Vasoactive Receptors in Abdominal Blood Vessels of the Dogfish Shark, *Squalus acanthias*

David H. Evans*
Mount Desert Island Biological Laboratory, Salsbury Cove, Maine 04672; Department of Zoology, University of Florida, Gainesville, Florida 32611

Accepted 9/11/00

ABSTRACT

Previous studies have demonstrated that the ventral aorta of the dogfish shark, *Squalus acanthias*, responds to a variety of cell-signaling agents. To investigate the generality of vasoactive receptors in the shark vasculature, in particular a conductance artery (anterior mesenteric) and vein (posterior intestinal), I measured the effect of acetylcholine, endothelin, nitric oxide, natriuretic peptides, and prostaglandins on tension in isolated rings from these vessels. Both vessels responded to these agents, and responses to receptor-specific ligands for endothelin and natriuretic peptide receptors suggest that B-type endothelin receptors are expressed in both vessels and that the artery expresses both A- and B-type natriuretic peptide receptors; however, the vein (like the ventral aorta) expresses only the B-type natriuretic peptide receptor. My data suggest that a suite of signaling systems is ubiquitous in both arteries and veins in at least this elasmobranch species. Their role in hemodynamics and osmoregulation (perfusion of gill and rectal gland) remains to be determined.

Introduction

In the past 10 yr, I have described receptors for a suite of signaling agents in the smooth muscle of the ventral aorta of the dogfish shark (*Squalus acanthias*), which can control the diameter of that vessel. These include receptors for adenosine (Evans 1992), natriuretic peptides (Evans et al. 1993), endothelin (Evans et al. 1996), and nitric oxide and prostacyclin (Evans and Gunderson 1998*b*), most of which are presumed to be secreted by endothelial cells lining the vessel. In addition, I have demonstrated that muscarinic receptors are also present in this tissue (Evans and Gunderson 1998*a*), although the source of the putative ligand (acetylcholine) is unknown because the ventral aorta in elasmobranchs apparently is not innervated (Donald 1998). I decided to extend these experiments to two abdominal vessels in the dogfish, the anterior mesenteric artery and posterior intestinal vein (Fig. 1) in order to test the hypothesis that receptors for vasoactive agents are found throughout the systemic vasculature, including conductance veins. The artery was chosen to confirm that a smaller conductance artery expresses these receptors and also because a parallel vessel, the posterior mesenteric artery, supplies the shark rectal gland, whose role in shark osmoregulation is well established (e.g., Karnaky 1998). However, little is known about perfusion limitation as a control of the rectal gland, despite the fact that an early study (Shuttleworth 1983) demonstrated that both catecholamines and vasoactive intestinal peptide can alter intragland perfusion pressures. The posterior intestinal vein was chosen to determine if a conductance vein can respond to vasoactive agents and, therefore, plays more than a passive role in elasmobranch hemodynamics. Fish veins contain very little smooth muscle and have been suggested, therefore, to function primarily as compliant vessels to return blood to the heart (Satchell 1992). Such a proposition seems intuitive, especially because fishes are generally horizontal and, because of the hydrostatic pressure of the surrounding water, do not suffer from potential blood pooling. On the other hand, an early study (Poder et al. 1991) demonstrated that catfish (*Amiurus melas*) posterior cardinal veins constricted (in a concentration-dependent manner) when mammalian endothelin was applied, and other studies (e.g., Olson et al. 1991, 1997, 2000; Zhang et al. 1998) have shown that veins in the rainbow trout (*Oncorhynchus mykiss*) respond to human endothelin (ET-1), natriuretic peptides, sodium nitroprusside (a NO donor), and catecholamines. These studies suggest a more active role for veins in hemodynamics, at least in the teleost fishes.

Material and Methods

Dogfish sharks (~2–5 kg) were captured and maintained in running seawater tanks at the Mount Desert Island Biological Laboratory as described previously (e.g., Evans and Gunderson 1998*b*). Experimental animals were killed by pithing through the snout (to destroy both the brain and spinal cord), either the anterior mesenteric artery (AMA) or posterior intestinal vein (PIV; Fig. 1) was removed, and cross-sectional rings (approximately 3 mm in length) were mounted in elasmobranch

* E-mail: dhefish@zoo.ufl.edu.

