VASOACTIVE EFFECTS OF METAL IONS ON VENTRAL AORTIC RINGS FROM THE SHARK, SQUALUS ACANTHIAS

David H. Evans and Karl E. Weingarten
Department of Zoology, University of Florida, Gainesville,FL 32611

We have previously demonstrated that isolated ventral aortic rings from the dogfish (stripped of vascular endothelium) are responsive to the heavy metal cadmium, and have receptors for epinephrine, carbachol, adenosine, VIP, and atriopeptin (Evans & Weingarten, Bull. MDIBL 27, 84-85, 1987-88; Evans & Weingarten, this volume). The current study extends these studies to other metal species in an effort to determine if the Cd^{2+} toxicity was a generalized metal effect, or specific to that ion.

Isolated vascular rings were prepared from the ventral aorta of the dogfish shark as previously described (Evans & Weingarten, 1987-88; 1989, Ibid). Initial tension was set at 500 mg and maintained for approximately 30 minutes, until tension was stable. All metals were added cumulatively , as chloride salts, in aliquots to produce the desired concentration, accounting for slight volume changes. Rings were not pre-constricted or pre-dilated before addition of the metals.

Ni^{2+}, Sn^{2+}, and Hg^{2+} produced slight (10% or less) increases in the tension of the aortic ring of the dogfish shark, which reach significance at 10^{-5} M for Ni^{2+}, and only at 10^{-4} M for Sn^{2+} and Hg^{2+}. The degree of vasoconstriction is far below the 24% vasoconstriction produced by 10^{-5} M Cd^{2+} (Evans & Weingarten, this volume). Pb^{2+}, Cu^{2+}, and Co^{2+} produced slight, but insignificant, increases in tension; Zn^{2+} was without effect, even at 10^{-4} M.

It is therefore clear that the vasoactive effects of metal ions, and even heavy metals such as Hg^{2+}, Ni^{2+}, and Pb^{2+}, cannot be generalized. Our finding that Cd^{2+} is the most vasoactive metal is in accord with its possible role in producing hypertension (Kopp, J. In: Cadmium; E.C. Foulkes, Ed., Handbk. Exp. Pharmacol., Vol. 80, Springer Verlag, Berlin, pp. 195-280, 1986). A role for the other metals in the etiology of hypertension is even less clear. Ni^{2+} is apparently carcinogenic, produces contact dermatitis and has respiratory effects, but has not been implicated in hypertension (Goyer, R.A. In: Casarett and Doull's Toxicology, 3rd edition, Klaassen, C.D. et al., eds., Macmillan, New York, pp. 582-635, 1986). Excessive blood levels of Co^{2+}, like Cd^{2+}, has been found to be sometimes associated with increased blood pressure (Goyer, Ibid.), but Co^{2+}, again like Cd^{2+}, is a potent Ca-channel blocker, which should produce vasodilation rather than constriction (Dagher, G. et al., BBA 903, 218-228, 1987), and it has even been used to treat hypertension in humans (Schroeder, H.A. et al. J. Chronic Dis. 20, 869-890, 1967). Mercuric chloride has potent renal effects, and also apparently produces vasoconstriction in preglomerular vessels (Balazs, T. et al. In: Casarett and Doull's Toxicology, 3rd edition, Klaassen, C.D. et al., eds., Macmillan, New York, pp. 387-411, 1986). Pb^{2+} has also been found to produce "changes in arterial elasticity" (Balazs, Ibid.), but the association between plasma Pb^{2+} levels and hypertension is debatable (Parkinson, D.K, et al. Br. J. Ind. Med. 44, 744-748, 1987; Rabinowitz, M. et al. Hypertension 10, 447-451, 1987; Sharp, D.S. et al. Med. Toxicol. 2, 210-232, 1987). Inorganic Sn^{2+}, Cu^{2+} and Zn^{2+} have not been implicated in hypertension to date.

In summary, the efficacy of inorganic metals in producing constriction of the shark ventral aorta follows the order: $Cd^{2+} > Ni^{2+} > Hg^{2+} > Sn^{2+}$; Pb^{2+}, Cu^{2+}, Co^{2+}, and Zn^{2+} are without effect. This order of potency suggests that the role of Ni^{2+} in producing vascular hypertension should be examined in greater detail. (Supported by NSF DCB-8801572 to DHE and NIEHS 1 P50 ES 03828-03 the Center for Membrane Toxicity Studies).