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Forearm Venous Responses to Stimulation of Adrenergic Receptors *

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The properties of the adrenergic receptors in the veins or capacitance vessels of man have not been defined completely. Norepinephrine causes constriction of resistance vessels by stimulation of alpha receptors (2); it also causes constriction of the veins or capacitance vessels (3–5). Isoproterenol causes dilatation of resistance vessels by stimulation of beta receptors (6), but reports of its action on the capacitance vessels are conflicting. It appears to cause forearm venous constriction when administered systemically (7), but dilatation is said to occur with infusion into the brachial artery (8). The experiments to be reported here were done to investigate the effects of stimulation of alpha and beta receptors in the veins of the forearm of man in a systematic fashion.

Methods

The subjects were healthy male volunteers ranging in age from 21 to 27 years. They were studied while lying in the supine position. Drugs that stimulate or block adrenergic receptors were infused or injected through polyethylene tubes inserted into the left brachial artery or into a systemic vein. Forearm blood flow and venous distensibility were measured in the left forearm with a water plethysmograph. In some experiments, transmural venous pressure was recorded through polyethylene tubes inserted into superficial veins in the segment of forearm enclosed in the plethysmograph. Arterial pressure was recorded intermittently through a three-way stopcock connected to the tube in the brachial artery with Sanborn or Statham pressure transducers. Heart rate was obtained by counting pulses on the arterial pressure tracing. Water level in the plethysmograph was measured electrically (9). Pressures and water level were recorded with a Sanborn direct-writing oscillograph.

The plethysmographic method for measuring venous distensibility has been described previously (7, 10, 11). Only a brief description is included here. To make the measurement, the forearm is enclosed in a plethysmograph, and water is added so that the pressure it exerts on the arm is greater than venous pressure but less than diastolic arterial pressure. The arterial inflow drives the pressure within the veins to a level slightly greater than the external water pressure. The difference between the pressure within the veins and the water pressure surrounding them is the distending or transmural pressure. Transmural pressure was measured in superficial forearm veins in many of the experiments reported here and in many other experiments by placing the reference level of the pressure transducer at the level of the surface of the water in the plethysmograph. Under resting conditions and under the circumstances described here, transmural pressure is low. It ranges from about 0.5 to 2.0 mm Hg, and it is constant and reproducible in a given subject. The volume of blood in the vessels of the extremity at this low transmural pressure is about 1.3 ml per 100 ml of tissue (12). Under resting conditions, this volume also is constant and reproducible in a given subject; it is called the "base-line" volume. Increases in volume in response to congestion of the extremity take place primarily in vessels whose resting pressures are less than 10 mm Hg (12). Venous pressure-volume curves may be obtained by increasing transmural pressure in a stepwise fashion to 30 mm Hg by inflating a cuff on the arm proximal to the plethysmograph and recording the associated changes in forearm volume (Figure 1). In previous work using this method, curves were constructed by plotting each level of volume in ml per 100 ml of forearm against its corresponding level of transmural pressure. In most of the experiments reported here, transmural pressure was increased to 30 mm Hg by a single inflation of the cuff. Pressure was then held constant until forearm volume became stable or was increasing at only a negligible rate. The volume at a transmural pressure of 30 mm Hg is the same with stepwise or

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TABLE I

*Forearm responses to infusions of isoproterenol into the brachial artery**

Subject	Dose of isoproterenol	C	LD		HD	
		VD	ΔBF	VD	ΔBF	VD
	μg/min	*ml/100 ml*		*ml/100 ml*		*ml/100 ml*
C. J.	0.10–0.20	4.7	↑	4.7	↑	4.6
D. G.	0.15–0.30	4.8	↑	5.2	↑	5.0
D. L.	0.15–0.30	4.3	↑	4.1	↑	4.0
S. D.	0.15–0.30	4.9	↑	5.3	↑	5.6
D. K.	0.15–0.30	4.8	↑	4.8	↑	5.0
J. H.	0.15–0.30	5.1	↑	5.1	↑	5.1
D. S.	0.15–0.30	4.8	↑	4.8	↑	4.8
D. H.	0.15–0.30	4.6	↑	4.7	↑	5.4
G. C.	0.30–0.60	3.9	↑	3.7	↑	3.7
R. M.	0.40–0.80	4.9	↑	4.9	↑	4.6
T. H.	0.60–1.20	4.2	↑	4.0	↑	4.0
V. R.	0.60–1.20	5.2	↑	5.2	↑	5.4
M. R.	0.60–1.20	4.8	↑	4.7	↑	4.8
B. R.	0.60–1.20	2.7	↑	2.7	↑	2.6
Mean		4.55		4.56		4.61
Mean difference from C				0.01		0.06
SE				0.05		0.09
p				>0.8		>0.5

