Helping small youngsters to grow

Endocrinologists are finding that some problems of growth might better be corrected in the hypothalamus rather than the pituitary gland

by Joan Lynn Arehart

Why children grow is a complex subject. Growth hormone, secreted by the pituitary gland in the brain, is undoubtedly the predominant hormone involved. But there is not a one-to-one correlation between how much growth hormone a child has in his or her body and the rate at which the body grows. Endocrinologists are finding that other pituitary hormones come into play as well. They include thyroid stimulating hormone (TSH), which in turn stimulates the thyroid gland to produce thyroxin; adrenocorticotrophic hormone (ACTH), which stimulates the adrenal gland; luteinizing hormone (LH), which turns on the sex glands, and so forth. So failure to grow may result from a deficiency in growth hormone alone or, more commonly, to a deficiency in several of the other hormones.

Now both American and European scientists have found that some other crucial chemicals are involved in growth. They are the hypothalamic releasing factors that turn on and off the various pituitary hormones. "In fact, these are the first really documented examples of hypothalamic deficiencies in humans," says Melvin Grumbach, chairman of the department of pediatrics at the University of California School of Medicine. Other principal investigators include Grumbach's coworkers, Selma Kaplan and Bruce Coston; Robert Blizzard, pediatric endocrinologist at Johns Hopkins University and a team of researchers at the Médecine des Enfants Clinique in Louvain, Belgium.

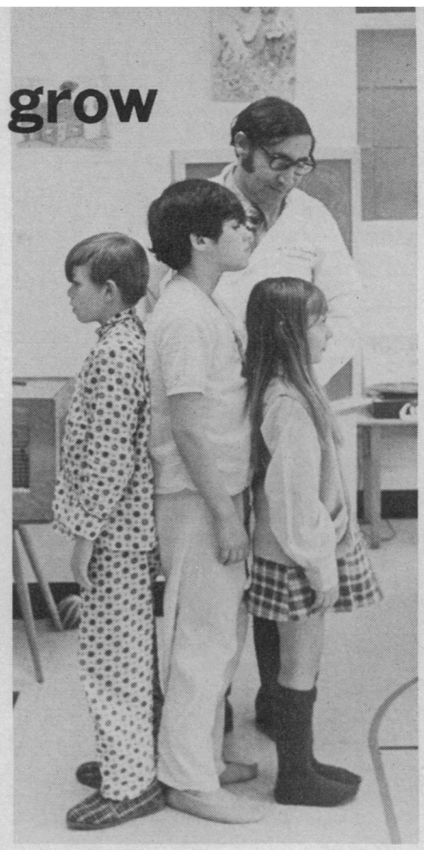
Univ. of Calif.

Grumbach: Look to hypothalamus.

What these researchers have done, essentially, is give tyrotropin-releasing factor (TRF), synthesized by Andrew Schally of the New Orleans Veterans Administration Hospital three years ago, to some 100 children diagnosed with growth problems secondary to growth-hormone deficiencies. Most of the children treated by all three groups of investigators responded to treatment with TRF. This indicates the cause of their thyroid deficiency was not in the thyroid gland or pituitary gland but in the hypothalamus. The culprit, in sum, was a deficiency of TRF.

Schally recently synthesized human growth hormone-releasing factor (GH-RF), as have some scientists at Merck, Sharp & Dohme. So the pediatric endocrinologists would like to obtain some of the synthetic GH-RF for similar studies in children with primarily growth-hormone related growth problems. They anticipate they will again find that a number of youngsters fail to grow not from a lack of growth hormone, but from a lack of its releasing factor. Schally cautions, though, that there are certain problems in clinical testing, and clinical application of GH-RF is some way off yet.

Schally is confident that the difficulties will be overcome, though, and when they are, the availability of a synthetic GH-RF will be a boon to clinical treatment. Thousands of children in the United States and Europe are estimated to suffer from growth difficulties related to growth hormone. Also, while children with thyroid-related growth deficiencies can be treated with synthetic thyroxin, if TRF and TSH are not available, growth-hormone deficiencies can be treated only with natural growth hormone. And there is a woeful shortage of it, says Salvatore Raiti, director of the National Pituitary Agency,



NPA

Raiti: Shortage of growth hormone.

the agency that parcels out the material to clinicians around the United States. "Some hundred pituitary glands obtained at autopsy are required to treat one child for growth hormone-related dwarfism," says Raiti. "Of the some 20,000 American boys and girls who are severly stunted because of GH deficiencies, only 515 received GH in 1971, and over 1,500 have been treated during the past 10 years."

Choh Hao Li of the University of California reported synthesis of human growth hormone in January 1971 (SN: 1/16/71, p. 41). But part of this sequence has been shown not to be entirely correct by Hugh D. Niall of the Massachusetts General Hospital. Raiti estimates it could well be a decade before human growth hormone is synthesized in large enough quantities to become commercially available. So he, like the TRF investigators, believes that synthetic GRF might be a more immediate answer to growth hormone-related dwarfism.

Hormone imbalances are not the only cause of growth failure in children. Hypoglycemia, or low blood sugar, is common in low weight infants. Tumors, trauma, diseases and genetic factors may be a cause. But, says Marvin Cornblath, a growth researcher and director of pediatrics at the University of Maryland Medical School, in hormone-related growth deficiency research, "The releasing factors are certainly the hottest area now." □