Endocrine Problems in Critically Ill Children

An Overview

Tara Trimarchi, MSN, RN, CRNP

The endocrine system maintains the physiologic functions of multiple other organ systems. Due to the multisystem nature of the endocrine system, endocrine diseases may be either due to or the result of complex illness. In children, developmental changes in organ systems create an additional layer of complexity to endocrine disease, thus children with endocrine problems frequently require critical care. This article will provide an overview of common endocrine problems encountered in critically ill children with attention to disorders that are unique to pediatrics.

□ Review of the Endocrine System

The endocrine system is a network of glands that secrete hormones into the bloodstream and target cells possessing receptors that respond to circulating hormones. Hormones are grouped into 3 categories based on their chemical structure: steroid, peptide, and amine. Characteristics and mechanisms of action of hormones are listed in Table 1. The primary functions of endocrine hormones...
TABLE 1 □ Categories of Hormones

<table>
<thead>
<tr>
<th>Steroids</th>
<th>Peptides</th>
<th>Amines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical structure</td>
<td>Short chains of amino acids and proteins; synthesized from precursor molecules that are cleaved by enzymes</td>
<td>Derivatives of the amino acid tyrosine</td>
</tr>
<tr>
<td>Type of glands</td>
<td>Pituitary gland; parathyroid gland; pancreas; heart; stomach; liver; kidneys</td>
<td>Thyroid gland; adrenal medulla</td>
</tr>
<tr>
<td>Storage and secretion</td>
<td>Stored in secretory granules until release is stimulated</td>
<td>Stored in secretory granules until release is stimulated</td>
</tr>
<tr>
<td>Mechanism of action</td>
<td>Water soluble; does not penetrate the cell plasma membrane; binds to the outer plasma membrane of cells; binding generates a chemical signal from a second messenger system that activates intracellular processes</td>
<td>Water soluble; does not penetrate the cell plasma membrane; binds to the outer plasma membrane of cells; binding generates a chemical signal from a second messenger system that activates intracellular processes</td>
</tr>
</tbody>
</table>

include regulation of growth and sexual maturation; energy production and utilization by cells (metabolic rate) including glucose homeostasis, fluid, and electrolyte balance; and circulatory function. Although endocrine regulation of growth and sexual maturation is a significant issue in general pediatrics, disorders of energy production and utilization, fluid and electrolyte balance, and circulatory function are the endocrine causes of critical illness in children.1,2

Hormone secretion by glands is designed to maintain a delicate balance of cellular functions and thus relies on feedback cycles between physiologic responses and circulating hormone levels.1 An endocrine response typically consists of the sequential release of hormones from various glands until a final hormone exerts a physiologic affect in a target organ. The most common control mechanism for endocrine systems is a negative feedback loop in which rising serum levels of a hormone serve to decrease further hormone secretion by a gland in the sequence. An understanding of the sequence of hormone release and control systems aids in the diagnosis and treatment of endocrine problems. Disorders of the endocrine system can be classified as: (1) overproduction of a hormone, (2) underproduction of a hormone, and (3) nonfunctional receptors that cause target cells to become insensitive to hormones.1,2

□ The Role of the Nervous System in Endocrine Functions

Interplay between the endocrine system and nervous system regulates the secretion of many hormones.1 The pituitary gland, often thought of as the “master gland” of the endocrine system, is located at the base of the brain and is connected to the hypothalamus. The neurons in the hypothalamus directly control the release of pituitary hormones. The pituitary gland has 2 components: the anterior and posterior lobes. Hypothalamic neurons secrete “releasing” hormones into a portal circulatory system that bypasses systemic circulation and delivers the hormones directly to the anterior pituitary. In response to hypothalamic hormones, the anterior pituitary releases its own hormones. Hormones
of the anterior pituitary gland are listed in Table 2. In contrast, other hypothalamic neurons extend the length of the pituitary stalk and reach the posterior pituitary, where they release hormones for storage and later secretion by the gland. Hypothalamic hormones that are stored and released by the posterior pituitary are also listed in Table 2. In both cases, the brain itself is acting as a gland. Frequently, the hormones released by the pituitary gland serve to stimulate the release of hormones from other glands and thus, diseases of the nervous system commonly cause systemic endocrine problems in critically ill children. In addition, disorders of vasopressin or anti-diuretic hormone (ADH) and atrial natriuretic peptide, due to brain injury can substantially impact fluid volume status in the critically ill child.

