Foreword

Endocrine Issues in Pediatric Critical Illness

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The management of critically ill children requires a thorough understanding of the complex interplay of multiple physiologic systems. There is considerable emphasis placed on the neurologic, cardiovascular, and respiratory systems in pediatric critical care training programs¹ with less time spent on the understanding, assessment, and management of endocrine pathophysiology. This is perhaps due to the complexity of the endocrine system in addition to the relative paucity of research in this area. This issue is meant to highlight areas of emerging interest within the endocrine system in critically ill children.

Although there have been previous reviews of endocrine issues in critically ill children,^{2–4} these reviews are either becoming outdated, address a small number of endocrine issues,^{2,3} or are focused on children with preexisting endocrine disease.⁴ This journal issue seeks to fill the current gap by providing comprehensive articles on eight key hormones, summarizing both physiology and up-to-date clinical research in pediatric critical care. These include vitamin D, melatonin, brain natriuretic hormone (BNP), vasopressin, thyroid, glucose control, endocrine management of organ donors, and procalcitonin. These particular areas were chosen either because of the recent emergence of new literature (glucose control, vitamin D, vasopressin, thyroid) or to highlight the need for further research in these areas (melatonin, BNP, calcitonin, endocrine management of the organ donor). We deliberately excluded a review on cortisol as it is the hormone that critical care practitioners are most familiar with and there have been no recent studies in this area.⁵

This issue begins with a review on vitamin D deficiency in pediatric critical illness. Numerous observational studies suggest that vitamin D deficiency may not only be common in this patient population,^{6,7} but that it is clinically significant. This is a very exciting area of research as it is possible to rapidly normalize vitamin D status through loading dose enteral cholecalciferol supplementation.⁸ As a simple, safe and inexpensive medication, this intervention could benefit critically ill children worldwide.

The next two reviews focus on the roles of the thyroid gland in critical illness. The primary role of the thyroid

gland is the control of the body's metabolic rate through the production of thyroid hormones. Numerous studies have demonstrated a decrease in serum triiodothyronine (T₃) and a concomitant increase in reverse triiodothyronine (rT₃) levels with critical illness.⁹ Researchers originally felt that these changes were an adaptive response to decrease metabolic demand and anabolism during critical illness. However, more recent evidence, originating from both animal and human interventional studies, suggests that these changes may actually represent a maladaptive response and that thyroid hormone replacement during clinical illness may have beneficial effects on clinical outcomes.¹⁰ If confirmed, thyroid hormone supplementation could provide clinicians with a simple, inexpensive, and widely available method for augmenting outcomes in pediatric critical care. One of the other, less known, roles of the thyroid gland is to produce procalcitonin in response to increased serum calcium. Procalcitonin levels have been used to determine prognosis in severe infections¹¹ and to rationalize the use of antibiotics¹² in critically ill adults. Although limited, early research on the role of procalcitonin as a marker of acute infection in critically ill children appears promising¹³ and has the potential to significantly improve the allocation of antibiotics in pediatric intensive care units (PICUs) across the globe.¹⁴

Melatonin, the next hormone in the review, also has the potential to affect a large number of critically ill children through its well-known effects on circadian rhythm,¹⁵ analgesia, and sedation.¹⁶ Studies in critically ill adults suggest an improvement in sleep quality¹⁷ and a decreased need for additional sedation.¹⁸ Unfortunately, there have been no studies on the exogenous administration of melatonin in critically ill children outside of the neonatal age group. Melatonin has been extensively studied and used in outpatient populations¹⁹ and in neonates without deleterious effects²⁰; studies demonstrating safety in critically ill children and adults are lacking. Given its potential for effectiveness and given that it demonstrated safety profile in other populations, the use of melatonin in PICU patients appears to be an exciting new area for critical care researchers.

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The review on melatonin is followed by another hormone, BNP that is starting to generate more interest in the pediatric population. Although BNP levels are a widely used marker of cardiac stress and function in adults,²¹ their role within the pediatric population remains unclear. Available pediatric evidence suggests that BNP levels may be useful in detecting the presence of cardiac disease,²² prognosticating its severity,²³ and differentiating cardiac from respiratory disease in children.²⁴ However, the diversity of patient populations, small sample sizes, lack of multicenter work, and paucity of guidelines and/or consensus recommendations have led to inconsistent and limited use of this potentially promising marker.

Vasopressin is the next hormone highlighted in the review. Different from the aforementioned hormones, it has a well-established place in the PICU, and is often used for the treatment of diabetes insipidus, gastrointestinal bleeding, cardiac arrest, and shock. Outside of diabetes insipidus, widespread application of this hormone is based on physiologic rationale and long-standing use, instead of sound clinical trial evidence. Trials in critically ill children have failed to show a benefit of vasopressin on clinically important outcomes in either shock or cardiac arrest and some trials, albeit underpowered, have suggested potential harm.^{5,25} This review reminds us of the available literature and recommends caution when using vasopressin for these conditions until larger trials are conducted.

The last reviews in this issue focus on the endocrine management of two clinical scenarios rather than the role of specific hormones. The first scenario is that of stress hyperglycemia that is a common occurrence in critically ill children.²⁶ The literature has been divided as to the significance of critical illness associated hyperglycemia and whether normalization of blood glucose levels improves clinical outcomes or saves health care spending. This review provides justification for another randomized controlled trial on glycemic control in critically ill children by highlighting the limitations of the existing studies. The final review describes the endocrine management of the neurologically diseased pediatric patient. There has been a significant amount of literature on the endocrine management of organ donors with relatively little clinical trial evidence to guide management in either adults or pediatrics. This review discusses the endocrine physiology of pediatric organ donors and the evidence for their management.

Our goals in putting together this special issue on endocrine issues in pediatric critical care were to summarize areas of endocrine physiology, discuss the existing literature along with its limitations, and highlight areas for future research. We hope that this issue will serve as a useful reference for trainees, clinicians, and researchers alike.

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