

Pituitary Adenomas: An Overview

MARCY G. LAKE, DO, U.S. Naval Hospital, Sigonella, Italy

LINDA S. KROOK, MD, Naval Hospital, Bremerton, Washington

SAMYA V. CRUZ, MD, U.S. Naval Hospital, Rota, Spain

Prolactinomas and nonfunctioning adenomas are the most common types of pituitary adenomas. Patients with pituitary adenomas may present initially with symptoms of endocrine dysfunction such as infertility, decreased libido, and galactorrhea, or with neurologic symptoms such as headache and visual changes. The diagnosis may also be made following imaging done for an unrelated issue in an asymptomatic patient; this is termed a pituitary incidentaloma. Oversecretion of hormones from a dysfunctional pituitary gland may result in classic clinical syndromes, the most common of which are hyperprolactinemia (from oversecretion of prolactin), acromegaly (from excess growth hormone), and Cushing disease (from overproduction of adrenocorticotropic hormone). In the diagnostic approach to a suspected pituitary adenoma, it is important to evaluate complete pituitary function, because hypopituitarism is common. Therapy for pituitary adenomas depends on the specific type of tumor, and should be managed with a team approach to include endocrinology and neurosurgery when indicated. Dopamine agonists are the primary treatment for prolactinomas. Small nonfunctioning adenomas and prolactinomas in asymptomatic patients do not require immediate intervention and can be observed. (*Am Fam Physician*. 2013;88(5):319-327. Copyright © 2013 American Academy of Family Physicians.)

► Patient information:

A handout on this topic, written by the authors of this article, is available at <http://www.aafp.org/afp/2013/0901/p319-s1.html>. Access to the handout is free and unrestricted.

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Author disclosure: No relevant financial affiliations.

Pituitary adenomas are the most common type of pituitary disorder.¹ They are benign neoplasms that account for 10% to 15% of all intracranial masses. Few large studies have delineated the exact prevalence, but a recent study of the inhabitants of a community in the United Kingdom found the overall prevalence to be higher than previously reported, at 77.6 per 100,000 persons.² Although autopsy and radiologic studies indicate that the prevalence may be as high as 20%, the majority of these tumors are incidentalomas without clinical significance.^{3,4} Whether during an evaluation of symptoms commonly presented to them, or through incidental discovery of a pituitary mass, family physicians are often the first to consider the diagnosis of a pituitary adenoma.

Classification

Pituitary adenomas are categorized based on primary cell origin and type of hormone secreted (*Table 1*⁵⁻¹²). If the adenoma does not secrete a sufficient level of hormones to be detectable in the blood or to result in clinical manifestations, it is considered nonfunctioning. Prolactinomas comprise 40% to 57% of all adenomas, followed by nonfunctioning adenomas (28% to 37%), growth

hormone-secreting adenomas (11% to 13%), and adrenocorticotropic hormone (ACTH)-secreting adenomas (1% to 2%). Pituitary adenomas that secrete follicle-stimulating hormone (FSH), luteinizing hormone (LH), or thyroid-stimulating hormone (TSH) are rare.^{2,13} Tumors are also categorized based on size. If the tumor is 10 mm or larger, it is considered a macroadenoma; if it is less than 10 mm, it is considered a microadenoma. Microadenomas are slightly more common than macroadenomas (57.4% vs. 42.6%).¹³

Pathophysiology

The pituitary gland sits inferior to the hypothalamus (*Figure 1*). It is surrounded caudally by the sphenoid bone in a basketlike structure called the sella turcica, and superiorly by the optic chiasm. The sella turcica forces an expanding adenoma superiorly, leading to compression of the optic nerve and headaches from mass effect. Additionally, destruction or compression of the pituitary gland may cause complete or partial hypopituitarism.⁵

Pituitary adenomas are benign tumors that arise from one of the five cell types that comprise the anterior pituitary (lactotrophs, gonadotrophs, somatotrophs, corticotrophs, and thyrotrophs). Tumors rarely form from a combination of these cells. Pituitary

