Maturational Changes in the Pharmacological Characteristics and Actomyosin Content of Canine Arterial and Venous Tissue

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ABSTRACT. The purpose of this study was to compare the pharmacological characteristics and actomyosin content of arterial and venous tissue at different times during development. Rings of arteries (femoral, renal, carotid, pulmonary) and veins (saphenous, pulmonary, jugular) were obtained from 1 wk, 1 month, and adult dogs, mounted at their optimal length for force development and the contractile response to potassium chloride and phenylephrine determined. The strain at optimal length was less at all ages in pulmonary artery and pulmonary and jugular veins than in other vessels. All vessels exhibited an increase in maximum contractile response with development but the increase was greater for phenylephrine. In general, the magnitude of the maximum response of the jugular and pulmonary veins and pulmonary artery was less than other vessels at all ages. The sensitivity (half maximum response) either increased or was unchanged in arteries with development, while in the veins it either decreased or was unchanged. The relaxant effects of verapamil and isoproterenol were determined on potassium chloride contracted vessels. Arterial tissue was minimally responsive to isoproterenol at all ages while venous tissue either increased its responsiveness (saphenous, pulmonary) with development or remained highly responsive (jugular). Verapamil, unlike isoproterenol, was an effective relaxant of all vessels. The actomyosin content (mg/mm) of femoral and renal arteries and saphenous and jugular veins increased with development but this increase was accompanied by a parallel increase in total protein so that the ratio (actomyosin/total protein) was unchanged. In jugular veins from adult dogs this ratio was smaller than in arterial tissue. In general, it can be concluded that arterial and venous tissues increase their maximum contractile response during maturation. Because the maximum response to agents with different mechanisms of action (potassium chloride, phenylephrine) increased at different rates, the increase must be due to more than a quantitative increase in contractile material, possibly to differences in the rate of maturation of their respective excitation-contraction coupling processes. However, when maturational changes in other characteristics are compared, differences are observed between arteries and veins as well as between vessels within a given class,
indicating intervessel heterogeneity in maturation. (*Pediatr Res* 21: 152–158, 1987)

Abbreviations

PSS, physiological salt solution
l_i, initial length
KCl, potassium chloride
l_o, optimal length
PE, phenylephrine
ED50, concentration that produces half maximum response
SDS, sodium dodecyl sulfate

It has been demonstrated by several investigators (1–5) that the mechanical responsiveness of arterial tissue to constrictor and dilator agents changes during the development of the animal (for more complete reviews see References 6 and 7). In general, the maximum response to constrictor agents increases while the sensitivity (ED50) either does not change or increases. The particular alteration in sensitivity observed may depend on the constrictor agent used, the age range studied, or the animal species from which the vessel was obtained. Work from this laboratory (8) suggests that the increase in maximum contractile response that occurs in developing rat aorta between the ages of 1 and 2 months can be explained in part by an increase in the actomyosin content of the vessel; however, changes in maximum contractile response occurring earlier (5) or later (8) are not due to changes in contractile protein content.

The response to vasodilator agents that operate via the β adrenergic receptor has been shown to increase early in development and then decrease after maturation (9–12). The effect of relaxing agents that do not operate through this receptor (*e.g.* nitroglycerin, adenosine, PGI 2) remains constant (10, 12–14). The changes in the effectiveness of β receptor agonists with maturation may be due to a decreasing effectiveness of cyclic AMP to produce relaxation (13) or to a decrease in receptor number.

The majority of work has concentrated on developmental changes in arterial tissue and few studies have determined if venous tissue undergoes similar changes. Where venous tissue has been examined (15, 16) with regard to the effect of isoproterenol, no loss in effectiveness was observed at ages where arterial tissue had a reduction in responsiveness. The purpose of these studies was to examine more extensively changes in the contractile and dilator response of venous tissue from both the pulmonary and systemic vascular beds with the objective of determining in a given species whether veins and arteries undergo similar developmental changes.