Vasopressin (Anti-diuretic Hormone)

Vasopressin is formed by the hypothalamus and secreted by the posterior pituitary. The primary role of vasopressin is regulation of serum osmolality. Vasopressin is released in response to low mean arterial blood pressure and/or increased serum osmolality and serves to increase water re-absorption by the collecting ducts of the kidneys.

Atrial Natriuretic Peptide

In addition to vasopressin and aldosterone, atrial natriuretic peptide (ANP) also plays an important role in sodium homeostasis. The heart is known to secrete ANP in response to stretching of the atria due to hypervolemia, and it is also suspected that excited neurons secrete the hormone as well. ANP increases glomerular filtration rate by dilating renal vessels and increases sodium and, to a lesser extent, water secretion into the urine. In addition to the glandular responses of the brain, functions of the adrenal gland, thyroid gland, and the pancreas are also of great importance in pediatric critical care.

The Role of Adrenal Hormones

The adrenal glands are made up of an inner medulla and outer cortex. The adrenal medulla is composed of modified neurons that secrete amine hormones such as the catecholamines: epinephrine and norepinephrine. The sympathetic nervous system stimulates the adrenal medulla to secrete these amine hormones in response to stress and to maintain circulation. The adrenal cortex produces 3 types of steroid hormones:
sex steroids, mineralcorticoids that maintain electrolyte balance, and glucocorticoids that respond to stress by modulating serum glucose levels and suppressing the inflammatory response. Adrenal hormones of importance in pediatric critical care include catecholamines, the mineralcorticoid aldosterone, and the glucocorticoid cortisol.\textsuperscript{1,2}

**Catecholamines**

Epinephrine and norepinephrine are the catecholamines secreted by the adrenal medulla. Catecholamines play an important role in maintaining mean arterial blood pressure. Through their effects on adrenergic receptors, catecholamines increase vascular tone, heart rate, and myocardial contractility.\textsuperscript{1}

**Aldosterone**

Aldosterone is a mineralcorticoid secreted by the adrenal cortex. Aldosterone is primarily secreted in response to low mean arterial blood pressure as part of the renin-angiotensin system, and in response to increased serum potassium and decreased serum sodium levels.\textsuperscript{1} To a lesser extent, corticotropin (ACTH) from the anterior pituitary also triggers the release of aldosterone. Aldosterone stimulates sodium and water retention and potassium secretion by the kidneys.\textsuperscript{1}

**Cortisol**

Cortisol is secreted by the adrenal cortex in response to release of ACTH from the anterior pituitary, which is released in response to corticotropin-releasing hormone (CRH) from the hypothalamus.\textsuperscript{1} This sequence of hormone releases is triggered by stress responses in the body. Cortisol serves to conserve sodium and water, elevate serum glucose levels through conservation of glucose utilization by cells, maintain blood vessel tone and capillary membrane integrity, and suppress inflammation. Cortisol also influences both the production of catecholamines by the adrenal medulla and the number and sensitivity of adrenergic receptors to catecholamines.\textsuperscript{1,2}

□ The Role of Thyroid Hormones

The thyroid gland is made up of follicles that secrete thyroglobulin. Thyroid-stimulating hormone (TSH) secreted by the anterior pituitary in response to thyrotropin-releasing hormone (TRH) from the hypothalamus, converts thyroglobulin to thyroxine, \( T_4 \).\textsuperscript{1} \( T_4 \) is then cleaved to the active thyroid hormone, triiodothyroxine, \( T_3 \). Thyroid hormone serves to increase basal metabolic rate and stimulate tissue growth. Specific cellular processes controlled by thyroid hormone include increased activity of Na/K-ATPase pumps that generate action potentials for electrical impulses and muscle contraction, oxygen extraction and adenosine triphosphate (ATP) production by cell mitochondria, carbohydrate, lipid, and protein metabolism and development of nervous and muscle cells.\textsuperscript{1} Thyroid hormone also influences hematopoiesis.\textsuperscript{1}

□ The Role of the Pancreas: Insulin and Glucagon

The major endocrine role of the pancreas is regulation of glucose homeostasis. Serum glucose level is controlled by the hormones insulin and glucagon, both of which are secreted by beta islet cells of the pancreas.

