Deconstructing misconceptions: The relevance of androgens for human health

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Emily Warrender August 21, 2025

Alexandra Cara and Carol F. Elias from the University of Michigan Medical School provide insights into the critical role of androgens in human health, including their vital roles throughout various life stages

Androgens are a class of steroid hormones best known for their role as male sex hormones. They promote the development of male reproductive organs, shape secondary sex characteristics (i.e., male pattern facial hair, deeper voice), and maintain reproductive health. However, females also produce androgens, though their importance is often overlooked. While testosterone is the main androgen produced in the testes, androgens are also produced in the ovaries, adrenal glands, and adipose tissue in individuals with testes or ovaries, depending on life stage.

Androgens exert their effects by binding to androgen receptors (AR) or estrogen receptors (ERs) after conversion to estrogens via the enzyme aromatase. Upon hormone binding, AR or ERs canonically act in the genome as transcription factors, changing the expression of multiple genes, or non-canonically via rapid non-nuclear signalling, ultimately altering the individual's physiology.

Levels of circulating androgens vary greatly with age and reproductive status

One of the earliest role of androgens occurs during embryonic development. Before gonadal differentiation, embryos possess two undifferentiated duct systems that can develop into either male- or female-typical reproductive tracts.

If the SRY gene is present, it induces a pattern of gene expression that is necessary for testicular development. This phenomenon occurs early during embryonic development, and once testes are present, they begin releasing androgens. Embryonic androgens promote the formation of internal reproductive organs such as the seminal vesicles, vas deferens, and epididymis. Testosterone is then converted to dihydrotestosterone (DHT) via the enzyme 5-alpha-reductase, which is necessary for the development of male-typical external genitalia.

Between one and three months of age, individuals with testes experience a temporary surge in testosterone known as the 'mini puberty of infancy.' During this hormonally sensitive period, testosterone can promote changes in select androgen-responsive brain nuclei. Afterwards, testosterone falls to very low or undetectable levels until puberty, when it rises again to reach adult concentrations.

In individuals with ovaries, androgens also rise significantly during puberty, and their levels fluctuate throughout the menstrual cycle, peaking during the mid-follicular and luteal phases. Of interest is the contribution of adrenal androgens to the total circulating pool of androgens in both pre- and post-menopausal individuals.

Adequate androgen levels are essential for maintaining overall health

In people with testes, low androgen levels (hypoandrogenism) caused by androgen deficiency, insufficiency, or deprivation (such as during prostate cancer treatment) lead to reduced sperm production and infertility, loss or lack of development of secondary sex characteristics, and sexual dysfunction.

Endogenous (naturally occurring) androgen excess in people with testes is rare. When it does occur, it is usually due to adrenal or testicular tumors or congenital adrenal hyperplasia. Symptoms may include early puberty, increased muscle mass, short stature, and infertility. Androgen excess can also result from misuse of anabolic steroids or testosterone prescriptions. Some people use high doses of testosterone to build muscle, boost red blood cell production, or gain advantage in sports competition. However, long-term exposure to excess androgens can suppress sperm production, leading to infertility, and may also increase the risk of cardiovascular disease, liver damage, and prostate cancer.

In people with ovaries, androgen levels are much lower than in people with testes, but lower than the physiological range can negatively affect fertility and sexual health. It also decreases bone density, potentially leading to osteoporosis or increased fracture risk. Causes of androgen deficiency can include aging (menopause), primary or secondary hypogonadism, adrenal insufficiency, use of oral contraceptives, premature ovarian insufficiency, or surgical removal of the ovaries. Hypoandrogenism in females has an important, albeit overlooked, impact on mental health. Depression, low energy, fatigue, decreased sense of wellbeing, and anhedonia are a few examples.

Conversely, elevated androgens in females have profound effects on reproductive health. It may be caused by adrenal or ovarian tumors, Cushing’s syndrome, adrenal hyperplasia, or certain medications. Symptoms of high androgen levels are excess body and facial hair growth (hirsutism), male- pattern of hair loss, increased acne, irregular or absent ovulation, subfertility or infertility, insulin resistance, abdominal adiposity, increased risk of type 2 diabetes, abnormal cholesterol levels, higher risk of cardiovascular diseases, depression, and anxiety. Some of these symptoms are grouped in what is called polycystic ovary syndrome (PCOS), prevalent in 10-20% of people with ovaries at reproductive age.

Androgens have important effects on energy balance and body composition through sex-specific actions on a variety of metabolic tissues. Experimental animal models with a loss-of-function mutation in AR develop obesity later in life due to decreased energy expenditure and reduced thermogenesis, insulin resistance, impaired

glucose tolerance, and accumulation of triglycerides in skeletal muscle and liver. Similar phenotypes are seen in males with hypoandrogenism, including increased adiposity, decreased muscle mass, and decreased bone density.

Interestingly, androgen deficiency in males usually promotes metabolic dysfunction similarly to elevated androgens in females. Hyperandrogenism in individuals with ovaries can decrease insulin sensitivity in muscle, liver, and adipose tissue, diminish liver glycogen synthesis, promote visceral adiposity accrual by increasing adipocyte size and inhibiting lipolysis, and cause beta cell dysfunction via increased basal hypersecretion of insulin, inadequate or exaggerated glucose-induced insulin secretion. Overall, these impairments heighten the risk of type 2 diabetes and metabolic syndrome.

AR is highly expressed in multiple organs, including the brain

The role of androgens in brain development is relatively well understood, but the direct effect of androgens in the adult brain is only partially described. Studies from different laboratories, including ours, have shown that androgens play a relevant role in neuroendocrine reproductive function and behavior, anxiety and depression, neuroprotection, learning, and memory. However, the effects of specific neuronal populations and circuitry responsive to androgens have not been completely demonstrated, and the causes and mechanisms underlying disorders of androgen imbalance mediated by brain AR are poorly understood. This is particularly important for gender diverse and intersex individuals who seek gender- affirming hormone treatment (GAHT). The consequences and potential effects of hormone therapy on specific brain function are largely unknown. Encouraging sustained support for research on androgens in the brain is essential for the development of safer and more effective therapies as well as the wellbeing of countless individuals.

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