Pituitary and Adrenal Disorders

HOW TO RECEIVE CREDIT

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Faculty

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Jane C. Norman, RN, MSN, CNE, PhD, received her undergraduate education at the University of Tennessee, Knoxville campus. There she completed a double major in Sociology and English. She completed an Associate of Science in Nursing at the University of Tennessee, Nashville campus and began her nursing career at Vanderbilt University Medical Center. Jane received her Masters in Medical-Surgical Nursing from Vanderbilt University. In 1978, she took her first faculty position and served as program director for an associate degree program. In 1982, she received her PhD in Higher Education Administration from Peabody College of Vanderbilt University. In 1988, Dr. Norman took a position at Tennessee State University. There she has achieved tenure and full professor status. She is a member of Sigma Theta Tau National Nursing Honors Society. In 2005, she began her current position as Director of the Masters of Science in Nursing Program.

Faculty Disclosure

Contributing faculty, Amanda Perkins, MSN, DNP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Jane C. Norman, RN, MSN, CNE, PhD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Audience

This course is designed for nurses in all practice settings.

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Course Objective

As health care becomes more complex, it is essential that the theoretical concepts of the basis of illness (pathophysiology) be well understood. The purpose of this course is to reinforce the scientific rationales for the interventions nurses perform and the decisions nurses make as patients move through the ever-changing struggle with their pituitary or adrenal illness.

Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the anatomy and physiology of the pituitary and adrenal glands.
2. Outline the action of the hormones excreted by the pituitary and adrenal glands.
3. Describe key aspects of the assessment of patients with pituitary or adrenal disorders, including appropriate diagnostic tools.
4. Discuss the presentation and diagnosis of diabetes insipidus.
5. Outline the options for the treatment of diabetes insipidus.
6. Review the presentation and management of syndrome of inappropriate antidiuretic hormone secretion (SIADH).
7. Evaluate the signs/symptoms, diagnosis, and treatment of growth hormone deficiency.
8. Identify acromegaly and gigantism and appropriate approaches to their treatment.
9. Describe the clinical presentation and diagnosis of Addison disease.
10. Evaluate approaches to the treatment of Addison disease, including identification and management of adrenal crises.
11. Discuss the identification and diagnosis of Cushing syndrome.
12. Evaluate various treatment options for Cushing syndrome, including surgical considerations.
13. Review the signs/symptoms, diagnosis, and treatment of primary aldosteronism.
14. Analyze the clinical presentation, diagnosis, and treatment of pheochromocytoma.
15. Identify psychosocial/lifestyle considerations for patients with pituitary or adrenal disorders.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Body activities, homeostasis, and the response to stress are controlled by two distinct, but interacting systems: the nervous system and the endocrine system. The nervous system creates an immediate but short-lived response, operating on the principles of electricity, through impulse conduction. The endocrine system has a slightly slower onset and a longer duration of action and uses highly specific hormones to control its response chemically.

The endocrine system is composed of many glands scattered throughout the body; these glands secrete unique and potent hormones directly into the bloodstream. Most hormones direct their action to target glands or tissues at distant receptor sites, thereby regulating critical body functions such as urinary output, cellular metabolic rate, and growth and development. Hormonal secretions typically are regulated by negative feedback; information about the hormone level or its effect is fed back to the gland, which then responds accordingly.

Endocrine diseases result from an abnormal increase or decrease in the secretion of hormones. This divergence from normal hormone quantities may be the result of hyperplasia, hypertrophy, or atrophy of an endocrine gland. Changes in gland size that affect the gland's production and secretion of a hormone often result from an insult to the gland, such as infection, radiation, trauma, surgical intervention, or inflammation.

As noted, the principal functional units in the system are the endocrine glands: the pituitary, thyroid, parathyroid, adrenal, and pineal glands; the cells of the islets of Langerhans in the pancreas; the gonads (ovaries and testes); and the thymus. The kidneys also perform an endocrine function. Some of these glands are solely endocrine in function, whereas others form parts of larger organs that may have both endocrine and nonendocrine functions. The pituitary, thyroid, parathyroid, pineal, and adrenal glands have distinct endocrine functions. This course will focus on the pathophysiology of the pituitary and adrenal glands.

Because of the complex actions of the pituitary and adrenal glands, as well as their interaction with each other and with other body systems, their dysfunctions have a variety of causes and clinical manifestations. Pituitary disorders encompass a diverse set of conditions, including diabetes insipidus, SIADH (syndrome of inappropriate antidiuretic hormone secretion), acromegaly, and growth hormone deficiency. Common adrenal disorders include Cushing syndrome, Addison disease, hypoaldosteronism, and hyperaldosteronism. Because the pituitary and adrenal glands work together closely, there is often overlap in the pathophysiology of these disorders.

Dysfunction of the pituitary or adrenal gland is associated with many physical and mental symptoms, with significant impact on patients, families, health services, and society. When caring for patients with these types of disorders, there are key skills necessary to accurately interpret diagnostic testing, identify comorbidities, and effectively manage care.

ANATOMY AND PHYSIOLOGY

HYPOTHALAMUS

The hypothalamus plays an important role in the regulation of homeostasis within the body. It is necessary for automatic functions of the nervous system, regulation of the glands of the endocrine system, emotional responses, and behaviors [1]. It may help to think of the hypothalamus as a control center—it monitors information about the body and makes necessary changes based on the information obtained.

The hypothalamus functions as an integral part of both the endocrine and nervous systems. In its neural role, it receives and processes innervations from the thalamus, cerebral cortex, spinal cord, and brainstem. This results in the control of such bodily functions as temperature, respiration, arterial blood pressure and circulation, and metabolism. The hypothalamus also controls certain behavioral functions, including the emotional states of fear, anxiety, anger, rage, pleasure, and pain, as well as the states of sleep, wakefulness, and alertness. The hypothalamus, as

it is influenced by the autonomic nervous system, affects all the unconscious activities of the body [2; 3]. In its endocrine role, the hypothalamus has two regulatory functions:

- Regulating the anterior pituitary gland by producing and secreting releasing factors
- Producing and secreting two hormones (oxytocin and antidiuretic hormone [ADH]) stored in the posterior pituitary gland

Hypothalamic-releasing factors are proteins that act on the anterior pituitary gland to stimulate or inhibit the release of tropic hormones. Other inhibiting factors and releasing factors have been identified; it is thought, although still unproven, that the hypothalamus may produce both an inhibiting and a releasing factor for each of the anterior pituitary hormones [2; 3].

The release or inhibition of these hypothalamic hormones is controlled by various neurotransmitters, such as serotonin, acetylcholine, norepinephrine, and dopamine. The tropic hormones released from the anterior pituitary gland then act upon a target gland or tissues to produce a specific response. In regulating the secretion of these releasing factors, the hypothalamus processes input from both the circulatory and nervous systems [2; 3].

PITUITARY GLAND

The pituitary gland (hypophysis) is located in the sella turcica at the base of the skull. It lies just below the hypothalamus and is connected to it by a stalk containing blood vessels and nervous tissue. The pituitary gland is composed of an anterior and posterior lobe (adenohypophysis and neurohypophysis, respectively), each of which performs specific functions, as well as a rudimentary intermediate lobe [4].

In response to the releasing factors from the hypothalamus, the anterior pituitary gland secretes several hormones, some of which control hormonal secretions by other glands. The anterior pituitary hormones secreted include thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), growth hormone, luteinizing hormone (also called interstitial cell-stimulating hormone in men), follicle-stimulating hormone, and prolactin. In general, growth hormone, ACTH, and TSH are concerned with metabolic activities, whereas luteinizing hormone, follicle-stimulating hormone, and prolactin are concerned with reproduction. ACTH, TSH, follicle-stimulating hormone, and luteinizing hormone exert their effects on target glands, either increasing their size or their secretions. Prolactin and growth hormone directly affect the metabolism of specific target tissues [5].

Most of the disorders affecting the pituitary gland originate in the anterior lobe. The effects of pathology on the anterior pituitary gland can be broadly summarized as hyperpituitarism and hypopituitarism [6; 7].

The most common cause of hyperfunction of the anterior pituitary gland is a neoplastic secreting tumor, usually a benign adenoma. Tumors of the pituitary gland exert their effects through either pressure on structures in the brain, causing visual symptoms and headaches, or excessive secretion of one or more of the anterior pituitary hormones, which results in increased stimulation of one or more target glands.

One of the pathophysiologic manifestations of these tumors is hypersomatotropism, which can result in acromegaly in adults and gigantism in children. Other effects of hypersomatotropism include goiter (from stimulation of the thyroid) and diabetes mellitus (from the diabetogenic effect of growth hormone). Cardiomegaly and hypertension can also occur. Visual impairment and eventual blindness are possible because of compression of tissues by an expanding tumor. Amenorrhea in women and loss of libido and potency in men may occur because compression from the expanding tumor leads to gonadal deficiencies from loss of healthy gonadotropin-producing cells [6; 7].

Hyperfunction of the anterior pituitary gland can be secondary to pathology of the anterior pituitary gland or to injury to the hypothalamus resulting in a decrease or absence of hypothalamic-releasing factors. Hypothalamism may be manifested by isolated hormonal deficiencies or by a deficiency of both the anterior and posterior pituitary hormones (panhypopituitarism). The exact hormonal deficit and its etiology are important to understanding patients' symptoms and signs [6; 7].

ADRENAL GLANDS

The adrenal glands are paired and located in the retroperitoneal space at the upper pole of the kidney. Because of this position, they may be referred to as the suprarenal glands. Each adrenal gland consists of an outer portion (the cortex) and an inner portion (the medulla), which differ in both anatomic structure and function [8].

The adrenal cortex is composed of three zones, or groups of different cells: the zona glomerulus (the outer layer of cortical cells that secretes the mineralocorticoids), the zona fasciculate (the middle layer of cortical cells that secretes the glucocorticoids), and the zona reticularis (the layer of cortical cells proximal to the medulla that secretes the adrenal sex hormones androgens and estrogen). The adrenal glands receive an abundant blood supply. The medulla of the adrenal gland functions as part of the sympathetic nervous system, whereas the cortex has only minimal nervous system innervation [8].

In response to stimulation by ACTH from the anterior pituitary gland, the adrenal cortex secretes three major types of hormones: glucocorticoids (cortisol), mineralocorticoids (aldosterone), and sex hormones (androgens, estrogen, and progesterone). These hormones affect metabolism, fluid balance, and the development of secondary sex characteristics, respectively. All three types of hormones secreted by the adrenal cortex are structurally similar steroids, which results in some overlapping of their effects [5; 9].

The primary causes of hypercortisolism (Cushing syndrome), originating from within the adrenal cortex itself, include neoplastic and bilateral hyperplasia. In iatrogenic hypercortisolism, an exogenous source (e.g., prolonged use of glucocorticoids or ACTH) is responsible for the hypercortisolism. The normal adrenal glandular tissue may be atrophic, and ACTH levels are suppressed [10].

Hyperfunction of the adrenal cortex results in three major disorders: Cushing syndrome, primary aldosteronism, and excessive production of sex hormones characterized by virilizing changes in women, feminizing changes in men, and precocious sexual development in children. These changes often cause serious psychologic issues related to self-esteem and body image.

Hypofunction of the adrenal cortex, or adrenal insufficiency, results in a decreased secretion of glucocorticoids, mineralocorticoids, and sex hormones. The causes of adrenal insufficiency can be grouped into two categories: primary (based on pathology occurring within the gland itself) and secondary (arising from an undersecretion of ACTH due to pathology in the pituitary gland or the hypothalamus). Primary causes may be acute or chronic [11].

Primary adrenal insufficiency (Addison disease) is characterized by a failure of the adrenal cortex to produce sufficient corticosteroids. Acute severe symptoms of Addison disease are referred to as addisonian or acute adrenal crisis.

The adrenal medulla is considered a part of the sympathetic division of the autonomic nervous system, which controls the secretion of its hormones. Because the functions of the sympathetic nervous system and the functions of the hormones of the adrenal medulla are the same, they can compensate for each other. Thus, the medullary hormones are not essential to life but play an important role in the body's response to stress. About 15% of the hormonal secretion by the adrenal medulla is norepinephrine and 75% is epinephrine [5].

Pathophysiology of the adrenal medulla is rare and is usually associated with hyperfunction. The clinical manifestations seen in hyperfunction of the adrenal medulla are related to the excessive secretion of epinephrine and norepinephrine [12]. Pheochromocytoma is the most common cause of adrenal medulla hyperfunction. Other disorders associated with hyperfunction of the adrenal medulla include neurofibromatosis carcinomas (of the thyroid) and hyperparathyroidism [12].

HORMONES

A hormone may be defined as a "chemical substance synthesized by an endocrine gland and secreted into the bloodstream, which carries it to other sites in the body where its actions are exerted" [5]. Hormones may function independently, in conjunction with other hormones, or as a step in a series of related actions. They may influence the action, metabolism, synthesis, and/or transport of another hormone, which is one of the integrative aspects of the endocrine system. Hormones can be differentiated into two major categories: local (with specific local effects) and general (transported by the circulation to distant sites, where they have a physiologic effect) [13].

Only target cells have the capability to respond to a specific hormone in a characteristic way. Their response depends on the presence of specific receptors for a particular hormone. This response is called hormone-target cell specificity, and the process is known as hormone-receptor binding. The initial interaction between a hormone and its target cell receptor initiates a chain of biochemical events that eventually provokes a cellular response. This often involves a hormone-induced change in the activity of a specific enzyme found in the target cell that might change the rate of reactions within the cell, change the growth of the cell, or control the cell's secretion. Because cells are exposed to many hormones, complex hormone-hormone interactions can occur in target cells. These interactions may be inhibitory, synergistic, or permissive (i.e., one hormone, by its presence, potentiates the effect of the second hormone) [13].

Hormones include steroid, polypeptide, amino acid, catecholamine, or iodothyronine structures. The steroidal hormones are aldosterone, cortisol, and the estrogens and androgens. The receptors involved in hormonal-receptor binding differ for steroidal and nonsteroidal hormones. The receptors for most nonsteroidal hormones are located on the outer surface of the plasma membrane of the target cells, whereas the receptors for the steroidal hormones are soluble proteins within the cytoplasm of the target cell. The physiology of hormone receptors is an expanding area of research in endocrinology [13].

Most hormones are not secreted at a constant rate. After secretion into the bloodstream, they circulate in a free form or are bound to proteins. Polypeptide hormones and the catecholamines are essentially unbound in the circulation. These free hormones are directly available to the target tissues, and only they can affect the target cells. The protein-bound forms are thought to represent a hormonal reserve, because the protein binding may prevent excretion of the hormone by the kidney. The amount of circulating free hormone is usually quite small and exists in equilibrium with the bound fractions [13].

There are five major influences of the secretion of hormones by the endocrine glands: the hypothalamus, hypothalamic-releasing factors, anterior pituitary hormones, the autonomic nervous system, and nutrient and ion concentrations in the plasma. The hypothalamus affects hormone secretion by secreting a series of peptides called releasing factors, which stimulate or inhibit the release of hormones by the anterior pituitary gland. The hypothalamus also directly manufactures oxytocin and antidiuretic hormones (ADH or vasopressin). The hypothalamic-releasing factors cause the interior pituitary gland to secrete growth hormone, prolactin, TSH, the gonadotropic hormones follicle-stimulating hormone, luteinizing hormone, and ACTH. The anterior pituitary hormones directly control the release of thyroid hormone (T3 and T4), cortisol, testosterone in men, and estrogen and progesterone in women [13]. In some patients with excessive hormone levels caused by a tumor of the involved

endocrine gland, feedback inhibition does not suppress the overproduction of the hormone, and the tumor functions autonomously [14; 15].

Diurnal variation is another of the control mechanisms affecting hormonal secretion. A 24-hour cyclical variation in the secretory rates of certain hormones can be seen. For example, growth hormone levels are highest in the first 90 minutes after sleep begins. These circadian rhythms have been found to be different for each hormone. It is evident that the endocrine system affects all aspects of the organism. Through the hormonal secretion of its glands, the system controls and regulates the metabolic processes of anabolism and catabolism, the function of muscles, growth and reproduction, energy production, stress reactions, electrolyte balances, and personality development [14; 15].

Antidiuretic Hormone (ADH)

The storage and release of ADH are influenced by such factors as plasma osmolality, blood volume, physiologic and psychological stress, and input from the central nervous system. ADH is produced in the hypothalamus and then transported to the posterior pituitary gland where it is stored. In the posterior pituitary gland, oxytocin and ADH are bound to the protein neurophysin and released into the circulation in response to specific physiological stimuli [3].

ADH plays an important role in the reabsorption of water by the kidneys; decreased ADH leads to diuresis, and increased ADH leads to fluid retention [16]. ADH is typically responsible for osmoregulation, but this changes when a person has a reduction in blood volume, which shifts ADH from osmoregulation to blood volume regulation [17]. ADH induces water reabsorption via vasopressin 2 receptors in the kidneys [18]. The main osmotic stimulus for ADH secretion is increased plasma osmolality and the main non-osmotic stimulus is hypovolemia [18]. The osmotic threshold for ADH is approximately 280–290 mOsm/Kg [17]. As such, ADH levels will significantly decrease when plasma osmolality drops below this level. Plasma osmolality greater than 280–290 mOsm/kg will lead to increased ADH release [17].

Growth Hormone

Growth hormone, also referred to as somatotropin, is produced in the pituitary gland [19]. An estimated 50% of the cells in the anterior pituitary are somatotrophs (cells that secrete growth hormone) [20]. Secretion of growth hormone by the anterior pituitary gland occurs in a pulsatile manner, and the majority (up to 70%) occurs at night during non-REM (typically stage 3) sleep [21; 22]. Therefore, the amount and quality of sleep plays an important role in growth and development.

Growth hormone-releasing hormone (GHRH) is secreted from the hypothalamus, so growth hormone levels are primarily under hypothalamic control [22; 23]. Growth hormone activates hormone-sensitive lipase (which results in metabolism of fat for energy), affects insulin sensitivity, and stimulates the formation of insulin-like growth factor in the liver [20; 24].

Growth hormone can first be detected in the fetus near the end of the first trimester, with levels peaking at 20 weeks and decreasing after birth [21]. It will fall to adult levels until puberty, when levels increase [21]. After puberty, the levels decrease again and remain relatively stable until mid-adulthood, when they undergo another drop [21]. Levels of growth hormone may be increased during fasting or exercising and decreased in those with central obesity [21; 23].

In addition to its role in normal development, growth hormone is necessary for the maintenance of bone health. It stimulates osteoblast differentiation and proliferation and increases calcium absorption in the intestines [23]. Further, it plays a role in appetite, cognitive function, energy, memory, mood, neuroprotection, and sleep [25].

Glucocorticoids

The glucocorticoids function in carbohydrate, fat, and protein metabolism and play an important role in the body's response to stress and emotional well-being. The principal glucocorticoid secreted by the adrenal cortex is cortisol, which constitutes 95% of cortical production; corticosterone and cortisone are also produced.

Glucocorticoids act on all cells in the body [26]. Cortisol, the main glucocorticoid, is secreted based on the circadian rhythm and in response to stress; for this reason, it is also known as the stress hormone. When the body is experiencing stress, the pituitary gland secretes ACTH, which stimulates the production and release of cortisol [27]. Cortisol also plays a role in nutrient metabolism, immune response to inflammation, regulation of blood pressure, blood glucose levels, and body fluid homeostasis [28; 29].

Mineralocorticoids

The principal and most potent mineralocorticoid secreted by the adrenal cortex is aldosterone. Desoxycorticosterone and corticosterone are also secreted, but their actions are of minor importance. Aldosterone enters the circulation and travels to the kidney, where it binds to a specific receptor in the cytoplasm of the epithelial cells of the distal convoluted tubules. This receptor initiates a series of biochemical events that result in the major physiologic action of aldosterone [5; 9].

Aldosterone increases the reabsorption of sodium and the secretion of potassium. This is accomplished as an exchange of sodium ions for potassium or hydrogen ions, which results in the excretion of potassium and hydrogen into the urine and the retention of sodium. As sodium is reabsorbed into the blood, it brings with it water and chlorides, which mechanically increases the blood volume. This action of aldosterone is vital to the maintenance of the extracellular fluid volume. Aldosterone also promotes sodium reabsorption to a lesser degree from the sweat glands, salivary glands, and gastrointestinal (GI) tract [2; 3].

Aldosterone is an important factor in the maintenance of circulatory blood volume homeostasis through its effect on the electrolyte balance and its control of blood volume. It is the most potent hormonal regulator of electrolyte excretion. The secretion of aldosterone is regulated by three (or possibly four) major mechanisms: the renin-angiotensin system, ACTH, plasma potassium levels, and perhaps prostaglandins.

