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RESEARCH ON CARDIAC PRESSORECEPTORS

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FOREWORD

This research has been conducted by the Physiological Institute of the University of Göttingen, Göttingen, Germany, under AF [redacted] Grant 61(052)-541 for the Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio. Mr. D. Rosenbaum, Altitude Protection Branch, Physiology Division, Biomedical Laboratory, Aerospace Medical Research Laboratories, was technical monitor for the Air Force. This research supported Project No. 7163, "Physiology Research," and Task No. 716302, "Vital Organ Function in Mammals." This research was started 1 January 1962 and completed 31 January 1964.

This technical report has been reviewed and is approved.

WAYNE H. McCANDLESS
Technical Director
Biomedical Laboratory

ABSTRACT

Pressoreceptor reflexes affecting coronary blood flow were investigated. No indication of reflexly induced changes of coronary vascular resistance has been found. Peripheral vegal stimulation resulted in a 25% increase in diastolic flow indicating vagal influence on the resistance of coronary vessels. Adrenaline injected into a coronary branch led to dilation prior to its effect on the contractile force of the heart.

The effects of two representative catecholamines on coronary blood flow were investigated. Using a beta-receptor blocking agent, both constrictor and dilator effects have been observed following adrenergic stimuli.

Separate pressure elevation in the main trunk of the left coronary artery caused peripheral dilation. Bradycardia was also observed. Although this is believed to be a part of a depressor reflex action, there is no evidence that there exists within the coronary vessels a separate reflexogenic area comparable in intensity to the aortic arch and carotid sinus. Moreover, branches from the aortic nerve must be assumed to be distributed as far as the coronary ostis. In such event, the coronary area must be considered to contribute a part of the systemic activation.

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SECTION I

INTRODUCTION

Pressoreceptors within the mammalian heart have been shown to exist by several authors (refs 1 and 2). One group demonstrated vagal nerve impulses appearing synchronously with diastole or systole; the other group showed functional activities of these receptors by demonstrating that peripheral reflex dilatation originated from receptor zones of the heart muscle itself. It therefore seemed worthwhile to consider whether the reflex dilation includes the coronary bed as well. Section II deals with an investigation of reflex dilatation of coronary vessels. (The results did not reveal a strong reflex control of coronary circulation, although a dilator principle conducted in the vagal nerve could be shown to be probable.)

Section III elucidated the adrenergic influence on coronary vessels. By means of β-receptor blocking agents, both constrictor and dilator effects could be observed following adrenergic stimuli.

Experiments (section IV) of a third and last study studied whether or not the pressoreceptor areas exist within the coronary bed. The results point to the possible existence of reflex areas around the ostia of coronary vessels, but give no evidence of such areas within the course of these vessels.

SECTION II

EFFECT OF STIMULATION OF RECEPTOR AREAS IN HEART AND CAROTID SINUS ON CORONARY BLOOD FLOW

Methods

Experiments were carried out on 17 dogs in barbituric anaesthesia (Inactin). By left costal incision the heart was rendered accessible for coronary cannulation. Usually the descending branch of the left coronary artery was cannulated and perfused under constant pressure. The blood was taken from the femoral artery and pumped into a constant pressure reservoir, from which the blood was led to the coronary cannula, passing through a Kolin-type electromagnetic flowmeter (ref 3). This flowmeter allowed measurement of the whole cycle of coronary flow per heart beat or alternately mean flow (fig 1). To study coronary reflexes elicited from areas of the heart itself, a distending balloon was introduced either into the right or the left atrium, where the pressoreceptors are known to exist. To supplement such studies, the distending balloons were also introduced into both carotid sinus regions and the behavior of coronary flow was recorded. Finally, in order to investigate possible dilating fibers running in the vagus nerve to coronary vessels, the peripheral end of the cut vagus nerve in the neck was stimulated electrically. Sympathetic fibers to the heart were not stimulated; instead, adrenergic substances added to the perfusing system were investigated. (See section III.)

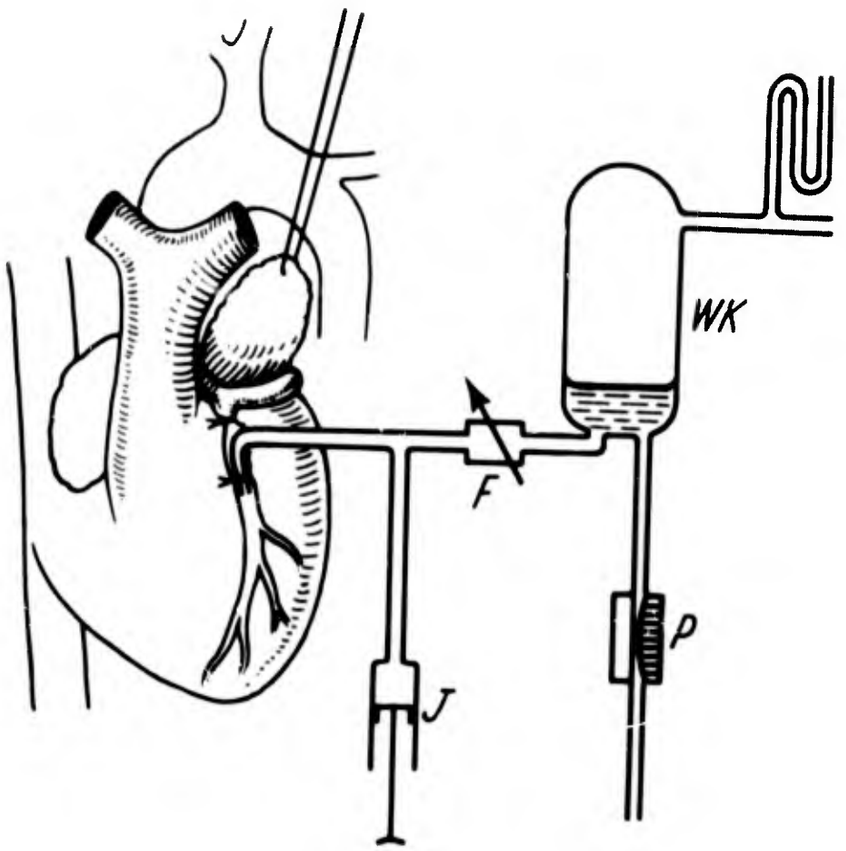

Figure 1: Schematic Drawing of Setup Used to Measure Coronary Flow in the Descending Branch of Left Coronary Artery at Constant Perfusion Pressure.

WK Air chamber and blood reservoir under constant pressure.

P Pump (sigma type) that pumps blood from the femoral artery into the air chamber.

F Cannulating electromagnetic flowmeter (Kolin type modified by Gregg).

J Syringe used for injections and continuous infusions of vasoactive substances.

