This exaggerated increase in growth was due to generalized overgrowth of the skeleton and to an enlargement of most tissues and organs. These results provided experimental evidence for the existence of a growth hormone (somatotropin) of hypophysial origin.

Smith and Allen, working independently, demonstrated that growth and metamorphosis of larval amphibians (frog tadpoles) were prevented by extirpation of the anlage (tissue primordium) of the epithelial (nonneural component) pituitary [13]. The larval animals were also light in color compared to normal intact tadpoles. These early experiments provided evidence for the existence of a pituitary thyroid-stimulating hormone and a melanocyte-stimulating hormone. Subsequently, other researchers provided evidence for the existence of other pituitary hormones regulating adrenal and gonadal function and numerous other physiological processes. This chapter will discuss the nature and endocrine role of the pituitary hormones.

ANATOMY OF THE PITUITARY GLAND

The pituitary gland (also known as the hypophysis) is composed of tissues that are derived from two diverse origins [12]. An understanding of the origin and development of the pituitary is critical to an understanding of the structure-function relationships of this endocrine gland. Early anatomists believed that the structural components of the pituitary (from the Latin *pituita*, or phlegm) gland were concerned with the removal of phlegm or mucus from the cavities of the brain. The comparative anatomy of the pituitary of many vertebrates has been reviewed in an important monograph by Holmes and Ball [16]. The ultrastructural characteristics of the anterior pituitary cells have been described in detail elsewhere [10].

Developmental Anatomy

The human pituitary is composed of an *adenohypophysis* (glandular or epithelial hypophysis) and a *neurohypophysis* (Fig. 5.1). The former derives from an inward invagination of the oral ectoderm of the stomodeum (primitive mouth cavity) known as Rathke's pouch (Fig. 5.2). The neuronal component arises from the neural ectoderm of the floor of the forebrain. Rathke's pouch elongates and becomes constricted at its attachment to the oral epithelium. A remnant of the connection between Rathke's pouch and the stomodeal ectoderm may persist as a "pharyngeal" pituitary. An infundibular process develops as a diverticulum of the floor of the diencephalon. The infundibulum increases in size because of neuroepithelial cell proliferation. Nerve fibers grow into the infundibulum from hypothalamic nuclei. The neuroepithelial cells then differentiate into *pituicytes* (neuroglial-like elements), which are dispersed between the neuronal endings within the infundibulum.

Cells of the anterior wall of Rathke's pouch proliferate to give rise to the pars distalis or anterior pituitary [10]. Continued proliferation of these cells leads to reduction of the lumen of Rathke's pouch to a *residual cleft* and a separation of the cells of the posterior wall from the anterior pituitary. Those cells adjacent to the

Pituitary Gland (Hypophysis)