Although chiefly affecting the secretion of cortisol, ACTH is also thought to affect aldosterone production for short periods. This appears to be related to crises, during which ACTH causes an increase in the secretion of glucocorticoids and stimulates the production of aldosterone. This effect of ACTH is thought to be minor and secondary to that of the renin-angiotensin system and serum potassium levels [3].

The ratio of serum sodium levels to serum potassium levels is another important regulator of aldosterone secretion. If the serum potassium level rises or the serum sodium level decreases, changing the sodium-potassium ratio, the adrenal cortex will be stimulated to produce aldosterone. Prostaglandins are also thought to be involved in aldosterone secretion through the relation of sodium and water excretion and the release of renin [5; 9].

Adrenal Medullary Hormones

The primary hormones secreted by the adrenal medulla are norepinephrine and epinephrine. Norepinephrine increases the contraction of the blood vessels, which increases peripheral resistance and causes the blood pressure to rise. This hormone also dilates the pupils of the eyes, increases the force and rate of myocardial contraction, and inhibits the activity of the GI system. It causes peripheral vasoconstriction, which diverts blood away from less-needed areas (e.g., the GI tract) toward the heart and skeletal muscles in a "fight-or-flight" response. Because of the length of time norepinephrine is retained in the circulation (two to three circulation times), it has an effect ten times larger than that of the sympathetic nervous system [5].

Epinephrine increases body metabolism and, in conjunction with glucagon, elevates the plasma glucose levels by glycogenolysis (the conversion of glycogen to glucose). Epinephrine also inhibits the secretion of insulin and elevates blood lipid levels by promoting lipolysis. These actions provide the body with a plasma glucose source for increased energy expenditure. Epinephrine is also able to constrict the arterioles of the skin selectively (causing pallor) while dilating the blood vessels of the heart and skeletal muscles, again vital to the stress response [5].

It is important to remember the permissive role of the glucocorticoids with respect to catecholamines. In the absence of cortisol, the vasoconstrictive and metabolic responses mediated by norepinephrine and epinephrine will not occur [5; 9].

Through innervation from the sympathetic nervous system, the secretion of the adrenal medullary hormones is influenced by emotional stresses (e.g., fear, anxiety) and physiologic stresses (e.g., childbirth, injury, cold, hypoxia, immobilization, physical exercise). The relation between the psychologic-emotional state and the endocrine system is one of the body's major homeostatic mechanisms for protecting the individual from harm and physiologic stresses in a way that preserves integrity [9].

NURSING ASSESSMENT

Assessment of pituitary and adrenal issues should begin with a nursing history, followed by a physical examination. Exams should include determination of the patient's signs and symptoms, past medical history, family history, and any medications or supplements that the patient is taking. During the physical assessment, nurses should use the skills of inspection, olfaction, auscultation, percussion, and palpation. Vital signs and the patient's weight should also be obtained during the patient assessment.

PHYSICAL ASSESSMENT

Vital Signs

Patients with suspected pituitary or adrenal disorder should have their height and weight assessed and compared with growth charts. A careful developmental and familial growth history may help in the interpretation of abnormalities. Blood pressure should be measured in both arms initially and in at least two positions (e.g., supine and seated). Apical and radial pulse rates, rhythm, and quality should be evaluated, along with respiratory rate, rhythm, and depth. The patient's temperature should also be recorded [30].

General Appearance

Whether a patient's appearance closely matches his or her chronologic age should be noted. The symmetry and proportionality of the body parts should be assessed. Weight distribution and any abnormal movements of the extremities or face (e.g., spasms or twitching of facial muscles) should be noted. A plethoric (round, erythematous), "moon" face suggests Cushing syndrome [30].

Skin, Hair, and Nails

Pituitary and adrenal dysfunction can affect the temperature and texture of the skin. For example, pheochromocytoma is associated with increased skin temperature with sweating. Ecchymoses often accompany Cushing syndrome, and vitiligo has been seen in patients with adrenal insufficiency. Other possible skin lesions include skin infections (e.g., furuncles, carbuncles), ulcerations, and diabetes-related skin changes (e.g., candidiasis, diabetic dermopathy, diabetic xanthoma) [30]. The texture and distribution of body hair should also be considered.

Eyes

Nurses should pay careful attention to any changes in visual acuity or visual fields defects. Patients whose disorders induce hyperglycemia may display diabetic retinopathy (e.g., retinal edema, microaneurysms, retinal hemorrhages, exudates). Patients with these conditions require immediate referral to an ophthalmologist [30].

Cardiorespiratory System

The patient's heart rate and rhythm should be assessed, with attention to murmurs or extra heart sounds. In pheochromocytoma, hypertension, tachycardia, and atrial fibrillation may be noted. Cushing syndrome often leads to congestive heart failure, as manifested by lethargy, dyspnea on exertion, paroxysmal nocturnal dyspnea, and cough. Hypertension can accompany Cushing syndrome, and hypotension can accompany adrenal insufficiency. Because of the interrelation between cardiac and respiratory systems, cardiac pathology often produces changes

in the lungs (e.g., pleural effusions, congestive heart failure). Therefore, the lungs should be assessed for abnormal breath sounds, rales, rhonchi, wheezes, and pleural friction rubs [30].

Abdomen and Genitals

The abdomen should be assessed for any asymmetry that might indicate ascites, enlargement of an organ, or a mass. Auscultation may detect bruits (especially over the renal arteries), and palpation can uncover abdominal pain [30].

Assessment of the genitalia is important in the evaluation of patients with pituitary/adrenal dysfunction, because changes in sexual development and reproductive function often occur. The appearance and any abnormalities of the patient's genitals should be noted. The presence or absence of secondary sex characteristics is recorded, including agreement between the genital, hormonal, and psychologic sex of the patient [30].

Neuromuscular System

Patients should be evaluated for current and past fractures, as may be seen in Cushing syndrome. Other issues may include bone pain, joint pain, and generalized muscle weakness. The neurologic and endocrine systems work closely together to maintain the homeostasis of the internal environment and to help cope with stress. Therefore, pathology in the nervous system often affects endocrine function (e.g., a benign tumor of the pituitary gland can cause hypersecretion of anterior pituitary hormones) and pathology in the endocrine system can be reflected in the nervous system [30].

Nurses should conduct a careful neurologic evaluation, including assessment of mental status, cranial nerves (as dysfunction of cranial nerves I and II is associated with enlargement of the pituitary gland), motor and sensory function, the cerebellum, and deep tendon and superficial reflexes. Ataxia can occur in hypocalcemia and acromegaly. Thoroughness in examination and accuracy in recording findings are essential, and all abnormal findings require additional evaluation [30].

DIAGNOSTIC TESTS

Single measures of endocrine function are rarely sufficient to support a diagnosis but nevertheless should be an integral part of the whole data base. In pituitary and adrenal testing, be aware of the importance of patient preparation and adhere strictly to the testing protocols. Patient and environmental influences that might modify the test results are important nursing considerations [31]. This section will focus on some of the most commonly used tests; general screening tests, such as complete blood count and basic metabolic panel, will not be discussed but are usually part of the workup.

Serum and Urine Osmolality

Serum osmolality testing provides information about the number of particles dissolved in the serum, while urine osmolality provides information about the kidney's ability to concentrate urine [32]. Serum and urine osmolality are controlled by ADH [33]. The release of ADH reduces the amount of fluid output by the kidneys, increasing blood volume and decreasing serum osmolality while simultaneously increasing urine osmolality. Serum osmolality is also increased in patients with hypernatremia and decreased in those with hyponatremia. The opposite is true for urine osmolality—it is increased with hyponatremia and decreased with hypernatremia. Certain medications can affect serum and urine osmolality (***Table 1***).

Cumulatively, serum and urine osmolality will help to estimate the ability of the kidney tubules to concentrate or dilute urine and can be used to aid in the diagnosis of diabetes insipidus and SIADH [33]. The normal range for serum osmolality in adults is 280–300 mOsm/kg, and the normal range for urine osmolality is approximately 250–900 mOsm/kg [32; 33]. Normal reference ranges may vary slightly depending on the source or laboratory. Diabetes insipidus is associated with elevated serum osmolality, while decreased values would be indicative of SIADH.

MEDICATIONS THAT IMPACT SERUM AND URINE OSMOLALITY	
Effect	**Medications/Drugs**
Increased serum osmolality	Corticosteroids Glycerin Insulin Mannitol
Decreased serum osmolality	Carbamazepine Chlorpromazine Hydrochlorothiazide Cyclothiazide Doxepin Lorcainide MDMA/Ecstasy
Increased urine osmolality	Anesthetic drugs Furosemide Mannitol Octreotide Vincristine
Decreased urine osmolality	Captopril Demeclocycline Glyburide Lithium Octreotide Tolazamide Verapamil
Source: [32]	*Table 1*

Urine osmolality tests use the first-voided urine specimen, which is thought to represent the maximum concentration ability of the kidneys [34]. Prior to this test, the patient should be asked about recent alcohol use and blood transfusions, as both can interfere with the results [33]. Alcohol should be avoided for at least 12 hours prior to the collection of the serum sample [33].

Water Deprivation Test

A water deprivation test involves withholding water from the patient for 6 to 17 hours while monitoring body weight, vital signs, urine volume, and urine osmolality every 1 to 2 hours [16; 35]. Blood samples are also obtained two hours after the start of fluid deprivation and before giving desmopressin [35]. At the end of the test, desmopressin is given and urine osmolality is tested [18]. Water deprivation typically leads to more concentrated urine and increased weight [16]. Extended deprivation results in a urine osmolality level greater than 800 mOsm/kg (considered maximally concentrated) [18]. In patients with complete central diabetes insipidus, urine osmolality will remain less than 300 mOsm/kg during water deprivation but will increase by more than 50% after the administration of desmopressin [18]. With nephrogenic diabetes insipidus, urine osmolality will remain less than 300 mOsm/kg throughout the test and administration of desmopressin will not induce an increase in urine osmolality [18]. Although the test is fairly easy, interpreting the results can be a challenge [35].

If any of the following develop during a water deprivation, the test should be halted [35]:

- Body weight decreased by more than 3%
- Symptoms of orthostatic hypotension, with a heart rate increase of 15% or a mean arterial blood pressure decrease of 15%
- Increase in plasma sodium level to 150 mmol/L or more

Hypertonic Saline Test

The hypertonic saline test can be used to aid in the diagnosis of diabetes insipidus. This procedure involves the administration of a 250-mL bolus of 3% hypertonic saline; the patient is given a 5% glucose infusion and is instructed to drink 30 mL of water per kg of body weight within one hour. Rapid sodium measurements are taken every 30 minutes; plasma osmolality, serum sodium, urea, and glucose are also monitored [18; 35]. If the sodium level rises above 147 mmol/L, the infusion should be stopped. If copeptin is being measured, it should be done at this point [18]. With the hypertonic saline test, a plasma copeptin measurement of 4.9 pmol/L or less indicates complete or partial central diabetes insipidus [35].

The advantages of measuring copeptin are that small amounts of serum are needed, the samples collected are stable for one week at room temperature, and results are available within two hours [18; 35]. The release of copeptin is triggered by osmotic stimuli and volume depletion [18]. Research has shown that measuring osmotically stimulated copeptin is a useful diagnostic tool [35]. Levels may be measured with a water deprivation or hypertonic saline test, but results are more accurate with hypertonic saline than water deprivation [35]. Baseline copeptin levels should be obtained followed by levels prior to desmopressin [35]. Basal plasma copeptin levels of less than 2.6 pmol/L are indicative of complete central diabetes insipidus [35]. If the ratio of copeptin to plasma sodium is less than 0.02 pmol/L, partial central diabetes insipidus is suggested [35].

Growth Hormone Stimulation Test

As noted, growth hormone is secreted by the anterior pituitary gland periodically throughout the day, with levels highest at night. Due to the episodic nature of growth hormone secretion, random checks are rarely useful [32]. However, to assess for growth hormone deficiency or acromegaly, a growth hormone test is often completed together with a growth hormone suppression test, growth hormone stimulation test, and insulin-like growth factor test [33]. Before testing, the patient should avoid eating, drinking, and exercising for 10 hours [33]. The typical normal value is less than 5 ng/mL in men, less than 10 ng/mL in women, and 0–10 ng/mL in children [33]. Decreased levels are associated with a deficiency, and increased levels are associated with acromegaly.

The growth hormone stimulation typically takes two to five hours to complete and is typically started in the morning with a baseline blood sample [36]. Medication (arginine, glucagon, or insulin) will be given intravenously to stimulate the pituitary gland to release growth hormone [36]. Blood samples may be obtained at baseline and 30, 60, 90, and 120 minutes after administration of the testing agent [33]. Prior to growth hormone stimulation and suppression tests, patients should avoid strenuous activity for at least 12 hours [32]. If the patient has normal values throughout this test, growth hormone deficiency can be ruled out. However, failure of growth hormone levels to increase as expected is an indicator that the patient may have a growth hormone deficiency.

Insulin Tolerance Test

Because hypoglycemia stimulates growth hormone secretion, an insulin tolerance test may also be used to assess growth hormone sufficiency [21]. An insulin tolerance test involves hypoglycemia induced by an intravenous (IV) injection of insulin [37]. With this test, regular insulin is administered intravenously to drop the patient's glucose levels below 40 mg/dL [21]. Within 30 to 60 minutes, growth hormone levels are measured and should reflect a peak. Throughout the course of this test,

the patient may experience signs and symptoms of hypoglycemia, including dizziness, anxiety, tremors, sweating, and tachycardia. Seizure and/or loss of consciousness are possible, so close monitoring during the test is necessary [21].

Cortisol Levels

The body typically responds to stress by triggering the pituitary to make ACTH, with a resultant elevation in cortisol [37]. Blood is drawn at the start of the test and every 30 minutes for 2 hours [37]. In patients with Cushing syndrome, cortisol levels are higher than expected [32]. This test is not appropriate for persons taking insulin or on hemodialysis [32]. Patients should be instructed to report signs and symptoms of hypoglycemia.

Growth Hormone Suppression Test

Growth hormone suppression tests are used to aid in the diagnosis of acromegaly. After the baseline blood sample is obtained, the patient is instructed to drink a solution containing glucose within five minutes [38]. Blood samples are then obtained after 60 and 120 minutes [33]. If possible, glucocorticoids should be halted prior to the test [38]. In general, this test is not used for screening—it is only ordered if a patient presents with signs and symptoms of acromegaly [38]. If growth hormone levels stay the same or increase during the test, acromegaly is suggested [38].

Insulin-like growth factor regulates the effects of growth hormone, but it remains stable throughout the day [39]. Testing Insulin-like growth factor levels is indicated for patients with suspected acromegaly or to monitor the effectiveness of growth hormone treatment [39; 40]. Elevated levels in the presence of elevated growth hormone levels are indicative of acromegaly [39].

ACTH Stimulation Test

ACTH stimulation testing involves the infusion of cosyntropin (a synthetic form of ACTH) as either intravenous or intramuscular injection [32]. Cortisol levels are collected at baseline, 30 minutes, and (in some cases) 60 minutes after the medication bolus [32]. Normal baseline cortisol levels are greater than 5 mcg/dL; normal levels at 30 to 60 minutes are 18–20 mcg/dL [32]. In response to the cosyntropin infusion, the adrenal cortex should release two to five times the amount of normal plasma cortisol levels within 30 minutes [24]. Prior to undergoing ACTH stimulation testing, patients should abstain from nicotine, alcohol, cortisol-affecting medications, and strenuous activity for at least 12 hours [32]. Some patients may be instructed to remain in bed for one hour prior to the test [32].

Urinary Free-Cortisol Test

For the 24-hour urinary free-cortisol test, urine is collected over 24 hours to measure the amount of unbound cortisol filtered by the urinary system [41]. The accuracy of this test is dependent on the patient's glomerular filtration rate and urinary volume [41]. Normal cortisol levels in a 24-hour urine collection are 450–700 nmol/L [42]. Elevated levels indicate Cushing syndrome, while low levels could indicate Addison disease.

Low-Dose Dexamethasone Suppression Test

The low-dose dexamethasone suppression test (LDDST) is completed by administering low doses of dexamethasone at night, followed by a blood draw in the morning [28]. For this test, the patient is given 1 mg of dexamethasone orally at 11 p.m. and cortisol levels are measured at 8 a.m. [32]. Alternately, dexamethasone may be given every 6 hours for 48 hours, followed by a blood sample 6 hours after the last dose [28]. Cortisol levels are expected to be less than 1.8 mcg/dL when the sample is taken [32]. Administration of dexamethasone decreases cortisol levels, so an elevated finding is indicative of abnormality. This test is used to distinguish between Cushing syndrome and Cushing disease (specifically

caused by a pituitary tumor that secretes excessive ACTH) [32]. However, certain medical conditions can affect the results of the test, including severe obesity, pregnancy, dehydration, uncontrolled diabetes, severe weight loss, alcohol withdrawal, severe injury, and stress [33].

Corticotropin-Releasing Hormone Stimulation Test

The corticotropin-releasing hormone stimulation test can help to distinguish between Cushing syndrome and Cushing disease [32]. Corticotropin-releasing hormone is given intravenously and eight cortisol and ACTH levels are collected, one at baseline and the others at 5, 15, 30, 60, 120, and 180 minutes after administration [32]. The expected result in healthy individuals is a peak in cortisol (greater than 20 mcg/dL) and a two- to four-fold increase in ACTH within 30 to 60 minutes [32]. Higher cortisol levels are associated with Cushing disease; cortisol levels that fail to increase may indicate ectopic ACTH secretion [32].

Inferior Petrosal Sinus Sampling

Bilateral inferior petrosal sinus sampling (IPSS) can be used to distinguish Cushing disease from ectopic ACTH secretion [43]. This test is guided by fluoroscopy, typically while the patient is under general anesthesia, and will take 60 to 90 minutes [43; 44]. Catheters are inserted through both the left and right femoral veins and advanced to the petrosal sinuses [43]. Samples are drawn simultaneously from the inferior petrosal sinus and the peripheral veins for plasma ACTH five minutes and one minute before administration of 1–100 mcg corticotropin-releasing hormone in a peripheral vein. Samples for plasma ACTH are collected at 2, 5, and 10 minutes after administration. A peripheral sample for plasma cortisol is also taken along with each sample for plasma ACTH.

ACTH should be in higher concentrations when measured from a sample collected close to the gland [43]. Possible complications associated with this test include a groin hematoma and rarely subarachnoid hemorrhage, brainstem injury, brainstem stroke, and infection [43]. Though less accurate, jugular vein sampling is a less-invasive alternative to IPSS [43].

If a tumor is the cause of excess ACTH, this test will help to identify the location [44]. Additionally, comparing results from the right and left sides can help identify the best approach to remove the tumor while maintaining some functional pituitary tissue [44].

Other Tests and Imaging

The late-night salivary cortisol test measures cortisol in the saliva at night, when the levels typically drop; levels will remain elevated in patients with Cushing syndrome [28]. Serum or urinary cortisol, aldosterone, and/or ACTH may also be assessed.

The diagnostic investigation of anterior pituitary dysfunction often involves an x-ray, computed tomography (CT), or most commonly, magnetic resonance imaging (MRI) scan of the skull. A cerebral flow brain scan or echoencephalogram also may be used. In the presence of a pituitary tumor, a widening of the sella turcica (the bony seat of the pituitary gland) may be visualized. To further detect the presence of a brain tumor, a complete neurologic evaluation may be done, including assessment of the patient's visual fields [34].

NURSING DIAGNOSES

The nursing diagnosis forms the basis of the plan of care for the patient and provides guidelines for its implementation and evaluation. Because pituitary/adrenal dysfunction has widespread effects, many nursing diagnoses can be used in caring for these patients. Each patient's actual problem is unique, however, and requires a skillful assessment. Recognition of the specific problem and its etiology is integral to a comprehensive, well-executed nursing care plan [45].

INEFFECTIVE INDIVIDUAL COPING

Because of the profound physiologic and psychosocial stresses on the patients with these conditions, it is not unusual for them to be fearful and have difficulty coping. Feelings of anxiety can be directly related to the disorder (as in pheochromocytoma) or exogenous, resulting from feelings of unexplained apprehension about the situation [45].

Pituitary/adrenal disorders often require the patient and family to make major changes in lifestyle. Patients may require lifelong pharmacotherapy and medical/nursing supervision. They also may face the possibility of major surgery and may have some degree of transitory or permanent sensory loss [45].

