Until recently, critically ill hyperglycemic patients without a history of diabetes generally weren’t considered candidates for insulin until their serum glucose levels exceeded 220 mg/dL. New evidence disputes that thinking and requires a new understanding of the causal relationship between stress-induced hyperglycemia and outcomes in the critically ill.

Keeping a patient’s blood glucose level below 220 mg/dL improves outcomes in postacute myocardial infarction (MI) and stroke. Even in patients without diabetes, postsurgical outcomes are improved by tight glycemic control through aggressive insulin therapy.

Normal glucose metabolism
In a healthy person, blood glucose concentrations are tightly regulated within a narrow range of about 80 to 100 mg/dL with little fluctuation, despite variation in oral intake of food. Under normal circumstances, a postprandial increase in blood glucose concentration stimulates the release of insulin from the pancreas (specifically the beta cells), resulting in decreased hepatic glucose production and an increase in peripheral glucose uptake, maintaining blood glucose homeostasis. After uptake into the skeletal muscle, glucose is directed to glucagon formation (pathway for carbohydrate storage) or glycolysis (used in the Krebs cycle, resulting in energy production). The liver can also store excess glucose or convert it to fatty acids for storage in adipose tissue.

When patients experience critical illness or major insults to the body, such as surgery, sepsis, or MI, metabolic compensation becomes more complex and a profound neuroendocrine and cytokine response known as the stress response occurs.

Hyperglycemia’s path
The precise pathophysiology behind the complications associated with hyperglycemia in critical illness extends beyond a simple elevation in blood glucose levels. Critical illness induces a number of adaptive changes in the body’s neuroendocrine functions. An increase in counterregulatory hormones, such as glucagon, epinephrine, norepinephrine, and growth hormone, results in an increase in hepatic glucose production and a subsequent decrease in peripheral glucose uptake. In addition, critical illness

Glucose control in the ICU
Many patients in the ICU have an increased metabolic response because of stress and other pathologic processes. One characteristic of this increased response is increased gluconeogenesis and peripheral insulin resistance. This in turn leads to hyperglycemia, which has a proven link to higher mortality and morbidity in ICU patients. A prospective observation study was done in an ICU that involved developing and implementing a glucose control protocol with a nurse-managed insulin therapy algorithm. Every measured blood glucose value and hourly and daily insulin dose were documented in 36 patients before and 44 patients after implementing this protocol.

Findings
After implementation of the protocol, the median blood glucose level decreased from 133 mg/dL to 100 mg/dL. The median amount of insulin used each day increased from 28 units to 35 units. Overall, diabetic patients continued to have higher blood glucose levels than nondiabetic patients, despite an increase in insulin use. The study concluded that glucose protocols help decrease glucose levels for patients in the ICU.

Nursing practice implications
To help patients achieve their optimum glucose levels:
• Monitor blood glucose levels frequently.
• Notify the healthcare provider about abnormal glucose levels in a timely manner.
• Administer insulin as scheduled to help decrease fluctuations in glucose levels.
• Be aware of medications that may increase glucose levels, such as corticosteroids.

**Safe Haven**

exacerbates the circulation of abnormal levels of cytokines, which mediate the inflammatory response and are thought to stimulate counterregulatory hormone secretion during illness. The resulting hyperglycemia is often called *stress diabetes*. Stress hormones stimulate gluconeogenesis by enhancing the production of substrates, including alanine, which is derived from skeletal muscle; lactate, produced from glycolysis; and glycerol, released from adipocytes. The normal inhibitory effects of insulin and glucose on gluconeogenesis are also lost during critical illness.

In healthy people, a combined infusion of epinephrine, cortisol, and glucagon induces a state of insulin resistance, resulting in hyperglycemia, despite elevated insulin levels. Tissue injury activates the hypothalamic-pituitary-adrenal axis and the renin-angiotensin-aldosterone system and releases cytokines, initiating a cascade of inflammatory enzymes. A complex relationship exists between cytokines, the neuroendocrine system, and the immune system. The cytokine (tumor necrosis factor-alpha) activates glucocorticoid release, which inhibits antibody production and natural killer cell activity. Immune system cells also have receptors for many neuroendocrine factors, such as adrenocorticotropic hormone and growth hormone, which further predisposes peripheral tissues to an increase in insulin resistance.

**Hyperglycemia in the critically ill**

Hyperglycemia hurts clinical outcomes and increases mortality in critically ill medical and surgical patients. Hyperglycemia can correlate to increased cerebral lactate, resulting in local brain tissue acidosis that decreases mitochondrial function and increases cerebral infarct size. Hyperglycemia can also adversely affect the ischemic brain by disrupting the blood-brain barrier and promoting cerebral edema.