**Insulin**

Insulin is an anabolic or energy-producing hormone that increases glucose uptake into cells and, thus, lowers serum glucose levels. In addition to glucose uptake, insulin also stimulates the formation of glycogen (glycogenesis), protein synthesis, and formation of adipose. Insulin is secreted by the pancreas in response to high serum glucose levels.\textsuperscript{1}

**Glucagon**

Glucagon is the counter-regulatory hormone to insulin. Glucagon increases serum glucose levels by stimulating the breakdown of glycogen stores (glycogenolysis) and by increasing the production of new glucose molecules (gluconeogenesis) from amino acids and fatty acids. Glucagon is secreted by the pancreas in response to low serum glucose levels.\textsuperscript{1}

□ Disorders of the Endocrine System in Children

Endocrine disorders that are associated with or that cause critical illnesses in children
Disorders of Fluid and Sodium Balance

SYNDROME OF INAPPROPRIATE ANTI-DIURETIC HORMONE SECRETION: The syndrome of inappropriate anti-diuretic hormone (SIADH) secretion is the result of excess vasopressin secretion from the hypothalamus. Excess vasopressin results in increased water reabsorption by the kidneys with subsequent hypervolemia and dilutional hyponatremia.\(^1,2\) The most characteristic manifestations of SIADH are urine output <0.5cc/kg per hour and hyponatremia. In addition, children with SIADH may show signs of hypervolemia, including weight gain, hypertension, reflex bradycardia, and change in mental status. Laboratory data consistent with SIADH includes a low serum sodium (typically <130 mEq/L), serum osmolarity less than 280 mOsm/L and a concentrated urine specific gravity.\(^2,5\) Causes of SIADH include: central nervous system (CNS) injury or infection (particularly tumor or injury to the hypothalamus), disease or injury of the posterior pituitary, holoprosencephaly (mid-brain hypoplasia) or anencephaly, spinal cord injury or surgery, liver disease, lung disease, and chemotherapy.\(^2,4,5\) Treatment of SIADH includes: central nervous system (CNS) injury or infection (particularly tumor or injury to the hypothalamus), disease or injury of the posterior pituitary, holoprosencephaly (mid-brain hypoplasia) or anencephaly, spinal cord injury or surgery, liver disease, lung disease, and chemotherapy.\(^2,4,5\) Treatment of SIADH includes fluid restriction, close monitoring of fluid intake, urine output, urine specific gravity, and serum sodium, as well as vital sign monitoring and serial neurologic assessments. Severe hyponatremia with accompanying change in mental status and/or seizure may be treated with a loop diuretic, such as Furosemide or with hypertonic (3%) saline administration.\(^2,5\)

DIABETES INSIPIDUS: In contrast to SIADH, diabetes insipidus (DI) is the result of vasopressin deficiency (central DI) or insensitivity to vasopressin by receptors in the kidneys (nephrogenic DI). Diabetes insipidus causes an increase in dilute urine output and hypertonic dehydration. Children with DI present with urine output >4cc/kg/hr, urine specific gravity less than 1.010 and an elevated serum sodium (>145 mEq/L).\(^2\) Children with DI may also show signs and symptoms of dehydration including tachycardia and hypotension. Severe DI may precipitate hypovolemic shock.\(^2\) Causes of central DI are the same as those for SIADH, however, severe traumatic brain injury that has progressed to brain death is more often associated with DI than with SIADH.\(^6,7\) Nephrogenic DI is typically a congenital, genetic disorder of the kidneys. Treatment of DI includes administration of synthetic vasopressin, which in the acute setting is most often administered in the form of intravenous aqueous arginine vasopressin, replacement of urinary fluid loss, and vigilant monitoring for signs of dehydration and impending shock.\(^2,4–6\)

CEREBRAL SALT-WASTING SYNDROME: Cerebral salt-wasting syndrome (CSW) is due to increased circulating atrial natriuretic peptide (ANP), which results in increased sodium secretion into the urine with resulting hyponatremia and a mild to moderate increase in urine output and dehydration. Low serum sodium with normal to elevated urine output and a normal to slightly elevated specific gravity are the hallmarks of CSW. Children with CSW will also have high urine sodium content (>80 mEq/L).\(^2\) Causes of CSW are the same as the causes of SIADH and DI, but in addition to CNS disease, CSW is also associated with congestive heart failure and other endocrine diseases, such as diabetic keto-acidosis, Cushing’s syndrome, and hyperaldosteronism.\(^2\) Normal to high urine output and high urine sodium differentiates CSW from SIADH as the cause of hyponatremia in a critically ill child. Table 3 compares and contrasts SIADH, DI, and CSW. Treatment of CSW includes sodium replacement and vigilant monitoring.\(^2,5\)

