Disorders of the Pituitary Gland

Raven Raye, R.T.(R)(T)
Natasha Hadrych-Rosier, MHA, MBA, R.T.(R)(T)

After completing this article, the reader should be able to:
- Explain the role of the pituitary gland in maintaining homeostasis.
- Identify anatomy of the pituitary gland and nearby structures.
- Describe treatment options available for pituitary adenomas and disorders.
- Discuss various disorders of the pituitary gland.

The pituitary gland is often called the “master gland” of the body; it produces hormones, which are then delivered through the bloodstream to different receptors in an effort to maintain homeostasis, or a balanced biological system. The pituitary gland is a small endocrine gland found at the base of the brain and situated within the sella turcica, a saddle-like compartment in the skull posterior to the nasal passages. This 2-lobed gland, which is roughly the size of a kidney bean, lies inferior to the hypothalamus and is connected to both the brain and the hypothalamus. The hypothalamus signals the pituitary gland to increase or decrease hormone production (see Figure 1).

Although commonly referred to as a single gland, because of its 2 lobes, the pituitary gland is sometimes referred to as 2 separate glands. The anterior lobe, called the adenohypophysis, produces hormones that mainly cause additional hormone production in the adrenal glands, the thyroid gland, and the reproductive organs. Although the adenohypophysis mostly has indirect influence, it also synthesizes and stores somatotropin (growth hormone, GH) and prolactin, which regulates the growth and development of the breasts and the production of milk. The posterior lobe of the pituitary gland, also referred to as the neurohypophysis, more directly influences the body systems’ hormones. Through either direct or indirect hormone production, the pituitary gland

Figure 1. The pituitary gland in relation to facial features and anterior cranial anatomy.
### Disorders of the Pituitary Gland

#### Figure 2. Illustration of the 2 lobes of the pituitary gland posterior (A) and anterior (B) and the hormones they release in response to the hormones produced by the hypothalamus. The hormone targets and their effects also are listed. Used under the Creative Commons Attribution 3.0 Unported license. OpenStax College via Wikimedia Commons.

Abbreviations: ACTH, adrenocorticotropin hormone; ADH, antidiuretic hormone; CRH, corticotropin-releasing hormone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone-releasing hormone; GHIH, growth hormone-inhibiting hormone; GnRH, gonadotropin releasing hormone; LH, luteinizing hormone; OT, oxytocin; PIH, prolactin inhibiting hormone; PRH, prolactin releasing hormone; PRL, prolactin; TRH, thyrotropin releasing hormone; TSH, thyroid-stimulating hormone.

<table>
<thead>
<tr>
<th>Posterior Pituitary Hormones</th>
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<tr>
<td>Releasing hormone (hypothalamus)</td>
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<tr>
<td>ADH</td>
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<td>OT</td>
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<th>Anterior Pituitary Hormones</th>
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<tr>
<td>Releasing hormone (hypothalamus)</td>
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<tr>
<td>GnRH</td>
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<tr>
<td>GnRH</td>
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<td>TRH</td>
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<td>PRH (inhibited by PIH)</td>
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<tr>
<td>GHRH (inhibited by GHIH)</td>
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<td>CRH</td>
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Contributes to controlling metabolism, physical growth, sexual development, blood pressure, urination, and many other key functions to maintain the body's homeostasis.  

**Figure 2** and the **Table** provide a list of hormones the pituitary gland produces and the effect each hormone has on the body.

The pituitary gland comprises several types of cells, each responsible for producing specific hormones. Pituitary lesions develop from one of these cell types. Two-thirds of pituitary tumors occur in the adenohypophysis. Although pituitary gland tumors can cause damage to the nerves, brain, or bony structures, more than 90% are slow-growing, benign, and treatable. Discovering a pituitary adenoma is fairly common, and as many as 1 in 5 adults might have a pituitary tumor. For example, if a patient is being assessed for headaches, inner ear problems, or trauma, a magnetic resonance (MR) scan of the brain might be performed, and sometimes pituitary adenomas are incidental findings on these examinations.

Individuals can easily overlook some symptoms of pituitary lesions; however, large lesions often are accompanied by vision loss, specifically peripheral vision, from the pressure of the lesion on the optic chiasm. The types of headache vary in each person and depend upon the size of the lesion. The lesion generally interferes with normal function of the pituitary gland, causing hypothyroidism, hyperthyroidism, or hypogonadism. Diabetes insipidus also can occur with some pituitary lesions, causing a feeling of dehydration and frequent urination. Unlike hyperglycemic diabetes, diabetes insipidus has no effect on glucose levels. Instead, diabetes insipidus affects renal function, and the kidney does not retain fluid because of inadequate levels of the hormone vasopressin.

**Epidemiology**

Nonfunctioning pituitary adenomas account for about 30% of adenomas diagnosed in adults but only 3% to 6% of pituitary adenomas in children. Most adenomas are functional lesions, which means they secrete a hormone that expresses clinical features. For example, hypersecretion of a hormone or compression of local structures by a lesion can disrupt physical and sexual development in children. Fewer than 0.1 per million

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Abbreviation</th>
<th>Function</th>
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<tbody>
<tr>
<td>Prolactin</td>
<td>PRL</td>
<td>Stimulates milk production, affects sex hormones from the ovaries in women and the testes in men.</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>GH</td>
<td>Stimulates growth during childhood, maintains muscle and bone mass in adults, and affects fat distribution throughout the body.</td>
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<tr>
<td>Adrenocorticotropic hormone</td>
<td>ACTH</td>
<td>Stimulates the production of cortisol, or stress hormone, by the adrenal glands and helps maintain blood pressure and glucose levels.</td>
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<tr>
<td>Thyroid-stimulating hormone</td>
<td>TSH</td>
<td>Stimulates the thyroid gland, which regulates metabolism, energy, growth and development, and the activity of the nervous system.</td>
</tr>
<tr>
<td>Antidiuretic hormone, also called vasopressin</td>
<td>ADH</td>
<td>Regulates water balance in the body.</td>
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<tr>
<td>Oxytocin</td>
<td>OT or OXT</td>
<td>Stimulates contraction of the uterus and milk delivery in preparation for childbirth in women and semen production in men.</td>
</tr>
<tr>
<td>Luteinizing hormone</td>
<td>LH</td>
<td>Regulates testosterone in men and estrogen in women.</td>
</tr>
<tr>
<td>Follicle-stimulating hormone</td>
<td>FSH</td>
<td>Stimulates sperm production in men and ovulation in women. LH and FSH work in harmony for the normal function of the ovaries and testes.</td>
</tr>
<tr>
<td>Melanocyte-stimulating hormone</td>
<td>MSH</td>
<td>Secreted during fetal development, early childhood, and pregnancy, and as a result of some diseases. MSH regulates the pigment in cells and skin. This hormone is released by the intermediate lobe of the pituitary gland.</td>
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individuals younger than 20 years of age are estimated to receive a pituitary adenoma diagnosis.  