Physiological and Biochemical Zoology 74(1):120–126. 2001. 1522-2152/2001/7401-0062$03.00

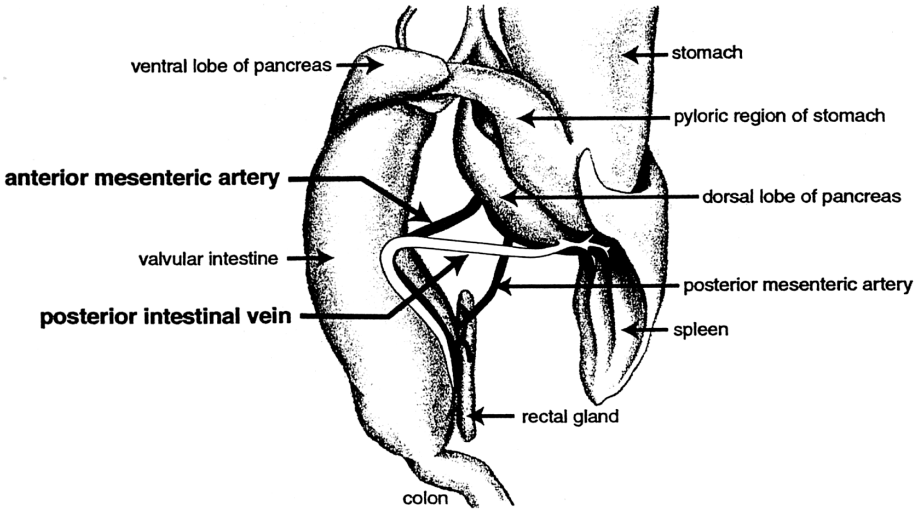

Figure 1. Drawing of the shark abdominal vessels and associated organs used in this study; redrawn from Gilbert (1982)

Ringer's solution in organ baths maintained at 12°C as described previously (Evans and Gunderson 1998*b*). Initial tensions were set at 200 mg (PIV) or 1000 mg (AMA) for 30–60 min because preliminary experiments determined that the respective rings were most responsive at those tensions. Tension was recorded by either Gould-Statham or WPI strain transducers connected to either a Gilson Duograph or a Biopac MP100WS system, using AcqKnowledge III software and a Macintosh Powerbook 140 computer. After the rings reached a stable tension, putative agonists were added cumulatively to the 10-mL experimental bath in increments totaling <4% of the initial volume. Each agonist was added only after a stable tension had been achieved subsequent to addition of the previous agonist. Solutions of acetylcholine (ACh; Sigma), ET-1 (American Peptide), sarafotoxin S6c (SRX S6c, an ET_B-specific agonist; American Peptide), sodium nitroprusside (SNP; Sigma), porcine C-type natriuretic peptide (pCNP; Peninsula Laboratories), eel atrial natriuretic peptide (eANP; Peninsula Laboratories), carbaprostacyclin (CPR; stable prostacyclin agonist), and PGE_1 (prostaglandin E_1; Cayman Chemicals) were made as described previously (Evans et al. 1996; Evans and Gunderson 1998*b*) and stored at −20°C until diluted. A saturated NO solution (distilled water) was prepared as described previously (Evans and Gunderson 1998*b*). Initial experiments consisted of the sequential addition of ACh (0.1 mM), ET-1 (0.1 μM), SNP (0.1 mM), NO (4.2 μM), CNP (0.1 μM), CPR (1 μM), and PGE_1 (1 μM) to a given ring. In subsequent experiments, to differentiate between ET_A and ET_B receptors, paired rings were exposed to 0.1 μM of either ET-1 or SRX S6c, followed by the addition of either 0.1 μM eANP or pCNP, to differentiate between A-type natriuretic peptide receptors (NPR-A) and B-type natriuretic peptide receptors (NPR-B).

All data are expressed as mean ± SE (N = number of fish). Tension changes were compared to 0 (tension before agonist addition) and accepted as significant when $P < 0.05$, using a one-sample t-test (Prism; GraphPad software, San Diego, Calif.).

Results

With the exception of the stable prostacyclin agonist carbaprostacyclin, all of the putative vasoactive agents produced significant changes in tension of the isolated anterior mesenteric arterial rings (Fig. 2). ACh was the most potent contractile agent (nearly 100% increase in tension); the apparent high variance of its effect was largely due to a single preparation that showed a 3,800 mg change in tension. ET-1 (45% increase in tension) was also constrictory, as were the NO donor SNP (3%) and NO itself (6%). Porcine CNP and PGE_1 produced relatively small (6%–8%) but significant dilations of the arterial rings. The ET_B-specific agonist SRX S6c was as constrictive as ET-1, and both pCNP and eANP dilated the arterial rings (Fig. 3).

