TABLE 62-3 SCREENING TESTS FOR PITUITARY DISORDERS

DISORDER	TESTS
PITUITARY TUMOR	
Acromegaly	IGF-I OGTT: measure blood sugar and GH (0, 60, 120 min)
Prolactinoma	Basal serum prolactin
ACTH-secreting tumor	24-hr urine-free cortisol and creatinine level 1-mg overnight dexamethasone suppression test 11 PM salivary cortisol Serum ACTH Dexamethasone-CRH test Bilateral inferior petrosal sinus sampling
TSH-secreting tumor	Serum TSH, FT4, FT3
Gonadotropin-secreting tumor	FSH, LH, alpha subunit
HYPOPITUITARISM	
GH deficiency	IGF-I GH provocative test: ITT Arginine-GHRH Glucagon stimulation test
Gonadotropin deficiency	Women: basal estradiol, LH, FSH Men: 8 AM fasting testosterone (total; free), LH, FSH
TSH deficiency	Serum TSH, free T_4
ACTH deficiency	ACTH Provocative test: ITT Metyrapone test Cosyntropin-stimulation test (1 μg and 250 μg)

ACTH, Adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone–releasing hormone; IGF-I, insulin-like growth factor-I; ITT, insulin tolerance test; LH, luteinizing hormone; OGTT, oral glucose tolerance test; T_4, thyroxine; TSH, thyroid-stimulating hormone; TFT, thyroid function test.

Prolactinomas and hyperprolactinemia are more common in women, with a peak prevalence between 25 and 35 years of age. The mean prevalence of patients medically treated for hyperprolactinemia is approximately 20 per 100,000 in men and approximately 90 per 100,000 in women. Prolactinomas are rare in childhood or adolescence.

Clinical Presentation

The clinical presentation of a prolactinoma varies with the age and gender of the patient. Typically, the patient is a young woman with menstrual irregularities, galactorrhea, and infertility. Galactorrhea occurs in 50% to 80% of affected women. Men may report a decrease in libido and erectile dysfunction as result of hypogonadism caused by reduced secretion of LH and FSH. Typically, however, their tumors are diagnosed after symptoms of tumor compression appear, including headache, neurologic deficits, and vision changes. Galactorrhea and gynecomastia are rare in men. Because of the early presentation of menstrual irregularities in women, microprolactinomas are more common in women; macroprolactinomas are more frequent in men and in postmenopausal women.

Diagnosis and Differential Diagnosis

Hyperprolactinemia is diagnosed by a single measurement of serum prolactin; a level above the upper limit of normal confirms the diagnosis. For prolactinomas, serum prolactin levels typically parallel tumor size. A prolactin level greater than 250 ng/mL usually indicates the presence of a prolactinoma. Dynamic testing is not needed to diagnose hyperprolactinemia.

Two types of artifacts can occur during the standard measurement of prolactin: the presence of macroprolactin and the hook effect. When a patient with mild hyperprolactinemia does not have the expected clinical features of hyperprolactinemia (e.g., galactorrhea, menstrual disturbance, infertility), one should consider the presence of macroprolactin. Although 85% of circulating prolactin is monomeric, serum also contains the macroprolactin, a polymeric form of prolactin that is biologically inactive. Most commercially available prolactin assays do not detect macroprolactin, but it can be detected inexpensively in the serum by polyethylene glycol precipitation. The estimated incidence of macroprolactin accounting for a significant proportion of hyperprolactinemia is 10% to 20%. The hook effect should be considered whenever a patient has a very large pituitary mass but only a mild elevation in prolactin. The hook effect is an assay artifact that occurs when very high serum prolactin concentrations saturate antibodies in the standard two-site immunoradiometric assay, resulting in falsely lower levels. This artifact can be overcome by repeating the prolactin measurement on a 1 : 100 serum sample dilution.

Physiologic increases in prolactin occur with pregnancy, physical or emotional stress, exercise, and chest wall stimulation. Other causes for hyperprolactinemia include some drugs, such as metoclopramide and risperidone, that can increase prolactin to greater than 200 ng/mL. Mild to moderate hyperprolactinemia (25 to 200 ng/mL) in the presence of a larger pituitary mass is more likely to be caused by a non–prolactin-secreting tumor with infundibular stalk compression and inhibition of dopamine transport to the lactotroph. Other causes include hypothalamic-pituitary disorders, systemic disorders, and neurogenic and idiopathic etiologies.

Treatment and Prognosis

Medical management with a dopamine agonist—bromocriptine or cabergoline—is the recommended treatment. The dopamine agonists normalize prolactin, decrease tumor size, and restore gonadal function in more than 80% of patients with prolactinomas. Because of the rapidity and efficacy of the dopamine agonists in treating these tumors, they are also the initial treatment for macroprolactinomas that have caused compromise in vision, neurologic deficits, or pituitary dysfunction.

Cabergoline, the newer agent, is preferred to other dopamine agonists because it has higher efficacy in normalizing prolactin levels and shrinking tumor size and has fewer side effects. The most common side effects seen with dopamine agonists are nausea, vomiting, orthostatic lightheadedness, dizziness, and nasal congestion. Because of the concern for cabergoline-related cardiac valvulopathy that was reported in patients who had Parkinson's disease treated with high doses of cabergoline and the possible long-term need for treatment, bromocriptine could be used in young patients if it is tolerated. Transsphenoidal resection of the tumor is indicated for patients who cannot tolerate the dopamine agonists or who do not respond to medical treatment. No treatment is required for patients who have microprolactinomas that are asymptomatic.