ALTERATION IN THOUGHT PROCESSES

Central nervous system involvement may produce a variety of problems in patients, ranging from headaches and lethargy (e.g., with pheochromocytoma) to outright psychosis (e.g., Cushing syndrome). Alterations in thought processes and perception pose difficulties not only for patients but for their families and friends as well [46].

ALTERATION IN COMFORT

Some patients with pituitary or adrenal dysfunction will have problems with thermal regulation. For example, patients with pheochromocytoma or hypoglycemia often experience excessive sweating. Those with acromegaly often experience joint pain [45; 46].

DISTURBANCE IN SELF-CONCEPT

Changes in the skin and hair occur in patients with pituitary or adrenal dysfunction and can contribute to disturbances in body image. Increases in skin pigmentation may occur in patients with Addison disease. Ecchymosis develops in patients with Cushing syndrome due to changes in the fragility of the capillaries. Facial flushing is often a sign of pheochromocytoma. Hirsutism is a problem for patients with adrenal tumor or hyperplasia and is an especially bothersome body image issue for women [45; 46].

Patients with these disorders may have an impaired ability to manage self-care or maintain their home environment. They are at increased risk for injury because of weakness, fatigue, and visual disturbances. For example, weakness of the musculoskeletal system is seen in patients with acromegaly and Cushing syndrome. Patients with Cushing syndrome have an increased incidence of fractures. Fatigue often accompanies adrenal insufficiency, hypoglycemia, and acromegaly. Patients with pituitary tumors may have some level of visual impairment [45; 46].

Sexual dysfunction may occur as loss of libido or impotence. Menstrual problems are also relatively common [45; 46].

ALTERATION IN NUTRITION AND BOWEL ELIMINATION

Anorexia and weight loss are common in patients with adrenal insufficiency, pheochromocytoma, and hyperkalemia [45; 46]. Alteration in bowel elimination, specifically diarrhea, may be seen in patients with Addison disease, while constipation can occur in patients with hypercalcemia and pheochromocytoma [45; 46].

ALTERATION IN FLUID VOLUME

Actual or potential fluid volume deficits occur in patients with posterior pituitary disorders. In addition, patients with Cushing syndrome may develop congestive heart failure. Patients with hypercalcemia and hyperaldosteronism may have polydipsia and polyuria [45; 46].

DIABETES INSIPIDUS

Diabetes insipidus is a rare disorder of the posterior pituitary caused by insufficient production or utilization of ADH and characterized by polyuria, polydipsia, and hypernatremia. It is seen in approximately 3 out of 100,000 people in the United States and is more common in adults but can develop in individuals of all ages [47]. Risk factors for the development of diabetes insipidus include tumors, trauma, medications, and alcohol consumption [16].

PATHOPHYSIOLOGY

The underlying cause of diabetes insipidus is generally either pituitary (central) or nephrogenic. More rarely, it may develop during pregnancy or related to a mental disorder.

Central Diabetes Insipidus

Approximately 50% of patients have primary central diabetes insipidus, also known as pituitary or primary diabetes insipidus. This form is associated with familial and congenital factors as well as with subclinical encephalitis. Secondary diabetes insipidus is diabetes insipidus arising from a variety of causes, including hypophysectomy, tumors (e.g., metastatic carcinoma of the breast, craniopharyngiomas), trauma (e.g., basilar skull fractures), vascular lesions (e.g., hemorrhage, aneurysm), infection (e.g., syphilis, encephalitis, meningitis), histiocytosis, and granulomatous disease (e.g., sarcoidosis, tuberculosis) [45; 46].

Patients with central diabetes insipidus have an impaired ability to synthesize and secrete vasopressin (ADH) [26; 47]. In most healthy people, ADH is secreted by the pituitary gland when plasma osmolality increases, but this does not occur in those with central diabetes insipidus [48]. Central diabetes insipidus is classified as either complete or partial, depending on the level of ADH present in the body [18].

A variety of factors can lead to central diabetes insipidus, including genetic mutation, medications (e.g., beta-adrenergic agents, ethanol, halothane, phenytoin, opioid antagonists), head (pituitary) trauma, intracranial tumor, infection (e.g., meningitis, encephalitis, tuberculosis), autoimmune disease, disorders of the hypothalamus or pituitary gland, and brain surgery [26; 48]. Rarely, central diabetes insipidus may be the result of snakebite. One genetic cause is Wolfram syndrome, an autosomal dominant disorder associated with diabetes mellitus, diabetes insipidus, optic nerve atrophy, and sensorineural hearing loss [48]. The most common causes are trauma and malignancy.

Lesions and autoimmune disorders can lead to the destruction of vasopressin neurons in the hypothalamus, while surgery and trauma can damage or destroy the vasopressin neurons [49]. It is important to note that the body's ability to synthesize vasopressin is greater than the body's needs, so up to 80% to 90% of the vasopressin neurons in the hypothalamus can be destroyed before diabetes insipidus develops [49].

A transient form of polyuria may develop in patients post-trauma or post-surgery, but it usually resolves within four days [49]. In rare cases, these patients may develop a permanent form of diabetes insipidus [49].

Nephrogenic Diabetes Insipidus

In patients with nephrogenic diabetes insipidus, the kidneys do not respond normally to vasopressin [26]. The underlying etiology of this condition may be genetic/congenital, medication-induced kidney damage (e.g., with amphotericin, cisplatin, clozapine, demeclocycline, furosemide, lithium [most common], methicillin), renal or urinary tract infection, or chronic disease processes (e.g., amyloidosis, chronic renal failure, polycystic kidney disease, sickle cell disease, Sjögren syndrome) [18; 26; 50]. Acquired nephrogenic diabetes insipidus is more common than the hereditary form [50].

The genes associated with the hereditary form of nephrogenic diabetes insipidus prevent the kidneys from responding to ADH [50]. Infants with hereditary nephrogenic diabetes insipidus will develop signs and symptoms of the disease within a few months of birth [50].

Gestational Diabetes Insipidus

Gestational diabetes insipidus is a type of transient diabetes insipidus that develops in 2 to 4 of every 100,000 pregnancies [51]. During pregnancy, ADH production is increased and plays a role in the increased blood volume. At the same time, placental vasopressinase, which metabolizes ADH, is increased [51]. This is more commonly seen in

pregnancies with multiple fetuses because of the increased placental mass [18; 51]. In the majority of cases, the patient will have a normal delivery and healthy newborn [51]. After delivery, vasopressinase levels will decrease by approximately 25% each day, reaching undetectable levels at four to six weeks postpartum and resulting in resolution of the disorder [51].

It is important to note that some patients may have undiagnosed diabetes insipidus prior to pregnancy, with symptoms not becoming apparent until after they become pregnant [51]. If the patient has undiagnosed diabetes insipidus discovered during pregnancy, it is classified as central or nephrogenic, depending on the underlying pathophysiology.

Psychogenic Diabetes Insipidus

In rare cases, patients may develop a psychiatric condition involving the consumption of large amounts of fluids [26]. This is not true of diabetes insipidus, but it can be life-threatening and has been associated with increased morbidity and mortality. In psychogenic cases, the function of the pituitary gland and kidneys remain intact, and extracellular fluid dilution develops and inhibits ADH secretion, leading to diuresis [52]. The increased fluid intake leads to functional diabetes insipidus [52].

This condition can be seen in patients with a variety of mental health disorders, including autism, schizophrenia, schizoaffective disorder, and bipolar disorder [53]. Schizophrenia is a common cause, with 11% to 20% of patients with schizophrenia developing psychogenic diabetes insipidus [53].

For some patients, increased fluid intake is a compulsion rather than a response to thirst [53]. Another subset of patients believes that increased water intake is healthy [53]. These individuals typically do not have a mental health disorder but are rather misinformed about the risks of overconsumption of water.

SIGNS AND SYMPTOMS

Patients with diabetes insipidus present with polyuria, nocturia, polydipsia, increased serum osmolality, decreased urine osmolality, and decreased urine specific gravity [16; 26]. Many report extreme thirst, even at night, leading to increased fluid intake at all hours [52]. In addition to drinking throughout the day, patients with diabetes insipidus often have a preference for cold or ice water [18]. An intact thirst drive will often prevent severe dehydration and maintain homeostasis in those affected [48]. In some cases, the thirst mechanism is faulty because of damage to osmoreceptors in the hypothalamus, leading to decreased fluid intake and severe dehydration [49].

Patients with diabetes insipidus will have dilute and light-colored urine. Polyuria will develop regardless of normal contributing factors to urine output, such as fluid intake. Patients may urinate as much as 10–20 L/day [26]. In most cases, the urine will be hypotonic and serum osmolality will increase [16; 26]. In patients with a serum osmolality of 300–330 mOsm/kg, symptoms may not be apparent [49]. Patients with severe dehydration may develop weakness, postural dizziness, confusion, azotemia, hyperglycemia, secondary hyperaldosteronism with hypokalemia, and coma [49]. Under normal circumstances, an increase in serum osmolality would result in a drop in blood pressure and subsequent secretion of ADH [16]. Additionally, when a patient has increased serum osmolality they will often be very thirsty [16]. Thirst will lead to increased fluid intake, which increases fluid in the vasculature and restores fluid balance. However, in patients with diabetes insipidus, this does not occur, further increasing the risk for dehydration and hypovolemic shock [16].

Serum sodium levels will be normal or increased, with hypernatremia typically developing if the patient does not drink enough water to account for the increased urine output [26]. Patients with hypernatremia may present with altered mental status, myoclonus (muscle jerking), seizures, and focal deficits [26]. If untreated, the patient may progress to an altered level of consciousness or death [16].

Infants with congenital nephrogenic diabetes insipidus present with enuresis, poor intake, poor weight gain, poor growth (failure to thrive), irritability, fevers, diarrhea, and vomiting [50]. If a child with this condition develops dehydration on multiple occasions, it can lead to problems with growth and development [50].

As many as 50% of patients with underlying diabetes insipidus will have increased signs and symptoms during pregnancy [51]. Patients with underlying diabetes insipidus do not have increased levels of ADH during pregnancy, so the symptoms of diabetes insipidus may become apparent [51]. Patients are at increased risk for dehydration and hypernatremia if they experience diabetes insipidus during pregnancy [51]. However, during pregnancy, thirst is triggered at lower serum osmolality levels, which can act as a protective factor [51].

Patients with an exacerbation of a mental illness may also increase their fluid intake; this increase is not related to the regulation or maintenance of homeostasis [53]. Patients with psychogenic diabetes insipidus drink more than 3L of fluids per day [52]. In patients with compulsive fluid intake, drinking fluids calms an acute anxiety and the compulsion can be so strong that they will drink from inappropriate and unhealthy water sources (e.g., toilets) [53]. Individuals who compulsively drink fluids may also have comorbid nicotine, alcohol, and/or eating disorders [53]. Patients with psychogenic diabetes insipidus urinate as often as every 30 minutes, and the urine is dilute, with decreased specific gravity and decreased osmolality [52]. These patients may also report fatigue and constipation [52].

Patients with psychogenic diabetes insipidus typically do not drink fluids at night, which can help differentiate it from true cases of diabetes insipidus [53]. Most patients with diabetes insipidus will develop hypernatremia due to the fluid deficit, but patients with psychogenic diabetes insipidus may develop hyponatremia [53]. If hyponatremia develops in these patients, it is important to determine if it is the result of excessive fluid intake or another cause (e.g., medication) [53]. Patients with schizophrenia and diabetes insipidus typically have lower body weight and increased rates of alcohol consumption and smoking compared with patients without diabetes insipidus [53].

DIAGNOSIS

The diagnosis of diabetes insipidus can be a challenge, and misdiagnosis carries the risk for severe complications [35]. Diabetes insipidus is diagnosed by routine screening tests, such as specific gravity of urine, plasma sodium levels, osmolality tests, and water-deprivation and water-loading tests. If serum osmolality is greater than 300 mOsm/kg and urine osmolality is less than 300 mOsm/kg, the diagnosis is likely diabetes insipidus [48]. Diagnosis is confirmed if a deficiency of ADH is demonstrated and the patient's kidneys are shown to respond normally to ADH. In response to a water-deprivation challenge, patients with diabetes insipidus will demonstrate an inability to increase the specific gravity and osmolality of the urine [54; 55]. Differential diagnosis involves other causes of polyuria. A brain scan, skull x-rays, visual field testing, and full neurologic examination may be indicated to rule out the presence of a tumor.

Differentiation between the types of diabetes insipidus can be a challenge but is essential because treatment will vary based on the type identified [18]. Patients with central diabetes insipidus will respond to vasopressin with decreased urine output and increased urine osmolality [48]. If the patient has nephrogenic diabetes insipidus, there will be no response to the vasopressin [48].

A newer diagnostic tool is copeptin, a surrogate marker for ADH [18]. High basal copeptin levels are accurate in diagnosing nephrogenic diabetes insipidus [18]. The copeptin test can also be used during pregnancy, unlike the water deprivation test [51]. In nonpregnant patients, the copeptin test can be combined with the water deprivation test, which increases diagnostic accuracy of both tests [18]. It can also be combined with the administration of hypertonic saline [18].

Diagnosis of psychogenic diabetes insipidus usually requires a multidisciplinary approach [52]. The care team may include primary care, endocrinologists, nephrologists, and psychologists.

TREATMENT

The treatment plan for patients with diabetes insipidus depends on the type and the associated signs and symptoms.

Central Diabetes Insipidus

For patients with mild cases of central diabetes insipidus, treatment may be as simple as increasing fluid intake [56]. However, most patients will require ADH replacement therapy. In acute cases, patients are given intravenous or subcutaneous vasopressin [16]. Long-term treatment involves the administration of desmopressin orally, subcutaneously, or intranasally [16]. The most common adverse effect of desmopressin administration is hyponatremia, although fluid retention can also develop [48]. Intranasal desmopressin can result in eye irritation, headaches, dizziness, rhinitis, epistaxis, coughing, and flushing [48]. If diabetes insipidus is caused by pituitary tumor, hypophysectomy may be required [16].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Society for Endocrinology recommends that for those patients with central diabetes insipidus and normal serum sodium and who require maintenance intravenous fluid therapy, the type and volume administered should be equivalent to the daily requirements appropriate for other patients without central diabetes insipidus. This should be given together with the agreed, prescribed dose of desmopressin.

(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6013691. Last accessed July 19, 2024.)

Level of Evidence: Expert Opinion/Consensus Statement

For infants with congenital central diabetes insipidus, the preferred treatment is usually thiazide diuretics [48]. Thiazide diuretics work by inhibiting the amount of sodium lost by the kidneys, which can lead to decreased water loss [57]. However, thiazide diuretics can paradoxically decrease urine flow in some [16]. As such, urine output should be closely monitored in these patients.

Nephrogenic Diabetes Insipidus

Poorly managed nephrogenic diabetes insipidus can cause pain, infection, damage to the genitourinary system, and kidney failure [50]. Appropriate treatment will help to prevent these complications. In many cases, treatment is palliative [57]. A low-sodium diet may be prescribed to help decrease the amount of urine made by the kidneys [56]. As with all types of diabetes insipidus, fluid intake should be increased. Hydrochlorothiazide may be given to help manage symptoms and decrease urine output [56]. Patients may also be prescribed indomethacin, a nonsteroidal anti-inflammatory drug that increases urine concentration [57].

Most of the secondary causes of nephrogenic diabetes insipidus can be reversed [18]. If medications are the cause, their use should be reconsidered. If the underlying cause is lithium, it can take months to years for renal function to recover completely [18].

Infants with nephrogenic diabetes insipidus should intermittently be offered water. Patients unable to take in enough fluid to replace urine output may require a feeding tube [57]. School-aged children should have a plan in place with their school to ensure adequate access to a bathroom and to fluids. The school nurse and teachers should be included in the plan.

Gestational Diabetes Insipidus

Desmopressin is the treatment of choice for gestational diabetes insipidus, with minimal side effects for the patient and fetus [51]. It is important to consider that the dosage should usually be increased as the pregnancy progresses [51]. It is also important to correct any hypernatremia that develops.

Patients with diabetes insipidus during pregnancy are at increased risk for recurrence during any future pregnancies [51].

Psychogenic Diabetes Insipidus

For patients with psychogenic diabetes insipidus, behavioral therapy may be beneficial [52]. Medication reconciliation should be done to eliminate agents that impair water excretion, if possible [53]. The treatment of psychogenic diabetes insipidus in children should involve parents/caregivers [52]. In general, adequately addressing the underlying mental health issue will help to resolve the diabetes insipidus. Patients with psychogenic diabetes insipidus due to health misinformation should be given education on appropriate water intake [53].

In some cases, clozapine may be given to help normalize sodium levels and decrease fluid intake [53]. The choice to use this medication should be made carefully, because it is associated with significant side effects [53]. Vasopressin V2 receptor (V2R) antagonists (vaptans) may also be given to normalize serum sodium levels [53]. These medications should be used cautiously and the patient observed closely because they can lead to dehydration and renal damage [53].

Unlike the treatment of other diabetes insipidus types, these patients may be placed on fluid restriction [53]. Weight measurements can help identify patients who will benefit from fluid restriction. If the patient's weight increases, it may be an indicator for fluid restriction. Providing ice chips may also help control fluid intake for patients with psychogenic diabetes insipidus [53].

Surgical Resection

If diabetes insipidus is caused by a pituitary tumor, this must be addressed in order to resolve symptoms. Hypophysectomy can involve the resection of a small tumor or the complete removal of the pituitary gland. The major indications for hypophysectomy are a primary neoplasm of the pituitary gland (adenoma) and the need to halt the growth and spread of other endocrine-dependent malignancies (e.g., breast, ovary, or prostate cancer).

Though historically used, transcranial and transsphenoidal approaches to hypophysectomy are major surgical procedures and have largely been replaced by less invasive options, such as radiation therapy. However, in some cases, surgical resection is required. Because of the risk of damaging the pituitary and the proximity of the optic nerves, optic chiasm, carotid arteries, cavernous sinus, and hypothalamus to the operative area, the surgery involves some risk.

The surgical approach is most commonly transsphenoidal selective tumor resection guided by fluoroscopy [58]. With this type of surgery, the tumor is approached through the sphenoid sinus, avoiding brain tissue. A cut is made along the nasal septum or under the upper lip, near the base of the nose. In addition to the avoidance of brain tissue, this procedure is often associated with fewer side effects and cosmetic effects compared with other surgery types [59]. Drawbacks are that it is more time-consuming and is difficult to perform on large tumors, which often require craniotomy for removal [59]. After a transsphenoidal approach, the patient may report sinus congestion and headaches lasting for one to two weeks postoperatively [59].

Transfrontal craniotomy is indicated when the tumor extends beyond the pituitary fossa and is impinging on the optic chiasm, because this procedure provides the best view of the operative field [60]. With this technique, an opening is made in the skull and the pituitary is accessed through the brain, increasing the risk of brain injury [59]. Complications can include brain damage, stroke, blindness, meningitis, leakage of cerebrospinal fluid, bleeding, diabetes insipidus, and adverse reactions to anesthesia [59].

Transient cerebrospinal fluid leaks can occur following removal of the nasal packings. Most leaks respond to conservative measures aimed at keeping the intracranial pressure low [59]. Lifelong hormonal replacement is necessary if the entire gland is removed [60].

Prior to surgery, patients with diagnosed pituitary tumors should be observed for symptoms and signs of pituitary apoplexy, including severe headache, changes in level of consciousness, diplopia, loss of vision, and shock. Pituitary apoplexy occurs when there is spontaneous hemorrhage into the tumor secondary to rupture of the blood vessels or rapid enlargement of the adenoma with resulting infarction [61].

Postoperative care of patients who have undergone transfrontal craniotomy should also be closely observed for signs/symptoms of [61]:

- Increased intracranial pressure (e.g., hypertension, bradycardia, change in pupil size and reaction to light, changes in level of consciousness, changes in mental or neurologic status)
- Adrenal insufficiency
- Hypothyroidism (which may develop over several weeks)
- Meningitis (e.g., elevated temperature, headache, motor restlessness, photophobia, nuchal rigidity)
- Fluid imbalance (which may indicate transient or permanent diabetes insipidus)

Most patients recover rapidly from transsphenoidal surgery. Patients may report a temporary loss of smell. Oral hygiene is important to keep the oral mucosa moist. Tooth brushing is usually contraindicated because of possible tension on the suture line. Nasal packs are usually removed in 48 to 72 hours [62]. Headache may be a problem in the postoperative period and should be assessed as a possible symptom of meningitis.

