α₁-Adrenergic Receptors in Pulmonary and Systemic Vascular Smooth Muscle Alterations With Development and Pregnancy

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α₁-Adrenergic receptors mediate vasoconstriction in the pulmonary and systemic vasculature. In sheep the in vivo vasoconstrictor response to α₁-adrenergic stimulation is less in the pulmonary circulation compared with the systemic circulation of the fetus, the response increases in both vascular beds with fetal and postnatal development, and it decreases in the systemic vasculature with pregnancy. In an effort to determine the mechanisms underlying these differences, α₁-adrenergic receptor binding characteristics were determined by using [³H]prazosin in intrapulmonary and systemic (thoracic aorta) vascular smooth muscle (VSM) from late-gestation fetal lambs and from pregnant and nonpregnant ewes. α₁-Adrenergic receptor density was less in fetal intrapulmonary VSM that in fetal aortic VSM (12.4±1.5 versus 29.4±3.2 fmol/mg protein, p<0.05), and it was less (p<0.05) in the fetus compared with the pregnant ewe in both intrapulmonary and aortic VSM (51.0±5.2 and 76.5±5.9 fmol/mg protein, respectively). α₁-Adrenergic receptor density in intrapulmonary VSM was similar in the pregnant and nonpregnant ewe (61.9±7.2 fmol/mg protein), whereas in aortic VSM it was less (p<0.05) in pregnant ewes compared with nonpregnant ewes (101.0±5.5 fmol/mg protein). α₁-Adrenergic receptor affinity was similar in all the VSM sources tested. β-Adrenergic receptor density was studied for comparison, and it was similar in intrapulmonary and aortic VSM and unchanged in the fetus versus the pregnant ewe (18.9±3.0 versus 19.3±2.7 versus 23.0±5.8 versus 14.5±2.9 fmol/mg protein in fetal intrapulmonary, fetal aortic, adult intrapulmonary, and adult aortic VSM, respectively). Thus, there are differences between vascular beds, maturational changes, and pregnancy-associated alterations in VSM α₁-adrenergic receptor density that are specific to this adrenergic receptor type. It is speculated that these differences in receptor number may partly explain the disparate vasoconstrictor responses to α₁-adrenergic stimulation found in the pulmonary vasculature compared with the systemic vasculature, in the fetus compared with the adult, and in the pregnant state compared with the nonpregnant state. (Circulation Research 1990;67:1193–1200)

Vasoconstriction is mediated by α₁-adrenergic receptors in the pulmonary and systemic vasculature.¹ It has been shown that the vasoconstrictor response to α₁-adrenergic stimulation and/or inhibition varies between these two vascular beds, and there also appear to be alterations in α₁-adrenergic mediation of vasomotor tone with development and pregnancy. Both in vitro and in vivo studies in fetal sheep have demonstrated that the response to α₁-adrenergic stimulation is less in the pulmonary circulation compared with the systemic circulation.²,³ In addition, it has been demonstrated in vivo that the vasomotor response to α₁-adrenergic stimulation or inhibition increases with fetal and postnatal development in sheep, as well as in other species.²–⁸ Furthermore, the pulmonary and systemic vasoconstrictor responses to α₁-adrenergic stimulation in vivo have been observed to decrease with pregnancy in some animal models.⁹–¹¹

In an effort to determine the mechanisms underlying these differences, the present study was designed to define α₁-adrenergic receptor binding characteristics in intrapulmonary and systemic (thoracic

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vascular smooth muscle (VSM) from the late-gestation fetal lamb and from the pregnant and nonpregnant ewe. These differences in response to \( \alpha_1 \)-adrenergic receptor activation may be due to differences in receptor density, which has been shown to correlate with VSM sensitivity in some studies.\(^{12,13} \) \( \beta \)-Adrenergic receptor binding characteristics were also examined to determine if the findings for \( \alpha_1 \)-adrenergic receptors are common to other VSM adrenergic receptor types. Based on the results of the studies examining physiological parameters,\(^{2-11} \) the following hypotheses were tested: 1) \( \alpha_1 \)-adrenergic receptor density is lower in pulmonary than in systemic VSM in the fetal lamb, 2) \( \alpha_1 \)-adrenergic receptor density is lower in fetal compared with adult VSM, and 3) the density of \( \alpha_1 \)-adrenergic receptors in VSM decreases with ovine pregnancy.

