Genetic Steroid Disorders: Chapter 3G. Genetic Deficiencies of Cytochrome P450c17 (CYP17A1): Combined 17-Hydroxylase/17,20-Lyase Deficiency and Isolated 17,20-Lyase Deficiency

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Steroid 17-hydroxylase 17,20-lyase (cytochrome P450c17, CYP17A1) occupies a critical position in the pathways of human steroidogenesis, regulating the classes of steroid hormones produced by cells of the adrenal glands and gonads. CYP17A1 catalyzes two major reactions: the 17-hydroxylase and 17,20-lyase reactions. Mutations that compromise all CYP17A1 activities cause combined 17-hydroxylase/17,20-lyase deficiency, which presents as hypertension, hypokalemia, and sexual infantilism. A few mutations selectively impair 17,20-lyase activity, and some mutations in cofactor proteins cytochrome P450-oxidoreductase and cytochrome b5 also selectively disrupt 17,20-lyase activity. This chapter reviews the genetics, clinical presentation, management, and history of these disorders.

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