

Late-Onset Adrenal Hyperplasia in Hirsutism

The investigators studied the incidence of late-onset adrenal hyperplasia as a cause of hirsutism, its association with the major histocompatibility complex, and its clinical expression. Their patient population included 400 women seen for hirsutism. Twenty-four (6%) were found to have late-onset adrenal hyperplasia.

Nonclassical, late-onset forms of adrenal hyperplasia, in which sexual ambiguity is not present at birth but virilization occurs during childhood or after puberty, have been described. However, these late forms are extremely variable in age at appearance, in degree of hyperandrogenism, and in association with abnormalities of the menstrual cycle. An elevated basal plasma 17-hydroxyprogesterone (17-OHP) level—especially its dramatic elevation after adrenocorticotrophic hormone (ACTH) stimulation—leads to the diagnosis of "partial" adrenal 21-hydroxylase deficiency.

All 400 women had ACTH stimulation tests in which 17-OHP and adrenal androgens were measured. In addition, the 24 identified as having late-onset adrenal hyperplasia due to 21-hydroxylase deficiency had human leukocyte antigen (HLA) typing since this form, like the classical form, is linked to the major histocompatibility complex. The families of these 24 patients underwent HLA typing as well.

Basal cortisol concentrations did not differ from normal values, but the increase after ACTH was significantly lower than normal. By contrast, 17-OHP levels were higher than normal and strikingly increased after ACTH. Plasma androstenedione was high in all but three patients and plasma testosterone levels, although often elevated, were normal in nine patients. Urinary excretion of 3 α -androstenediol was higher than normal in most cases.

HLA typing showed HLA B-14 in 75% of the index patients, but in only

11.7% of a control population. AW-33, B-14 was 40 times more common in the patients. The family members who had HLA typing were divided into three groups: HLA identical, one haplotype in common (heterozygotes), and no haplotypes in common (normal). As expected, the basal and post-ACTH 17-OHP concentrations in the heterozygotes were intermediate between those values in the normals and those in the homozygotes.

Kuttann F, Couillin P, Girard F, et al: *N Eng J Med* 1985;313:224.

Editor's comment—*This study represents the accumulation of large amounts of interpretable data on hirsute women and their families. The results indicate the utility of the ACTH stimulation test as part of the diagnostic evaluation of hirsute women and, by implication, in children of both sexes with premature adrenarche.*

More importantly, this study points to the remarkable variability in the expression of androgen excess in these women and their families. Hirsute women with similar androgen profiles can have totally dissimilar menstrual alterations. Siblings with HLA-identical haplotype may or may not have the same androgen profile or clinical presentation. The facts that both symptomatic and asymptomatic forms of late-onset adrenal hyperplasia occur in the same family, that they are biochemically identical and are linked with the same HLA antigens, and that they are strongly associated with HLA B-14, suggest that the genetic mutation in the symptomatic and asymptomatic forms is the same.

The consideration of late-onset adrenal hyperplasia should be mandatory not only in the hirsute adolescent and adult, but also in the child with premature adrenarche.

Use of Plasma SmC/IGF-1 Measurements to Monitor the Response to Nutritional Repletion in Malnourished Patients

The purpose of this study was to evaluate the usefulness and sensitivity of somatomedin C/insulin-like growth factor I (SmC/IGF-I) concentrations as an indication of short-term nutritional rehabilitation in malnourished patients. Six malnourished adults were studied during a period of ten to 16 days of parenteral or enteral nutritional therapy. These patients had a variety of gastrointestinal disorders that led to malnutrition. A statistically significant increase in plasma SmC/IGF-I concentrations was reported from a baseline (mean \pm SD) of 0.67 ± 0.15 U/ml to 0.93 ± 0.38 U/ml after two days of refeeding. By the 16th day of nutritional therapy, the SmC/IGF-I had fallen to 1.28 ± 0.49 U/ml from a peak of 1.80 ± 0.44 at day 10. All patients were in positive nitrogen balance throughout the duration of the study. In contrast, the levels of prealbumin, transferrin, and retinal-binding protein did not reflect significant changes.

In summary, the findings of this study suggest that plasma SmC/IGF-I is a more sensitive indicator of improved nutritional status during short-term nutritional rehabilitation in malnourished patients than other plasma proteins that are frequently used to assess nutritional status.

Clemmons DR, Underwood LE, Dickerson RN, et al: *Am J Clin Nutr* 1985;41:191.

Editor's comment—*This paper demonstrates the validity of SmC/IGF-I levels as an indicator of short-term nutritional status. This may, therefore, be useful in evaluating the response to treatment in various forms of nutritional dwarfism, as well as the compliance of the patients with dietary intervention.*