe and other parts of the world. Radiation and radioactivity are presented in traditional and SI units as well (rad/gray, rem/sievert; curie/becquerel) and their conversion factors are summarized in chapter Thyroid gland imaging. The ranges of normal reference of hormone and drug values may slightly differ in some working places and laboratories. There may also be individual variations including day-to-day variations and variations over the course of hours of hormone secretion and in relation to the physiology of the subject, including obesity, pregnancy, and exercise.

The chapter on therapy presents proven generic drugs and principles of management strategy for particular endocrine disorders. Therapy requires accurate diagnosis and detailed knowledge of the patient because no drug generates the same therapeutic effects on each person. Readers are encouraged to confirm the information about new drugs contained herein with other sources.

This monograph is intended not only for pre-graduate and post-graduate students but also for all young colleagues interested in clinical endocrinology and diagnostic imaging. We are aware that this manuscript does not and cannot cover all the details of the art of endocrinology, but even so have tried to present a wide variety of endocrine diseases with an emphasis on clinical use.

Ars longa, vita brevis.

Acknowledgement

We would like to acknowledge the input of Dr. Radek Pádr, Senior Consultant, Department of Radiology, Charles University in Prague, for most of the presented interventions, Prof. Dr. Petr Vlček, CSc., Head of the Department of Endocrinology and Nuclear Medicine, Charles University in Prague, and Prof. Dr. Karel Benda, DrSc., Professor of Radiology, Masaryk University Brno, for their review of the manuscript and constructive comments.

Prague, December 2011 *J. Brunová, J. Bruna*

1. Pituitary Gland

1.1 Embryology remarks

Pituitary gland (hypophysis) is formed from two sources during first eight weeks of fetal life. The **epithelial distal part** of the pituitary gland (adenohypophysis), which includes the pars anterior, pars intermedia, and pars tuberalis, originates from the primitive stomatodeal ectoderm called **Rathke's pouch**. The anterior wall of the proximal portion of Rathke's pouch grows faster and forms distal part of the pituitary (adenohypophysis). The proximal portion of Rathke's pouch closes early but a remnant often persists into postnatal life as a cleft or residual basipharyngeal canal that lies between the distal part and neural part. Occasionally Rathke's pouch gives rise to a cyst, and later in postnatal life to a tumor (Fig. 1.1).