Results

The main problem of investigations on coronary reflexes is to find a criterion of smooth muscle response in coronary vessels, since only blood flow and perfusion pressure are measured. It is commonly known, since Gregg's work in this field (ref 4), that mean flow measurements do not furnish a definite answer to our problem as two factors influence coronary flow: the extravehicular resistance, due to mechanical forces of the heart beat, and the intravascular resistance, due to the state of contraction of the vascular smooth muscles. As Gregg pointed out, a vascular smooth muscle response can only be judged from measurements taken during diastole when no mechanical forces influence coronary flow. However, another fallacy must be considered: any change in mechanical work, due either to change of the contractile force or to change of heart rate and peripheral factors, induce changes of the overall coronary resistance. Therefore, any study on coronary reflex behavior is confronted with the almost unavoidable interference of metabolically- and nervously-induced processes on coronary vessels.

a. Experiments with distenting balloons in auricles.

In two experiments rubber balloons were introduced into either the left or right auricle. Figure 2 shows results of an experiment in which the balloon was inflated over a period of 30 seconds. Arterial pressure decreased to low values, as was expected; the mean coronary flow decreased only slightly; however, the phasic recording revealed a definite drop of diastolic flow, indicating that the tone of coronary vessels had increased. The almost constant mean flow was due to the fact that systolic inhibition of phasic flow was markedly reduced.

b. Experiments with distending balloons in both carotid sinuses.

Figure 3 shows the effect of inflation of the two balloons lying in each of the carotid sinuses. No effect was observed, although blood pressure dropped about 40 mmHg and consequently the work of the heart dropped also. In a few cases, slight increases (25%) of diastolic coronary flow were observed during inflation.

c. Experiments with inflation of lungs.

Another, though indirect, approach to influencing the activity of depressor zones in the heart muscle is made by inflation of the lungs, with subsequent decrease of the filling of the heart. In most experiments a slight decrease of mean flow, as has been noted in auricular distension experiments, could be observed. Figure 4 demonstrates the recording taken in the same experiment as shown in figure 3. In any case, almost no change in flow can be seen.

d. Experiments with peripheral vagal stimulation.

In 14 animals vagal stimulation led to a very characteristic course of coronary flow changes. After the onset of stimulation and subsequent arrest of the heart beat, coronary flow obtained a value close to the diastolic flow, indicating that intravascular resistance had not changed. After 2 sec of continued vagal stimulation, a definite increase of flow could be observed, lasting

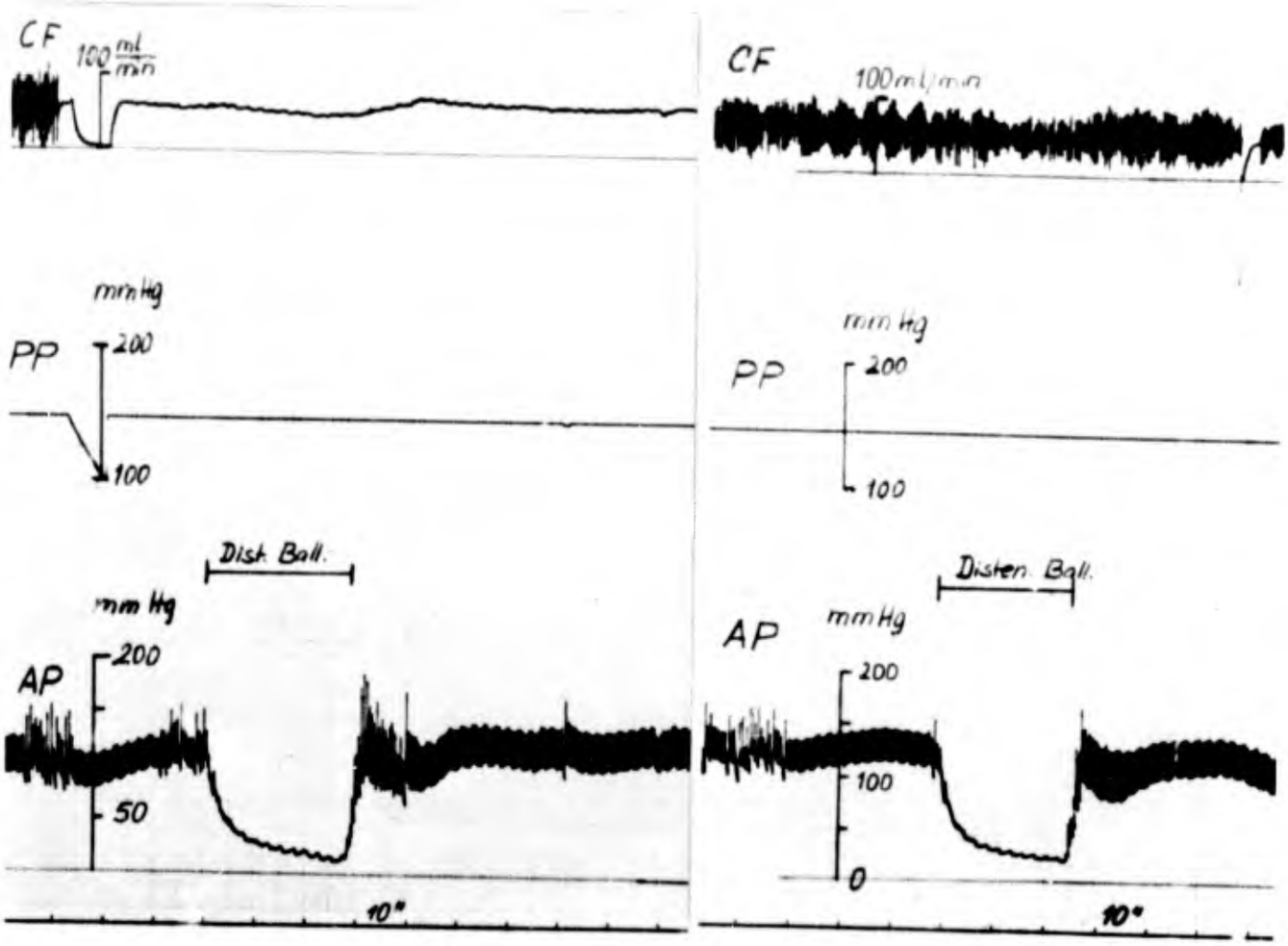

Figure 2: Response of Mean and Phasic Coronary Flow to Distension of the Left Atrium. Left top: mean coronary flow, right top phasic flow. Top at tracing represents diastolic phase of flow.

PP Perfusion pressure.
Lowest tracings arterial pressure.
Balloon distension for 30-sec periods.

CF Coronary flow

AP Arterial pressure

Each division on bottom line represents 10 seconds.