Pituitary adenomas account for only 2.7% of all supratentorial tumors (ie, those that occur in the upper part of the brain) in children and are far more common in adults. However, research involving individuals with hypopituitarism has not demonstrated any correlation with gender, ethnicity, geographic location, or age that suggests a pattern. 

Pituitary Adenoma Pathophysiology  

Although there is no definitive cause of pituitary lesions, the hypothalamus might overstimulate the pituitary gland to produce hormones, which is a possible cause of tumors. Pituitary adenomas might result from or have their growth influenced by factors such as hypothalamic dysfunction. Hypothalamic dysfunction can result from genetic disorders, eating disorders, head trauma, surgery, radiation, tumors, or any physical damage to the hypothalamus that alters the pituitary gland’s ability to maintain homeostasis. In addition, significant data indicate that pituitary tumor genesis is a result of intrinsic pituicyte genetic disruption. Pituicytes are fusiform cells of the gland’s stalk and posterior lobe. X-inactivation studies, which analyze conditions linked to the X chromosome, suggest that most pituitary adenomas arise from a single cell undergoing a clonal event.

Most of these lesions develop spontaneously, but evidence suggests that some pituitary disorders or diseases can be passed from parent to child or carried to future generations if a gene change occurs in a reproductive cell. Although rare, an individual with certain family traits or history is more likely than others to develop a pituitary adenoma. However uncommon hereditary cases may be, several conditions, such as gigantism and acromegaly, are linked to heredity.

The familial syndrome multiple endocrine neoplasia type 1 (MEN 1) results in the simultaneous development of lesions in the endocrine glands, such as the pituitary, pancreas, and parathyroid. Individuals who have MEN 1 develop pituitary adenomas approximately 25% to 50% of the time. It has been suggested that 1% to 5% of pituitary lesions present within the same family. Individuals with a family member who has MEN 1 or Carney complex are at greater risk than others for developing pituitary lesions.

Carney complex is rare; only 750 people have been identified with this disorder, which is characterized by several types of tumors. People with Carney complex can develop benign tumors in the heart called cardiac myxomas, which can block blood flow in the heart, or they can develop myxomas on other internal organs or the skin. Carney complex also might cause adrenal disease leading to Cushing syndrome; tumors in the thyroid, testes, and ovaries; or pituitary adenomas that usually result in excess GH leading to acromegaly.

Pituitary adenomas are primarily caused by the oversecretion of a hormone. Clinicians initially use 3 characteristics to differentiate and classify a pituitary adenoma: size, growth rate (aggressiveness), and the effect on hormone production. Adenomas less than 1 cm in diameter are called microadenomas, and those larger than 1 cm in diameter are classified as macroadenomas. Nearly all adenomas of the pituitary gland are benign and have a slow growth rate. However, more aggressive lesions can occur. These aggressive pituitary adenomas have a higher growth rate and an increased chance of recurrence.

Pituitary adenomas can be classified according to their cellular makeup, size, type of hormone production, and other characteristics. If a lesion affects the amount of hormone secreted by the pituitary gland, it is classified as a functional or hormone-active lesion. Functional lesions are attributed to acromegaly, Cushing syndrome, gigantism, and prolactinoma. These lesions can secrete excessive amounts of hormones, which means they are secretory functional lesions. Lesions that cause a deficiency in the release of hormones are nonsecretory functional lesions. Some secretory tumors, such as somatotrophic adenomas and corticotropic adenomas, secrete too much of a hormone. Depending on the type of tumor, the excess hormones can affect growth or the function of the adrenal or thyroid glands. Lesions that secrete too much luteinizing hormone or follicle-stimulating hormone are less common. If a tumor does not influence the amount of hormone being released, it is classified as clinically nonfunctional. Pituitary adenomas are further classified as hyposecretory, hypersecretory, or having tumor mass effect.

Hypossecratory Tumors  

Hypossecratory tumors release too little hormone causing insufficient levels. A nonsecretory tumor can
interfere with the pituitary gland’s ability to manufacture certain hormones, and if large secretory tumors compress the pituitary gland, they can cause decreased secretion of certain other hormones. In addition, treatment of a tumor with surgical resection or radiation therapy can cause a decrease in secretion. Even though an adenoma is nonfunctional, it can be problematic when the size or location of the lesion leads to hormonal hyposecretion. Symptoms that can indicate a nonfunctional pituitary lesion include:

- Loss of appetite.
- Weight fluctuation.
- Fatigue or general lethargy.
- Hypoglycemia.
- Joint pain.
- Frequent nocturia.
- Sexual dysfunction – impotence, infertility, or decreased libido.

**Hypersecretory Tumors**

When a pituitary lesion releases too much of a hormone, it is hypersecretory. This interference with normal hormone levels can result in a state of target organ hormone deficiencies, including hypogonadism and hypothyroidism. Prolactin is often affected by hypersecretory lesions, and some medications used to treat psychiatric conditions also can induce an increase of prolactin levels in patients. In some instances, hyperplasia of the pituitary, resulting in enlargement of the sella turcica, occurs with long-term hypersecretion. In rare cases, ectopic tumors (outside of the pituitary gland) can secrete pituitary hormones.

Hypersecretory pituitary lesions that occur in children include prolactinoma, corticotropinoma (Cushing syndrome), and somatotropinoma (gigantism). Hyperpituitarism, or the primary hypersecretion of pituitary hormones resulting from a pituitary microadenoma, is found more often in adults than children. Another less common disorder in children is thyrotropinoma, a lesion that secretes thyroid-stimulating hormone. Typically, these disorders have been found in children aged older than 11 years. To date, there has been no report of a child developing gonadotropinoma, a pituitary adenoma that secretes gonadotropin and causes visual field loss, headache, hypogonadism, and hormonal hypersecretion syndromes.

**Prolactinoma**

The most common secretory pituitary adenoma is prolactinoma. Prolactinomas cause the overproduction of the prolactin hormone and account for 40% of all pituitary tumors. The risk of developing a prolactinoma increases with age; 93% of occurrences are in individuals over the age of 12 years, with girls being 4 to 5 times more likely to develop a prolactinoma than boys. In pediatric cases, age and sex have an effect on the development of a prolactinoma. Prolactinomas originate from the same daughter cells as do somatotropes (growth cells) and thyrotropes (thyroid cells). This shared foundation means that tests might show results for somatotropins and thyrotropins when testing for prolactinoma. Iglesias and Diez demonstrated that this condition occurs more often in women than men between the ages of 20 and 50 at a rate of almost 10:1.

In adults, symptoms of prolactinoma can include headaches, visual disturbances, mood changes, and osteoporosis. Prolactinomas also can cause changes in menstruation, amenorrhea, infertility, milk discharge unrelated to childbirth, as well as vaginal dryness, painful intercourse, and reduced libido in women, and reduced libido and impotence in men.

Children with a prolactinoma usually have one or a combination of the following symptoms: headache, vision problems, and a slow growth rate. Boys usually develop larger lesions than do girls, and the boys’ lesions are accompanied by higher levels of prolactin. Boys with a prolactinoma might have low levels of testosterone (hypogonadism) that result in increased breast tissue (gynecomastia). Girls might show slowed development of breasts or low levels of estrogen.