Table 1. Classification and Clinical Presentation of Pituitary Adenomas

<i>Cell type</i>	<i>Hormone secreted</i>	<i>Clinical syndrome</i>	<i>Presentation</i>	<i>Corresponding diagnostic tests</i>
Corticotroph	Adrenocorticotropic hormone	Cushing disease	<p>Symptoms Labile mood, proximal muscle weakness, skin changes, changes in facial features, weight gain, depression, hirsutism, decrease in libido, menstrual changes</p> <p>Signs Thin skin, striae/bruising, central obesity, moon facies, plethora, hypertension, acne, glucose intolerance, neutrophilia, lymphocytopenia, eosinopenia</p> <p>Morbidity Diabetes mellitus, cardiac disease, osteoporosis</p>	<p>24-hour urine free cortisol</p> <p>Late-night salivary cortisol</p> <p>1-mg overnight dexamethasone suppression</p>
Gonadotroph	LH/FSH, alpha- and beta-subunits	No specific syndrome	Symptoms from mass effect; hypopituitarism; silent (nonfunctioning)	LH/FSH
Lactotroph	Prolactin	Hyperprolactinemia	<p>Symptoms General: galactorrhea, decrease in libido, infertility</p> <p>Men: gynecomastia, impotence</p> <p>Premenopausal women: oligomenorrhea or amenorrhea</p> <p>Signs Gynecomastia, hypogonadism (testicular atrophy, breast shrinkage, hair loss)</p> <p>Morbidity Osteoporosis</p>	Serum prolactin
Somatotroph	Growth hormone	Acromegaly, gigantism (if occurs before closure of growth plate)	<p>Symptoms Increase in hand and foot size, change in facial features (large mandible), carpal tunnel symptoms, hyperhidrosis, fatigue, proximal muscle weakness, decrease in libido, menstrual changes</p> <p>Signs Hypertension, coarse facial features, left ventricular hypertrophy, cardiomyopathy, visceromegaly, hypercalciuria, goiter</p> <p>Morbidity Cardiac disease, diabetes, sleep apnea, increased risk of colon cancer, osteoporosis</p>	<p>Serum insulinlike growth factor 1 levels</p> <p>Oral glucose suppression test (75-g load) followed by growth hormone measurement after two hours</p>
Thyrotroph	Thyroid-stimulating hormone	Hyperthyroidism	Hyperthyroid symptoms	Thyroid-stimulating hormone, thyroxine
<i>Tumor type</i>	<i>Hormone secreted</i>	<i>Clinical syndrome</i>	<i>Presentation</i>	<i>Corresponding diagnostic tests</i>
Mixed-cell adenomas	Any combination of hormones	Varies based on dominant hormone	Symptoms from mass effect; hypopituitarism; silent (nonfunctioning)	No specific corresponding test
Nonfunctioning adenoma	None	No specific syndrome	Symptoms from mass effect; hypopituitarism; silent (nonfunctioning)	No specific corresponding test
Pituitary carcinoma	None	No specific syndrome	Symptoms from mass effect; hypopituitarism; silent (nonfunctioning)	No specific corresponding test

FSH = follicle-stimulating hormone; LH = luteinizing hormone.
Information from references 5 through 12.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Serum prolactin level should be measured in all patients with signs or symptoms of pituitary adenoma.	C	7, 9, 34
Evaluation of a suspected pituitary mass should include magnetic resonance imaging.	C	7, 21
Patients with pituitary adenomas affecting the optic chiasm on imaging should have formal visual field testing.	C	7
Symptomatic prolactinomas and macroprolactinomas should be treated medically with dopamine agonists.	B	9, 17
Cabergoline is the preferred dopamine agonist for the treatment of prolactinomas.	B	23, 24
Patients who have growth hormone- and adrenocorticotropic hormone-secreting tumors and those with symptomatic nonfunctioning macroadenomas should be referred for surgical removal.	B	7, 25, 30

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

adenomas are true neoplasms with a monoclonal cell origin.¹⁴ Hypersecretion or diminished inhibition of the hormones of the hypothalamic-pituitary axis can lead to the constellation of endocrine symptoms often seen in patients with pituitary adenomas.

Clinical Features

Pituitary adenomas present clinically in three ways: syndromes of hormone hypersecretion or deficiency; neurologic manifestations from mass effect of an expanding gland; or an incidental finding on imaging done for an unrelated issue.