ALDOSTERONE DEFICIENCY: In addition to disorders of vasopressin and ANP, disordered aldosterone secretion may also result in fluid and electrolyte abnormalities. Although
TABLE 3 ■ Comparison of Endocrine Disorders of Fluid and Sodium Balance

<table>
<thead>
<tr>
<th>Syndrome of Inappropriate Anti-diuretic Hormone</th>
<th>Diabetic Insipidus</th>
<th>Cerebral Salt-wasting Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravascular volume</td>
<td>Hypervolemia</td>
<td>Hypovolemia</td>
</tr>
<tr>
<td>Serum sodium</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Urine output</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Urine sodium</td>
<td>Normal</td>
<td>Normal to hypovolemia</td>
</tr>
<tr>
<td>Primary treatment</td>
<td>Fluid restriction</td>
<td>Vasopressin and fluid replacement</td>
</tr>
<tr>
<td>Serum sodium</td>
<td>Low</td>
<td>Normal to high</td>
</tr>
<tr>
<td>Urine output</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>Normal</td>
<td>Normal to high</td>
</tr>
<tr>
<td>Urine sodium</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>Primary treatment</td>
<td>Fluid restriction</td>
<td>Sodium replacement</td>
</tr>
</tbody>
</table>

Disorder of Circulatory Function

ADRENAL INSUFFICIENCY: Adrenal insufficiency, which may lead to the shock syndrome of “adrenal crisis,” is the result of deficient cortisol and aldosterone and associated decreases in catecholamine release and adrenergic receptor sensitivity. In addition to hyponatremia, hyperkalemia, and hypovolemia due to aldosterone deficiency, children experiencing adrenal crisis also develop decreased myocardial contractility, vasodilation, capillary leak, and hypoglycemia due to cortisol deficiency. Adrenal insufficiency may quickly precipitate shock and/or contribute to circulatory failure that is refractory to resuscitation with fluids and inotropic and vasoactive drugs.

Primary adrenal insufficiency is due to intrinsic disease of the adrenal gland of which the causes include Addison’s disease, congenital adrenal hypoplasia, autoimmune adrenalitis, adenoleukodystrophy, and adrenal hemorrhage that is frequently the result of traumatic injury (including birth trauma) or sepsis with disseminated intravascular dissemination (DIC). Adrenal hemorrhage in the setting of sepsis is called Waterhouse-Friderichsen syndrome. In addition to adrenal hemorrhage due to sepsis with DIC, septic shock is also associated with global suppression of adrenal function in the absence of hemorrhage. Neonates, particularly premature and very low birth-weight infants, may have relative primary adrenal insufficiency, and thus corticosteroid replacement is routinely administered in critically ill neonates with refractory shock.

Secondary adrenal insufficiency is due to disrupted communication between the hypothalamus, pituitary gland, and adrenal gland, or the hypothalamic-pituitary-adrenal (HPA) axis. Secondary adrenal insufficiency then, may be the result of either deficient CRH from the hypothalamus or ACTH from the pituitary. Diseases of the CNS and pituitary gland may cause secondary adrenal insufficiency; however, abrupt discontinuation of exogenous corticosteroid (prednisone, methylprednisolone, dexamethasone, or hydrocortisone) is one of the most common causes of secondary adrenal insufficiency and adrenal crisis in children. Any critically ill child who is experiencing refractory shock and has previously been administered corticosteroids should be suspected as having adrenal crisis.

