

Recognition of Children With Psychosocial Short Stature: A Spectrum of Presentation

The conclusion of Gohlke et al is that psychosocial short stature (PSS) should be considered in every patient with "idiopathic" growth hormone deficiency (GHD) or when growth hormone (GH) treatment is ineffective in a child with presumed GHD. Symptoms such as hyperphagia, abnormal eating habits, disturbed behavior, global developmental lag, enuresis, or encopresis should prompt consideration of PSS, especially when there is a possibility of associated sexual abuse, which is frequently present in patients with this symptom complex.

Forty of the 65 children studied were single family cases; however, 25 represented multiple cases within 12 families. In half of the families, the parents were divorced or separated. The educational and work background of the parents was usually in the lower and unskilled categories. Unemployment of fathers was significantly excessive.

Sex distribution was equal. A remarkable finding was that only 29% of full-term newborns had a birth weight >3,000 g. Twenty-one percent of all patients were premature (<37 weeks). Bone age was delayed by an average of 1.9 years. Body mass index was normal in all patients.

Fifty-four percent had eating problems, 42% behavioral problems, 26% encopresis, and 18% nocturnal enuresis; 12% urinated in inappropriate places or as an aggressive act. Many suffered physical abuse as well as psychological abuse. Bizarre eating habits, etc, were common in the physically abused. The authors noted that their data after assessment were very different from the data given in the physician referral letters; items such as hyperphagia, enuresis, and encopresis were not mentioned at all in referral letters but were often obtainable when inquiry was made.

Three case histories were presented that emphasized different important aspects of this syndrome. In case No.1, failure to respond to GH treatment as expected in a child with presumed GHD was present. GH insensitivity may be the presenting sign of PSS. In case No. 2, separation of the affected children with PSS from the abusing family did not result in catch-up growth. When this happens, an adverse environment should be looked for in the second home. In addition, some patients who have an adequate initial response to GH subsequently fail to grow at an

appropriate rate for a child with GHD under treatment; when this occurs, PSS should be suspected. The authors emphasize that not all PSS patients have classic findings of PSS. Case No. 3 demonstrated that abuse cannot always be proven, although several features of PSS may be present.

In the discussion, emphasis is made that a detailed psychological history should be taken for hyperphagia, polydipsia, and hoarding or scavenging food in all children suspected of having GHD.

Gohlke BC, et al. *J Pediatr Endocrinol Metab* 1998;11:509-517.

Editor's comment: *This syndrome is underdiagnosed in most pediatric clinics. These 65 children with PSS presented over a 7-year period to the pediatric endocrine clinic at Great Ormond Street. This syndrome is much more common than most pediatric endocrinologists believe, and the diagnosis often is not made because the physician does not think of the possibility. In retrospect, I myself have missed the diagnosis several times, although I am considered an authority in the field. Exemplary is my misdiagnosing GHD initially but finally diagnosing PSS in presumed GHD children who were not responding to GH satisfactorily.*

This article is abstracted because of its importance and because clinicians dealing with short stature need to consider the syndrome, know its variations, and suspect its presence, particularly in children of low normal or low birth weight and in short children who come from disrupted homes.

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Previous publications relating to PSS appearing in *Growth, Genetics, & Hormones* are listed immediately below.

Abuse or Psychosocial Dwarfism: An Update. 1985;1(4):1-4.

Physiological GH Secretion During the Recovery From PSS. A Case Report. 1989;5(2):14.

Psychosocial Growth Failure: A Positive Response to GH and Placebo. 1992;8(4):13.

Letter to and Letter from the Editor. 1993;4(1):9.

A New Stress-Related Syndrome of Growth Failure and Hyperphagia in Children Associated With Reversibility of GH Insufficiency. 1997;13(1):9-11.

A Prolactin-Releasing Peptide in the Brain

The investigators isolated a gene for a 7-transmembrane, G-protein-associated, orphan receptor, itself expressed primarily in the pituitary; they then transfected this receptor into Chinese hamster ovary cells and thereafter isolated 2 peptides from hypothalamic extracts that bound to this receptor and had specific prolactin-releasing activity. They identified the bovine, rat, and human genes coding for these peptides. The human gene encodes an 87 amino acid peptide with a 22 amino acid signal peptide, prolactin-releasing 31 amino acid (amino acids 23-53) and 20 amino acid (amino acids 34-53) peptides, and a carboxyl terminal 34 amino acid sequence. The carboxyl terminal glycine of both peptides must

be amidated for full bioactivity. The prolactin-releasing activity of the 31 amino peptide (PrRP31) was comparable to that of thyrotropin-releasing hormone. This report also demonstrated the importance of the arachidonic acid signal transduction pathway in prolactin secretion, as it was this signal that was employed to monitor the isolation and identification of these peptides.

Hinuma S, et al. *Nature* 1998;393:272-276.