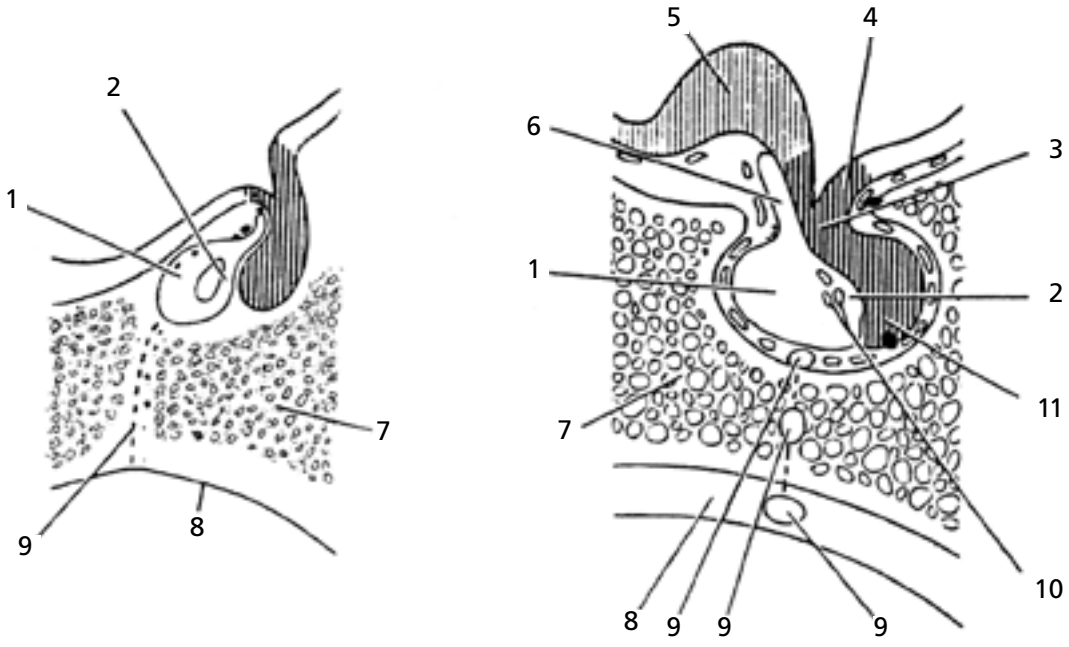

Fig. 1.1 Diagram of pituitary development – midsagittal section of the hypothalamus. 1 – anterior pituitary (adenohypophysis), 2 – pars intermedia of pituitary, 3 – infundibulum (pituitary stalk), 4 – foundation of eminentia medialis, 5 – chiasma opticum, 6 – anterior part of infundibulum, 7 – foundation of the sphenoid bone, 8 – upper pharynx, 9 – residual cranio-pharyngeal (base-pharyngeal) canal, a possible locations of accessory adenohypophysis, 10 – colloid deposits, 11 – posterior pituitary (neurohypophysis)

The neural portion originates from neuroectoderm of the diencephalon, includes infundibulum (pars infundibularis), neural stalk, and neurohypophysis (posterior pituitary), which adheres with pars intermedia of adenohypophysis (Fig. 1.1).

Histologic differentiation:

- *Acidophilic (eosinophilic) cells = α cells* are noticeable at about the third month of fetal life and produce growth hormone (GH) = somatotropin (STH) and lactogenic hormone prolactin (PRL).
- *Basophilic cells = β cells* appear a little later and are responsible for the secretion of corticotropin = adrenocorticotropin hormone (ACTH), thyrotropin = thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), interstitial-cell-stimulating hormone (ICSH) and melanocyte-stimulating hormone (MSH).
- *Chromophobe cells adenomas* are associated with hypopituitarism but may secrete prolactin, TSH and GH.

Pituitary hormones are synthesized early: The growth hormone and adrenocorticotropin hormone can be demonstrated at about the 9th week of gestation, and are followed by the appearance of glycoprotein hormones: a thyroid-stimulating hormone, a follicle-stimulating hormone, and a luteinizing hormone. Hormones of neurohypophysis, vasopressin = antidiuretic hormone (ADH) and oxytocin are synthesized in the hypothalamus and are found at about the 10th week of gestation. The neurosecretory material in the posterior lobe can be recognized at about the 20th week of gestation.

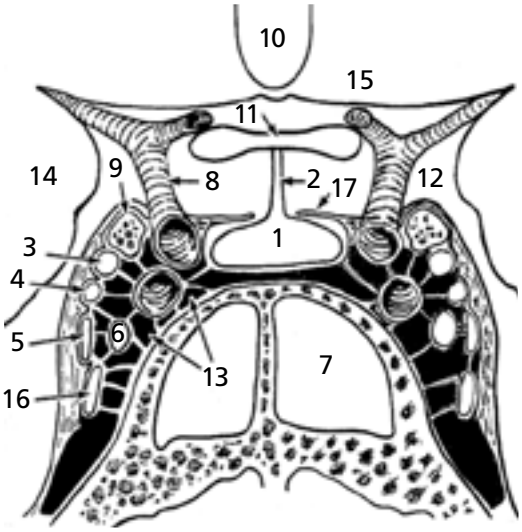

Fig. 1.2 Diagram of the sellar and parasellar structures in a coronal image. 1 – pituitary gland, 2 – pituitary stalk, 3 – nervus oculomotorius, 4 – n. trochlearis, 5 – ophthalmic branch of the n. trigeminus, 6 – n. abducens, 7 – sphenoidal sinus, 8 – arteria carotis interna, 9 – anterior clinoid processus, 10 – third ventricle, 11 – chiasma opticum, 12 – cistern suprasellaris, 13 – venous space of the cavernous sinus, 14 – medial wall of the middle fossa cranialis, 15 – hypothalamus, 16 – maxillary branch of the n. trigeminus, 17 – diaphragma sellae (according to AG Osborn, Diagnostic neuroradiology, Mosby – St. Louis 1994)

