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MOLECULAR PATHOGENESIS OF ACHONDROPLASIA

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INTRODUCTION

Achondroplasia (OMIM 100800) is by far the most common chondrodysplasia in humans with an estimated prevalence to be one in 15 000 to 40 000 live births. It is the prototype of short-limbed dwarfism and the archetype of a group of disorders that range from the much more severe thanatophoric dysplasia (TD) to the less severe hypochondroplasia.¹ These disorders share a common qualitative clinical phenotype dominated by short limbs, long trunk, large head with frontal bossing, and midfacial hypoplasia.²

Infants with achondroplasia typically present with mild-to-moderate limb

shortening, moderate craniofacial manifestations, and a lumbar gibbis. These features typically become more noticeable over time. The gibbis usually gives way to a lumbar lordosis, and infants and children with achondroplasia are at risk for spinal cord compression at the foramen magnum, as well as obesity. Average adult height for men with achondroplasia is 131 ± 5.6 cm; for women it is 124 ± 5.9 cm.

Thanatophoric dysplasia is much more severe in general. It is usually lethal in the perinatal period, but on rare occasions infants survive with a poor prognosis. Craniofacial abnormalities are much more dramatic. The thorax appears long but narrow and is associated with severe respiratory distress. Two types of TD (TDI and TDII: OMIM 18700 and 18760) can be distinguished radiographically. SADDAN dysplasia refers to a clinical phenotype

From The Editor's Desk

Dear Colleague:

The latest issue of GGH includes the highlights of 2 important annual meetings in our field. The printed journal contains the highlights of the Endocrine Society's meeting held in June in Boston. The online journal also contains highlights from the European Society of Pediatric Endocrinology meeting held in July in Rotterdam. The lead article by Dr. William A. Horton, "Molecular Pathogenesis of Achondroplasia," elucidates the advances that have occurred in the understanding of the mechanisms of growth alterations of these patients. A look at the future with potential therapeutic considerations adds value to the clarification of the pathophysiology of the disease. Additionally, there are 17 reviews of recent papers that were selected by the Editorial Board. Altogether, the journal will stimulate you and enhance your continuous medical education efforts. I am very pleased to note that we continue to expand the content and size of the e-reviews; for example, this issue contains 11 reviews of papers with editorial comments. As well, new clinical practice guidelines continue to be added to the website. In order to provide more reviews, the index of volume 22 (2006) is now only online. Moreover, all issues and subjects are searchable online.

Finally, it is the time of year that I take the opportunity to wish you all the best for the holiday season and best wishes for the New Year.

Sincerely,
Fima Lifshitz, MD

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