other authors only demonstrated vasoconstriction to acetylcholine in cat cerebral arteries in vitro[17]. The vasodilation caused by acetylcholine (0.01–10 μM) was abolished by atropine (0.4 μM), a muscarinic receptor blocking agent. However, neurogenic vasodilation to TNS was unaffected by this concentration of atropine (Figure 3). The maximum dilation to TNS (25 Hz) was matched by acetylcholine at 0.01–0.05 μM.

Preliminary electronmicroscopic observations (LEE, SU and BEVAN, unpublished data) do not support the idea that the neuromuscular gap in cat cerebral arteries is too narrow to permit the entry of atropine to block the action of the transmitter, as has been proposed for the rat vas deferens[18]. There may, however, be atropine-resistant cholinergic receptors, such as have been described in bladder smooth muscle[19]. Neurogenic vasodilation (8 Hz), however, was not potentiated by physostigmine (7 μM) suggesting that neither the muscarinic nor the nicotinic effect of acetylcholine was involved.

It is of interest that in the presence of muscle tone, cat cerebral arteries invariably relaxed to nerve stimulation. Rabbit cerebral arteries, on the other hand, showed predominantly a contraction upon stimulation of the intramural nerves. Only occasionally was a small relaxation clearly apparent after adrenergic blockade (LEE, SU and BEVAN 1975)[20]. In the dog basilar artery neither contraction nor relaxation has been demonstrated[21], even though relaxation to potassium ions does occur[22]. These observations suggest that significant species differences occur not only in types of innervation but in their relative importance in one particular species.

Summary. The results presented provide strong support for the presence of vasodilator innervation in the cat cerebral arteries. The dilator innervation is neither adrenergic nor cholinergic and does not originate in the superior cervical ganglia. The nature of the vasodilator transmitter is unidentified. Such innervation, however, may be involved in the regulation of cerebral blood flow, especially in view of the capability of some cat cerebral vessels to develop intrinsic muscle tone.

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Altered Arterial Connective Tissue in Racing Greyhound Dogs

The greyhound breed of dog has been shown to have hemodynamic characteristics different from those of mongrel dogs[1–3]. The greyhound is under evaluation in our laboratories as a possible animal model for hypertension, since it has hemodynamic characteristics resembling those described[4] for human essential hypertension, i.e., high cardiac index (CI), low total peripheral resistance (TPR) in young greyhounds, changing to low CI, high TPR in older greyhounds[3].

In recent years vascular wall components have received attention as to their role in vascular disease from two aspects: 1. the role of wall changes in contributing to the pathological state, and 2. the response of wall components to mechanical and chemical stress of the disease state[5–9], such as increased pressure in hypertension. These two aspects are very difficult to separate.

We have been particularly concerned with collagen and elastin changes in vascular wall in pathological states. We have shown previously that renal hypertensive dog vessels tend to have a lower collagen to elastin ratio, a finding that would imply increased distensibility of the vessel[10]. We have also shown that human coronary arteries which are calcified exhibit a lower collagen to elastin ratio, indicating a response of the vessel to pathological change[11].

Because of the increased blood pressure and increased cardiac index of these greyhound dogs we thought that they would be a useful animal model for documenting changes in wall components in relation to hemodynamic mechanical stress. This report, accordingly, presents the findings as to vascular connective tissue in greyhound dogs as compared to that in normal mongrel dogs, previously reported[12].

Methods. 9 healthy greyhound dogs, obtained from racing kennels, were anesthetized with pentobarbital, 30 mg/kg, and studied for hemodynamic characteristics[1–3]. At the end of the hemodynamic studies specimens of the following arteries were quickly dissected: carotid, coronary, ascending aorta, abdominal aorta, renal proximal mesenteric, distal mesenteric, small mesenteric branches, and femoral. The vessels were dried and defatted as previously described[12]. Collagen and elastin were separated by the method of NEUMAN and LOGAN[13] and hydrolyzed overnight in 6 *N* HCl. Hydroxyproline was deter mined and collagen and elastin calculated as previously described[12].

Results. The composition of the vessels is given in the Table: % collagen, % elastin, and collagen/elastin ratio (C/E). It can be seen that in 3 vessels, the carotid artery, abdominal aorta, and femoral artery, the percent collagen

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Collagen and elastin composition and C/E ratio of greyhound and mongrel dogs[a]