* C refers to control observations. LD refers to observations made at the low dose of isoproterenol, and HD refers to observations made at the high dose of isoproterenol. VD is the forearm venous volume at a transmural venous pressure of 30 mm Hg. ΔBF indicates the direction of change in forearm blood flow from the control during infusion of isoproterenol; ↑ indicates an increase, → indicates no change, and ↓ indicates a decrease.

single inflation of the cuff provided the congesting pressure is held constant until the volume of the forearm is no longer changing. The values for venous distensibility reported in the tables are stable volumes present at a transmural pressure of 30 mm Hg. A decrease in this volume indicates reduced distensibility or constriction; an increase indicates increased distensibility or dilatation.

In using this method for measuring venous distensibility, it is necessary in the resting or control state to be sure that external water pressure on the arm is greater than the natural venous pressure; it is desirable, but not absolutely necessary, to have the water pressure higher than any level of venous pressure that might be reached during an intervention. In human subjects, injections of norepinephrine into the brachial artery have caused pressure in small veins of the hand (veins about 1 mm in diameter) to rise to 20 mm Hg (13). Systemic infusions of norepinephrine in doses in excess of those used in the experiments reported here have caused small vein pressure to rise to 16 mm Hg (14). Because of the possibility that small vein pressures might rise to levels approaching 20 mm Hg with the interventions which we employed, we placed the lower surface of the arm in the plethysmograph at the level of the right atrium and added water so that the pressure it exerted on the upper surfaces of the arm was at least 20 mm Hg. In addition to this, we observed the base-line volume continuously before and during drug infusions (Figure 1). An increase in base-line volume would indicate that pressure in some of the veins had risen above water level. Base-line volume did increase with intra-arterial infusions of isoproterenol (Figure 1). This usually was transient; it was attributed to the initial surge of blood into the veins as flow increased suddenly. In most cases, base-line volume returned to the original level before the congesting cuff was inflated. Occasionally, the base-line volume remained slightly elevated. This did not require a correction because the value with which we were concerned was the forearm volume, at 30 mm Hg transmural venous pressure, measured with reference to the control or resting volume. A change in base-line volume because of an increase in pressure in small veins would have no effect on the volume at a transmural pressure of 30 mm Hg unless intraluminal pressure reached heights greater than 30 mm Hg above the water. Since water pressure was at least 20 mm Hg, intraluminal pressure would have to have risen to more than 50 mm Hg without the knowledge of the observer to have caused an error in the measurement of the venous responses.

The initial slope of the volume record as the veins fill is an index of the rate of blood flow into the forearm (Figure 1). Mean arterial pressure did not change in the experiments in which drugs were infused into the brachial artery. With pressure constant, increases or decreases in flow indicate dilatation or constriction of resistance