Materials and Methods

Animal Model

The sheep has been used extensively by several groups of investigators\(^{2-11} \) in studies examining physiological parameters to assess \( \alpha_1 \)-adrenergic mediation of both pulmonary and systemic vasomotor tone during fetal and postnatal development and during pregnancy. As such, it is an excellent animal model for the investigation of the variations in VSM \( \alpha_1 \)-adrenergic receptor binding characteristics in different vascular beds with maturation and pregnancy. The VSM studied was obtained from three groups of mixed-breed sheep. They were fetal lambs at 125–140 days gestation \((n = 16)\), with term being 144±3 days, pregnant ewes at 125–140 days gestation \((n = 15)\), and nonpregnant ewes \((n = 17)\). All the pregnant ewes were multiparous and had singletons or twins, with the exception of one set of triplets. The ewes were housed in the Animal Resources Center of the University of Texas Southwestern Medical Center and were given standard animal chow and water ad libidum. The study protocol was approved by the Institutional Review Board for Animal Research.

Tissue Preparation

The pregnant ewe and fetus(es) were anesthetized with sodium pentobarbital (50 mg/kg) given intravenously to the ewe, and the fetus(es) was delivered by cesarean section. The thoracic contents of the ewe and fetus(es), including the thoracic aorta, were immediately removed en bloc and were placed into ice-cold 0.01 M phosphate-buffered saline (pH 7.4). The thoracic contents of nonpregnant ewes were removed in a similar manner. Further tissue preparation was performed in a cold room at 4°C. The pulmonary arterial tree was rapidly dissected from the lung parenchyma, the thoracic aorta was isolated, and both were placed in fresh ice-cold phosphate-buffered saline. Fat and connective tissue were removed, the adventitia was grossly dissected from the arteries until the homogeneous medial layer was reached, and the endothelium was scraped off with a cotton-tipped applicator. Removal of the endothelium was verified by demonstrating a lack of increase in cyclic GMP content with acetylcholine stimulation in arteries treated in the above manner compared with those with intact endothelium (authors’ unpublished data).\(^{14} \) The remaining medial layer was the source of the VSM examined. To have sufficient quantities of VSM (particularly fetal) for the receptor binding studies with tritiated radioligand, the intrapulmonary VSM examined was obtained from the media of third to sixth generation pulmonary arteries, with the vast majority coming from the proximal branches.\(^{15} \) The systemic VSM examined for comparison was obtained from the media of the thoracic aorta. The thoracic aorta was chosen for study because it also arises from the heart and is located in the thoracic cavity and because sufficient VSM can be obtained from it for the study of \( \alpha_1 \)-adrenergic receptors in fetal systemic VSM.

\( \alpha_1 \)-Adrenergic Receptor Radioligand Binding Studies

After the removal of the endothelium, the medial tissue was transferred into ice-cold 0.25 M sucrose buffer, pH 7.4, with 10 mM Tris base. Intrapulmonary or aortic VSM from one or two fetuses or from a single ewe (1.5–2.5 g wet wt) was placed in 20.0 ml buffer. The tissue was washed in the sucrose buffer twice, and the plasma membranes were prepared at 4°C by methods modified from those of Wei et al.\(^{16} \) The tissue was minced with scissors and was homogenized twice with a Polytron (Brinkmann Instruments, Westbury, N.Y.) at setting No. 8 for 10 seconds. The homogenate was centrifuged at 4°C at 1,500g for 10 minutes, and the resulting supernatant was filtered through two layers of gauze and then centrifuged at 4°C at 100,000g for 30 minutes. The pellet formed was resuspended in 25 mM glycylglycine buffer, pH 7.4, yielding a protein concentration of 150–200 \( \mu \)g/ml, as determined by a modification of the Lowry method.\(^{17} \) The final membrane preparation was free of collagen, which was removed during the first centrifugation,\(^{16} \) and the protein concentration of the preparation was not influenced by elastin because it does not cross-react in the protein assay.

