

## Foreword



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Once again, the *Endocrinology and Metabolism Clinics of North America* has assembled a cadre of world experts to review a number of very important aspects of acute endocrinology. Dr. Greet Van den Berghe, a world-renowned expert in critical care medicine has compiled this extremely topical issue.

The opening presentations cover thyroid storm and myxoedema coma, two classic endocrine emergencies. Nayak and Burman describe the normal physiology of thyroid hormone metabolism and the etiology of thyroid storm, which usually occurs in cases of Graves' disease. As they outline in their very practical review, signs and symptoms affect many organ systems of the body, and once the diagnosis is made, there are a number of therapeutic choices. Most cases will respond to medications, but occasionally, emergency surgery is required. The review by Wartofsky describes the fortunately uncommon occurrence of myxoedema coma, although patients with severe undiagnosed myxoedema are probably more common than thought, and myxoedema should always be considered in severely ill patients. Once again, multiple systems are affected, and signs and symptoms maybe quite subtle, especially in the elderly. Serum thyroid-stimulating hormone measurements are easily obtainable and are the mainstay for screening. As Wartofsky points out, because hypothyroidism may be secondary to hypopituitarism, corticosteroids should be used simultaneously to starting treatment for myxoedema, to avoid an adrenal crisis.

Pheochromocytomas are not very common and are often difficult to detect, although these should always be thought of when presenting symptoms are unusual. Paroxysmal hypertension, sweating, palpitations, and headaches

are the classic symptoms, yet are absent in over half of the cases. In cases of pheochromocytoma emergencies, multi-system failure can be seen, particularly with hypertensive encephalopathy, arrhythmias, and shock. Both alpha and beta adrenergic blockades are necessary; in the review by Brouwers and colleagues, there is a very explicit description of the management of such life-threatening conditions.

Both hyperglycemia and hypoglycemia may become critical conditions. Kitabchi describes the events occurring in hyperglycemic ketoacidosis, primarily, although not exclusively, an event seen in Type 1 diabetics, and non-ketotic hyperosmolar coma, seen more commonly in Type 2 diabetics. Despite our understanding of these conditions and of the appropriate management required, both are still relatively common, and may reflect poor management of patients with diabetes; thus, this review is timely and appropriate. The article on hypoglycemia by Guettier and Gorden, on the other hand, describes the classic causes and evaluation of patients with hypoglycemia and the management of the primary cause. Drug-induced hypoglycemia remains the most common type of hypoglycemia, particularly in patients with diabetes, and should be treated rapidly and effectively, because it often presents as an emergency condition.

Adrenal insufficiency may be primary or secondary to hypothalamic–pituitary disorders and requires immediate diagnosis and replacement therapy. The article by Bouillon is a practical approach that suggests that during the diagnosis, it may be necessary to institute therapy immediately to avoid a deterioration of the patient’s condition.

The article by Langouche and Van den Berghe describes an interesting summary of studies that outline the hormonal deficiencies seen in acute and chronic illness. In both circumstances, peripheral hormone deficiency occurs. In acute illness, this is despite increased secretion of hypothalamic–pituitary hormones and suggests a degree of peripheral hormone resistance. In contrast, in chronic illness, there is an overall reduction in central hormone secretion. The concept is based on numerous studies and has a powerful message for the academic.

Mesotten and Van den Berghe then address the question of the growth hormone (GH)/insulin-like growth factor (IGF) in critical illness. There is a good although incomplete understanding of the effects of critical illness on this axis. On the other hand, use of rhGH or rhIGF-1 in these patients remains essentially a research opportunity. Both hormones have numerous effects in addition to protein anabolism, and these negative effects on metabolism may preclude their use; indeed, one study using GH in intensive care patients was associated with increased mortality.

Mebis and colleagues describe the alterations in the hypothalamic–pituitary–thyroid axis in critical illness, known to most clinicians as the “euthyroid sick syndrome.” They also discuss the question of replacement of triiodothyronine (thyroxine is ineffective) under these circumstances, and although they don’t give a clear answer to this question (because there isn’t

one), they correctly suggest that thyrotropin-releasing hormone replacement maybe more appropriate and safer.

Similarly, in the excellent article by Müller, there is a discussion, backed by studies, which suggests that a degree of “relative adrenal insufficiency” exists in cases of critical illness. However, as the author points out, the uncontrolled use of glucocorticoids under these circumstances may sometimes be more harmful than helpful. Judicious use is, therefore, suggested as we await the outcome of large controlled studies on this topic.

Catecholamines are widely used in maintaining tissue perfusion in patients with critical illnesses, although some of the side effects are quite serious and include increased oxygen consumption and enhanced gluconeogenesis. Dopamine, on the other hand, may suppress release of certain hormones and interfere with the body’s immune response. Vasopressin has become the new wonder drug in maintaining cardiovascular stability, although its side effect profile is as yet undefined. All of these issues are covered in a very scholarly article by Bassi, Radermacher, and Calzia.

In their classic studies on intensive insulin therapy in medical and surgical intensive care patients, Van den Berghe and coworkers showed phenomenal improvements in outcomes. Vanhorebeek and Van den Berghe describe many studies of their own and by others on the mechanisms that may play a role in the success of an intensive insulin therapy program. In addition to blood glucose control, it is apparent that insulin therapy has effects on other metabolic parameters, such as lipids, and on tissue mitochondrial health. Insulin may also have nonmetabolic effects, such as on proinflammatory mediators, that may help explain the results.

Sodium and water imbalances are critical issues in patients with severe illnesses and are very commonly encountered. These conditions are divided into hyposmolar disorders (excess water relative to solute) and hyperosmolar disorders (excess solute relative to water), making appropriate evaluation and management extremely important. A very practical expose is discussed by Verbalis.

In summary, this issue is a must read for endocrinologists, internists, and intensivists, contributing greatly to the understanding of important endocrinological disorders and providing practical guidelines to their treatment.

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