PROSTAGLANDIN E IS THE ENDOTHELIUM-DERIVED RELAXING FACTOR IN THE SHARK (*SQUALUS ACANTHIAS*) VENTRAL AORTA

David H. Evans and Mark Gunderson
Department of Zoology, University of Florida, Gainesville, FL 32611

In mammals, the vascular endothelium produces a variety of vasoactive molecules, including C-type natriuretic peptide, endothelin, various prostaglandins (PGs), and the gas nitric oxide (NO), which is considered to be the dominant endothelium-derived relaxing factor (EDRF; e.g., Vane, Philos. Trans. R. Soc. Lond [Biol] 343: 225-246, 1994; Inagami et al., Annu. Rev. Physiol. 57: 171-189, 1995). Our previous studies have suggested that the dominant EDRF in sharks is a prostaglandin, rather than NO, because neither L-Arg nor sodium nitroprusside (NO precursors) produce dilation in isolated rings of ventral aortic smooth muscle (VSM) from *Squalus acanthias* (Evans and Gunderson, Bull. MDIBL 34: 109, 1995), and the nitric oxide synthase inhibitor L-NAME does not inhibit the A23187-induced dilation of intact aortic VSM rings (Evans and Gunderson, Bull. MDIBL 35: 94, 1996). On the other hand, indomethacin (PG synthesis inhibitor) does inhibit this dilation, and both PGI_2 (prostacyclin) and PGE_1 dilate intact rings (Ibid). To test further the hypothesis that PGs are the dominant EDRF in shark aortic VSM, we tested the ability of two more NO donors, SIN (Jones et al., Am. J. Physiol. 266: L9-L16, 1994) and SNAP (Kowaluk and Fung, J. Pharm. Exp. Therap. 255: 1256-1264, 1990), to produce dilation and the ability of PGI_2 and PGE_1 to stimulate dilation in a concentration-dependent manner.

Rings of VSM from the ventral aorta of *S. acanthias* were prepared as described previously (e.g., Evans, J.Comp. Physiol. 162: 179-183, 1992; Evans and Gunderson, Op. Cit., 1996). SIN (3-morpholinosydnonimine hydrochloride) and SNAP (s-nitroso-n-acetylpenicillamine) were dissolved in distilled water and a 25% DMSO/75% distilled water solution, respectively, and were applied (at 10^{-4} M) to endothelium-free rings after pre-constriction with 10^{-4} M acetylcholine (ACh). In another series of experiments, PGI_2 and PGE_1 were dissolved in elasmobranch Ringer's and DMSO, respectively, and applied to endothelium-free rings in a concentration range of 10^{-9} to 3×10^{-6} M. Maximal final DMSO concentrations were 0.2% and <5% for the SNAP and PGE_1 experiments, respectively.

Application of 10^{-4} M ACh produced a contraction of 226 ± 18 mg (mean ± se, N = 6) above the 500 mg initial tension, demonstrating that the rings were responsive. Subsequent application of either SIN (10^{-4} M; Δ = +43 ± 10 mg, N=5) or SNAP (10^{-4} M; Δ = +20 ± 6 mg, N = 5) did not dilate the rings. Interestingly, PGI_2, the major dilatory PG in mammalian vessels (Armstrong et al., Circ. Res. 43 (Suppl. 1): 112-119, 1978), also did not produce dilation (Δ = +81 ± 127 mg; N = 3), in contrast to our experiments last year which demonstrated a small dilation (Δ = -95 ± 48 mg, N = 8) in response to 10^{-6} M PGI_2. PGE_1, on the other hand, did produce a distinct concentration-dependent dilation, with an EC_{50} of approximately 0.1 uM (N = 6) and a final tension change of -594 ± 80 mg (N = 6), even most substantial than that measured last year in respone to a single dose of 10^{-6} M PGI_2 (-389 ± 121 mg; N = 8). We conclude, therefore, that PGE, rather than PGI_2 is the dominant EDRF in the endothelium of the shark aortic VSM. (Supported by NSF IBN-9306997 and a Grant in Aid (9507715S) from the Maine Affiliate of the American Heart Association).