# Chapter 1
# Introduction

**Jean-Charles Preiser**

> The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them. William Henry Bragg

One of the most challenging tasks on earth is to bring people together and to build bridges to promote the cross-fertilization of knowledge!

In the field of care of the critically ill, this statement can be translated into the integration of new discoveries or major advances in the understanding of physiology into unbiased evaluations of new therapeutic strategies adapted from novel experimental findings. Conversely, basic science should be open to clinical data and able to understand and to integrate clinical concerns into research questions. This book aims to bridge the new knowledge gathered in experimental research with new clinical results.

Historically, the *"stress response"* was quoted by the Canadian physiologist Hans Selye, who discovered the mechanisms of the "fly or fight response" designed to restore the homeostasis needed for an independent life, as described by Claude Bernard. Some of the basic and adaptive mechanisms were preserved over the evolution, in keeping with the Darwinian theory of evolution.

Now, the changes and improvements in the practice of medicine allow patients to survive critical illness, allow surgeons to perform risky interventions, allow anesthesiologists to sedate very weak patients, etc. The support of the vital functions prolongs the lifespan of a critically ill thanks to improvements in pharmacological agents, in the technology of ventilators, renal replacement therapies, and extracorporeal membrane oxygenators. However, the metabolic and functional consequences of the critical illness can last weeks or months, representing a major burden for the society and cannot be supported by any dedicated device. Only a few drugs

J.-C. Preiser, MD, PhD
Department of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, 808 route de Lennik, Brussels 1070, Belgium
e-mail: Jean-Charles.Preiser@erasme.ulb.ac.be



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and nutritional formulas can slightly influence metabolism. Therefore, a detailed knowledge of the intimate mechanisms of the stress response is warranted to help clinicians to support the adaptive and desirable metabolic responses while trying to minimize the maladaptive ones.

In this book, several world-leading experts accepted to share their knowledge and to summarize the current understanding of the metabolic response to stress, including the cellular and subcellular mechanisms, the use of macro- and micronutrient as energy substrates during catabolism or anabolic resistance typically associated with critical illness. The roles and patterns of endocrine mediators will be discussed in detail. The final section will address difficult clinical situations, as examples of how the new findings can be translated into daily practice.

Specifically, in the first section, the bioenergetics of the stress response has been revisited in detail by C Faisy, using the concept of stress as a challenge to the equilibrium at each level of the body. The successive phases of the metabolic response to stress were being reviewed in a temporal and clinically relevant sequence. Novel insights as hibernation and mitochondrial mechanisms of adaptation have been updated by J Grip, N Tardif, and O Rooyackers, while the development of anabolic resistance has been reviewed by JP Thissen. The ensuing alterations in the use of lipids, carbohydrates, and protein metabolism were updated by Ph Calder, P Singer, L Tappy, A Norberg, F Liebau, and J Wernerman, whereas the current roles of micronutrients have been reviewed by MM Berger. A Thooft, R Machado, and myself summarized the related issue of stress hyperglycemia.

In Part 2, the current understanding of the functional changes of hormonal systems has been described by L Langouche and G Van den Berghe for the thyroid axis and P Marik for the adrenal system. The roles and relevance of new important endocrine mediators, the enterohormones released from the gastrointestinal tract, and the adipokines released from fat tissue have been reviewed by M Plummer, A Reintam, A Deane, K Robinson, J Prins, and B Venkatesh.

In Part 3, the clinical views and attitudes in situations accompanied by challenging metabolic alterations have been addressed. The issue of severe undernutrition was revisited by P Singer and J Cohen; the specificities of traumatic brain injury by H Quintard, C Ichai, and JF Payen; the particular aspects of sepsis and organ failures by V Fraipont and myself; morbid obesity by M Coeffier and F Tamion; and the issues related to burn injury by A Abdullahi, D Patsouris, SR. Costford, and MG Jeschke.

I would like to thank wholeheartedly each one of the authors who brought his own contribution and his personal stone to the huge enterprise of understanding the metabolic response to stress, an indispensable step to improve the quality of care and the quality of the lives of the survivors of critical illness.