



NASET Q & A Corner

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Adrenal Glands Disorders

The adrenal glands, located on the top of each kidney, are responsible for releasing different classes of hormones. Adrenal gland disorders occur when the adrenal glands do not work properly. They can be classified into disorders where too much hormone is produced or where too little hormone is produced. These disorders can occur when the adrenal gland itself is affected by a disease process due to genetic mutation, tumors, or infections. Or, sometimes the cause is a problem in another gland, such as the pituitary, which helps to regulate the adrenal gland. In addition, some medications can cause the adrenal gland not to function properly. When the adrenal glands produce too few or too many hormones, or when too many hormones are introduced by an outside source, significant disorders can develop. The focus of this issue of *NASET's Q & A Corner* will be to address issues pertaining to adrenal gland disorders

What are the adrenal glands?

The adrenal glands, located on the top of each kidney, are responsible for releasing different classes of hormones.

The outer part of the gland, called the adrenal cortex, produces the hormones cortisol (pronounced *KAWR-tuh-sohl*) and aldosterone (pronounced *al-DOS-tuh-rohn*). The inner part of the gland, called the adrenal medulla (pronounced *muh-DUHL-uh*), produces the hormones adrenaline and noradrenaline.

These hormones control many important functions in the body, including¹:

- Maintaining metabolic processes, such as managing blood sugar levels and regulating inflammation
- Regulating the balance of salt and water
- Controlling the "fight or flight" response to stress
- Maintaining pregnancy
- Initiating and controlling sexual maturation during childhood and puberty

The adrenal glands are also an important source of sex steroids, such as estrogen and testosterone.

What are adrenal gland disorders?

Adrenal gland disorders occur when the adrenal glands do not work properly. They can be classified into disorders where too much hormone is produced or where too little hormone is produced.

These disorders can occur when the adrenal gland itself is affected by a disease process due to genetic mutation, tumors, or infections. Or, sometimes the cause is a problem in another gland, such as the pituitary, which helps to regulate the adrenal gland. In addition, some medications can cause the adrenal gland not to function properly. When the adrenal glands produce too few or too many hormones, or when too many hormones are introduced by an outside source, significant disorders can develop.

What are some types of adrenal gland disorders?

Adrenal Gland Tumors

Most adrenal gland tumors are noncancerous. They often do not cause symptoms or require treatment. However, adrenal gland tumors can produce and thus cause excess levels of a variety of different hormones.

Adrenal tumors can cause:

- Cushing's syndrome, by producing and thus raising body levels of cortisol
- Primary hyperaldosteronism, by creating excess levels of aldosterone
- Pheochromocytoma, by producing too much adrenaline

Adrenocortical Carcinoma

This is a cancerous adrenal tumor that tends to develop in the outer layer of the adrenal gland. Cancerous adrenal tumors are often found years after they start growing, at which point they typically have spread to other organs.

Cushing's Syndrome

Cushing's syndrome is a rare disease that results from having too much cortisol hormone in the body. In some cases, Cushing's syndrome develops from prolonged or excess use of steroid medications. In other cases, the body itself produces too much cortisol. This can happen for several reasons, including the presence of tumors (abnormal growths) such as a:

- Tumor of the pituitary gland
- Tumor of the adrenal gland
- Tumor in another part of the body (these are called "ectopic" tumors and are more commonly found in the pancreas, lung, or the thyroid gland)

Congenital Adrenal Hyperplasia (CAH)

CAH is a common genetic disorder that prevents the body from making enough cortisol. People with CAH sometimes also have other hormone imbalances. For example, their bodies might not make enough aldosterone but might make too much androgen. Aldosterone is a hormone that controls blood pressure as well as the amount of salt and potassium in the body. Androgen hormones promote the development of male sexual organs.

Pituitary Tumors

The pituitary gland is located at the base of the brain. It releases hormones that affect many of the body's functions. Among those hormones is the adrenocorticotrophic (pronounced *a-DREE-noh kawr-tuh-koh-TRO-pic*) hormone (ACTH), which stimulates the adrenal glands to release the hormone cortisol.

Sometimes, benign (noncancerous) pituitary tumors or—more rarely cancerous tumors¹—may grow on the pituitary gland, which can cause a variety of problems. Some pituitary tumors release too much ACTH,

which, in turn, can cause the adrenal glands to produce too much cortisol. Cushing's disease refers to pituitary tumors that cause Cushing's syndrome.

