Acetylcholine-Induced Coronary Vasoconstriction and Vasodilation in Tranquilized Baboons

Delvin R. Knight, You-Tang Shen, Mark A. Young, and Stephen F. Vatner

To determine the effects of acetylcholine on the coronary bed in the baboon and whether the effects preceded or followed the action of acetylcholine on ventricular function, eight adult baboons (*Papio anubis*) were instrumented to measure left ventricular (LV) and mean arterial pressures, LV dP/dt, regional myocardial function, and coronary blood flow. Acetylcholine was injected locally through a catheter positioned in the coronary artery ostium using fluoroscopic guidance in intact sedated baboons. With heart rate held constant, intracoronary acetylcholine (0.5 µg/kg) reduced coronary blood flow by 82±4% from a baseline value of 34±4 ml/min without a significant change in mean arterial pressure and with a reduction in LV dP/dt of only 12±3%. The decrease in coronary blood flow occurred before either LV dP/dt or regional myocardial function fell in the region of the heart receiving acetylcholine. After the intense coronary constriction, a later phase characterized by dilation was observed. The changes in coronary blood flow with acetylcholine were unaffected by combined α- and β-adrenoceptor blockades but were abolished by muscarinic blockade. Low doses of acetylcholine elicited only coronary vasodilation. All doses of acetylcholine, administered directly into the iliac artery, also elicited only iliac vasodilation. Intracoronary acetylcholine in conscious dogs also induced only coronary vasodilation, whereas in conscious calves at higher doses, initial vasoconstrictor responses were observed, which also preceded reductions in regional myocardial function. These results suggest that the controversy surrounding the effects of acetylcholine can be reconciled on the basis of species, vascular bed studied, and dose. In the baboon, although lower doses of acetylcholine induce vasodilation, larger doses exert a direct vasoconstrictor effect on the coronary bed via a muscarinic mechanism. (*Circulation Research* 1991;69:706–713)

Cholinergic regulation of the coronary circulation remains one of the most intense controversies in coronary physiology. It has been generally accepted that in the canine model, cholinergic activation results in vasodilation of the coronary resistance vessels[^1]–[^4] and large coronary arteries.[^5] However, in other species, including normal human subjects and nonhuman primates, acetylcholine (ACH) has been shown to induce both coronary vasodilation[^3],[^4],[^6]–[^12] and coronary vasoconstriction.[^2],[^3],[^9]–[^17] Many of the studies have been conducted in isolated tissue,[^7],[^13],[^16] in acutely prepared, anesthetized animals,[^3],[^4],[^17] or in normal human subjects,[^6],[^8]–[^12],[^14],[^15] in which measurements are indirect and complications due to latent coronary artery disease might also complicate interpretation.[^18] Accordingly, the goal of the present study was to determine the coronary vascular effects of intracoronary ACH on the coronary resistance vessels in chronically instrumented, intact, tranquilized baboons. ACH was administered directly into the coronary artery to eliminate the complicating systemic effects of ACH. Increasing doses of ACH were used to determine dose-related effects. Because ACH may also elicit negative inotropic and chronotropic effects,[^19] heart rate was held constant and regional myocardial function was measured continuously in the distribution of the coronary artery in which ACH was administered. The underlying hypothesis was that if ACH induced primary vasoconstriction, then a decrease in blood flow would precede any decrease in mechanical function; conversely, if ACH induced coronary vasoconstriction secondary to changes in myocardial metabolic demand, then the effects on coronary
blood flow and vascular resistance would follow the effects on mechanical function. To determine if the coronary effects were unique, the effects of ACH, administered directly into the iliac artery, were also examined in conscious baboons. Finally, to further address potential species differences, effects of intra-coronary injection of ACH were examined in conscious dogs, in which vasodilatation has generally been observed, and in calves, in which coronary vasoconstriction has been reported in in vitro experiments.