\( \alpha_1 \)-Adrenergic receptor binding assays were performed with 100 \( \mu \)l membrane preparation in a total volume of 150 \( \mu \)l of the 25 mM glycylglycine buffer. The \( \alpha_1 \)-adrenergic receptor–specific radiolabeled antagonist \([^3H]prazosin\) was used.\(^{18} \) \([^3H]Prazosin\) was added at concentrations ranging from 100 to 2,000 pM, in the presence or absence of \( 10^{-5} \) M phentolamine to distinguish nonspecific from specific binding. Time to equilibrium assays were performed with 150 pM \([^3H]prazosin\), as were studies examining the affinity of the \( \alpha_1 \)-adrenergic receptors for agonists and antagonists \((10^{-10}–10^{-3} \) M \( l \)-norepinephrine, \( l \)-epinephrine, \( l \)-isoproterenol, prazosin, phentolamine, and yohimbine). Binding of \([^3H]prazosin\) to both intrapulmonary and aortic VSM membrane preparations reached equilibrium after 10 minutes of incubation and remained constant for at least an
Additional 20 minutes (Figure 1). As such, an incubation time of 20 minutes was used for all binding studies. Incubations were performed at 37°C and were terminated by rapid dilution with 4.0 ml ice-cold 50 mM Tris buffer, pH 7.4, with 10 mM MgCl₂ and by separation of bound and free ligand by filtration through Whatman GF/C filters (Whatman Inc., Clifton, N.J.) under vacuum, followed by three 4.0-ml rinses of the filters with the same buffer. After drying, the radioactivity collected on each filter was determined by liquid scintillation spectrometry (40% counting efficiency). All determinations were performed in duplicate. Binding curves were generated, and the density of receptors (B_max) and dissociation constant for the ligand (K_d) were determined from the specific binding data by computer analysis using a modification of the program LIGAND by Munson and Rodbard, adapted for microcomputers by G.A. McPherson (Elsevier BIOSOFT, Cambridge, UK).  

**β-Adrenergic Receptor Radioligand Binding Studies**  

In an effort to determine the specificity of any observed differences in α₁-adrenergic receptor binding characteristics, we examined those same parameters for β-adrenergic receptors on the intrapulmonary and aortic VSM plasma membrane preparations from the fetal and pregnant sheep. The membrane preparation was identical to that outlined above, except that the final pellet was resuspended in 5.0 mM HEPES buffer, pH 7.4, with 1.0 mM MgSO₄, achieving a final protein concentration of 50–100 μg/ml. The β-adrenergic receptor binding studies were performed with [³¹I]iodocyanopindolol ([³¹I]ICYP) over a concentration range of 10–100 pM in the presence or absence of 10⁻² M l-alprenolol to distinguish nonspecific from specific binding. The incubations, which were performed at 37°C for 120 minutes, were terminated by dilution and washing of the membranes with 20 mM KH₂PO₄ buffer, pH 7.4, with 1.0 mM MgSO₄. The separation of bound and free radioligand was accomplished as outlined above in the studies of the α₁-adrenergic receptor. The methods have been described in detail elsewhere.  

**Materials**  

l-Norepinephrine, l-epinephrine, l-isoproterenol as d-tartrate or d-bitartrate salts, prazosin HCl, phentolamine, and yohimbine HCl were obtained from the Sigma Chemical Co., St. Louis. 7-Methoxy-[³¹I]prazosin (82 Ci/mmol) and dl-[³¹I]ICYP (2,200 Ci/mmol) were from New England Nuclear/Dupont, Boston.  

**Statistical Analysis**  

Analysis of variance (ANOVA) with Newman-Keuls post hoc testing was used to compare binding characteristics between the various VSM sources and study groups and between the two receptor types. Nonparametric ANOVA was used when indicated. Significance was accepted at p<0.05. All results are expressed as mean±SEM.  

**Results**  

**α₁-Adrenergic Receptors**  

The radioligand binding curves depicted that specific binding of [³¹I]prazosin to α₁-adrenergic receptors in intrapulmonary and aortic VSM from all three study groups was saturable, and LIGAND analysis confirmed that a one-site model was appropriate (p<0.05). Representative specific binding curves and Scatchard plots for intrapulmonary and aortic VSM from fetal, pregnant, and nonpregnant sheep are shown in Figure 2.  

Furthermore, agonist and antagonist displacement curves (Figure 3) yielded an order of agonist potency of l-norepinephrine > l-epinephrine > l-isoproterenol and an order of antagonist potency of prazosin > phentolamine > yohimbine. This is characteristic of binding to an α₁-adrenergic receptor. The displacement curves illustrated in Figure 3 represent the mean values from three or four experiments performed in duplicate with each agonist and antagonist on membranes from intrapulmonary VSM from nonpregnant ewes. Identical displacement curves were obtained for aortic VSM membranes, and they were also similar for the three groups of sheep examined.  