A major complication in the postoperative period is hypopituitarism, which may develop into Addisonian crisis and transient or permanent diabetes insipidus. As such, these patients should be watched closely for symptoms and signs of Addisonian crisis (e.g., weakness, lethargy, fever, nausea, hypotension, dizziness) and diabetes insipidus. In the immediate postoperative period, intake and output should be measured and used as a guide to fluid balance; the specific gravity of urine should be checked after each voiding [62].

After total ablation of the pituitary gland, amenorrhea and infertility will result. For men, testosterone may relieve changes in libido and impotence secondary to the surgery. Estrogen may be prescribed for women to relieve atrophy of the vaginal mucosa. Human pituitary gonadotropins have been successful in treating infertility in patients posthypophysectomy, especially women [62].

Postoperative teaching should focus on medications prescribed, including their purpose and side effects, and the importance of regular follow-up care.

Nursing Interventions

When caring for any patient with diabetes insipidus, close monitoring of the patient's fluid balance is necessary. Nurses should also monitor the patient for dehydration, especially if the patient is confused, unconscious, or otherwise unable to communicate (e.g., infants), because these patients are unable to make their needs known regarding fluid intake. This is best done with daily weights and frequent intake and output monitoring. Patients should be assessed for signs and symptoms of fluid deficit, such as poor skin turgor and dry mucous membranes.

Treatment of diabetes insipidus may include the administration of hypotonic intravenous fluids to increase fluid in the vasculature without increasing serum sodium levels [16]. These patients should be closely monitored for fluid overload [16]. Oral fluids should be encouraged for most patients with diabetes insipidus, except those with psychogenic diabetes insipidus. Nurses should also be vigilant for signs of hypovolemic shock, including hypotension and tachycardia. Any of these potential complications should be addressed promptly.

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION (SIADH)

Clinically, SIADH is the opposite of diabetes insipidus, with ADH levels increased as opposed to decreased. It is seen more commonly as an individual ages but can develop at any age [17]. A major risk factor for SIADH is hospitalization, and a high number of SIADH cases develop in hospitalized patients older than 30 years of age [24].

PATHOPHYSIOLOGY

The syndrome of inappropriate antidiuretic hormone, or SIADH, is a condition characterized by autonomous release of ADH without regard to plasma osmolality. The body is unable to dilute the urine appropriately, so fluid is retained, which expands the extracellular fluid compartment and leads to hyponatremia. There may also be sodium loss by the kidneys because of a lack of aldosterone [26].

The cause of SIADH is multifactorial and may include genetic, nervous system, malignancy, pulmonary disease, surgery, and medication factors [16]. Hereditary SIDAH is referred to as nephrogenic SIADH and is the result of a functional mutation in the vasopressin 2 receptors in the kidneys that leads to these receptors staying in an active state [17].

Conditions that increase intracranial pressure can lead to the development of SIADH, including head trauma, stroke, meningitis, lesions, hemorrhage, and hydrocephalus [16; 24; 26]. Vasopressin-secreting tumors of the lung and brain are another potential cause of SIADH; small cell lung cancer is responsible for 70% of the cancer-related causes of SIADH [16; 26; 63]. Pulmonary disease (e.g., cystic fibrosis, chronic obstructive pulmonary disease) can lead to SIADH, although the exact mechanism is not fully understood [16].

Medications associated with SIADH include carbamazepine, oxcarbazepine, chlorpropamide, cyclophosphamide, selective serotonin reuptake inhibitors (SSRIs), antipsychotics, hormones (i.e., vasopressin, desmopressin, and oxytocin), and antihistamines [16; 26]. Of these medications, SSRIs and carbamazepine are the most commonly associated medications [24]. The illicit drug 3,4-methylenedioxy-methamphetamine (MDMA or Ecstasy/E/Molly) induces release of ADH and increases thirst, which causes SIADH and is linked to more severe signs and symptoms [17].

SIGNS AND SYMPTOMS

SIADH is also associated with serum hypo-osmolality, concentrated urine, increased urine specific gravity, decreased urine output, weakness, lethargy, headache, anorexia, nausea, vomiting, mental status changes, seizures, cerebral edema, cerebral hemorrhage, asterixis, myoclonus, pulmonary edema, and coma [26; 64]. Hyponatremia and decreased extracellular fluid volume lead to a fluid shift into the cells [17]. The osmotic fluid shifts associated with this condition cause cerebral edema and subsequent increased intracranial pressure [26]. When cerebral edema occurs, there is also a loss of potassium and amino acids from brain cells [24].

In patients with chronic SIADH, solute loss is more prominent than water retention [17]. This can lead to the development of hyponatremia in a euvolemic state. In those with SIADH, ADH is secreted even in instances in which the ADH should be decreased, leading to the reabsorption of water, increased fluid in the bloodstream, dilutional hyponatremia, and an increase in the extracellular fluid volume. Dilutional hyponatremia may be manifested by a bounding pulse, increased or normal blood pressure, muscle weakness, headache, personality changes, nausea, diarrhea, convulsions, and coma [16]. The patient with hyponatremia may also develop gait disturbance, memory and cognition problems, dizziness, and an increased risk for falls.

Hyponatremia can be classified as mild (130–134 mEq/L), moderate (125–129 mEq/L), or profound (less than 125 mEq/L) [64]. In patients with mild-to-moderate hyponatremia, the only signs and symptoms may be nausea and malaise [17]. As hyponatremia worsens, patients will develop additional signs and symptoms, and serum sodium levels less than 120 mEq/L can lead to coma and respiratory arrest [17]. The speed at which the hyponatremia develops is correlated with the neurologic manifestations [26]. If the patient develops acute hyponatremic encephalopathy, the condition may be reversible, but it could also lead to permanent deficits [17]. Vomiting is considered an ominous sign [17].

Hyponatremia that develops quickly can lead to cerebral edema and potential brain herniation [63]. When the body has time to adapt to the cerebral edema, it displaces solutes (e.g., potassium) from the brain and into the extracellular spaces [63]. In those with chronic hyponatremia, the body adapts and the condition can be asymptomatic, even with serum sodium levels less than 120 mEq/L [17]. Although these patients may be asymptomatic, nausea and vomiting are seen in approximately one-third of patients [17]. However, rapid drops in sodium levels can result in delirium, confusion, and seizures, even if the drop is minimal [17].

DIAGNOSTIC TESTS

In all patients with suspected SIADH, hypothyroidism and adrenal insufficiency should be ruled out [17]. Patients should be asked about a history of head injury, chronic pain, smoking, weight loss, respiratory symptoms, drug use, and any new symptoms experienced [17]. The physical exam should include an assessment of the patient's volume status, skin turgor, mucous membranes, neurologic status, and vital signs. There is no specific diagnostic tool or test for SIADH, but the Bartter-Schwartz criteria, developed in 1967, are still used today to aid in diagnosis [17]. The following are the criteria for this tool [17]:

- Serum sodium <135 mEq/L
- Serum osmolality <275 mOsm/Kg
- Urine sodium >40 mEq/L
- Urine osmolality >100 mOsm/kg
- Absence of clinical evidence of volume depletion
- Absence of other causes of hyponatremia
- Correction of hyponatremia with fluid restriction

Selection of appropriate diagnostic tests is vital, because it will affect the successful correction of hyponatremia and patient success rates [65]. Although a variety of tests are used, the three cardinal tests assess urine osmolality, plasma osmolality, and urine sodium [65]. Patients with SIADH will have decreased serum sodium, increased urine sodium, decreased serum osmolality, increased urine osmolality, decreased blood urea nitrogen (BUN), and concentrated urine [16; 66]. Urine osmolality will be greater than 50 mOsm/Kg, and often greater than 100 mOsm/kg [64]. Serum ADH will also be increased.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The European Society of Endocrinology recommends that if clinical assessment indicates that the volume of extracellular fluid is not overtly increased and the urine sodium concentration is >30mmol/L, other causes of hypotonic hyponatremia should be excluded before implicating SIADH.

(https://academic.oup.com/ndt/article/29/suppl_2/i1/1904943. Last accessed July 19, 2024.)

Level of Evidence: Expert Opinion/Consensus Statement

TREATMENT AND NURSING INTERVENTIONS

Treatment of SIADH is directed toward its underlying cause. Approaches will differ for acute and chronic disease [63]. One of the main goals of treatment is the correction of hyponatremia, with a target serum sodium level of more than 130 mEq/L [17]. Even mild cases of hyponatremia are associated with a variety of safety risks, including gait instability, falls, osteoporosis, bone fractures, attention deficit,

and increased mortality [67]. Although these risks are known, many patients admitted to the hospital with SIADH are discharged with continued hyponatremia [65].

In elderly patients a common cause of hyponatremia is chronic SIADH, and these patients may have aging-related safety risks exacerbated by low serum sodium levels [67]. Additionally, chronic SIADH is associated with a decreased bone mass, increasing the risk for fractures [63].

It is important to slowly increase sodium levels, because increasing the concentration too quickly can lead to osmotic demyelination syndrome and poor outcomes [17; 64]. Osmotic demyelination syndrome, also known as central pontine myelinolysis, is seen more often in those treated with hypertonic saline or tolvaptan [65; 68]. Rapid correction of sodium leads to a fluid shift and essentially dehydration of the brain cells, which causes degeneration and demyelination of the myelin [68]. Patients with euvolemic hyponatremia (as opposed to hypervolemic hyponatremia) have an increased risk for rapid sodium correction and the development of osmotic demyelination syndrome [66]. Other risk factors include alcohol use disorder, malnutrition, liver disease, hypokalemia, hyponatremia lasting longer than two days, and decreased serum sodium concentration in conjunction with decreased BUN prior to the start of therapy [66; 68]. With this in mind, these laboratory values should be assessed/considered prior to initiating treatment.

The signs and symptoms associated with osmotic demyelination typically arise in two to six days. The first signs and symptoms include changes in level of consciousness and difficulty or inability to speak [68]. Patients may also develop dysarthria, dysphagia, paraparesis, quadriparesis, spastic quadriplegia, confusion, disorientation, obtundation, pseudobulbar palsy, encephalopathy, and coma [68]. These signs and symptoms are the result of noninflammatory demyelination of the pons [68]. In severe cases, a type of locked-in syndrome can develop, whereby the patient is paralyzed and unable to communicate but fully awake [17]. The effects of this condition may be partially reversible, but in many instances, they are permanent. Prevention involves avoidance of sodium increases of more than 8 mEq/L in 24 hours or 0.5–1 mEq/L per hour [17]. Treatment focuses on addressing symptoms and lowering the serum sodium concentration [68].

Patients with mild-to-moderate SIADH may require fluid restriction, which will lead to the release of aldosterone and the conservation of sodium by the kidneys [17; 24]. The recommended fluid intake is often 600–800 mL per day, which can be a significant challenge for many patients [24; 67]. In fact, the major challenge with fluid restriction is non-compliance, and patient education will play an important role in the patient's plan of care. Fluid restriction should be used cautiously in patients with an increased risk for hypovolemia.

If fluid restriction is unsuccessful or if the patient is acutely ill and symptomatic, hypertonic 3% saline may be administered to help increase serum sodium levels; this is typically reserved for patients with severe hyponatremia [17]. This intervention should be completed cautiously, because when the solution is administered too rapidly the fluid shifts can damage the brain [24]. The initial dose is 100 mL hypertonic 3% saline bolus in the first three to four hours [17]. Serum sodium levels are then checked within two to three hours, and the results will help to guide continued treatment [17]. These patients should be closely monitored for fluid overload. Because of the risks of severe side effects, isotonic saline should only be used in hyponatremic emergencies [65].

In some cases, loop or thiazide diuretics may be ordered to help rid the body of excess fluid. Use of diuretics is often reserved for patients with cardiac symptoms [24]. Patients prescribed diuretics may take oral salt tablets or increase dietary salt intake to decrease the urine concentration [17].

Conivaptan is a vasopressin 2 receptor antagonist that may be ordered for severe cases of hyponatremia [16]. This agent is given intravenously and blocks the action of ADH at the kidney level [16; 66].

Tolvaptan is also a vasopressin 2 receptor antagonist, but it is given orally [17]. This medication is hepatotoxic and should be avoided in patients with pre-existing liver disease. Tolvaptan increases sodium levels at a faster rate than other methods, but it can increase the rates too rapidly, leading to osmotic demyelination syndrome [65]. Potential side effects include dry mouth, polydipsia, liver toxicity, and polyuria [63]. It is also important to consider that this medication can be quite costly.

Other medications that may be used in the treatment of this condition are lithium and demeclocycline [17]. Demeclocycline, an antibiotic that blocks the action of ADH at the tubules of the kidney, is administered at a dose of 600–1,200 mg/day in divided doses [24]. Both of these medications are nephrotoxic and associated with undesirable side effects.

If a secreting tumor is the underlying cause of SIADH, the tumor may need to be removed [16]. The removal and additional treatment of the tumor will depend on a variety of factors, including whether the tumor is malignant or benign. If medications are associated with this condition, they should be stopped, if possible.

Patients with SIADH should be monitored for patent airway. For patients without respiratory symptoms, the head of the bed should be kept low (i.e., 10 degrees or less) [24]. Keeping the head of the bed low will enhance venous return and left atrial filling pressure, leading to a decrease in the release of ADH [24].

Other nursing interventions include closely monitoring intake and output, daily weight checks, assisting with hemodynamic monitoring, and neurologic checks. Because the most common indicator of SIADH is decreased serum sodium levels, the patient's laboratory values should be monitored closely [24]. Urinary output may be monitored hourly, with notation of color, clarity, and odor. In most patients with SIADH, urinary output will be decreased and urine will appear concentrated. If the patient on fluid restrictions complains of a dry mouth, hard candies, dry mouth lozenges, or moisturizing mouth swabs may be offered. Patients should also be educated on SIADH and treatment, with an emphasis on the importance of adhering to fluid restriction and increased salt intake.

GROWTH HORMONE DEFICIENCY

Growth hormone deficiency is usually the result of genetic mutations or structural defects in the brain and can affect children and adults [69]. Acquired growth hormone deficiency in adults is due to malnutrition, trauma (e.g., traumatic brain injury [TBI], Sheehan syndrome), infection (e.g., meningitis, encephalitis), radiation therapy, brain tumors, or the treatment of acromegaly [69; 70]. In children, malnutrition, neglect, and/or emotional stress can lead to a growth hormone deficiency [16]. Cases in which there is no identifiable cause are classified as idiopathic.

Worldwide, malnutrition is the most common cause of growth hormone deficiency [16]. The prevalence of growth hormone deficiency in children is 1.8 to 2.9 per 10,000 population [71]. Approximately 6,000 new cases of adult-onset growth hormone deficiency are diagnosed each year in the United States [21].

PATHOPHYSIOLOGY

Congenital growth hormone deficiency can be genetic or the result of structural changes in the brain. It appears to have a hereditary factor; approximately 5% to 30% of children with growth hormone deficiency have a first-degree relative with the disorder [20]. These patients have an increased risk for other pituitary hormone abnormalities and anatomic differences of the pituitary gland [20]. Three abnormalities are commonly seen in patients with congenital growth hormone deficiency: interrupted or thin pituitary stalk; absent or ectopic posterior pituitary gland (i.e., the posterior portion of the pituitary gland is in an abnormal position); and anterior hypoplasia or aplasia of the pituitary gland [20].

Genetic causes of growth hormone deficiency include growth hormone deficiency IA, IB, IIB, and III [69]. Growth hormone deficiency IA is an autosomal recessive disorder in which the fetus develops growth retardation in utero [69]. When these children are initially given growth hormone, they respond appropriately, but over time, they create antibodies to the growth hormone [69]. Growth hormone deficiency IB is an autosomal recessive disorder in which the child has some growth hormone and will respond to the administration of growth hormone [69]. Growth hormone IIB is an autosomal dominant disorder, and III is an x-linked disorder [69]. Both of these genetic disorders are similar to growth hormone deficiency IB [69].

Adult-onset growth hormone deficiency is typically caused by a pituitary tumor or brain trauma, but less common causes include surgery, radiation, infection, and hemorrhage [23; 69]. These contributing factors cause damage to the pituitary gland, leading to a growth hormone deficiency. Deficiency in adults can also be caused by persistent childhood growth hormone deficiency [23]. It is also important to consider that growth hormone secretion decreases with age [22].

Treatment of acromegaly suppresses growth hormone secretion and reduces insulin-like growth factor levels [22]. An estimated 30% to 75% of patients undergoing radiation therapy for acromegaly develop growth hormone deficiency, with increased risk associated with younger age, high doses of radiotherapy, and extended treatment [22]. This effect will be discussed in greater detail later in this course.

TBI has been associated with growth hormone deficiency; more severe TBI increases this risk [70]. However, growth hormone deficiency after a TBI is not well-known and can be easily missed [70]. The reported prevalence is variable due to a multitude of factors, but an estimated 2% to 30% of patients who have experienced a TBI will develop growth hormone deficiency within one month [25]. Further, an estimated 10% to 63.6% of patients in the chronic phase of TBI will develop growth hormone deficiency [25]. The underlying cause in these patients is ischemic injury to the pituitary gland, particularly the pituitary stalk, which is fragile and prone to injury [25]. In the secondary phase of TBI, ischemic, cytotoxic, and inflammatory changes can increase the risk for the development of a growth hormone deficiency [25].

In some cases, malnutrition, neglect, and/or emotional/environmental stress can lead to delayed growth [71]. This may be related to inflammation that develops due to chronic stress; increased inflammation is associated with decreased levels of insulin-like growth factor and growth hormone resistance [71].

Sheehan Syndrome

Sheehan syndrome is a rare postpartum pituitary dysfunction caused by pituitary necrosis [70]. This condition develops after severe hypotension and shock associated with hemorrhage during delivery [70]. A variety of hormonal deficiencies can develop in the patient with Sheehan syndrome, but growth hormone deficiency is one of the most common [72]. Although relatively rare in the United States, this disorder is still seen frequently in developing countries due to the lack of obstetric care [72].

Sheehan syndrome is characterized by hypopituitarism caused by ischemic pituitary necrosis developing after blood loss associated with childbirth [72]. The pituitary gland is susceptible to injury during and immediately after pregnancy because the anterior pituitary gland enlarges during pregnancy but does not develop an increased blood supply [72].

SIGNS AND SYMPTOMS

The signs and symptoms observed with growth hormone deficiency will vary depending on the age of the individual affected.

Children

Growth hormone deficiency can present in a variety of ways in children. Growth retardation, short stature, and delays in maturation are common signs [69]. Children with this deficiency typically have delays in longitudinal bone growth, and untreated growth hormone deficiency results in an average maximal height of 3–4 feet, although body proportions are normal. These children will also display slowed sexual maturation and, in some cases, cognitive deficits. Excess weight and a younger than expected appearance and voice may also be noted [73].

Children with growth hormone deficiency are typically within normal range for size at birth [69]. However, infants with anatomic changes in the pituitary gland are more likely to be born breech and to have jaundice, hypoxia, and hypoglycemia [20]. As these children grow, they will present with delayed development of the facial bones, slowed tooth eruption, fine hair, poor nail growth, and delayed lengthening of the long bones [69]. If the growth hormone deficiency is associated with malnutrition, changes in the child's weight will often be observed before delayed growth [71]. In infants, the fontanelles may take longer than expected to close [69]. Additional signs and symptoms include poor appetite, decreased strength, decreased muscle development, low energy, poor endurance, sleep difficulties, trouble concentrating, and fatigue [73].

Growth hormone deficiency can impact a child's daily, emotional, and social life [73]. The child may report a decreased ability to play sports or participate in social activities [73]. Short stature may lead to bullying, leaving the child to feel as if he or she is different and socially isolated.

Adults

Adults with a growth hormone deficiency may present with fatigue, weakness, obesity, decreased muscle mass, weakened bones, sexual dysfunction, elevated cholesterol levels, and insulin resistance [16; 69]. Decreased bone turnover and decreased bone mass are common, and adults with a growth hormone deficiency have a risk for fracture that is two to three times higher than their counterparts without growth hormone deficiency [23]. Early onset of deficiency (i.e., in childhood) and cigarette smoking can further increase this risk [23].

These patients are at an increased risk for cardiovascular and neurologic disorders. Growth hormone deficiency is associated with increased abdominal subcutaneous tissue, insulin resistance, hypercoagulability, increased total and low-density lipoprotein (LDL) cholesterol levels, decreased high-density lipoprotein (HDL) cholesterol levels, decreased exercise performance, and atherosclerosis [21]. All of these changes can increase the risk for cardiovascular complications.

As with pediatric patients, growth hormone deficiency can decrease adult patients' quality of life, and treatment has been shown to improve satisfaction with life [21; 22]. These individuals are more likely to be unemployed, on sick leave, or on disability [21]. Patients who develop a growth hormone deficiency after a TBI are more likely to develop depression and report a decreased quality of life [25].