The posterior intestinal vein responded to all agonists except NO with significant changes in tension (Fig. 4). In this vessel, the most significant constriction was produced by ET-1 (100% increase in tension), with smaller constrictions produced by ACh (25%), SNP (13%), and carbaprostacyclin (13%). Both pCNP and PGE_1 produced significant dilations (8%–10%). In this vessel, SRX S6c was as constrictive as ET-1, but only pCNP produced dilation; eANP produced no response (Fig. 5).

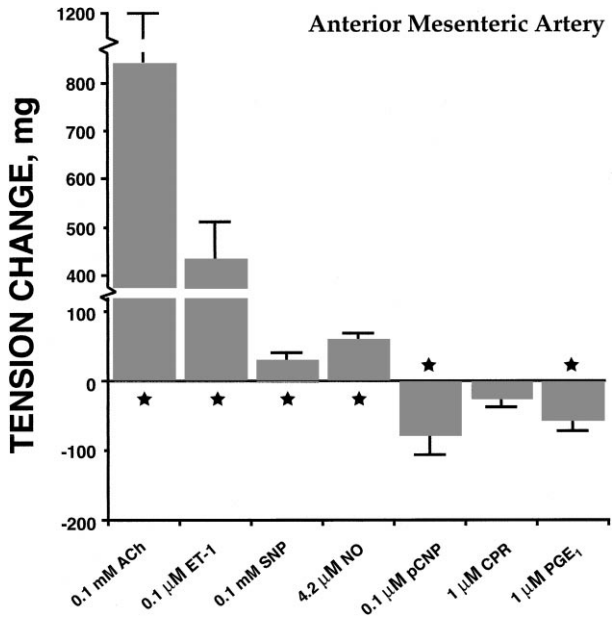

Figure 2. The effect of vasoactive agents on isolated rings of the anterior mesenteric artery of the spiny dogfish, *Squalus acanthias*. Abbreviations are as in the text. Mean ± SE, $N = 10$. Tension changes that were significantly different from 0 are marked with a star.

Discussion

It is clear that both abdominal vessels of *Squalus acanthias* respond to a variety of vasoactive substances, demonstrating that the vascular smooth muscle of a conductance artery and vein express the same array of receptors that have been described for the ventral aorta of this species (see "Introduction").

Cholinergic Receptors

Cholinergic receptors have been identified in the coronary artery of *Oncorhynchus mykiss* (Small et al. 1990; Farrell and Johansen 1995) as well as the ventral aorta, celiacomesenteric artery, and efferent branchial artery of the same species (Olson and Villa 1991; Miller and Vanhoutte 1992). The ventral aorta and celiacomesenteric artery of the Atlantic salmon (*Salmo salar*) also respond to acetylcholine (Sverdrup and Helle 1994; Sverdrup et al. 1994). Venous preparations have been examined from only one teleost species, *O. mykiss*. Olson and coworkers demonstrated that the anterior cardinal vein constricted when ACh was applied (Olson and Villa 1991), as did the posterior cardinal vein, intestinal vein, and ductus Cuvier (Conklin and Olson 1994). Interestingly, Olson et al. (2000) recently demonstrated that spontaneous contractions in the dorsal aorta from the yellow stingray (*Urolophus jamaicensis*) were inhibited by ACh, but no alteration in average tension was mentioned. These data suggest that elasmobranchs, as well as salmonid teleosts, express cholinergic receptors in systemic arteries and veins, but the generality of this finding will remain unclear until more taxa have been examined. It is interesting to note, however, that "there is no evidence for a cholinergic vasomotor innervation of the systemic vasculature of fishes" (Donald 1998, p. 416), so it is unclear where the ACh is coming from that may be activating these cholinergic receptors in vivo. However, overflow from cardiac nerves may be a source.

