# Contribution of endothelium-derived nitric oxide to exercise-induced vasodilation.

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BACKGROUND: Endothelium-derived nitric oxide is an important modulator of resting vascular tone in animals and humans. However, the contribution of nitric oxide to exercise-induced vasodilation is unknown. METHODS AND RESULTS: The effect of NG-monomethyl-L-arginine (L-NMMA), an inhibitor of nitric oxide synthesis, on exercise-induced vasodilation was studied in 18 healthy subjects (mean +/- SD, 40 +/- 10 years; 10 women). Acetylcholine was used to test the efficacy of L-NMMA in inhibiting stimulation of nitric oxide synthesis and sodium nitroprusside to test the specificity of L-NMMA in inhibiting endothelium-dependent vasodilation. Intermittent handgrip exercise and infusions of acetylcholine and sodium nitroprusside were performed during intra-arterial infusion of 5% dextrose (control) and L-NMMA (4 to 16 mumol/min). Forearm blood flow was determined by strain-gauge plethysmography. Forearm oxygen extraction was measured from arterial and venous oxygen saturations. In a separate study, 10 subjects performed exercise during infusions of 5% dextrose, L-arginine (the substrate for nitric oxide production), and D-arginine (the stereoisomer that is not a substrate for nitric oxide production). L-NMMA reduced exercise blood flow by 7 +/- 13% (P = .04), increased exercise resistance by 18 +/- 20% (P = .02), and increased exercise oxygen extraction by 16 +/- 17% (P < .001). The degree of inhibition of acetylcholine-induced vasodilation with L-NMMA correlated positively with the degree of reduction in exercise blood flow (r = .55, P = .02). The highest dose of L-NMMA (16 mumol/min) produced the greatest effect; exercise blood flow was reduced by 11 +/- 14% (P = .03), and vascular resistance increased by 26 +/- 23% (P = .005). L-NMMA did not affect the forearm vasodilation produced by sodium nitroprusside. Exercise blood flow, resistance, and oxygen extraction were not significantly modified by infusions of either L- or D-arginine. **CONCLUSIONS: Inhibition of nitric oxide synthesis reduces exercise-induced vasodilation in the human forearm, indicating that nitric oxide plays a role in exercise-induced vasodilation. Increased availability of nitric oxide substrate does not enhance exercise-induced vasodilation in healthy subjects. These findings have important implications for disease states in which endothelium-derived nitric oxide production is impaired.**

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