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Introduction

Critical illness is a modern phenomenon resulting from medical advances which allow the survival of patients who would have previously died. The effects of critical illness are manifold and not least among them are the profound changes seen in metabolic and hormonal systems. Some of these processes are disease specific and others are common to many aetiologies of critical illness. There are a number of reasons why it is important to understand these metabolic processes. Firstly, and potentially most importantly, this knowledge may allow the rational use of pharmaceutical interventions aimed at improving outcome. Secondly, the changes may have prognostic significance whether or not they have a causal role in outcome or are just markers for disease severity. Prognostic relationships suggest that a number of the metabolic changes seen in acute illness may be important in determining outcome.

It has been proposed that critical illness falls into two metabolically distinct phases – acute and chronic [1]. It seems likely that the acute phase has evolved to optimise survival in the face of a temporary non-catastrophic injury or illness. Before modern medicine the organism would have survived or died and it seems unlikely therefore that there would have been pressure for the evolution of a chronic response. The chronic response we see today may thus represent human physiology reacting to circumstances which it has not evolved to deal with and its responses may thus be inappropriate and even deleterious to survival.

The obvious implication of this reasoning is that interventions that modify the endocrine/metabolic response may be beneficial. A number of important studies have attempted to do this and these are discussed in the relevant chapters. In general, early small studies have been promising but larger better designed studies, often using a sledgehammer approach, have either shown no benefit or actual harm. In the light of these findings recent work has begun to suggest that subtle interventions may be of benefit.

It is important to differentiate pharmacological approaches, i.e. the use of hormones at doses far in excess of the normal physiological levels, from physiological doses, i.e. the use of hormones at doses designed to mimic the normal responses to stress. An example of this difference would be the comparison of the large negative trials of glucocorticoids [2], and the more recent encouraging lower dose trials [3]. There was a 90-fold difference in glucocorticoid dosage between the studies.

A number of common themes emerge from the chapters not least of which is the idea that cytokines may provide a mechanism to link the specific insult, e.g. sepsis, trauma or burns, to the endocrine disturbance. This point is made in a number of chapters with remarkable consistency of findings – time and again the finger of suspicion points to IL-6, IL-1 and TNF- α . In addition to the common mechanisms many of the chapters detail the specific effects of particular underlying pathologies such as sepsis, trauma and burns.

Heller and Robinson open with a careful consideration of carbohydrate metabolism and discuss the changes seen in peripheral glucose uptake and hepatic glucose output in illness. The roles of lactate, alanine, glutamine and glycerol as gluconeogenic substrates and the possible effects of cytokines as a common pathway between diverse disease processes and perturbations of glucose homeostasis are discussed.

Moving from sugar to salt, Arieff provides a comprehensive review of hyponatraemia and hypernatraemia. Body fluids, solutes, osmolality, the role of the kidneys, thirst and its regulation are considered. The clinical effects of abnormal sodium concentrations are described and the mechanisms, predominantly changes in the size of brain cells are discussed. The major effects of gender and age on the ability to tolerate deranged salt homeostasis is detailed and the changes seen in specific conditions, such as heart failure, AIDS, liver failure, cancer and surgery, are discussed.

Calcium metabolism has received less attention than some of the other metabolic changes in illness and Lind and Ljunghall go some way towards redressing the balance. They briefly describe the important physiological roles of calcium, phosphate and magnesium and their homeostatic mechanisms in health before detailing work which suggests that there is hypersecretion of parathyroid hormone from an early stage of illness. They also describe the effects of calcium supplementation on haemodynamic indices.

Hennemann and Krenning describe the characteristic changes seen in thyroid hormone concentrations during illness and also the underlying pathophysiological processes. The tissue effects of reduced thyroid hormone concentrations and studies in which subjects have been given exogenous thyroid hormones in an attempt to correct the low thyroid hormone state are reviewed.

The hypothalamo-pituitary-adrenal axis has been extensively studied in acute illness. Newell-Price and Trainer review the normal physiology, methods of assessing the axis and the effects of specific disease processes on the axis. They describe the adrenal adaptation to stress and the biphasic changes seen in the axis as acute illness becomes chronic. The incidence of adrenal failure in acute illness and the results of important studies of the effects of exogenous glucocorticoids in acute illness are described.

Fletcher reviews the hypogonadism of acute illness and analyses the relative contributions of central and peripheral processes. The effects of specific disease processes are detailed before the results of trials of the use of androgens as anabolic agents are discussed.

Two chapters examine the GH/IGF-I axis. Ghigo et al. review in detail the physiology and pathophysiology of the axis. They describe the major molecules and receptors which form the axis and also review the control of GH secretion. They consider the effects of sleep, age, exercise, fasting and obesity on GH secretion and then consider the neuroendocrine control of GH secretion and interactions with other metabolic factors such as fatty acids, glucose, thyroid hormones and glucocorticoids. Botfield and Hinds briefly review the physiology of the GH/IGF-I before moving on to examine the anabolic properties of GH and IGF-I. They review GH dosages, side-effects and compare the effects of separate and combined GH and IGF-I treatment in terms of metabolic changes and more importantly functional outcomes.

We hope that this volume will both provide an overview of the current state of knowledge of endocrine and metabolic function in acute illness and stimulate further research in this important area.

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References

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