Adenohypophysis

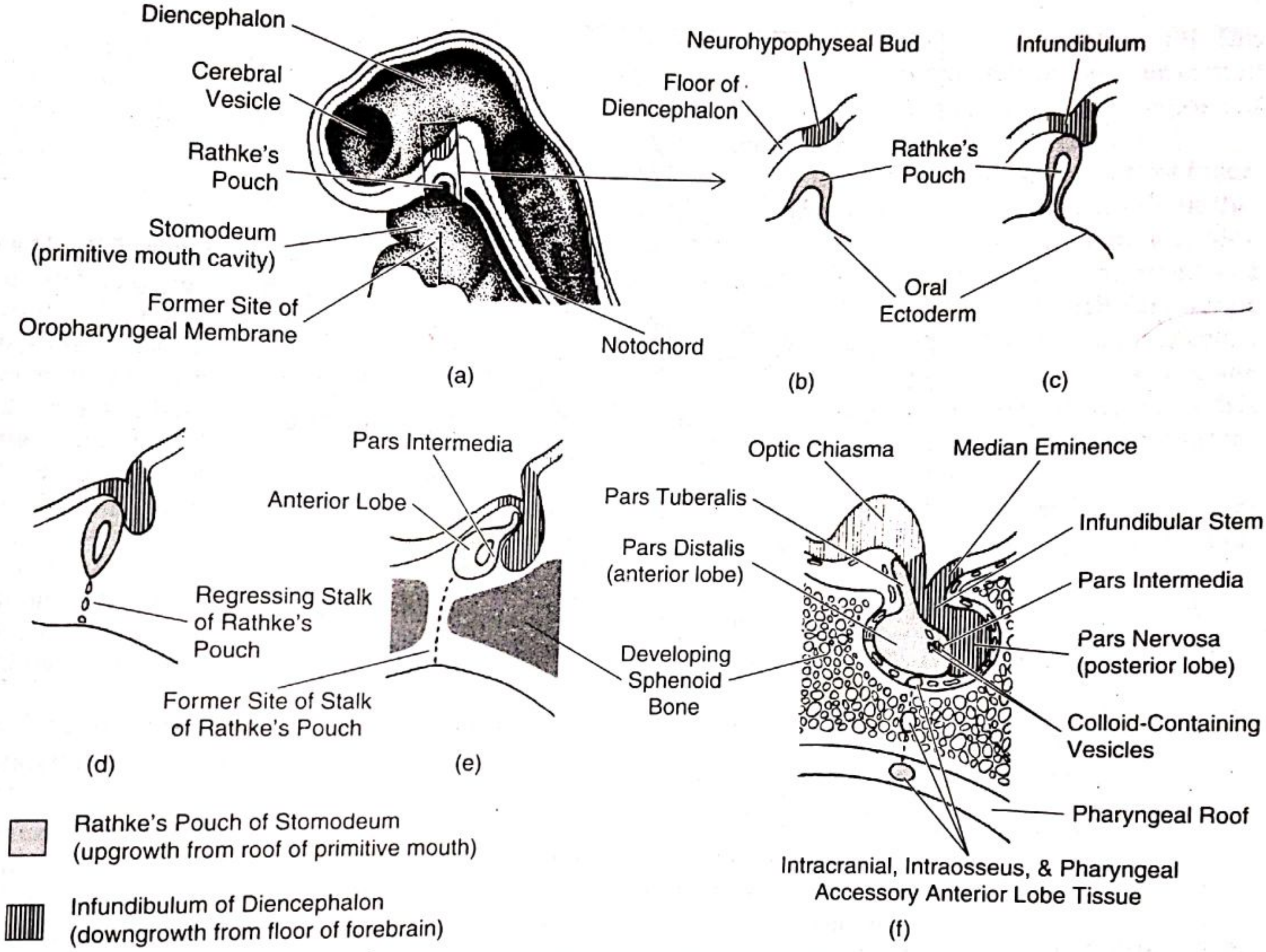

Figure 5.2 Developmental anatomy of the pituitary. (From K. L. Moore, *The Developing Human,* "Clinically Oriented Embryology," 2nd ed., 1977. Courtesy of W. B. Saunders Company.)

infundibulum may proliferate to give rise to a pars intermedia of considerable size in some species. Failure of the adenohypophysis to contact the developing neurohypophysis results in the inability of the pituitary cells to form a pars intermedia. In birds, the adenohypophysis is separated from the neurohypophysis by a layer of connective tissue and a pars intermedia does not develop. In humans, the fetal pars intermedia regresses and is absent in the adult (see Chap. 8). Dorsal extensions of the anterior pituitary surround the infundibular stalk to give rise to the *pars tuberalis*. The pars tuberalis may provide an important anatomical link between the pars distalis and the hypothalamus. The definitive pituitary in many species consists of the pars distalis, the pars intermedia, the pars tuberalis, and the pars nervosa (Fig. 5.3). The intimate anatomical relationship between the pituitary gland and the overlying brain provides an important clue to understanding the essential functional relationship of the components of the brain-pituitary axis [9, 10, 14, 17].