METHODS

Animals. Dogs of either sex in three different age groups were used in the study. The 1-wk group consisted of dogs 3 to 7 days of age, the 1-month group consisted of dogs 4 to 5 wk of age and the adult group consisted of animals between 1 and 2 yr of age. The 1-wk and 1-month animals were obtained from pregnant bitches housed in the vivarium. All animals were killed with an overdose of pentobarbital given either intreperitoneally in the one week and one month animals or intravenously in the adult animals.

Vessel preparation. At least four different vessels were removed from each animal and immediately placed in a PSS of the following composition (mM): NaCl, 132; KCl, 4.7; $MgSO_4$, 1.2; $NaHCO_3$, 18; $CaCl_2$, 2: glucose, 5 where they were cleaned of adhering fat and connective tissue. The pulmonary artery used was one of the first branches from either the right or left pulmonary artery that ran within the lobe of the lung. If the vessel was to be used for mechanical studies it was placed in an isolated tissue bath as described below. If it was to be used for protein determination, the wet weight was determined and it was frozen in liquid nitrogen and pulverized in a percussion mortar precooled in liquid nitrogen.

Determination of mechanical properties. A segment at least 5-mm long was cut from each vessel and threaded onto two stainless steel rods, one permanently fixed to an immovable support and the second connected by a movable stage micrometer to a Grass FT03 force transducer. The output of the force transducer was displayed on a Grass Model 7 polygraph. For vessel segments from neonatal animals, the rods were 26 gauge and for the segments from adult animals they were 23 gauge. After threading the segments, they were lowered into an isothermic tissue chamber containing 37C PSS which was continuously bubbled with 95% O_2/5% CO_2. Immediately upon placing the segment within the chamber, the l_i of the segment was determined by moving the rod attached to the force transducer. The distance, as indicated by the micrometer, between the fixed and movable rods at which tension was first detected was designated l_i. The vessel segment was then stretched to a length that was 50% greater than l_i and allowed to equilibrate for at least 1 h.

After the equilibration period, sufficient KCl was added to the bath to raise the concentration to 30 mM and the mechanical response followed for 5 min at which time fresh PSS was placed in the bath. This stimulation with KCl was repeated at least three times to ensure reproducible mechanical responses. The segment length was then set at 10% of l_i and after a 15-min equilibration period it was stimulated with 30 mM KCl. The steady state tension was noted and fresh PSS placed in the chamber. When the response to KCl had completely waned, the segment length was increased another 10% of l_i and the stimulation repeated. This sequence was continued until the l_o for tension development was determined. The vessel was then set at this length for all subsequent concentration-response determinations. The strain at l_o [$(l_o - l_i)/l_i$] was calculated for each vessel.

The concentration-response relationship for KCl or PE was determined as described by Van Rossum and Van den Brink (17) and the ED50 concentration determined by probit analysis of the concentration-response relationship. To determine the effect of isoproterenol or verapamil, the ED50 concentration of KCl was added to the bath and after attainment of the steady state response, increasing amounts of isoproterenol or verapamil were added. The effect of either agent was expressed as a percentage of the mechanical response to the ED50 concentration of KCl.

At the end of the experiment, the wet weight of the vessel segment was determined and the wall cross-sectional area calculated from the relationship between wet weight, length (l_o) and density [wt/($l_o \times$ D), D = 1.05 g /cm^3 (18)].

Determination of contractile protein content. The actin and myosin heavy chain content of femoral and renal arteries and saphenous and jugular veins was determined as described previously (8). Vessels, cleaned of adhering fat and connective tissue, were frozen in liquid nitrogen and pulverized in a percussion mortar cooled in liquid nitrogen. It was necessary to combine vessels from both the right and left sides of the neonatal animals to obtain sufficient material for analysis. At least 10 mg (wet weight) of tissue was used. The pulverized tissue was placed in a solution (25 μl/mg tissue) consisting of 25 mM sodium phosphate, 2% β mercaptoethanol, 2% sodium dodecylsulfate, and 5 μg/ml of the proteinase inhibitors leupeptin and pepstatin. The suspension was heated at 37° C for 15 min, centrifuged at 2500 $\times$ g for 10 min at room temperature, and the supernatant removed. The remaining tissue pellet was extracted two more times and the tissue pellet remaining after the third extraction dissolved in 2 M NaOH. The protein content of the three supernatant samples and the dissolved tissue pellet were determined by the micro-Kjeldahl method. The total protein content of the tissue was derived from the sum of the protein contents of the three supernatants, plus the protein remaining in the tissue pellet.

