

# Hormonal Effects on Respiration and Metabolism of Steroid Hormones

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There is a growing public awareness that sex hormones can have an impression on a spread of physiological processes. Yet, despite almost a century of research, we still don't have a transparent picture on the consequences of sex hormones on the regulation of breathing. Extensive information has gathered appearance that estrogen, progesterone and testosterone can impact respiratory capacity in creatures and people. Several disorders of breathing like obstructive apnea (OSA) and sudden infant death syndrome (SIDS) show clear sex differences in their prevalence, lending weight to the importance of sex hormones in respiratory control.

A number of hormones, including hypothalamic neuropeptides acting as neurotransmitters and neuromodulators within the CNS, are involved within the physiologic regulation of breathing and participate in adjustment of inhaling disease. Additionally to central effects, some hormones also control breathing at peripheral chemoreceptors or have local effects on the lungs and airways. Estrogen and progesterone seem to guard from sleep-disordered breathing, whereas testosterone may predispose thereto. Progesterone and thyroxine have for quite some time been known to animate breath. More recently, several hormones like corticotropin-releasing hormone and leptin are suggested to act as respiratory stimulants. Somatostatin, dopamine, and

neuropeptide Y have a depressing effect on breathing. Animal models and experimental human studies suggest that also many other hormones could also be involved in respiratory control.

Steroid hormones are synthesized primarily within the gonads, adrenal glands, and therefore the fetoplacental unit. Cholesterol, which is the common precursor of all steroid hormones, is first converted to pregnenolone, and therefore the steroidogenic pathway, then diverges towards the formation of sex hormones, glucocorticoids, or mineralocorticoids. Within the steroid hormone pathway, pregnenolone is first converted to progesterone, which is an intermediate for the synthesis of androgens and estrogens. Estrogens are synthesized from androgens by the formation of an aromatic A ring, and this reaction is catalyzed by the enzyme aromatase. Sex steroid hormones act via their receptors: estrogen via estrogen receptor (ER)  $\alpha$  or ER $\beta$ , progesterone via progesterone receptor (PR)-A or PR-B, and androgens via the androgen receptor (AR). Simplistically speaking, ligand-bound sex steroid receptors dimerize and bind to specific DNA response elements to modulate transcription. In recent years, newer concepts of sex steroid receptor signaling have emerged, including rapid cellular activation pathways that don't involve direct alteration of gene transcription. Importantly, all sex steroid receptors are shown to be expressed in lung tissue.

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