**Materials and Methods**

Eight male baboons (*Papio anubis*) weighing 25–35 kg were premedicated with ketamine hydrochloride (8 mg/kg i.m.). General anesthesia was induced with sodium thiopental (2 mg/kg i.v.) and was maintained with halothane (0.5–1.0 vol%). With the use of sterile technique, the chest was opened through a midline sternotomy, the pericardium incised, and the heart exposed. A miniature solid-state pressure gauge (Konigsberg Instruments, Inc., Pasadena, Calif.) was implanted in the left ventricular (LV) chamber. Pacing electrodes were implanted on the right atrium. Heparin-filled Tygon catheters were implanted in the ascending aorta and left atrium. The right coronary artery was carefully dissected, and a lightweight Doppler ultrasonic flow transducer was implanted. In three of these animals, a hydraulic occluder was implanted on the right coronary artery distal to the flow transducer, and ultrasonic segment length gauges were implanted in the right ventricular myocardium in the center of the region supplied by the right coronary artery to measure regional myocardial segment length. In one baboon, a flow transducer and occluder were implanted on the left circumflex coronary artery, and ultrasonic wall thickness gauges were implanted transmurally across the LV free wall in the center of the myocardium supplied by that artery to measure regional myocardial wall thickness. The myocardium supplied by the instrumented coronary artery was identified by occluding the artery for 15 seconds to create a cyanotic area before the ultrasonic crystals were implanted. Placement of the crystals also was verified visually under fluoroscopy by injection of radiopaque dye into the instrumented artery during the experiment, which illuminated the area of myocardium supplied by the coronary artery studied. In four baboons, the iliac artery was instrumented to measure the effects of ACH on iliac blood flow. In these animals, general anesthesia was induced with sodium thiopental (2 mg/kg i.v.) and halothane (0.5–1.0 vol%). With the use of sterile technique, a midline abdominal incision was made, a Doppler ultrasonic flow transducer was implanted on the iliac artery, and a heparin-filled Tygon catheter was then implanted in the terminal aorta. All transducers and catheters were tunneled to the back of the animal and buried in subcutaneous pouches. Animals used in this study were maintained in accordance with the guidelines of the Committee on Animals of Harvard Medical School and the National Institutes of Health Guide for the Care and Use of Laboratory Animals (Department of Health and Human Services Publication No. [NIH] 85-23, revised 1985).

All experiments were performed 2–6 weeks after operations, when the animals had recovered from surgery and no signs of infection were present. On the day of the experiments, the baboons in which coronary blood flow was measured were sedated with ketamine hydrochloride (8–10 mg/kg i.m.) and were placed on a fluoroscopic table; the instrumentation then was exteriorized with the use of a local anesthesia (lidocaine 2%). Lidocaine was also used to isolate either the right carotid or the right brachial artery for catheterization with a 6F guide catheter. With the use of fluoroscopic guidance, a Judkins angiographic catheter was placed in the coronary ostium of the instrumented artery. Placement of the catheter in the ostium was verified by injection of radiopaque contrast dye. Artery patency was verified by continuous monitoring of coronary blood flow. A small catheter made of PE10 tubing was inserted through the Judkins catheter into the coronary artery for intracoronary administration of pharmacological agents and measurement of coronary arterial pressure. Supplemental doses of ketamine (3–5 mg/kg i.m.) were administered throughout the duration of the protocol. At the end of the experiments, the acutely implanted catheter was removed, the carotid or brachial artery repaired, and the incision closed.

During the experiments, heart rate was held constant by atrial pacing, and doses of ACH (0.01, 0.05, 0.5, and 1.0 µg/kg) were administered through the coronary catheter. At least a 15-minute hiatus was allowed between each injection, and the responses were compared with a saline injection. The 0.5 µg/kg dose of ACH was used for further studies, because it was the largest concentration of drug that would not induce systemic effects. On separate days, the dose of 0.5 µg/kg was repeated after the administration of β- and α-adrenergic receptor blockers with propranolol (1 mg/kg i.v.) and phenolamine (2 mg/kg i.v.), respectively. Efficacy of the blockers was determined by the absence of hemodynamic effects to isoproterenol (0.2 µg/kg i.v.) and norepinephrine (0.2 µg/kg i.v.). ACH (0.5 µg/kg i.c.) was again administered after muscarinic receptor blockade with atropine (0.1 mg/kg i.v.) in the presence of α- and β-adrenergic receptor blockers. In three of the baboons, the vasoconstriction observed with ACH (0.5 µg/kg i.c.) was mimicked by use of the hydraulic coronary artery occluder to reduce coronary blood flow mechanically to the same level and for the same duration as previously observed with ACH (0.5 µg/kg i.c.). The baboons in which iliac blood flow was measured were restrained in a primate chair, and the instrumentation was exteriorized as described above. ACH (0.05, 0.5, 1.0, and 2.5 µg/kg) was administered through the terminal aortic catheter. Again, at least a 15-minute hiatus was allowed between each injec-
tion, and the responses were compared with a saline injection.

