venous injection of agonists or antagonists of α -adrenoceptor subtypes in anesthetized open-chest dogs.

For this purpose, total spinal anesthesia was performed and mean arterial pressure was maintained at about 80 mmHg by continuous intravenous infusion of epinephrine. The measurement of MCP was made before and after intravenous injection of phenylephrine (PHE, 10 μ g/Kg, α_1 -agonist), prazosin (PRA, 150 μ g/Kg, α_1 -antagonist), BHT 920 (BHT, 5 μ g/Kg, α_2 -agonist) or yohimbine (YOH, 30 μ g/Kg, α_2 -antagonist), in one minute, and the response of MCP to these agonists and antagonists were obtained.

1) PHE (α_1 -agonist) increased MCP from 10.0 $\pm$ 0.4 mmHg (mean $\pm$ SE) to 10.9 $\pm$ 0.4 mmHg (N=6).

2) PRA (α_1 -antagonist) decreased MCP from 10.0 $\pm$ 0.5 mmHg to 8.5 $\pm$ 0.7 mmHg (N=5).

3) After pretreatment with PRA (α_1 -antagonist), MCP increasing action of PHE (α_1 -agonist) was blocked. MCP before pretreatment with PRA was 9.3 $\pm$ 0.4 mmHg and MCP after PRA+PHE was 7.7 $\pm$ 0.3 mmHg (N=5).

4) BHT (α_2 -agonist) increased MCP from 9.0 $\pm$ 0.3 mmHg to 10.1 $\pm$ 0.3 mmHg (N=6).

5) YOH (α_2 -antagonist) decreased MCP from 9.8 $\pm$ 0.2 mmHg to 7.7 $\pm$ 0.3 mmHg (N=5).

6) Pretreatment with YOH (α_2 -antagonist) caused MCP increasing action of BHT (α_2 -agonist) to be eliminated. MCP before YOH was 9.6 $\pm$ 0.4 mmHg and MCP after YOH+BHT was 8.3 $\pm$ 0.5 mmHg (N=5).

It is thus suggested that α_1 -adrenoceptor subtype is present in the systemic capacitance vessels (results 1, 2 and 3) and α_2 -adrenoceptor subtype is also present in the systemic capacitance vessels (results 4, 5 and 6). Furthermore it is suggested that both α_1 - and α_2 -adrenoceptor are acting in the direction of constricting the systemic capacitance vessels.

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CHARACTERISTICS OF CORONARY ADRENOCEPTORS

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The characteristics of the porcine coronary adrenoceptors were investigated and compared with those of the porcine aorta. [3 H](-)-dihydroalprenolol ([3 H]DHA) and [3 H]prazosin binding to sarcolemmal fractions from porcine coronary artery (CA) and aorta (AO) were used. In the binding isotherms, there were no major differences in the K_d values of these two radioligands between CA and AO. However, the B_{max} values of [3 H]DHA for CA and AO were 258 and 37 fmol/mg protein, respectively and those of [3 H]prazosin were 12 and 525 fmol/mg protein, respectively. β -Adrenergic agonists competed with [3 H]DHA binding sites in CA, with the order of potency of (-)-isoproterenol (IP) > (-)-norepinephrine (NE) > (-)-epinephrine (EP) > (+)IP. In case of AO, the potency order was (-)IP > (-)EP > (-)NE. The K_i value of ($\pm$)bisoprolol, a highly β_1 -selective antagonist, for coronary β -receptors (35 nM) was 56 times lower than that for AO (2000 nM). From these results, we concluded that; 1) α_1 - and β -adrenoceptors are present in porcine vascular smooth muscle cells, 2) β -receptors of CA are predominantly of the β_1 -type, while those of AO are of the β_2 -type, 3) as to the relative population of the adrenoceptors, CA is β -dominant ($\beta/\alpha_1=22$), while AO is α_1 -dominant ($\beta/\alpha_1=0.07$). The predominance of β -adrenoceptors and their relatively high affinity for NE (because they are of the β_1 -type) may account for the weak contraction, or relaxation, of the CA induced by NE, reported by other investigators in the

experiments dealing with the responses of isolated coronary strips.

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DUAL CONTROL OF MAXIMAL CORONARY VASODILATORY EFFECTS OF ADENOSINE BY α_1 -ADRENOCEPTOR STIMULATION

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Potent α_1 -adrenoceptor stimulation elicits coronary vasoconstriction. To test the hypothesis that moderate α_2 -stimulation inversely augments the coronary vasodilatory effect of adenosine, 23 dogs were studied. The left anterior descending coronary arterial flow (CBF) was measured during maximal coronary vasodilation with adenosine under α_1 - and α_2 -stimulation. To stimulate α_1 -adrenoceptors, norepinephrine (NE) was infused at the dose from 0.03 μ g/kg/min to 0.6 μ g/kg/min under pretreatments (PT) of prazosin and propranolol, and for α_2 -adrenoceptor stimulation same doses of NE were infused under PT of yohimbine and propranolol. Changes in CBF (ml/100g/min) during infusions of adenosine under α_1 - and α_2 -stimulations were:

	UN	PT	Ado	NE/0.24	0.48	0.6
α_1 -	91 $\pm$ 2	91 $\pm$ 2	340 $\pm$ 9	401 $\pm$ 17 [#]	306 $\pm$ 25*	218 $\pm$ 19 [#]
α_2 -	93 $\pm$ 2	94 $\pm$ 2	267 $\pm$ 14	236 $\pm$ 18 [#]	208 $\pm$ 18 [#]	204 $\pm$ 19 [#]

UN=untreated Ado=adenosine NE: μ g/100g/min Mean $\pm$ SE

* P <0.05 and [#] P <0.01 vs each value of PT with Ado
Without adenosine infusion, NE decreased baseline CBF dose-dependently. On the other hand, moderate/potent α_2 -attenuation reduced/augmented the maximal coronary blood flow. These results indicate that adenosine-induced maximal coronary vasodilation is still regulated by α_2 -adrenoceptor activity in a dual fashion: Moderate α_2 -stimulation augmented maximal vasodilation whereas potent α_2 -stimulation reduced maximal vasodilation. This dual effect may play a pivotal role in the regulation of CBF during exercise or myocardial ischemia wherein the sympathetic activity and adenosine release are enhanced.

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EFFECTS OF A NOVEL COMPOUND, Y-19638 HAVING ANTICHOLINERGIC AND CALCIUM BLOCKING ACTIONS ON ISOLATED HUMAN CORONARY ARTERY

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Methyl 3-diethylaminomethyl-7-methyl-5-(3-nitrophenyl)-5,8-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate hydrochloride (Y-19638) is a newly synthesized compound having anticholinergic and calcium channel blocking effects. We evaluated the effects of this compound on the isolated human coronary artery in comparison with these of nitrendipine and atropine. The proximal portions