Pheochromocytoma

Pheochromocytomas are part of a larger family of tumors called paragangliomas. Pheochromocytoma is a paraganglioma that develops in the adrenal medulla. It produces adrenaline, causing excess levels of this hormone in the body. In most cases, the tumors are not cancerous and do not spread to other parts of the body. In about 10% of cases, the tumors are cancerous.

Adrenal Gland Suppression

The normal activity of the adrenal glands can be suppressed when people take steroid medications (medicines that act like cortisol in the body) such as prednisone, hydrocortisone, or dexamethasone. Steroid medications, most often prednisone, may be prescribed to treat certain types of arthritis, severe allergic reactions, autoimmune (pronounced *awh-toh-im-YOON*) diseases, and other conditions.

Ordinarily, the dose of steroids is tapered slowly before the drug is stopped completely. When steroid medications are stopped suddenly, after being taken for several weeks or more, the adrenal glands may be unable to produce steroid hormones (most importantly, cortisol) in sufficient amounts for several weeks or even months.¹

Addison's Disease

This rare disorder develops when the adrenal glands do not make enough cortisol. In most cases of Addison's disease, the body also fails to make enough of the hormone aldosterone.

Addison's is an autoimmune disease—a condition in which the immune system mistakenly attacks the body's own tissues and cells. In the case of Addison's disease, this reaction results in damage to the adrenal glands.

Hyperaldosteronism

This is a disorder in which the body produces too much aldosterone. The excess aldosterone is either produced by an adrenal gland tumor that typically affects one adrenal gland or from abnormal growth of both glands, called "adrenal hyperplasia."

What are the symptoms of adrenal gland disorders?

When the adrenal glands produce too many hormones, the symptoms vary depending on the disorder. These include:

Cushing's Syndrome

Common symptoms of Cushing's syndrome (due to an adrenal, pituitary, or ectopic tumor) can include:

- Upper body obesity, round face and neck, and thinning arms and legs
- Skin problems, such as acne or reddish-blue streaks on the abdomen or underarm area
- High blood pressure
- Muscle and bone weakness
- Moodiness, irritability, or depression
- High blood sugars
- Slow growth rates in children

Women may also have increased growth of hair on their face and body and experience menstrual irregularities. Men may become less fertile and have a reduced or absent sex drive.

Hyperaldosteronism

The main symptom is moderate to high blood pressure (hypertension), which can be difficult to control. Other symptoms include:

- Low potassium levels
- Muscle cramping or spasms
- Excessive urination, sometimes at night
- Headache
- Generalized weakness

Congenital Adrenal Hyperplasia (CAH)

Symptoms of CAH range from mild to serious. Some people with mild CAH are never diagnosed because their symptoms do not cause them any problems.

Symptoms of the mild form of CAH, which can be diagnosed in children or adults, may include¹:

- Shorter than average final height
- Early signs of puberty (in children)
- Acne
- Irregular menstrual periods and possible trouble getting pregnant (in women)
- Excess facial hair (in women)

Symptoms of the severe form of CAH, which is diagnosed in children, may include¹:

- Dehydration
- Low blood pressure
- Low blood sugar level
- Trouble keeping enough salt in the body
- Altered development of the external genitalia in girls, which is noted at birth and may require surgery to correct
- Shorter than average final height
- Early signs of puberty
- Irregular periods and possible trouble getting pregnant (in women)
- Excess facial hair (in women)
- Benign testicular tumors and infertility (in men)

Pheochromocytoma/Paraganglioma

Most people with pheochromocytoma have high blood pressure (hypertension) because the tumor causes the adrenal gland to produce too much adrenaline or noradrenaline. Other symptoms may include²:

- Rapid heart rate
- Headache
- Sweating
- Episodes of high or low blood pressure
- Anxiety or panic attack
- Shaking (tremors) of the hands
- Pale skin
- Blurred vision
- Weight loss

- Constipation
- Abdominal pain
- High blood sugar
- Psychiatric disturbances

Addison's Disease

Symptoms can vary, depending on what causes the disease. Symptoms typically include^{3,4}:

- Weight loss
- Weakness
- Extreme fatigue
- Nausea and/or vomiting
- Low blood pressure
- Patches of darker skin
- Craving for salt
- Dizziness upon standing
- Depression

How many people are affected by or at risk of adrenal gland disorders?

The number of people affected depends on the specific disorder.

Cushing's Syndrome

Cushing's syndrome is uncommon, affecting about 10 to 15 out of every 1 million people each year. This syndrome can occur at any age, but it occurs most often in adults between the ages of 20 and 50 years old. Women are affected five times more frequently than are men.