The preferred treatment approach for a prolactinoma is medication. Dopamine agonist tablets are successful in reducing tumor size and reducing or eliminating symptoms in 80% to 90% of prolactinoma patients. Adverse effects of dopamine agonists include nausea and dizziness. If medical therapy is not effective, surgical intervention might be necessary. However, the patient still will need medical therapy to control pituitary failure or hypopituitarism before surgery. If cortisol and thyroid hormone levels are too low, a life-threatening situation is likely. Low levels of cortisol can affect blood pressure, glucose levels, and
the body’s response to stress. Low thyroid hormone levels can slow body functions and metabolism and lead to coma. Radiation is rarely used to treat large prolactinomas; however, if surgery and medication fail to treat macroprolactinomas successfully, irradiation is the preferred treatment. If the tumor is small and stable, it may be monitored closely without any treatment.\textsuperscript{7,24,35}

**Tumor Mass Effect**

Tumors that grow large enough to press against a disease-free pituitary gland or other areas of the brain might cause tumor mass effect. When a tumor’s size causes displacement of other brain tissue or blocks cerebrospinal fluid, intracranial pressure increases, creating a mass effect that causes several symptoms.\textsuperscript{34} Symptons of tumor mass effect include visual field disturbances, headaches, and abnormal control of eye movements.\textsuperscript{4} Pituitary lesions that produce tumor mass effect are usually 10 mm in diameter or greater and can be secretory or nonsecretory.

**Pituitary Apoplexy**

A sudden increase in a pituitary tumor’s size causes several acute symptoms; the condition is called pituitary apoplexy. An apoplectic event occurs when a lesion has hemorrhaged or has outgrown its blood supply, causing the necrotic tissue to swell. The result is an acute headache; sudden vision loss in connection with the headache can indicate the need for emergency surgical intervention. In addition, insufficiency of the pituitary gland can be caused by an apoplectic event, with symptoms not presenting until days or weeks after the event.\textsuperscript{15,35}

**Pituitary Adenoma Detection and Diagnosis**

Often, pituitary lesions are found incidentally when imaging examinations, usually computed tomography (CT) or MR scans, are performed that include the pituitary gland. Radiologists must evaluate and report everything they see on each scan. If a lesion is present and the radiologist does not note it and communicate the findings to the ordering physician, the radiologist and the ordering physician can be financially liable.\textsuperscript{38} Including incidental findings in the final imaging report is not necessarily sufficient for the radiologist to avoid liability. According to the American College of Radiology, the physician also must directly communicate any additional findings, especially if they conflict with preliminary findings, to the ordering physician and other support staff to ensure appropriate follow-up with the patient.\textsuperscript{36}

As a result of this practice, the number of incidental findings is on the rise. In 2010, Lumbreras et al performed a systematic review on the frequency of incidental findings from diagnostic imaging examinations.\textsuperscript{37} After reviewing a combination of nearly 300 abstracts and articles, they determined that incidental pituitary findings accounted for approximately 24% of findings in all types of imaging except CT. CT examinations alone showed a higher rate of incidental pituitary-related findings of just over 31% of all findings reported.\textsuperscript{37}

The term *pituitary incidentalomas* has been coined to represent the incidental findings of pituitary lesions on CT and MR imaging examinations.\textsuperscript{38} Some evidence supports the incidental findings of lesions using positron emission tomography-CT when there is increased uptake of fluorodeoxyglucose in nonfunctional pituitary adenomas.\textsuperscript{38} Some maintain that pituitary microadenomas presenting as incidental findings from diagnostic imaging examinations is rare because of the need for pituitary focused imaging. Although this might be true for definitive diagnoses, evidence suggests that abnormalities evident on imaging scans that include the pituitary gland might lead to a definitive diagnosis.\textsuperscript{39} The occurrence of pituitary incidentalomas of smaller than 10 mm ranges from 4% to 20% for CT and 10% to 38% for MR examinations.\textsuperscript{40}

The methods used to detect a pituitary lesion, whether malignant or benign, include laboratory analyses and diagnostic imaging. Laboratory analysis of blood and urine can identify abnormalities in hormone levels. A neuro-ophthalmological evaluation to assess the patient’s visual field might be performed. Routine analysis of hormone levels can be conducted for all hormones produced by the pituitary gland if a lesion is suspected. Elevated or deficient levels of any hormone can indicate the histology of a lesion. A pituitary adenoma diagnosis also can be made if pituitary function tests are performed. An endocrinologist who specializes in pituitary gland function and disease can perform these tests to analyze blood hormone levels.\textsuperscript{15,41,42}
In addition, MR and CT scans of the brain are used to evaluate abnormalities in pituitary gland tissue. MR scans are preferred for evaluating the pituitary gland and detecting pituitary lesions. With specific protocols developed for the detection of pituitary lesions, doctors can use MR scans to reliably detect lesions as small as 4 mm (see Figure 3). Use of images from 3T MR scanners can lead to detection of even smaller lesions. When a pituitary lesion is suspected and the hormone levels support that suspicion, further examination using MR imaging generally is used. However, an occult pituitary microadenoma or an ectopic tumor might be missed on diagnostic imaging. The use of abdominal or chest scanning often can reveal ectopic lesions such as carcinoid tumors, pancreatic islet-cell tumors, or bronchial neoplasms. Although CT is suitable for detecting larger adenomas, it is insufficient when smaller lesions are a possibility. It is important to know whether the abnormality is malignant or benign, but this is sometimes difficult to determine even when a biopsy and histology are performed. In fact, unless there is definitive spread to distant organs, a malignant lesion could be mistaken for a benign one.

**Pituitary Disorder Treatment Options**

The purpose of treatment is to control the lesion’s growth and correct hormone imbalances. Most lesions can be treated with available therapy options specific to the disorder or hormone affected. In general, treatments can include surgery, radiation therapy, medical regimens, or a combination of the 3 options.

**Surgery**

Surgical resection occurs in 3.6% to 6% of all pituitary adenomas. Two types of surgery are typically performed for pituitary adenomas: endoscopic transnasal transphenoidal surgery and transcranial surgery. Endoscopic transnasal transphenoidal surgery is accomplished by approaching the pituitary gland through an incision inside the patient’s nose (transnasal) to access the sphenoid sinus (transsphenoidal) (see Figure 4). The anterior wall of the sphenoid sinus is then opened to reach the sella turcica, where the pituitary gland typically lies. The endoscope provides a panoramic view on a high-definition television screen so the surgeon can see the tumor, cut open the...
covering surrounding it, and remove pieces of the lesion with a curette.46

A cerebral spinal fluid leak can occur if the tumor or the surgery compromises the dura mater above the pituitary gland. In these cases, a small piece of fat can be used as a graft to stop the leakage.47 Following surgery, the patient’s bed is elevated 30° to decrease the cerebral spinal fluid pressure in the head, and the nostrils are packed to stop bleeding.48 This minimally invasive technique minimizes the discomfort and complications associated with major surgery and the amount of time the patient spends in the hospital.15