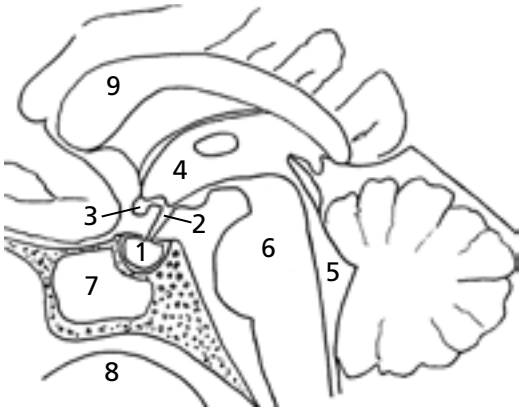

Fig. 1.3 Diagram of the pituitary and surrounding structures in the midsagittal section. 1 – pituitary gland, 2 – pituitary stalk (infundibulum), 3 – chiasma opticum, 4 – third ventricle, 5 – fourth ventricle, 6 – pons Varoli (pont), 7 – sphenoid sinus, 8 – space of the epipharynx, 9 – corpus callosum

1.2 Anatomy remarks

The sellar region is a complex area composed of the bony sella turcica, pituitary gland, and adjacent structures (Fig. 1.2–1.4).

Bony sella. The bony sella turcica (pituitary fossa) is a cup-shaped depression in the central sphenoid bone that contains the pituitary gland and inferior part of the infundibular stalk.

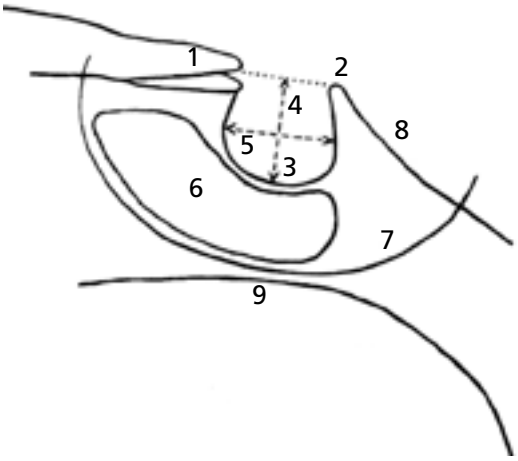

Fig. 1.4 Bony fossa measurement. 1 – anterior clinoid processes, anterior processes of the sphenoid bone (processes allae parvae ossis sphenoidei), 2 – posterior clinoid processus (dorsum sellae processus), 3 – bottom of the sella, 4 – depth of the sella – vertical diameters of the sella, 5 – length of the sella – ventrodorsal diameter of the sella, 6 – sphenoid bone sinus, 7 – bottom of the middle fossa of the skull base, 8 – clivus, 9 – space of the pharynx

The pituitary gland. The pituitary gland lies in the sella at the base of the brain in the central part of the middle cranial fossa. Lateral aspects of the pituitary gland are close to the cavernous sinus, medial wall of internal carotid artery, and the oculomotor, trochlear, and abducent nerves. The pituitary gland is composed of two lobes – anterior pituitary (adenohypophysis) and posterior pituitary (neurohypophysis). The pituitary gland is oval in shape, bilaterally symmetric with diameters about 13 mm (8–16 mm) transversally (width, latero-lateral diameter), ≈ 12 mm (9–14 mm) antero-posteriorly (length, ventro-dorsal diameter) and ≈ 6 mm (female 4–10 mm, male 3–7 mm) vertically (height, cranio-caudal diameter).

The volume of the pituitary gland is usually calculated as:

$\mathbf{V = ½ \times length \times height \times width}$

or from the formula for an ellipsoid:

$\mathbf{V = a \times b^2 \times \pi/6}$ (a = longer diameter)

The average weight of the pituitary gland is 0.6 g (0.4–0.8 g) in adults and 0.1 g at birth. An increase in weight occurs during puberty, pregnancy and lactation, and a reduction in old age. In multiparous women, the pituitary gland weighs somewhat more than in nulliparous women or in men.

Note: In our study of adult people with growth failure due to primary pituitary dwarfism we also measured the volume of the pituitary gland on MR images in a reference group of 16 normal adult subjects without any pituitary and growth problems (age 42.9 years). Results have confirmed a relatively wide variation of pituitary size. The largest diameter of pituitary gland was transverse diameter – width 13.3 mm (10–14 mm), followed by sagittal diameter – length 12.1 mm (9–13 mm) and vertical diameter – height 6.2 mm (5–9 mm). The average volume of the pituitary gland in normal subjects was 654 mm^3 (270–914 mm^3) (Bruna, Brunova, 2002).

