

Endocrinology

Introduction

This chapter provides a basic approach to endocrine issues in an austere or combat environment. The emphasis is on signs and symptoms and an index of suspicion for serious, potentially life-threatening situations. Hormone dosing is best determined using accurate height and weight to allow exact calculation of body surface area.

$$\text{Surface area (m}^2\text{)} = \sqrt{\frac{\text{Ht (cm)} \times \text{Wt (kg)}}{3,600}}$$

When this information is not available, use the estimates obtained from a Broselow tape.

Diabetes Mellitus

- Diabetes is defined as follows:
 - Fasting blood sugar > 126 mg/dL
 - Random blood sugar > 200 mg/dL in association with symptoms of diabetes
 - Blood sugar > 200 mg/dL 2 hours after an oral glucose tolerance test
- Symptoms of diabetes mellitus include polyuria, nocturia, polydipsia, and polyphagia
- Weight loss will often occur with diabetes mellitus type 1 (DM1), but can occur with diabetes mellitus type 2 (DM2)
 - Children with the above symptoms who are not overweight should be suspected of having DM1 if their blood sugar is elevated
 - Management of DM2 depends on the presentation at the time of diagnosis
 - ▶ Random blood sugar < 200 mg/dL without marked elevations 1–2 hours after meals can often be managed by diet, exercise, and weight loss without the initiation of medications

- ▶ Random blood sugar > 200 mg/dL will require medication
 - ▷ Use caution when initiating antidiabetic medication regimens in austere environments with limited laboratory or clinical follow-up
 - ▷ Consider the risk of hypoglycemia
 - ▷ For an overweight, newly diagnosed patient with DM2 with random blood sugar between 200 and 300 mg/dL, administer metformin 500–1,000 mg once or twice a day
 - ▷ Insulin should be strongly considered in a hyperglycemic, nonacute patient with random blood sugar > 300 mg/dL, although oral therapy may be safer (see below)

Diabetic Ketoacidosis

- Diabetic ketoacidosis (DKA) is diagnosed when a patient has:
 - D: high glucose
 - K: ketones in the blood
 - A: acidosis
- Perform a brief history and physical examination to assess for shock and degree of volume depletion (Table 30-1)

Table 30-1. Assessing Dehydration in the Pediatric Patient with Diabetes

Parameter	Mild	Moderate	Severe
Estimated volume deficit (%)	3	6	10
Clinical signs			
Perfusion	Normal	Normal or ↓	↓
Heart rate	Normal	↑	↑
Blood pressure	Normal	Normal or ↓	Normal or ↓
Labs			
HCO ₃	Normal	10–20	< 10
pH	Normal	> 7.20	< 7.20
Glucose	300–400	400–600	> 600
BUN	< 20	< 30	> 25

BUN: blood urea nitrogen
 HCO₃: bicarbonate

- Physicians frequently overestimate the degree of fluid depletion
- The best data are the patient's actual weight loss (use outpatient records if available)
- Obtain results from the following laboratory tests:
 - Chemistry panels, including calcium, magnesium, and phosphorous, if available
 - Arterial blood gas (ABG) or venous blood gas (VBG) analysis
 - Serum ketones test
 - Urinary analysis
 - C peptide test
 - Consider looking for an infectious trigger via complete blood count with differential, urine culture, etc
- Obtain intravenous (IV) access and begin correcting deficit slowly, unless patient is in shock
 - Give normal saline (NS) 10–20 mL/kg over 1 hour
 - The rest of the deficit should be replaced over 48 hours to avoid dropping serum osmoles too quickly and precipitating cerebral edema
 - Placing two large IVs allows treatment through one and sampling through the other
- Insulin therapy need not be viewed as emergent therapy, but should be initiated as soon as possible
 - Use regular insulin (100 units in 100 mL NS) with insulin drip at 0.05–0.1 units/kg/h
 - **Do not bolus with insulin!** It can precipitously drop glucose levels and serum osmolarity, exacerbating risk of cerebral edema
 - The goal of therapy should be a drop in serum glucose of 50–100 mg/dL/h (start on the low end of the range and increase over time)
 - Plastic tubing binds insulin; run insulin through before using
 - Blood sugar checks should be done every hour
 - In mild DKA, especially in the austere environment, if no IV access is available, intramuscular insulin can be given every 3 hours, rather than using an insulin drip
 - ▶ The dose of IM regular insulin is 0.1–0.3 units/kg
 - ▶ Start at the low end and increase over time to avoid in-