If the patient has a large tumor invading the brain, a transcranial approach might be necessary to access the tumor. Surgeons either remove the tumor through a small incision in the upper side of the skull or through a minimally invasive technique called a keyhole microcraniotomy in which a small incision is made in an eyebrow.49

With an experienced surgeon, there is an 80% success rate for those undergoing this surgical procedure. If the initial surgery is unsuccessful, or results in only a temporary cure, the procedure can be repeated and often has better results.50,51 A temporary reduction in hormone levels usually accompanies a successful surgery. Patients are typically placed on hormone replacement therapy to normalize hormone levels for some time after surgery.45

However, if the adrenal gland is responsible for the overproduction of cortisol, as in Cushing syndrome, and the lesion has malignant attributes on diagnostic radiographic examinations, surgical intervention is appropriate. The removal of a single adrenal gland is performed if the lesion is small and well defined, and can be accomplished with laproscopic techniques (laparoscopic adrenalectomy).52,53

### Radiation Therapy

If surgery is inappropriate for the patient, unsuccessful, or only partial resection of the tumor is accomplished, radiation therapy is an option.44 Radiation therapy can be administered using either photon or proton therapy. Because there are a limited number of proton therapy centers, proton therapy is not widely available.45 Most often, conventional radiation therapy with photons is used in one of the following ways: external beam radiation therapy, including 3-D conformal radiation therapy and intensity-modulated radiation therapy (IMRT); and stereotactic radiosurgery (SRS).

#### Three-dimensional Conformal Therapy

Three-dimensional conformal radiation therapy uses MR imaging or CT for treatment planning.33 The use of CT makes it possible to outline the tumor and surrounding structures in 3-D renderings. The treatment team adjusts the beams to deliver radiation to the entire tumor while sparing normal tissue.49 This treatment usually is delivered in 1.8 Gy to 2 Gy in several fractions to achieve a total dose of between 45 Gy and 50.4 Gy.33 Following external radiation for pituitary lesions, patients could require several months to years before they feel better.45,56 Although 3-D treatment is not used as often in current protocols, it is still a viable treatment approach for some patients or cases. The technique is generally effective in preventing tumor growth.11

#### Intensity-Modulated Radiation Therapy

IMRT delivers radiation treatments by using computer and mechanically driven beam shaping devices called multileaf collimators, which can provide exceptional beam shaping and customizable radiation doses that cannot be achieved with 3-D conformal radiation therapy. After the radiation oncologist determines the treatment parameters, the medical dosimetrist develops an inverse plan using the end criteria as guidance. The computer system develops an appropriate treatment plan for IMRT that limits dose to normal surrounding tissues and structures while ensuring the maximum radiation dose to the area of interest.57 Because IMRT can provide more coverage and conformal treatment, normal brain tissue is not unnecessarily irradiated.57

#### Stereotactic Radiosurgery

SRS for pituitary adenomas is most often delivered by a linear accelerator with external photons using dedicated SRS systems.58 However, the use of protons also is possible.45 A cyclotron is a particle accelerator that energizes protons for proton therapy.59 Proton beams are easier to shape than photon beams. Protons irradiate
normal tissue as they pass through it to reach a tumor but then deposit most of the radiation in the target so less radiation is delivered to surrounding tissues compared to when photon beams are used. This means that larger amounts of radiation can be delivered in a single dose with less damage to normal tissue. Proton therapy is particularly helpful when treating children with pituitary disorders because more healthy tissue is spared, and the long-term risks associated with treatment are less severe.

Whether photon or proton beams are used, delivering high doses of radiation means that the utmost precision is required. SRS uses micro-multileaf collimators to deliver extremely precise dose distribution to a specific target while sparing surrounding structures. Candidates for SRS treatments are patients whose lesions are no larger than 2.5 cm to 3 cm and that are at least 0.2 cm to 0.3 cm from the optic chiasm. A 2009 study of 26 patients being treated with CyberKnife reported that total radiation doses ranged from 14 Gy to 24 Gy; the treatment was delivered in a single fraction to 5 patients, and 21 patients received the total dose in 3 fractions. Another study published in 2010 involving 100 patients reported treating patients using CyberKnife with 17 Gy to 21 Gy in 3 fractions, or 22 Gy to 25 Gy in 5 fractions.

The precise targeting used in SRS treatments can offer more rapid results for patients, but SRS is accompanied by an increased risk of adverse effects, including nerve injury resulting in impaired vision. The severity of the injury depends on the nature of the tumor. Still, the risk of serious injury from SRS is low.

Adverse Effects
Risks are associated with any type of radiation treatment to the brain, but the benefits usually outweigh the risks. For conventional SRS treatment, single doses should remain equal to or less than 2 Gy, and total doses must not exceed 50 Gy to minimize risks. Some patients experience fatigue, patchy hair loss, and skin erythema and dryness. Risk of hair loss and erythema might be greater with proton therapy. Headache and nausea are less common adverse effects. The most common adverse effect from radiation therapy for pituitary adenomas is hypopituitarism, with an incidence rate of 13% to 56%. Optic neuropathy, vascular changes, neuropsychological disorders, and secondary malignancies are rare, and brain necrosis is an extremely rare but possible long-term adverse effect.

Radiation therapy usually results in lower hormone production. Therefore, even if a pituitary adenoma does not affect the patient’s hormone production, treatment with conventional radiation therapy can cause abnormally low hormone levels. Hormone deficiencies usually do not occur immediately. Some patients’ hormone levels decrease within 1 to 2 years following completion of radiation therapy, but it can take 10 to 20 years following radiation treatments for a patient to develop a deficiency. An endocrinologist can prescribe replacement hormones to treat deficiencies.

Radiation therapy can control tumor growth in 80% to 98% of patients who have nonsecreting pituitary lesions. For functional lesions, growth is controlled in 67% to 89% of patients.

Medical Management
Medical management is specific to the cause or origin of the lesion or disorder and how it affects each individual. The main objective of medical therapy is to remove, shrink, or compensate for pituitary lesions and their effects on an individual. For example, GH-producing tumors often receive adjuvant or primary therapy with dopamine and somatostatin analogues or with GH-receptor agonists to hinder GH action.

