

Skinny**SCIENCE**®

MEDICAL NEWS

EDUCATIONAL SERIES

L-ARGININE M2®

Influence of L-Arginine^{M2}

on the Anabolic Action of Androgens

No. 22885
August 2008

This Series is published at
SkinyScienceEDU.com

Influence of L-Arginine^{M2} on the Anabolic Action of Androgens

In humans, androgens are responsible for growth, muscle development, and the induction of the male phenotype, including differentiation of extra-genital tissues.

Androgen actions are mediated through the androgen receptor (AR), which has been identified as a nuclear receptor. Androgen-AR complexes regulate transcription of the androgen-receptive genes. Various growth factors and hormone, such as growth hormone (GH) and insulin-like growth factors modulate the actions of androgens.

AMINO ACIDS & ANDROGENS

Dietary amino acids provide a significant role in growth-related gene regulation. Dietary arginine is the most significant amino acid involved in the actions of androgens and arginine is required for the anabolic actions of androgens in humans and some mammals, including testosterone.

Arginine is relevant to the anabolic action of testosterone, which is mediated by alterations in the Insulin-Like Growth Factor (IGF) system. Dietary (oral) arginine plays a major role in the anabolic action of testosterone, as arginine modulates androgen action, though not exclusively, through an influence on insulin-like-growth factors; IGFs and IGF-B's.

Conversely, dietary arginine deficiencies alter the expression of IGF-1, IGF-BP1 and IGF-1R in the kidney and IGF-BP1 in the liver.

Changes and deficiencies in the levels of plasma arginine affects the action of muscle and kidney testosterone, which acts independently of the mechanisms involved in the interaction between testosterone and arginine.

SUPPLEMENTAL L-ARGININE

In humans and mammals, oral ingestion of the amino acid L-arginine improves protein anabolism, leading to increased lean muscle mass and reduced adipose tissue fat.

Dietary L-arginine regulates the homeostasis of plasma arginine, including protein turnover and prevention of catabolism (muscle wasting). The primary regulator of arginine levels in adult humans remains dietary arginine intake. Low dietary intake of arginine results in decreased plasma and tissue arginine levels.

Dietary restriction of arginine influences the metabolic action of testosterone, which is the major determinant of gender dimorphism.

GROWTH HORMONE (GH)

Additionally, dietary arginine in therapeutic doses produces testosterone and other anabolic hormones via growth hormone (GH). Arginine-stimulated GH is the primary mechanism involving the production of testosterone and other anabolic hormones.

Therapeutic doses (10,000 mg +) of oral arginine can produce growth hormone (GH), if it is stimulated to cross the Blood-Brain-Barrier (BBB). This mechanism involves both the pituitary and hypothalamus glands and requires oral ingestion of 10 grams of L-Arginine, taken with a Blind Amino Acid Rider, at bedtime on an empty stomach.

GH is the most prominent anabolic hormone and both growth hormone and IGF insulin-like growth factors modulate androgen action, interacting with different co-activators or co-repressors. GH, IGF-factors, serum L-arginine, and BBB crossover of L-arginine, all translate to increased testosterone in humans. These specific mechanisms can act in tandem or individually.

When oral L-arginine acts as a secretagogue of growth hormone (GH) in humans by crossing the BBB during Delta sleep, the anabolic/androgen interactions take place in a metabolically coordinated fashion, increasing and balancing levels of GH, testosterone, and IGF-factors.

IGF, GH & TESTOSTERONE

L-arginine is a potent secretagogue of GH in humans, and both GH and IGF-1 enhance testosterone, and arginine modulates androgen actions via its influence on GH and IGF. IGF's and IGFBP's are also important regulators of testosterone action on skeletal muscle mass.

IGF-RELATED CANCERS

The actions of testosterone are commonly misaligned as culprits in the development of hormonal cancers.

It is now known that IGF-related cancers, such as prostate cancer, are encouraged by ingestion of red meat and high-purine foods, and *not* by regeneration of age-related decline in anabolic hormones, such as testosterone.

As age-related testosterone drops, prostate cancer risk *increases*, showing that testosterone is not the culprit in the development of prostate cancer, though reduction of testosterone is recommended once prostate cancer has been diagnosed.

IN CONCLUSION

Dietary L-arginine increases anabolic hormones in humans and lean muscle mass by producing GH, testosterone, and IGF factors. Further, L-arginine is capable of re-instating GH in humans following the hypothalamic/pituitary juncture cessation of GH production, caused by aging.