DIAGNOSTIC TESTS

The diagnosis of congenital causes of growth hormone deficiency is often delayed until slow growth is observed in a child [69]. It is common to see initial diagnosis around 5 years of age, when children start school or when puberty is delayed (10 to 13 years of age for girls, 12 to 16 years of age for boys) [69]. Diagnostic tests for a growth hormone deficiency include serum growth hormone levels, growth hormone stimulation test, pituitary MRI, and bone density tests.

The Endocrine Society recommends recommend that the insulin tolerance test and the GHRH-arginine test have sufficient sensitivity and specificity to establish the diagnosis of growth hormone deficiency in adults.

(https://academic.oup.com/jcem/article/96/6/1587/2833853. Last accessed July 19, 2024.)

Strength of Recommendation/Level of Evidence: 1/⊕⊕⊕⊕ (Strong recommendation based on high-quality evidence)

Although growth hormone levels can be measured, these tests can be unreliable because hormones are not secreted in consistent amounts throughout the day. Additionally, a variety of medications can affect growth hormone levels and interfere with diagnostic testing [32]. As such, a medication review should be conducted to determine if any could interfere with testing. Medications that can affect the results include insulin, estrogen, amphetamines, oral contraception, and corticosteroids; the herbal supplement St. John's wort can also impact findings [33].

A more reliable test is the growth hormone stimulation test, which measures the response of growth hormone to hypoglycemia [16]. Medications that may be used in stimulation testing are clonidine, arginine, and glucagon [20]. In the patient with a growth hormone deficiency, growth hormone levels would not elevate as expected.

An MRI is usually completed to assess for tumors, and a bone density test will provide information about bone strength and possible disorders (e.g., osteopenia, osteoporosis). In patients with congenital growth hormone deficiency, an MRI will help to identify abnormal pituitary anatomy rather than for definitive diagnosis. However, conducting an MRI can be challenging for pediatric patients and may require sedation to remain calm and still for approximately 45 minutes.

Diagnosis of a growth hormone deficiency after TBI can be challenging because many of the signs and symptoms associated with each condition overlap [25]. It is important to consider that increases in the severity of TBI likewise increase the risk of growth hormone deficiency [25]. As such, patients with a severe TBI should be evaluated. In these patients, plasma insulin growth factor is not a useful measure, because it lacks sensitivity and accuracy [25]. Instead, an insulin tolerance test, GHRH levels, and/or glucagon stimulation test should be used [25].

The diagnosis of growth hormone deficiency due to Sheehan syndrome is often delayed, in some instances for many years [72]. This is often because it is overlooked by healthcare professionals, and it should be considered as part of the differential diagnosis in women presenting with suggestive signs and symptoms [72].

TREATMENT AND NURSING INTERVENTIONS

The treatment of growth hormone deficiency is most commonly the administration of synthetic human growth hormone. If hormone replacement is initiated during childhood, the patient will usually reach a normal height in adulthood; even those with short stature can catch up [71; 74]. The goal is to start hormone replacement before the child drops below the third percentile for height [21].

Growth hormone replacement is also appropriate therapy for adults and can lead to increased bone turnover, expanded remodeling space, decreased fracture risk, and over time, increased bone density [23]. It is interesting to note that some research has shown that the positive effect on bone density is more pronounced in men than women [23].

Somatropin, a recombinant growth hormone, may be used for both children and adults with a growth hormone deficiency. This medication increases skeletal growth in children and increases bone density in adults [75]. Somatropin is administered as a subcutaneous injection, usually in the evening to mimic the body's normal rhythm [21]. The onset of action is typically within three months of the initiation of treatment [75]. Starting treatment early will help prevent delayed growth in children. In most cases, somatropin is administered to children when delayed growth is identified, with doses increased when the child is going through puberty and discontinued when skeletal maturation is reached [69]. However, testing should be completed to determine if the patient should continue treatment, as early cessation can lead to negative consequences in adulthood [69]. Adverse effects of somatropin include edema of the hands and feet, hyperglycemia, hypothyroidism, insulin resistance, pancreatitis, pain at the injection site, lipodystrophy, carpal tunnel syndrome, and arthralgia [21; 75]. Lipodystrophy can be prevented by rotating injection sites. Concurrent use of corticosteroids can decrease the effectiveness of somatropin [75].

During somatropin treatment, children should have growth (height and weight) assessed every three to six months [75]. In adolescence, patients' growth and puberty should be monitored every six months [74]. Because this medication has been linked to hypothyroidism, thyroid function should be periodically checked. Somatropin treatment is ineffective in the presence of hypothyroidism, so treatment of the condition is vital [75]. Patients should also be monitored for hyperglycemia, especially patients diagnosed with diabetes. In addition, patients given somatropin after epiphyseal closure should be monitored for signs and symptoms of acromegaly.

Somapacitan, a long-acting human growth hormone analog, was approved for use in adults with growth hormone deficiency in 2020 [76]. This medication is administered as a once-weekly injection [76; 77]. The initial dose is 1.5 mg, but the dose can be increased by 0.5–1.5 mg per week (to a maximum 8 mg per week) every two to four weeks based on clinical response and insulin-like growth factor-1 levels. Potential adverse effects include back pain, joint pain, indigestion, sleep disorders, dizziness, tonsillitis, edema of the extremities, vomiting, adrenal insufficiency, hypertension, increased blood creatinine phosphokinase, weight gain, and anemia [76]. The dose should be reduced if needed for adverse reactions or elevated insulin-like growth factor-1 levels. Somapacitan is contraindicated in patients with malignancy, diabetic retinopathy, and acute critical illness [76; 77]. Discontinuation of therapy should be considered if no apparent benefits are achieved after 12 to 18 months.

In 2021, the FDA approved lonapegsomatropin (Skytrofa) for treatment of pediatric patients 1 year of age and older who weigh ≥11.5 kg and who have growth hormone deficiency. Lonapegsomatropin is administered subcutaneously once weekly. Lonapegsomatropin is initially dosed at 0.24 mg once weekly, then titrated based on individualized patient response [78; 79; 80]. The FDA approved lonapegsomatropin based on one clinical trial of 161 patients with growth hormone deficiency and short stature. The trial was conducted at 54 sites in 14 countries around the world, including in the United States, to assess efficacy and safety [80]. Common side effects include viral infection, fever, cough, nausea and vomiting, diarrhea, arthralgia, arthritis, and increased blood phosphate levels [80].

Growth hormone replacement therapy should continue over a prolonged period of time, in some cases for the patient's entire life. Patients receiving this treatment should be taught self-administration techniques.

Due to the length of treatment, adherence can be a challenge. Factors that may affect adherence include cost, length of treatment, and decreased understanding of treatment. Transition to adolescence is an important challenge to adherence [74]. Factors that may negatively affect adherence in adolescence include peer group conflict and loss of a sense of control. This is also a period of increased independence during which adolescents may want to take a more central role in managing their own care.

Poor compliance with or delayed therapy can lead to poor growth in children and to increased weight, changes to bone metabolism and density, and changes to cardiac structure and function (e.g., exercise intolerance, bradycardia, dilated cardiomyopathy) in adults [74]. Cognitive/psychological changes associated with poor compliance may include fatigue, sleep disturbance, decreased motivation, decreased self-esteem, and isolation [74].

With adherence in mind, empowering patients is important. For pediatric patient, parents/caregivers and the patient should be educated, offering choices (whenever possible), rewards, and age-appropriate educational materials [74]. Adolescent patients should be asked how they feel about their treatment and allowed to make decisions so they feel a sense of control. Adult patients should be encouraged to attend regular follow-up appointments and be provided with education on the benefits of treatment. Phone alerts or text or e-mail reminders may be beneficial [74]. Because cigarette smoking can increase the risk for fracture in adults with a growth hormone deficiency, patients should be advised to quit smoking and provided with cessation tools and resources.

DISORDERS OF HYPERSOMATOTROPISM

Hypersecretion of somatotropin by the anterior pituitary results in gigantism (before puberty) or acromegaly (after puberty). The crucial factor is the time onset of the disorder. If the hypersecretion of growth hormone occurs during the individual's growth period before the epiphyses of long bones have closed, gigantism will occur. Acromegaly occurs after epiphyseal closure [81; 82].

ACROMEGALY

Acromegaly is a rare condition, with approximately 3 to 14 of every 100,000 people diagnosed [83]. It is seen most commonly in adults between 30 and 40 years of age and more frequently in women than men [16; 24]. Acromegaly is most commonly caused by pituitary tumors (e.g., adenomas, hypothalamic adenomas), but pituitary hyperplasia and genetic mutation are other possible etiologies.

Pathophysiology

As noted, acromegaly develops when there is excessive growth hormone after the closure of the growth plates [83]. Bones will specifically increase in width rather than length. Subcutaneous connective tissues, organs, and glands may also enlarge [16].

Patients with acromegaly have increased levels of somatotropin and insulin-like growth factor [22]. Insulin-like growth factor alters the metabolism of blood glucose and lipids, increasing the risk for type 2 diabetes, hypertension, and cardiovascular disease [83]. Patients with acromegaly may also have an abnormal production of glucocorticoids, mineralocorticoids, and gonadotropins [24].

The majority of cases of growth hormone hypersecretion (more than 90%) are caused by benign pituitary adenomas [19; 83]. In the United States, it is estimated that about 16% of the population (more than 50 million people) have pituitary tumors, although most are undiagnosed. Approximately 13,000 people are diagnosed with pituitary tumors each year; 25% of these tumors will lead to acromegaly [21]. It is possible for patients to develop a malignant pituitary adenoma that is responsible for acromegaly, but this occurs in less than 1% of cases [24]. The disorder may also be caused by hypothalamic adenomas that increase the amount of GHRH, which, in turn, increases growth hormone levels [19]. Other types of tumors, such as those found in the hypothalamus, pancreas, lungs, chest, or abdomen, can also lead to acromegaly [83]. These tumors can secrete their own growth hormone, although it is more common for them to produce GHRH [83]. Additional possible causes include pituitary hyperplasia and excess GHRH [16].

Acromegaly has been shown to run in families, and several mutated genes have been associated with acromegaly, including *AIP*, *MEN1*, *CDKN1B*, *PRKARIA*, *SDHx*, *GPR101*, and *GNAS* [84]. The most common genetic cause of acromegaly is familial isolated pituitary adenoma syndrome [84]. Less common causes are Carney complex, multiple endocrine neoplasia, and sporadic acromegaly [84]. The exact mechanisms behind familial isolated pituitary adenoma are not fully understood [84].

Signs and Symptoms

The term acromegaly refers to enlargement of the acral parts—the head, hands, and feet—and these patients often present with enlargement of facial features, excessive growth of the hands and feet, and hypertrophy of soft tissues. The signs and symptoms may develop slowly and not become apparent for years [19].

Patients with acromegaly will have lateral changes to the bones of the face, and the mandible will enlarge and protrude. The space between the patient's teeth may widen and teeth may become displaced, which can lead to problems chewing and eating. The tongue and salivary glands often enlarge, leading to trouble with speaking and eating [16; 21]. In addition to the tongue thickening, the lips and nose also enlarge, impeding breathing and possibly causing sleep apnea [83]. The patient's hair and skin may become thick, coarse, and oily [83]. Approximately 70% of patients with acromegaly report oily skin with increased sweating and unpleasant odor [21].

Some patients describe skin tags that become larger and darker [83]. Joint changes are seen in approximately 70% of patients with acromegaly, and joint pain and osteoarthritis often develop [19]. Growth hormone can increase bone resorption and turnover, increasing the risk for fracture [21].

Patients with pituitary enlargement may complain of headaches and visual disturbances (e.g., diplopia) as a result of the adenoma pushing on the brain and cranial nerves III, IV, and VI [16; 19; 24]. If the tumor presses on other pituitary tissue, it can lead to menstrual changes, erectile dysfunction, thyroid hormone changes, and decreased circulating cortisol [83]. The headaches may be severe and can interfere with the patient's ability to perform daily tasks [21]. If cranial nerve V is involved, the patient may also complain of facial pain [21].

Patients with acromegaly often have a reduced life expectancy because of associated cardiovascular, respiratory, metabolic, and neoplastic conditions [22]. Cardiac disease, including cardiomyopathy, arrhythmias, hypertension, and diastolic overload, is seen in approximately 60% of patients with acromegaly [21]. As many as 50% of patients will develop hypertension [21].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Endocrine Society suggests evaluating all patients presenting with acromegaly for associated comorbidities, including hypertension, diabetes mellitus, cardiovascular disease, osteoarthritis, and sleep apnea.

(https://academic.oup.com/jcem/article/99/11/3933/2836347. Last accessed July 19, 2024.)

Strength of Recommendation/Level of Evidence: 2|⊕⊕○○ (Weak recommendation based on low-quality evidence)

Diagnosis

The slow progression of acromegaly often delays diagnosis and treatment [83]. This is a problem, because associated health conditions can develop and cause significant damage during this period [83]. The first step is in an accurate physical exam and history. Patients should be observed for any enlargement in facial features; it may be helpful to ask the patient to bring in an older photograph for comparison [24]. Patients should also be asked about any changes that they have noticed, such as an increase in ring or shoe size [16]. An oral exam may be significant for an enlarged tongue; if present, respiratory issues may be a concern. Patients should be asked about any problems chewing, eating, or swallowing or with sleep (e.g., snoring and excessive daytime sleepiness, which may be signs of sleep apnea). When speaking with the patient, assess for and note any difficulty speaking. The nurse should ask the patient about skin changes, sweating, increased body odor, changes to body hair, and skin tags, and an assessment of the patient's integumentary system should be conducted. Patients should be asked about a history of headaches or visual changes, either of which would warrant additional investigation.

Appropriate diagnostic tests include serum insulin-like growth factor, growth hormone levels, serum glucose, MRI, CT scan, bone density scans, and x-rays [24; 83]. Insulin-like growth hormone levels are more than five times greater in patients with acromegaly than in those without the disease [24; 83]. For patients with moderately elevated insulin-like growth factor, an oral glucose tolerance test may also be ordered. This test consists of the patient drinking a sugary liquid, typically containing 75 mg of glucose, and blood samples taken after one and two hours to measure growth hormone [24; 83]. Under normal conditions, growth hormone levels would drop after consumption of glucose, but this will not occur in patients with acromegaly. Theoretically, blood tests of growth hormone levels would also be elevated, but these tests may be unreliable. Elevated blood glucose levels are also common in these patients.

Bone density testing is completed to identify any weakening of the patient's bones, and x-rays are done to identify bone enlargement. An MRI should be conducted to visualize pituitary and any other tumors.

Treatment and Nursing Interventions

The changes associated with acromegaly usually develop over 7 to 10 years, but the best outcomes are associated with early identification and treatment [24]. Left untreated, this condition can result in early mortality and decreased quality of life [83]. However, treatment allows patients with acromegaly a normal life expectancy and quality of life [83].

In most cases, the goal of treatment is to control the size of the underlying tumor, to return growth hormone and insulin-like growth factor levels to normal, and to improve symptoms and manage any associated conditions [83]. It is particularly important to address any cardiovascular complications, as these are the main cause of excess mortality [21].

Surgical Intervention

A common treatment option is the surgical removal of the pituitary adenoma by endoscopic, transnasal, or transsphenoidal route [24; 83]. For 60% of patients, surgery will result in cure, and in many cases, pituitary function may be preserved [24]. However, some may require hypophysectomy, with fluoroscopy-guided removal of the pituitary gland along with any adenoma or other tumors [83].

Possible postoperative complications include bleeding, cerebrospinal fluid leaks, sodium imbalances, fluid imbalances, decreased pituitary hormones, diabetes insipidus, hypopituitarism, and meningitis [24; 83]. Postsurgical nursing interventions include [24]:

- Assess neurologic status
- Assess for pain
- Assess for nasal drainage
- Elevate the head of the bed
- Educate about the avoidance of activities that increase intracranial pressure
- Check blood glucose and serum sodium levels

If present, clear nasal drainage should be checked for glucose to ensure that it is not cerebral spinal fluid [24]. The head of the bed should be elevated to promote drainage and to make breathing easier. Patients should be advised to avoid coughing, straining for a bowel movement, or any other activity that can increase intracranial pressure for up to two months following the procedure. Tooth brushing can cause damage to the surgical incision site and should also be avoided. After the removal of pituitary adenoma, hypoglycemia may develop as growth hormone and insulin-like growth factor levels drop [24]. Approximately 20% of patients have associated pituitary damage and may require replacement of glucocorticoids, gonadotropins, and thyroid hormone [24].

Radiation Therapy

Radiation therapy is another treatment option for patients with acromegaly caused by malignancy. It is typically a second-line option if surgery and/or pharmacotherapy are ineffective [83]. It is important to understand that it can take years for this treatment to improve symptoms [83]. Further, this therapy can impair fertility and approximately 50% of patients will require hormone replacement [83].

Pharmacotherapy

Medications used in the treatment of acromegaly include somatostatin analogs, dopamine agonists, and growth hormone-receptor antagonists [83]. These medications are initiated in patients who do not have remission following surgical removal of adenoma or in patients for whom surgery and/or radiation therapy is contraindicated [24].

Somatostatin analogs (e.g., octreotide, lanreotide) work by slowing the release of growth hormone [78; 83]. In some cases, these medications can effectively reduce the size of the pituitary tumor [83]. Octreotide suppresses growth hormone, insulin, and glucagon and helps to normalize growth hormone and insulin-like growth factor levels in patients with acromegaly [75]. Octreotide is available in short- and long-acting forms [24]. The short-acting form is given as a 100-mg subcutaneous injection three times daily; the long-acting form is given as a 10- to 30-mg intramuscular injection once monthly [24]. Lanreotide is a treatment option for patients with acromegaly who are not candidates for or who have not responded to other treatment options [75].

Lanreotide is given as a 60- to 120-mg subcutaneous injection monthly and is intended to be administered by a healthcare professional [75]. Potential side effects of somatostatin analogs include cramps, bradycardia, orthostatic hypotension, gas, diarrhea, gallstones, and hair loss [83]. Octreotide has been linked to dizziness, bradycardia, and orthostatic hypotension, so pulse and blood pressure should be monitored in these patients prior to and periodically throughout treatment. Patients should be advised to move slowly and not operate vehicles or heavy machinery until they know how they respond to the medication. Octreotide can also increase fertility in ovulating patients, so precautions to prevent pregnancy are necessary [75]. GI side effects are common when starting lanreotide but will often decrease with time [75].

Dopamine agonists (e.g., bromocriptine) are a treatment option to inhibit growth hormone production and tumor growth, but they are not as effective as somatostatin analogs [83]. Growth hormone-receptor antagonists (e.g., pegvisomant) decrease growth hormone levels and may be given orally. Potential side effects include GI upset, nausea, vomiting, headache, postural hypotension, dizziness, nasal congestion, and cold-induced vasospasm [21]. Laboratory changes may also be noted, including increased serum BUN, aspartate transaminase (AST), alanine transaminase (ALT), creatine phosphokinase (CPK), alkaline phosphatase, and uric acid levels [75]. Due to the risk of severe hypotension with the first dose, patients should be supervised when treatment is initiated.

Growth hormone antagonists (e.g., pegvisomant) are given to lower insulin-like growth factor levels [24]. Pegvisomant is used for patients with acromegaly who do not respond to other therapies and are not candidates for surgery or radiation [75; 78]. It binds to growth hormone receptor sites and blocks the effects of growth hormone, decreasing the manifestations of acromegaly [75]. Pegvisomant is given as a daily subcutaneous injection and takes two weeks to start working [24; 75]. Insulin-like growth factor levels should be checked within four to six weeks of the onset of therapy and every six months thereafter [75]. Side effects include hypertension, peripheral edema, lipohypertrophy, increased glucose tolerance, elevated liver enzymes, increased fertility, dizziness, and back pain [75].

If the therapy regimen includes injectable medications, patients should receive instruction on injection technique and should be able to demonstrate appropriate medication administration. Patients with acromegaly often experience changes to their self-concept [24]. Nurses should inquire about how the condition is affecting their life and help develop a plan of care based on the information obtained from the patient.

GIGANTISM

Gigantism starts in infancy or childhood and is characterized by continuous growth of the body until epiphyseal closure occurs. In adults, it is defined as a height greater than 80 inches; in children, it is defined as three standard deviations above the mean for the child's age as measured on a growth curve. Adults with gigantism may be as tall as 8 feet and weigh more than 300 pounds. Some individuals may develop associated acromegaly features (i.e., very large heads, hands, and feet) in adulthood [82].