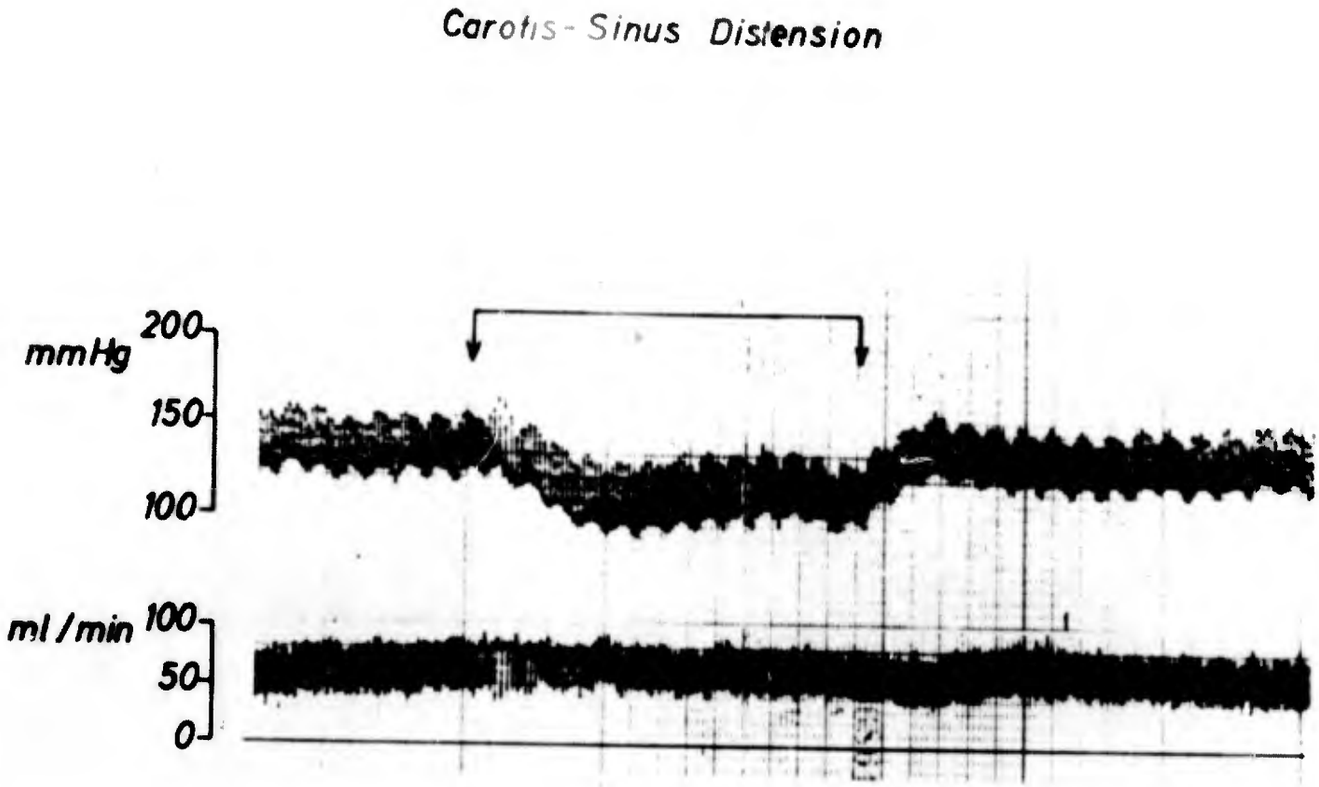

Figure 3: The Effect of Bilateral Distension of Carotid Sinuses on Phasic Coronary Flow. Balloon distension for period of 1 minute.

Note constancy of flow (coronary vessel perfused under constant pressure).

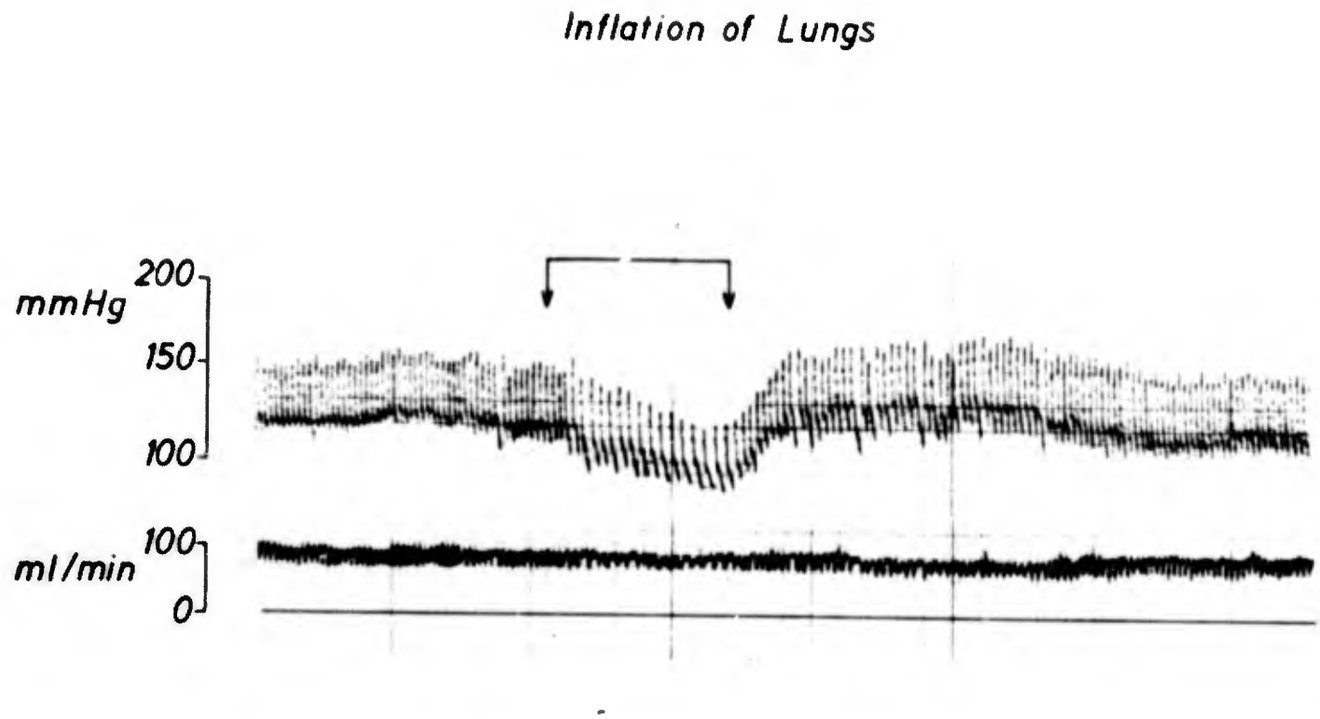

Figure 4: Effect of Positive Pressure Inflation of Lungs on Phasic Coronary Flow (constant perfusion somewhat elevated over that in figure 3).

Note cardiac slowing during 30 second period of inflation.

for a period of about 10 sec , regardless of whether or not the heart started to beat. Figure 5 gives an example of a great number of similar recordings.

e. Experiments with adrenaline dilation.

As mentioned above, sympathetic nerve stimulation has not been carried out in these experiments. Since adrenaline is considered to be the adrenergic transmitter substance, the effects of this substance were taken as being similar to those expected after sympathetic nerve stimulation. Figure 6 gives an example of the effect of adrenaline administered to the perfusing system. (See fig 1.) Diastolic and systolic flow increased during the first 10 sec after adrenaline injection. This first phase is followed by a later decrease in systolic flow, probably due to the increased force of contraction induced by adrenaline. Nevertheless, the high diastolic flow (about +60% of control) was that of an adrenergic stimulus and is of a dilating nature.