HORMONAL

A pituitary adenoma may present as a distinct syndrome of hormone hypersecretion, the most common of which are hyperprolactinemia, acromegaly, and Cushing disease (Table 1⁵⁻¹²). Another hormonal manifestation of

a pituitary adenoma is either partial or complete hypopituitarism, most often hypogonadism. This is a result of interference with normal hormone secretion, either from direct compression of the pituitary gland or (in the case of hyperprolactinemia) inhibition of the pulsatile secretion of LH, leading to inadequate gonadal stimulation.⁶ The clinical presentation depends on the patient's sex. In women, the clinical presentation also depends on whether the patient is premenopausal or postmenopausal. Fatigue and loss of libido are common in men and women. Men may have erectile dysfunction, whereas premenopausal women often experience oligomenorrhea or amenorrhea^{6,11} (Table 1⁵⁻¹²).

NEUROLOGIC

The most common neurologic symptoms in patients with pituitary adenomas are headaches and visual changes. Neurologic symptoms are more common in nonfunctioning adenomas or gonadotroph adenomas because these tumors do not secrete sufficient hormones to cause endocrine-type symptoms, and their diagnosis often is delayed until patients present with symptoms of mass effect.¹¹ Headaches, which are believed to result from stretching of the dural sheath, are nonspecific and do not necessarily correlate with tumor size.⁵

When the tumor enlarges, it compresses the optic chiasm superiorly, primarily causing visual field deficits, most often bitemporal hemianopia.⁶ If the adenoma expands laterally into the cavernous sinus, it has the potential to affect the cranial nerves housed there, including cranial nerves III (oculomotor), IV (trochlear), and VI (abducens). With more severe compression or direct invasion of the optic nerve, decreased visual acuity may occur. In contrast with headaches, visual disturbances tend to correlate with tumor size. They also tend to occur insidiously,

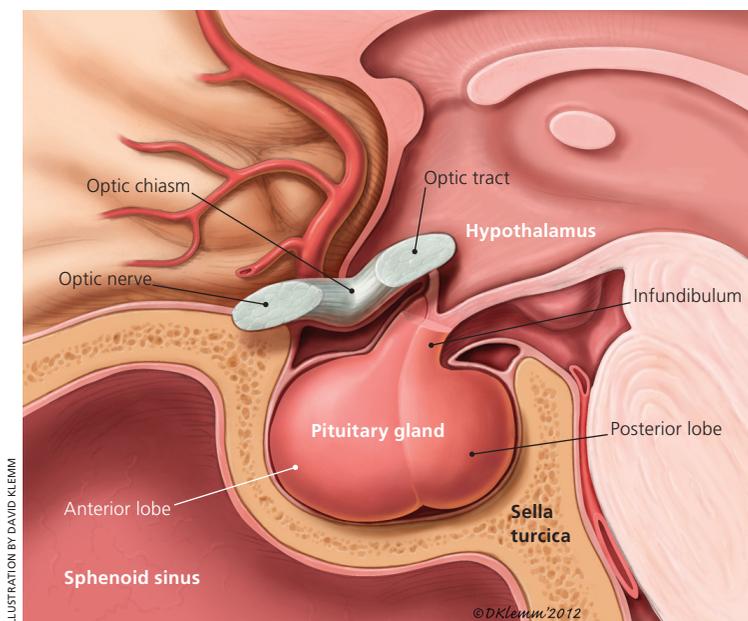


Figure 1. Anatomy of the pituitary gland.