To examine the coronary responses to ACh in other species, nine calves and two dogs were instrumented for measurement of LV and aortic pressures and left circumflex coronary blood flow. With the use of general anesthesia as described above and a left thoracotomy incision, a Silastic catheter was implanted in the circumflex coronary artery, proximal to the Doppler flow transducer, for intracoronary injection of ACh (0.5 μg/kg).20 In four calves, ultrasonic wall thickness gauges were implanted on opposing surfaces of the left circumflex coronary artery to measure coronary artery diameter and also transmurally across the LV free wall in the center of the myocardium supplied by the instrumented artery to measure regional myocardial wall thickness.

In all experiments, data were recorded on a 14-channel magnetic tape recorder (Bell and Howell Co., Denver, Colo.) and monitored on a multichannel oscillograph ( Gould Instruments, Cleveland, Ohio). Coronary blood flow was measured with a Doppler ultrasonic flowmeter, which had been calibrated previously against the electromagnetic flowmeter, and was found to be linear with reliable zero flow reference.21 Mean arterial pressure and mean coronary blood flow were derived using resistance-capacitance filters with 2-second time constants. Heart rate was measured continuously with a cardiotachometer triggered by a signal from the pulsatile aortic pressure and was held constant by electrical stimulation with a Grass S9 stimulator. Coronary vascular resistance was calculated as the quotient of aortic or coronary arterial pressure and coronary blood flow. LV pressure was measured with the implanted miniature pressure gauge, which was calibrated in vitro as well as in vivo during the experiments by systolic arterial pressure and diastolic left atrial pressure sampled through the catheters and measured with Statham P23ID strain-gauge manometers (Statham Instruments, Oxnard, Calif.). LV dP/dt was derived by differentiating the LV pressure signal with an operational amplifier connected as a differentiator with a frequency response of 700 Hz. A triangular signal with known slope (rate of change) was substituted for the pressure signal to calibrate the differentiator directly. Regional myocardial wall thickening or segment length shortening and left circumflex coronary artery diameter were measured with an ultrasonic transit time dimension gauge previously described in detail.22 Late diastolic coronary blood flow and regional systolic myocardial wall thickening and segment length shortening were calculated for each beat before and throughout the reduction in coronary blood flow. These data were plotted simultaneously to determine the temporal flow-function relation.

All data are reported as mean±SEM. Because responses were biphasic, the data comparing baseline and ACH early and late responses were analyzed using Student's t test with a Bonferroni correction for multiple comparisons.23

Results

Effects of Intracoronary Acetylcholine in Baboons

Table 1 shows the effects of intracoronary ACH in baboons. With heart rate held constant, intracoronary ACH (0.01 μg/kg) elicited only an increase in coronary blood flow (Figure 1) and a decrease in coronary resistance. The higher doses of ACH induced a biphasic response, that is, intense vasoconstriction followed by vasodilation (Figure 2). There was a dose-related decrease in mean coronary blood flow and increase in late diastolic coronary resistance during the initial response to ACH (Figure 1), and a dose-related decrease in late diastolic coronary resistance and increase in mean coronary blood flow during the late responses to ACH. Intracoronary ACH (0.5 μg/kg) induced intense initial coronary vasoconstriction (i.e., coronary blood flow fell by 82±4%), with maximal vasoconstriction at 10±1 seconds, and a later vasodilation (i.e., coronary blood flow rose by 121±12%), which was maximal at 23±2 seconds. The time required for the coronary response to return to baseline was 109±13 seconds.