An aliquot from each of the three tissue supernatant samples was combined with a glycerol-pyronin-Y (0.1% pyronin-Y in glycerol) solution (5 μl of supernatant/μl glycerol-pyronin-Y) and applied to a 10% T polyacrylamide-SDS gel at 15–70 μg of protein per well. On the same gel, known amounts (0.8–9.4 μg) of purified skeletal muscle actin and myosin (Sigma Chemical Co.) were also applied. After electrophoresis and Coomassie blue staining, the amount of actin and myosin heavy chain in each of the three tissue supernatants was determined from desitometric scans of the purified proteins and tissue samples as previously described (8). The actin and myosin heavy chain content of the three extracts from the vessel segments were added together to give the amount of contractile protein in the segment. Approximately 90% of the extractable actin and myosin heavy chain was removed in the first two extractions. The quantity "actomyosin" was defined as the sum of the amounts of actin and myosin heavy chain.

The various tissue protein values were normalized to length and tissue wet weight. Normalization to tissue length provides information about the absolute amount of protein present whereas normalization to tissue wet weight reflects the amount present relative to all tissue components (19).

Statistical treatment. One-way analysis of variance was used to determine if a given vessel parameter changed with age or if at a given age a parameter varied between vessel types. If a statistically significant change was indicated, the Duncan's multiple range test was used to identify specific intergroup differences. The Student's t test was used to test for statistical significance of the maximum contractile response to KCl and PE for a given vessel at a given age. For all statistical tests, a p value of 0.05 or smaller was taken as indicating a significant difference.

RESULTS

The strain at the optimal length for force development (Table 1) remained constant with maturation in all vessels examined except the femoral artery where the strain decreased. At any given age, the strain needed to achieve l_o was always lowest in the jugular and pulmonary veins and the pulmonary artery and greatest in the renal artery.

For all vessels studied, the maximum contractile response to KCl and PE increased with maturation (Tables 2 and 3). Comparison of the relative changes in maximum response to KCl and PE in a given vessel with maturation indicated that the maximum response to PE increased more (8.4 ± 1.0 times) than did the maximum response to KCl (4.4 ± 0.5 times; $p < 0.05$) with the greatest increases in response to PE occurring after 1

Table 1: *Strain at* l_0*

	Wk (W)	Mo (M)	Adult (A)	Change with age†
Femoral artery	5.3 ± 0.6 (19)	5.6 ± 0.7 (37)	3.3 ± 0.4 (32)	W = M > A
Renal artery	4.6 ± 0.5 (27)	7.0 ± 1.0 (30)	5.1 ± 0.4 (28)	W = M = A
Carotid artery	2.9 ± 0.3 (24)	2.7 ± 0.2 (38)	3.5 ± 0.2 (35)	W = M = A
Pulmonary artery	0.9 ± 0.04 (19)	1.0 ± 0.01 (11)	1.2 ± 0.1 (10)	W = M = A
Saphenous vein	3.3 ± 0.3 (32)	5.8 ± 0.7 (33)	4.5 ± 0.7 (24)	W = M = A
Jugular vein	0.5 ± 0.1 (3)	1.0 ± 0.2 (4)	0.6 ± 0.05 (5)	W = M = A
Pulmonary vein	0.6 ± 0.1 (3)	1.5 ± 0.1 (3)	1.0 ± 0.05 (4)	W = M = A
Intervessel comparison‡	1,2 > 3,4,5,6,7	1,2 > 3,4,6,7	1,2,3 > 4,6,7	
	3 > 4	5 > 4,6,7	5 > 1,4,6,7	
	5 > 4,6,7			

* All values mean ± SEM with number of observations in parentheses.
† Within vessel comparison of the effect of age with > indicating a statistically significant difference.
‡ Intervessel comparison at each age group with > indicating a statistically significant difference between the numbered groups.