Hormone Disorders

Cushing Syndrome
Cushing syndrome is caused by the body’s overproduction of cortisol, or hypercortisolism, for any reason other than a pituitary tumor. Cortisol regulates various functions in the body, such as blood pressure, inflammatory response, immune system function, and balance of glucose, energy, protein, carbohydrates, and fat metabolism. Managing the body’s response to stress is one of the most crucial functions of cortisol. This is clearly exhibited in trained athletes and during the last trimester of pregnancy, which is associated with elevated levels
of cortisol.62 Individuals who are depressed or who have malnutrition, alcoholism, or panic disorders also display elevated cortisol levels.4,12,32,65,68

Cushing syndrome can be induced by long-term continued exposure to elevated levels of the cortisol hormone from excessive use of glucocorticoids, cortisol, or other corticosteroid medications. Medications such as prednisolone or prednisone often are used to treat conditions such as asthma, lupus, rheumatoid arthritis, or other inflammatory issues.4,69

Cushing disease refers to Cushing syndrome that is caused by benign pituitary adenomas.76 Although this distinction is important to note, literature surrounding Cushing often refers to these conditions as Cushing syndrome. These pituitary lesions are much smaller than other pituitary adenomas and are responsible for the increased amounts of adrenocorticotropic hormone (ACTH).4,12,32,43 In either the syndrome or the disease, the hypothalamus sends a corticotropin-releasing hormone to the pituitary gland, signaling the need to produce ACTH. ACTH causes the adrenal glands to produce cortisol and release the hormone into the cardiovascular system.4,50 The hormone can be produced from ectopic sources (ie, outside the pituitary gland), but this is extremely rare. For example, small-cell lung cancer and bronchial carcinoid tumors can produce ACTH.71 When this occurs, Cushing syndrome develops just as if the ACTH came from the pituitary gland.4,12,27,28,52,53

Cushing syndrome was first described in 1932 by Dr Harvey Cushing, who identified 8 patients who exhibited the following similar signs43:

- Central body obesity.
- Glucose intolerance.
- Hypertension.
- Excessive hair growth.
- Osteoporosis.
- Kidney stones.
- Irregular menses.
- Emotional variation.

Cushing syndrome more often affects individuals between the ages of 20 and 50 years.40 It is estimated that for every million people, between 10 and 15 are affected annually.44 Cushing syndrome is 3 times more likely to affect women than men.9 Pituitary adenomas result in 60% of cases of ACTH-dependent Cushing syndrome. Research also has shown that only 5% of ACTH-dependent Cushing syndrome patients develop benign or malignant lesions in a lung, the pancreas, thyroid, or thymus gland.93 One-quarter of individuals with ACTH-independent Cushing syndrome develop benign lesions of the adrenal cortex called adrenal adenoma.92 Malignant lesions that develop from the adrenal cortex are called adrenocortical carcinomas; they are rare and develop in only 10% of individuals with ACTH-independent Cushing syndrome.4,12,27,28,52 If the adrenal glands develop lesions and those lesions comprise cortisol-producing cells, the adrenal glands produce excessive amounts of cortisol.92 The pituitary gland can monitor the levels of the different hormones and compensate when it senses an excess or insufficient amount of a hormone. This helps physicians to distinguish whether excessive levels of a hormone are caused by the pituitary gland or the adrenal glands.4,52,72

Some patients develop Cushing syndrome because they inherit an increased tendency to develop tumors. Primary pigmented micronodular adrenal disease develops in children and young adults and causes small cortisol-producing lesions in the adrenal glands. Hormone-secreting lesions of the parathyroid glands, pancreas, and pituitary gland occur when an individual develops MEN 1. If an individual has MEN 1, Cushing syndrome might be caused by pituitary, ectopic, or adrenal gland tumors.72

Corticotropinoma, also referred to as “the obesity tumor,” is the second most common childhood pituitary adenoma.9 In 2010, Azevedo et al reported a case of a 15-year-old girl with a recurring corticotropinoma that caused symptoms of Cushing syndrome. The patient was treated surgically, but the tumor recurred 4 years later and caused the same symptoms.93 This lesion is seen almost twice as often in girls than boys; it can present at all ages, but usually is seen in children before they reach puberty. The incidence of these adenomas increases in pubescent and postpubescent individuals.8,24,66 Some studies suggest that excessive release of ACTH can increase the risk in boys, but the older they get the less likely they will be to develop corticotropinoma.8,24

Symptoms

The symptoms associated with Cushing syndrome include4:

- Obesity of the upper body.
- A rounded face.
Individuals with Cushing syndrome can experience other common symptoms, such as slow healing from infections, acne, cuts, or insect bites.4,50,52,66,72 In addition, men and women experience sexual symptoms. Men might have a decreased sperm count and lack of interest in intercourse. Women might have irregular menses or amenorrhea and increased hair growth on their neck, face, trunk, and upper legs (see Figure 6).4,66

**Diagnosis**

Several tests can be used to confirm the overproduction of cortisol. Clinicians might order a 24-hour urine test, or they can use a dexamethasone suppression test to measure the cortisol levels in a patient’s blood. If indicated, an MR of the brain or a corticotropin-releasing

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- Increased neck fat.
- Thinning of the arms and legs.
- Easy bruising.
- Purplish pink striae.
- Thinning of the skin.
- Skin that does not heal.

Children with Cushing syndrome exhibit obesity combined with a slowed growth rate. Striae begin to develop on the lower portion of the body, abdomen, breasts, and arms. Patients experience a noticeable weakening of the bones with routine daily activities; weakened bones can lead to backaches, and fractures of the ribs and spine are possible from bending and standing from a seated position. Some individuals gain weight on the upper back between their shoulders, developing a dorsocervical fat pad (see Figure 5).66

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**Figure 5.** Physical signs of Cushing syndrome include the dorsocervical fat pad (A) and abdominal striae (B). Reprinted from Wikispaces.com under a Creative Commons Attribution Share-Alike 3.0 License.

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**Figure 6.** Photograph of Anne Jones, who had hirsutism, circa 1900. It is not confirmed whether Jones had hirsutism a result of Cushing syndrome. Public domain file via Wikimedia Commons.
Disorders of the Pituitary Gland

Gigantism

Gigantism is characterized by having a stature much larger than other individuals of similar age and sex, usually by more than 2 standard deviations. Somatotropinomas can cause gigantism in children, and the tumors develop in the anterior portion of the pituitary gland. The tumors are more commonly associated with local invasion of surrounding structures, such as the sphenoid, optic nerves, and brain.\(^\text{4,24,76}\)

Robert Wadlow, who was also known as the Alton Giant, was born in 1918 and was the tallest person in documented history, standing at 8 feet, 11 inches tall. Wadlow was diagnosed with gigantism, and he died from complications related to the disorder when he was 22 years old. Neuropathy, a symptom of gigantism, caused him to have little sensation in his feet. As a result, he died on July 15, 1940, from a fatal infection from a blister on one of his feet.\(^\text{77}\)

Gigantism is usually recognized in children or adolescents who are much taller than their peers and who might have disproportionately large features. Gigantism affects both sexes equally, and there does not appear to be a correlation with a specific race or ethnic group.\(^\text{4,24,76}\) In 2008, only 100 cases were reported in the United States, and associated morbidity and mortality rates are not accessible because so few individuals have this condition.

Elevated prolactin levels often accompany excessive levels of somatotropin in children with gigantism. Research has indicated the reason for elevated prolactin is that mammosomatotroph cells in the pituitary gland are responsible for the secretion of both somatotropin and prolactin. When the pituitary begins overproducing somatotropin from these cells, the cells also overproduce prolactin. Somatotropin-producing lesions in children are far more invasive and aggressive than the lesions that develop in adults.\(^\text{4,24,76}\) In addition, benign pituitary tumors composed of mammosomatotroph cells lead to the overproduction of IGF-1.

