excruciating headache, diplopia due to pressure on the oculomotor nerves, and hypopituitarism. In severe cases, it can cause cardiovascular collapse, loss of consciousness, and even sudden death. The combination of mass effects from the hemorrhage and the acute hypopituitarism makes pituitary apoplexy a true neurosurgical emergency.

- *Ischemic necrosis of the pituitary and Sheehan syndrome:* Sheehan syndrome, also known as postpartum necrosis of the anterior pituitary, is the most common form of clinically significant ischemic necrosis of the anterior pituitary. During pregnancy the anterior pituitary enlarges to almost twice its normal size. This physiologic expansion of the gland is not accompanied by an increase in blood supply from the low-pressure venous system; hence, there is relative hypoxia. Any further reduction in blood supply caused by obstetric hemorrhage or shock may precipitate infarction of the anterior lobe. Because the posterior pituitary receives its blood directly from arterial branches, it is much less susceptible to ischemic injury and is therefore usually not affected. Pituitary necrosis may also be encountered in other conditions, such as disseminated intravascular coagulation and (more rarely) sickle cell anemia, elevated intracranial pressure, traumatic injury, and shock of any origin. Whatever the pathogenesis, the ischemic area is resorbed and replaced by a nubbin of fibrous tissue attached to the wall of an empty sella.
- *Rathke cleft cyst:* These cysts, lined by ciliated cuboidal epithelium with occasional goblet cells and anterior pituitary cells, can accumulate proteinaceous fluid and expand, compromising the normal gland.
- *Empty sella syndrome:* Any condition or treatment that destroys part or all of the pituitary gland, such as ablation of the pituitary by surgery or radiation, can result in an *empty sella* and the *empty sella syndrome*. There are two types: (1) In a *primary* empty sella, a defect in the diaphragma sella allows the arachnoid mater and cerebrospinal fluid to herniate into the sella, expanding the sella and compressing the pituitary. Classically, this occurs in obese women with a history of multiple pregnancies. Affected individuals often present with visual field defects and occasionally with endocrine anomalies, such as *hyperprolactinemia*, due to interruption of inhibitory hypothalamic inputs. Sometimes the loss of functioning parenchyma is sufficient to produce hypopituitarism. (2) In *secondary* empty sella, a mass, such as a pituitary adenoma, enlarges the sella and is then either surgically removed or undergoes infarction, leading to loss of pituitary function.
- *Hypothalamic lesions*: As mentioned earlier, hypothalamic lesions can also affect the pituitary by interfering with the delivery of pituitary hormone-releasing factors. In contrast to diseases that involve the pituitary directly, hypothalamic abnormalities can also diminish the secretion of ADH, resulting in diabetes insipidus (discussed later). Hypothalamic lesions that cause hypopituitarism include *tumors*, which may be benign (e.g., craniopharyngioma) or malignant; most of the latter are metastases from tumors such as breast and lung carcinoma. Hypothalamic insufficiency can also appear following irradiation of brain or nasopharyngeal tumors.
- *Inflammatory disorders and infections*, such as sarcoidosis or tuberculous meningitis, can involve the hypothalamus and cause deficiencies of anterior pituitary hormones and diabetes insipidus.
- *Genetic defects:* Congenital deficiency of transcription factors required for normal pituitary function is a rare cause of hypopituitarism. For example, mutation of the pituitary-specific gene *PIT-1* results in combined pituitary hormone deficiency, characterized by deficiencies of GH, prolactin, and TSH.

The clinical manifestations of anterior pituitary hypofunction vary depending on the specific hormones that are lacking.

- Children can develop growth failure *(pituitary dwarfism)* due to growth hormone deficiency.
- Gonadotropin (LH and FSH) deficiency leads to amenorrhea and infertility in women and decreased libido, impotence, and loss of pubic and axillary hair in men.
- TSH and ACTH deficiencies result in symptoms of hypothyroidism and hypoadrenalism, respectively, and are discussed later in the chapter.
- Prolactin deficiency results in failure of postpartum lactation.
- The anterior pituitary is also a rich source of MSH, synthesized from the same precursor molecule that produces ACTH; therefore, one of the manifestations of hypopituitarism includes pallor due to a loss of stimulatory effects of MSH on melanocytes.

Posterior Pituitary Syndromes

The clinically relevant posterior pituitary syndromes involve ADH and include *diabetes insipidus* and *secretion of inappropriately high levels of ADH*.

- ***Diabetes insipidus.* ADH deficiency causes *diabetes insipidus*, a condition characterized by excessive urination (polyuria) due to an inability of the kidney to resorb water properly from the urine.** Diabetes insipidus can occur in a variety of conditions, including head trauma, tumors, inflammatory disorders of the hypothalamus and pituitary, and surgical complications. The condition can also arise spontaneously, in the absence of an identifiable underlying disorder. Diabetes insipidus from ADH deficiency is designated as *central* to differentiate it from *nephrogenic* diabetes insipidus, which is a result of renal tubular unresponsiveness to circulating ADH. The clinical manifestations of these two disorders are similar and include the excretion of large volumes of dilute urine with a lower than normal specific gravity. Serum sodium and osmolality are increased by the excessive renal loss of free water, resulting in thirst and polydipsia. Patients who can drink water generally compensate for the urinary losses, but patients who are obtunded, bedridden, or otherwise limited in their ability to obtain water may develop life-threatening dehydration.
- ***Syndrome of inappropriate ADH (SIADH) secretion.* ADH excess causes resorption of excessive amounts of free water, resulting in *hyponatremia*.** The most