Pediatric endocrinology will undergo an extraordinary revolution this century. It has also become increasingly apparent that experiences and exposure throughout fetal life and childhood can have important effects on many diseases that develop much later during adult life. Alterations to the endocrine system mediate many of these long-term effects, and understanding how these changes occur and how they translate into compromised health in adulthood have become additional questions that confront pediatric endocrinologists [1–3].

I shall quote just a few examples of the great challenges that wait to be tackled in the near future [2].

There is increasing evidence that the hypothalamus is involved in the regulation of energy balance and glucose homeostasis and, ultimately, the occurrence of diabetes. In humans, however, studies on the brain’s control of metabolism and the endocrine system are difficult to perform, and only translational research will provide robust data that can be translated into clinical practice. If it were not for this lack of data, the world of pediatric medicine would be at the final stages of research [4,5].

For almost a century, endocrine research has focused on the interaction between hormones and their receptors, providing major advances in the understanding of endocrine system physiology. More recently, the research focus has shifted to the pathways downstream of such receptors. The study of intracellular hormone signaling has revealed that some endocrine diseases may originate from alterations in signal transduction. It is easy to foresee that further investigations will reveal that many as of yet unexplained endocrinopathies are the result of subtle alterations in intracellular signaling [6].

Novel genes have recently been found to play a pivotal role in the regulation of reproduction and growth. Genome-wide association analysis has revealed the influence of many unexpected genes in the control of growth, puberty, and diabetes [7]. This new large-scale genetic approach challenges researchers to obtain more complete descriptions of the susceptibility architecture of endocrine traits and to translate the information gathered into improvements in clinical management [8]. However, the mechanisms through which genetic information is translated into phenotypic features and diseases as well as those underlying the interaction between hundreds of genes are still largely unknown. Genetic manipulation of experimental species, which utilizes transgenic and gene-knockout technology, has led and will lead to important advances in determining the relationship between genes and the function of their encoded proteins in the intact organism [9].

Alterations in the embryo–fetal and early postnatal hormonal environment, caused by either maternal diet or exposure to environmental factors, can modify the epigenome, and these modifications are inherited in somatic daughter cells and maintained throughout life, ultimately leading to permanent metabolic and endocrine changes. We are at the beginning of the epigenomics era which may provide important insights that can be translated into interventions to revert epigenetic programming [10]. The early prevention of
adult diseases is at present a primary objective of pediatrics in general and pediatric endocrinology in particular. Obesity, diabetes, hypertension, and cardiovascular disease in adulthood may originate during embryo-fetal development and early postnatal life. Therefore, elucidation of the environmental, (epi)genetic, and endocrine mechanisms leading to long-term metabolic risk represents the primary task of pediatric endocrinologists [8–11].

The last three decades have witnessed growing concerns over the potential adverse effects that may result from exposure to a group of chemicals that have the potential to alter the normal functioning of the endocrine system in wildlife and humans. Potential adverse outcomes in both wildlife and humans have focused mainly on reproductive and sexual development and function, altered immune and nervous system function, thyroid function, and hormone-related cancers. Analysis of the human data in isolation, while generating concerns, has so far failed to provide firm evidence of direct causal associations between exposure to endocrine disruptors and adverse health outcomes. Our current understanding of the effects posed by endocrine disruptors on humans is incomplete. Uncertainty over the possible effects of chronic exposure to a number of chemicals with endocrine-disrupting potential and the fundamental role played by the endocrine system in maintaining homeostasis make the study of the effects posed by exposure to these chemicals a worldwide research priority [10–12].

Further challenges come from the development of novel therapeutic approaches for endocrine diseases in childhood [13]. New drug formulations, individualized treatment based on pharmacogenomics, as well as gene and stem cell therapies represent further research fields for pediatric endocrinologists of the 21st century.

Below are just a few examples of the potential research fields:

- Long-acting growth hormone;
- Novel long-acting or ultra-rapid-acting insulin;
- New therapies for diseases such as achondroplasia;
- New panel genes research.

The above challenges present a real opportunity for the future and are key challenges for both pediatricians and their patients.

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References


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