Discussion

In the experiments in which depressor areas within the heart and in the carotid sinus were stimulated, only slight changes of coronary diastolic flow were observed. In the auricular distension experiments, the drop in diastolic flow can best be explained by the decrease in mechanical work of the heart subsequent to the drop in arterial pressure. In the experiments with carotid sinus distension, a much less decrease of pressure, and therefore of work, may be responsible for almost no change in diastolic flow. The occasionally observed increase in diastolic flow may be due to an activation of sympathetic discharge to the heart, originated by a release of pressoreceptor areas in the aorta and heart. In this case, one must assume that the stimulation of carotid sinus areas was not followed by an effective sympathetic inhibition.

The most interesting finding in this series, coronary dilation during vagal stimulation, is difficult to explain. One fallacy could vitiate the argument of direct dilating effect of impulses conducted in vagal fibers: under conditions of perfusion of a severed coronary artery, a drop in general blood pressure much below the perfusion pressure would allow the flow to increase through collaterals to other coronary areas. However, the vagal dilating effect lasts only 10 sec, whereas the arterial pressure is still comparatively low after that period. In addition to this, it can be assumed that the proposed dilating fibers fatigue sooner than the other vague fibers. Another more likely explanation could be derived from experiments by Krayer and Feldberg (ref 5), who showed that ACh, set free during vagal stimulation, then appeared in the blood of the coronary sinus in concentrations of 0.5 μg %. However, the amount is too little to be responsible for the dilation of coronary vessels. Injections of ACh of the same order of magnitude into the right auricle had no effect on our preparation. This failure was probably due to the fact that ACh had to pass on to the femoral artery and the perfusing system before it could reach the coronary vessel under examination. A direct injection of the same amount of ACh (2-4 μg) into the perfusing system has a powerful dilating effect. It therefore seems necessary that ACh originated by vagal stimulation should reach the coronary arterioles directly, which seems improbable, as no vagal fibers are known to reach coronary vessels themselves. The fibers are confined only to the conducting system of the heart; from this region, the ACh detected by Krayer and Feldberg may be drained and washed out by coronary venous blood in the right auricle.

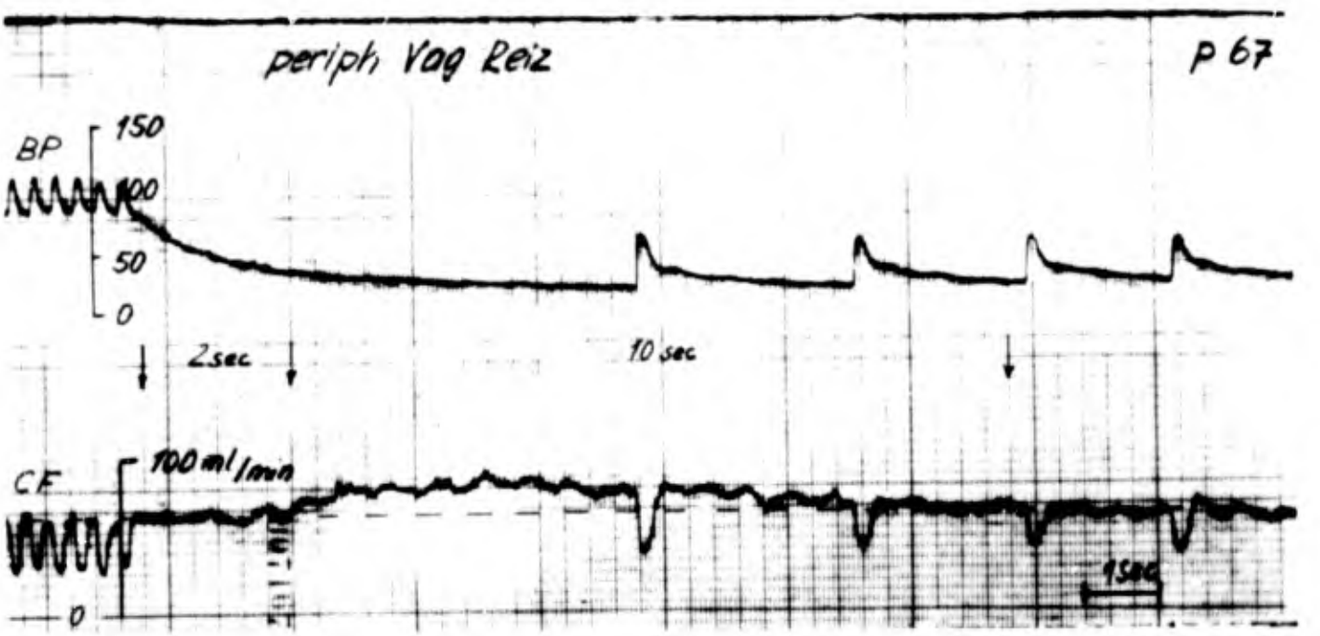

Figure 5: The Influence of Peripheral Vagus Stimulation on Phasic Coronary Flow (for exp. see text).