Endothelin Receptors

ET-1 (0.1 μM) was a much more effective constrictor than ACh (0.1 mM) in the vein of *S. acanthias* (Fig. 4), but in the artery, ACh produced twice the constriction (Fig. 2). However, since there was a 1,000-fold difference in concentration, it is apparent that ET-1 is much more vasoactive than ACh in both vessels. It should be noted that there were much more substantial ET/SRX-induced constrictions in the comparative experiment (Fig. 3) versus the cumulative experiment (Fig. 2) where the ring was preconstricted with ACh before the ET was added. Because the experiments were performed a year apart (but in the summer in both cases), one cannot rule out population effects, but it is easier to suppose that the ET response was blunted by the previous ACh exposure. They both produce the same second messengers, inositol triphosphate and Ca^{2+}, so maximal intracellular concentrations may have been reached before the full ET effect was possible. In the ventral aorta, both 0.1 mM ACh and 0.1 μM ET-1 produced near-maximal responses (Evans et al. 1996; Evans and Gunderson 1998*a*) of the same magnitude (D. H. Evans and M. P. Gunderson, unpublished data), which supports the hypothesis that ET-1 has a greater efficacy than

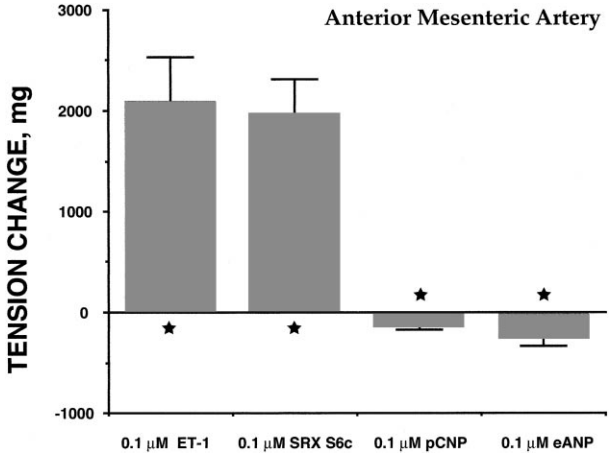

Figure 3. The effect of the addition of the ET_B-receptor agonist SRX S6c versus the ET_A/ET_B-receptor agonist ET on the AMA rings, followed by either pCNP (NPR-B agonist) versus eANP (NPR-A and NPR-B agonist); $N = 4$–6 in each case. Tension changes that were significantly different from 0 are marked with a star.

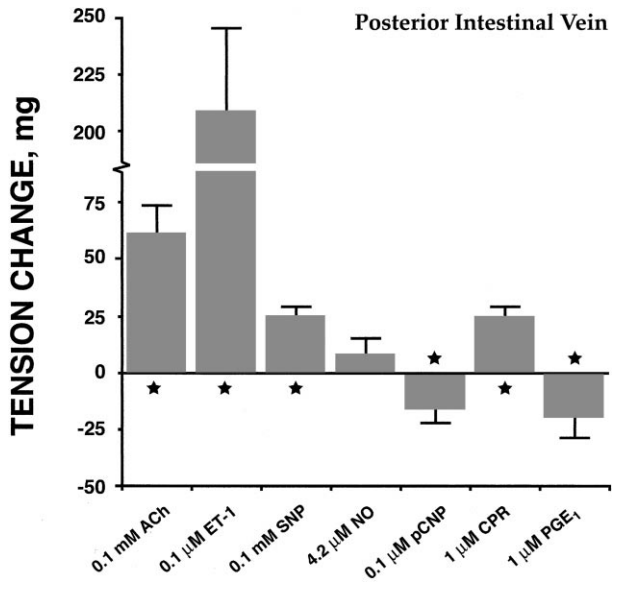

Figure 4. The effect of vasoactive agents on isolated rings of the posterior intestinal vein. $N = 8$. Tension changes that were significantly different from 0 are marked with a star.

ACh in the shark vasculature. In both the vein and artery (Fig. 3) as well as in the ventral aorta (Evans et al. 1996), the ET_B-specific agonist SRX S6c was as effective as ET-1 in constricting the vessels, so it appears that the vascular endothelin receptor in at least *S. acanthias* is of the ET_B type. In mammals, the receptor that mediates ET-1-induced constriction in arteries is usually ET_A (e.g., Sumner et al. 1992; Auguet et al. 1993; Buchan et al. 1994), although the ET_B receptor has been found to mediate constriction in mammalian veins and some arteries (e.g., Moreland et al. 1992; Seo et al. 1994; Teerlink et al. 1994; White et al. 1994). I have found that SRX S6c has little effect on the ventral aorta of at least one species of teleost (*Anguilla rostrata*, American eel; Evans and Harrie 2001), which suggests that the dominant endothelin receptor expressed in the vascular smooth muscle of teleosts and elasmobranchs may be different. Data on other teleosts and elasmobranchs as well as agnathans, such as a hagfish or lamprey, might allow more definitive statements about the evolution of endothelin receptors in the vascular smooth muscle of the early vertebrates.

