

Binding Protein for Human Growth Hormone: Effects of Age and Weight

The authors studied the age-related changes in serum levels of high-affinity growth hormone-binding protein (GHBP) measured by gel chromatography on a long (100 cm) column of Sephacryl S200. This GHBP is considered to be identical to the extracellular portion of the hepatic receptor to growth hormone (GH). The method measures the 85-kd complex containing the GHBP, after addition of ^{125}I -labeled human GH of the 22-kd type in the serum to be studied. The results are expressed as the percentage of radioactivity eluting in the 80- to 90-kd range.

Sera from 250 normal infants and children were studied. GHBP was very low in cord sera, with an average of $3.3\% \pm 0.7\%$, and stayed near this level up to age 2 months. Then it sharply increased during infancy and reached $12.7\% \pm 3.9\%$ at 18 to 24 months of age. Further increase during childhood was slower, with the mean level after age 18 years attaining $19.7\% \pm 7.1\%$, and a wide range of individual values between 7% and 40% in children ages 7 to 18 years, with no obvious change at puberty. There was no difference between females and males at any age.

Correlation with age was significantly positive in the younger children ($r=0.31$, $P<0.005$) but below the level of significance in the older group ($r=0.15$). Correlations with height and weight were calculated. Only 2 significant correlations were found: a moderately positive correlation with weight expressed as standard deviations (SD) for age in the patients aged at least 2 years ($r=0.42$, $P<0.0001$), and a weak negative correlation with height SD for age in older children ($r=-0.17$, $P<0.025$). Partial correlation analysis showed no change of the correlation with weight when height was excluded, and a small change of the negative correlation with height when weight was excluded ($r=0.22$).

From these data, the authors point out that nutrition affects GHBP levels. The high serum GHBP found in most overweight children is considered as likely to reflect an increased number of peripheral GH receptors. This could reflect the usually low serum GH concentrations in obesity, contrasting with normal levels of insulin-like growth factor 1 (IGF-1) and normal or sometimes increased growth velocity. The authors comment on other aspects of their results, and compare their data with those previously reported by other authors.

Holl RW, Snehotta R, Siegler B, et al. *Horm Res* 1991;35:190-197.

Editor's comment: Among many studies of the main serum GHBP, this one seems of special value since it involves a great number of normal individuals from birth to adulthood, uses a most reliable technique, and calculates partial correlations in order to exclude the "pseudocorrelations" resulting from the physiologic relationships between age, height, and weight during childhood and adolescence. Not only the positive correlation with weight and probable correlation with nutritional status but also the negative correlation with the SD of height are reported. The study in newborns and infants suggests to the authors a relationship between GHBP, probably GH receptors, and the developmental switch from more or less

GH-independent intrauterine growth regulations to GH-dependent postnatal growth mechanisms. The data appear to be a valuable contribution to the presently poor insight we have on early postnatal changes in the regulation of longitudinal growth.

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2nd Editor's comment: Dr. Paul Martha, Jr, and colleagues recently presented a paper at the American Pediatric Society/Society of Pediatric Research (APS/SPR) meetings that supplements the data reported by Holl et al. For the purpose of broadening the perspectives regarding GHBP for our readers, the abstract by Martha et al is reprinted here from the program of the APS/SPR meeting.

A LONGITUDINAL ASSESSMENT OF SERUM GROWTH HORMONE-BINDING PROTEIN IN NORMAL BOYS DURING PUBERTY

Recent studies suggest the high-affinity serum GHBP may serve an important role in regulating normal body growth in humans. Therefore, we evaluated the relationships among GHBP, linear growth, and GH secretion over time in normally growing boys ($n=11$). On 154 occasions over 4.0 to 5.1 years, a physical exam, height and weight measurement, 24-hour GH study, and serum GHBP measurement were performed. GHBP levels varied widely among the group and spanned a 12-fold range (40 to 504 pmol/L; coefficient of variation [CV] = 51%). However, individual subjects' values varied within much more narrow limits (intrasubject mean CV = 30%, mean range 3.1-fold, $P<0.05$). The individual subjects' overall mean GHBP correlated inversely with the overall mean 24-hour GH level ($r=-0.61$, $P<0.05$) and correlated directly with mean body mass index SD score ($r=0.69$, $P=0.018$). For individual subjects, GHBP did not correlate with growth velocity or age. GHBP levels (pmol/L) according to age (years) at the time of study were as follows:

Age	<11	11-11.9	12-12.9	13-13.9	14-14.9	15-15.9	16-16.9
GHBP	208±24	241±39	196±36	175±24	161±27	217±29	200±39

No statistical differences were detectable among groups, therefore these data indicate that although serum GHBP concentrations for each child fluctuate over time during puberty, they do so within relatively narrow limits more characteristic of the individual child than of the larger population. The maintenance over time of a positive correlation between GHBP to body mass index SD score and an inverse relationship to mean GH secretion level lends further support to the concept that these factors are intimately and inextricably interrelated to normal growth and development. The data do not support the existence of an increase in GHBP levels confined specifically to the period of active pubertal development.

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