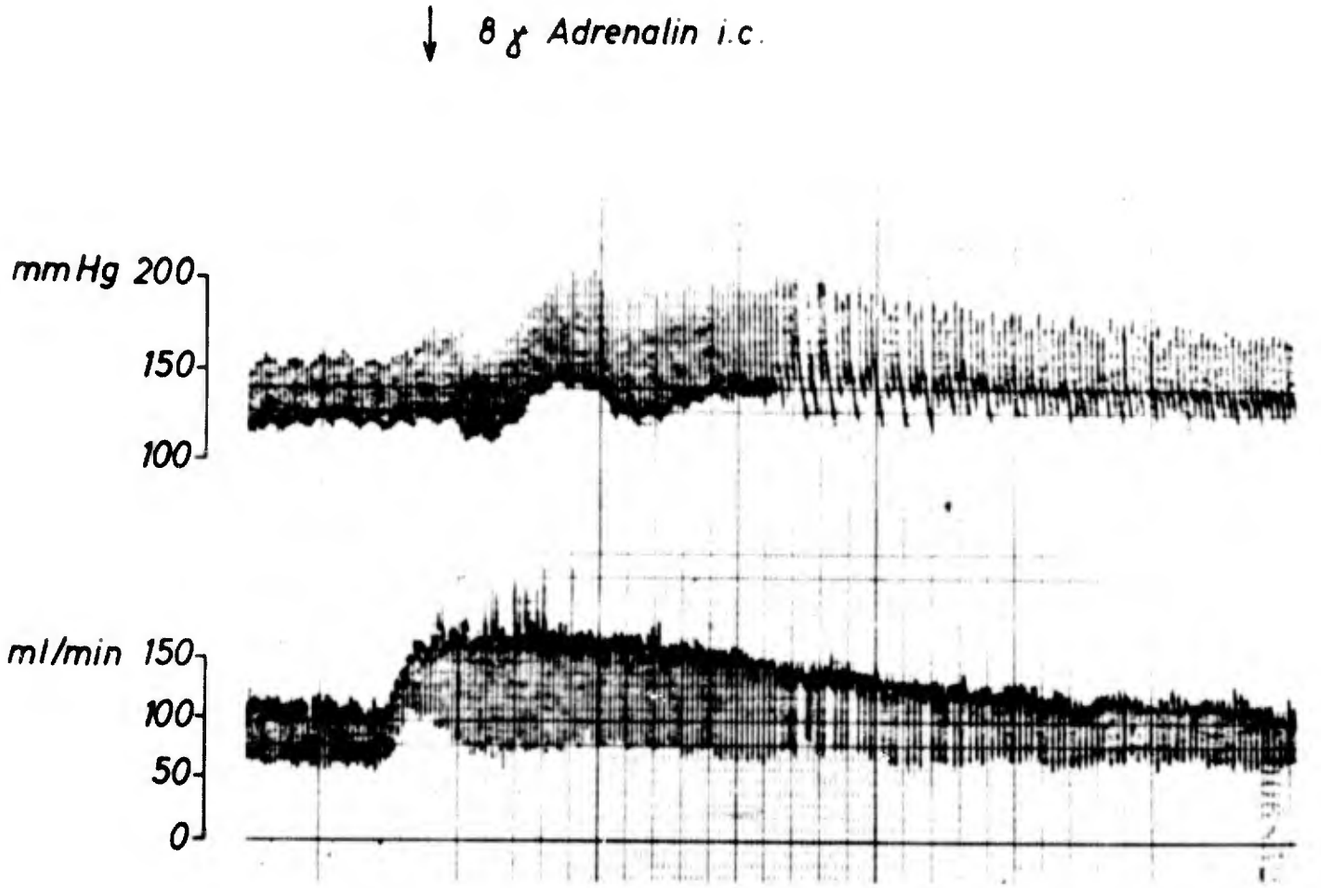

Figure 6: Result of Injection of 8 μg Adrenaline Into the Coronary Perfusion System. Note immediate and relatively prolonged increase in diastolic and systolic flow (timescale the same as in figures 3 and 4).

SECTION III

EFFECT OF ADRENERGIC TRANSMITTER ON ALPHA- AND BETA-RECEPTORS WITHIN THE CORONARY BED ON CORONARY BLOOD FLOW

Introduction

Although very little evidence for a reflex action on coronary vessels could be obtained, it seemed worthwhile to us to reinvestigate the coronary effect of adrenergic substances which are believed to act directly on the smooth muscles of the coronary vessels. Since noradrenaline and adrenaline are assumed to be the sympathetic transmitters, a study of these substances should at least allow some insight into the sympathetic action on coronary vessels, regardless of whether they are reflex in nature, or activated from higher centers.

As we have already shown (section II, fig 6), adrenaline injected into the coronary perfusion leads to a dilation before the effect of contractile force on the heart sets in. It is generally accepted that adrenaline has dilatory effects at low concentrations in vessels of skeletal muscles. With increasing concentrations in the plasma, a constrictor response appears. This dual effect of adrenaline has led to the theory of alpha and beta receptors. These are not understood as anatomical structures comparable to other chemo- or mechanoreceptors. The term is used to indicate receptor areas on the mechano-receptors. The term is used to indicate receptor areas on the macromolecular basis located within the smooth muscle membrane itself. The theory fits well with the fact that competitive substances block either the alpha or beta responses.

In recent years a beta-blocking substance, nethalide (ref 6) has been introduced, which has a fairly long continuing effect, enabling several catecholamine compounds to be studied and compared with each other.

Methods

Experiments were carried out on five dogs under barbituric (inactin) anesthesia. The experimental setup used in this part is identical to that described in section I (see fig 1). The study was confined to the effects of two representative catecholamines: isoproterenol, a mainly beta-receptor stimulant, and arterenol, a mainly alpha-receptor stimulant. These substances were added to the perfusing system by an automatic syringe. The beta-blocking agent, nethalide, was given intravenously so that all beta-receptors in the animal were blocked.

Results

In the upper record, figure 7 shows the coronary dilating effect during 10 μg isoproterenol infusion into the perfused coronary vessel. Since the substance enters the general circulation after passing through the heart, the beta-receptor stimulation effect in the peripheral vessels leads to dilation and subsequent decrease in mean arterial pressure. After methalide administration the coronary flow was reduced and isoproterenol infusion was followed by a much smaller increase in flow.

The coronary bed behaves quite differently when arterenol is infused, as shown in figure 8. This substance has only a very small, if any, stimulating effect,

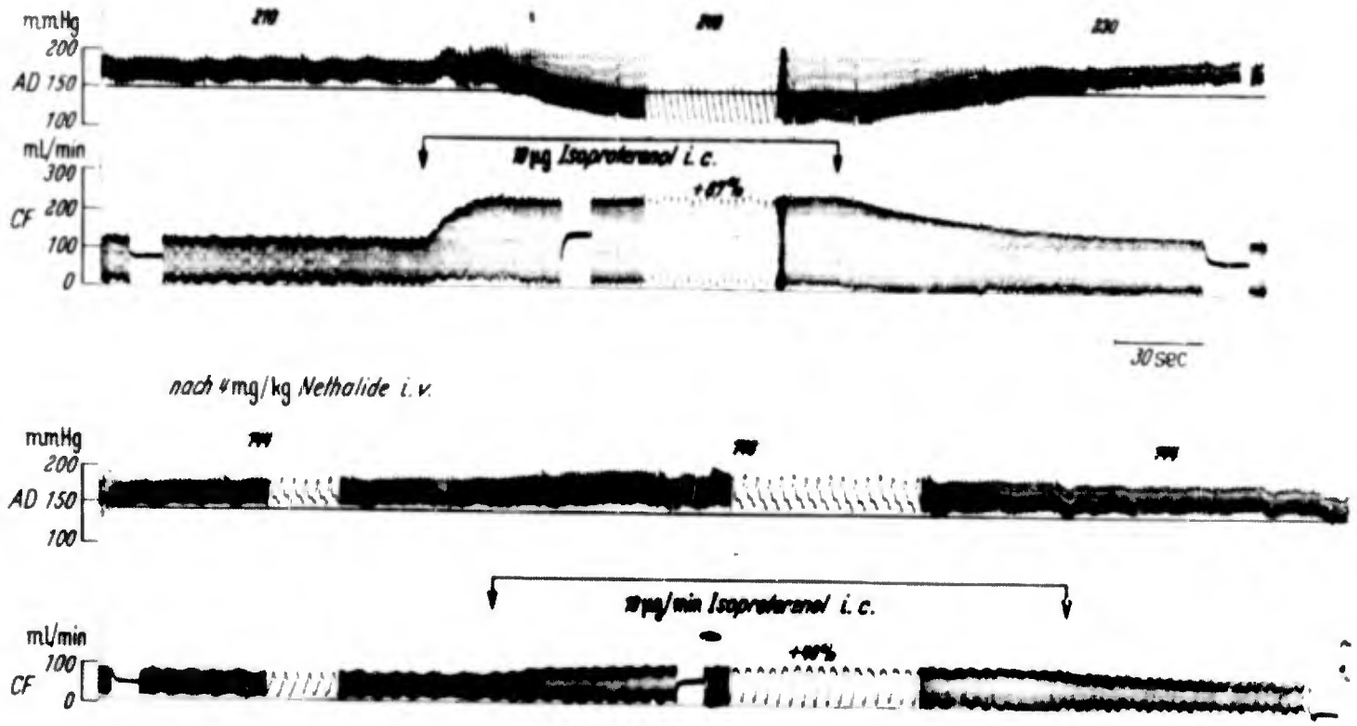

Figure 7: Effect of Isoproterenol on Coronary Flow Before and After Nethalide Administration

Upper half of figure--effect of initial infusion of isoproterenol. Lower half--effect of same dosage following intravenous injection of Nethalide.