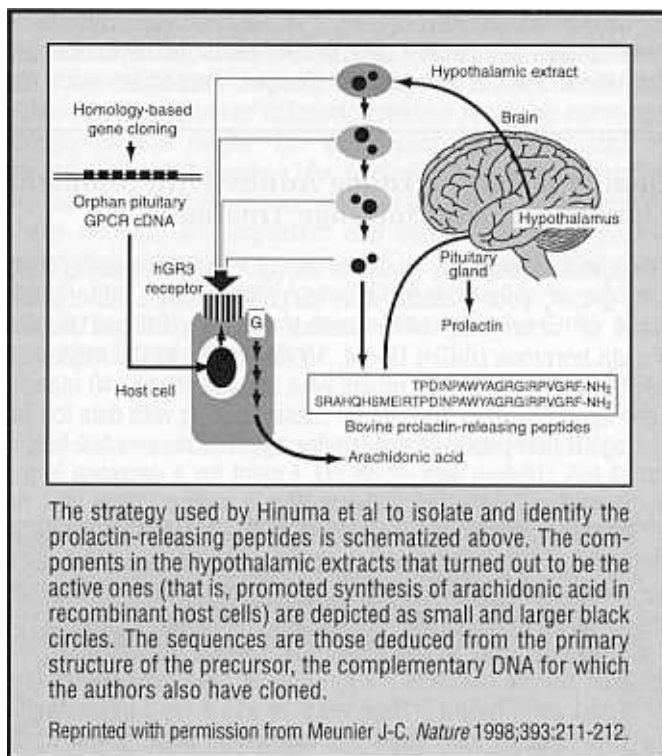
Editor's comment: *A specific prolactin-releasing substance to complement the prolactin inhibitory activity of dopamine has*

long been sought and now appears to have been isolated. The physiologic role of the prolactin-releasing peptides is unclear, and their diagnostic or therapeutic relevance remains to be assessed. The "reverse" process by which the prolactin-releasing peptides were found (ie, identification of an orphan receptor and then its ligands) indicates the revolution in biologic investigation in which we have the privilege of participating. Details concerning the lactotroph cell membrane receptor specific for the prolactin-releasing peptides are awaited. Meunier's comments and entire article (*Nature* 1998;393:211-212) are exceedingly worthwhile reading.

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GH Dependence and GH Withdrawal Syndrome in GH Treatment of Short Normal Children: Evidence From Growth and Cardiac Output

Lampit et al evaluated the efficacy of interrupted growth hormone (GH) therapy in prepubertal children with idiopathic short stature (ISS). Their protocol was to treat normal short children for a period of 3 years or until they reached the 25th percentile and then to discontinue therapy at a young age (no more than 9 years of age) and follow them until final height. The criteria for ISS were height <-2 SD, growth rate more than -1 SDS, bone age $<75\%$ of chronologic age, and serum GH concentration following arginine stimulation of >10 $\mu\text{g/L}$. Thirty-four children were studied, 12 of whom served as a control group. In addition to measuring the children, Doppler echocardiographic evaluation was performed before recombinant human GH (rhGH) therapy, yearly for 2 years during therapy, and at 6 and 12 months after the cessation of therapy.

The children receiving rhGH were treated until their height reached the 25th percentile but for no longer than 3 years, even if they had not reached this percentile. Nineteen of the children completed 3 years of rhGH therapy (0.9 mg/m^2 daily). During the first year of treatment, the growth velocity accelerated as expected. After withdrawal of rhGH, growth decelerated in every child over a 6-month period to a velocity that was significantly lower than pretreatment values. The growth velocity recovered to pretreatment values by the fourth semiannual measurement. Height SDS also increased in the treatment group and then declined somewhat in the second year of therapy. The GH response to arginine was not significantly different after rhGH therapy. Insulin-like growth factor 1 (IGF-1) and IGF-binding protein 3 (IGFBP-3) remained unchanged throughout the

study. However, systolic and diastolic parameters fell significantly during the initial 6 months of rhGH withdrawal and remained low for 12 months. Aortic cardiac output also fell significantly during the initial 6 months of rhGH withdrawal. No child had any symptoms referable to these cardiac changes.

The authors state that these data suggest that it may be feasible to interrupt rhGH prior to puberty in order to achieve an improved final height, but they will not know this for certain until the patients reach their final height. More interestingly, their report suggests that rhGH treatment is associated with the development of a physical adaptation to continuous high levels of GH. The rhGH withdrawal symptoms were not induced by alterations of serum GH or IGF-1.

Lampit M, et al. *Eur J Endocrinol* 1998;138:401-407.

Editor's comment: This is a fascinating report. It has become more and more apparent that adults with GH deficiency (GHD) have significant improvement in cardiac function when they are restarted and maintained on replacement therapy. It would appear that the administration of rhGH to children who do not manifest GHD induces a dependency on rhGH for cardiac function.

Indeed, when rhGH is interrupted there is a significant reduction in cardiac output. Although the authors state that there have been no clinical symptoms associated with the cardiac findings, the effect of either longer periods of rhGH administration or longer