A POSSIBLE ROLE FOR SUPEROXIDE OR PEROXYNITRITE IN THE NO-INDUCED CONSTRICTION OF AORTIC VASCULAR SMOOTH MUSCLE IN THE DOGFISH SHARK, *SQUALUS ACANTHIAS*.

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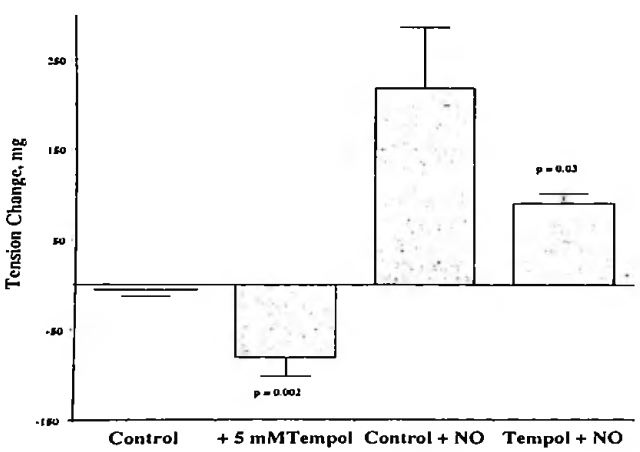
Contrary to vascular smooth muscle in mammals, the ventral aorta of the shark responds to L-arginine (NO precursor), sodium nitroprusside (NO donor), and NO itself by constricting rather than dilating (Evans, D.H. and Gunderson, M.P., Am. J. Physiol. 274: R1050-R1057, 1998). Recent evidence suggests that many of the cytotoxic effects of NO are secondary to the interaction of NO with superoxide ions (SO) and the generation of the very reactive peroxynitrite ion (PN; e.g., Beckman, J.S. and Koppenol, W.H., Am. J. Physiol. 271: C1424-1437, 1996). In fact, generation of these molecules is now thought to be the basis for a variety of diseases, including arthritis, atherosclerosis, diabetes, ischemia-reperfusion injury, and Alzheimer's disease. We hypothesized that SO or PN may be involved in the NO-induced constriction of vascular rings from the shark ventral aorta.

Isolated rings of the ventral aorta from *S. acanthias* were prepared as described previously (Evans and Gunderson, *Ibid*). To test our hypothesis, and to determine if SO is generated tonically from this tissue, we exposed uncontracted (ca. 500 mg tension), endothelium-intact rings to 5 mM Tempol (4-hydroxy-2,2,6,6-tetramethyl piperidinoxyl), a membrane-permeable superoxide dismutase mimetic (e.g., Nilsson, U.A. J. Biol. Chem. 264: 11131-11135, 1989) before and after NO was added to a nominal concentration of 8.4 μM. Rings were run as matched pairs (N = 10), with the control ring receiving the same volume of Tempol carrier (dist. water) and both rings receiving the same volume (200 ul) of saturated NO solution.



It is clear that inhibition of the production of SO (by the addition of Tempol) reduced the resting tension of the rings significantly (ca. 20%). Moreover, the response to NO was reduced by ca. 50%. These data suggest that vascular smooth muscle from the shark synthesizes and releases SO tonically, which constricts the vessel because PN is produced after reaction of the SO with NO. This hypothesis is supported by the subsequent reduction in the constrictory effect of NO, when only PN is being produced. Direct addition of PN will test this hypothesis. (Supported by NSF IBN-9604824 to DHE)