An overabundance of IGF-1 that often occurs prior to the fusion of the epiphyseal plates usually causes gigantism. Most growth-related gigantism cases are caused by hepatocytes creating more IGF-1 in response to the presence of somatotropin. Although pituitary adenomas that secrete somatotropin occur infrequently and usually are isolated, they can present when other conditions also exist. An individual with gigantism might also have MEN, Carney complex, or McCune-Albright syndrome, which affects bones, skin, and hormone-producing tissues.\(^\text{4,24,78,79}\)

Intracranial or ectopic influences also can cause the release of the growth hormone-releasing hormone test can be used to determine the cause of increased cortisol levels. Another test used to measure ACTH levels is inferior petrosal sinus sampling, an invasive examination that measures the levels of ACTH in the peripheral blood. Because cortisol is secreted in varying amounts over a 24-hour period, measuring the levels of ACTH in the blood once or even twice is not an effective testing method.\(^\text{4,12}\) Instead, sampling urine over a 24-hour period is much more reliable.\(^\text{74}\) A diagnosis of Cushing syndrome is appropriate when the 24-hour cortisol levels are more than 100 µg.\(^\text{4,12}\)

Treatments are specific to the causes of the excess production of cortisol but can include surgery, radiation therapy, cortisol-inhibiting drugs, or chemotherapy.\(^\text{66}\) If the excess cortisol is caused by long-term exposure to glucocorticoid medications used to treat other disorders, physicians gradually reduce the glucocorticoid dosage to the lowest dose possible that effectively controls symptoms.\(^\text{66}\) Several treatment options are available for treating Cushing-induced ACTH-secreting pituitary adenomas. Medications such as aminoglutethimide, metyrapone, and ketoconazole can be used individually or in combination to maintain an appropriate level of cortisol.\(^\text{67,75}\)

If response to initial treatments is unsuccessful or there are other patient health concerns, radiation therapy should be considered. Radiation therapy has a 60% to 80% chance of controlling hormonally active tumors, but it depends on the type and size of tumor. Radiation therapy also can control tumor growth 95% of the time.\(^\text{66}\) Without treatment, Cushing syndrome can become an extremely serious illness, eventually leading to death. A lesion can recur after its initial removal; outcomes vary depending on the tumor’s initial characteristics.\(^\text{56}\)

Three specific disorders involving growth hormones can occur: gigantism, dwarfism, and acromegaly. These disorders are linked to somatotropin and insulin-like growth factor 1 (IGF-1), but there are some differences in how these hormones operate within the body.\(^\text{4,24,76}\)
(GHRH), which can cause an excess of GH to be released. An increase in GHRH levels also might be a cause of gigantism; several patients with gigantism or acromegaly have been reported to have excess levels of GHRH.23,24,78,80

When an individual has gigantism, the resulting growth abnormalities do not develop symmetrically and cause physical disfigurement (see Figure 7). Therefore, these individuals also experience abnormal development of internal organs, which leads to additional complications. The following are signs that a child might have gigantism4,24:

- Headaches.
- Vision problems.
- Hearing problems.
- General weakness.
- Obesity.
- Macrocephaly.
- Osteoarthritis.
- Neuropathy.
- Cardiovascular diseases.
- Delayed onset of puberty.
- Irregular menstruation in girls.

**Acromegaly**

In contrast to gigantism, acromegaly is the result of an excess of IGF-1 that occurs after the epiphyseal growth plates are fused.4,24 Acromegaly is more common than gigantism and affects men and women equally82; however, the condition’s rarity and the gradual progression of the disease are reasons it can remain undiagnosed for a long time. The typical delay between the onset of symptoms and diagnosis is 12 years.83 When a person develops acromegaly, the size of the limbs and face increases as in gigantism. Patients and family members often do not notice the slow physical changes. It is only when patients’ physical appearance is compared with the appearance of their younger selves that changes become apparent.

People with acromegaly are 2 to 3 times more likely than the general population to die prematurely.83,84 The most frequent causes of death for people with acromegaly are cardiovascular and respiratory complications.41 Andre Roussimoff, who was also known as Andre the Giant, suffered from acromegaly. Roussimoff grew to be 7 feet, 4 inches tall and made a name for himself as an actor and wrestler before dying from a myocardial infarction in 1993 at the age of 46 years.44

**Symptoms**

The symptoms of acromegaly mirror those of gigantism, including excessive sweating, osteoarthritis, vision problems, cardiovascular problems, neuropathy, an increased size of the hands and feet, and amenorrhea in women. However, some symptoms differ from those in gigantism4,17,82,85:

- Limited mobility.
- Mood swings.
- Skin tags.
- Memory loss.
- Enlarged tongue.
- Colon polyps.
- Impotence.
- Reduced libido.

In addition, patients might experience enlargement of the vocal cords, causing a deepening of the voice or even
an obstructed upper airway, leading to severe snoring or sleep apnea. The chest often increases in size, becoming more barrel-shaped, and many internal structures, such as the liver, kidneys, and spleen, increase in size.4,5,6

Although acromegaly results from the same influences as gigantism, the literature states that many people who have acromegaly also develop additional benign lesions, such as uterine myomas or prostatic hypertrophy.6 Research has shown that up to 30% of people with acromegaly also have a premalignant colon polyp at the time of diagnosis.6,8 Approximately 5% of these patients will have been diagnosed with a lesion of the colon, but there is insufficient research to demonstrate the overall impact that colon cancer has on patients with acromegaly.8

Complications from acromegaly can be prevented with early detection and treatment using the same surgical and radiation therapy approaches as other pituitary lesions. Transsphenoidal surgery results in a 42% to 65% remission rate.57,58 Radiation therapy is recommended for patients with persistent postsurgical disease and provides an 85% to 95% success rate in managing the pituitary lesion.57,87

If the condition is managed with the use of somatostatin analog medications, such as octreotide, the patient typically exhibits a corrective response of 65% to 70%, with few adverse effects.4 If surgery is unsuccessful or the patient is not a good surgical candidate, these medications also can be used as an independent, follow-up, or adjuvant treatment. However, although the use of octreotide offers decreased levels of GH and IGF-1, the tumor shrinks only nominally and in only 20% to 50% of patients.88 Octreotide also can be used in patients who are awaiting radiation therapy. Lanreotide, another somatostatin analog medication, is helpful to reduce tumor size in newly diagnosed acromegaly.88

The dopamine-receptor agonists bromocriptine and cabergoline can be used as adjuvant treatments to suppress the secretion of GH by binding with pituitary dopamine type 2 receptors.4,5,31 Prolactin levels also can be suppressed when dopamine-receptor agonists are used; however, there is little to no effect on the circulating GH and IGF-1 or the size of the tumor. The mechanism of action of dopamine-receptor agonists is unclear, and although this adjuvant treatment is fairly effective, it can be used in conjunction with octreotide for better results.4,5,31