Table 2. *Response of arterial tissue to KCl and PE**

	Max K (mN/mm²)	Max PE (mN/mm²)	K ED50 (mM)	PE ED50 ($\times 10^{-6}$ M)
Pulmonary artery				
Wk (W)	4.9 ± 1.0 (14)†	NR (5)†	46.1 ± 3.2 (14)	NR (5)
Mo (M)	12.8 ± 2.1 (12)†,‡	0.4 ± 0.4 (3)†,‡	43.9 ± 3.2 (12)	7.4 ± 7.4 (3)
Adult (A)	21.6 ± 3.9 (6)	10.4 ± 4.5 (5)†	36.0 ± 1.2 (6)	5.2 ± 0.5 (5)
Changes with age§	W < M < A	M < A	W = M > A	W > M > A
Femoral artery				
Wk (W)	16.0 ± 1.8 (19)	12.5 ± 3.9 (7)†	34.8 ± 2.1 (19)	3.4 ± 1.4 (7)
Mo (M)	47.9 ± 5.2 (18)	35.7 ± 5.9 (10)	36.3 ± 1.9 (8)	2.1 ± 0.4 (10)
Adult (A)	55.0 ± 14.2 (10)‡	128.9 ± 13.8 (7)‡	31.7 ± 2.3 (10)	0.9 ± 0.1 (7)
Changes with age	W < M = A	W < M < A	W = M = A	W = M > A
Carotid artery				
Wk (W)	23.5 ± 3.0 (11)‡	9.0 ± 1.6 (11)†,‡	40.9 ± 3.7 (11)	6.0 ± 1.0 (11)
Mo (M)	44.1 ± 4.7 (19)‡	12.0 ± 3.6 (9)‡	39.6 ± 1.7 (19)	4.5 ± 2.1 (9)
Adult (A)	73.2 ± 11.1 (11)	48.9 ± 9.7 (11)†	32.2 ± 1.4 (11)	3.1 ± 0.6 (11)
Changes with age	W < M < A	W = M < A	W = M > A	W = M = A
Renal artery				
Wk (W)	18.5 ± 3.0 (12)	24.6 ± 6.6 (10)	41.4 ± 2.3 (12)	2.1 ± 0.3 (10)
Mo (M)	46.3 ± 5.5 (16)	31.2 ± 4.8 (8)	39.0 ± 2.6 (16)	2.5 ± 0.4 (8)
Adult (A)	58.4 ± 17.1 (10)‡	169.0 ± 28.7 (7)‡	34.0 ± 1.5 (10)	1.9 ± 0.3 (7)
Changes with age	W < M = A	W = M < A	W = M > A	W = M = A

* All values mean ± SEM with number of observations in parentheses.
† Significantly less than other vessels at the same age.
‡ $p < 0.05$ Max K *vs* max PE.
§ Within vessel comparison of the effect of age with > indicating a statistically significant different between age groups.

month of age. In general, venous vessels developed less maximum response than arterial vessels at all ages; however, the saphenous vein and pulmonary artery were exceptions.

The sensitivity of these vessels to KCl and PE changes in some but not all vessels with maturation (Tables 2 and 3). In the pulmonary, carotid, and renal arteries, the sensitivity to KCl increased while in the pulmonary and saphenous veins it decreased. Only the sensitivity of pulmonary and femoral arteries to PE increased.

Examination of the responsiveness to the β receptor agonist isoproterenol (Fig. 1) indicated that the femoral, renal, pulmonary, and carotid arteries from animals of all ages were minimally responsive, while its effectiveness increased with development in the pulmonary and saphenous veins and remained constant in the jugular vein. In contrast, the calcium channel blocker, verapamil, significantly reduced the ED50 response to KCl in all systemic arteries and veins (Fig. 2) from either 1-wk or 1-month animals. The verapamil response of pulmonary arteries from 1-

wk and 1-month animals was less than the response of any other vessel.