High plasma glucose levels on admission are associated with an increased risk of heart failure, the need for coronary artery bypass grafting, cardiogenic shock, and increased mortality following acute MI. An MI meta-analysis revealed an association between stress hyperglycemia, increased risk of in-hospital mortality, and heart failure or cardiogenic shock. Insulin can inhibit inflammatory growth factors, which may be important in acute MI. Insulin also inhibits lipolysis. Elevated free fatty acids are associated with cardiac dysrhythmias and poor outcomes.

Acute hyperglycemia affects all major components of innate immunity and impairs the patient’s ability to fight infection. Hyperglycemia inhibits the release of IL-1 from macrophages, impairs phagocytosis, and causes the release of oxygen radicals from neutrophils.

Critically ill patients often develop a diffuse polyneuropathy, which presents as a tetraparesis (weakness of all four extremities; also known as quadriparesis) with muscle atrophy. In most patients, the course is self-limited and good recovery occurs if the underlying critical illness resolves. Polyneuropathy, however, severely impairs ventilator weaning and early mobilization.

**Intensive insulin therapy**

You can best achieve tight glycemic control in the ICU with a continuous insulin infusion (see *Glucose control in the ICU*). This therapy lowers glucose levels mainly by stimulating skeletal muscle glucose uptake, rather than affecting hepatic glucose handling. The American Diabetes Association recommends keeping the blood glucose level of critically ill patients as close to 110 mg/dL as possible and less than 180 mg/dL.

I.V. insulin has a quick onset of action and a short half-life (about 7 minutes), which makes it responsive to rapid adjustments. (Note that only regular insulin is appropriate for I.V. use.) In comparison, subcutaneous insulin is absorbed slower and less predictably, especially in patients whose peripheral circulation may be compromised. And I.V. insulin administered as a sliding scale rather than a continuous infusion has been associated with poor glycemic control and frequent episodes of hypoglycemia. Check your patient’s blood glucose levels every 1 to 2 hours when using a continuous insulin infusion.

One risk associated with aggressive insulin therapy is hypoglycemia (blood glucose level of 40 mg/dL or less). Clinical manifestations include anxiety, weakness, fatigue, confusion, behavioral changes, loss of consciousness, and seizures. Many of these are difficult to observe in critically ill patients, so ensure close patient monitoring.

**Hyperglycemia treatment protocols**

To improve glycemic control and lower rates of hypoglycemia, use standardized protocols developed by in-house multidisciplinary teams. Benefits of a tight glycemic protocol include:

- application of evidence-based best practice
- standardization of care
- decreased variability in care
- reduced medical errors and complications
- improved patient outcomes
- decreased costs.

Such protocols standardize the approach to tight glycemic control and reduce the variation that occurs with individual preference. Protocol development is a process that requires the careful attention of healthcare providers. Recommendations for insulin infusion adjustments must
be based on patient conditions and should be clearly defined. Also, be sure to follow guidelines for preventing, identifying, and treating hypoglycemia.

**Nursing considerations**

Critically ill patients have many risk factors for developing hyperglycemia; one that’s often overlooked is excessive I.V. dextrose. High concentrations of dextrose can be found in dialysis solutions, I.V. medications mixed in dextrose solutions, and total parenteral nutrition (TPN).

Patients at risk for developing hyperglycemia include those on glucocorticoid medications, catecholamine vasopressors, and prolonged bed rest. Corticosteroids can increase insulin resistance in peripheral tissues. Differences in duration of action among corticosteroids can cause varying patterns of insulin resistance in some patients. Corticosteroids often administered in tapering dose schedules create the need to anticipate varying insulin requirements. In the absence of critical illness, bed rest alone can contribute to reduced skeletal muscle insulin sensitivity.

The obvious complication of aggressive insulin therapy is hypoglycemia. Frequent monitoring of blood glucose levels via bedside glucose monitoring is the safest way to prevent swings in blood glucose and is a significant part of any tight glycemic control protocol, requiring quick and easy access to glucose monitoring equipment. Other considerations include following guidelines for adjusting insulin if you stop tube feedings or TPN, change administration rate or formula, or interrupt delivery.

Insulin therapy is a straightforward and inexpensive way to avoid the staggering costs of long-term complications of critical illness. By understanding the risk factors associated with developing hyperglycemia, as well as the effects of hyperglycemia on patient outcomes, you can help keep your critically ill patient normoglycemic.

**Selected references**