Signs and Symptoms

Untreated, patients with gigantism have an increased death rate of approximately twice the normal average for the population. These patients experience progressive debilitation, but treatment can be very effective [81; 82]. They generally present with [81; 82]:

- Extremely large size
- Enlargement of the heart, liver, spleen, kidneys, pancreas, thyroid, parathyroid, adrenals, soft tissues, and/or peripheral nerves
- Increased metabolic rate
- Incomplete or slow development of secondary sex characteristics
- Glucose intolerance with resulting hyperglycemia and diabetes mellitus
- Possible excess secretion of other anterior pituitary hormones (e.g., prolactin, ACTH)

More advanced signs include extreme muscular weakness and crippling osteoarthritis, which may be associated with a severe kyphosis [81; 82].

The symptoms of gigantism are usually attributable to the effects of compression of the adjacent tissues by the pituitary tumor or by metabolic changes. Symptoms include headache, which may be mild to severe and persistent; bitemporal hemianopia and other visual field defects (e.g., changes in color perception, diplopia) due to pressure in the optic chiasm; and seizures and stroke resulting from increased intracranial pressure [81; 82].

Treatment

Because the underlying pathophysiology of gigantism is similar to acromegaly (usually pituitary tumor), the approach to treatment is generally the same. However, because most of these patients are children, patient and family education should be adjusted. Patients should be allowed opportunities to discuss their feelings and ask questions about the changes in their physical appearance. Children with gigantism require information about the reasons for the changes in physical appearance and also what might occur in the future. These patients are often coping with major differences in body size and shape as compared with peers, and this can result in bullying and insecurity [55].

ADDISON DISEASE

Addison disease, also known as primary adrenal insufficiency, develops when the adrenal glands do not produce enough of the hormones cortisol and aldosterone. In the United States, Addison disease affects approximately 1 out of every 100,000 people and is seen more commonly in women than men [27; 37]. This disorder is typically diagnosed among individuals 30 to 50 years of age, but it can develop at any age [37]. Addison disease may be caused by an autoimmune disease, genetics, infections, adrenalectomy, hemorrhage, cancer, amyloidosis, adrenoleukodystrophy (ALD), or medications, or as a side effect of the treatment of Cushing syndrome [85].

PATHOPHYSIOLOGY

As discussed, the adrenal glands are found above each kidney and produce cortisol, a glucocorticoid and aldosterone, a mineralocorticoid. In patients with Addison disease, an abnormality of the adrenal cortex leads to inadequate amounts of circulating cortisol and, in some cases, aldosterone [86].

Autoimmune disease is the most common cause of Addison disease, accounting for approximately 80% to 90% of all cases [37]. Autoimmune Addison disease, also referred to as autoimmune adrenalitis, results in atrophied adrenal glands and an inability to produce hormones in sufficient amounts. Cells destroyed by the inflammatory response are replaced by fibrotic tissue [87]. In these patients, the cells in the adrenal cortex are damaged but the medulla remains intact [87].

Risk for Addison disease is increased in those with a family history of the disease, with heritability accounting for 97% of cases in a Swedish twin study [24]. In addition, other autoimmune conditions have been associated with an increased risk of Addison disease, including vitiligo, type 1 diabetes, and hypothyroidism [45].

Viral, bacterial, or fungal infection or parasitic infestation of the adrenal glands can lead to changes, and childhood infections may predispose a patient to Addison disease [87]. Worldwide, tuberculosis is the most common cause of Addison disease, although this is not routinely seen as a cause in developed countries [45; 87]. Many infections that damage the adrenal glands are opportunistic, meaning they develop in immunocompromised individuals [87]. Serious infections (e.g., sepsis) require that the body be able to rapidly activate glucocorticoid production, which can lead to adrenal failure and, in some instances, adrenal crisis [87]. However, it has been hypothesized that infections highlight or exacerbate existing adrenal insufficiency rather than initiating it [87].

Patient who undergo bilateral adrenalectomy, as may occur with Cushing syndrome treatment, require steroid replacement or they will develop adrenal insufficiency and subsequent adrenal crisis. However, unilateral adrenalectomy rarely causes Addison disease unless the patient experiences severe adrenal stress, in which case the reduced adrenal reserve may be depleted [88]. Conditions that increase the risk for adrenal stress include sepsis, cardiopulmonary disturbance, trauma, and postoperative complications [88].

Hemorrhage (usually in response to infection or trauma) or malignant cells in the adrenal glands can cause damage and negatively affect the glands' ability to secrete cortisol and aldosterone [85]. Amyloidosis is a condition whereby the protein amyloid accumulates and causes damage to the adrenal glands, leading to decreased amounts of cortisol in the body [85]. Medications (e.g., antifungals, general anesthesia) can also lead to the development of Addison disease [37; 85].

Adrenal crisis is a serious complication of Addison disease that can result in death if not identified and treated appropriately. Anything that increases the cortisol needs of the body can lead to this condition. In the patient with Addison disease, the body is unable to increase the amount of circulating cortisol in the body, leading to a cortisol deficit. The decline in cortisol and aldosterone directly affects the liver, stomach, and kidneys [89].

SIGNS AND SYMPTOMS

Addison disease is associated with vague, gradually developing (insidious) symptoms that can make diagnosis a challenge [37]. Signs and symptoms associated with this disorder are due to hormone deficiency, with the majority being attributable to decreased cortisol levels, although aldosterone plays a role as well [86]. In many cases, signs and symptoms do not develop until approximately 90% of the adrenal cortex is destroyed, and in some patients, symptoms are not recognized until adrenal crisis develops [85; 86].

The most common signs and symptoms of Addison disease are chronic fatigue, lethargy, muscle weakness, loss of appetite, weight loss, increased urination, increased thirst, and abdominal pain [37; 85]. Other potential signs and symptoms include nausea, vomiting, diarrhea, hypotension, irritability, depression, joint pain, salt cravings, hypoglycemia, dizziness, reduction in underarm and pubic hair, muscular pain, irregular or no menstruation, decreased libido, darkening of the skin, slowed growth in children, neurologic disturbances, depression, impaired concentration, and hypersensitivity to tastes and smells [37; 90].

Cortisol plays a significant role in glucose metabolism, and decreases in cortisol levels can lead to hypoglycemia. Aldosterone acts on the kidneys to increase water retention and blood volume, and decreases in aldosterone levels can lead to hypotension, tachycardia, and salt cravings [16; 32; 86].

Melanodermia, color changes of the skin, is a potential side effect of Addison disease and most often presents in areas of the body most exposed to sunlight, such as the face, neck, knuckles, elbows, knees, and creases of the palms [24; 90]. Darkening of scars may also be seen [89]. Pigment changes seen with Addison disease are due to the stimulant effect of excess ACTH on the melanocytes to produce melanin [86].

Electrolyte changes (e.g., hyponatremia, hyperkalemia, hypercalcemia) may occur with Addison disease [90]. As such, these patients should be closely monitored and may require supplementation and/or a modified diet. The patient with this disorder may also develop lymphocytosis and anemia [86].

Late symptoms of adrenal insufficiency are hypotension, dizziness, syncope, nausea, vomiting, diarrhea, abdominal pain, joint pain, back pain, muscle cramps, chronic exhaustion, skin changes, and decreased libido [85]. Signs and symptoms of adrenal crisis are hypotension, hypoglycemia, hyponatremia, hyperkalemia, vomiting, diarrhea, weakness, confusion, severe dehydration, severe pain in the lower back and abdomen, GI pain, and loss

of consciousness [37; 90]. Patients with later stage Addison disease may present with pale, cold, clammy skin; sweating; rapid, shallow breathing; and severe muscle weakness [85]. Untreated, adrenal crisis can lead to coma and death.

Patients in adrenal crisis lose large amounts of sodium and water, causing a fluid deficit with resulting hypotension and tachycardia [16]. The patient will often present with hyperkalemia, which can lead to cardiac abnormalities. The decreased cortisol levels in Addison disease will cause decreased glucose output by the liver and decreased digestive enzymes [89].

DIAGNOSTIC TESTS

For most patients with Addison disease, diagnosis will be made around 40 years of age, and it is not uncommon for these patients to see multiple physicians before a diagnosis is made [86]. In cases of primary adrenal insufficiency, diagnosis of Addison disease may be delayed up to one year in as many as half of all cases [90]. Misdiagnosis is also common due to the vague signs and symptoms associated with the condition [86].

As discussed, the diagnostic tests that may be used for suspected Addison disease include ACTH stimulation test, serum cortisol levels, insulin tolerance test, antibody testing, and a CT scan or MRI. Aldosterone, serum cortisol, urine cortisol, blood glucose, and electrolyte levels may also be assessed [16; 85]. In these patients, cortisol, aldosterone, sodium and glucose levels would all be low in persons with Addison disease; potassium will be elevated [85]. If the patient becomes dehydrated, BUN and hematocrit levels should be checked and will likely both be elevated. A complete blood count may be checked to determine if the patient has lymphocytosis or anemia.

After completion of the ACTH stimulation and insulin tolerance tests, an antibody test may be ordered. If the antibody test is positive, diagnosis of autoimmune Addison disease may be made with no further testing [37]. The CT scan or MRI may be helpful to evaluate the adrenal glands and/or pituitary gland. These imaging studies can determine if the glands are small in size or if they are enlarged due to infection, bleeding, or malignancy [37]. If tuberculosis is suspected, testing to rule out tuberculosis should be conducted.

TREATMENT AND NURSING INTERVENTIONS

When a patient develops Addison disease, glucocorticoids are typically prescribed. Those with autoimmune Addison disease will require lifelong glucocorticoid treatment, and even with steroid replacement, these patients have an increased risk for morbidity, mortality, and decreased quality of life [87].

Hormone replacement should be carefully planned to ensure the best outcome for the patient. Under typical circumstances, two-thirds of the daily dose is given in the morning and one-third in the evening to mimic the natural circadian rhythm of cortisol levels [16]. Increased doses of hormones are required during times of stress, as this will mimic what normally happens in the body; this includes during illness, infection, accident, injury, invasive medical procedures, and strenuous exercise [85]. If the patient is vomiting, IV or intramuscular hydrocortisone may be necessary [27]. Patients should be educated on self-administration of injectable medications.

The most often prescribed corticosteroid for the treatment of Addison disease is hydrocortisone; however, prednisone or dexamethasone may be used [37]. In patients who are deficient in both cortisol and aldosterone, fludrocortisone is the agent of choice [37]. Fludrocortisone aids in the retention of sodium and loss of potassium, and patients taking this medication should be monitored for signs and symptoms of fluid overload. This involves daily weights and assessment of new onset of edema in the lower extremities. Patients who do not make sufficient amounts of aldosterone should be advised to consume high-salt foods, especially if they are craving salt and on hot days.

One side effect of long-term corticosteroid therapy is an increased risk for osteoporosis [37]. As such, calcium and vitamin D supplementation may be necessary, and patients should be educated about incorporating these nutrients into the diet. Corticosteroids can also lead to mood swings and insomnia [85]. Treatment for these side effects is guided by impact on the patient's life and patient preference.

It may also be necessary to restore fluid, electrolyte, and hormone imbalances [24]. The IV fluid typically used for these patients is 5% dextrose in 0.9% sodium chloride to address glucose and sodium imbalances [24]. Electrolyte disturbances are addressed by adding electrolytes to IV fluid, hanging individual bags of specific electrolyte(s), or oral supplementation.

Nursing assessments should include questions about any recent stressors, such as illness, infection, or traumatic events. It is important to inquire regarding the use of steroids or recent surgery, particularly on the adrenal and/or pituitary glands. Identifying associated signs and symptoms (e.g., increased urination, salt cravings) is important. Standard nursing care includes monitoring vital signs, daily weights, intake and output, and laboratory values. Patients who report increased urination should be monitored for dehydration and signs/symptoms of hypovolemia (e.g., hypotension, tachycardia). Understanding that stress can play a role in this disorder, patients should be assessed for coping abilities and educated about stress reduction strategies. It may also be helpful to ask about the patient's support systems. Patients should be encouraged to wear a medical alert bracelet or necklace to help ensure appropriate care, such as the administration of glucocorticoids if the patient is ill or injured and unable to provide a medical history [85].

Adrenal Crisis

When at all possible, it is important to prevent an adrenal crisis. Risk factors for adrenal crisis include GI infection, febrile infection, surgery, strenuous physical activity, discontinuation of glucocorticoids, psychiatric distress, and accidents [90]. If untreated, these patients can go into shock, followed by coma and death [89]. If adrenal crisis is suspected, treatment should be started quickly to restore fluid balance and cortisol levels [16; 91]. Replacement fluids should contain glucose. Cortisol levels are restored with the administration of intravenous glucocorticoids. If IV access is not readily available, glucocorticoids can be given intramuscularly [91]. Glucocorticoids are administered either on an around-the-clock schedule or as a continuous infusion [91]. If necessary, electrolytes should be replaced. For children with adrenal crisis, additional challenges include an increased incidence of hypoglycemia, ensuring weight-based dosing for medications, and difficulty attaining IV access [91].

Patient education is essential for the prevention of adrenal crisis. Patients should be aware of the risk factors in addition to associated signs and symptoms. Specific medication orders should be given for sick/stress days, and an emergency hydrocortisone kit should be available at all times [91].

CUSHING SYNDROME

As discussed, Cushing syndrome is a disorder of excess cortisol, and the effects of this disorder can be seen in nearly every body system [24]. It is most commonly seen in individuals between 20 and 50 years of age and is three times more common in women than men [92]. Cushing syndrome affects 40 to 70 people per 1 million population in the United States [28]. Nearly 90% of cases are among adults, but children can be affected [24].

PATHOPHYSIOLOGY

Cushing syndrome is further classified as iatrogenic (or exogenous), primary, secondary, or ectopic [24]. Iatrogenic Cushing syndrome is the most common form and is the result of long-term glucocorticoid therapy [21]. Both primary and secondary Cushing syndrome develop as a result of endogenous causes (e.g., adrenal tumor). Primary Cushing syndrome is typically caused by adrenal gland malignancy, while secondary Cushing syndrome (also referred to as Cushing disease) is the result of excessive secretion of ACTH by a pituitary tumor, usually an adenoma [24]. Ectopic Cushing syndrome arises from the endogenous production of ACTH by one of at least 25 different extrapituitary malignancies, including carcinoma of the lung and of several organs in the GI tract. Secondary Cushing syndrome is the most common (66%) endogenous type of the disease. When this condition is seen in infants, it is most commonly caused by an adrenal carcinoma [24].

As noted, Cushing syndrome is most commonly caused by long-term, high-dose glucocorticoid (e.g., prednisolone, dexamethasone) therapy, often used for the treatment of chronic conditions, such as asthma and chronic obstructive pulmonary disease (COPD) [21; 28]. Symptoms associated with exogenous Cushing syndrome typically do not develop until the patient has been taking corticosteroids for at least one month [24].

In comparison, endogenous Cushing syndrome is relatively rare, occurring in 2 to 3 out of every 1 million people [41]. Cushing disease (secondary Cushing syndrome) makes up approximately 70% of all endogenous cases [21]. It is important to note that the terms Cushing syndrome and Cushing disease are not synonymous. Cushing syndrome encompasses cortisol changes from a variety of internal (endogenous) or external (exogenous) causes, while Cushing disease is only endogenous disease caused by a pituitary tumor or hyperplasia of the pituitary gland [29; 92].

SIGNS AND SYMPTOMS

A variety of signs and symptoms may be observed in patients with Cushing syndrome, including round ("moon") face; flushed face; weight gain above the collarbone and/or on the back of neck ("buffalo hump"); purple striae on the chest, armpits, and abdomen; acne; excessive facial hair; easy bruising; thin skin; rapid central weight gain; thin extremities; hypertension; skin ulcers; headache; muscle weakness; weak bones; menstrual irregularities; decreased libido; erectile dysfunction; hyperglycemia; emotional disturbances; and slowed growth in children [29; 92; 93]. Visceral fat deposits are one of the most common and often one of the first symptoms [21]. The distribution of fat deposits is different than what is typically seen with obesity [21]. For example, fat deposits are commonly seen on the face and clavicular area, both anterior and posterior; extremities often remain thin unless edema develops [21].

Many of the signs and symptoms associated with this disorder are due to the protein-wasting effect of cortisol [21]. Muscle wasting, thin skin, and striae develop because of the catabolic effect of cortisol on the tissues [16]. Purple/red striae occur then the skin becomes thin and stretched over areas of fat deposits [21]. This sign is most commonly seen on the abdomen, flank, breast, hips, and axillae [21]. The patient's skin may be red and warm to the touch due to inflammatory changes [21]. Patients with Cushing syndrome bruise easily and have fragile skin that is prone to tears. Wound healing is slowed due to the increased cortisol levels and subsequent hyperglycemia [21]. Lower extremity edema may develop and is often due to increased capillary permeability and sodium/fluid retention [21].

Children and adolescents with Cushing syndrome may present with growth delay or arrest (most common), weight gain/obesity, virilism, hirsutism, delay of secondary sexual development, and muscle weakness [94].

Women with Cushing syndrome may display signs of androgen imbalance, including oligomenorrhea or amenorrhea; infertility; excess hair on the face, neck, chest, abdomen, and thighs; thinning of the hair on the scalp; and polycystic ovary syndrome [16; 28; 94]. In addition to increasing the risk for infertility, Cushing syndrome may also increase the risk for miscarriage, perinatal death, premature birth, intrauterine growth restriction, pre-eclampsia, and eclampsia [21; 58]. Men may experience erectile dysfunction and decreased fertility and libido [28].

The symptoms of Cushing syndrome often overlap significantly with metabolic syndrome [41]. These symptoms include obesity, glucose impairment, insulin resistance, dyslipidemia, and hypertension, all of which may persist after diagnosis and treatment of Cushing syndrome [41]. Patients with Cushing syndrome will have an increased risk for heart attack, cardiac failure, and left ventricular hypertrophy [41]. These persisting conditions can lead to a decreased quality of life and an increased risk morbidity and mortality.

Patients with this condition may also present with emotional, behavioral, and cognitive effects, such as mood changes, increased irritability, anxiety, depression, sleep problems, memory problems, and fatigue [29; 93]. Anxiety and bipolar disorder are the most common psychiatric disorders associated with Cushing syndrome [41]. In children, obsessive compulsive disorder may be seen, as well as a declining school performance [41].

The catabolic effect of cortisol can cause changes to the patient's bones [16]. Up to 40% of patients with Cushing syndrome will develop osteoporosis and 20% of patients with this disorder will develop compression fractures of the spine [21]. Patients may also have a spontaneous rupture of the Achilles tendon [94]. The patient may also develop kyphosis and decreased height. Individuals with Cushing disease are more prone to opportunistic infections [94].

Many patients with Cushing syndrome report a decreased quality of life. Appropriate diagnosis and treatment can lead to improvements in patient health and well-being.

DIAGNOSTIC TESTS

Diagnosis of Cushing syndrome may be difficult because cortisol levels are variable and will fluctuate throughout the day [93]. Misdiagnosis is common because the disease typically progresses slowly, making symptom identification more difficult [92]. Diagnosis is based on a medical history, physical exam, and laboratory tests. Through the diagnostic process, differential diagnosis is a consideration, as several conditions can mimic the syndrome. Patients should be evaluated for recent use of oral, cream, or inhaled steroids, most commonly hydrocortisone, prednisone, and dexamethasone [92]. Estrogen-containing oral contraceptive pills can increase cortisol and glucose levels, making diagnosis a challenge [21]. When testing for Cushing syndrome, estrogen therapy should be discontinued for six weeks prior to the test, if possible [21].

Diagnosis is especially challenging during pregnancy, because cortisol and glucose levels normally increase during this time [21]. Understanding that pregnancy and oral contraceptives may increase blood glucose and cortisol levels, Cushing syndrome testing should utilize saliva or urine samples in these patients [21].

After Cushing syndrome is diagnosed, it is necessary to determine the underlying cause [41]. This can often be accomplished with a dexamethasone-corticotropin-releasing hormone test [28]. This test can distinguish Cushing syndrome from non-Cushing causes of elevated cortisol. Similarly, bilateral inferior petrosal sinus sampling can be used to differentiate pituitary from ectopic Cushing syndrome [41].

CT or MRI is necessary to identify pituitary or adrenal tumors; MRI is the preferred imaging technique for Cushing syndrome [21]. CT scan can be used, but it is less reliable and may lead to false positive findings [21]. Additional laboratory tests may show neutrophilia and decreased lymphocytes and eosinophils [21].