There was an increase with development in the amount of actomyosin per unit length in all vessels (Table 4). The ratio of actomyosin to total protein did not change with age, and the amount of actomyosin per tissue weight increased significantly only in the saphenous vein. These ratios were lower in the jugular vein than in other vessels at most ages. The weight ratio of actin to myosin heavy chain did not change in the arterial tissue but increased in the veins with development. There were no intervessel differences in this ratio at any age.

DISCUSSION

As demonstrated by other investigators using vessels from a variety of animals, the maximum contractile response to KCl and PE of all vessels studied (Tables 2 and 3) increased during development. The explanation for the increasing maximum con-

Table 3. *Response of venous tissue to KCl and PE**

	Max K (mN/ mm²)	Max PE (mN/ mm²)	K ED50 (mM)	PE ED50 (×10⁻⁶ M)
Saphenous vein				
Wk (W)	13.3 ± 2.4 (19)	12.6 ± 1.6 (10)	30.2 ± 2.1 (19)	1.6 ± 0.4 (10)
Mo (M)	32.5 ± 3.8 (16)	22.4 ± 4.6 (8)	36.7 ± 2.8 (16)	1.2 ± 0.2 (8)
Adult (A)	53.3 ± 7.0 (10)†	112.8 ± 29.2 (7)†	39.9 ± 3.2 (10)	1.4 ± 0.2 (7)
Changes with age‡	W < M < A	W < M < A	W < M = A	W = M = A
Jugular vein				
Wk (W)	1.9 ± 0.1 (3)§		36.2 ± 1.7 (3)	
Mo (M)	3.6 ± 0.9 (4)§		31.1 ± 4.8 (4)	
Adult (A)	11.8 ± 5.2 (5)§		39.4 ± 3.8	
Changes with age	W < M < A		W = M < A	
Pulmonary vein				
Wk (W)	1.8 ± 0.1 (3)§		26.9 ± 3.3 (3)	
Mo (M)	4.2 ± 2.6 (3)§		26.5 ± 0.7 (3)	
Adult (A)	11.4 ± 2.6 (5)§		38.3 ± 4.2 (5)	
Changes with age	W < M < A		W = M < A	

* All values mean ± SEM with number of observations in parentheses.
† $p < 0.05$ max K *vs* max PE.
‡ Within vessel comparison of the effect of age with > indicating a statistically significant difference between age groups.
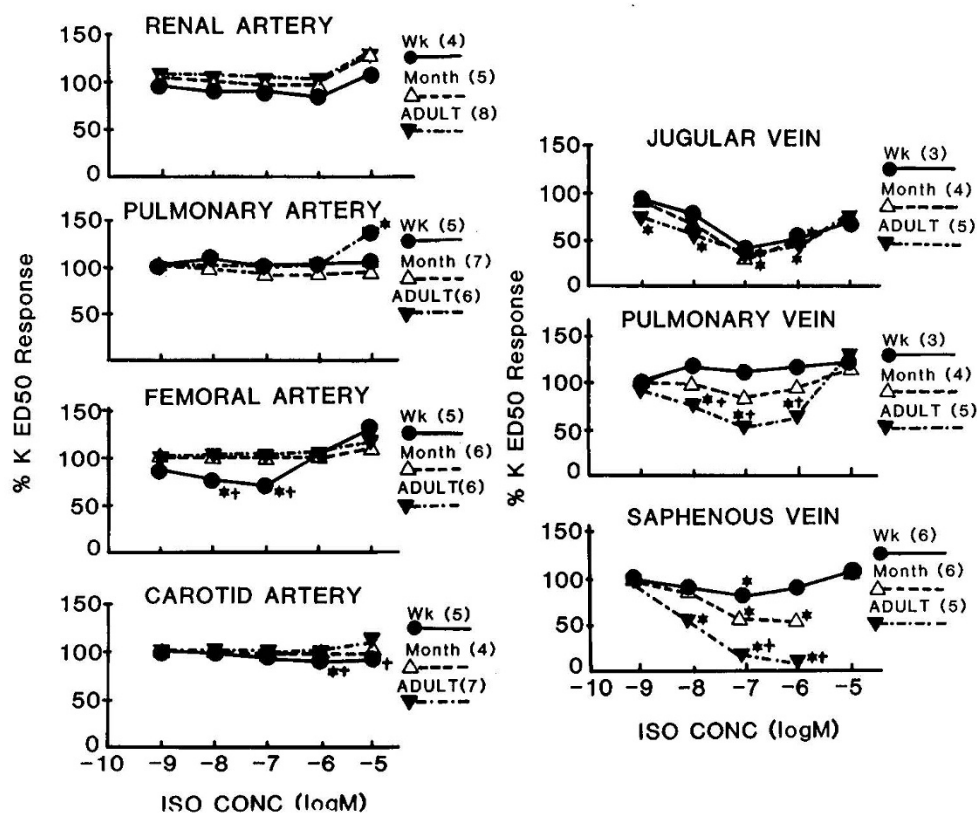§ Significantly less than other vessels at the same age.