Table 2. Diagnostic Tests Useful in the Evaluation of a Suspected Adenoma

Test	Indication	Abnormal (reference range)*	Clinical notes
24-hour urine free cortisol	Cortisol excess	Elevated (10 to 84 mcg total per 24-hour period)	Urine collection must be accurate and total High false-positive rate in women taking estrogen Diagnostic if four times greater than normal
Adrenocorticotrophic hormone	Determine source of excess cortisol	Elevated (6 to 48 pg per mL [1 to 11 pmol per L])	Levels will be elevated with pituitary or ectopic source of excess cortisol
Estradiol	Hormone deficiency in females	Low (1.5 to 3 pg per mL [6 to 11 pmol per L])†	Not accurate in women taking oral contraceptives or hormone therapy Values vary based on phase of menstrual cycle
Free T ₄	Thyroid deficiency	Low (4.2 to 13 ng per dL [54 to 167 pmol per L])	Low T ₄ with normal or low TSH indicates secondary hypothyroidism (possibly from pituitary dysfunction)
Late night salivary cortisol	Cortisol excess	Elevated (< 0.01 to 0.09 mcg per dL)	Midnight sample
Low-dose dexamethasone suppression	Initial test for cortisol excess	Elevated (serum cortisol ≥ 1.8 ng per dL)	1 mg of dexamethasone given at 11 p.m., cortisol test at 8 a.m. Abnormal if cortisol levels fail to decrease to < 1.8 ng per dL High false-positive rate in women taking estrogen Further testing needed to rule out the source of excess cortisol and to rule out "pseudo-Cushing syndrome"
Oral glucose suppression	Acromegaly (excess growth hormone) confirmatory test	Elevated (0 to 1 ng per mL)‡	Failure of growth hormone to decrease to < 1 ng per mL two hours after administering 75 g of oral glucose
Serum alpha-subunit	Determine if nonfunctioning or gonadotroph-secreting tumor	Elevated (0.04 to 1.23 ng per mL)‡	Test for the alpha subunit common to LH, FSH, TSH, and hCG May be overproduced in some pituitary adenomas (most commonly gonadotroph- and thyrotroph-secreting types) Useful if elevated LH/FSH levels and etiology of elevation is unknown
Serum cortisol	Cortisol deficiency	Low (8 to 19 mcg per dL [221 to 524 nmol per L])	Early morning testing If < 13 mcg per dL (359 nmol per L), patient should undergo dynamic testing

continued

FSH = follicle-stimulating hormone; hCG = human chorionic gonadotropin; LH = luteinizing hormone; T₄ = thyroxine; TSH = thyroid-stimulating hormone.

*—Reference ranges vary widely with performing laboratory. Values given for adults.

†—Varies with age, sex, and hormonal status.

‡—Varies widely with age.

so that many patients are not aware of them until they are specifically tested.¹⁵ Other neurologic presentations, such as cerebrospinal fluid rhinorrhea, seizures, and pituitary apoplexy, can occur but are uncommon.

INCIDENTAL

Increased use and sensitivity of computed tomography (CT) and magnetic resonance imaging (MRI) have identified many pituitary lesions that otherwise might not have been detected. Autopsy and radiology studies suggest that between 10% and 20% of all pituitary adenomas may be unsuspected or found incidentally.^{3,4}

Diagnostic Approach

The diagnostic approach to a suspected pituitary adenoma depends on the presenting symptoms. There is no evidence from controlled trials to guide a specific investigative approach, and recommendations are based largely on expert opinion and extrapolation from observational studies.^{6-9,16,17}

HORMONAL SYMPTOMS

A patient who presents with symptoms of hormone excess likely has a functioning adenoma. Evaluation can be geared toward the specific hypersecretory

Table 2. Diagnostic Tests Useful in the Evaluation of a Suspected Adenoma (continued)