Congenital Adrenal Hyperplasia (CAH)

CAH is one of the most common genetic disorders, affecting approximately 1 in 100 people. Mild CAH is more common than severe CAH. Severe CAH, also referred to as complete or classic CAH, is estimated to occur in 1 in 14,000 people. CAH affects men and women equally, although it is found more frequently in people from certain ethnic backgrounds, including those of Ashkenazi Jewish, Hispanic, and Italian heritages.

Pituitary Tumors

Although a large number of people have pituitary tumors (up to 20% of the world's population), most of these tumors are not cancerous, do not cause symptoms, and are never diagnosed. Cancerous tumors in the pituitary are very rare; only about 100 cases have ever been reported.

Pheochromocytoma

Pheochromocytomas are very rare. Only about 800 cases of pheochromocytoma are diagnosed each year in the United States. Although they can occur at any age, they occur most commonly in middle age. A pheochromocytoma can be life threatening if not diagnosed and treated. In approximately one-third of pheochromocytoma cases, there is a family history of the disease. Researchers have identified multiple genes as being associated with the tumors.

Paraganglioma

Paragangliomas also are very rare. Only about 2 in every 1 million people are affected. These tumors can occur at any age. Up to 25% of paragangliomas are caused by genetic syndromes.⁸

Addison's Disease

Addison's disease is diagnosed in 1 to 4 of every 100,000 people. It affects men and women of all ages.

Hyperaldosteronism

Hyperaldosteronism was thought to occur only in about 1% of all patients with hypertension. However, recently, this estimate has changed to greater than 10%.

What causes adrenal gland disorders?

Adrenal gland disorders can be caused by a problem in another gland, such as the pituitary gland, or when a disease or infection affects one or both of the adrenal glands. Specific disorders can develop when the adrenal glands produce too few or too many hormones, or when too many hormones are introduced from an outside source.

Cushing's Syndrome

Cushing's syndrome occurs when the body is exposed to high levels of the hormone cortisol over a long period of time.

Sometimes Cushing's syndrome develops when people take certain hormones for asthma, rheumatoid arthritis, lupus, and other inflammatory diseases. The syndrome also can occur when hormones are taken to suppress the immune system so that a patient's body will not reject a transplanted organ.

Other people develop Cushing's syndrome because their bodies produce too much cortisol. Other causes of Cushing's syndrome include pituitary adenomas (a type of benign tumor), ectopic adrenocorticotrophic hormone syndrome, adrenal tumors, or familial Cushing's syndrome. Cushing's syndrome due to tumors occurs more commonly in women.

Congenital Adrenal Hyperplasia (CAH)

CAH is a group of inherited disorders of the adrenal glands. It affects men and women equally. Both parents must carry the gene in order for a child to be born with CAH. Researchers have identified the location of the gene that causes the most common forms of CAH as chromosome 6.

Pituitary Tumors

Scientists have not yet discovered what causes pituitary tumors. Most pituitary tumors are not inherited; only a small percentage of cases run in families.

Pheochromocytoma/Paraganglioma

Most of the time, these tumors are "sporadic," meaning why they develop is not associated with any known risk factor or genetic mutation. However, an increasing number of patients—greater than 20%—that have genetic mutations responsible for tumor development.⁷ In these patients, family members may also be affected.

Addison’s Disease

In all cases of Addison’s disease, the adrenal glands do not produce enough of the hormone cortisol. In most cases, the glands also make too little of the hormone aldosterone.⁸ This is also termed primary adrenal insufficiency. This disease can be caused by an autoimmune disorder, infection (for example, tuberculosis), or other rare diseases that cause infiltration and thus destruction of the adrenal glands (for example, sarcoidosis or amyloidosis). The most common cause of Addison’s disease in developed countries is autoimmune disorders.

Hyperaldosteronism

There are two causes of hyperaldosteronism. One cause is an excessive growth of normal cells in both adrenal glands. The other cause is a noncancerous tumor in one of the glands. There are no known gene mutations associated with this disorder at this time. However, rarely, hyperaldosteronism can run in families.

How do health care providers diagnose adrenal gland disorders?

Methods for diagnosing adrenal gland disorders differ depending on the specific disorder. For example, the severe form of congenital adrenal hyperplasia (CAH) is most commonly identified during newborn screening, whereas paraganglioma is diagnosed using blood and urine tests.

Cushing’s Syndrome

If a health care provider suspects Cushing’s syndrome, he or she may order one or more of the three screening tests currently in use for this disorder. One of the tests screens for elevated cortisol levels in saliva, whereas another test looks for elevated cortisol levels in the urine over 24 hours. A third test determines whether a synthetic steroid, called dexamethasone (pronounced *dek-suh-METH-uh-sohn*), suppresses cortisol production by the body.