TREATMENT

Surgery

As noted, the underlying cause of Cushing syndrome will guide the development of a plan of care [58]. If a tumor is the cause, surgery is often necessary. Surgery is effective and is associated with decreased morbidity and mortality [21]. Prior to surgery, hypertension and hyperglycemia should be well-controlled.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Endocrine Society recommends initial resection of primary lesion(s) underlying Cushing disease, unless surgery is not possible or is unlikely to significantly reduce glucocorticoid excess.

(https://academic.oup.com/jcem/article/100/8/2807/2836065. Last accessed July 19, 2024.)

Strength of Recommendation/Level of Evidence: 1/⊕⊕⊕⊕ (Strong recommendation based on high-quality evidence)

An adrenalectomy is the surgical removal or resection of one or both of the adrenal glands. In a subtotal adrenalectomy, only part of an adrenal gland is excised [60]. In most cases, the major goal of adrenalectomy is to reduce hyperfunction secondary to a tumor or hyperplasia of the glands (e.g., pheochromocytoma) or in advanced cases of cancer of the breast and prostate.

Laparoscopic adrenalectomy is the criterion standard for benign adrenal conditions [95]. A number of approaches are appropriate given the location of the adrenal glands, including trans-sphenoidal microsurgery, posterior or lateral retroperitoneal, transthoracic, and lateral transperitoneal [93]. Rarely, an open adrenalectomy may be required for large tumors or complicated cases.

Preoperative nursing care focuses on stabilization of the patient. In a patient with Cushing syndrome, this involves controlling hypertension, hyperglycemia, and hypokalemia. However, it also requires attention to decreased resistance to stress and infection, emotional liability, and edema [61]. The environment should be organized to provide maximum physical and emotional rest for the patient. Hyperadrenocorticism has an impact on the emotions, and patients may require additional support and reassurance. Patients should also be monitored for symptoms or signs of infection [61; 95].

Serum electrolytes and urinary glucose and acetone levels will be monitored at regular intervals. Any fluid and electrolyte imbalances should be corrected in the preoperative period, because they may be exacerbated in the postoperative period. Intake, output, and weights should be recorded to assess the degree of fluid retention [54].

In the postoperative period, dietary selections should be centered on controlling hypertension, hyperglycemia, and hypokalemia. If a patient with excessive hyperadrenocorticism has protein depletion (hypoproteinemia), as reflected by a low serum albumin level, he or she may be prescribed a high-protein diet [96].

Corticosteroids are administered preoperatively as well as during surgery to prevent renal insufficiency in the postoperative period. Intravenous fluids are usually started and infused slowly to allow prompt administration of corticosteroids and vasopressors if needed [54].

Patient teaching before adrenalectomy should include [54]:

- What to expect in the immediate postoperative period (i.e., the patient will be in the recovery room or intensive care unit until stable, and vital signs will be monitored regularly)
- The importance of coughing, deep breathing, and early ambulation for prevention of complications
- The nature of the procedure, its indication, and its expected outcome, including the need for lifelong medication and medical supervision

The greatest postoperative concern after adrenalectomy is adrenal insufficiency. Also important are possible hypotension caused by the rapid withdrawal of mineralocorticoids, electrolyte imbalances, and infection resulting from suppression of the immune system. The surgical hazards associated with adrenalectomy include possible injury to the spleen, liver, duodenum, and common bile duct as well as hemorrhage [54].

Postoperative nursing care of the patient following adrenalectomy includes frequent monitoring of the vital signs, including level of consciousness and blood pressure. Blood pressure is monitored every 15 minutes in the immediate postoperative period until it is stabilized. Any unexplained or significant fall in blood pressure should be reported immediately, because it may indicate immediate impending adrenal insufficiency. Complaints of chest pain should also be reported, because they may indicate cardiac involvement or a pulmonary embolism [54].

Patients should also be monitored for signs and symptoms of Addisonian crisis. Early signs of adrenal insufficiency may be subtle, including restlessness, dehydration, and tachycardia. Later signs (preceding overt shock) are increased weakness, hypotension, increased temperature, and vomiting. Addisonian crisis requires prompt intervention with increased corticosteroids, hypertonic saline solution, or both. In rare cases, peripheral vasoconstrictors may be used [54; 55].

If the tumor is removed but the gland remains, the gland may start to function again over time [29]. However, the patient may require supplemental cortisol until function returns [29]. Blood hormone levels should be checked at intervals after surgery to assess glandular function. In instances in which the gland is removed along with the tumor, lifelong cortisol replacement will be necessary. Surgery is often paired with radiation therapy and/or chemotherapy.

Pharmacotherapy

Three medication classes may be used in the treatment of Cushing syndrome: somatostatin analogs (central-acting inhibitors of ACTH), adrenal steroidogenesis inhibitors, and antiglucocorticoids [92]. Pasireotide, a somatostatin analog, is used to reduce ACTH to normal levels [92]. It is administered by subcutaneous or intramuscular injection and is effective in approximately 25% of patients; for others, it may decrease but not fully resolve symptoms [92]. It may take up to two months for the full effects of the agent to be seen [92]. Common side effects associated with pasireotide include fatigue, headache, hypertension, edema, alopecia, hyperglycemia, GI upset, anorexia, and injection-site reactions [75]. Ketoconazole, metyrapone, mitotane, and etomidate are adrenal steroidogenesis inhibitors that are used off-label to decrease cortisol levels in patients with Cushing syndrome [92]. For example, when administered at a dose of 400–1,200 mg per day, the antifungal ketoconazole effectively decreases cortisol production [58]. Mifepristone is a antiglucocorticoid commonly used to treat hypertension associated with Cushing syndrome [92]. A variety of side effects are associated with this medication, including but not limited to anxiety, headache, dizziness, fatigue, edema, hypothyroidism, hypocalcemia, GI upset, dry mouth, uterine bleeding, and dyspnea [75].

Radiation Therapy

Treatment of Cushing syndrome may also include targeted radiation therapy, known as stereotactic radiosurgery [92]. Stereotactic radiosurgery involves the application of x-ray beams to destroy the DNA of abnormal tissue [97]. This can reach small and/or difficult to reach areas in the body while decreasing the risk for damage to healthy tissue [97]. Stereotactic radiosurgery is associated with fewer side effects than other types of radiation therapy [97]. When side effects do develop, they may include fatigue, skin irritation at the site of treatment, hair loss at the site of treatment, headache, and GI upset [97].

Nursing Interventions

Standard nursing care for patients being treated for Cushing syndrome includes a medication review, vital signs, intake and output assessment, laboratory test monitoring, and infection prevention. Nurses should inquire about weight gain, paying particular attention to patient reports of the face becoming more "round" or a "hump on their back." Photographic comparison of the patient's previous appearance may be helpful. To assess for skin thinning, examine the skin on the back of the hand for striae, skin color, and skin texture [21]. The patient's muscle strength should be assessed by asking the patient to rise from sitting without using their hands or arms; the muscle wasting that occurs with Cushing syndrome tends to occur in the lower extremities [94]. The nurse should also examine the patient's extremities, noting if they appear thin or atrophied.

Electrolyte monitoring is important because potassium levels are often low and sodium levels are often high, requiring treatment and monitoring [42]. Patients may be encouraged to consume a high-potassium, low-sodium, and high-protein diet [16]. Patient education should include dietary recommendations and the importance of the various nutrients.

Patients with suspected Cushing syndrome should be asked about the use of steroids [94]. If Cushing syndrome is caused by long-term glucocorticoid use, the dose is usually decreased slowly over an extended period of time [28]. The nurse should also provide education to the patient about any medications and/or treatment ordered.

PRIMARY ALDOSTERONISM

Primary aldosteronism, also known as Conn syndrome or hyperaldosteronism, is a condition caused by excessive production of aldosterone by the adrenal cortex. It is characterized by hypertension, excessive urinary loss of potassium, and retention of sodium. Primary aldosteronism is thought to be the underlying cause in 1% to 2% of patients with diagnosed hypertension.

Primary aldosteronism originates from one of three sources: single adrenocortical tumor (generally a benign adenoma), bilateral hyperplasia of the adrenal cortices, or tumor of the juxtaglomerular cells of the kidney (which produce renin autonomously). A secondary form of aldosteronism occurs when increased renal secretion of renin leads to the increased production of aldosterone. The increase renin secretion results from other pathologic processes in the body, such as heart failure or cirrhosis. The production of aldosterone it triggers in turn initiates a cycle of pathologic changes, resulting in increased fluid retention, further compromising cardiac and hepatic function [98; 99].

SIGNS AND SYMPTOMS

The major clinical manifestations of primary aldosteronism are hypertension, excessive urinary loss of potassium resulting in hypokalemia, and retention of sodium (hypernatremia). The hypertension is usually a moderate elevation in diastolic blood pressure. Patients may complain of headaches, and on physical examination, early hypertensive retinopathy and cardiomegaly may be noted [98; 99].

Symptoms of hypokalemia range from mild fatigue to profound weakness. Patients may complain of paresthesia, loss of stamina, muscular weakness, and intermittent periods of paralysis. If hypokalemia alkalosis occurs, resulting in tetany, physical examination may elicit positive Trousseau and Chvostek signs [98; 99].

Because of the increased reabsorption of sodium and water, hypernatremia and hypervolemia occur. Generally, edema is not present. The hematocrit may appear abnormally low as a result of the hemodilution. In addition to these major clinical signs, the patient with primary aldosteronism may also have severe polydipsia, polyuria, and nocturia resulting from the renal tubules' inability to respond appropriately to ADH [98; 99].

Primary aldosteronism should be suspected in all patients with hypertension, particularly the young. Findings of comorbid hypertension, hypokalemia (potassium level less than 3.5 mEq/L), and excessive mineralocorticoid production (increased serum aldosterone levels) suggest the diagnosis. These findings become more significant if an excessive excretion of urinary potassium is found along with hypernatremia and decreased excretion of urinary sodium [98; 99].

DIAGNOSIS

For the diagnosis of primary aldosteronism, a spironolactone test may be used in conjunction with assessment of serum potassium levels. Spironolactone is an aldosterone antagonist and, when given orally for three to four days, will stop the urinary excretion of potassium and restore serum levels to normal. Serum potassium levels have been shown to drop again five to seven days after the drug is halted [98; 99].

To identify and localize an aldosterone-producing adenoma, various techniques may be used. Noninvasive procedures such as CT, MRI, and fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET)/CT are the most commonly used imaging studies to assess potential adrenal masses. Invasive procedures, such as arteriography and retrograde adrenal venography, are rarely used for this purpose [98; 99].

TREATMENT

The two main approaches to the treatment of primary aldosteronism are surgery and pharmacotherapy. Surgery is indicated when there is a unilateral aldosterone-producing tumor. In cases of hyperplasia, a subtotal or total adrenalectomy may be performed. Postoperatively, the return of normal aldosterone secretion by the remaining adrenal tissue may take several months. Following resection of the tumor, blood pressure will return to normal in most patients, but in one-third it may be lowered only slightly [100; 101].

If surgery is not possible or declined by the patient, mineralocorticoid receptor antagonists (e.g., spironolactone, eplerenone) and lifestyle changes may be necessary to help control symptoms [102; 103]. Possible side effects of these medications include gynecomastia, hyperkalemia, and hyperglycemia. Lifestyle changes, including weight loss, exercise, and low-sodium diet, and smoking cessation, will also be necessary.

In patients with primary aldosteronism due to bilateral adrenal disease, the Endocrine Society recommends medical treatment with a mineralocorticoid receptor antagonist (e.g., spironolactone). (https://academic.oup.com/jcem/article/101/5/1889/2804729. Last accessed July 19, 2024.)

Strength of Recommendation/Level of Evidence: 1|⊕⊕○○ (Strong recommendation based on low-quality evidence)

Nursing Interventions

The nursing care of patients with primary aldosteronism should include daily weights and measurement of intake and output to assess the degree of fluid retention and loss, as well as frequent assessment of blood pressure, pulse, and respiratory rate.

Symptoms and signs of increased blood pressure (e.g., headaches, changes in visual acuity, hypertensive retinal changes) should also be noted. Patients should also be observed for symptoms and signs of cardiac decompensation and congestive heart failure (e.g., increasing shortness of breath, jugular venous distention, rales at lung bases, orthopnea, and paroxysmal nocturnal dyspnea), and irregularities in heart rate and rhythm [100; 101].

Symptoms and signs of hypokalemia, muscle weakness, cramping, fatigue, and skin breakdown should also be noted. Patients should be assessed for paresthesia and tetany. It is vital that these individuals take adequate rest. The recommended diet is low in sodium and high in protein and potassium. Calories may be restricted if weight reduction is desired [100; 101].

Patients with primary aldosteronism should receive instruction on the nature of the disorder (e.g., pathophysiology, symptoms and signs, prognosis) and the goals of the treatment plan. If pharmacotherapy is indicated, patients should be familiar with its purpose, action, dosage, administration, and side effects. Patient teaching on diet, physical activity, and regular medical follow-up should also be provided. If surgery is done, patients should be aware of the time frame for resumption of adrenal function, the potential need for postsurgical medication therapy, and signs of surgical complications [100; 101].

Patients who are able should take and record their blood pressure and pulse regularly. Nurses can provide instruction on how to interpret the findings and when to report issues. If patients are unable to self-monitor, a caregiver or family member may be engaged in the capacity [100; 101].

PHEOCHROMOCYTOMA

Pheochromocytomas are tumors that arise from chromaffin cells in the adrenal medulla. While tumors originate in the adrenal medulla, they may rarely develop in the sympathetic ganglia of the abdomen, bladder, or chest; these are referred to as extra-adrenal pheochromocytomas or catecholamine-secreting paragangliomas. Pheochromocytomas characteristically produce both catecholamines (epinephrine and norepinephrine), although some tumors may release only one of the catecholamines. Hypersecretion of epinephrine elevates blood pressure by increasing the strength of contractions of the heart and increasing cardiac output. Norepinephrine causes arteriolar vasoconstriction, increasing peripheral vascular resistance to blood flow. Both of these effects result in marked elevation of both diastolic and systolic blood pressure, which is characteristic of pheochromocytoma [104; 105].

Pheochromocytomas are thought to occur more often than clinically recognized and are often diagnosed due to incidental findings when investigating other unrelated issues. Pheochromocytomas are also often asymptomatic or vaguely symptomatic for some time. Tumors that produce primarily epinephrine are typically associated with profuse diaphoresis, palpitations, tremors, anxiety, heat intolerance, and pallor followed by flushing. Tumors that produce primarily norepinephrine are associated with fewer symptoms; when symptoms are present, they are similar to those of essential hypertension [104; 105].

Most (70%) pheochromocytomas are benign, unilateral adrenal tumors; however, 10% are benign bilateral or multiple, 10% are extra-adrenal, and 10% are malignant. Men and women are equally affected, and the peak incidence is in the fourth and fifth decades of life, although they can occur at any age. Pheochromocytomas can also be found in association with certain familial neurofibromatosis disorders (e.g., neurofibromatosis, hemangioblastoma), hyperparathyroidism, and thyroid medullary carcinoma [104; 105].

SIGNS AND SYMPTOMS

Both epinephrine- and norepinephrine-producing tumors may secrete catecholamines paroxysmally, episodically, or continuously. The most severe symptoms are usually seen in patients with paroxysmally functioning tumors because of the rapid and marked changes in serum catecholamine levels. About 40% of patients with pheochromocytoma have paroxysmal hypertension, whereas the remainder experience either sustained or labile elevations in blood pressure [105].

Paroxysmal attacks vary in frequency, severity, and duration. Both the onset and resolution tend to be abrupt, with the average attack lasting a few minutes to a few hours. In many patients, these attacks may occur without warning, but others may be able to identify a prodrome of dermal paresthesia and increasing anxiety. Paroxysmal attacks may be precipitated by emotional changes (e.g., laughing, sexual activity, pain), postural changes (especially flexion or bending of the body), and/or physical exertion. Attacks may increase in frequency and duration over time and can result in pulmonary edema, cerebral hemorrhage, or ventricular fibrillation [105].

Symptoms of pheochromocytoma include headache, diaphoresis, and intense palpitations. The patient may also complain of extreme anxiety, tinnitus, excessive weakness, tremor, blurred vision, vertigo, dyspnea, and angina. After the attack, the patient may report a feeling of extreme weakness and exhaustion [100; 106; 107].

Signs of pheochromocytoma include marked elevation of the diastolic and systolic blood pressure (which may rise as high as 200 to 300/150 mm Hg), often with excessive diaphoresis, anxiety, dilation of the pupils, and tachycardia. Orthostatic hypotension and hypertensive retinopathy may occur in patients with persistently functioning tumors. Hyperglycemia and glycosuria are also frequently associated with pheochromocytoma because catecholamines can inhibit insulin production [100; 106; 107].

DIAGNOSIS

Pheochromocytoma should be suspected in patients with hypertension who have symptoms and signs of sympathetic hyperactivity, although only an estimated 0.2% of hypertension is related to pheochromocytoma. Diagnosis of pheochromocytoma is based on the presence of symptoms, laboratory confirmation, and imaging modalities. Biochemical testing of the serum and/or urine will reflect continuous production of catecholamines and their metabolites (metanephrines) [108]. In the past, pharmacologic tests (e.g., histamine test, phentolamine-blocking test) were used, but these have largely been replaced by more reliable and safer urinary assays [102].

After excessive catecholamine secretion has been determined, imaging studies are done to confirm the diagnosis and localize the tumor [100; 107]. PET is the preferred approach, coupled with CT. The American College of Radiology recommends FDG-PET/CT scan to detect metastatic disease [109].

TREATMENT

The definitive treatment of pheochromocytoma is surgical excision of the tumor. In the 10% of patients who are not surgical candidates (because of malignant pheochromocytoma with metastases or serious medical problems), control of symptoms is attempted with cytoreductive techniques, radiopharmaceuticals, chemotherapy, radiotherapy, and experimental therapies.

Surgical resection of a pheochromocytoma is considered high-risk due to the potential impact on heart rate and blood pressure. The Endocrine Society recommends that all patients with hormonally functional pheochromocytoma undergo preoperative blockade to prevent perioperative cardiovascular complications. The recommended preoperative treatment of choice is alpha-adrenergic receptor blockers [110]. This treatment should continue for 7 to 14 days before surgery. During this period, patients should also be instructed to adhere to a high-sodium diet and to increase fluid intake. Adjustments should be made prior to surgery in response to blood pressure, heart rate, and blood glucose level monitoring.

The usual operative approach is minimally invasive (laparoscopic) adrenalectomy. Open resection is reserved for large (i.e., >6 cm) or invasive pheochromocytomas to ensure complete tumor resection, prevent tumor rupture, and avoid local recurrence [110]. Partial adrenalectomy may be appropriate for selected patients.

Because of the possibility of extreme fluctuations in the blood pressure in the immediate postoperative period, blood pressure should be monitored every 15 minutes until stabilized; the time to stabilization may be extended in patients with pheochromocytoma. Nurses should be alert for sudden elevation in blood pressure in the early postoperative period, which may reflect a release of epinephrine and norepinephrine from the tumor as it was being excised. An alpha-adrenergic blocking agent may be used intravenously if the blood pressure rises excessively [60].

Severe hypotension may also develop postoperatively and can lead to shock. Metaraminol or norepinephrine, usually administered via IV infusion, may be used to help stabilize the patient. The dosage and flow rate will depend on accurate blood pressure measurements [60]. All patients who have undergone resection of a pheochromocytoma should be advised to change positions slowly to avoid orthostatic hypotension.

Discharge planning should stress the need for lifelong medical supervision. Following successful resection, patients should undergo regular follow-up, including measuring plasma or urine levels of metanephrines, to diagnose persistent (recurrent or metastatic) disease. Pheochromocytomas recur in 10% to 13% of cases [55].

EVIDENCE-BASED PRACTICE RECOMMENDATION

For patients who have undergone treatment for pheochromocytoma, the Endocrine Society suggests lifelong annual biochemical testing to assess for recurrent or metastatic disease.

(https://academic.oup.com/jcem/article/99/6/1915/2537399. Last accessed July 19, 2024.)

Strength of Recommendation/Level of Evidence: 2|⊕⊕○○ (Weak recommendation based on low-quality evidence)

PSYCHOSOCIAL/LIFESTYLE INFLUENCES AND EFFECTS

The pituitary and adrenal glands have far-reaching effects on both physiologic and psychological function, and dysfunction can contribute to major developmental and psychosocial crises. To provide comprehensive patient care, nurses should be aware of these potential crises and their manifestations [81; 82].