Oral dietary arginine supplementation may be used as a stand-alone treatment for low testosterone in humans, and as an adjunct to improve the pharmacologic action of synthetic analogs of testosterone used in clinical therapy.

MEDICAL NEWS EDUCATIONAL SERIES

L-ARGININE M2 ®

Influence of L-Arginine^{M2}

on the Anabolic Action of Androgens

No. 22885

August 2008

REFERENCES

Wu G & Meininger CJ 2002 Regulation of nitric oxide synthase by dietary factors. Annual Review of Nutrition 22 61–86.

Bhasin S, Woodhouse L & Store TW 2001 Proof of the effect of testosterone on skeletal muscle. Journal of Endocrinology 170 27–38.

Boger RH & Bode-Boger SM 2001 The clinical pharmacology of L -arginine. Annual Review of Pharmacology and Toxicology 41 79–99.

A Cremades¹, C Ruzafa, F Monserrat, A J López-Contreras and R Peñafiel. Journal of Endocrinology (2004) 183; Influence of dietary arginine on the anabolic effects of androgens

Appleton J 2002 Arginine: clinical potential of a semi-essential amino acid. Alternative Medicine Review 7 512–522.

Obled C, Papet I & Breuille D 2002 Metabolic bases of amino acid requirements in acute diseases. Current Opinion in Clinical Nutrition and Metabolic Care 5 189–197.

Bardin CW & Catterall JF 1981 Testosterone: a major determinant of extragenital sexual dimorphism. Science 211 1285–1294.

Castillo L, Ajami A, Branch S, Chapman TE, Yu YM, Burke JF & Young VR 1994 Plasma arginine kinetics in adult man: response to an arginine-free diet. Metabolism 43 114–122.

Barbul A 1986 Arginine: biochemistry, physiology and therapeutic implications. *Journal of Parenteral and Enteral Nutrition* **10** 227–238.

Berard MP, Zazzo JF, Condat P, Vasson MP & Cynober L 2000 Total parenteral nutrition enriched with arginine and glutamate generates glutamine and limits protein catabolism in surgical patients hospitalized in intensive care units. *Critical Care* **28** 3637–3644.

Field CJ, Johnson I & Pratt VC 2000 Glutamine and arginine: immunonutrients for improved health. *Medical Science in Sports and Exercise* **32** S377–S388.

Berger FG & Watson G 1989 Androgen-regulated gene expression. *Annual Reviews of Physiology* **51** 51–65.

Björntorp P 1996 Growth hormone, insulin growth factor I and lipid metabolism: interactions with sex steroids. *Hormone Research* **46** 188–191.

Brinkman AO, Blok LJ, de Ruiter PE, Doesberg P, Steketee K, Berrevoets CA & Trapman J 1999 Mechanisms of androgen receptor activation and function. *Journal of Steroid Biochemistry and Molecular Biology* **69** 307–313.

Cui XL, Iwasa M, Iwasa Y, Ohmori Y, Yamamoto A, Maeda H, Kume M, Ogoshi S, Yokoyama A, Sugawara T & Funada T 1999 Effects of dietary arginine supplementation 16 on protein turnover and tissue protein synthesis in scald-burn rats. *Nutrition* **15** 563–569.

Cynober L, Le Boucher J & Vasson MP 1995 Arginine metabolism in mammals. *Journal of Nutritional Biochemistry* **6** 402–413.

Dhanakoti SN, Brosnan JT, Herzberg GR & Brosnan ME 1990 Renal arginine synthesis: studies in vitro and in vivo. *American Journal of Physiology (Endocrinology and Metabolism)* **259** E437–E442.

Efron D & Barbul A 2000 Role of arginine in immunonutrition. *Journal of Gastroenterology* **35** (Suppl 12) 1220.

Fafournoux P, Bruhat A & Jousse C 2000 Amino acid regulation of gene expression. *Biochemical Journal* **351** 1–12.

Gross KL, Hartman WJ, Ronnenberg A & Prior RL 1991 Arginine-deficient diets alter plasma and tissues amino acids in young and aged rats. *Journal of Nutrition* **121** 1591–1599.

Hannan CJ, Friedl KE, Zold A, Kettler TM & Plymate SR 1991 Psychological and serum homovanillic acid changes in men administered androgenic steroids. *Psychoneuroendocrinology* **16** 335–343.

Hobbs CJ, Plymate SR, Rosen CJ & Adler RA 1993 Testosterone administration increases insulin-like growth factor-I levels in normal men. *Journal of Clinical Endocrinology and Metabolism* **77** 776–779.