Note decrease in heart rate and slight fall in arterial pressure accounting for the reduced coronary flow following Nethalide administration. Subsequent administration of the same dosage of isoproternol is much less effective.

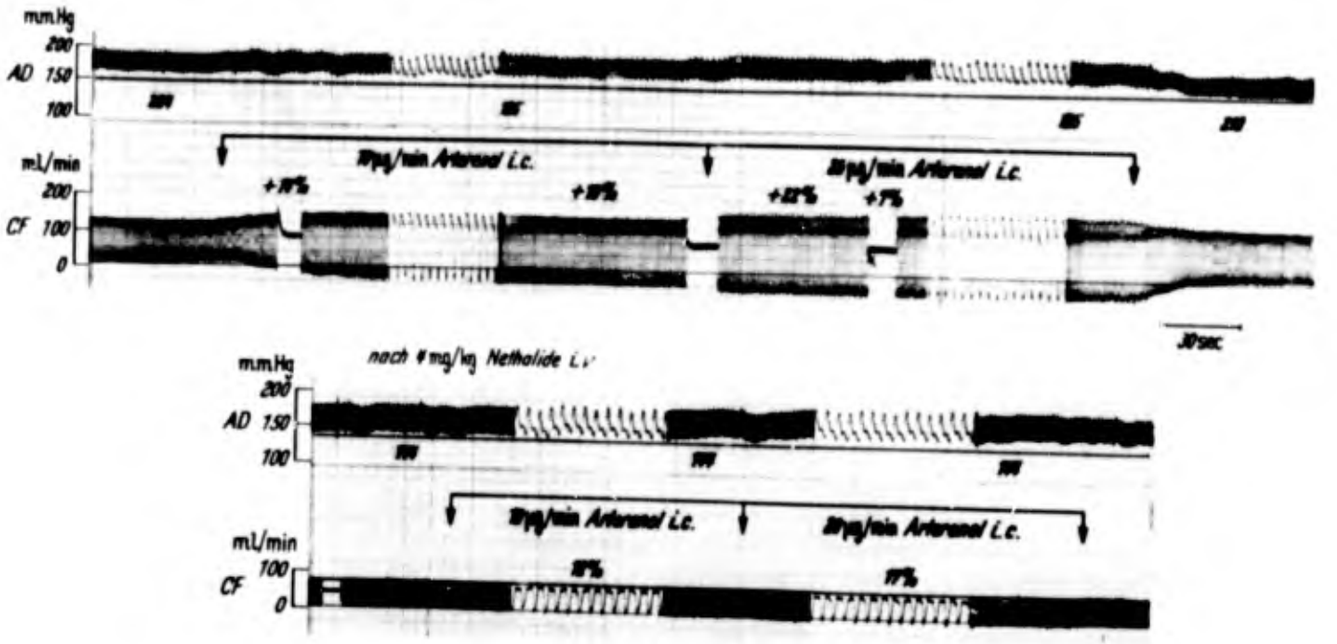

Figure 8: Experiment Similar to That in Figure 7 Using Arterenol. Note slight increase of coronary flow following Arterenol infusion reversed by Nethalide.

as is known from studies on skeletal muscle. The increase of mean coronary flow amounts to +14% and +7%, respectively, the latter following the higher concentration of infused arterenol. In this case, nethalide blocks the small beta activity completely and, leaving the alpha effect intact, shows that arterenol is able to constrict coronary vessels (-12% and -17% of controlled flow in the respective concentrations). Figure 9 summarizes these results in five experiments on heart rate, blood pressure, and coronary flow.

Discussion

Two findings of this part should be discussed:

1. The strong dilating effect of the adrenergic substance isoproterenol and its blockage by nethalide.

The dilating effect could be secondary to the increase of contractile force and subsequent increase of metabolic needs, known to be evoked by isoproterenol in the mammalian heart. This objection against direct dilating effects of catecholamines cannot be invalidated without measurements of the energy output of the heart under these conditions. Preliminary investigations of myocardial O_2-consumption have shown that in both instances, under either proterenol or arterenol infusions, the increase in O_2-consumption was found to be almost equal. This would mean that the higher diastolic coronary flow during isoproterenol infusion is due to an additional dilating stimulus, or the minor increase in diastolic coronary flow during arterenol infusion is due to constrictor stimulus superimposed on a metabolic increase in flow. The decision can be made by comparing the relatively small constrictor action of arterenol (average -10%) with the dilation observed, which is only 50% of the isoproterenol dilation. We therefore believe that, in addition to the metabolically induced dilation of coronary vessels, a definite dilating action of catecholamines exists.

2. Arterenol after beta-receptor blockage has definite constrictor effects on coronary vessels.

The apparent vasoconstrictor action of arterenol after beta-receptor blockage is comparatively small. It might be interesting to study this effect on the non-beating heart to obtain the range of constriction without interference with the dilating action of metabolites. The question of whether the small constrictor potency of this adrenergic compound plays a role in the physiological conditions which regulate coronary tone cannot be answered until the proposed experiments have been performed. Decreases of coronary flow to an extent greater than 10% were found by Szentivanyi (ref 7) after electrical stimulation of separated accelerant fibers, and are probably not due to vasoconstriction. The conclusions are based on mean flow measurements and the extracoronary resistance, therefore, cannot be estimated. These experiments should be repeated with phasically recording flowmeters.