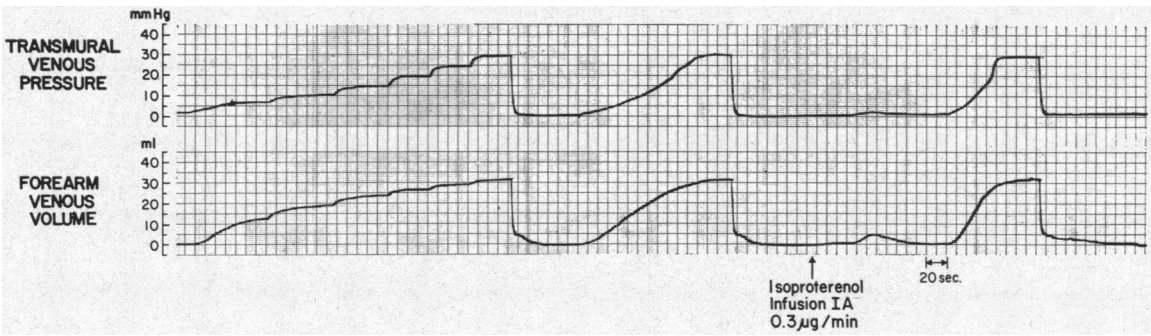

FIG. 1. PRESSURE-VOLUME CURVES FROM FOREARM VEINS BEFORE AND DURING INTRA-ARTERIAL IA INFUSION OF ISOPROTERENOL. In this experiment, the external water pressure on the arm was about 20 mm Hg. Transmural venous pressure was measured in a superficial vein in the segment of forearm enclosed in the plethysmograph. The reference level of the manometer corresponded to the level of water in the plethysmograph. Transmural pressure (upper left tracing) was increased in increments by inflating the cuff on the arm proximal to the plethysmograph. The changes in forearm volume from the "base line" (see text) are recorded on the lower graph. To obtain the middle set of pressure and volume tracings, transmural pressure was increased to 30 mm Hg with a single inflation of the cuff. The arrow indicates the beginning of the isoproterenol infusion. For the right-hand tracing, transmural pressure was increased again to 30 mm Hg with a single inflation of the cuff. The increased slope of the volume record during infusion of isoproterenol indicates an increase in the rate of blood flow into the forearm. The same forearm venous volume at the same transmural pressure before and during infusion of isoproterenol indicates no change in venous distensibility (see text).

vessels. The plethysmographic method, therefore, provided information concerning the effects of the stimuli on both resistance and capacitance vessels simultaneously in the same segment of forearm.

Transmural pressure in the forearm veins was measured as the difference between the pressure within the veins and the pressure surrounding them. This was done by placing the reference level of the venous pressure transducer at the level of the surface of the water in the vertical cylinder attached to the top of the plethysmograph. The diameter of the cylinder was large so that maximal volume increases in the forearm raised water level only a few millimeters. The error introduced by this change in water level was so small that no correction was made for it.

The actual rate of blood flow into the forearm was not calculated. Directional changes were determined from changes in the slope of the volume record and are identified in the tables by arrows. Statistical comparisons of venous responses were made by the paired *t* test (15).

The drugs employed in these experiments were *dl*-isoproterenol hydrochloride, *l*-epinephrine chloride, *l*-norepinephrine bitartrate, phentolamine methanesulfonate, and nethalide.[1] The dose of norepinephrine is given in terms of the base. The doses of all other agents are expressed in terms of their salts. All drugs were diluted in 5% glucose in water and infused at room temperature. Infusion rates were 1.2 and 2.4 ml per minute. No measurable changes in forearm blood flow or venous distensibility were observed when 5% glucose was infused into the brachial artery at these rates.

[1] Nethalide was supplied by Ayerst Laboratories, New York, N. Y., as Ay 6204.

Results

Forearm vascular responses to infusions of isoproterenol into the brachial artery. Observations on forearm venous distensibility and blood flow were made in 14 subjects before and during infusions of isoproterenol hydrochloride into the brachial artery. Two doses of isoproterenol were given to each subject (Table I). The venous collecting cuff was inflated at the end of the second minute of infusion. One to 4 minutes was required for transmural pressure to reach 30 mm Hg. Transmural pressure was held at this level until forearm volume became constant or was changing at only a negligible rate. The infusion was then discontinued, and a rest period of 10 minutes was allowed before the next infusion was started.

No measurable systemic effects were noted during isoproterenol infusions except in four subjects who had slight increases in heart rate and some widening of pulse pressure at an infusion rate of 1.2 μg per minute. Blood flow increased with each infusion in each experiment (Table I, Figure 1) indicating dilatation in resistance vessels.

TABLE II

*Forearm responses to infusion of isoproterenol into the brachial artery**

Subject	Dose of isoproterenol	Before adrenergic blockade			After nethalide			After phentolamine		
		C	I		C	I		C	I	
		VD	ΔBF	VD	VD	ΔBF	VD	VD	ΔBF	VD
	μg/min	*ml/100 ml*		*ml/100 ml*	*ml/100 ml*		*ml/100 ml*	*ml/100 ml*		*ml/100 ml*
G. C.	0.60	3.9	↑	3.7	3.6	→	3.7	3.7	↑	3.7
R. M.	0.80	4.9	↑	4.6	4.8	→	4.7	4.9	↑	5.0
T. H.	1.20	4.2	↑	4.0	4.3	→	4.0	4.3	↑	4.0
V. R.	1.20	5.2	↑	5.4	5.2	→	5.3	5.1	↑	5.1
M. R.	1.20	4.8	↑	4.8	4.4	→	4.2	4.6	↑	4.5
Mean		4.60		4.50	4.46		4.38	4.52		4.46
Mean difference from C				−0.10			−0.08			−0.06
SE				0.09			0.08			0.07
p				>0.3			>0.3			>0.4

* For abbreviations and symbols see footnote to Table I. I refers to observations made during infusion of isoproterenol.