Fig. 1. Concentration-response relationship for isoproterenol of arterial and venous tissue from dogs of different ages. The mechanical response to isoproterenol is expressed as a percent of the initial contractile response of the vessel to the ED50 concentration of KCl. All values are means, *error bars* have been deleted for clarity and the number of observations for each age group is in parentheses. * $p<0.05$ relative to 100%; † $p<0.05$ relative to 1-wk response.

tractile response during development is unknown, but could be due to factors independent of the contractile agent used as well as to factors dependent on the mechanism of agonist action. Factors independent of the contractile agonist include the position of the vessel on its active length tension curve, the contractile protein content, the sensitivity of the contractile proteins to

calcium, and the orientation of the contractile filaments and/or cells within the vessel wall. Factors dependent on the agonist used include the source(s) of calcium available for agonist-induced release and the ability of the agonist to release these calcium pools.

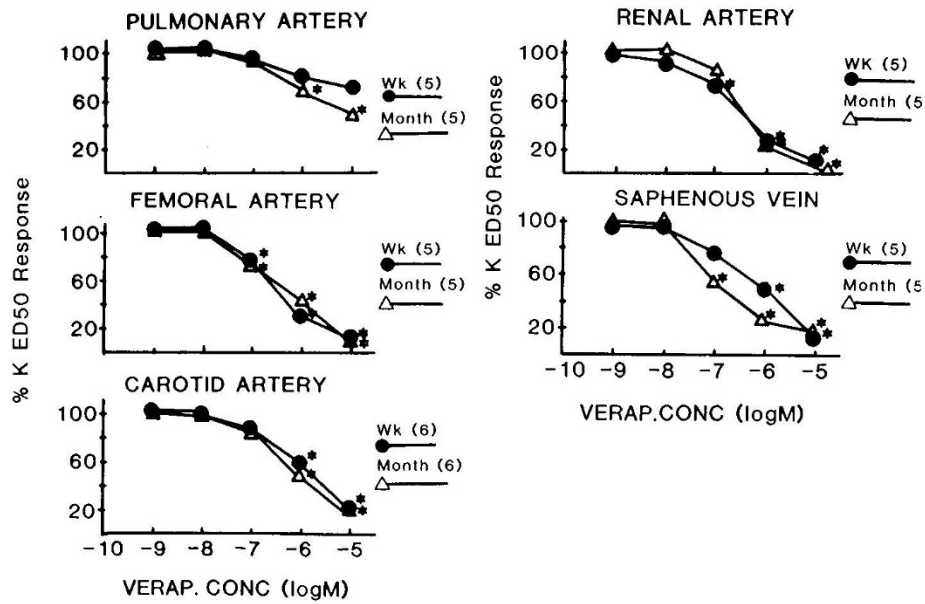The maximum contractile response to KCl and PE was deter-

Fig. 2. Concentration-response relationship for verapamil of arterial and venous tissue from dogs of different ages. The mechanical response to verapamil is expressed as a percent of the initial contractile response of the vessel to the ED50 concentration of KCl. All values are means, *error bars* have been deleted for clarity and the number of observations for each age group is in parentheses. * $p < 0.05$ relative to 100%.