Addison’s disease

To diagnose Addison’s disease, a health care provider may administer a blood test to measure cortisol and adrenocorticotrophic hormone (ACTH) levels. Then he or she may perform an ACTH stimulation test, an hour-long test during which a synthetic (man-made) form of ACTH (hormone produced by the pituitary gland) is administered through an intravenous (IV) line. The health care provider measures blood levels of various hormones before and after the ACTH is given and interprets these values to determine if adrenal insufficiency (lack of cortisol) is present.

Congenital Adrenal Hyperplasia (CAH)

The most common way that health care providers identify CAH in infants is through a newborn-screening blood test. If the first screening test indicates that the infant may have CAH, the health care provider will order another blood test to confirm the diagnosis. In some cases, female infants may have visible genital abnormalities that lead health care providers to suspect CAH as the cause. In these cases, health care providers will order an additional test to confirm the diagnosis. The milder form of CAH, when suspected, can also be diagnosed by the ACTH stimulation test.

Pituitary Tumors

The first step in diagnosing pituitary tumors is through a physical exam. This exam includes a neurologic examination and evaluation for signs of excessive hormone secretion. A health care provider may also conduct a vision test to determine whether the growth of a pituitary tumor has affected sight or peripheral vision. If results of this test lead the health care provider to suspect a pituitary tumor, he or she will order

one or more tests of the patient's endocrine function. To confirm the diagnosis, the health care provider may ask for a test of the patient's visual field (the area visible at a given instant without moving the eyes) or a magnetic resonance imaging scan of the patient's head.

Pheochromocytoma/Paraganglioma

If a health care provider suspects a paraganglioma, he or she may administer a blood or urine test. The test measures the levels of catecholamines (pronounced *kat-i-KOL-uh-meens*), which are hormones that increase the heart rate, blood pressure, rate of breathing, and amount of energy available to the body, and metanephrines (pronounced *met-uh-NEF-reens*)—molecules into which catecholamines are broken down by the body.

Hyperaldosteronism

If a health care provider suspects hyperaldosteronism, he or she may order blood and urine tests to check for high levels of aldosterone and low levels of potassium. The health care provider also may order a computed tomography scan to determine whether a noncancerous tumor or other abnormal growth of the adrenal glands is present.

What are the treatments for adrenal gland disorders?

Health care providers use a variety of surgical and medical treatments for adrenal gland disorders. These include

- Surgery to remove tumors in the adrenal gland or, when appropriate, surgery to remove the one or both of the adrenal glands
- Minimally invasive surgery performed through the nostrils to remove tumors in the pituitary gland
- Medication to stop the excess production of hormones
- Hormone replacement

Cushing's Syndrome

The treatment for Cushing's syndrome depends on the cause. If medication causes the excess cortisol, a health care provider can change the patient's dosage or try a different medication to correct the problem. If the Cushing's syndrome is caused by the body making too much cortisol, treatments may include oral medication, surgery, radiation, or a combination of these treatments.

Congenital Adrenal Hyperplasia (CAH)

CAH cannot be cured, but it can be treated and controlled. People with CAH can take medication to help replace the hormones their bodies are not making. Some people with CAH need only these medications when they are sick, but other people with CAH may need to take medication every day.

Pituitary Tumors

The most widely used treatment for non-cancerous pituitary tumors is transsphenoidal adenectomy (pronounced *a-dee-na-MEK-ta-me*). Using a microscope and small instruments, the health care provider removes the tumor through a nostril or opening below the upper lip. Radiation is also used.

Pheochromocytoma/Paraganglioma

The usual treatment for pheochromocytoma/paraganglioma is removal of the tumor through surgery. In most cases, removing the tumor improves the patient's blood pressure control. This treatment seems to be more effective in patients whose high blood pressure is sporadic than in those patients whose high blood pressure is long lasting.

Addison's Disease

Addison's disease is treated by replacing the cortisol and/or aldosterone that the body is lacking. People with Addison's disease take oral medication each day to replace these hormones. They may also need to consume additional salt.

Hyperaldosteronism

The treatment for hyperaldosteronism caused by an excessive growth of normal cells in both adrenal glands is medications that block the effect of aldosterone. The treatment for hyperaldosteronism caused by a non-cancerous tumor in one adrenal gland is removing the affected gland using laparoscopic (pronounced *la-puh-re-SKOP-ic*) surgery. This type of surgery is minimally invasive, involving only small incisions in the abdomen, and is usually easier to recover from than is traditional surgery.