... Vascularization, and Innervation

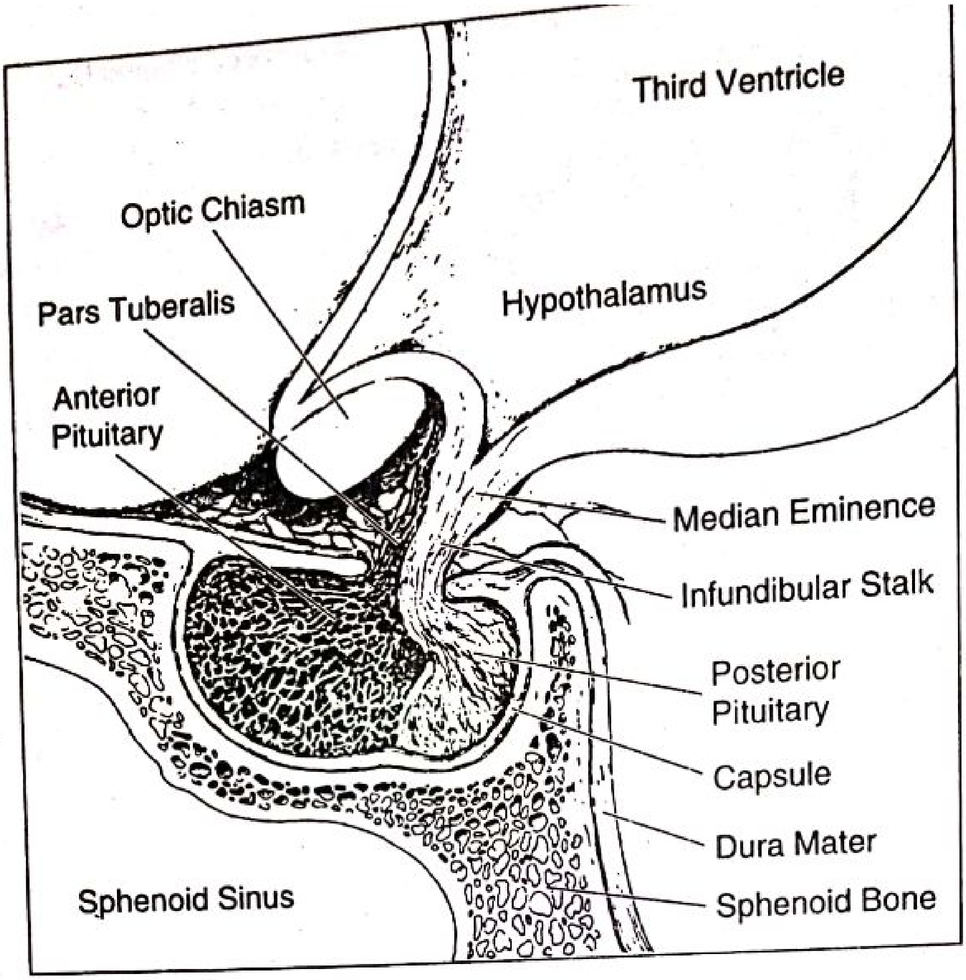

Figure 5.3 The pituitary gland of humans. In the adult human, unlike most mammals, the pars intermedia is absent. (From R. Guillemin and R. Burgus, "The Hormones of the Hypothalamus," with permission [14]. ©1972 by Scientific American, Inc. All rights reserved.)

The pituitary gland receives its blood supply from the superior and inferior hypophysial arteries. The anterior and posterior branches of the superior hypophysial artery penetrate the hypophysial stalk, as well as the hypothalamus (Fig. 5.4). The pars distalis is vascularized by hypophysial portal vessels that arise from the capillary beds within the median eminence of the hypothalamus. This hypophysial portal system provides an important link for carrying hormonal information from the CNS to the pituitary (Chap. 6). Whether the anterior lobe receives blood exclusively from the portal circulation, or whether some additional direct arterial blood supply is available, is unresolved. The pars nervosa receives a separate blood supply from the inferior hypophysial artery. The pars intermedia, if present, is relatively avascular. Physiologists have generally assumed that all hormones produced by the adenohypophysis are released directly into the efferent portal veins to be carried through the systemic circulation to distant target tissues. There is evidence that some adenohypophysial venous blood may be shunted to the neurohypophysis [3]. This circular path of blood flow may permit adenohypophysial venous blood to be carried up the infundibular process to the brain. This observation carries the important implication that pituitary hormones might be able to modify CNS function.

Except for neurovascular elements, there is no evidence that neurons innervate or otherwise directly influence the cell activity of the human pars distalis or that of most other mammals. Neuronal elements may affect cellular hormone secretion within the pars distalis of some teleost fishes. The cells of the pars intermedia of amphibians and some mammals are surrounded by a plexus of catecholaminergic neurons that regulate MSH secretion from the melanotrophs (MSH-secreting cells). Such a direct neuronal innervation is absent from the pars intermedia of some reptiles. The pars nervosa is composed of axonal endings of neurons whose cell bodies are located in hypothalamic nuclei, and in mammals, the paraventricular and supraoptic nuclei (Fig. 5.5).

The gross morphology of the pituitary differs considerably between the vertebrate classes and often between species of the same class. At the cytological level the individual cell types may be intermingled to varying degrees (as in tetrapods) or separated into zones (as in most teleost fishes). There is no distinct neural lobe in fishes. The neural lobe is, however, characteristic of tetrapods, and this may be related to the terrestrial manner of life of these vertebrates, where one or both neurohypophysial hormones may be of adaptive importance (see Fig. 8.2). The size of the pars intermedia varies considerably between species, and all birds lack a pars intermedia. This is not a unique feature, as the pars intermedia is not present in some mammals (elephants, whales, adult humans).