The main treatment of primary adrenal insufficiency is administration of high-dose corticosteroids, usually in the form of intravenous hydrocortisone. Secondary adrenal insufficiency may also be treated with...
Findings, Causes, and Treatment of Adrenal Crisis

<table>
<thead>
<tr>
<th>Finding</th>
<th>Cause</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Hypotension/circulatory collapse | Cortisol deficiency and associated decreased catecholamine production and receptor sensitivity | For cases of refractory shock (use hydrocortisone sodium succinate preparation):[^21]  
  - Children: Initial 50 mg/kg, repeat in 4 hours and/or every 24 hours as needed[^26]  
  - Adolescents and adults: 500 mg to 2 g every 2 to 6 hours[^21]  
  For acute adrenal insufficiency without refractory shock:  
  - Immediate administration of hydrocortisone 1 to 2 mg/kg dose followed by stress dose of hydrocortisone 4 to 6 hours later[^26] (may use either hydrocortisone sodium succinate or sodium phosphate preparation)  
  1. Hydrocortisone stress dose:  
     - Children: 25 to 150 mg/day in divided doses every 6 to 8 hours[^21]  
     - Older children/adolescents: 150 to 250 mg/day in divided doses every 6 to 8 hours[^21]  
     - Adults: 300 mg/day in divided doses every 8 hours[^21]  
  2. Hydrocortisone physiologic maintenance doses:  
     - Oral: 0.5 to 0.75 mg/kg/day or 20 to 25 mg/m²/day divided every 8 hours[^21]  
     - IM or IV: 0.25 to 0.35 mg/kg/day or 12 to 15 mg/m²/day once daily[^21]  
| Hyponatremia             | Aldosterone deficiency                                               | Fludrocortisone acetate:  
  - Infants and children: 0.05 to 0.1 mg/day by mouth[^21]  
  - Adults: 0.1 to 0.2 mg/day with ranges of 0.1 mg 3 times/week to 0.2 mg/day by mouth[^21]  
  - Emergency replacement of sodium for change and mental status and/or seizure using hypertonic 3% saline solution  
| Hyperkalemia             | Aldosterone deficiency                                               | Fludrocortisone acetate:  
  - Infants and children: 0.05 to 0.1 mg/day by mouth[^21]  
  - Adults: 0.1 to 0.2 mg/day with ranges of 0.1 mg 3 times/week to 0.2 mg/day by mouth[^21]  
  - Emergency management of hyperkalemia resulting in ECG changes

Hypothyroidism: Although hypothyroidism with acute thyrotoxicosis is encountered in pediatrics, hypothyroidism is the more common disorder associated with critical disease in children.[^11] Thyroid hormone is essential for the growth and development, particularly of the CNS. Because the developing fetus is almost entirely dependent on maternal thyroid hormone, maternal hypothyroidism is associated with small-for-gestational-age newborns who have severe CNS underdevelopment, as well as with spontaneous abortion.[^11] During years 1 through 6 of life, the thyroid hormone continues to be crucial to the developing nervous system, and hypothyroidism is known to cause irreversible cognitive delays. Due to the importance of the thyroid hormone on early childhood development, newborns are routinely screened for hypothyroidism.[^11] Congenital hypothyroidism may be due to an enzyme defect in the synthesis of thyroxine, dysgenesis of the thyroid gland, or...
presence of maternal antibodies to thyrotropin receptors. The incidence of congenital hypothyroidism is as high as 1/4,000 births. It is also important to note that preterm newborns have quantitatively less circulating thyroid hormone than term newborns and that sequelae of prematurity, such as respiratory distress syndrome, may further reduce thyroid hormone levels in the first week of life. Many premature infants require temporary thyroid hormone replacement.

Acquired hypothyroidism in older children also occurs. The most common cause of acquired hypothyroidism in children is chronic lymphocytic thyroiditis. Autoimmune diseases and genetic syndromes, such as Trisomy 21, Turner’s syndrome, and Kleinfelter’s syndrome, however, are also associated with hypothyroidism. In addition, hypothyroidism may be encountered in children with either congenital or acquired problems of the hypothalamus or pituitary gland.

Signs and symptoms of hypothyroidism may be completely absent until 6 months of age. Subtle signs of hypothyroidism in the young infant include, unconjugated hyperbilirubinemia, a large tongue, flat nasal bridge, periorbital edema, and persistent hypothermia. Other assessment findings in children with hypothyroidism are listed in Table 5.

In addition to true hypothyroidism, the euthyroid sick syndrome is also encountered in critically ill children. The euthyroid sick syndrome is due to disruption of thyroid hormone regulation and TSH sensitivity in prolonged serious illness. Because hypothyroidism can result in decreased oxygen utilization and energy production with resulting multisystem organ failure, it is particularly deleterious in critical illness and may contribute to refractory shock. Table 6 lists the laboratory evaluation that is useful in diagnosing both true hypothyroidism and euthyroid sick syndrome.

