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<p>This article reviews factors that contribute to excessive weight gain in children and outlines current knowledge regarding approaches for treating pediatric obesity. Most of the known genetic causes of obesity primarily increase energy intake. Genes regulating the leptin signaling pathway</p>	

are particularly important for human energy homeostasis. Obesity is a chronic disorder that requires long-term strategies for management. The foundation for all treatments for pediatric obesity remains restriction of energy intake with lifestyle modification. There are few long-term studies of pharmacotherapeutic interventions for pediatric obesity. Bariatric surgical approaches are the most efficacious treatment but, because of their potential risks, are reserved for those with the most significant complications of obesity.

Metabolic Syndrome in Pediatrics: Old Concepts Revised, New Concepts Discussed 549

Ebe D'Adamo, Nicola Santoro, and Sonia Caprio

The worldwide epidemic of childhood obesity in the last decades is responsible for the occurrence in pediatrics of disorders once mainly found in adults, such as the metabolic syndrome. A key factor in the pathogenesis of metabolic syndrome is insulin resistance, a phenomenon occurring mainly in obese subjects with a general resistance to the insulin effect only on carbohydrates metabolism. Given that the metabolic syndrome is driven by obesity, the prevalence of the latter will strongly influence the prevalence of metabolic syndrome. This article addresses the causes of metabolic syndrome and the relevance of obesity in the pediatric population.

Nutrition and Bone Growth in Pediatrics 565

Galia Gat-Yablonski, Michal Yackobovitch-Gavan, and Moshe Phillip

Children's growth is a hallmark of their normal development and the association between nutrition and linear growth in children is well accepted. Growth requires an adequate supply of many different nutritional factors, some form the "building materials," whereas others play regulatory roles. In this article we describe the growth of the growth plate and discuss the role of nutritional affected hormones on this process. In addition we describe the effect of local regulators and nutritional factors on the growth process and suggest the involvement of new regulatory factors in the translation of nutrition to growth.

Growth Hormone: The Expansion of Available Products and Indications 587

Sherry L. Franklin and Mitchell E. Geffner

Growth hormone is a widely used hormone. This article describes its historical use, current indications and studies for possible future uses.

Strategies for Maximizing Growth in Puberty in Children with Short Stature 613

Nelly Mauras

The approach to the child with growth retardation who is in puberty remains an important clinical challenge. The use of high-dose growth hormone (GH), suppression of puberty with GnRH analogs in combination

with GH, and the use of selective inhibitors of the aromatase enzyme with aromatase inhibitors (also in combination with GH) are all therapeutic choices that have been studied. Aromatase blockade effectively blocks estrogen production in males with a reciprocal increase in testosterone, and a new generation of aromatase inhibitors, including anastrozole, letrozole and exemestane, is under investigation in adolescent subjects with severe growth retardation. This class of drugs, if judiciously used for a window of time, offers promise as an adjunct treatment of growth delay in pubertal patients with GH deficiency, idiopathic short stature, testotoxicosis, and other disorders of growth. These evolving uses of aromatase inhibitors, however, represent off-label use of the product, and definitive data on their efficacy are not available for each of the conditions mentioned. Safety issues regarding bone health also require further study.

Recombinant Human Insulin-Like Growth Factor-1 Treatment: Ready for Primetime

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George M. Bright, Jessica R. Mendoza, and Ron G. Rosenfeld

The combination of targeted gene knockout studies in animals and human mutational analysis has demonstrated the key role of the IGF system in mammalian growth, both in utero and postnatally. The concept of IGF deficiency as a diagnostic category for children with growth failure first was proposed in the mid 1990s, and has gained support through the demonstration of patients with mutations in key components of the growth hormone (GH)-IGF axis, as well as the widespread use of IGF-I assays for evaluating short stature. The US Food and Drug Administration has approved IGF-I therapy for treating children who have severe primary IGF deficiency, defined as a height SD score ≤ -3 and a serum IGF-1 SD score ≤ -3 , normal serum GH. Recent studies have demonstrated the efficacy and safety of IGF-I therapy in such patients, and investigations are in progress to determine optimal dosing. The availability of IGF-I therapy thus has expanded the therapeutic tool chest available to endocrinologists caring for children who have growth failure.

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