advertently administering excessive amounts of insulin

- Preferred fluid choice is $\frac{1}{2}$ NS with potassium
 - Use potassium chloride and potassium phosphate to administer 40 mEq/L (even though the patient is hyperkalemic, the total-body potassium is low)
 - **Add glucose when blood sugar drops into the 250–300 mg/dL range**
 - Always anticipate the next bag needed and order it ahead of time from the pharmacy (ie, $D_5 > D_{10} > D_{12.5}$)
- Cerebral edema is a major concern; perform neurological checks hourly
 - When faced with a deteriorating mental status, consider performing a computed tomography (CT) scan of the head to look for cerebral edema
 - Administer mannitol (dose 0.25 g/kg) for progressive neurological deterioration or focal neurological examination
 - There is a high risk for cerebral edema when fluids are administered at $> 4,000 \text{ mL/m}^2/\text{day}$
- Check glucose hourly, VBG or ABG tests and chemistry panels every 4 hours, and urinary analysis every void (or more frequently when necessary)
- Do not reduce insulin prematurely if glucose is falling—give more glucose!
 - Giving enough glucose ($D_5 > D_{10} > D_{12.5}$) allows room to provide enough insulin to correct the acidosis
- Transition to subcutaneous (SQ) insulin from insulin drip when patient is expressing hunger, the acidosis is mostly gone, and there is food immediately available
 - Turn off the drip, administer the SQ insulin, and wait 30 minutes before feeding
 - Typically, rehydration without glucose will need to be continued once the patient is eating

Diabetes Management

- Dietary management is generally the same in DM1 and DM2
 - Dietary treatment of diabetes consists of a well-balanced diet, low in refined and simple sugars
 - The diet should be approximately 55% carbohydrate, 30% fat, and 15% protein

- Carbohydrate intake should favor complex carbohydrates
 - ▶ In general, infants and toddlers (0–3 y) will need 30–45 g carbohydrate per meal
 - ▶ Older children (4–12 y) need 45–60 g carbohydrate per meal
 - ▶ Teenagers (13–18 y) need 75–90 g carbohydrate per meal
- Insulin therapy
 - Insulin therapy and timing depends on the type of insulin available (Table 30-2)

Table 30–2. Types and Action Times of Insulin

Type of insulin	Onset	Peak (h)	Duration (h)
Lispro/aspart	10–15 min	1–2	2–4
Regular	30–60 min	2–4	6–9
NPH	1–2 h	3–8	12–15
Lente	1–2 h	3–14	18–20
Ultralente	2–4 h	6–14	18–20
Glargine	1–2 h	2–22	24

NPH: Neutral Protamine Hagedorn

- ▶ In theater, it is likely that only Neutral Protamine Hagedorn (NPH) and regular insulin are available
- ▶ Start with a total daily dose of 0.6 units/kg/day if the initial glucose at diagnosis is < 500 mg/dL
 - ▷ **Initial glucose at diagnosis > 500 mg/dL and no acidosis:** use a total daily dose of 0.8 units/kg/day
 - ▷ **Initial glucose at diagnosis > 500 mg/dL and acidosis present:** use a total daily dose of 1.0 unit/kg/day
 - ▷ **Initial glucose level at diagnosis unavailable:** start with 0.8 units/kg/day
- ▶ Morning insulin should constitute $\frac{2}{3}$ of the total daily dose
 - ▷ This amount should be divided further to $\frac{2}{3}$ NPH and $\frac{1}{3}$ regular insulin (Exhibit 30-1)
 - ▷ This dose should be given about 20 minutes before breakfast
- ▶ The evening dose should constitute $\frac{1}{3}$ of the total daily dose

Exhibit 30-1. Case Study: Insulin Dosing using Neutral Protamine Hagedorn and Regular Insulin

A 30-kg patient presents with an initial blood glucose of 558 mg/dL and serum bicarbonate of 20 mEq/L.