Hypothyroidism is treated with the administration of synthetic T4, levothyroxine. Levothyroxine may be administered intravenously or enterally. Intravenous T3 may also be administered as a continuous infusion in critical care.

HYPOGLYCEMIA: Hypoglycemia is defined as a serum glucose level ≤60 mg/dL. Hypoglycemia is caused by poor adaptation to fasting, excessive insulin production, and deficient glucagon production. Hypoglycemia is a very common problem in sick neonates and young infants and is most frequently due to inadequate glycogen stores. In addition, neonates born to diabetic mothers may continue to secrete large amounts of insulin after birth, thus resulting in hypoglycemia due to transient hyperinsulinism. Persistent forms of hyperinsulinism may be also present during infancy and are listed in Table 7. Persistent hyperinsulinemic hypoglycemia in infancy (PHHI) is treated with frequent or continuous feedings, medications such as diazoxide and somatostatin analogues (octreotide) and subtotal pancreatectomy. Other causes of hypoglycemia in infants as well

### Table 5 - Signs of Hypothyroidism

- Course, dry hair
- Dry skin
- Hypotonia and hyporeflexia
- Bradycardia
- Hypotension
- Hypothermia
- Gastric dysmotility and constipation
- Anemia
- Growth delay

### Table 6 - Laboratory Evaluation of Hypothyroidism and Euthyroid Sick Syndrome

<table>
<thead>
<tr>
<th>Hypothyroidism</th>
<th>Euthyroid Sick Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>T₄</td>
<td>Low</td>
</tr>
<tr>
<td>T₃</td>
<td>Low</td>
</tr>
<tr>
<td>Reverse T₃</td>
<td>Low</td>
</tr>
<tr>
<td>TSH</td>
<td>High</td>
</tr>
</tbody>
</table>

T₄, thyroxine; T₃, triiodothyronine; TSH, thyrotropin-releasing hormone.

### Table 7 - Causes of Pediatric Hyperinsulinism

- Beta islet cell hyperplasia (Beckwith-Wiedemann syndrome)
- Islet cell dysmaturation syndrome
- Nesidioblastosis
as in older children include hypopituitarism and/or adrenal insufficiency, liver failure, and inborn errors of metabolism, such as glycogen storage disease and drug ingestion, particularly poisoning with oral hypoglycemic agents. Regardless of age, signs and symptoms of hypoglycemia are: depressed level of consciousness, seizure, tremors, hypotonia, apnea, tachycardia, diaphoresis, and anxious behavior. Management of hypoglycemia includes the administration of glucose and may include glucagon administration in children with adequate glycogen stores or glycogen storage disorders.

TYPE I DIABETES MELLITUS AND DIABETIC KETOACIDOSIS: Although the incidence of type II (non-insulin dependent) diabetes mellitus in children is rising, type I diabetes is more likely to be encountered in pediatric critical care. Unlike type II diabetes mellitus, which is due to insensitivity of receptors to insulin and is common in adults, Type I diabetes mellitus (also called juvenile diabetes and insulin-dependent diabetes mellitus, IDDM) is most common in children and the result of deficient insulin production. Although intrinsic diseases of the pancreas, such as cystic fibrosis, may cause insulin deficiency, idiopathic autoimmune destruction of the beta islet cells of the pancreas is the most common cause of type I diabetes. In the absence of insulin, glucose uptake into cells is impaired and a state of intracellular energy debt ensues. In response to the lack of availability of glucose for energy production, gluconeogenesis, or the breakdown of proteins and lipids to make amino acids and fatty acids available as energy substrates, occurs in type I diabetes. The “keto acids” acetoacetic acid and beta-hydroxybutyric acid, by-products of fatty acid oxidation, are released in cases of prolonged insulin deficiency. The presence of high levels of circulating acetoacetic acid and beta-hydroxybutyric acid results in “ketoacidosis.” The constellation of severe hyperglycemia (serum glucose $\geq 180$ mg/dL or 10 mmol/L) and ketoacidosis in the child with type I diabetes is called diabetic ketoacidosis (DKA). In addition to acidosis, children with DKA also experience electrolyte abnormalities, such as hyperkalemia and hyperphosphatemia and hyperosmolarity with osmotic diuresis, resulting in dehydration and hypernatremia. History and physical assessment findings associated with DKA are listed in Table 9. Often, DKA is the first presentation of type I diabetes in a child. Other factors that are known to precipitate DKA in the child with type I diabetes include noncompliance with, or transition of home insulin and diet regimen, and concurrent infection.