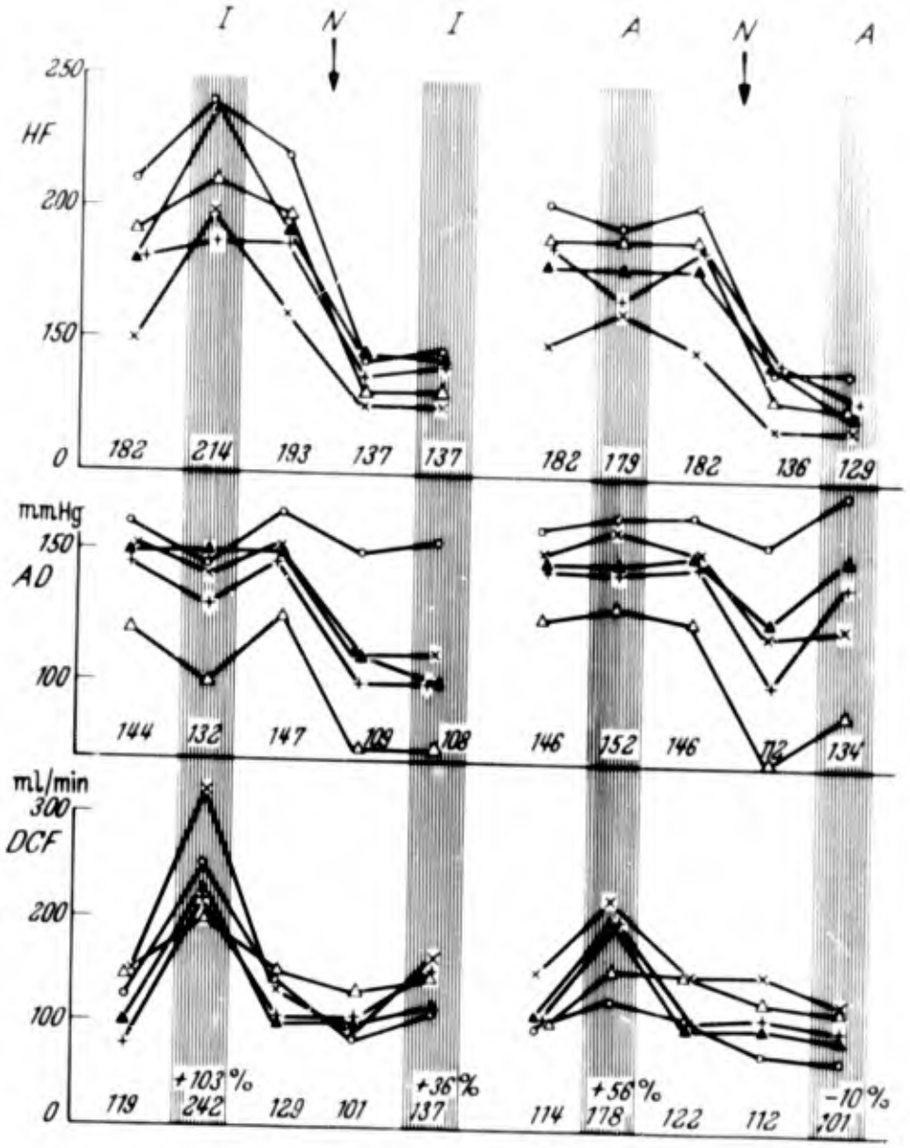

Figure 9: Summary of 5 Experiments of Isoproterenol (Left) and Arterenol (Right) Before and After Nethalide. From top to bottom: heart rate, mean arterial pressure, and diastolic coronary flow.

I = Isoproterenol
N = Nethalide
A = Arterenol

HF = heart rate beats/min.
AD = mean arterial pressure mm Hg
DCF = diastolic coronary flow ml/min.

SECTION IV

STIMULATION OF PRESSORECEPTORS IN THE CORONARY BED AND ITS EFFECT ON THE PERIPHERAL CIRCULATION

Introduction

This part deals with the problem of whether or not functional pressoreceptors—analogous to the classical depressor areas—are present in the coronary arteries. This question has been discussed and attacked by several investigators. Dawes (ref 8) mentions in a round table discussion that he never observed any depressor reflex action with increased perfusion pressure in a separately perfused coronary branch. In the course of the work reported here, a paper was published by Okinaka et al (ref 9), who found decreases of blood pressure during increase pressure in the coronary perfusion system.

Methods

The experimental procedure requires a separate perfusion of coronary vessels in order to make possible changes of local pressure in the coronary bed. Conveniently, the left coronary artery is separately perfused by a catheter introduced by way of the common carotid artery. This technique was developed by Gregg in 1957 (ref 10). In order to investigate possible pressoreceptors situated in the walls of coronary artery branches, it is necessary to introduce Gregg's cannula without tying the vessel; otherwise, any nerve fibers along the walls near the base of the arteries would be destroyed by the ligature. In the four dogs anesthetized with chloralose or inactin, the left coronary artery was made accessible by an intercostal incision. The cannula, introduced through the left common carotid artery, was directed into the ostium of the left coronary.

In four other dogs with closed chest, the cannula, introduced in the same manner, was directed into the left coronary ostium under x-ray control. The injection of radiopaque material (Urografin-Schering) revealed the course to be followed by the catheter. In both preparations the cannula was kept in position by means of an elastic fixation.

Since the animal lies on its right side, the direction of the main trunk of the left coronary artery is vertical. Because of this vertical course the heart rides on the tip of the cannula. Nevertheless, any movement of the intrathoracic organs (deep breathing, strong heart contractions) may impose a shift of the cannula in either direction, deeper into or out of the coronary artery.

Perfusion pressure of the cannulated coronary artery was maintained by a blood reservoir connected with a 50-liter air chamber. The reservoir was kept continually filled with blood pumped out of either the right carotid or a femoral artery. The air chamber pressure could be changed suddenly to pressures as high as 400 mmHg providing pressure for blood perfusion of the coronary.

In one series of experiments, Gregg's cannula was tied into the left coronary artery or one of its branches. Any depressor effect evoked during pressure elevation of the coronary perfusion would indicate that pressoreceptors are located in the course of the coronary bed. A positive finding in this case would indicate that sensory nerve would join the arteries below the ligature.

As an indicator of reflex vasodilation an innervated but isolated hind paw was used which was separately perfused under constant pressure (ref 11). The blood flow was measured by a rotameter of a modified Shipley type.

The experimental setup is seen in figure 10. The following recordings are taken: blood flow through isolated paw by rotameter I, arterial systemic pressure by strain gauge I and coronary perfusion pressure by strain gauge II. In some experiments, pressure in the cranial part of the ligated carotid artery was registered. Rotameter II was not recorded, but served as a control of correct perfusion. Injections could be made into either the coronary cannula or into the aortic arch as indicated in figure 10.

Results

a. Experiments with Gregg's indwelling cannula without tying into a coronary branch.

In order to test the responsiveness of the preparation, the systemic pressure was elevated by injections of small doses of adrenaline IV. The extent of dilation in the hind paw could then be compared with responses due to pressure elevation in the coronaries.

Table 1 demonstrates the extent of reflex dilation in the hind paw following pressure elevation in the left coronary artery, as well as in systemic arteries, expressed in percentages of blood flow increase. The data shown in this table are mean values and are representative of a large number of tests:

1. The responses to both coronary and systemic pressure elevations are very variable from experiment to experiment. Within one experiment, however, the magnitude of the responses is quite constant.

2. In three of eight experiments the effect of systemic pressure elevation (SPE) exceeded that of the coronary pressure elevation (CPE), whereas two experiments showed a significantly higher response following CPE. In five experiments the response to CPE was positive; in two the reflex was not elicited. In one experiment the response during CPE could not be checked because of early death of the animal. Only in two experiments (V and VIII) did bradycardia occur during pressure elevation in the coronary artery, whereas SPE never failed to cause bradycardia.

In figure 11, records of experiment no. VIII are shown. This experiment is an example of a relatively low responsiveness to coronary pressure elevation. In figure 3b and d, a perfusion pressure elevation in the coronary arteries from 100 to 300 mmHg was followed by an increase in blood flow in the hind paw of 24% and 17%. The adrenaline test and infusion of saline solution, however, did not reveal much greater dilations. In some instances there was no response to CPE (fig 3c).

b. Experiments with Gregg's cannula tied into a coronary branch.