The isoproterenol infusions caused no significant change in venous distensibility.

Five of the 14 subjects received an intrabrachial infusion of 15 mg of nethalide, a beta receptor blocking agent (16). Control observations were repeated 3 minutes later. Then isoproterenol was infused at the higher of the two doses given previously. Nethalide blocked the dilator effect of isoproterenol on resistance vessels, but had no effect on the venous responses (Table II, Figure 2).

One mg of phentolamine, a drug known to block alpha receptors in resistance vessels (17), was injected into the brachial artery of the same five subjects after the blocking effect of nethalide on resistance vessels had disappeared. Control observations were repeated 3 minutes later. Then isoproterenol was reinfused at the higher dose. Phentolamine did not block the effect of isoproterenol on the resistance vessels, nor did it alter the response of the capacitance vessels (Table II).

Forearm vascular responses to infusions of isoproterenol into the brachial artery during intravenous infusion of norepinephrine. Five subjects

TABLE III

*Forearm responses to infusion of isoproterenol into the brachial artery during intravenous infusions of norepinephrine**

Subject	Dose of isoproterenol	Dose of norepinephrine	C	I		NE		NE+I	
			VD	ΔBF	VD	ΔBF	VD	ΔBF	VD
	μg/min	*μg/kg/min*	*ml/100 ml*		*ml/100 ml*		*ml/100 ml*		*ml/100 ml*
S. D.	0.3	0.2	5.1	↑	5.2	↓	3.8	↑	3.8
T. A.	0.3	0.2	5.0	↑	5.2	↓	4.1	↑	3.3
W. W.	0.6	0.2	5.4	↑	5.3	↓	3.6	↑	2.7
D. L.	0.6	0.1	3.8	↑	3.9	↓	3.2	↑	3.2
D. G.	0.6	0.2	5.0	↑	5.3	↓	3.7	↑	2.0
Mean			4.86		4.98		3.68		3.00
Mean difference					−0.12†		−1.34‡		−0.68§
SE					0.07		0.19		0.32
p					>0.1		<0.01		>0.1

* See footnote to Table I. I refers to observations made during infusion of isoproterenol into the brachial artery. NE refers to observations made during intravenous infusion of norepinephrine. NE+I refers to observations made during simultaneous infusions of isoproterenol into the brachial artery and norepinephrine into a systemic vein.

† Mean difference from C.

‡ Mean difference from I.

§ Mean difference from NE.