Jansson JO, Eden S & Isakasson O 1985 Sexual dimorphism in the control of growth hormone secretion. *Endocrine Reviews* **6** 128–150.

Jousse C, Bruhat A, Ferrara M & Fafournoux P 1998 Physiological concentration of amino acids regulates insulin-like-growth-factor-binding protein 1 expression. *Biochemical Journal* **334** 147–153.

Kadi F, Bonnerud P, Eriksson A & Thornell LE 2000 The expression of androgen receptors in human neck and limb muscle: effects of training and self-administration of androgenic-anabolic steroids. *Histochemistry and Cellular Biology* **113** 25–29.

Kitiyakara C, Chabrashvili T, Jose P, Welch WJ & Wilcox CS 2001 Effects of dietary salt intake on plasma arginine. *American Journal of Physiology (Integrative and Comparative Physiology)* **280** R1069–R1075.

Kuhn CM 2002 Anabolic steroids. *Recent Progress in Hormone Research* **57** 411–434.

Morris SM Jr 2002 Regulation of enzymes of the urea cycle and arginine metabolism. *Annual Review of Nutrition* **22** 87–105.

Niermann GL & Watson GL 1999 Growth hormone and insulin-like growth factor-I enhance beta-glucuronidase gene activation by androgen in mouse kidney. *Molecular and Cellular Endocrinology* **153** 47–55.

Veldhuis JD & Iranmanesh A 1996 Physiological regulation of the human growth hormone (GH)-insulin-like-growth factor type I (IGF-I) axis: predominant impact of age, obesity, gonadal function and sleep. *Sleep* **19** (Suppl 10) S221–S224.

Pieper GM & Dondlinger LA 1997 Plasma and vascular tissue arginine are decreased in diabetes: acute arginine supplementation restores endothelium-dependent relaxation by augmenting cGMP production. *Journal of Pharmacology and Experimental Therapeutics* **283** 684–691.

Preiser JC, Berre PJ, Van Gossum A, Cynober L, Vray B, Carpentier Y & Vincent JL 2001 Metabolic effects of arginine addition to the enteral feeding of critically ill patients. *Journal of Parenteral and Enteral Nutrition* **25** 182–187.

Reyes AA, Karl IE & Klahr S 1994 Role of arginine in health and renal disease. *American Journal of Physiology (Renal Physiology)* **267** F331–F346.

Rosenfeld RG, Rosenbloom AL & Guevara-Aguirre J 1994 Growth hormone (GH) insensitivity due to primary GH receptor deficiency. *Endocrine Reviews* **15** 369–390.

Ruzafa C, Monserrat F, Cremades A & Peñafiel R 2003 Sexual dimorphism of arginine metabolism in mice: influence of dietary arginine. *Journal of Nutritional Biochemistry* **14** 333–341.

Sheffield-Moore M 2000 Androgens and the control of skeletal muscle protein synthesis. *Annals of Medicine* **32** 181–186.

Sheffield-Moore M & Urban RJ 2004 An overview of the endocrinology of skeletal muscle. *Trends in Endocrinology and Metabolism* **15** 110–115.

Shi HP, Efron DT, Most D, Tantry US & Barbul A 2000 Supplemental dietary arginine enhances wound healing in normal but not inducible nitric oxide synthase knockout mice. *Surgery* **128** 374–378.

Tincello DG, Saundres PTK, Hodgins MB, Simpson NB, Edwards CRW, Hargreave TB & Wu FCW 1997 Correlation of clinical, endocrine and molecular abnormalities with in vivo responses to high-dose testosterone in patients with partial androgen insensitivity syndrome. *Clinical Endocrinology* **46** 497–506.

Urban RJ, Bodenbun YH, Gilkison C, Foxworth J, Coggan AR, Wolfe RR & Ferrando A 1995 Testosterone administration to elderly men increases skeletal muscle strength and protein synthesis. *American Journal of Physiology (Endocrinology and Metabolism)* **269** E820–E826.

Verhoeven G & Swinnen JV 1999 Indirect mechanisms and cascades of androgen action. *Molecular and Cellular Endocrinology* **151** 205–212.

Visek WJ 1986 Arginine needs, physiological state and usual diets: a re-evaluation. *Journal of Nutrition* **116** 36–46.

Wu G & Morris SM Jr 1998 Arginine metabolism: nitric oxide and beyond. *Biochemical Journal* **336** 1–17.

Yu YM, Ryan CM, Burke JF, Tompkins RG & Young VR 1995 Relations among arginine, citrulline, ornithine, and leucine kinetics in adult burn patients. *American Journal of Clinical Nutrition* **62** 960–968.