Test	Indication	Abnormal (reference range)*	Clinical notes
Serum insulinlike growth factor 1	Excess growth hormone	Elevated (76 to 328 ng per mL [10 to 43 nmol per L])‡	High sensitivity Normally elevated during pregnancy May be low in patients with poorly controlled diabetes mellitus, liver disease, hypothyroidism, and malnutrition
Serum LH/FSH	Gonadotroph-secreting tumor	Elevated FSH (2 to 35 mIU per mL [2 to 35 IU per L])† LH (1.5 to 50 mIU per mL [1.5 to 50 IU per L])†	In postmenopausal women, elevated LH/FSH levels are normal Value for menstruating women varies based on phase of menstrual cycle
	Hypogonadism	Low FSH (2 to 35 mIU per mL)† LH (1.5 to 50 mIU per mL)†	
Serum macroprolactin	Hyperprolactinemia	Present	Biologically inactive form of prolactin, with no pathologic association Useful to check in patients with hyperprolactinemia who have moderate elevations (100 to 300 mcg per L [4,348 to 13,043 pmol per L]) of serum prolactin with unknown etiology or when radiographic findings and clinical presentation are not consistent with serum prolactin level
Serum prolactin	Hyperprolactinemia	Elevated (3 to 24 mcg per L [130 to 1,043 pmol per L])	≥ 250 mcg per L (10,870 pmol per L) highly suggestive of prolactinoma Moderate elevations (25 to 249 mcg per L [1,087 to 10,826 pmol per L]) should prompt investigation of other causes of hyperprolactinemia Serum level correlates with tumor size; when level does not correlate with size, consider serial dilutions
Serum TSH	Evaluate thyrotroph-secreting tumor	Elevated (0.5 to 4.8 mIU per L)	May be atypically normal in relation to free T ₄
	Thyroid hormone deficiency	Low (0.5 to 4.8 mIU per L)	
Testosterone (total)	Hormone deficiency in males	Low (350 to 1,030 ng per dL [12 to 36 nmol per L])‡	Total (free + protein-bound) alone is generally an accurate picture of testosterone level
Testosterone (free)		Low (52 to 280 pg per mL)‡	Measurements should be taken at 8 a.m.

FSH = follicle-stimulating hormone; hCG = human chorionic gonadotropin; LH = luteinizing hormone; T₄ = thyroxine; TSH = thyroid-stimulating hormone.

*—Reference ranges vary widely with performing laboratory. Values given for adults.

†—Varies with age, sex, and hormonal status.

‡—Varies widely with age.

Information from references 6 through 12, and 17 through 19.

syndrome (Table 1⁵⁻¹²). Hormone deficiencies should also be evaluated because hypopituitarism is present in up to 30% of adenomas,^{13,16} and because of the need to address deficiencies in future treatment regimens. Consensus guidelines recommend obtaining an endocrine panel as an initial set of laboratory tests.^{7,9} This includes serum prolactin, insulinlike growth factor 1 (IGF-1), LH/FSH, TSH, thyroxine (T₄), and an initial test for cortisol excess—a 24-hour urine free cortisol, a late night salivary cortisol, or a low-dose dexamethasone suppression test. The 24-hour urine free cortisol,

late night salivary cortisol, and overnight dexamethasone suppression tests have similar accuracy (positive likelihood ratio [LR+] = 10.6, negative likelihood ratio [LR-] = -0.16; LR+ = 8.8, LR- = 0.07; and LR+ = 16.4, LR- = 0.06, respectively).¹² Dexamethasone suppression and 24-hour urine free cortisol tests have the highest specificity (97% and 91%, respectively) and the most evidence to support their use^{8,18} (Table 2^{6-12,17-19}). When the diagnosis remains uncertain after these initial studies, dynamic endocrine function tests should be performed, usually in consultation with an endocrinologist.



Figure 2. Macroadenoma (arrow) on computed tomography.

A higher serum prolactin level (250 mcg per L [10,870 pmol per L] or more) suggests a prolactinoma over other causes of hyperprolactinemia (e.g., hypothyroidism, medications, non-prolactin-secreting pituitary adenomas, pregnancy, renal failure).^{9,17} A serum prolactin level greater than 500 mcg per L (21,739 pmol per L) is diagnostic for a macroprolactinoma (98% specificity), although only about one-third of persons with prolactinoma have levels that high (35% sensitivity).¹⁷ Non-prolactin-secreting pituitary tumors may cause moderate elevations in prolactin through compression of the pituitary stalk, resulting in loss of inhibition of prolactin release; this is termed the stalk effect.^{6,17}

NEUROLOGIC SYMPTOMS

If a pituitary mass is suspected, MRI is the best initial imaging study.⁷ MRI is 61% to 72% sensitive and 88% to 90% specific for sellar masses.^{20,21} The study should be done with and without gadolinium enhancement. CT is limited by its inability to precisely image the optic chiasm. If an MRI is contraindicated or unavailable, CT done with thin sections (1.5 mm or less) and in a coronal plane will improve imaging of the pituitary region²² (Figures 2 and 3).

