
Adrenal Androgens in Humans and Nonhuman Primates: Production, Zonation and Regulation

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Abstract

The synthesis and secretion of large quantities of the adrenal androgens, dehydroepiandrosterone (DHEA) and its sulfoconjugate DHEA sulfate (DS), is a phenomenon that appears limited to humans and some non-human primates. Both hydroxylase and lyase activities of the enzyme 17 α -hydroxylase/17,20-lyase cytochrome P450 (P450c17) are necessary for DHEA production and are differentially regulated during adrenal development. Production of DHEA and DS occurs in the zona reticularis (ZR) of adults and the fetal zone of fetal primate adrenal glands, which is the primary substrate for maternal estrogen production during pregnancy. The onset of adrenal androgen production in childhood, referred to as adrenarche, corresponds with the establishment of the ZR: but the process is poorly understood, largely due to the lack of accessible animal models. Several nonhuman primates have been used to study adrenal function and remodeling, though none completely recapitulates human adrenarche, developmentally, functionally or temporally. This review will summarize the variations in adrenal androgen production and adrenal zonation in humans and nonhuman primates throughout life. It is hoped that recent studies demonstrating adrenarche in the rhesus will put in proper context the significance of adrenal zonation in nonhuman primates as valid models for human adrenal development and function.

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The mammalian adrenal cortex is remarkably zonal in its cellular organization and functional ability to secrete steroids. The major zones of the mature cortex, the outermost zona glomerulosa (ZG), and beneath it the zona fasciculata (ZF), secrete mineralocorticoids, and glucocorticoids, respectively. In addition, in humans and some nonhuman primates, the zona reticularis (ZR) located between the ZF and the medulla secretes androgens [1]. The secretion of adrenal androgens in primates is profoundly dynamic, reflecting the development of the ZR postnatally and also the functional capacity for androgen synthesis by the transient fetal zone (FZ) prenatally. In humans, dehydroepiandrosterone (DHEA) and its sulfoconjugate (DS) are the principal androgens secreted from the FZ and ZR, though these zones are distinctly different morphologically and in their appearance developmentally. This is reflected