Table 4. *Protein content of arterial and venous tissue**

	TP/mm (mg/mm)	TP/ww (mg/gww)	AM/mm (mg/mm)	AM/ww (mg/gww)	AM/TP (mg/gww)	A/M (mg/mg)
Femoral artery						
Wk (6)	0.13 ± 0.06	272 ± 107	5 ± 1	12 ± 4	81 ± 24	1.2 ± 0.4
Mo (7)	0.21 ± 0.05	157 ± 32	14 ± 3	10 ± 2†	79 ± 21	1.7 ± 0.5
Adult (7)	0.83 ± 0.20	175 ± 30	69 ± 8	22 ± 5	135 ± 29	1.3 ± 0.2
Changes with age‡	W = M < A	W = M = A	W = M < A	W = M = A	W = M = A	W = M = A
Renal artery						
Wk (3)	0.25 ± 0.17	429 ± 283	14 ± 6	23 ± 10	89 ± 44	0.9 ± 0.08
Mo (6)	0.22 ± 0.05	267 ± 91	22 ± 6	20 ± 4	121 ± 42	1.7 ± 0.05
Adult (4)	0.57 ± 0.07	157 ± 40	94 ± 22	26 ± 4	180 ± 63	1.9 ± 0.3
Changes with age	W = M < A	W = M = A	W = M < A	W = M = A	W = M = A	W = M = A
Saphenous vein						
Wk (3)	0.08 ± 0.05	116 ± 64	3 ± 1	5 ± 1†	68 ± 21	1.5 ± 0.4
Mo (5)	0.11 ± 0.03	97 ± 24	8 ± 2†	7 ± 2†	78 ± 7	1.1 ± 0.3
Adult (7)	0.79 ± 0.08	223 ± 16	59 ± 8	16 ± 2	78 ± 12	2.4 ± 0.3
Changes with age	W = M < A	W = M = A	W = M < A	W = M < A	W = M = A	W = M < A
Jugular vein						
Wk (7)	0.24 ± 0.06	137 ± 49	5 ± 1	4 ± 1†	49 ± 14	1.2 ± 0.2
Mo (8)	0.33 ± 0.04	140 ± 19	8 ± 1†	4 ± 1†	26 ± 7†	1.0 ± 0.3
Adult (8)	1.15 ± 0.23	200 ± 25	28 ± 5†	4 ± 1†	23 ± 5†	2.2 ± 0.3
Changes with age	W = M < A	W = M = A	W = M < A	A = M = W	W = M = A	W = M < A

* All values means ± SEM with the number of observations in parentheses.

† Significantly less than other vessels at the same age.

‡ Within vessel comparison of the effect of age with > indicating a statistically significant difference between age groups and A = adult, M = mo, W = wk.

mined with all vessels at their optimal length for force development; therefore, the changing maximum response with development cannot be explained by the position of the vessel on its active length tension curve. The strain at the optimal length for force development (Table 1) changed with development only in the femoral artery where it decreased. Cox et al. (2) also reported a decrease in strain in mesenteric and renal arteries from maturing dog. A decrease with development in the strain necessary to achieve l_o could be due to an increase in the stiffness of elastic material in series with the contractile filaments and/or the orientation of the muscle cells within the vessel wall so that a smaller percentage change in length is needed to move the contractile filaments to their optimal position for force development. Alternatively, the absence of a change in strain at l_o would suggest minimal changes in these vessel characteristics with development.

As indicated in Table 4, the absolute amount of actomyosin (mg/mm) increased during development; however, the proportion of the total protein made-up by actomyosin did not change in the vessels examined. These results suggest that the increasing maximum contractile response was not due to an increased proportion of contractile protein as was observed in developing rat aorta (8). However, it has recently been demonstrated (20) that during development of the rat aorta the relative proportion of nonmuscle (β) and muscle (α)-like actin changes with the amount of muscle-like actin increasing. Increases in maximum force generation may parallel increases in specific actin variants even though force does not parallel changes in total actin content. The present data do not permit the elimination of other agonist independent factors such as contractile element orientation and contractile protein sensitivity to calcium from playing a role in the increasing maximum contractile response with development.