Administer 0.8 units/kg/day \times 30 (24 units/day).

Morning:

$\frac{2}{3}$ of the total dose = 16 units total (10 units NPH and 6 units of regular insulin before breakfast)

Evening:

The remaining $\frac{1}{3}$ total dose = 8 units total (4 units of NPH and 4 units of regular insulin before dinner)

NPH: Neutral Protamine Hagedorn

- ▷ This amount should further be divided to $\frac{1}{2}$ NPH and $\frac{1}{2}$ regular insulin
- ▶ This dosing plan places a child at risk for low blood sugar; the child should have small snacks in the mid-morning, midafternoon, and at bedtime when this insulin plan is used
- Children on insulin should have multiple blood sugar checks per day
- A combination of rapid-acting insulin (lispro or aspart) and glargine is preferable to the regular and NPH insulin combination, if available, because it more closely approximates normal physiology (further pediatric endocrinology consultation is recommended)
- In an austere environment, use a goal blood sugar of 150 mg/dL

Hypoglycemia

- Signs and symptoms
 - Nonspecific in infancy, but can include cyanotic episodes, apnea, respiratory distress, refusal to feed, myoclonic jerks, convulsions, somnolence, hypothermia, sweating, etc
 - For older children, symptoms include anxiety, weakness, hunger, shakiness, sweating, tachycardia, nausea, vomiting, headache, visual disturbances, lethargy/lassitude, restless-

- ness, mental confusion, somnolence/stupor, convulsions, bizarre neurological signs, decreased intellectual ability, personality changes, bizarre behaviors, etc
- Other suggestive physical findings include hepatomegaly, short stature, large size for gestational age (newborn), and hemihypertrophy of an extremity
 - The definition of hypoglycemia is < 40 mg/dL in the first month of life (older infants, children, and teenagers should be able to maintain a blood sugar > 60 mg/dL)
 - The differential diagnosis includes a host of congenital metabolic and hormonal disorders, systemic disease, and drug intoxications; the presence of urine ketones may be helpful in diagnosis
 - If urine ketones are positive, it is likely that a transient abnormality exists that can be treated with IV or oral glucose therapy
 - The absence of ketones in the face of profound hypoglycemia generally represents an excess of insulin secretion or the presence of a disorder of fatty acid metabolism
 - Treatment varies by age
 - Neonates: 2–4 mL/kg 10% dextrose in water (D₁₀W) IV bolus
 - Children: 2–4 mL/kg 25% dextrose in water (D₂₅W) IV, administered slowly
 - ▶ Follow each immediately by continuous glucose infusion
 - ▶ If IV therapy is unavailable, oral or nasogastric therapy should be undertaken in a child that is awake and able to tolerate it
 - If a child is actively seizing or comatose due to low blood sugar, administer 1 mg of glucagon intramuscularly
 - ▶ Be aware that vomiting is common after glucagon administration; lay children on their sides after giving glucagon

Thyroid

- Hypothyroidism
 - Hypothyroidism can be congenital or acquired
 - ▶ Congenital hypothyroidism is almost impossible to recognize early on