Diabetic ketoacidosis is a life-threatening form of shock that is commonly encountered in pediatric critical care. Treatment of DKA includes fluid resuscitation, administration of insulin, and correction electrolyte abnormalities. Table 10 outlines a typical care plan for the child with DKA. The most serious complications of DKA include coma and the development of cerebral edema. The cause of cerebral edema in children experiencing DKA is not well understood, but is association with correction of acidosis using bicarbonate and overhydration have been reported in the past. Although more recent research has refuted the association between treatment interventions and the development of cerebral edema, use of bicarbonate and large volume, rapid fluid resuscitation should be avoided when possible in children.
TABLE 9  
History and Physical Assessment Findings Associated With Diabetic Ketoacidosis

<table>
<thead>
<tr>
<th>History</th>
<th>Physical Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria</td>
<td>Altered mental status (signs of elevated ICP)</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Recent viral illness/URI or other signs and symptoms of infection</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Lethargy/depressed level of consciousness/dizziness</td>
<td></td>
</tr>
<tr>
<td>‘Difficulty breathing’/tachypnea</td>
<td>Poor peripheral perfusion</td>
</tr>
<tr>
<td>Family history positive for juvenile diabetes type I</td>
<td>Tachypnea</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Abdominal tenderness</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Signs of concurrent infection</td>
</tr>
</tbody>
</table>

URI, upper respiratory infection; ICP, intracranial pressure.

experiencing DKA. In addition to management of the physiologic derangements associated with type I diabetes and DKA, it is also important that the critical care team include patient-family teaching regarding chronic disease management into the care of hospitalized children.

Patient-Family Teaching for Critically Ill Children With Endocrine Disease

Providing education to children with critical endocrine disease and their families can pose a challenge to the critical care team. In general, patient-family teaching in critical care requires recognition of teachable moments in the midst of a crisis and adaptation of standardized teaching plans to patients’ unique situations. The success of patient-family teaching is dependent on continuity of care and clear communication among multidisciplinary providers.

Issues that make patient-family teaching as it relates to critical endocrine disease particularly complicated include: explaining the complex physiology of endocrine disease, preparing families to manage both the acute and chronic manifestations of endocrine disorders, including transition to self-care by the child when developmentally appropriate, and teaching technical skills such as subcutaneous and intramuscular injections, maintenance of insulin pumps, and intranasal administration of medications such as the form of synthetic vasopressin that is often used to treat chronic diabetes insipidus. Patients and families must also be prepared to identify and prevent factors that precipitate critical endocrine disease, such as the development of concurrent infections, and growth spurts that necessitate changes in the dose of hormone replacement. For example, management of chronic type I diabetes requires “sick-day rules,” or a plan for adjusting insulin dose and serum glucose monitoring when a sick child has decreased food intake. It is particularly important that the parents of very young children who cannot adequately communicate their needs are taught to recognize physiologic changes, such as change in the number of wet diapers, excessive sleeping, changes in heart rate and respiratory pattern, and seizure activity that are markers of endocrine abnormalities. In addition, all family members who will care for children with endocrine disorders require education related to emergency management of associated life-threatening complications. Emergency management training may include administration of stress dose steroids to children with adrenal insufficiency who are experiencing an intercurrent illness, treatment of hypoglycemia, keeping a patient safe during a seizure, and infant-child cardiopulmonary resuscitation.

Summary

In summary, endocrine disease in pediatric critical care encompasses complex, multiorgan system problems. Abnormalities of the endocrine system in children are frequently due to other underlying diseases including
 TABLE 10  ■ Treatment of Diabetic Ketoacidosis