The densities of the α₁-adrenergic receptors and the dissociation constants for [³¹I]prazosin binding in the intrapulmonary and aortic VSM from fetal and pregnant adult sheep are compared in Figure 4. The percent specific binding at K_d was generally greater than 95%. α₁-Adrenergic receptor density (B_max) was lower in the intrapulmonary than in the aortic VSM from both the fetuses and the pregnant ewes; the density in intrapulmonary VSM was 42% and 67% of the density in aortic VSM from the two groups, respectively. In the intrapulmonary arteries, the receptor density in fetal VSM was 24% of the density in adult VSM. Similarly, in the thoracic aorta, receptor density in fetal VSM was 38% of the density in adult VSM. The dissociation constants were similar for all
the VSM sources, with mean values ranging from 133 to 235 pM, indicating that there was high affinity of the receptor for the radioligand.

The \( \alpha \)-adrenergic receptor binding characteristics for the VSM from the pregnant and nonpregnant ewes are compared in Figure 5. Similar to the findings for the VSM from fetal and pregnant sheep, the density of receptors was less in the intrapulmonary arteries than in the thoracic aorta from the nonpregnant ewes, with the density in the intrapulmonary VSM 61% of that in the aortic VSM. The receptor density was similar in the intrapulmonary VSM from the pregnant and nonpregnant ewes. In the aortic VSM, however, receptor density was 25% less in the pregnant group compared with the nonpregnant group. The dissociation constants for the radioligand were similar in the intrapulmonary and aortic VSM from the pregnant and nonpregnant ewes.

**Comparison of \( \alpha \)- and \( \beta \)-Adrenergic Receptors**

The radioligand binding curves for the \( \beta \)-adrenergic receptor studies exhibited saturability, and LIGAND analysis confirmed that binding of \( [125I] \)ICYP was to a single homogeneous population of receptors (data not shown). Radioligand binding also demonstrated high affinity, with the dissociation constants in the picomolar range; the dissociation constants were similar in fetal intrapulmonary and aortic VSM (15.2±2.4 versus 20.1±5.8 pM, \( n=6 \)), but they were lower in adult intrapulmonary compared with aortic VSM (24.5±4.2 versus 38.3±4.4 pM, \( n=6, p<0.05 \)). We have demonstrated that VSM \( \beta \)-adrenergic receptors in fetal as well as adult sheep are primarily of the \( \beta_2 \)-adrenergic subtype.23

**Figure 2.** Panel A: Representative curves for specific binding of \( [3H] \)prazosin to intrapulmonary and aortic vascular smooth muscle plasma membranes from a fetal lamb ( ), a pregnant adult ewe (○), and a nonpregnant adult ewe (●). Specifically bound \( [3H] \)prazosin is plotted as a function of the concentration of \( [3H] \)prazosin. Each point was determined in duplicate. Panel B: Scatchard plots of specific \( [3H] \)prazosin binding to intrapulmonary and aortic vascular smooth muscle plasma membranes in panel A. The ratio of bound to free (B/F) \( [3H] \)prazosin is plotted as a function of specifically bound \( [3H] \)prazosin.

**Figure 3.** Displacement curves illustrating inhibition of specific \( [3H] \)prazosin binding by adrenergic agonists and antagonists. These studies were performed with intrapulmonary artery vascular smooth muscle plasma membranes from nonpregnant adult sheep prepared as described in "Materials and Methods." The percent inhibition of specific \( [3H] \)prazosin binding is plotted as a function of increasing concentration of agonist or antagonist. Values shown are mean values from three or four experiments with each agent, each performed in duplicate.
The radioligand binding studies with $^{125}$I]ICYP revealed that the density of $\beta$-adrenergic receptors was similar in the intrapulmonary compared with the aortic VSM from the fetal lambs and also from the pregnant ewes (Figure 6). This is in contrast to the observation that the density of $\alpha_1$-adrenergic receptors is lower in intrapulmonary compared with aortic VSM in these two groups. In addition, $\beta$-adrenergic receptor density was similar in fetal compared with adult intrapulmonary or aortic VSM. This is in contrast to the increased density of $\alpha_1$-adrenergic receptors in adult compared with fetal VSM.