There have been promising strides in treating acromegaly with the use of pegvisomant, a hepatic GH-receptor antagonist, which returns IGF-1 levels to normal.88 When administered subcutaneously, pegvisomant appears to suppress GH and IGF-1 levels.4,17,89 Pegvisomant has not been tested in children with gigantism, although one case study reported success in a 12-year-old girl treated with pegvisomant for pituitary gigantism.88 If IGF-1 levels can be normalized, the patient’s risk of death also returns to normal.57,24

The resolution of symptoms depends on the individual. In some cases, sweating stops almost immediately, and blood pressure and glucose levels return to normal. Skin thickening takes longer to resolve, but osteoarthritis and bone changes from acromegaly usually are permanent.4,34

Dwarfism

Dwarfism is a short stature caused by a genetic or medical condition. The average adult height for people with dwarfism is 4 ft.90 Dwarfism can be either disproportionate or proportionate.90 Disproportionately short stature indicates that the individual has an average-sized trunk, but short limbs. It is possible for an individual to develop a short trunk, but still have disproportionate limbs larger than the person’s trunk would suggest. In general, the individual’s head is disproportionally larger than the body and limbs.90,91 In addition to the overall disproportionate appearance of the individual, people with this form of dwarfism typically have a prominent forehead, flattened nose, bowed legs, and a swayed back. When dwarfism and hydrocephalus are present, there is an increased probability that the person also will have neurological complications from the hydrocephalus.90,91

Disproportionate dwarfism, with hands and feet of normal size but a shortened trunk, neck, arms, and legs, is caused by a rare disorder known as spondyloepiphyseal dysplasia congenita.92 People with this condition have mild changes in facial features, including flattened cheekbones. Cleft palate and nearsightedness are possible, and approximately 25% of people with spondyloepiphyseal dysplasia congenita have hearing loss.92 Problems with vision and hearing can lead to slower motor skill development. Other complications of this disorder are hip deformities, clubfoot, and kyphosis.90,91 Although the condition is present at birth, symptoms might not appear until a child is 5 to 10 years old.93
Unlike disproportionate dwarfism, proportionate dwarfism is evident at birth or in early childhood and limits overall growth and development. The person’s physical characteristics are small, but proportional to each other. Proportionate dwarfism can be caused by chemical, endocrine, nutritional, or other abnormalities. In addition, because the disorder affects the child’s overall growth, it can affect social development. The most common cause of dwarfism is achondroplasia, a genetic condition that causes arms and legs to be proportionally smaller than the head and trunk. Achondroplasia affects approximately 1 in 15,000 to 1 in 40,000 people, and causes 70% of dwarfism. Adenohypophyseal hypoplasia might be responsible for the abnormal growth of these individuals.

Dwarfism can be attributed to hormone deficiencies as a result of faulty pituitary gland function or even poor nutrition, as in psychosocial dwarfism, but genetic disorders usually are the cause. Although the parents might be of average height, a random mutation in one parent’s sperm or egg occurs in 80% of people with dwarfism. Most often, the deficiency cannot be traced to a specific genetic mutation.

Characteristics of dwarfism usually begin to appear in childhood, with height falling under the third percentile on standard pediatric growth charts. People who have dwarfism also have decreased functionality of other endocrine systems, with the exception of the parathyroid glands, because the pituitary gland is not functioning correctly.

Several health problems and risk factors are associated with dwarfism, such as hydrocephalus, joint problems, scoliosis, spinal stenosis, and heart and respiratory problems. Other genetic conditions, problems with metabolism and hormone balances, and kidney disease also are associated with dwarfism. However, with appropriate medical attention and care, most individuals with dwarfism live active lives, with no increased risk of early mortality.

**Diagnosis**

Routine wellness checks that include checking a child’s weight, height, and head circumference allow pediatricians to track the child’s growth on a standardized chart to determine whether there is a growth problem. Several dwarfism disorders demonstrate distinct skeletal and facial feature development, and the physician can order radiographic examinations to help determine which form of dwarfism the child may have. Although usually not necessary for diagnosis, genetic tests can be used to specifically identify dwarfism disorders that are related to specific genes. Once the specifics of the condition are established, a physician can plan an appropriate treatment approach.

**Treatment**

Treatment for dwarfism generally does not increase height, although it can help with other problems caused by the condition. Surgery is available to those who need skeletal structure correction. For instance, if staples are placed in the ends of the long bones at the location of the epiphyseal plates, surgeons can manage the direction in which the bones grow.

Although controversial for various reasons among those with dwarfism, limb lengthening can be performed on an individual with dwarfism through a scaffolding procedure. In this procedure, the surgeon separates the bones of a limb into 2 or more sections. The sections are then affixed using screws, pins, and braces. Periodic adjustments to the tension are made to allow for the gradual regrowth of bone, eventually creating a longer bone.

Injections of synthetic GH can be prescribed for children with dwarfism. Injections are administered daily until the child reaches a maximum adult height that is usually similar to that of others in their family who do not have dwarfism. However, for children with achondroplasia, supplemental GH does not increase their final adult height. Estrogen hormone therapy is necessary for young girls when they begin puberty for sexual development. The individual likely will have to receive estrogen until she is ready for menopause.

**Pituitary Adenoma Metastasis**

Metastatic spread to the pituitary gland is uncommon unless cancer is already widespread. Generally, metastatic spread to the pituitary occurs from cancers in the lung, gastrointestinal tract, and breast. Lung and breast cancers have a high incidence of cerebral metastases. Clinically, patients have signs of hormonal imbalances, which can lead to the misdiagnosis of a pituitary adenoma. Patients also might experience...
visual problems from tumor mass effect, or the tumor can extend into the cavernous sinuses.\textsuperscript{69}

Metastases originating from the pituitary gland can spread to the lungs, liver, or heart; however, this is rare. If a pituitary lesion is the primary malignancy, organs most at risk for distant metastases include:\textsuperscript{4}

- Brain.
- Spinal cord.
- Meninges.
- Adjacent bony structures.

Treatment options for metastatic spread to the pituitary gland can include surgery, radiation therapy, and chemotherapy; however, because this type of tumor is rare and is associated with end-stage disease, treatment usually is only palliative.\textsuperscript{79} Complications are common with surgery and include heavy bleeding; local invasion of the surrounding bone or sinuses makes resection difficult.\textsuperscript{100} There do not appear to be any improvements in survival from treatment, although palliative therapy can improve an individual’s quality of life.\textsuperscript{101} The average survival time is approximately 6 months following a diagnosis of metastatic invasion of the pituitary gland.\textsuperscript{101}

There is debate regarding whether treating metastatic pituitary gland tumors with radiation should focus on only the parasellar region or the whole brain. Adverse effects of irradiation are reduced when treatment is confined to the parasellar area. Conversely, tumor invasion of the meningeal pathways is more likely when treatment is limited. The data available do not support one approach over the other, although it appears that whole-brain treatments with radiation might be used more often when there are multiple lesions in the brain involving more than just the pituitary gland.\textsuperscript{101}

**Conclusion**

The pituitary gland, although small, plays an important role in maintaining the body’s endocrine system. Benign pituitary adenomas often cause abnormal hormone levels that have significant effects on growth in children and young adults. Malignant pituitary lesions or metastatic spread to the pituitary gland is unlikely. Radiation therapists might encounter patients with pituitary disorders and will benefit from an understanding of the effects of these conditions on their patients.