Artery	Collagen (%)			Elastin (%)			C/E		
	Greyhound	Mongrel[a]	*P* Value	Greyhound	Mongrel[a]	*P* Value	Greyhound	Mongrel[a]	*P* Value
Carotid	43.0 ± 2.4	50.7 ± 2.1	< 0.025	29.0 ± 1.8	20.1 ± 1.0	< 0.0005	1.55 ± 0.16	2.55 ± 0.13	< 0.0005
Coronary	46.6 ± 2.0	47.9 ± 2.6	N.S.	19.3 ± 1.3	15.6 ± 0.7	< 0.025	2.49 ± 0.18	3.12 ± 0.21	< 0.025
Ascending aorta	18.2 ± 0.6	19.6 ± 1.2	N.S.	46.9 ± 1.2	41.1 ± 2.1	< 0.025	0.39 ± 0.02	0.49 ± 0.04	< 0.025
Abdominal aorta	41.6 ± 1.4	45.5 ± 1.7	< 0.05	33.2 ± 1.1	30.1 ± 1.7	N.S.	1.28 ± 0.06	1.58 ± 0.15	< 0.05
Renal	41.5 ± 1.3	42.6 ± 1.6	N.S.	22.3 ± 1.2	18.7 ± 1.8	N.S.	1.92 ± 0.14	2.46 ± 0.27	< 0.05
Mesenteric proximal	38.0 ± 1.2	38.1 ± 1.7	N.S.	27.5 ± 2.1	26.5 ± 1.7	N.S.	1.44 ± 0.12	1.51 ± 0.15	N.S.
Mesenteric distal	35.8 ± 1.1	37.4 ± 1.4	N.S.	22.1 ± 0.9	22.4 ± 1.5	N.S.	1.65 ± 0.08	1.72 ± 0.11	N.S.
Mesenteric branches	34.8 ± 0.8	36.1 ± 1.5	N.S.	22.4 ± 1.1	21.8 ± 0.9	N.S.	1.57 ± 0.08	1.69 ± 0.10	N.S.
Femoral	40.5 ± 1.3	44.5 ± 1.4	< 0.05	29.3 ± 1.3	24.5 ± 1.6	< 0.05	1.40 ± 0.06	1.89 ± 0.14	< 0.005

[a] Reference[12].

was significantly reduced. There was a tendency for the percent elastin to be increased, significantly in 4 of the vessels. The most striking results are seen, however, when the components are expressed as C/E. The C/E was significantly reduced in all but the mesenteric vessels. This decrease in C/E was especially marked in the carotid and femoral arteries. Even the mesenteric vessels showed a tendency to decreased C/E, but the differences were not statistically significant.

Discussion. The collagen to elastin ratio has been suggested as an index of distensibility of vessels[12], based on connective tissue composition, since collagen fibres are relatively stiff and elastin fibres quite extensible[14]. We have confirmed this correlation of C/E with stiffness in a series of puppies in which we measured both C/E and stiffness of the carotid artery[15]. It has been pointed out that in documenting changes in wall components, the total accumulation may differ from the percentage composition. Thus WOLINSKY[8] found little change in percentage composition in hypertensive rat aortic wall, but total amount was increased. The use of C/E, on the other hand, is a more relevant index as to stiffness, since it is the relative amounts of the two fibres which will influence passive stiffness[12]. The use of this ratio, also, eliminates weighing errors.

The current results and those of previous hemodynamic studies would suggest that the decreased C/E might represent a response of the vessel wall to increased pressure and/or flow, as compared with mongrel dogs. These dogs had blood pressures and cardiac indexes greater than mongrels. Since the greyhound has well developed skeletal muscles, the marked decrease in C/E in the femoral could represent an accommodation to the increased flow to these muscles. Likewise, the elevated heart weight to body weight ratios in greyhounds would necessitate high coronary flow. On the other hand, one could envision mesenteric vessel function in greyhounds as being not much different from that of mongrels.

The significance of these findings of differences in wall components in response to hemodynamic stress is that they suggest that one must consider both cause and effect in evaluating changes in wall components. Previous studies have indicated that vessels become stiffer with hypertension, and various wall components have been implicated[5]. The present results indicate that one should consider the factor of response of wall components as well as their etiological role. Ideally, studies on wall components in hypertension should include animals in the pre, early and late hypertensive stages, to help sort out the cause and effect.

In our studies the C/E in ascending aorta was significantly lower in greyhounds than mongrels, thus producing a more distensible vessel. Accordingly the pulse pressure associated with cardiac injection would be lower, and this would lower hydraulic work of heart associated with pulsatile pressure and flows. MILNOR[16] presented the concept that pulsatile work represented a penalty the heart must pay because it functions as an intermittent pump: thus, decreased C/E allows a smaller fraction of external work of the heart to be expended as pulsatile work and may allow for more efficient cardiac function. This lowered C/E in the ascending aorta, therefore, may represent an adaptive response of the vascular system beneficial to the animal.

Summary. Vascular collagen and elastin contents and the ratio of collagen/elastin (C/E) were studied in racing greyhound dogs, a breed which exhibits increased cardiac output. As compared to mongrel dogs, vascular C/E was lower, suggesting a greater distensibility of vessels as an adaptive response to hemodynamic stress.

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