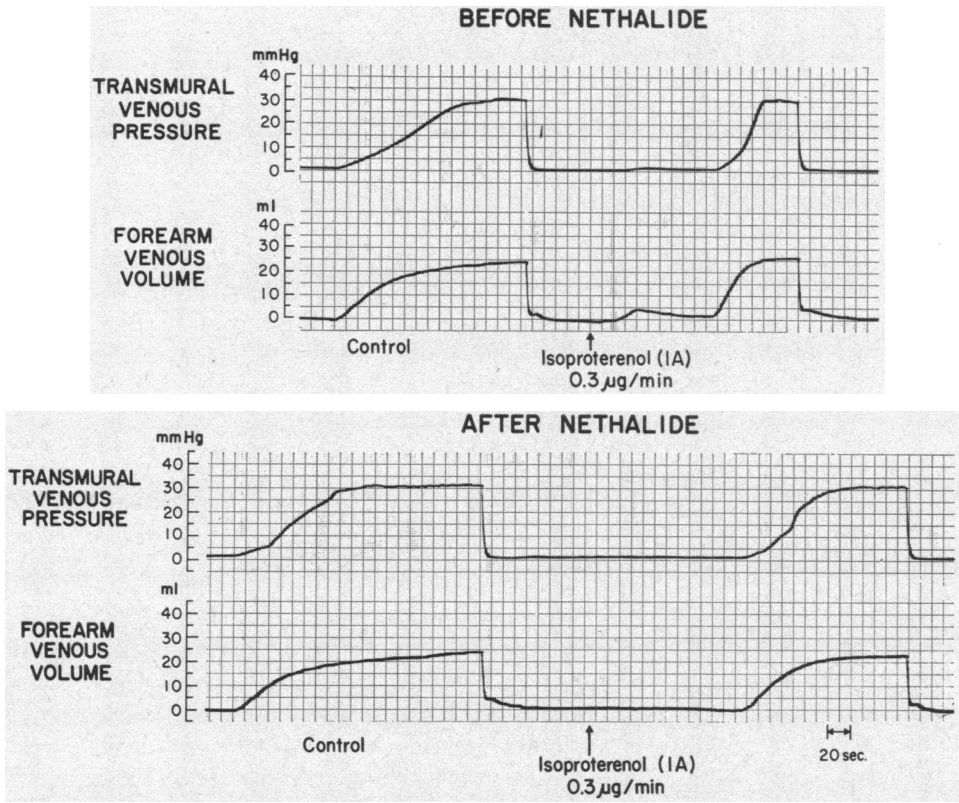

FIG. 2. EFFECTS OF ISOPROTERENOL BEFORE AND AFTER INFUSION OF NETHALIDE INTO THE BRACHIAL ARTERY. Before nethalide (upper panel) isoproterenol caused an increase in forearm blood flow and no change in venous distensibility (see legend for Figure 1). Nethalide (lower panel) blocked the increase in blood flow, but had no appreciable effect on the response of the veins.

received infusions of isoproterenol into the brachial artery as in the first group of experiments. Blood flow increased in response to the isoproterenol, but again there were no changes in venous distensibility (Table III). Norepinephrine bitartrate in doses of 0.1 or 0.2 µg of norepinephrine base per kg per minute was then infused into a systemic vein, and observations were made again at the end of 5 minutes. There were increases in mean arterial pressure that averaged 12 mm Hg and decreases in heart rate that averaged 9 beats per minute. Forearm blood flow and venous distensibility decreased in each instance (Table III). The norepinephrine infusion was continued, and isoproterenol was reinfused into the brachial artery. Observations were made again at the end of 2 minutes of infusion of isoproterenol. In each case isoproterenol caused an increase in blood flow indicating that it antagonized the constrictor effect of the norepinephrine on the resistance vessels. There was no increase in venous distensibility indicating no antagonism of the constrictor effect on capacitance vessels (Table III).

Forearm vascular responses to infusions of epinephrine into the brachial artery. Observations on forearm venous distensibility and blood flow were made in six subjects before and during infusions of epinephrine hydrochloride into the brachial artery. Two doses of epinephrine were given to each subject (Table IV). The venous collecting cuff was inflated at the end of the second minute of infusion. Forearm volume was allowed to stabilize at a transmural venous pressure of 30 mm Hg. The cuff was then deflated and the infusion was discontinued. Venous distensibility and blood flow were allowed to return to control levels before the next infusion was started.

No measurable systemic effects of epinephrine

TABLE IV

*Forearm responses to infusions of epinephrine into the brachial artery**

Subject	Dose of epinephrine	C	LD		HD	
		VD	ΔBF	VD	ΔBF	VD
	μg/min	*ml/100 ml*		*ml/100 ml*		*ml/100 ml*
T. H.	0.0625–0.125	4.2	↓	3.4	↓	3.2
V. R.	0.0625–0.125	5.3	↓	4.7	↓	4.3
R. M.	0.125 –0.25	4.4	↓	3.6	↓	3.2
C. J.	0.125 –0.25	4.7	↓	3.9	↓	3.1
M. R.	0.125 –0.25	4.8	→	4.1	↓	3.1
D. S.	0.125 –0.25	4.7	↓	4.0	↓	3.1
Mean		4.68		3.95		3.33
Mean difference from C				−0.73		−1.35
SE				0.03		0.13
p				<0.001		<0.001

* See footnote to Table I.

were noted during the infusions. Blood flow decreased in five of the six experiments with the low dose of epinephrine and in all six with the high dose, indicating constriction of resistance vessels. Venous constriction occurred with each infusion. The degree of constriction was greater with the larger dose (Table IV).