Nitric Oxide Responses

The constrictory response to either NO itself (AMA) or the NO donor SNP (AMA and PIV) corroborates earlier data on the ventral aorta of *S. acanthias* (Evans and Gunderson 1998*b*). In mammals, NO plays a myriad of roles in cell signaling (e.g., Moncada et al. 1991; Griendling and Alexander 1996; Grisham et al. 1999), and its role as the endothelium-derived relaxing factor is well established (e.g., Furchgott and Zawadzki 1980; Godecke et al. 1998). Like in mammals, vascular smooth muscle in teleost fishes generally relaxes in response to NO, but only a very few number of species have been examined. One study (Miller and Vanhoutte 1992) found that NO did not dilate the isolated ventral aorta of *O. mykiss*, but three other studies found that SNP and nitroglycerine did dilate the isolated ventral aorta as well as the coronary, celiacomesenteric, and efferent branchial arteries and anterior cardinal vein of the same species (Small and Farell 1990; Small et al. 1990; Olson and Villa 1991). In addition, L-arginine (NO precursor) dilated the in situ, perfused trout coronary system, and two inhibitors of nitric oxide synthase (NOS) constricted this preparation (Mustafa et al. 1997). Further, injection of SNP into intact trout produced a significant fall in ventral and dorsal aortic blood pressure and gill resistance (McGeer and Eddy 1996; Olson et al. 1997). SNP produced a small decrease in the perfusion pressure in saline-perfused swim bladders from the European eel (*Anguilla anguilla*; Schwerte et al. 1999), and I found that both SNP and NO dilated the isolated ventral aorta of the congeneric American eel (*A. rostrata*; Evans and Harrie 2001). Finally, the acetylcholine-induced increase in cerebral blood flow in the crucian carp (*Carassius carassius*) was inhibited by NOS inhibitors (Hylland and Nilsson 1995), suggesting involvement of NO. It appears, therefore, that teleosts may express at least some components of the usual NO-mediated EDRF (endothelium-derived relaxing factor) axis, but its role in the control of vascular tension remains unclear and controversial (e.g., Olson and Villa 1991; Farrell and Johansen 1995; Mustafa et al. 1997).

There is no ready explanation for how NO constricts vessels in the spiny dogfish shark, although one might hypothesize that

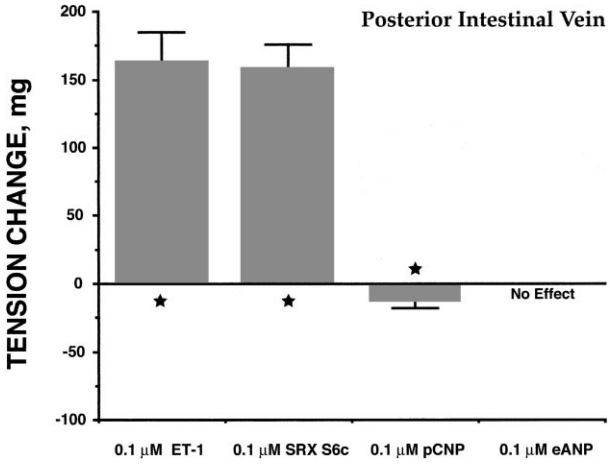

Figure 5. The effect of the addition of the ET_B-receptor agonist SRX S6c versus the ET_A/ET_B-receptor agonist ET on the PIV rings, followed by either pCNP (NPR-B agonist) versus eANP (NPR-A and NPR-B agonist); $N = 6–10$ in each case. Tension changes that were significantly different from 0 are marked with a star.

it is mediated via reaction with superoxide ions to produce the very reactive peroxynitrite (e.g., Beckman and Koppenol 1996). In fact, preliminary experiments have shown that preincubation of shark aortic rings with a superoxide dismutase mimetic (Tempol; e.g., Nilsson et al. 1989), which would therefore inhibit the production of both superoxide and peroxynitrite, not only dilated the nonstimulated vessel but also inhibited the NO-induced constriction by 60% (D. H. Evans and J. E. C. Hagen, unpublished data). In addition, the putative superoxide generator pyrogallol constricted isolated rings from the ventral aorta (D. H. Evans and J. Nowacki, unpublished data). Studies (Evans and Harrie 2001) have found that SNP and NO both produce a significant constriction of the isolated ventral aorta of the hagfish (*Myxine glutinosa*), and NO produces a biphasic response (slight initial constriction, larger subsequent dilation; both significant) in the ventral aorta of the lamprey (*Petromyzon marinus*). Both of these agnathan species preceded the elasmobranchs in vertebrate evolution, so it appears that the vascular function of the NO signaling system may be different in the early vertebrates.

