

## Growth Without GH: The "Invisible" GH Syndrome

Four children with normal growth velocity, relatively low growth hormone (GH) concentrations as measured by radioimmunoassay (RIA), increased GH concentrations by radioreceptor assay (RRA), markedly increased RRA:RIA ratios, and normal somatomedin C assays were described. These unusual findings suggest the presence of a biologically active GH that is not detected by the usual RIA for GH. Therefore, the structure of the GH molecule in these children is believed to be unusual.

The authors postulate that the

GH molecule(s) secreted by these patients may be a product of the human growth hormone (hGH)-V gene rather than a product of the hGH-N gene, which is normally responsible for GH production. This gene was previously reported by other authors to be unexpressed, since no messenger RNA (m-RNA) derived from it could be detected in human cells.

Bistrizter T, Lovchik JC, Chalew SA, et al. *Lancet* 1988;i:321.

**Editor's comment**—*The hypothesis expressed by the authors is tenable on the basis of the data presented, although not proven. To prove the hypothesis, m-RNA*

*for the hGH-V gene would have to be demonstrated in the patient(s). The findings are intriguing regardless. Assay measurements in these patients are the opposite of patients previously described by Kowarsky et al (J Clin Endocrinol Metab 1978;47:401); those patients had very low RRA:RIA ratios and slow growth, and were believed to secrete biologically inactive but immunoreactive GH. The four patients reported in the current article resemble some acromegalic patients (reported by Hizuka et al in J Clin Endocrinol Metab 1982;55: 545) who also had significantly higher GH concentrations on RRA than on RIA.*

Robert M. Blizzard, M.D.

## Placental Chromosomal Mosaicism Is Responsible for Variations in Growth Rates: Three Reports

If the placentas of children with unexplained intrauterine growth retardation (IUGR) are examined for a chromosomal aneuploidy, a surprisingly large number (perhaps as many as one third of cases of IUGR) will have chromosomal mosaicism confined to the placenta, with a normal cell line and an abnormal cell line. Now that chorionic villus sampling is being done on a regular basis for prenatal diagnosis, it has been found that about 5% of placentas have placental mosaicism with one normal cell line and another with a variety of different chromosomal aneuploidies. These findings suggest that there is a common explanation for IUGR that cannot be attributed to other causes such as maternal smoking or a syndrome: namely, the presence of cytogenetic abnormalities confined to the placenta. Most interesting are the new reports that mosaicism confined to the placenta may also be responsible for allowing fetuses with certain types of chromosomal problems to be carried to term.

Kalousek and McGillivray have recently reported the presence of

a normal cell line in all of the placentas recovered from fetuses with trisomy 18 and trisomy 13 that were born alive. By contrast, trisomic fetuses that are miscarried spontaneously as abortuses or stillbirths do not have mosaicism or cytogenetically normal cells in their placentas. It appears that the normal cell line allows such fetuses to survive long enough to be born alive at term.

Kalousek DK, Dill FJ. *Science* 1983;221:665-667.

Kalousek DK, Dill FJ, Pantzar T, et al. *Hum Genet* 1987;77:163-176.

Kalousek DK, McGillivray BG. *Am J Hum Genet* 1987;41:A278.

**Editor's comment**—*Since the placenta is fetal in origin, we have assumed that it has the same chromosomes as the baby. The work described in these reports suggests that 5% of placentas have some cells that are cytogenetically different from those of the baby. When the placenta has abnormal cells but the baby has only normal cells, the baby may have IUGR. When the baby has abnormal cells but the placenta has some normal cells, the abnormal fetus may survive to term.*

Judith G. Hall, M.D.

## Mapping and Screening in Families With Multiple Endocrine Neoplasia Type 2A: Four Reports

Recently, multiple endocrine neoplasias type 2A have been mapped to chromosome 10. A number of polymorphic DNA markers around the gene allow prediction in most families of those individuals who are carriers of the gene. In addition, prospective screening annually for manifestations of the disease appears to be effective in prevention of morbidity and mortality. For example, provocative tests to guarantee the release of calcitonin can be used to monitor whether or not "medullary" thyroid carcinoma is present, and 24-hour urine screening for both epinephrine excretion and the ratio of urinary epinephrine to norepinephrine allows detection of proliferation of the adrenal medulla before life-threatening manifestations occur.

An 18-year follow-up study of a large family by Gagel et al suggests that total thyroidectomy, when done at the first appearance of increased calcitonin secretion, is curative since there were no recurrences or metastatic diseases in their patients. Parathyroid dis-

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