If a patient presents with visual symptoms, or if imaging reveals impingement on the optic nerve, the patient should be referred for formal visual field testing and a complete ophthalmologic examination.⁷ Early referral for visual field testing should be considered even in the absence of presenting symptoms, because unrecognized deficits occur in approximately 10% of incidentally discovered pituitary adenomas.^{15,16}

INCIDENTALOMA

When a pituitary mass is discovered incidentally, diagnostic studies should be geared toward determining if the mass is functioning or nonfunctioning (Figure 4⁷).



Figure 3. Macroadenoma on magnetic resonance imaging.

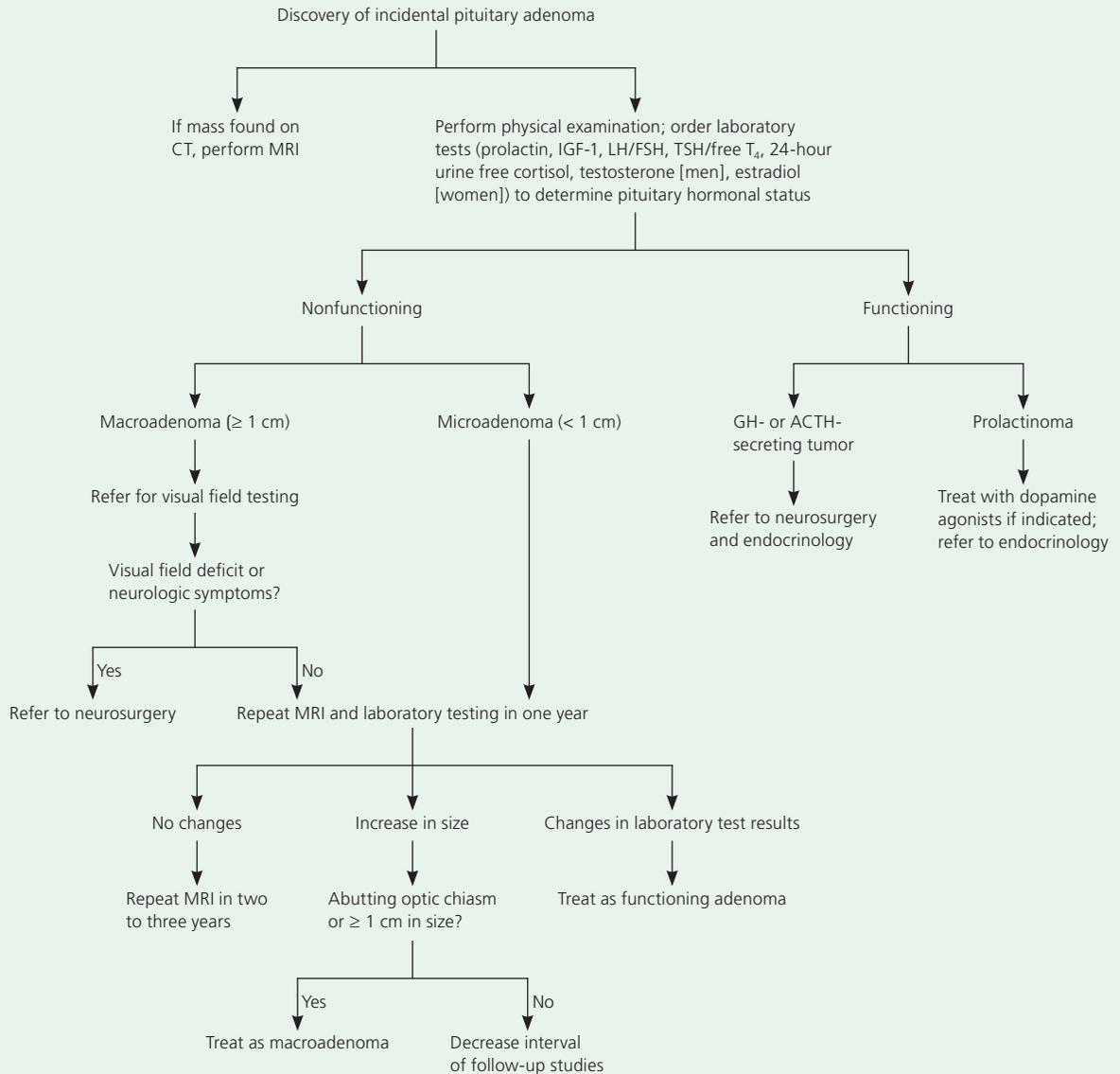
There is debate over the extent of laboratory assessment warranted in the evaluation of incidentalomas, especially microadenomas. The Endocrine Society's 2011 clinical practice guidelines for pituitary incidentalomas recommend a complete assessment of pituitary function, even if the patient is asymptomatic.⁷ The basis for this recommendation stems from the effectiveness of prolactinoma treatment and the value of identifying growth hormone- and ACTH-secreting adenomas early to avoid associated long-term morbidity. Most patients do not require surgical intervention, although prospective biochemical monitoring and repeated imaging are recommended by expert panel guidelines.⁷ Clinical trials of the best approach to monitoring these patients have not been done.