Natriuretic Peptide Receptors

As in the ventral aorta of *S. acanthias* (Evans et al. 1993), porcine C-type natriuretic peptide dilated both the AMA and PIV (Figs. 2, 4), although the responses were relatively small. The efficacy of a CNP in these vessels suggests that natriuretic peptide type B (NPR-B), rather than type A (NPR-A), receptors are expressed in shark vessels. This proposition is supported by the cloning of dogfish CNP from cardiac extracts (Schofield et al. 1991) as well as the cloning of a NPR-B from the shark rectal gland (Aller et al. 1999). Eel ANP was without effect on the PIV (Fig. 5), but it dilated the AMA (Fig. 3), suggesting that NPR-A receptors also may be expressed in this vessel.

Prostanoid Receptors

Although both vessels responded to prostanoids, the characterization of the type of receptor involved is difficult. The AMA did not appear to respond to carbaprostacyclin, the stable prostacyclin agonist, but the PIV contracted when carbaprostacyclin was applied (Figs. 2, 4), suggesting the presence of the IP prostacyclin receptor (e.g., Narumiya et al. 1999) in at least the vein. However, the IP receptor mediates dilation, not constriction, in the ventral aorta of this species (Evans and Gunderson 1998*b*) as well as in mammalian blood vessels (via an increase in intracellular cAMP [cyclic AMP]; e.g., Narumiya et al. 1999). On the other hand, it has been demonstrated that IP ligands can also bind to both the EP_1 and EP_3 (prostaglandin E receptors) receptors, which mediate an increase in intracellular Ca^{2+} or decrease in intracellular cAMP, respectively, and thereby could produce constriction or inhibit dilation (Narumiya et al. 1999). Since PGE_1 dilated both vessels (as it does the ventral aorta of *S. acanthias*; Evans and Gunderson 1998*b*), one might suggest that an EP_2 or EP_4 receptor is present, both of which increase intracellular cAMP levels (Narumiya et al. 1999). On the other hand, PGE_1 also binds to the IP receptor (Narumiya et al. 1999), which would produce dilation. In short, my experiments have determined that prostanoid receptors are expressed in both vessels, but only measurements of intracellular second messengers, radio-ligand binding experiments, or molecular cloning and expression protocols would allow characterization of the specific prostanoid receptor(s) expressed in these vessels.

In summary, my data demonstrate for the first time that a variety of receptors for vasoactive signaling agents are expressed in an abdominal artery and vein of *S. acanthias*. Since this suite of receptors has been characterized in a major artery (ventral aorta) of this species as well (see "Introduction"), it appears that the entire conductance vasculature of the spiny dogfish shark expresses a complex array of vasomotor control systems. Their role in maintaining normotension, not to mention control of rectal gland perfusion (and thereby osmoregulation), remains to be determined.

Acknowledgments

Appreciation is expressed to Mark Gunderson and Joe Hagen, whose technical expertise made these experiments possible. This research was supported by National Science Foundation grant IBN9604824.

Literature Cited

Aller S.G., I.D. Lombardo, S. Bhanot, and J.N. Forrest, Jr. 1999. Cloning, characterization, and functional expression of a CNP receptor regulating CFTR in the shark rectal gland. Am J Physiol 276:C442–C449.

Auguet M., S. Delaflotte, P.E. Chabrier, and P. Braquet. 1993. Characterization of endothelin receptors mediating contraction and relaxation in rabbit saphenous artery and vein. Can J Physiol Pharmacol 71:818–823.

Beckman J.S. and W.H. Koppenol. 1996. Nitric oxide, superoxide, and peroxynitrite: the good, the bad, and ugly. Am J Physiol 271:C1424–C1437.

Buchan K.W., H. Magnusson, K.F. Rabe, M.J. Sumner, and I.S. Watts. 1994. Characterisation of the endothelin receptor mediating contraction of human pulmonary artery using BQ123 and Ro 46-2005. Eur J Pharmacol 260:221–225.