**Discussion**

In the present study, we have successfully defined $\alpha_1$-adrenergic receptor binding characteristics in intrapulmonary and systemic (thoracic aorta) VSM from the late-gestation fetal lamb and the pregnant and nonpregnant ewe. The binding of $[^3]H$prazosin to the VSM membranes exhibited the pharmacological characteristics expected for labeling of $\alpha_1$-adrenergic receptors, including the attainment of equilibrium and saturation, high affinity specific binding to a single population of receptors, and the proper order of agonist and antagonist potency. To our knowledge, $\alpha_1$-adrenergic receptors have neither been previously quantified in pulmonary VSM nor compared in pulmonary and systemic VSM.

The results of these studies provide important new information regarding the possible mechanism(s) underlying the differences between the pulmonary and systemic vascular bed and the developmental and pregnancy-related changes in $\alpha_1$-adrenergic mediation of vasomotor tone. First, our finding that $\alpha_1$-adrenergic receptor density is less in the pulmonary compared with the systemic VSM of the third trimester fetal lamb is consistent with the observations of Nuwayhid et al.\textsuperscript{2} that norepinephrine infusion results in a smaller increase in vascular resistance in the ovine fetal pulmonary compared with systemic circulation. In addition, these results are consistent with the work by Su et al.\textsuperscript{3} demonstrating that the maximal contractile response to norepinephrine is less in arterial strips of ovine fetal main pulmonary artery compared with thoracic aorta. Regarding developmental changes, our observation that receptor density is less in fetal compared with adult VSM is consistent with the data of Nuwayhid and colleagues\textsuperscript{4} that indicates that there is a greater fall in pulmonary and systemic blood pressure in response to phenoxylbenzamine in late-gestation compared with early-gestation fetuses, with the maximal response occurring in adult sheep. In addition, these findings agree with the work of these investigators showing that the rise in pulmonary and systemic vascular resistance with norepinephrine is increased with fetal and post-

**Figure 4.** Bar graphs comparing $\alpha_1$-adrenergic receptor binding characteristics in intrapulmonary and aortic vascular smooth muscle plasma membranes from fetal and pregnant adult sheep. Panel A: Receptor density ($B_{\text{max}}$). Panel B: Dissociation constant ($K_d$). Values are mean±SEM from six experiments. *$p<0.05$ vs. aorta; †$p<0.05$ vs. pregnant adult sheep.

**Figure 5.** Bar graphs comparing $\alpha_1$-adrenergic receptor binding characteristics in intrapulmonary and aortic vascular smooth muscle plasma membranes from pregnant and nonpregnant adult sheep. Panel A: Receptor density ($B_{\text{max}}$). Panel B: Dissociation constant ($K_d$). Values are mean±SEM from six experiments. *$p<0.05$ vs. aorta; †$p<0.05$ vs. nonpregnant adult sheep.
natal development. Furthermore, our results may be consistent with those of Wyse and coworkers, who have demonstrated in ovine ear arteries that the maximal contraction generated with electrical stimulation of postganglionic neurons or with norepinephrine increases with development from 110 days of gestation through to adulthood. Lastly, regarding pregnancy-related changes, the finding that receptor density is decreased in the systemic VSM during pregnancy may partly explain the attenuated systemic response to norepinephrine and phenylephrine demonstrated by Magness and Rosenfeld to occur during ovine pregnancy. Studies of the uterine vasculature by Ford and coworkers indicate that these changes in receptor density with pregnancy may be mediated by alterations in plasma progesterone and estrogen. Thus, our overall findings suggest that in the sheep the differences between the fetal pulmonary and systemic vascular bed and the developmental and pregnancy-related changes in the response to α₁-adrenergic stimulation or inhibition may be related to variations in the density of VSM α₁-adrenergic receptors.

The relation of α₁-adrenergic receptor binding characteristics to the sensitivity of VSM to norepinephrine has been examined in a variety of animal models. Regarding receptor number, Oriowo and coworkers demonstrated in six different cat arteries that approximately 80% of the variation in the sensitivity to norepinephrine was attributable to differences in α₁-adrenergic receptor number. In rat mesenteric artery, Colucci et al related changes in the sensitivity to norepinephrine after epinephrine administration to alterations in receptor number. Regarding receptor affinity for agonists, multiple studies have revealed the potential importance of this parameter in the determination of the sensitivity to norepinephrine, with several artery types in different species demonstrating significant covariance of tissue sensitivity and affinity of the α₁-adrenergic receptor for norepinephrine. Although agonist affinities were not quantified in the present study, the similarity of the agonist displacement curves for the different artery types suggests that affinity did not differ in the groups examined. It is evident that the comparative roles of receptor density and affinity in the determination of tissue sensitivity may differ between vascular beds, between physiological and pathological states, and between species, with the present results suggesting that, in the sheep, receptor density may be a more important determinant than affinity.

