Birth, Distress and Disease

This volume examines the role of steroids and peptides in the regulation of pregnancy and pregnancy outcome, and their long-term effects including possible influences on adult-onset diseases. During pregnancy the placenta acts as a central regulator and coordinator of maternal and fetal physiology, and of the onset of labor, through its production and regulation of steroids and peptides. Perturbations to this regulatory system can result in poor pregnancy outcome, such as preterm birth and low birth weight. These in turn are linked to diseases in later life. Intriguingly, many of these regulatory actions of steroids and peptides also occur in the brain. The induction and suppression of peptides by steroids appear to be the key to regulatory function in both brain and placenta. These various interweaving strands, linking basic sciences with obstetrics, are all reviewed in depth here producing a fascinating account of an important area of materno-fetal medicine.

Birth, Distress and Disease

Placental–Brain Interactions

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This volume is dedicated to the students and young (and not so young) scientists we confidently predict will extend and improve on the research presented here.

We would also like to acknowledge and thank certain individuals for the personal contributions they have made to one of us (JS): E. E. Krieckhaus; Ellen Oliver; and Stanley Schulkin.

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Preface

In the summer of 2002, a small one-day conference was held at the offices of the American College of Obstetricians and Gynecologists in Washington DC. The purpose of the conference was to consider the implications of the intriguingly converging research areas of peptide regulation by steroids in both brain and placenta, and how these research findings might enhance our understanding of the physiological processes of human gestation and parturition. An important subtext of the discussion was how events and processes at the beginning of life can affect health and well-being decades later. Among the participants were both clinicians and basic scientists; the research presented concerned both human studies and comparative research on animal models; the perspectives examined ranged from clinical medicine to evolutionary biology.

Our understanding of the physiological and regulatory processes that underlie the timing and progression of labor and delivery remains incomplete. Perhaps the most graphic indication of our inadequate understanding of this fundamental biological process is the current lack of accurate and effective clinical tools to either predict or prevent preterm birth. In the USA, the rate of preterm birth continues to rise, and half of preterm births are classified as idiopathic.

Progress is being made, however. A key paradigm shift is replacing the idea of the placenta as a largely passive organ mainly responsible for delivering nutrients to the fetus with the concept of the placenta as a metabolically active, transitory endocrine organ that serves as an important central regulator of maternal and fetal physiology. The placenta is now known to produce a wider array of steroids, peptides, cytokines and other regulatory molecules than does any other organ in the body, except possibly the brain.

In the mid-1980s, independent groups, some working on the brain and others on the placenta, made important discoveries regarding the differential regulation of one such neuropeptide, corticotropin-releasing hormone (CRH), by cortisol. Previously, the received view was that CRH release and production was negatively restrained by cortisol; the paradigmatic example of this was the negative feedback

system of the hypothalamic–pituitary–adrenal axis. It turns out that in several areas of the brain (e.g. central nucleus of the amygdala, bed nucleus of the stria terminalis) and in the placenta, CRH release and production is induced by cortisol. Neural CRH is important in the induction of adaptive behaviors in response to conditions where high alertness and metabolic effort are appropriate (e.g. dangerous, fear-inducing situations). Placental CRH appears to play an important role in human gestation, fetal development and parturition, possibly either reflecting or serving as a gestational 'clock'. Although initial enthusiasm for placental CRH as a predictor of preterm labor has been tempered, recent research has suggested that it, indeed, may have clinical value (Wadhwa *et al.*, 2004).

This volume was inspired by the talks and discussions that occurred during the meeting in Washington DC in the summer of 2002. We strove to put together a book that reflects the diversity of research relevant to understanding neural and placental physiology, their intriguing similarities, and how these diverse lines of research can contribute to understanding human biology and improving health. We could not include all relevant areas in a single volume, and we apologize to our colleagues and other scientists whose work is not represented here.

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