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<th>Title</th>
<th>Estimating the genetic potential in stature [11]</th>
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<td>Karlberg, J; Luo, ZC</td>
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Estimating the genetic potential in stature

J Karlberg; Z C Luo

Archives of Disease in Childhood; Mar 2000; 82, 3; ProQuest Medical Library pg. 270

Dr. Morley and colleagues comment:

We apologise for misquoting Stevens’ paper: this was an editing error when we amalga-
mated two papers. The reference for the statement “Iron fortification of milk for-
uila has been shown to reduce the inci-
dence of iron deficiency anaemia” should have been: Moffatt ME, Longstaffe N, Rovent
J, Dureux C. Prevention of iron deficiency and psychomotor decline in high risk infants

The iron content of the three milks was also misquoted and should have been: cows’ milk 0.5 mg/litre; iron fortified formula 12 mg/litre; unfortified formula 0.9 mg/litre. This correction strengthens rather than weakens our conclusions.

Estimating the genetic potential in stature

Editor. Midparental height is an important measure in estimating a child’s target height—the potential in stature. Height reference values that allow for paren-
tal height are more appropriate for growth evaluation in paediatricians. We read with interest the recent paper by Wright and Cheetham on the strengths and limitations of parental heights as a predictor of attained height. The authors concluded that midparental height was a useful indicator of the expected height for children when their parents were of average stature but forbade-
ing when used to assess short children. We have recently reported the same findings based in 2402 Swedish children. We observed that the regression coefficient between midparental height and a child’s final height was approximately 0.6 in standard deviation scores for children aged 8 years of age in the paper by Wright and Cheetham.

We believe that the linear function of midparental height could be used to estimate a child’s target height with greater accuracy than either regression or corrected midparental height, which Wright and Cheetham implicitly used to rep-
resent a child’s target height. The meaning of midparental height is different for children with short, average, and tall parents. The parents’ heights not only reflect the par-
tents’ genotype in stature, but also mirrors the extrinsic influence on their parents during their own growth span. This provides a biologically meaningful explanation of the so-called “regression to the mean” pheno-
menon. For instance, the intrinsic genetic potential in stature of short parents is usually much greater than their measured heights; conversely, short parents, who usually grow considerably taller due to a better manifestation of the intrinsic growth potential.

We agree that short children attending pacificare clinics are usually shorter than their target height, whatever method is used for estimation. The height of parents is important for clinical evaluation of short children. A short child with tall parents is certainly more likely to have a pathological cause than a short child of short parents. It is not appropriate to consider midparental height itself as a simple measure of target height. Clearly, midparental height is not misleading for any child if its linear function is used for estimating a child’s target height—the genetic potential in stature.

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1 Wright CM, Cheetham TD. The strengths and limitations of parental heights as a predictor of attained height. BMJ 1996;313:627-30.

GFIBP-3 as a predictor of growth hormone deficiency

Editor. We read with interest the paper by Mitchell and colleagues and wish to add our own observations on this subject. In 1996, the Regional Endocrine Laboratory started to provide a service for the measurement of insulin-like growth factor binding protein (IGFBP-3) following early reports that this was a good marker of growth hormone secretion. We then undertook a retrospective audit of the measurement of serum insulin-like growth factor (IGF-I) and IGFBP-3 as predictive markers of growth hormone deficiency (GHD) in children undergoing growth hormone stimulation tests (glucose and insulin tolerance tests). Between October 1996 and January 1998, 93 children had simultaneous measurements of IGF-I and 76 children had measurements of IGFBP-3. We defined GHD as a peak growth hormone level of < 20 mU/litre and complete GHD as a peak < 10 mU/litre in response to a stimulation test. The results for IGF-I and IGFBP-3 were compared to reference ranges for age available to the laboratory and classified as low or normal. The reference range for IGF-I was constructed by the laboratory using their own assay and that for IGFBP-3 being supplied by the manufacturers of the kit (Nichols Institute, Santa Juan Capistrano, California, USA). We calculated their sensitivity and specificity as predictors of GHD using the usual cut off levels and the likelihood ratio—with that is, the likelihood that the result would be seen in someone with— as opposed to someone without GHD deficiency. Eight children had both a low IGF-I and IGFBP-3, which produced a sensitivity of 22.2% and specificity of 99.4%. The likelihood ratio ratio of 2.3 in predicting GHD. Therefore the combination of a low IGF-I and low IGFBP-3 would be highly suggestive of GHD, but a significant number of children with GHD will have normal values for either of these two markers.

This is consistent with the idea that a single measure of IGFBP-3 performed no better than IGF-1 as a marker of growth hormone secre-
tion despite previous claims. Neither marker had a high likelihood ratio and would therefore not be good as a single predictive test. Although we realise that some of the normal IGFBP-3 results could have been attributed from the presence of IGFBP-3 protease activity interfering with the assay in children with radiometric induced GHD this is not likely to alter our findings significantly.

Thus we agree with Mitchell et al and other authors that IGFBP-3 measurements are not good predictive markers of growth hormone secretion and do not replace the need for careful clinical evaluation and growth hor-
mone stimulation tests in short, slowly growing children.

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Letters, Book reviews, Westminster briefing

Table 1: Sensitivity and specificity of IGF-I and IGFBP-3 for predicting growth hormone (GH) deficiency

<table>
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<tr>
<th>IGF-I</th>
<th>IGFBP-3</th>
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<tr>
<td>Sensitivity</td>
<td>57.5%</td>
</tr>
<tr>
<td>Specificity</td>
<td>76.3%</td>
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<tr>
<td>Likelihood ratio</td>
<td>1.85</td>
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IGF-1

Sensitivity: 57.5%
Specificity: 76.3%
Likelihood ratio: 1.85

IGFBP-3

Sensitivity: 26.3%
Specificity: 76.3%
Likelihood ratio: 1.5