Table 1. Effects of Intracoronary Acetylcholine (0.5 μg/kg) in Eight Tranquilized Baboons

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Early constriction</th>
<th>Late dilation</th>
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<tbody>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>96±4.5</td>
<td>-6±2.4</td>
<td>-3±1.3</td>
</tr>
<tr>
<td>Left ventricular systolic pressure (mm Hg)</td>
<td>106±4.4</td>
<td>-4±3.3</td>
<td>0±3.7</td>
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<tr>
<td>Left ventricular dP/dt (mm Hg/sec)</td>
<td>2,513±195</td>
<td>-274±61*</td>
<td>-31±38</td>
</tr>
<tr>
<td>Mean coronary blood flow (ml/min)</td>
<td>34±3.7</td>
<td>-28±3.3*</td>
<td>+42±7.4*</td>
</tr>
<tr>
<td>Late diastolic coronary blood flow (ml/min)</td>
<td>39±4.2</td>
<td>-32±3.8*</td>
<td>+61±10.3*</td>
</tr>
<tr>
<td>Late diastolic coronary resistance (mm Hg/ml/min)</td>
<td>2.62±0.35</td>
<td>+14.28±2.91*</td>
<td>-1.59±0.21*</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>124±6</td>
<td>0±0</td>
<td>0±0</td>
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</table>

*Different from baseline, p<0.05.
Regional myocardial function was measured during the injection of intracoronary ACH (0.5 µg/kg) in three baboons. In these experiments, the fall in late diastolic coronary blood flow preceded any reduction in regional myocardial function (Figure 3). Regional myocardial function fell at a later time, clearly after blood flow was already reduced (Figure 4). In three of the baboons, coronary arterial stenoses were induced by inflation of the hydraulic occluder to mimic the ACH response (Figure 5). Coronary stenosis, which reduced coronary blood flow to the same level and for the same duration as did ACH (0.5 µg/kg), resulted in a reactive hyperemic response on release of the occluder, peaking at 25±6 seconds.

Intracoronary ACH (0.5 µg/kg) was repeated after systemic β- and α-adrenoceptor blockades in intact, tranquilized baboons (Figure 2). With heart rate held constant at 121±5 beats/min, combined β- and α-adrenoceptor blockades significantly reduced (p<0.05) baseline mean arterial pressure from 92±5 to 73±6 mm Hg and LV dp/dt from 2,513±195 to 1,429±138 mm Hg/sec, but did not significantly affect baseline coronary blood flow values. After administration of β- and α-blockades, intracoronary ACH (0.5 µg/kg) induced similar initial decreases (80±7%) and subsequent increases (140±36%) in coronary blood flow when compared with the coronary responses in the same animals without blockades. Muscarinic receptor blockade with heart rate held constant did not alter baseline coronary blood flow.

**Figure 1.** Percent changes±SEM in initial coronary blood flow responses to intracoronary acetylcholine (0.01, 0.05, 0.5, and 1.0 µg/kg) for eight tranquilized baboons. Acetylcholine induced coronary vasodilation at the lower dose but caused coronary vasoconstriction at the moderate to higher doses.

**Figure 2.** Effects of intracoronary acetylcholine (ACH) (0.5 µg/kg) on measurements of phasic and mean arterial pressures and right coronary blood flow in an intact, tranquilized baboon. In the absence of major systemic effects, ACH induced a biphasic response; during the initial phase, coronary blood flow was reduced to zero in this animal. Neither β-adrenergic receptor blockade with propranolol nor the addition of α-adrenergic receptor blockade with phentolamine eliminated the coronary constriction induced by ACH. However, the coronary constriction was abolished by muscarinic receptor blockade with atropine.

**Figure 3.** Effects of intracoronary acetylcholine (ACH) (0.5 µg/kg) on measurements of left ventricular (LV) pressure, LV dp/dt, phasic and mean arterial pressures, phasic coronary blood flow, and right ventricular (RV) segment length in a tranquilized baboon. Coronary blood flow fell substantially before any decrease in systolic segment length shortening.
Flow and hemodynamic parameters but abolished the effects of any dose of intracoronary ACH.

Effects of Intrailiac Acetylcholine in Baboons

Figure 6 shows the effects of intrailiac ACH in baboons. ACH at doses of 0.05, 0.5, 1.0, and 2.5 μg/kg administered locally through a catheter in the terminal aorta induced only vasodilation in the iliac circulation. Baseline values for iliac blood flow varied from 102±10 to 115±13 ml/min. ACH increased iliac blood flow by 107±11%, 144±12%, 161±39%, and 279±91% at doses of 0.05, 0.5, 1.0, and 2.5 μg/kg, respectively. ACH did not affect mean arterial pressure at the lower doses but decreased mean arterial pressure by 9±3% and 10±1% from baseline values of 104±6 and 107±4 mm Hg at doses of 1.0 and 2.5 μg/kg, respectively.