Therapy

There are three primary treatment goals for pituitary adenomas: reducing hormone hypersecretion and its clinical manifestations; decreasing tumor size to improve symptoms of mass effect; and correcting hormone deficiencies (Table 3^{9,10,23-27}).

The majority of prolactinomas can be managed medically with dopamine agonists. Dopamine agonists approved for use in the United States are bromocriptine (Parlodel) and cabergoline. By inhibiting the release of prolactin from the anterior pituitary, these medications resolve hyperprolactinemia symptoms, reduce tumor size, and often restore reproductive function.^{9,17,28} Several controlled trials have shown improved effectiveness and better patient tolerance of cabergoline over bromocriptine. Patient-oriented outcomes such as quicker restoration of normal vision, faster return of regular menses, and fewer gastrointestinal adverse effects were noted in those using cabergoline.^{23,24}

Approach to the Evaluation and Management of a Pituitary Incidentaloma



ACTH = adrenocorticotropic hormone; CT = computed tomography; FSH = follicle-stimulating hormone; GH = growth hormone; IGF-1 = insulinlike growth factor 1; LH = luteinizing hormone; MRI = magnetic resonance imaging; T₄ = thyroxine; TSH = thyroid-stimulating hormone.

Figure 4. Approach to the evaluation and management of a pituitary incidentaloma.

Adapted with permission from Freda PU, Beckers AM, Katznelson L, et al.; *Endocrine Society. Pituitary incidentaloma: an Endocrine Society clinical practice guideline.* *J Clin Endocrinol Metab.* 2011;96(4):899.

The most common adverse effects of dopamine agonists are nausea, vomiting, and fatigue. Long-term use of high-dose ergoline-derived dopamine agonists for Parkinson disease increases the risk of cardiac valvular regurgitation. However, this same association has not been found with use of short-term, lower-dose agents in the treatment of prolactinomas.²⁹

Although dopamine agonists are not approved for use during pregnancy, both bromocriptine and cabergoline are thought to be safe.²⁸ Because of the greater body of

published evidence on bromocriptine, it is the recommended dopamine agonist for initiation during pregnancy.^{9,28} Expert consultation is advised for all women with a prolactinoma who intend to become pregnant.

Medical management of growth hormone- and ACTH-secreting tumors is less effective than for prolactinomas, and surgery via transsphenoidal resection is the preferred treatment.^{7,25,30} Somatostatin analogues such as octreotide (Sandostatin) and lanreotide (Somatuline) inhibit growth hormone secretion and somatotroph proliferation. They