The extrapolation of the results of our studies of VSM radioligand binding to the in vivo responses to norepinephrine infusions, however, should be made with a degree of caution because a variety of processes besides receptor activation by agonist may influence in vivo responsiveness. The direct, nonvascular effects of agonist infusion must be considered, such as effects on cardiac output. In addition, alterations in vascular beds other than the one being studied are possible, with secondary effects occurring in the vasculature of interest. Furthermore, local processes within the blood vessel should be kept in mind when one is attempting to explain disparate vasomotor responses. These include differences in norepinephrine uptake by neuronal and nonneuronal cells, differences in the degree of stimulation of other receptor types such as β- and α₂-adrenergic, and differences in the effects on non-VSM cells such as the endothelium. In addition, one must also consider variations in postreceptor events within the VSM as a possible explanation for differences in responses. Moreover, it is possible that the interpretation of the results of the radioligand binding studies should be somewhat tempered because the VSM receptors examined are from specific locations in the pulmonary and systemic vascular beds, which may not necessarily represent the situation in the resistance vessels. This potential limitation of the model and methodology used has been accepted to evaluate α₁-adrenergic receptors in fetal VSM.

Along with the investigations of α₁-adrenergic receptor binding characteristics, we studied β-adrenergic receptors in identical VSM plasma membrane preparations for comparison. Since the density of β-adrenergic receptors was similar in the various membrane preparations examined, in contrast to the
marked differences found in α₁-adrenergic receptor density, it is doubtful that the demonstrated differences for the latter receptor type can be explained simply by differences between groups in the yield of the plasma membrane preparations. Instead, they most likely represent true differences between the artery types and between the developmental groups. Furthermore, the contrasts in the developmental patterns for β- and α₁-adrenergic receptor density may be reflective of differences in the factors mediating the ontogeny of these two receptor types. As noted earlier, our previous study²³ suggests that the majority of β₁-adrenergic receptors in ovine VSM are of the β₁-adrenergic subtype. In general, the density of β₂-adrenergic receptors in the cardiovascular system appears to be regulated humorally by circulating catecholamines, whereas the number of α₁-adrenergic receptors seems to be regulated neurally.²⁷⁻²⁹ Furthermore, the ontogeny of these two components of the sympathoadrenal system appears to be dissimilar in the sheep, in that plasma catecholamine concentrations have been found to be similar in fetal and adult sheep in some studies, whereas the neural regulation of vasomotor tone in both vascular beds appears to increase with fetal and postnatal development.⁴⁻³⁰ As such, our contrasting results for the two receptor types may be explained in part by the thesis that the humoral mechanisms involved in β₁-adrenergic receptor development in ovine VSM are mature by late gestation, whereas the neuronal mediation of α₁-adrenergic receptor density undergoes maturation both in utero and after birth. To our knowledge, the studies involving sympathectomy and adrenalectomy in fetal and developing sheep that would be necessary to test this hypothesis have not yet been performed.

In summary, α₁-adrenergic receptor binding characteristics were determined in pulmonary and systemic VSM from late-gestation fetal lambs and pregnant and nonpregnant ewes in an effort to determine the mechanisms underlying the differences between vascular beds and the developmental and pregnancy-related changes in α₁-adrenergic mediation of vasomotor tone. The pulmonary VSM was derived from intrapulmonary arteries, and the systemic VSM was obtained from the thoracic aorta. In all groups studied, receptor density was lower in pulmonary compared with systemic VSM, receptor density in both VSM types was lower in the fetus compared with the adult, and receptor density in systemic VSM was decreased with pregnancy. There were no evident differences in affinity for agonists. Parallel studies of VSM β-adrenergic receptors indicated that these changes are specific to the α₁-adrenergic receptor. It is speculated that these differences in α₁-adrenergic receptor density may partly explain the attenuated vasoconstrictor response to α₁-adrenergic stimulation in the pulmonary compared with the systemic vasculature of the fetal lamb, the increase in response in both vascular beds with fetal and postnatal development, and the attenuated systemic vasomotor response associated with pregnancy.

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References


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