

"Although epidemiologic studies have suggested that maternal and paternal passive smoke exposure increases cancer risk in children, the Finette study is the first demonstration of smoking-induced genetic damage in utero. It is noteworthy that a recent study by Hecht and colleagues (presented in August at the American Chemical Society meeting) found that urine from 19 of 31 neonates born to mothers that smoked during pregnancy contained metabolites of NNK (4-methylnitrosamino-1-(3-pyridyl)-1-butanone), a carcinogen found only in tobacco smoke. Metabolites were not found in urine samples from any infants born to non-smoking mothers.

Given the small sample size of the Finette study, additional investigations of the transplacental effects of passive smoke in newborns are required. These studies should include analysis of transplacental exposure of preterm infants and newborns to 'active' as well as passive cigarette smoke. (In adults a similar spectrum of p53 mutations in lung tumors from passive and active smokers has been found.) In addition, measurement of the 'rate' of tobacco consumption in actively smoking mothers as well as a more precise

quantitation of passive smoke exposure in non-smoking mothers should be obtained. V(D)J-recombinase-mediated HPRT deletions also occur spontaneously, thus the comparison of these changes in exposed and in unexposed groups is critical.

This study provides incontrovertible genetic evidence of the devastating effects of tobacco smoke particularly among the young, who suffer a greater risk from environmental toxicants, such as tobacco smoke, not only because of their smaller size but also because of their physiological immaturity. The time has come to proclaim an end to the exposure of preterm infants, newborns, and children of all ages to tobacco smoke."

My opinion is possibly a little more cautious than that of Sozzi et al. I agree the results must be confirmed. The causative nature of the deletions needs to be established before drawing firm conclusions. If the risk turns out to be true, the article provides an additional reason not to expose fetuses to tobacco smoke.

William A. Horton, MD

Monthly Measurements of IGF-1 and IGFBP-3 In Healthy Prepubertal Children: Characterization and Relationship With Growth: The 1-Year Growth Study

Gelander et al studied 65 prepubertal healthy children (38 boys and 27 girls) between the ages of 8 and 11 years (mean, 9.1 ± 0.85 years) with monthly determinations of insulin-like growth factor 1 (IGF-1) and IGF-binding protein 3 (IGFBP-3). In addition, measurements of height, weight, and lower leg length (using a knemometer) were recorded monthly by the same person between 0800 and 1000 hours. All biochemical analyses for each child were performed in the same assay. Additional data, including recent illness, food intake, and the daily mean temperature and number of hours of sunshine, also were recorded. Since concentrations of IGF-1 and IGFBP-3 are age dependent, the values were converted to SDS using prepubertal reference values.

Mean levels of IGF-1 in the children were significantly higher for the girls than for the boys ($P < 0.05$). By multiple stepwise regression analysis, height SDS, gender, and height velocity were significant parameters that explained 45% of the variance in IGF-1 SDS. The mean coefficient of variation for IGF-1 adjusted for age for each child was 13.9%, with a mean difference between samples taken at 3 monthly intervals from -0.4 to +0.3. These changes were correlated with changes in body mass index, but also were influenced negatively by illness and positively by outdoor temperature. Maximum changes over 3 months were related only to changes in temperature. The mean serum concentration of IGFBP-3 was comparable in boys and girls and correlated with the height SDS, weight SDS, height velocity, and weight gain. By using multiple regression analysis, 33% of the level of IGFBP-3 could be explained by gender, height SDS, and weight gain. The mean coefficient of variation for IGFBP-3 was 9.7%, and changes in IGFBP-3 were not related to recent illnesses and changes in body mass index. However, the changes in IGFBP-3 over 1 and 3 months correlated with season, evaluated as either changes in the outdoor temperature or hours of sunshine.

The authors noted that their data demonstrate considerable monthly variation in both IGF-1 and IGFBP-3 of such a magnitude that it exceeds the analytical precision of the measurements. This infor-

mation needs to be carefully considered when evaluating a single IGF-1 or IGFBP-3 concentration in a child who is not growing or whose growth is being evaluated. If repeated IGF-1 concentrations are to be used to evaluate treatment, the changes must exceed -0.4 to +0.4 SDS, whereas the changes for IGFBP-3 must exceed -0.6 to +0.3 to reflect a significant treatment effect. The data also demonstrate the importance of following more than 1 auxologic or biochemical variable. The seasonal variation in growth also has been demonstrated with these changes in IGF-1 and IGFBP-3.

Gelander L, et al. *Pediatr Res* 1999;45:377-383.

Editor's comment: This is an interesting, well-conducted study. The type of carefully collected information that Gelander and colleagues have provided can be of significant use in interpreting biochemical growth variables in short children, even those not receiving exogenous growth hormone. Knowing the coefficient of variation around the child's IGF-1 or IGFBP-3 level enhances the physician's ability to determine whether changes in these parameters are of biologic significance. Finally, it is of interest to have verification of the frequently observed finding that children grow up better when the weather is warmer.

William L. Clarke, MD

GROWTH, Genetics, & Hormones is published under an educational grant from Genentech, Inc. The information reflects the views of the editors and/or contributors and not necessarily those of the sponsor, grantor, or the publisher.

Published by:
405 Trimmer Road
PO Box 458
Califon, NJ 07830

Gardiner-Caldwell
SynerMed

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