1. First priority: Assess and stabilize airway and breathing.
2. Second priority: Assess and stabilize circulation (including acute management of severe hyperkalemia associated with acidosis)
   • Bolus with normal saline.
     -Brisk 10 to 20 mL/kg for circulatory failure—repeat as needed to regain circulation, but proceed with caution and avoid >40 mL/kg when possible.
     -Without ongoing circulatory collapse, bolus 5 to 20 mL/kg over 1 to 2 hours.2
   • Calculate volume deficit and replace (typically 10% to 20% dehydration).
     -Administer 0.9% saline at maintenance plus deficit correction over next 24 to 72 hours.2,15
   • Establish vascular access.
   • Minimum of 2 peripheral IV lines (largest bore possible)
   • Consider a separate “blood-drawing IV.”
   • Arterial line is indicated when patient has:
     -Profoundly altered mental status
     -Signs of uncompensated shock
     -Severe acidosis (pH < 7.0)
3. Third priority: Insulin administration
   • Use regular insulin 0.05 to 0.1 units/kg/hr.2,15,21
     -Start with low dose insulin infusion (do not bolus).2,15
     -Titrated according to drop in serum glucose.
     -Add 5% dextrose to intravenous fluids when serum glucose reaches 300 mg/dL.
   • Convert from regular insulin infusion to subcutaneously administered insulin preparations when ketoacidosis has resolved, as evidenced by the absence of ketones in the urine.2,15
   • Use of an infusion of regular insulin without a bolus loading dose is recommended to allow for careful titration of the drug dose in order to prevent rapid decreases in serum glucose levels. Similarly, addition of glucose to intravenous fluids is as serum glucose levels begin to decrease is recommended to slow the rate of decrease and to prevent iatrogenic hypoglycemia. A rapid decrease in serum glucose level is known to precipitate central pontine myelinolysis and may also be associated with development of global cerebral edema in patients with diabetic ketoacidosis (DKA).2,15,17

4. Manage electrolyte abnormalities
   • Adjust for true serum sodium:15
     -Serum sodium levels rise 1.6 mEq/L for every 100 mg/dL increase in serum glucose concentration.
   • To calculate true serum sodium:
     -Subtract 1.6 from sodium level for every 100 mg/dL of glucose above 100.
5. Treat potassium and phosphate imbalance.
   • Replace potassium and phosphorous as needed by adding to IV fluid bag (avoid single-dose administration to allow for more careful titration of supplemental electrolyte needs. Potassium will move between intracellular and extracellular compartments as insulin dosing is adjusted and acidosis resolves, and thus may result in rapid fluxes in serum levels). Guidelines for adding potassium supplements:
     K+ <3.5: Add 40 mEq/L to IV fluids.
     K+ 3.5 to 5.0: Add 30 mEq/L to IV fluids.
     K+ 5 to 5.5: Add 20 mEq/L to IV fluids.
     K+ >5.5: Do not add potassium to IV fluids.
   • Use potassium chloride, add potassium phosphate if phosphorous <3.
   • Add potassium supplementation only after a patient is assessed to have sufficient renal function.
   • Patients may present with hyperkalemia. Potassium will return to intracellular space with administration of insulin and correction of acidosis.2,15
     -Treat severe hyperkalemia (>7 mEq/L and ECG changes) with calcium and consider sodium bicarbonate administration.
6. Serial assessments
   • Serum glucose every 1 hr
     -Also check serum glucose after the initial fluid administration.
   • Dip urine for ketones with every void.
     -The absence of ketones and serum glucose <200 mg/dL indicates readiness for transition to subcutaneous dosing.
   • Measure serum electrolytes every 2 hours.
   • Continuous cardiac-respiratory monitoring, strict monitoring of fluid intake and output and neurological checks (minimum of every 1 hr during acute phase of illness)2,15

(continues)
TABLE 10 ■ Treatment of Diabetic Ketoacidosis (Continued)

7. Perform infection work-up (infection is the most frequent cause of DKA)
   • Obtain complete blood count with differential.
   • Obtain urine and blood cultures (and possibly respiratory samples).
   • Defer lumbar puncture for cerebrospinal fluid culture unless suspicion of meningitis is very strong and head computed tomography demonstrates no cerebral edema.
   • Consider broad-spectrum empiric IV antibiotics.
   • Monitor body temperature closely.
   • Evaluate for signs and symptoms of infection on history and physical examination.

8. Assess for chronic hyperglycemia
   • Obtain a glycosylated hemoglobin.
     —Hgb A1C level
     • In a patient with known diabetes, high percentages of Hgb A1C suggests chronic hyperglycemia due to poor compliance with insulin administration.15

9. Provide patient-family teaching

    • Rosenbloom AL. Cerebral edema in diabetic ketoacidosis and other acute devastating