Patients with pituitary and/or adrenal dysfunction may have to face the reality of coping with chronic illness or an acute life-threatening situation. Anger, fear, guilt, and denial are common initial reactions. Individual responses to this challenge vary according to the patient's past experiences, attitudes toward health and illness, coping patterns, and support system strength. It is not unusual to find patients with several years' history of a disease still working through their anger and denial. In pediatric cases, parents' feelings of guilt and denial should also be considered as part of a holistic plan of care [81; 82].

In many patients, lifestyle changes are necessary to manage the disease, reduce symptoms, and perform activities of daily living and tolerate stress. However, these changes are often reminders to the patient and family that the illness is serious and that their lives will be affected [81; 82].

SELF-CONCEPT AND SELF-ESTEEM

Patients with pituitary or adrenal dysfunction are often confronted with a change in self-concept and a loss of self-esteem arising from changes in body image, decreased functional abilities, sexual dysfunction, loss of autonomy, and limitations in the decision-making processes. Changes in self-concept and loss of self-esteem can interfere with the patient's ability to adhere with the treatment plan and accept the diagnosis and its implications. For example, patients with Cushing syndrome will often require time and support to adjust to the cosmetic implications of the "moon" face, upper back/neck fat deposits, and truncal obesity associated with that disorder. Some conditions will also affect patients'

ability to participate in activities as they once had or wish to. Individuals with Addison disease are required to take steps to avoid stressful situations. These pathophysiologic changes affect the patient's ability to function in normal situations, causing further stress and anxiety [81; 82].

Certain disorders, including pituitary tumor and dysfunction of the adrenal cortex and medulla, cause emotional liability and personality changes. This presents serious concerns for the patient, who often feels out of control or unrecognizable. The nurse can help both the patient and family to understand the relationship between the physiologic condition problem and the psychological changes [81; 82].

SEXUAL EXPRESSION AND REPRODUCTION

Often in disorders affecting the creation of the adrenocortical sex hormones, changes in libido and sexual potency concern patients and their sexual partner. Sensitive intervention by the nurse may relieve anxiety in the couple [82]. Unfortunately, sexual dysfunction is rarely addressed in the treatment plan for these patients. Research indicates that different domains of sexual health are affected by different disease processes, particularly in women. Specifically, hypercortisolism is associated with impaired lubrication, orgasm, sexual arousal, and satisfaction, while hyperprolactinemia and hypoandrogenism are associated with decreased sexual desire and arousal [111]. Treatment of the underlying condition may help, but if sexual dysfunction persists, it should be addressed by pharmacotherapy, adaptive practices, and psychotherapy. It is important to remember that pharmacotherapy cannot address important psychosocial factors of performance anxiety, poor self-confidence, partner sexual dysfunction, relationship conflict or poor communication, sexual factors in the relationship (e.g., sexual scripts, sexual satisfaction), and contextual factors (e.g., life stressors) [112]. Even when sexual dysfunction is primarily physiologic, virtually all patients experience negative psychologic and interpersonal effects. These include interpersonal conflict, depression, performance anxiety, and avoidance of sex.

OCCUPATIONAL AND ECONOMIC FACTORS

Occupational implications of pituitary/adrenal disorders include the possible need to change occupations or limitations in one's ability to work because of a physical disability. Patients with visual loss or changes in mentation often must make significant occupational adjustments. Patients may require adaptive equipment or may move to a different area to be closer to a source of health care or to access a special living environment. Economic factors may include the necessity for lifelong medications and medical supervision along with the increasing costs of diagnostic tests and hospitalizations [104; 105].

DIETARY FACTORS

The adjustment to new dietary requirements is a major challenge for patients with pituitary/adrenal disease. Patients who previously gave little thought to nutrition or balanced meals are often introduced into a life of fluid restrictions, special diets, and dietary supplements. These changes add extra strain to an already stressful situation and can also be an economic burden. Nurses should acknowledge the importance of dietary challenges and understand how they affect the patient and family, with particular consideration of how food features in the patient's culture. Patient teaching should include an exploration of dietary customs and how changes will be linked to improved health and quality of life [104; 105].

CULTURAL CONSIDERATIONS

As society becomes increasingly diverse, nurses are encountering a wide variety of cultural values and perceptions that influence health behavior in individuals and families. Because culture can have a strong influence on a patient's response to nursing interventions, nurses should be continually aware of these influences.

Cultural competence means being sensitive to differences in the values and beliefs that are shared by the members of an ethnic, cultural, racial, religious, or lifestyle preference of a group. Components of effective transcultural nursing include communication style, use of personal space, eye contact, and understanding of biologic variations. It is important to keep in mind, however, that there can be great variation among individuals within cultures. Therefore, stereotyping and making assumptions about an individual patient's beliefs based solely upon ethnic identification should be avoided.

In most cases, it is not necessary to develop a thorough understanding of each and every culture encountered in diverse healthcare settings. However, a certain degree of cultural competence can and should be developed. The first step in doing this is to recognize that cultural differences do exist. How these variations impact self-management can be explored in the needs assessment. This may include a sensitive exploration of the person's healthcare practices and the role of family members. Other culturally impacted areas may include beliefs about illness, diet, the role of the patient in self-care, gender roles, religious rituals, and communication styles.

Dietary preferences, meal preparation practices, and the symbolism of food represent an especially important area. When giving diet instructions, efforts should be made to consider the food preferences of the cultural group.

Cultural competence includes recognizing that cultural healthcare practices may differ from one's own beliefs about how an illness should be treated. Furthermore, cultural influences may not always be consistent with healthcare recommendations. This may be especially true for diseases that require significant behavioral adaptations. Americanized versions of traditional foods are high in salt, fat, and calories and are not recommended for people with restricted diets. Therefore, patients may experience a conflict between cultural values and those of the mainstream healthcare system.

CASE STUDIES

ACUTE ADRENAL INSUFFICIENCY (ADDISON DISEASE)

Present Illness

Patient A, a man 50 years of age, is admitted for diagnosis and initial management of suspected adrenal hypofunction with acute adrenal insufficiency. For the past five years, Patient A has been under considerable stress managing his failing contracting business. Initially, he dismissed his complaints of fatigue and weakness as job-related. Lately, the symptoms have been difficult to ignore and associated with anorexia, nausea, and vomiting. He has lost 30 pounds over the past three months without dieting. He complains of frequently feeling cold and has had two syncopal attacks in the month prior to admission. He reports that although he has spent essentially all this time indoors at the office, his skin has become as dark as his employees who work outdoors.

On the morning of admission, he did not wake at his usual early hour and told his wife that he felt gravely ill. His wife called the family physician, who instructed her to take Patient A to the emergency department. After evaluation in the emergency department, Patient A is admitted to the critical care unit (CCU).

Medical History

A medical history is obtained from Patient A's wife. She states that the patient has no allergies to medications but was very allergic to ragweed when they were first married. During the first 10 years of their marriage, Patient A had frequent asthma attacks requiring treatment with epinephrine injections. The asthma attacks diminished in frequency during his middle years, and his wife cannot remember when he last had an attack.

PATIENT A'S PHYSICAL EXAM RESULTS	
Parameter	**Findings**
General appearance	A thin, well-tanned man who seemed mildly confused Height: 6 feet 2 inches (188 cm) Weight: 190 pounds (86 kg)
Head and eyes	Normocephalic Numerous gray-brown freckles on forehead Pupils equal (4 mm), round, reactive to light and accommodation Normal fundoscopic exam Extraocular muscles full Nasal turbinates slightly reddened, with clear exudate Brown freckles on oral mucosa Pharynx clear
Ears	External ear canals clear Tympanic membranes clear and retracted
Neck	Supple, without masses or thyromegaly Nonpalpable cervical lymph nodes
Chest	Symmetrical excursion Areolas darkly pigmented Lungs clear to percussion and auscultation
Abdomen	Flat with active bowel sounds in all quadrants Normally unexposed skin appears tanned Soft, nontender, and without organomegaly or masses
Extremities	Pulses present, equal, and faint. Normal hair distribution
Genitourinary system	Within normal limits
Neurologic status	Oriented to person, place, and time but very slow to answer questions Cranial nerves II–XII grossly intact Deep tendon reflexes 1+ and symmetrical Bilateral plantar flexor responses
Cardiovascular system	Cardiac rhythm sinus bradycardia without ectopy Point of maximal impulse at sixth intercostal space 1 inch left of midclavicular line Heart sounds quiet with normal S1 and S2, without gallops, rubs, or murmurs
Vital Signs	
Blood pressure	100/60 mm Hg
Temperature	96.5° F
Heart rate	58 bpm
Respiratory rate	12 breaths per minute
Source: Author	*Table 2*

Patient A also has a history of coccidioidomycosis, which was active for several years late in adolescence and in early adulthood. Mrs. A has no recollection of being told of changes in the patient's routine chest x-rays for some time. Ten years previously, Patient A was diagnosed with hypertension, but his blood pressure has been well-controlled with daily exercise and dietary changes.

Patient A has been married to his wife for 35 years and has three grown children who live out of state. His contracting business had been successful until five years ago, when a decrease in housing starts resulted in a decline in business and increased financial stress.

Assessment and Diagnosis

Upon admittance to the CCU, a full physical exam is conducted (***Table 2***). A chest x-ray is done and shows normal lung fields and a smaller than expected heart. Several laboratory tests are ordered, with the following results:

- Serum chemistry results:
  - Sodium: 125 mEq/L
  - Potassium: 6.2 mEq/L
  - Chloride: 89 mEq/L
  - Carbon dioxide (CO_2): 19 mmol/L
  - Blood glucose: 45 mg/dL
  - BUN: 37 mg/dL
- Hematocrit: 50%
- White blood count: 3.5 x 10^9/L

Based on the results of the assessment, Patient A is diagnosed with possible acute adrenal insufficiency and possible Addison disease.

Management

Shortly after arriving in the CCU, Patient A vomits a large amount of bile-colored gastric contents and then develops coma and shock. His blood pressure is 60/10 mm Hg, his heart rate is 50 beats per minute, and his respiratory rate is 8 breaths per minute and gasping. He is quickly resuscitated with rapid IV infusion of normal saline, hydrocortisone sodium succinate (100 mg IV), tracheal intubation, and artificial ventilation. A double lumen nasogastric tube is inserted and connected to low constant suction. An indwelling urinary catheter is inserted and connected to a urine meter. Patient A's condition stabilizes as he becomes alert and orientated, has adequate spontaneous ventilation, and maintains adequate cardiac output and blood pressure. Efforts are made to confirm the diagnosis of Addison disease.

The physician orders diagnostic tests of adrenal, thyroid, and pituitary function. Results of the 24-hour urine collection assessed for 17-ketosteroids and 17-hydroxycorticosteroids indicates that adrenal secretion of cortisol, corticosterone, cortisone, and 11-hydroxycorticosternone is inadequate. The result of the plasma cortisol response to ACTH test confirms the diagnosis of Addison disease. The latest results of tests of thyroid and pituitary function are within normal limits.

Patient A is prescribed fludrocortisone acetate (0.1 mg daily) and hydrocortisone (20 mg daily) as replacement therapy. He responds well and is transferred out of the CCU four days after admission.

Study Questions

Consider the information that has been presented in this course regarding adrenal insufficiency and Addison disease.

1. What fluid and electrolyte imbalances are usually associated with adrenal insufficiency? How does the pathophysiology of adrenal insufficiently create these imbalances?
2. What are the expected results of the plasma cortisol response to ACTH test and 24-hour urine collection in adrenal insufficiency? How are the tests conducted?
3. What risks will subsequent critical illness pose for Patient A?
4. What nursing observation would be important in a critically ill patient with a history of adrenal insufficiency?
5. How might chronic adrenal insufficiency be managed during a critical illness?
6. What are the symptoms and signs of hypoadrenalism?
7. What is the most common type of hypoadrenalism?
8. What are the other causes of hypoadrenalism?
9. How is hypoadrenalism diagnosed?

DIABETES INSIPIDUS

Present Illness

Patient B, a man 26 years of age, is in the hospital recovering from surgical clipping of an aneurysm on the anterior communicating artery. Three days after surgery, he begins voiding large quantiles of very pale urine. His IV intake is 80 mL/hour, and his oral intake is minimal. The specific gravity of the urine is 1.002, and the patient's calculated urine output is more than 200 mL/hour for four consecutive hours. The nurse observes that during the past two hours Patient B's blood pressure has declined from 120/80 mm Hg to 110/70 mm Hg and that his heart rate has increased from 68 beats per minute to 110 beats per minute. The nurse notifies the neurosurgeon of the large unconcentrated urinary output and the changes in vital signs.

Medical History

Patient B has suffered chronic severe headaches, and the diagnosis of cerebral aneurysm led to the cerebrovascular procedure. The surgical procedure went well, and Patient B was recovering as expected.

Assessment and Diagnosis

Upon the onset of diuresis, a full physical exam is conducted (***Table 3***). Laboratory findings are:

- Plasma osmolality: 289 mOsm/L
- Urine osmolality: 108 mOsm/L
- Serum sodium level: 150 mEq/L

Based on the findings of the assessment, Patient B is diagnosed with diabetes insipidus secondary to manipulation of the pituitary.

Management

The neurosurgeon orders 2.5 units of aqueous vasopressin to be administered immediately intramuscularly. Following administration, urine output is reduced to 60 mL/hr in 30 minutes. The urine osmolality level two hours later is 760 mOsm/L. Patient B continues to be monitored to determine if the pituitary damage is permanent and if he requires long-term desmopressin therapy.

Study Questions

Consider the information that has been presented in this course regarding diabetes insipidus.

1. What are the key signs and symptoms of diabetes insipidus? How did it present in Patient B?
2. What is the action of vasopressin?
3. What are the main types of diabetes insipidus? What type does Patient B have?
4. What causes central diabetes insipidus? What causes nephrogenic diabetes insipidus?
5. What diagnostic test(s) can reveal whether diabetes insipidus is central or nephrogenic? How are these conditions treated?

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION

Present Illness

Patient C is a Hispanic man, 60 years of age. He is brought to the emergency department by his family because of acute mental confusion and combativeness. His wife and son report that he has been complaining of anorexia, a nonproductive cough, and unusual fatigue and weakness for the past seven months. During this time, he lost 40 pounds. In the past two weeks, Patient C has been unusually irritable and occasionally irrational. The day before admission, the patient's confusion and disorientation became so severe that he tried to hit his wife. Because she could not manage him alone, the patient's wife asked their son to come and stay with them.

The morning of the admission, Patient C has a seizure (with signs consistent with a tonic-clonic seizure), and the family transports the patient to the emergency department for evaluation.

Medical History

Patient C's wife reports that her husband drinks six 12-ounce beers daily and has smoked two to three packs of cigarettes per day for the 35 years of their marriage. She has no knowledge of Patient C's family medical history. In addition, Patient C has only rarely seen a physician for illnesses and has never had a routine physical examination.

PATIENT B'S PHYSICAL EXAM RESULTS	
Parameter	**Findings**
General appearance	A young African American man who appears his stated age and is alert and oriented Height: 5 feet 11 inches (180.5 cm) Weight: 190 pounds (86 kg)
Head and eyes	Normocephalic Dressing dry and intact No ecchymosis visible Pupils equal (4 mm), round, reactive to light and accommodation Normal fundoscopic exam Extraocular muscles full Nasal turbinates and oral mucosa pink and moist Pharynx clear
Ears	External ear canals clear Tympanic membranes clear
Neck	Supple, without masses or thyromegaly
Chest	Symmetrical excursion Lungs clear to percussion and auscultation
Abdomen	Flat with active bowel sounds in all quadrants Soft, nontender, and without organomegaly or masses
Extremities	Pulses present, equal, and moderate
Genitourinary system	Within normal limits
Neurologic status	Oriented to person, place, and time Cranial nerves II–XII grossly intact Deep tendon reflexes 1+ to 2+ and symmetrical Bilateral plantar flexor responses present
Cardiovascular system	Cardiac rhythm normal sinus without ectopy Point of maximal impulse at fifth intercostal space 2 cm left of midclavicular line Heart sounds normal S1 and S2, without gallops, rubs, or murmurs
Vital Signs	
Blood pressure	110/70 mm Hg
Temperature	98.4° F
Heart rate	69 bpm
Respiratory rate	11 breaths per minute
Source: Author	*Table 3*

Assessment and Diagnosis

Upon presentation to the emergency department, a full physical exam is conducted (***Table 4***). An electrocardiogram (ECG) is normal with nonspecific ST-T wave changes. Skull imaging is normal, but a chest x-ray visualizes a mass in the lower right lobe. Laboratory studies find:

- Blood chemistry levels:
  - Sodium: 115 mEq/L
  - Potassium: 3.8 mEq/L
  - Chloride: 80 mEq/L
  - Calcium: 7.2 mg/dL
  - Total protein: 5.8 mg/dL
- CO_2: 25 mmol/L
- BUN: 15 mg/dL
- Blood glucose: 90 mg/dL
- Creatinine: 0.9 mg/dL
- Serum osmolality: 235 mOsm/L
- Urine osmolality: 260 mOsm/L

PATIENT C'S PHYSICAL EXAM RESULTS	
Parameter	**Findings**
General appearance	A thin, disoriented, and irritable man who appears older than his stated age and coughs frequently Height: 5 feet 8 inches (173 cm) Weight: 149 pounds (68 kg)
Head and eyes	Normocephalic All structures normal
Ears	External ear canals clear Tympanic membranes clear
Neck	Supple, without thyromegaly Firm 2 x 3 cm lymph node in right supraclavicular area Jugular vein distention to the angle of the jaw while sitting up 45 degrees
Chest	Increased anteroposterior diameter and increased curvature to thoracic spine curvature Dullness to percussion in right base Lungs have scattered rhonchi and diminished breath sounds in the right base
Abdomen	Flat with active bowel sounds in all quadrants Soft with mild tenderness in right upper quadrant Liver palpable 5 cm below right costal margin
Extremities	Peripheral pulses present, equal, and bounding Normal hair distribution
Genitourinary system	Within normal limits
Neurologic status	Confused, oriented to self only Unable to follow instructions for cranial nerve exam Deep tendon reflexes symmetrically diminished, with bilateral plantar flexion
Cardiovascular system	Heart sounds are normal S1 and S2 with S3 with a soft systolic murmur the base No pericardial friction rub
Vital Signs	
Blood pressure	140/80 mm Hg, supine and standing
Temperature	98.9° F
Heart rate	100 bpm
Respiratory rate	18 breaths per minute
Source: Author	*Table 4*

Based on the findings of the assessment, Patient C is diagnosed with severe hyponatremia secondary to water intoxication. A lack of history for excessive water intake suggests SIADH.

Management

The physician suspects that Patient C has SIADH, and further diagnostic studies are planned and carried out. The supraclavicular lymph node is biopsied. The pathology report identifies the node as small-cell lung cancer.

Patient C's serum cortisol is 10 mcg/dL in the morning. A 24-hour urine collection is completed, and 17-ketosteroids excretion is 9 mg per day and sodium excretion is 150 mEq per day. Patient C's fluid intake is restricted, furosemide is administered, and hypertonic saline is carefully infused. As the patient undergoes diuresis, his serum sodium gradually returns to normal and his sensorium improves. His wife is relieved at the return of her normally gentle husband.

Extended management includes assessment of the underlying cause of the SIADH, assumed to be metastatic small-cell lung cancer. The patient is referred to an oncologist for further testing and treatment.

Study Questions

Consider the information that has been presented in this course regarding SIADH.

1. What are the key signs and symptoms of SIADH? What pathophysiology underlies these effects?
2. How do diabetes insipidus and SIADH present differently? How are they similar?
3. What studies assist in confirming the diagnosis of SIADH? What are the nursing responsibilities in conducting these tests?
4. What safety precautions should be implemented for Patient C because he is confused and oriented to self only?
5. What nursing observations and actions are required to compensate for patients who are not alert and/or do not have access to food and water and therefore cannot use normal physiologic mechanisms to achieve fluid and electrolyte balance?
6. What typically causes SIADH?
7. How is SIADH treated?

CONCLUSION

The pituitary and adrenal glands play a significant role in many functions in the body, and proper functioning is essential for the maintenance of health. Dysfunction in these glands can have detrimental effects and may lead to death if untreated. Although disorders of the pituitary or adrenal glands are not as easy to see or identify as many conditions, they are nonetheless relatively common among many patient populations.

This course has provided a brief overview of the anatomy and physiology of the pituitary and adrenal glands, assessment, common disorders, and care of the patient with pituitary/adrenal dysfunction. Nurses have a responsibility and duty to identify the signs and symptoms of these disorders and to care for patients appropriately and fully.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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