Hemodynamic Effects of Intracoronary Acetylcholine in Dogs and Calves

With heart rate held constant, intracoronary ACH (0.5 μg/kg) induced only coronary vasodilation in conscious dogs. Intracoronary ACH (0.5 μg/kg) in nine conscious calves induced intense coronary vasoconstriction (i.e., coronary blood flow fell by 69±4%), followed by vasodilation (i.e., coronary blood flow rose by 251±19%) (Figure 7). Beat-by-beat analysis of posterior LV wall thickening versus instantaneous coronary flow demonstrated that the decrease in coronary blood flow clearly preceded the decrease in regional ventricular function in calves (Figure 8), as was also observed in baboons (Figure 4). In four conscious calves, effects of intracoronary ACH (0.5 μg/kg) were examined on measurements

Figure 4. Beat-by-beat analysis of the effects of intracoronary acetylcholine (0.5 μg/kg) on measurements of late diastolic coronary blood flow (LDCBF) and left ventricular systolic wall thickening (SWT) in a baboon. The reduction in blood flow clearly precedes the fall in systolic wall thickening by approximately 15 seconds.

Figure 5. Effects of a brief period of coronary stenosis mimicking the initial vasoconstriction with acetylcholine on measurements of phasic and mean arterial pressures and right coronary blood flow in a tranquilized baboon. The reactive hyperemic response to the brief period of stenosis was similar to the vasodilation phase with acetylcholine (see Figure 2).

Figure 6. Effects of intrailiac administration of acetylcholine (ACH) (0.5 μg/kg) on measurements of phasic and mean arterial pressures and iliac blood flow in a conscious, intact baboon. In the absence of major systemic effects, ACH induced only vasodilation in the iliac bed.
of left circumflex coronary artery diameter. Initially, coronary diameter fell insignificantly but rose during the later phase ($p<0.05$) by $11 \pm 2\%$.

**Discussion**

Cholinergic control of the coronary circulation has been the subject of intense controversy. Initially, the controversy involved differences in results from studies in canine coronary vessels; that is, both coronary vasodilation and vasoconstriction were observed in response to cholinergic stimulation with ACH. Studies by Feigl\(^1\) clearly demonstrated that as long as the major factors that control myocardial oxygen consumption were held constant, ACH induced only coronary vasodilation in the dog. Studies in our laboratory confirmed this and extended Feigl's findings to large coronary arteries in the conscious dog.\(^5\) Experiments by Furchgott and Zawadzki\(^24\) further clarified this by demonstrating that intact endothelium was required for the vasodilator action of ACH.

**Figure 7.** Effects of intracoronary acetylcholine (ACH) (0.5 $\mu$g/kg) on measurements of left ventricular (LV) pressure, LV $dP/dt$, phasic and mean arterial pressures, phasic and mean left circumflex coronary blood flows, and heart rate in a conscious calf. In the absence of major systemic effects, ACH induced a biphasic response; that is, a decrease in coronary blood flow was followed by coronary vasodilation.

**Figure 8.** Effects of intracoronary acetylcholine (0.5 $\mu$g/kg) on measurements of late diastolic coronary blood flow (LDCBF) and left ventricular systolic wall thickening (SWT) represented as beat-by-beat response in a conscious calf. The reduction in blood flow clearly precedes the fall in systolic wall thickening.
in a variety of isolated vessel preparations. Accordingly, isolated vessels with endothelium inadvertently removed would respond differently to ACH than would vessels with endothelium intact.

The major finding of the present investigation is that ACH elicits both primary vasoconstriction and primary vasodilation in the baboon, which can be blocked completely by atropine. Coronary blood flow almost ceased at the higher doses without a significant change in heart rate and arterial pressure. This response was followed by a transient vasodilation during which blood flow rose above baseline. It could not be ascertained whether the secondary increase in blood flow was a direct effect of ACH on endothelium or was similar to a reactive hyperemic response. A very similar pattern could be elicited in the same animals during the hyperemic phase after release from a stenosis, which mimicked the constriction induced by ACH (Figure 5).