- ▶ Signs and symptoms
 - Macroglossia
 - Open posterior fontanelle
 - Developmental delay
 - Constipation
 - Coarse facial features, including broad nasal bridges, eyelid edema, flat facies, and large heads
- ▶ Treatment is oral thyroid replacement
 - Starting dose is 12–15 $\mu\text{g}/\text{kg}/\text{day}$ for neonates
 - Most children with congenital hypothyroidism are on 5 $\mu\text{g}/\text{kg}/\text{day}$ of levothyroxine by 1 year of age
 - Most infants require 37.5 μg daily (given as 1½ 25- μg tablets)
 - Pills should be crushed and given directly to the patient mixed in formula or applesauce—**DO NOT** make elixirs for this therapy (stability may be affected)
- ▶ Acquired hypothyroidism
 - ▶ Signs and symptoms
 - Constipation
 - Fatigue
 - Cold intolerance
 - Enlarged thyroid gland
 - ▶ Most children with acquired hypothyroidism require an initial dose of 2–3 $\mu\text{g}/\text{kg}/\text{day}$ of levothyroxine
- Hyperthyroidism
 - Symptoms in infants and children
 - ▶ Irritability
 - ▶ Flushing
 - ▶ Tachycardia
 - ▶ Hypertension
 - ▶ Poor weight gain
 - ▶ Goiter
 - ▶ Exophthalmos
 - ▶ Hepatosplenomegaly, jaundice, thrombocytopenia, and hypoprothrombinemia
 - Signs are typically subtle and slowly progressive; initial

signs of irritability and jitteriness should lead one to suspect sepsis or hypoglycemia first

- Treatment in infants and children is initiated with propranolol (1–2 mg/kg/day divided tid) and propylthiouracil (PTU) 5–10 mg/kg/day divided tid
- The female-to-male ratio of acquired hyperthyroidism in teenagers is 5:1
- Symptoms in teenagers
 - ▶ Tachycardia
 - ▶ Restlessness
 - ▶ Difficulty sleeping
 - ▶ Widened pulse pressure
 - ▶ Heat intolerance
 - ▶ Increased frequency of loose stools
 - ▶ Enlarged, nontender thyroid
- Etiology is generally autoimmune, but if a prominent thyroid nodule is palpable, it may be the cause
- Treatment in teenagers can be surgical resection of all or part of the thyroid gland, or medical or radioactive iodine ablation
 - ▶ Medical treatment consists of β -blocker therapy with atenolol (25–50 mg/day) until the marked symptoms have resolved, and with PTU at 5–10 mg/kg/day divided tid
 - ▷ If medical treatment is initiated, thyroid function tests should be obtained prior to therapy and sent to a referral lab (this should be possible in a deployment situation)
 - ▷ After the free thyroxine level has normalized or lowered, adding levothyroxine at 2 μ g/kg/day allows maintenance of a euthyroid state
 - ▷ The thyroid can be adequately suppressed while treating with PTU

Adrenal Disorders

- Adrenal insufficiency is uncommon; however, an index of suspicion for adrenal disorders is critical because they can be fatal
- A patient with known autoimmune conditions, such as dia-

betes or thyroid disease, has the potential to develop adrenal insufficiency

- Tuberculosis, human immunodeficiency virus, adrenal hemorrhage, and traumatic adrenal resection may also lead to adrenal insufficiency
- Signs and symptoms
 - Unexplained hypotensive shock
 - Progressive weakness, fatigue, dehydration, and hypotension are most common
 - Anorexia, nausea, vomiting, myalgias, and personality changes are possible
 - Other suggestive physical findings include hyperpigmentation of the skin and mucous membranes (especially the creases and the nipples)
 - Vitiligo and alopecia may also be associated
 - Laboratory evidence suggestive of adrenal insufficiency includes hyponatremia, hyperkalemia, and hypoglycemia
- If adrenal insufficiency is suspected, obtain a blood specimen in a serum separator tube (red, tiger, yellow)
 - Separate the serum and freeze the specimen
- Treatment includes aggressive IV fluid therapy (20 cc/kg bolus of NS followed by reassessment)
 - Pressor agents are sometimes required
 - Hydrocortisone hemisuccinate should be given urgently by IV (50 mg/m²)
 - ▶ Infants: 25 mg
 - ▶ Toddlers and young children (< 6 y): 50 mg
 - ▶ Older children and teenagers (> 6 y): 100 mg
 - Regular dosing (q6h) should be continued at a dose of 100 mg/m²/day, divided in equal doses
 - If the adrenals have been removed or primary adrenal disorders are suspected, mineralocorticoid therapy (fludrocortisone) will be necessary when the hydrocortisone dose is dropped below 100 mg/m²/day
 - ▶ Safe when the child stabilizes or the significant stressor (surgery, illness, etc) has resolved
 - ▶ Maintenance hydrocortisone dose is 12–15 mg/m²/day (divided tid)
 - ▶ Fludrocortisone dose is 0.1 mg bid for infants, and 0.1 mg qid in patients ≥ 1 year old