The anterior lobe (adenohypophysis) constitutes about 80% of the pituitary gland and can be divided into the following three parts:

1. Pars tuberalis (functionally associated with part of the infundibular stalk and median eminence of the hypothalamus)
2. Pars intermedia
3. Pars distalis

The posterior lobe, infundibular stalk, median eminence and supraoptic and paraventricular hypothalamic nuclei functionally belong to neurohypophysis.

The pituitary gland is covered by dura. The connective tissue of dura mater covering superior surface of pituitary is called sella diaphragm and has a small central opening 5 mm in diameter, which is penetrated by the hypophysial stalk. Above the sella diaphragm is suprasellar cistern, optic chiasm, median eminence, hypothalamus, and the third ventricle.

The **pars distalis** of pituitary gland is the main site of adeno-hypophysial hormone synthesis and discharge. The pars intermedium is rudimentary and its functional significance is in secretion of melanocyte-stimulating hormone. The pars tuberalis contains gonadotropes and thyrotropes.

The pituitary cells have a definite topographic representation within the gland. The prolactin and growth hormone secreting cells tend to be located predominate laterally, ACTH, TSH, FSH and LH secreting cells are located centrally. The secretion of these hormones is mediated by hormone-releasing factors produced in the hypothalamus and released into the hypophyseal portal system.

Normal variations of the anterior lobe

The shape, size, and signal intensity of the normal anterior lobe on MRI vary with the age, sex, and physiologic state of the individual. The pituitary gland of the neonate has a convex superior margin. Unlike the pituitary in an adult, the anterior lobe in the neonate has a homogenously high signal on T1-weighted images. This appearance reflects the intense hormonal activity that begins during fetal life and continues into the neonatal period.

By two months of age, the convexity of the superior margin of the gland flattens out, the signal intensity of the anterior lobe decreases, and the anterior lobe can be clearly discriminated from the bright spot of the posterior lobe. The gland may have a slightly concave superior margin throughout childhood but is not expected to reach a height of greater than 6 mm (measured on the midline sagittal image). The pituitary stalk diameter is approximately 2 mm and never should exceed the diameter of the basilar artery.

At puberty, the gland increases in size, reflecting a period of high hormonal activity. At this time, gender variation is noted. The height of the gland in males reaches a maximum of 8 mm. In females, the gland may become markedly convex in superior contour and reach 10 mm in height. Hormonal activity in puberty is not as intense as occurs in the neonatal period, and there is no concurrent increase in signal of the gland as in neonates. In children with central precocious puberty, the gland increases in height and obtains the convex superior border seen at the time of normal puberty. Following adolescence, the pituitary gland slowly decreases in size. With the exception of pregnancy, the pituitary gland remains relatively stable in appearance for most of adult life (Fig. 1.5). There is a gradual involution of the gland starting at approximately 50 years of age. But in women, a slight increase in height of the gland can be visible in the age of 50 to 59 years. It is suggested that this represents a compensatory gonadotropes hypertrophy responding to increased gonadotropin-releasing hormone (GnRH) resulting from a decreased feedback of circulating gonadal steroids. The hypertrophy of the gland during pregnancy and breast feeding is reflected on imaging as well (Fig. 1.6, 1.7). The gland obtains a markedly convex superior margin and increases in height up to 10 mm and the signal intensity of anterior lobe increases, too. This is presumably related to the same factors accounting for the hyperintense signal of the anterior lobe in neonates. This high signal persists into the immediate postpartum period, when the gland may reach a height as great as 12 mm. The pituitary stalk may increase in size but should not exceed 4 mm in diameter. During the second postpartum week the pituitary gland returns to its normal adult appearance.

Changes of the height and appearance of the pituitary gland may also be seen in patients with psychiatric nutritional problems.