The relative increase with development in the maximum PE response (8.4×) was greater than that for KCl (4.4×) indicating that part of the explanation for the increasing maximum response is related to the agonist used. A similar observation was made by Cox et al. (2) for KCl and norepinephrine. This implies that the effectiveness of a given agonist to activate the contractile system may increase during development. Since PE acts via α adrenergic receptors while KCl acts through nonreceptor mediated mechanisms, these observations imply that these two mechanisms of excitation-contraction coupling mature at different rates. The exact step involved is not known at present.

Unlike maximum contractile response, other measured parameters either did not change with development or the changes were different in arteries and veins. The sensitivity (ED50) to KCl or PE did not change in some vessels, but if a change occurred, arteries showed an increase while veins showed a decrease. The pulmonary artery was especially interesting in that in 1-wk animals it was unresponsive to PE but contracted on exposure to KCl indicating a functioning contractile system. By 1 month of age, the pulmonary artery responded to PE and increased its sensitivity to adulthood. It is apparent from these data and previously published data on developing rat aorta (5) that some vessels may not contain α receptors or may contain ineffective α receptors at birth. These observations indicate that a general statement cannot be made about developmental changes in vascular sensitivity to contractile agents because of intervessel heterogeneity.

The response to the β adrenergic agonist, isoproterenol, also varied between arteries and veins during development (Fig. 1). The majority of arteries examined was minimally relaxed by isoproterenol at all ages studied. Only the carotid and femoral arteries from 1-wk-old animals were relaxed significantly by isoproterenol. The veins, on the other hand, were all responsive with the pulmonary and saphenous veins increasing their responsiveness with age and the jugular remaining responsive at all ages. Since the Ca-channel blocker verapamil was effective at antagonizing KCl-induced tone, the inability of isoproterenol to

relax arterial tissue was not due to a general inability of this tissue to respond to vasodilators. These results are in contrast to those obtained on systemic arterial tissue from maturing rabbits (9, 10) and rats (5) where the effectiveness of isoproterenol increased during development. These results suggest an intervessel heterogeneity in β receptor function and that the maturation of β receptors in canine vessels is dissimilar to that of vessels from other species.

It is possible that the differential relaxing effect of isoproterenol is related to the contractile agent used. Possibly arterial tissue contracted with another agonist would be relaxed by isoproterenol but if this were the case, this observation would still indicate that β receptor-mediated relaxation was different in different canine vessels as well as that it underwent different maturational changes.

The observation that the pulmonary artery responded the least to verapamil of all vessels examined (Fig. 2) suggests a difference in the voltage sensitive Ca channels present in this tissue relative to systemic arteries and veins.

Finally, these data also provide some general characteristics of canine arteries and veins independent of developmental changes. At any given age, arteries require a greater strain to achieve l_o (Table 1), develop more maximum force (Tables 2 and 3), and have a higher relative amount of contractile protein than veins (Table 4). However, the saphenous vein and pulmonary artery appear to be exceptions with the saphenous vein having "arterial" characteristics and the pulmonary artery, "venous" characteristics. Since both of these vessels are exposed to low transmural pressure, the general characteristics of arteries and veins delineated above cannot be due to an adaptive response to the different pressures to which these two vessel groups are exposed.

In summary the following points can be made: 1) both arteries and veins increase their ability to develop force during maturation which is due to more than an increase in functioning contractile proteins; 2) if changes occur, arterial vessels increase their sensitivity to contractile agents without changing their β agonist responsiveness while veins decrease their responsiveness to contractile agents and increase their responsiveness to β adrenergic dilators; 3) at any given age, arteries require a greater strain to achieve l_o, develop more maximum force, and have a higher relative amount of contractile protein than veins.

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