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THE MOST FREQUENT HUMAN AUTOSOMAL RECESSIVE DISEASE. P Speiser, B Dupont, P Rubinstein, A Piazza, A Kastelan, MI New, Cornell Univ Med Col, Memorial Sloan-Kettering Cancer Ctr, New York Blood Ctr, New York NY; Stanford Univ Med Ctr, Stanford CA; Tissue Typing Ctr, Zagreb, Yugoslavia

Nonclassical steroid 21-hydroxylase deficiency (nc21OHD) is an autosomal recessive disease which results in a phenotypically variable syndrome of postnatal hyperandrogenism. Its prevalence is unknown because basal serum 17-OHP levels are not sufficiently elevated for detection with the microfilter paper technique used in screening for classical 21-OHD. We therefore ascertained the frequency of the nc21OHD gene using ethnic group-specific HLA-B-nc21OHD associations in conjunction with ACTH testing in obligate heterozygote parents. Confirmation of this approach was obtained by the affected sib pair method of Thomson and Bodmer. The gene frequency for nc21OHD was highest in Ashkenazi Jews (19.1%) and was also high in Hispanics (13.6%), Yugoslavs (12.5%), and Italians (5.8%). In other Caucasians studied it was 0.1%. Disease frequencies were 1/27 for Ashkenazi Jews, 1/53 for Hispanics, 1/63 for Yugoslavs, 1/333 for Italians, and 1/1000 for other Caucasians. Carriers of the HLA-B14 marker had a 32-fold increased risk of nc21OHD compared to controls. Linkage disequilibrium betweeen HLA-B14 and nc21OHD was significant in Ashkenazi Jewish, Hispanic, and Italian patients, but not in Yugoslavs or other Caucasians.
Conclusion: It appears that nc21OHD is the most frequent autosomal recessive genetic disorder in man.

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Adrenal 11-Oxo-Androgens In Human Peripheral Plasma

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The adrenal androgens are quantitatively the most important steroid hormones, but their physiological role remains still somewhat obscure in man. Far less information is available about those adrenal androgens which carry a functional group at C-11. Therefore we established RIA systems to get some information about 11-oxo-testosterone (11-oxo-T) and 11-oxo-androstendione (11-oxo-A) in man. Highly specific antisera were raised in rabbits. [1,2-3H]-11-oxo-T and [1,2-3H]-11-oxo-A were syntnesized from [1,2-3H]-cortisone. The plasma levels (nM±SD) of 11-oxo-T and 11-oxo-A were measured in healthy male and female subjects (20-40 years of age) at 8a.m. and 11p.m. Table: Mean plasma level of 11-oxo-T and 11-oxo-A (nM±SD)

	Males (n=22)			Females (n=22)		
	8a.m.	11p.m.	p	8a.m.	11p.m.	p
11-oxo-T	2.04±0.63	0.96±0.33	<0.01	2.18±0.89	0.96±0.89	<0.01
11-oxo-A	2.37±0.56	0.87±0.35	<0.01	3.16±0.43	1.15±0.52	<0.01

During ACTH stimulation tests 11-oxo-A increased 1.3-fold ($p<0.01$), while 11-oxo-T decreased by 30% ($p<0.02$). Dexamethasone suppression tests resulted in a decrease of 83% (11-oxo-T) and 87% (11-oxo-A), respectively. HCG administration on 3 consecutive days did not influence plasma concentrations of the 2 steroids. Our data demonstrate that 11-oxo-T and 11-oxo-A are present in male and female subjects in considerable amounts. There was no significant sex difference and it seems to be most likely that these steroids are mainly secretory products of the adrenal gland.