Conklin D.J. and K.R. Olson. 1994. Compliance and smooth muscle reactivity of rainbow trout (*Oncorhynchus mykiss*) vessels in vitro. J Comp Physiol B 163:657–663.

Donald J.A. 1998. Autonomic nervous system. Pp. 407–439 in D.H. Evans, ed. The Physiology of Fishes. CRC, Boca Raton, Fla.

Evans D.H. 1992. Evidence for the presence of A_1 and A_2 adenosine receptors in the ventral aorta of the dogfish shark, *Squalus acanthias*. J Comp Physiol B 162:179–183.

Evans D.H., M. Gunderson, and C. Cegelis. 1996. ET_B-type receptors mediate endothelin-stimulated contraction in the aortic vascular smooth muscle of the spiny dogfish shark, *Squalus acanthias*. J Comp Physiol 165:659–664.

Evans D.H. and M.P. Gunderson. 1998*a*. Functional characterization of a muscarinic receptor in the smooth muscle of the shark (*Squalus acanthias*) ventral aorta. Exp Biol Online 3:3.

———. 1998*b*. A prostaglandin, not NO, mediates endothelium-dependent dilation in ventral aorta of shark (*Squalus acanthias*). Am J Physiol 274:R1050–R1057.

Evans D.H. and A.C. Harrie. 2001. Vasoactivity of the ventral aorta of the American eel (*Anguilla rostrata*), Atlantic hagfish (*Myxine glutinosa*), and sea lamprey (*Petromyzon marinus*). J Exp Zool (in press).

Evans D.H., T. Toop, J. Donald, and J.N. Forrest, Jr. 1993. C-type natriuretic peptides are potent dilators of shark vascular smooth muscle. J Exp Zool 265:84–87.

Farrell A.P. and J.A. Johansen. 1995. Vasoactivity of the coronary artery of rainbow trout, steelhead trout, and dogfish: lack of support for nonprostanoid endothelium-derived relaxation factors. Can J Zool 73:1899–1911.

Furchgott R.F. and J.V. Zawadzki. 1980. The obligatory role of the endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. Nature 288:373–376.

Gilbert S.G. 1982. Pictoral Anatomy of the Dogfish. University of Washington Press, Seattle.

Godecke A., U.K. Decking, Z. Ding, J. Hirchenhain, H.J. Bidmon, S. Godecke, and J. Schrader. 1998. Coronary hemodynamics in endothelial NO synthase knockout mice. Circ Res 82:186–194.

Griendling K.K. and R.W. Alexander. 1996. Endothelial control of the cardiovascular system: recent advances. FASEB J 10: 283–292.

Grisham M.B., D. Jourd'Heuil, and D.A. Wink. 1999. Nitric oxide. I. Physiological chemistry of nitric oxide and its metabolites: implications in inflammation. Am J Physiol 276: G315–G321.

Hylland P. and G.E. Nilsson. 1995. Evidence that acetylcholine mediates increased cerebral blood flow velocity in crucian carp through a nitric oxide–dependent mechanism. J Cereb Blood Flow Metab 15:519–524.

Karnaky K.J., Jr. 1998. Osmotic and ionic regulation. Pp. 157–176 in D.H. Evans, ed. The Physiology of Fishes. CRC, Boca Raton, Fla.

McGeer J.C. and F.B. Eddy. 1996. Effects of sodium nitroprusside on blood circulation, acid-base balance, and ionic balance in rainbow trout: indications for nitric oxide induced vasodilation. Can J Zool 74:1211–1219.

Miller V.M. and P.M. Vanhoutte. 1992. Endothelium-dependent vascular responsiveness: evolutionary aspects. Pp. 3–20 in U.S. Ryan and G.M. Rubanyi, eds. Endothelial Regulation of Vascular Tone. Dekker, New York.

Moncada S., R.M.J. Palmer, and E.A. Higgs. 1991. Nitric oxide: physiology, pathophysiology, and pharmacology. Pharmacol Rev 43:109–142.

Moreland S., D.M. McMullen, C.L. Delaney, V.G. Lee, and J.T. Hunt. 1992. Venous smooth muscle contains vasoconstrictor ET_B-like receptors. Biochem Biophys Res Commun 184: 100–106.

Mustafa T., C. Agnisola, and J.K. Hansen. 1997. Evidence for NO-dependent vasodilation in the trout (*Oncorhynchus mykiss*) coronary system. J Comp Physiol 167:98–104.