Calcium and Vitamin D Disorders

- Hypocalcemia
 - Symptoms can range from nothing to severe (eg, tetany and seizures)
 - Long QT interval is apparent on electrocardiogram
 - Symptomatic hypocalcemia generally occurs when calcium levels in the blood are below 6 mg/dL
 - Managing acute hypocalcemia requires calcium and vitamin D
 - ▶ Administer 10% calcium gluconate at 1 mL/min, not to exceed 2 mL/kg
 - ▶ Give intravenously but with care; SQ infiltration of calcium can cause severe burns
 - ▶ Vitamin D is given as calcitriol at a dose of 20–60 ng/kg/day
 - ▶ Once acute symptoms have resolved, oral calcium should be given at 50–75 mg of elemental calcium per kilogram of body weight every 24 hours (oral calcium is much safer to give than IV calcium)
 - ▶ Vitamin D may be needed long term in some cases, such as in the presence of hypoparathyroidism
 - ▶ Hypocalcemia may not respond to therapy if the patient's magnesium level is also low (see Hypomagnesemia)
- Hypercalcemia
 - Severe hypercalcemia (> 13.5 mg/dL) requires treatment
 - Initiate treatment with IV NS to establish optimal fluid hydration
 - ▶ Once urine output is substantial (> 2 cc/kg/h), give furosemide at a dose of 1–2 mg/kg IV
 - ▶ If hypercalcemia persists, give hydrocortisone hemisuccinate 1 mg/kg IV every 6 hours
 - ▶ Bisphosphonates can also be used, but are not likely to be available in an austere environment
 - ▶ In the immobilized patient, it may be prudent to start a low-calcium diet and avoid vitamin D
 - ▶ Encourage copious fluid intake
- Hypomagnesemia
 - May cause hypocalcemia
 - Hypocalcemia will be resistant to treatment in the presence

- of untreated hypomagnesemia
- Treat magnesium levels below 1.4 mg/dL
- Treatment consists of 50% magnesium sulfate 0.1–0.2 mL/kg
 - ▶ Repeat the dose in 12–24 hours if the magnesium level remains low
- Rickets
 - The most common cause of rickets is vitamin D deficiency
 - Infants and children at risk for vitamin D deficiency typically have a history of prolonged breast-feeding and live in a northern latitude
 - Signs and symptoms
 - ▶ Rachitic rosary
 - ▶ Bowed legs
 - ▶ Bowing forearms
 - ▶ Frontal bossing
 - ▶ Craniotabes
 - ▶ Short stature
 - ▶ Suboptimal weight
 - ▶ Systemic symptoms, including hypotonia, weakness, anorexia, and delay in walking
 - ▶ Vitamin D deficiency can present as seizures when severe hypocalcemia is present
 - Radiographic evidence of vitamin D deficiency consists of cupping, widening, and irregularity of the distal metaphyses; there is also evidence of osteopenia with cortical thinning
 - Treatment in an urgent situation includes administering IV calcium and providing vitamin D treatment
 - ▶ In an otherwise normal child, ergocalciferol should be administered in doses of 1,000–2,000 international units (IUs) per day
 - ▷ Start at the higher end of the dose and wean to 1,000 IU/day after 2–4 weeks
 - ▶ Supplemental vitamin D should be continued until there is radiographic evidence of healing
 - ▷ This usually takes 2–3 months, but can take longer in cases of severe vitamin deficiency
 - ▶ If symptoms of vitamin D deficiency persist despite

- adequate replacement, changing vitamin D to 1,25-hydroxyvitamin D may alleviate the problem
- ▷ Calcitriol should be used at a dose of 20–60 ng/kg/day
 - ▷ This form of medication has a long half-life and care should be taken not to overdose this medication
- To prevent rickets, breast-fed babies should receive a daily multivitamin containing 400 IU of vitamin D