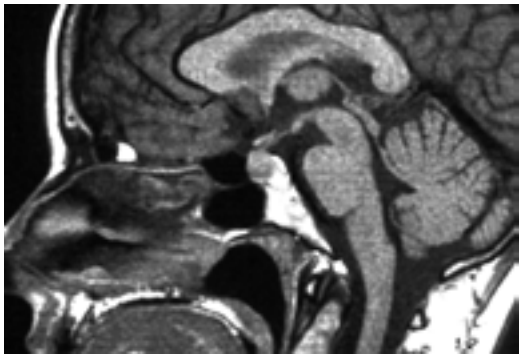

Fig. 1.5 Pituitary enlargement. Sagittal postcontrast T1GE image shows an enlarged pituitary gland in a pregnant patient

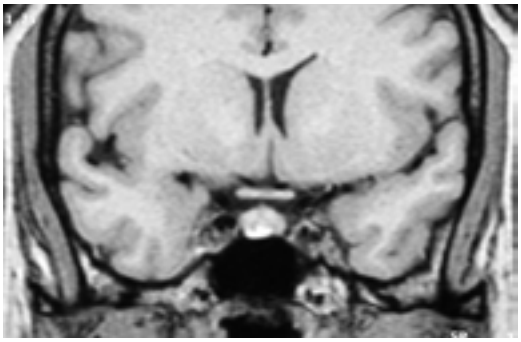

Fig. 1.6 Pituitary hyperplasia. Coronal MR T1 image of the pituitary region shows a diffuse enlarged pituitary gland with an area of hyperintensity from the floor – probably bleeding. Breastfeeding female 31 years old

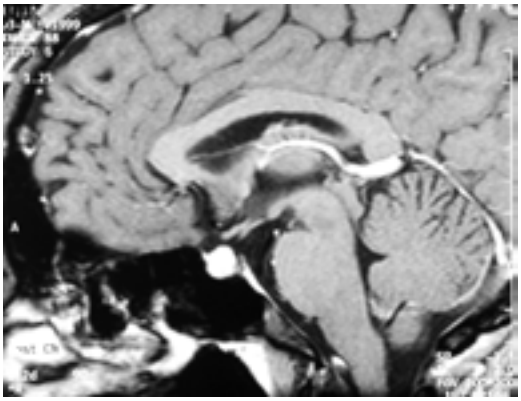

Fig. 1.7 Pituitary hyperplasia. Sagittal post-gadolinium MR T1 image of the pituitary region shows a diffuse homogenous enhancement of the enlarged pituitary gland. Breastfeeding female 31 years old

Adjacent structures

The suprasellar subarachnoid space lies above the sella diaphragm and is surrounded by the circle of Willis. The suprasellar cistern contains the optic nerves and chiasm and the upper part the infundibular stalk. The hypothalamus and anterior part of the third ventricle (optic recessus and pituitary recessus) are located just above the stalk.

Laterally, sella turcica is bordered by thin medial dural reflection of the cavernous sinus. The cavernous sinus is a multiseptated venous channel that contains the cavernous part of internal carotid arteries and cranial nerves: III – n. oculomotorius, IV – n. trochlearis, V – n. trigeminus (two branches: V1 – ophthalmic and V2 – maxillaris), and VI – n. abducens (see Fig. 1.2).

The sphenoid sinus occurs directly below the sella. Anteriorly, the sella floor is continuous with the tuberculum sellae and limbus sphenoidale. The dorsum of sella demarcates the posterior border of sella.

The cavernous sinus is best visible on coronal postcontrast CT and MR images or on magnetic resonance angiograms.

Blood supply

Main arteries supplying pituitary gland are the *superior and inferior hypophyseal arteries*. Both of them arise from the internal carotid arteries. The inferior hypophyseal artery originates more proximally from the infraclinoid portion of the internal carotid artery and the superior hypophyseal artery more distally from the supraclinoid part of the internal carotid artery. The superior hypophyseal arteries penetrate the infundibulum and terminate in the primary capillary bed of the hypophyseal portal system. The portal vessels run along the infundibulum and terminate in the sinusoids of the secondary capillary bed. The adenohypophysis does not have a direct arterial supply. It receives its blood from the hypophyseal-portal system, which also serves as the pathway by which hypothalamic releasing hormones reach these structures. The inferior hypophyseal arteries, branches of the cavernous portion of the internal cerebral artery, carry blood to the neurohypophysis (Fig. 1.8).