Narumiya S., Y. Sugimoto, and F. Ushikubi. 1999. Prostanoid receptors: structures, properties, and functions. Physiol Rev 79:1193–1226.

Nilsson U.A., L.I. Olsson, G. Carlin, and A.C. Bylund-Fellenius. 1989. Inhibition of lipid peroxidation by spin labels: relationships between structure and function. J Biol Chem 264: 11131–11135.

Olson K.R., D.J. Conklin, A.P. Farrell, J.E. Keen, Y. Takei, L. Weaver, Jr., M.P. Smith, and Y.T. Zhang. 1997. Effects of natriuretic peptides and nitroprusside on venous function in trout. Am J Physiol 273:R527–R539.

Olson K.R., D.W. Duff, A.P. Farrell, J. Keen, M.D. Kellogg, D. Kullman, and J. Villa. 1991. Cardiovascular effects of endothelin in trout. Am J Physiol 260:H1214–H1223.

Olson K.R., M.E. Forster, P.G. Bushnell, and D.W. Duff. 2000. Spontaneous contractions in elasmobranch vessels in vitro. J Exp Zool 286:606–614.

Olson K.R. and J. Villa. 1991. Evidence against nonprostanoid endothelium-derived relaxing factor(s) in trout vessels. Am J Physiol 260:R925–R933.

Poder T.C., S.D. Silberberg, and D. Rampe. 1991. Contraction of reptile, amphibian, and fish blood vessels by endothelin-1. Can J Physiol Pharmacol 69:215–217.

Satchell G.H. 1992. The venous system. Pp. 141–183 in W.S. Hoar, D.J. Randall, and A.P. Farrell, eds. Fish Physiology. Vol. 12A. Academic Press, San Diego, Calif.

Schofield J.P., D.S. Jones, and J.N. Forrest, Jr. 1991. Identification of C-type natriuretic peptide in heart of spiny dogfish shark (*Squalus acanthias*). Am J Physiol 261:F734–F739.

Schwerte T., S. Holmgren, and B. Pelster. 1999. Vasodilation of swimbladder vessels in the European eel (*Anguilla anguilla*) induced by vasoactive intestinal polypeptide, nitric oxide, adenosine and protons. J Exp Biol 202:1005–1013.

Seo B., B.S. Oemar, R. Siebenmann, L. Von Segesser, and T.F. Lüscher. 1994. Both ET_A and ET_B receptors mediate contraction to endothelin-1 in human blood vessels. Circulation 89:1203–1208.

Shuttleworth T.J. 1983. Haemodynamic effects of secretory agents on the isolated elasmobranch rectal gland. J Exp Biol 103:193–204.

Small S.A. and A.P. Farell. 1990. Vascular reactivity of the coronary artery in steelhead trout (*Oncorhynchus mykiss*). Comp Biochem Physiol C 97:59–63.

Small S.A., C. MacDonald, and A.P. Farrell. 1990. Vascular reactivity of the coronary artery in rainbow trout (*Oncorhynchus mykiss*). Am J Physiol 258:R1402–R1410.

Sumner M.J., T.R. Cannon, J.W. Mundin, D.G. White, and I.S. Watts. 1992. Endothelin ET_A and ET_B receptors mediate vascular smooth muscle contraction. Br J Pharmacol 107: 858–860.

Sverdrup A. and K.B. Helle. 1994. Differential patterns of relaxation by atrial natriuretic peptide in major blood vessels of two distantly related teleosts. Regul Pept 53:89–101.

Sverdrup A., P.G. Kruger, and K.B. Helle. 1994. Role of the endothelium in regulation of vascular functions in two teleosts. Acta Physiol Scand 152:219–233.

Teerlink J.R., V. Breu, U. Sprecher, M. Clozel, and J.P. Clozel. 1994. Potent vasoconstriction mediated by endothelin ET_B receptors in canine coronary arteries. Circ Res 74:105–114.

White D.G., H. Garratt, J.W. Mundin, M.J. Sumner, P.J. Vallance, and I.S. Watts. 1994. Human saphenous vein contains both endothelin ET_A and ET_B contractile receptors. Eur J Pharmacol 257:307–310.

Zhang Y., L. Weaver, Jr., A. Ibeawuchi, and K.R. Olson. 1998. Catecholaminergic regulation of venous function in the rainbow trout. Am J Physiol 274:R1195–R1202.