

Foreword



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These issues contain a potpourri of endocrinological conditions important to the pediatric endocrinologist.

The first issue begins with a discussion by Alfred Tenore and Daniela Driul on the human genome project's impact on our understanding of the genetics and the pathophysiology of many endocrine disorders, and on how the project can potentially lead to new drug targets and pharmacogenetics for these disorders. They discuss these new advances in understanding endocrine disorders that lead to hyposecretion of hormones and in others that lead to hypersecretion. In their article, they also outline the various technologies applied to discover disease-related genes, such as *menin* and *leptin*, and the techniques for diagnosing certain disorders and thus pointing the way to specific therapy. One such technique, for example, is that for identifying the *ret* oncogene in thyroid cancer. These and newer techniques will undoubtedly be critical for better understanding of the disease process, for making faster and more accurate diagnoses, and for developing more advanced therapies.

Congenital disorders of the thyroid gland, both hypothyroidism and hyperthyroidism, are presented by Ferenc Péter and Ágota Muzsnai. Their article describes the ontogeny of the thyroid gland and the genetics involved in this process. They also describe the role of the pregnant mother and placenta on the developing fetus and how the fetal-placental system may affect the neonate and the function of the thyroid to result in hypothyroidism, hyperthyroidism, or both.

The perinatal period is a critical time and neonates are not immune to endocrine disorders. Many of the derangements in endocrine function may be due to maternal disorders. If such disorders are known, the effects on the neonate can be anticipated. Often, however, the disorders are missed and the neonate represents the first indication. Hyman, Novoa, and Holzman discuss the possible abnormalities, which include thyroid (hypothyroidism), adrenal, parathyroid (hypocalcemia), and pancreatic (hypo- and hyperglycemia) abnormalities. Both the obstetrician and neonatologist should be on the alert for these readily treatable conditions.

Melissa Crocker and Jack Yanovski discuss childhood obesity, an important issue affecting our communities. Similar to the obesity epidemic in the adult population, this epidemic among children is leading to more type 2 diabetes in the young, as well as to other comorbidities. In their article, Crocker and Yanovski discuss the known endocrine disorders where obesity is found, genetic links to the disorder, and the hypothalamic mechanisms involved. Some medications approved for adult obesity have been shown in trials to be effective in treating childhood obesity. However, bariatric surgery is really the most effective treatment when behavioral therapy fails, though it should be reserved for very severe cases.

In their article on metabolic syndrome in the pediatric population, Ebe D'Adamo, Nicola Santoro, and Sonia Caprio describe this important and common scenario. More populations are demonstrating an alarming increase in overweight and obese children and adolescents. These overweight youngsters often demonstrate features of the metabolic syndrome, including dyslipidemia, hypertension, and impaired fasting glucose, though these are often not always in the adult range. Furthermore, growing evidence shows that early-onset metabolic syndrome is associated with complications. Unfortunately, most therapies are "off-label." It is hoped that, when more studies are performed in the adolescent population, therapies may become available. Meanwhile, a major effort needs to go towards lifestyle changes to reduce the burden of the metabolic syndrome.

Galia Gat-Yablonski, Michal Yackobovitch-Gavan, and Moshe Phillip describe an interesting paradigm: the role of nutrition on growth. While it is well established that major effects of pubertal growth is related to the growth hormone–insulin-like growth factor-1 axis, apparently nutritional and other hormones may also be important for this process. Thus, malnutrition together with inadequate insulin levels affects insulin-like growth factor-1 production because of a relative growth hormone resistance. Other hormones that may play a role include ghrelin, leptin, and various vitamins and micronutrients. Our understanding of these effects is obviously still limited and requires more research.

Recombinant human growth hormone is now widely available for use in the treatment of growth retardation in children as well as in adults with growth hormone deficiency, as defined by definitive criteria. Babies who are small for gestational age and children with growth hormone deficiency, idiopathic short stature, Turner syndrome, Prader-Willi syndrome, Noonan syndrome, chronic renal disease, and SHOX gene deficiency are all being treated to improve growth. As described in this practical article by Sherry Franklin and Mitch Geffner, a number of preparations are available to the endocrinologist and in many conditions the effectiveness of the drug is quite impressive.

Because growth hormone replacement therapy is only useful while the epiphyses are open, the child with growth retardation discovered during puberty presents a particular challenge. Dr. Mauras discusses this issue and presents an approach that includes high doses of growth hormone and the delaying of puberty progression with the use of gonadotropin-releasing hormone analogues. As outlined, there is also the possibility of using growth hormone with aromatase inhibitors, as it is well known that estrogen enhances epiphyseal closure.

Children with short stature are common and are initially investigated for growth hormone deficiency. Those that prove growth hormone–deficient are treated quite effectively with replacement growth hormone. Apparently a number of children either do not respond appropriately to growth hormone or have a deficiency of insulin-like growth factor-1 production as a primary defect. These individuals may be treated with recombinant human insulin-like growth factor-1, which until recently was

reserved for treating Laron-type dwarfism with growth hormone resistance due to a genetic disorder in the growth hormone receptor. Appropriate diagnosis and close monitoring are critical, as discussed by Bright, Mendoza, and Rosenfeld. In addition, they discuss the possibility of giving growth hormone and human insulin-like growth factor-1 therapy under certain circumstances.

This first issue covers some very important pediatric endocrine conditions with practical aspects as well. The authors are indeed the world experts in this area of research and therapeutics.

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