Venous blood is transported from the pituitary by neighboring venous sinuses – cavernous sinus and petrosal sinuses to the jugular veins.

Innervation

The adenohypophysis has no direct nerve supply, expect for a few sympathetic nerve fibers that penetrate the anterior lobe along the

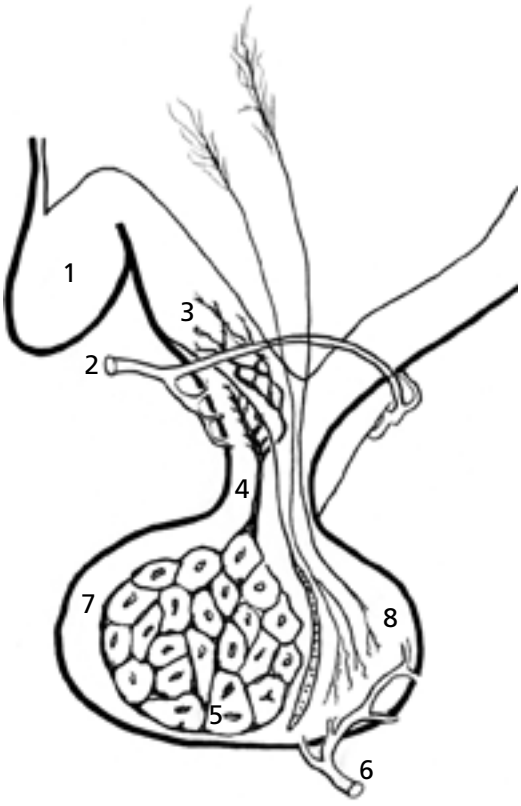

Fig. 1.8 Diagram of the vascular system of the pituitary gland – detail. 1 – chiasma opticum, 2 – a. hypophysalis superior, 3 – pituitary primary portal system, 4 – v. hypophysalis longa, 5 – pituitary secondary portal system, 6 – a. hypophysalis inferior, 7 – anterior pituitary – adenohypophysis, 8 – posterior pituitary – neurohypophysis (according to Tindall et al: Disorders of the pituitary, CV Mosby, St. Louis 1986)

vessels. The nerve fibers may affect adenohypophyseal blood flow but play no direct role in the regulation of anterior pituitary hormone secretion. The regulatory role of the hypothalamus is neurohumoral. It is done by stimulating and inhibiting hormones (factor) produced in the hypothalamus, which are transported by the portal vessels to the adenohypophysis.

The posterior lobe is richly innervated through the hypophyseal stalk by the supraoptico-hypophyseal and tubero-hypophyseal tracts. The supraoptico-hypophyseal tract transports the neurosecretory material along the nonmyelinated nerve fibers from the hypothalamus to the posterior lobe

1.3. Imaging of the pituitary region

Imaging of the pituitary gland, sellar and parasellar region and exact evaluation of the clinical and laboratory data is often crucial because different conditions of this region may present with similar clinical findings.

Imaging methods:

- Plain X-ray of skull
- Computed tomography (CT)
- Magnetic resonance imaging (MRI)
- Cerebral angiography
- Inferior petrosal venous sinus sampling (IPSS)

Plain X-ray of skull

Plain X-ray imaging was mainly used in the pituitary gland diagnosis before the introduction of CT and MR into clinical practice. At present X-ray of skull is usually performed from the other than pituitary imaging indications (skull anomaly, trauma, tumors – metastatic malignancy, myeloma and others). However, the examination may reveal an unexpected expansion in pituitary region or suspicious skeletal changes for example in acromegaly. X-ray offers the advantage of being a cheap and noninvasive method for evaluation of the *pituitary fossa* (synonyms: sella, hypophyseal fossa of sphenoid bone, sella Turcica, Turkish saddle) changes, adjacent sinuses and bony structures. They yield a certain amount of important information – size, cortical margin and shape of sella, bony erosion or compression, double contour of sella, sphenoid sinus changes, and calcifications in the region.

The sella has usually been evaluated on lateral X-ray image and less exactly by posterior--anterior axial or semi-axial Town's projection.

The ***normal diameters*** of the pituitary fossa on lateral plain X-ray can be slightly larger then the pituitary gland because of the fibrotic tis-