Critical Care for the Non-Critical Care Physician
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This summary will cover intensive care unit (ICU) management as it relates to the endocrine system.

Glycemic Control

General Considerations for Critically Ill Patients

Patients with critical illness frequently develop stress-induced hyperglycemia, even in the absence of underlying chronic diabetes. Excessive hyperglycemia should be avoided. In general, glucose levels should be maintained below 180-200 mg/dL. More intensive glucose control is discouraged, as this can increase the risk of dangerous hypoglycemic events. Episodes of hypoglycemia should be aggressively managed with IV bolus of 50 percent dextrose +/- continuous IV infusion of dextrose containing crystalloids.

Diabetic Ketoacidosis (DKA) versus Hyperosmolar Hyperglycemic Syndrome (HHS): Patients with underlying diabetes (Type 1 or Type 2) are at risk of developing DKA and/or HHS in times of critical illness. Both forms of hyperglycemic crisis result in osmotic diuresis and urinary wasting of electrolytes. Patients should be evaluated for electrolyte abnormalities and metabolic acidosis. High anion-gap metabolic acidosis is typical of DKA and is generally not seen in HHS. Serum osmolality and the presence of serum and urine ketones may also be helpful in distinguishing between the two conditions. Although hyponatremia is common in both conditions, it is important to recognize that hyperglycemia will falsely lower serum sodium levels. The true serum sodium (Na) level should be calculated with the following equation prior to any attempts at correction: Actual Na = Measured Na + 0.024 x (Serum Glucose - 100). Additionally, patients with both DKA and HHS are prone to significant and potentially life-threatening hypokalemia, which may be underappreciated in patients who are acidotic due to the extracellular shifting of potassium. Treatment of DKA and HHS both require 1) volume expansion, 2) careful correction of electrolyte imbalances, and 3) insulin administration. Insulin should NOT be administered until potassium (K) >3.3 mEq/L has been achieved, as this may precipitate dysrhythmias.

Considerations in Patients with Suspected or Confirmed COVID-19: The use of insulin infusions to control hyperglycemia is common in the ICU but should be carefully considered in patients with suspected or confirmed COVID-19, as this necessitates hourly glucose checks. When possible, consider using a combination of intermediate- or long-acting insulin with sliding scale correction scheduled every 4 hours if on enteral nutrition, or at pre-meal and bedtime (AC/HS) checks if taking food by mouth.

Thyroid Function

General Considerations for Critically Ill Patients

Euthyroid Sick Syndrome: Patients in the ICU frequently present with abnormal thyroid function tests that do not represent chronic thyroid dysfunction. Typical findings include decreased T3 (most common), normal or decreased T4, and normal or slightly decreased TSH levels. Euthyroid sick syndrome does not require thyroid hormone supplementation, although it may warrant periodic monitoring and follow-up.

Hypothyroidism: Patients with a known history of hypothyroidism should be continued on their home thyroid hormone replacement regimen as possible. The half-life of T4 (levothyroxine) is seven days, so brief interruptions in treatment need not be of significant concern. Due to cost, the enteral route of administration is preferred, although IV levothyroxine is also available if needed.

Occasionally, patients with untreated hypothyroidism will develop persistent hypotension, which resolves with adequate thyroid hormone supplementation. This can be considered in the differential diagnosis of unexplained hypotension.

Critical illness in patients with unrecognized or untreated hypothyroidism can, in rare cases, precipitate myxedema coma, a life-threatening form of decompensated hypothyroidism characterized by altered mental status and hypothermia and potentially accompanied by hyponatremia, hypoventilation, bradycardia, and hypotension. Myxedema coma requires immediate IV thyroid hormone supplementation and supportive care under the guidance of an endocrinologist. Stress dose steroid replacement may also be required.

Hyperthyroidism: Patients with a known history of hyperthyroidism should be continued on their home antithyroid regimen, most commonly methimazole or propylthiouracil. The half-lives of these medications are considerably shorter than that of levothyroxine, and care should be given to avoid significant interruptions in administration.

The stress of critical illness in patients with unrecognized or untreated hyperthyroidism can sometimes precipitate thyroid storm, a potentially fatal form of thyrotoxicosis. Symptoms of thyroid storm are non-specific and may be difficult to distinguish from other causes of critical illness, for example, sepsis. Patients are uniformly febrile, may be diaphoretic, are prone to tachycardia as well as dangerous tachyarrhythmias, and may develop signs of congestive heart failure. Management of thyroid storm includes supportive care, inhibition of peripheral thyroid hormone excess using beta blockade, and inhibition of thyroid hormone synthesis and release under the guidance of an endocrinologist.

Steroid Use in Critical Illness

General Considerations for Critically Ill Patients

Adrenal Insufficiency: During times of physiologic stress, cortisol production is expected to increase. Unfortunately, a variety of factors can blunt this response and its physiologic effects. Patients with either primary or secondary (e.g., chronic steroid use generally defined as a daily prednisone dose >5 mg for 3 months or longer) adrenal insufficiency are at significant risk for absolute adrenal failure/crisis when they become critically ill, due to the adrenal gland's inability to mount an appropriate stress response. In most cases, these patients should be started empirically on high-dose steroid replacement (proposed regimens include hydrocortisone 100 mg every 8 hours or hydrocortisone 50 mg every 6 hours) for the duration of their critical illness.

Patients without history of adrenal insufficiency remain at risk for developing relative or absolute adrenal insufficiency during critical illness. This presents as refractory hypotension, despite vasopressor therapy. Although serum cortisol levels in these patients may be low, often they are within the normal range and may even be elevated, but nevertheless insufficient given the level of physiologic stress. Although the measurement of cortisol levels before and after stimulation with ACTH has been proposed as a means of identifying patients with relative adrenal insufficiency, the value of this test has been heavily debated. Empiric use of stress dose hydrocortisone (with either regimen described above) can be considered, regardless of cortisol level, in patients with profound hypotension refractory to vasoactive medications.

Acute Respiratory Distress Syndrome (ARDS): The role of steroid use in ARDS has been controversial. Currently, steroids are recommended for use in ARDS precipitated by a steroid-responsive condition (e.g., sepsis). Additionally, steroids may be used to treat early, moderate-severe ARDS that has not

responded to other supportive therapies. The DEXA-ARDS trial, published in March 2020, proposes a regimen of dexamethasone 20 mg x 5 days, followed by 10 mg x 5 days, for the treatment of early, severe ARDS.

Considerations in Patients with Suspected or Confirmed COVID-19
In the early phases of the pandemic, steroids were not recommended in the treatment of viral pneumonia and ARDS in patients with COVID-19 due to concerns about prolonged viral clearance. However, the RECOVERY trial, published in July 2020, demonstrated a significant mortality reduction in patients with COVID-19 requiring supplemental oxygen therapy who were treated with dexamethasone 6 mg daily x 10 days. Steroids have subsequently become part of standard treatment at many centers.

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