Five of the six subjects received an intrabrachial infusion of 15 mg of nethalide. Control observations were repeated 3 minutes later. Then epinephrine was reinfused at the higher of the two doses given previously. Nethalide had no apparent effect on the blood flow response and no significant effect on the venous response to epinephrine (Table V).

One mg of phentolamine was injected into the brachial artery of the same five subjects. Control measurements were made 3 minutes later. Then epinephrine was reinfused at the higher dose. In this case phentolamine blocked or reversed the blood flow response; the venous response was blocked but not reversed (Table V).

Forearm vascular responses to intravenous infusions of isoproterenol before and after intra-arterial administration of phentolamine. Observations were made in six subjects at the end of 3 minutes of infusion of 5.8 μg of isoproterenol per minute into a systemic vein. Heart rate increased and mean blood pressure fell in each subject. The average increase in heart rate during

TABLE V

*Forearm responses to infusions of epinephrine into the brachial artery**

Subject	Dose of epinephrine	Before adrenergic blockade			After nethalide			After phentolamine		
		C	E		C	E		C	E	
		VD	ΔBF	VD	VD	ΔBF	VD	VD	ΔBF	VD
	μg/min	*ml/100 ml*		*ml/100 ml*	*ml/100 ml*		*ml/100 ml*	*ml/100 ml*		*ml/100 m*
T. H.	0.125	4.2	↓	3.2	4.3	↓	2.9	4.3	↑	4.3
V. R.	0.125	5.3	↓	4.3	5.3	↓	4.7	5.1	→	5.1
R. M.	0.25	4.4	↓	3.2	4.7	↓	3.3	4.9	→	4.4
C. J.	0.25	4.7	↓	3.1	4.5	↓	3.2	4.1	↑	4.2
M. R.	0.25	4.8	↓	3.1	4.4	↓	3.4	4.6	↑	4.3
Mean		4.68		3.38	4.64		3.50	4.60		4.46
Mean difference from C				−1.30			−1.14			−0.14
SE				0.15			0.15			0.11
p				<0.001			<0.01			>0.2

* See footnote to Table I. E refers to observations made during infusion of epinephrine.

TABLE VI

*Forearm responses to intravenous infusions of isoproterenol before and after intra-arterial administration of phentolamine**

Subject	Dose of isoproterenol	Before phentolamine			After phentolamine		
		C	I		C	I	
		VD	ΔBF	VD	VD	ΔBF	VD
	μg/min	*ml/100 ml*		*ml/100 ml*	*ml/100 ml*		*ml/100 ml*
J. H.	5.8	5.0	↑	4.0	4.9	↑	4.9
S. K.	5.8	5.1	↑	4.4	4.7	↑	4.7
D. K.	5.8	4.5	↑	4.1	4.6	↑	4.8
D. B.	5.8	4.2	↑	3.7	4.2	↑	4.1
F. B.	5.8	5.2	↑	4.1	5.1	↑	5.1
T. A.	5.8	5.1	↑	4.8	5.1	↑	5.3
Mean		4.85		4.18	4.76		4.82
Mean difference from C				−0.67			0.06
SE				0.13			0.05
p				<0.01			>0.3

* See footnotes to Tables I and II.

the infusion was 36 beats per minute; the average fall in mean arterial pressure was 7 mm Hg. Forearm blood flow increased and venous distensibility decreased in each experiment (Table VI).

The infusion of isoproterenol was repeated in each subject 5 minutes after injection of 1.0 mg of phentolamine into the left brachial artery. Isoproterenol caused changes in mean blood pressure, heart rate, and forearm blood flow that were similar to those seen before phentolamine. The decrease in venous distensibility in the left forearm, however, was blocked completely by the phentolamine (Table VI).

Discussion

Others have shown that infusions of norepinephrine into the brachial artery cause constriction of resistance vessels in the forearm, that infusions of epinephrine cause dilatation which is followed by constriction, and that infusions of isoproterenol cause only dilatation (18–20). According to Ahlquist, constriction results from stimulation of alpha adrenergic receptors in vascular smooth muscle, whereas dilatation results from stimulation of beta receptors (17, 21). Drugs, such as phentolamine or phenoxybenzamine, that block alpha receptors antagonize the constrictor actions of norepinephrine and epinephrine; they enhance the dilator action of epinephrine and have no effect on the dilator action of isoproterenol (2, 22). Drugs, such as nethalide, that block beta receptors antagonize the dilator actions of both epinephrine and isoproterenol (6). These reports show that norepinephrine stimulates alpha receptors, that isoproterenol stimulates beta receptors, and that epinephrine stimulates both alpha and beta receptors in resistance vessels (6, 22). The pharmacology of the adrenergic receptors in the veins or capacitance vessels is less well understood.