A potent vasoconstrictor response to ACH was observed at the moderate to higher doses in the coronary circulation. However, at the lowest dose, only coronary vasodilation was observed. In the iliac bed of the baboon, only vasodilation was observed with ACH at any dose studied. These differences in response to the higher doses in the coronary and iliac circulation and the differences between the higher and lower doses in the coronary circulation may reconcile some of the discrepancies reported by prior studies. Prior studies in anesthetized primates have reported both vasoconstriction and vasodilation, and prior studies in humans without atherosclerosis have also reported both vasoconstriction and vasodilation. It is conceivable that some of these differences among prior studies in primates, including humans, could be attributed to the dual action of ACH observed in the present study, as well as to the dose of ACH used. Most of the prior work in the field of endothelial vascular control has concentrated on large conductance vessels. More recently, increasing evidence suggests that endothelial mediated vasodilation also plays an important role in regulating resistance vessel caliber. Assuming that ACH vasodilation is mediated by endothelial mechanisms, the results of the current study suggest that in primates, endothelial control of resistance coronary vessels, as opposed to peripheral vessels in the limb, can be overpowered by direct vasoconstrictor effects of ACH at increasing concentrations. The recent study by Newman et al. also clearly demonstrates the importance of ACH concentration in determining whether coronary vasodilation or vasoconstriction is observed in humans.

When the effects of any intervention on the coronary circulation are examined, it is important to know if the changes in coronary blood flow are primary or secondary to changes in myocardial oxygen demands. The major determinants of myocardial oxygen consumption are heart rate, LV contractility, and afterload. Major changes in these parameters were not observed with ACH in the present investigation. However, it was considered that a local change in myocardial contractility could be missed by the measurements of global LV pressure and LV dP/dt. Accordingly, in a subset of animals, regional myocardial function was measured in the distribution of the coronary artery receiving the ACH. In all experiments, it was demonstrated clearly that coronary constriction occurred before the decrease in regional function. These two observations—that the initial ACH vasoconstriction essentially shut off coronary blood flow and that the decrease in coronary blood flow clearly preceded any decreases in regional ventricular function—indicate that the coronary vasoconstrictor effects were primary and not simply secondary to changes in myocardial oxygen demand.

Part of the controversy regarding the effects of ACH in the coronary circulation is due to differences in species studied. As mentioned above and confirmed in the present study only, coronary vasodilation is observed in normal canine coronary vessels with intact endothelium. However, in the conscious calf, both early vasoconstriction and later vasodilation were observed. In comparison with studies in the baboon, the vasoconstrictor phase in the calf was more transient, and the vasodilator phase was more intense and prolonged. A pattern intermediate between calf and baboon was recently observed in the coronary circulation of the pig. It is interesting to speculate that different subtypes of muscarinic receptors, which have been shown to be involved in mediating responses to ACH, may vary among species and in different beds within a species and could be responsible for these qualitative differences.

In several studies in normal human subjects and in isolated vessel experiments, ACH has been shown to constrict large coronary arteries. It was not determined in the present investigation whether ACH exerts its vasoconstrictor effects at the level of the small resistance vessels or at the level of larger coronary arteries. However, in selected instances, intracoronary injections of ACH were flushed with contrast media instead of saline, and no vasoconstriction of the larger coronary arteries was observed fluoroscopically. Although coronary dimensions were not quantitated, spasm of the large coronary arteries sufficient to reduce blood flow by an average of 82% was not observed. Furthermore, in a subset of calves studied, large coronary artery diameters were measured. In these experiments, only slight initial vasoconstriction was observed, followed by prolonged and more intense later vasodilation. The trivial vasoconstriction of the large coronary arteries occurred in the face of intense resistance vessel constriction, which in turn preceded any change in regional function in the portion of the left ventricle supplied by the coronary artery in which ACH was injected.

In summary, the extent to which ACH induces vasodilation or vasoconstriction depends not only on whether endothelium is intact, but also on the spe-
cies, ACH concentration, and vascular bed being studied. The primary action of ACH in the baboon was constriction in the coronary bed at higher doses and vasodilation at lower doses. This might be explained by an endothelial mediated vasodilation, which is revealed at lower doses but is overpowered by a direct smooth muscle vasconstrictor effect at higher concentrations. This dual coronary vascular action of ACH may help reconcile some of the controversy in this field.

References

KEY WORDS • cholinergic vasoconstriction • primate species • coronary blood flow • regional myocardial function
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