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Raven Raye, R.T.(R)(T), has been delivering radiation therapy since 1984. She now works part time at Memorial Hermann Southeast Hospital in Houston, Texas.

Natasha Hadrych-Rosier, MHA, MBA, R.T.(R)(T), is the radiation therapy manager at the American Society of Radiologic Technologists in Albuquerque, New Mexico.

Reprint requests may be mailed to the American Society of Radiologic Technologists, Communications Department, at 15000 Central Ave SE, Albuquerque, NM 87123-3909, or e-mailed to communications@asrt.org.

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Disorders of the Pituitary Gland

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Read the preceding Directed Reading and choose the answer that is most correct based on the article.

1. The ______ signal(s) the pituitary gland to increase or decrease hormone production.
   a. adrenal glands
   b. hypothalamus
   c. thymus
   d. thyroid gland

2. The ______ lobe of the pituitary is referred to as the adenohypophysis.
   a. superior
   b. anterior
   c. inferior
   d. posterior

3. Through direct or indirect hormone production, the pituitary gland is credited with controlling:
   1. metabolism.
   2. urination.
   3. blood pressure.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

4. More than 90% of all pituitary tumors are:
   a. slow-growing, benign, and curable.
   b. slow-growing, malignant, and inoperable.
   c. fast-growing, benign, and curable.
   d. fast-growing, malignant, and inoperable.

5. If an individual with a pituitary lesion feels dehydrated and urinates frequently, it likely indicates:
   a. diabetic effect.
   b. hyperglycemia.
   c. hypertension.
   d. diabetes insipidus.

6. Research suggests that pituitary adenomas may result from different factors, including:
   1. hyperglycemia.
   2. hypothalamic dysfunction.
   3. intrinsic pituicyte genetic disruption.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

continued on next page
7. Which of the following characteristics are used to differentiate and classify a pituitary adenoma?
   1. size
   2. aggressiveness
   3. effect on hormone production

   a. 1 and 2  
   b. 1 and 3  
   c. 2 and 3  
   d. 1, 2, and 3

8. A tumor that does **not** influence the hormones being released is classified as:
   a. clinically functional.  
   b. nonfunctional malignant.  
   c. clinically nonfunctional.  
   d. developmentally functional.

9. Symptoms that indicate a nonfunctional pituitary lesion include:
   1. hypoglycemia.  
   2. joint swelling.  
   3. frequent nocturia.

   a. 1 and 2  
   b. 1 and 3  
   c. 2 and 3  
   d. 1, 2, and 3

10. Which of the following statements is **true** regarding prolactinomas?
    a. They are the least common type of secretory pituitary adenoma.  
    b. The risk of developing a prolactinoma decreases with age.  
    c. Sex has no effect on development of a prolactinoma.  
    d. Girls are 4 to 5 times more likely to develop the tumor than are boys.

11. Boys with a prolactinoma might have the following signs and symptoms:
    1. gynecomastia.  
    2. hypogonadism.  
    3. high levels of testosterone.

    a. 1 and 2  
    b. 1 and 3  
    c. 2 and 3  
    d. 1, 2, and 3

12. A tumor that grows large enough to press against a disease-free pituitary gland or other areas of the brain can cause:
    a. hyosecretion.  
    b. tumor mass effect.  
    c. hypersecretion.  
    d. pituitary shrinkage.

13. Pituitary apoplexy occurs when a pituitary tumor:
    a. invades the sphenoid.  
    b. suddenly increases in size.  
    c. decreases in size spontaneously.  
    d. secretes less growth hormone.

14. ________ is the preferred method for detecting pituitary lesions.
    a. Magnetic resonance scanning  
    b. Computed tomography scanning  
    c. Cerebral angiography  
    d. Exploratory transsphenoidal resection

15. According to the article, typical procedures to treat pituitary adenomas include which types of surgery?
    1. endoscopic transethmoidal  
    2. endoscopic transsphenoidal  
    3. transcranial

    a. 1 and 2  
    b. 1 and 3  
    c. 2 and 3  
    d. 1, 2, and 3
16. Which of the following statements is **not true** regarding surgery for pituitary adenomas?
   a. Some surgery is performed intranasally.
   b. A cerebral spinal fluid leak can occur if surgery compromises the dura mater.
   c. In microcraniotomy, a small incision may be made above the lip.
   d. A transcranial approach may be necessary for a large tumor invading the brain.

17. To be a candidate for stereotactic radiosurgery, a patient should have a pituitary adenoma no larger than ______ cm to ______ cm.
   a. 0.5; 1
   b. 1.5; 2
   c. 2.5; 3
   d. 3.5; 4

18. According to the article, the **most common** adverse effect from radiation therapy treatment for a pituitary adenoma is:
   a. hair loss.
   b. headache.
   c. hypopituitarism.
   d. nausea.

19. Cortisol regulates various functions in the body, including:
   1. blood pressure.
   2. energy.
   3. fat metabolism.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

20. In Cushing syndrome and Cushing disease, the hypothalamus sends a signal to produce ______ hormone to the pituitary gland.
   a. prolactin-releasing
   b. thyroid-stimulating
   c. corticotropin-releasing
   d. luteinizing

21. Harvey Cushing’s evaluation of Cushing syndrome began with an examination of patients who exhibited the following similar issues:
   1. central body obesity.
   2. glucose intolerance.
   3. excessive hair growth.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

22. Cushing syndrome most often affects individuals between the ages of 20 and 50 years.
   a. true
   b. false

23. Research has shown that a small percentage of adrenocorticotropic hormone–dependent Cushing syndrome patients can develop benign or malignant lesions in the:
   1. lung.
   2. pancreas.
   3. thymus.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

24. Primary pigmented micronodular adrenal disease develops in children and young adults.
   a. true
   b. false

*continued on next page*
25. Children who have Cushing syndrome exhibit:
   1. obesity.
   2. decreased neck fat.
   3. slowed growth rate.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

26. Both ______ and ______ are specific disorders that occur involving growth hormones.
   a. gigantism; acromegaly
   b. micronodular adrenal disease; Cushing syndrome
   c. Cushing syndrome; acromegaly
   d. gigantism; micronodular adrenal disease

27. Children with gigantism generally have elevated levels of:
   1. prolactin.
   2. somatotropin.
   3. cortisol.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

28. An excess of insulin-like growth factor 1 after the epiphyseal plates have fused can cause:
   a. microadrenoma.
   b. gigantism.
   c. acromegaly.
   d. Cushing syndrome.

29. Research has shown that up to 30% of people with acromegaly also have a ______ at the time of diagnosis.
   a. peptic ulcer
   b. premalignant colon polyp
   c. malignant lung lesion
   d. metastatic brain lesion

30. Treatment for the spread of metastatic disease to the pituitary gland usually is only:
   a. surgical resection.
   b. stereotactic radiosurgery.
   c. chemotherapy.
   d. palliative.