Norepinephrine and epinephrine are known to cause forearm venous constriction, but neither appears to cause dilatation (3–5). The venous constriction that occurs in response to systemic infusion of these agents has been blocked by systemic administration of phentolamine (3), suggesting that the constriction results from stimulation of alpha receptors. In these experiments, however, both agonist and antagonist were administered systemically, leaving the question of the direct effects of epinephrine and norepinephrine on forearm veins unanswered. Systemic infusions of isoproterenol in large doses have caused forearm venous constriction (7), but this response does not necessarily represent a direct effect on the veins of the forearm. The conclusion that slight venous dilatation occurs with injection into the brachial artery was qualified and based on a limited amount of data (8).

In 14 experiments reported here, isoproterenol was infused directly into the brachial artery. A

wide range of doses was employed. In each instance, the resistance vessels dilated, but no change in venous distensibility was observed. The absence of a response despite the wide range of doses suggests that venous smooth muscle in the forearm is not stimulated by isoproterenol. The possibility was considered, however, that isoproterenol might stimulate both constrictor and dilator receptors equally. A dual action does occur in resistance vessels with epinephrine. Simultaneous and equal stimulation of both dilator and constrictor receptors, although unlikely, could explain the absence of a response. For this reason, isoproterenol was infused before and after blockade of beta receptors with nethalide and before and after blockade of alpha receptors with phentolamine. Neither agent unmasked a venous response even though nethalide blocked the dilator action on the resistance vessels.

Another possibility which was considered was that isoproterenol stimulates dilator receptors in the forearm veins but that dilatation could not occur in these experiments because the veins of the warm, comfortable, supine subjects were maximally dilated in the control state. To test this possibility, norepinephrine was administered by systemic intravenous infusion in a dose sufficient to cause constriction of both resistance and capacitance vessels. Isoproterenol was then infused into the brachial artery. In each instance, isoproterenol reversed the constriction in the resistance vessels, but did not diminish the constriction of the capacitance vessels, providing further evidence that the veins do not respond to stimulation with isoproterenol.

Epinephrine also was infused into the brachial artery in a wide range of doses. The initial increase in blood flow that is known to occur (18, 19) was seen, but it was replaced by constriction of resistance vessels by the time venous distensibility was measured. Epinephrine caused constriction of both resistance and capacitance vessels that was not altered by nethalide. Phentolamine, however, blocked or reversed the constriction of resistance vessels; it blocked completely but did not reverse the venous response. These experiments are consistent with other reported observations showing that epinephrine stimulates both alpha and beta receptors in resistance vessels (6, 22); they show, in addition, that epinephrine stimulates only alpha receptors in capacitance vessels.

A previous report (7) from this laboratory described forearm venous constriction with systemic administration of large doses of isoproterenol (5.8 μg per minute). This could have been a reflex effect possibly triggered by widespread vasodilatation or by some other systemic event. These experiments were repeated in connection with the present series. The results were the same; a decrease in venous distensibility occurred in each experiment. This response was associated with decreases in mean arterial pressure and increases in heart rate. It was not seen in four experiments in which isoproterenol was infused at a lower dose (1.2 μg per minute) that did not cause symptoms and produced only slight changes in arterial pressure and heart rate. It was not seen in two subjects in whom the systemic effects of the isoproterenol were blocked by 70 mg of nethalide. In each experiment, intra-arterial phentolamine blocked the forearm venous constriction induced by systemic administration of isoproterenol. The results of this group of experiments indicate that the venoconstrictor effect of large systemic doses of isoproterenol is of reflex origin, possibly related to the fall in mean arterial pressure, and mediated by alpha receptors.

Summary

The capacitance vessels of the forearm apparently lack beta or vasodilator receptors that are stimulated by isoproterenol. They do contain alpha or constrictor receptors that are stimulated by epinephrine but not by isoproterenol. Forearm venous constriction occurring with systemic infusions of large doses of isoproterenol is not a direct effect; it must be of reflex origin and mediated through alpha receptors.

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