Cytology

The cells of the pituitary are referred to as *acidophils, basophils*, or *chromophobes*, depending on their affinity for certain dyes used in histological stains (Table 5.1). Histochemical and immunocytochemical methods have provided definitive information on the specific cellular sources of each pituitary peptide hormone [27]. The cells of the pars distalis have been differentiated into somatotrophs, lactotrophs (mammotrophs), corticotrophs, thyrotrophs, and gonadotrophs [22]. These terms relate to the particular hormonal product synthesized by each of these cells.

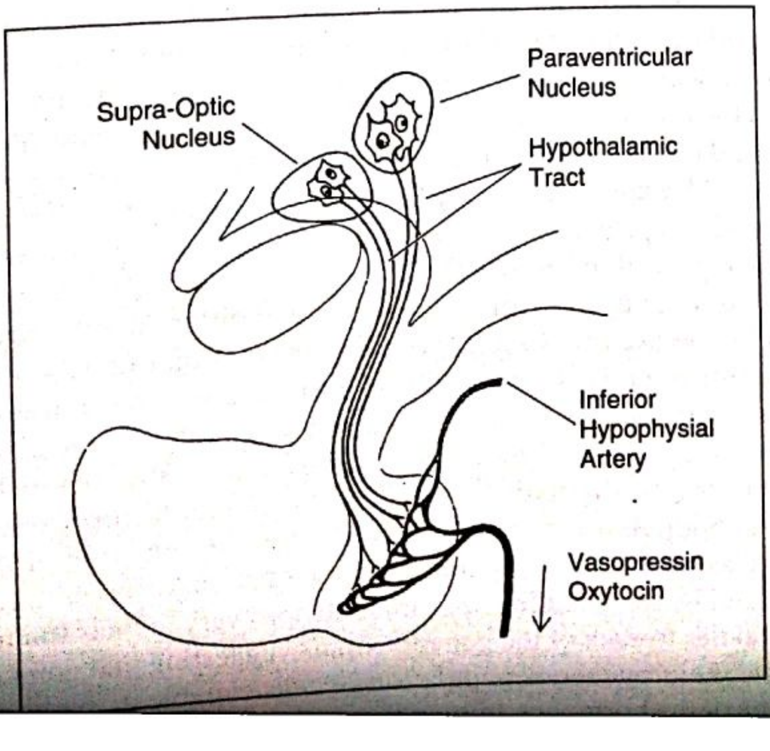

Figure 5.5 Neural components of the pituitary gland of humans [14]. (From R. Guillemin and R. Burgus, "The Hormones of the Hypothalamus," with permission [14]. ©1972 by Scientific American, Inc. All rights reserved.)

TABLE 5.1 Histochemical Classification of Pituitary Pars Distalis cells

Cell Type	*Hormone*		*Staining characteristic*
Corticotroph[a]	Corticotropin	(ACTH)	Basophil
Thyrotroph	Thyrotropin	(TSH)	Basophil
Gonadotroph			
FSH-gonadotroph	Follitropin	(FSH)	Basophil
LH-gonadotroph	Lutropin	(LH)	Basophil
Lactotroph (mammotroph)	Prolactin	(PRL)	Acidophil
Somatotroph	Growth Hormone	(GH)	Acidophil

[a]Cytological classification uses either the suffix -troph or -trope (e.g., corticotrope).

Somatotrophs and lactotrophs are acidophils, whereas the thyrotrophs and the gonadotrophs are basophils. The corticotrophs are basophils but are often referred to as chromophobes. The cells of the mammalian pars intermedia are also considered to be chromophobes. The extent to which a cell exhibits acidophilia, basophilia, or chromophobia may depend on the granular content (hormone-containing vesicles) of the cell, which often varies with the temporal secretory activity of the cell. These secretory vesicles may become depleted after continued secretory activity of the cells; in contrast, these granules may accumulate, at least transiently, if the cells stop releasing hormone. Granule synthesis may eventually decline if the cell is no longer stimulated to secrete its hormonal product. Except for the sparse pituicytes (glial-like cells), the pars nervosa contains only neuronal axonal endings.

Nongranulated, presumably nonsecretory cells are also present in the pars distalis, pars intermedia and