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**Non-genomic vascular actions of testosterone metabolites: Is there a beneficial role in the regulation of vascular tone and blood pressure?**

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The dogmatic view that testosterone (TES) exacerbates development of cardiovascular disease (CVD) in males is challenged by accumulating evidence from our labs. and others that TES and other androgens exert beneficial effects by inducing rapid vasorelaxation of vascular smooth muscle (VSM) via nongenomic mechanisms, independent of cytosolic androgen receptor (AR). TES appears to induce VSM relaxation *in vitro* by nitric oxide (NO)-induced activation of voltage-operated and Ca<sup>2+</sup>-activated K<sup>+</sup> channels and/or inactivation of L-type voltage operated Ca<sup>2+</sup> channels. Studies with TES analogs and metabolites reveal that androgen-induced vasodilation exhibits a structure-function relationship fundamentally different than the genomic actions on reproductive targets. Dihydro-metabolites of TES, such as 5b-dihydrotestosterone (5b-DHT) are more efficacious vasodilators than TES, but are devoid of androgenic activity. Since 5b-DHT vasodilates human umbilical artery, and is produced by the placenta, androgens may regulate fetoplacental blood flow and growth; thus a deficiency in 5b-DHT could contribute to development of preeclampsia. Recent studies from our labs. are the first to demonstrate that TES and 5b-DHT exert systemic hypotensive actions which involve direct vasodilatory actions on the peripheral vasculature, which, like isolated arteries, is structurally specific, AR-independent, and involves activation of neuronal NO synthase. Recent clinical studies reveal that androgen deficiency appears to exacerbate risk factors and pathologies associated with age and CVD. Thus, androgen replacement therapy with vasoselective androgens such as 5b-DHT, devoid of actions on the AR, may be an emerging therapeutic option for the treatment of preeclampsia in pregnant women and hypertension in aging men, and other vascular dysfunctions.

**Biography**

John N Stallone earned his PhD in medical physiology from University of Arizona College of Medicine and did Postdoctoral studies at University of Tennessee Health Sciences Center, Hypertension Training Program. He is Professor of Physiology & Pharmacology at Texas A&M University College of Veterinary Medicine. He has published nearly 50 papers in highly respected journals, is a Fellow of the American Physiological Society, and is a nationally and internationally recognized expert on the effects of the gonadal steroid hormones on the cardiovascular system in health and disease.

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