Table 3. Treatment Recommendations for the Most Common Pituitary Adenomas

<i>Tumor type</i>	<i>Treatment</i>	<i>Therapeutic goal</i>
Adrenocorticotrophic hormone–secreting adenoma	Surgical resection	Remove tumor or decrease in size
	Adrenostatic medication	Restore pituitary function
	Ketoconazole: 200 mg twice a day (maximum daily dosage: 1,200 mg)	Suppress excess cortisol
	Metyrapone (Metopirone): 250 mg four times a day (maximum daily dosage: 6,000 mg)	
	Mifepristone (Mifeprex): 300 mg once a day (maximum daily dosage: 1,200 mg)	
	Mitotane (Lysodren): 500 mg three times a day (maximum daily dosage: 9,000 mg)	
	Radiation therapy	
	Bilateral adrenalectomy	
Growth hormone–secreting adenoma	Surgical resection	Remove tumor or decrease in size
	Somatostatin analogues*	Restore pituitary function
	Octreotide (Sandostatin): 50 mcg subcutaneously three times a day or depot preparation, 20 mg every four weeks	Suppress growth hormone secretion
	Lanreotide (Somatuline): 90 mg subcutaneously every four weeks	Lower insulinlike growth factor 1 level
	Titration based on growth hormone and insulinlike growth factor 1 levels	
	Growth hormone antagonists*	
Pegvisomant (Somavert): 15 to 20 mg daily		
	Radiation therapy	
Nonfunctioning adenomas	No immediate therapy necessary unless macroadenoma or symptomatic Monitor with laboratory tests and imaging	Early intervention for increasing tumor size or hormone hyposecretion/hypersecretion
Prolactinoma	Dopamine agonists*	Decrease tumor size
	Cabergoline: 0.25 to 1 mg orally two times per week; increase by 0.25 mg to reach therapeutic goal	Lower prolactin level
	Bromocriptine (Parlodel): start with 1.5 to 2.5 mg orally daily; increase by 2.5 mg every two to seven days to reach therapeutic goal	Restore gonadal function

*—Dosage ranges are those given for adults.

Information from references 9, 10, and 23 through 27.

decrease the size of growth hormone–secreting tumors and the symptoms of growth hormone excess. The growth hormone receptor antagonist pegvisomant (Somavert) reduces the production of IGF-1, which is primarily responsible for the symptoms of acromegaly.²⁶ Medications that decrease or halt steroidogenesis at the adrenal gland (ketoconazole, metyrapone [Metopirone], mitotane [Lysodren], and mifepristone [Mifeprex]) are used to decrease symptoms in patients with ACTH-secreting tumors, and for palliation in persons unable to tolerate surgery (Table 3^{9,10,23–27}), but they have no effect on the tumor itself or in restoration of normal pituitary function.²⁷ Radiation and radiosurgery can decrease tumor size and enhance endocrine functioning, especially when used to treat post-resection residual adenoma.^{27,31,32}

Nonfunctioning microadenomas and microprolactinomas in asymptomatic patients do not require immediate treatment. However, a small percentage of these tumors will increase in size or cause new pituitary dysfunction, and therefore warrant monitoring.^{16,33} No clinical trials

have been done to compare a conservative approach with early therapy, so management and monitoring intervals are based on expert opinion. An expert guideline recommends a repeat MRI in 12 months and, if there is no increase in size, lengthening the imaging interval to two to three years.⁷ Biochemical testing via an endocrine panel is not recommended unless the tumor enlarges or the patient develops symptoms (Figure 4⁷). Measurement of prolactin alone may also be an effective strategy to monitor microadenomas; a cost analysis found this test to have the lowest cost per quality-adjusted life-year.³⁴

Data Sources: A PubMed search was completed in Clinical Queries using the key terms pituitary adenoma, prolactinoma, pituitary incidentaloma, Cushing's disease, and acromegaly in both diagnosis and treatment. The search included systematic reviews, meta-analyses, clinical practice guidelines, and clinical studies. We also used the National Guideline Clearinghouse, Essential Evidence Plus, the Cochrane database, UpToDate, and Google Scholar. Search dates: June 2011 and January 2012.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Navy Medical Department or the U.S. Navy at large.

The Authors

MARCY G. LAKE, DO, is a family physician at the U.S. Naval Hospital, Sigonella, Italy.

LINDA S. KROOK, MD, FACP, FACE, is an endocrinologist at the Naval Hospital, Bremerton, Wash.

SAMYA V. CRUZ, MD, is a family physician at the U.S. Naval Hospital, Rota, Spain. At the time this article was written, she was a family physician at the U.S. Naval Hospital, Guantanamo Bay, Cuba.

Address correspondence to Marcy G. Lake, DO, U.S. Naval Hospital, Sigonella, Italy, USNH Box 64, FPO, AE 09589-1000 (e-mail: marcy.lake22@gmail.com). Reprints are not available from the authors.

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