In the experiments with Gregg's cannula tied into the left coronary artery or one of its branches, any pressure elevation of the coronary profusion

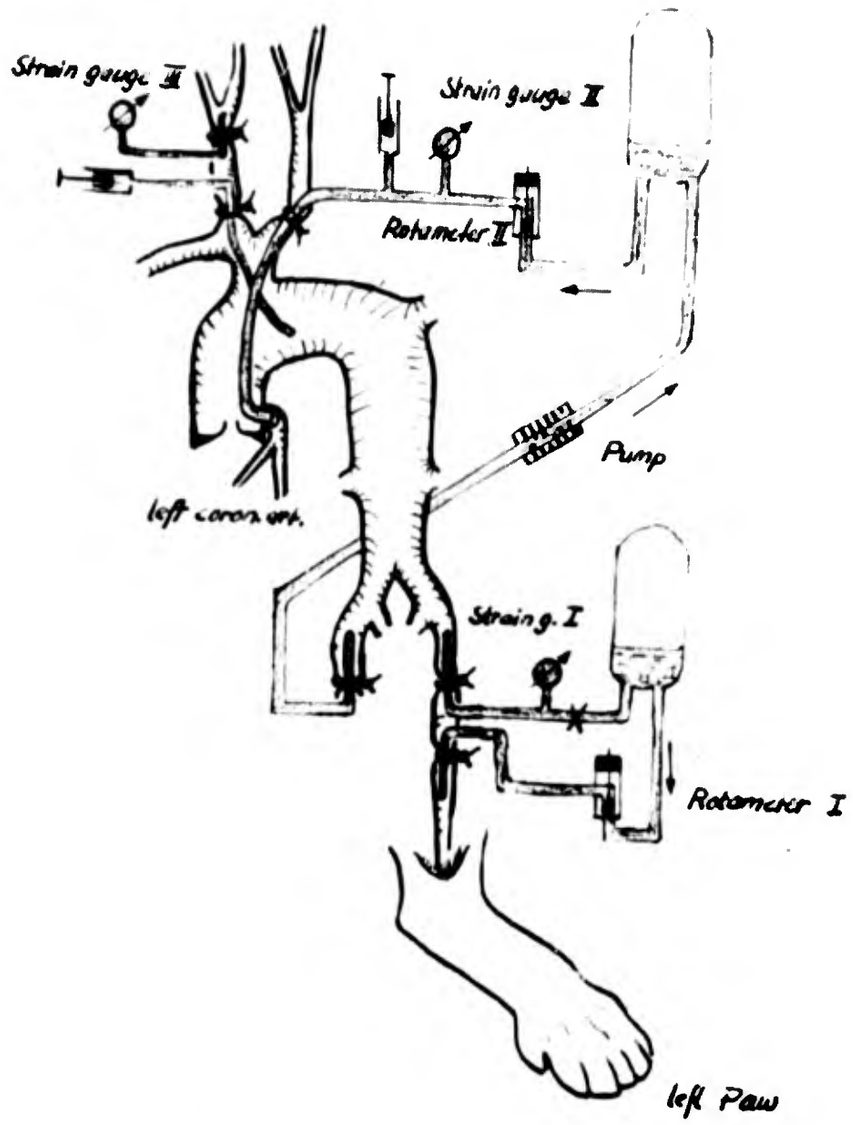

Figure 10: Schematic Drawing of Experimental Setup.

The part above at right shows the coronary perfusion system with sigma pump, buffering chamber, rotameter (II), strain gauge (II), syringe for coronary injection of drugs, and Gregg cannula.

On the upper left side of the drawing, a catheter introduced into the aorta is shown. It is used for systemic infusion of drugs. Strain gauge III is connected with the left carotid sinus for purposes not to be described in this paper. The lower part of the drawing shows the perfusion system of the left hind paw modified according to McDowell. Systemic pressure is measured by strain gauge I through a catheter introduced into the femoral artery.

TABLE I

REFLEX DILATATION IN HIND PAW VESSELS DURING SEPARATE ELEVATION OF THE SYSTEMIC AND OF THE CORONARY PRESSURE

A SURVEY OF EIGHT EXPERIMENTS ON DOGS

(Numbers in parentheses: positive responses)

Experiment	Anaesthesia and Preparation	Reflex dilatation of hind paw vessels following pressure elevation in:		Remarks
		systemic arteries	coronary arteries	
I	Chloralose open chest	not measured	+280% (6)	Very high sensitivity to systemic pressure elevation must be assumed although not measured. Therefore, positive results may be partially due to the slight pressure elevation in the classical depressor areas.
II	Inactin open chest	+53%	+120% (5)	Systemic pressure elevation (80%) was induced by adrenaline injection IV. See figure 3. Slight systemic pressure changes during elevation of coronary perfusion pressure
III	Chloralose open chest	+300%	+53%	Systemic pressure elevation was induced by adrenaline injection IV. Considerable increase of systemic pressure during elevation of coronary perfusion pressure
IV	Inactin open chest	+122%	not measured	Before coronary catheter was introduced the animal died.
V	Chloralose closed chest	+160%	+260% (4)	Reflex dilatation CPE is accompanied by 30% pressure fall and bradycardia. In the course of the experiment heart infarcation occurred and no further reflex response due to CPE could be observed.
VI	Inactin closed chest	+50%	0%	No reflex dilatation following CPE. Fast deterioration of the preparation to be recognized in continuously diminishing response to SPE.
VII	Inactin closed chest	+47%	0%	
VIII	Chloralose closed chest	+50%	+24% (11)	Slight and inconstant reflex response throughout the experiment following CPE bradycardia.

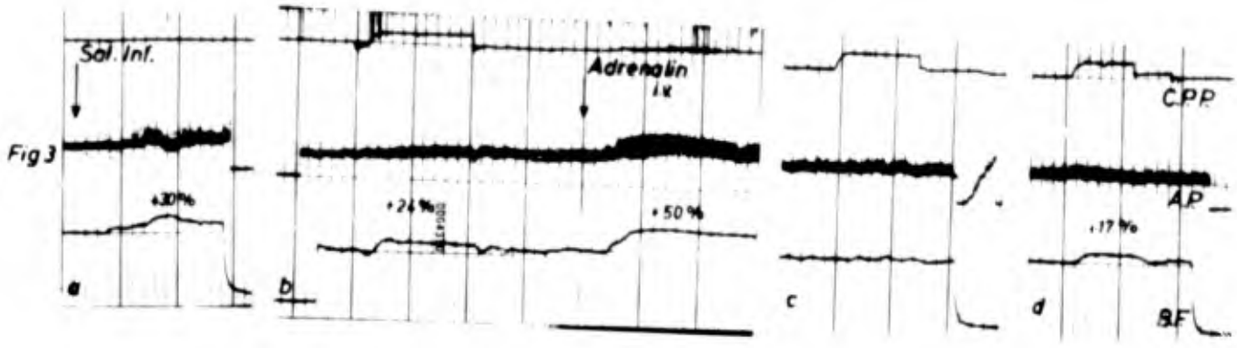

Figure 11: Reflex Dilatation in the Hind Paw (B.F.):

a. Following infusion of 200 cc. of saline;

b. Following coronary pressure elevation (CPP) from 100 to 300 and following systemic pressure elevation (AP) from 120 to 250 mmHg after adrenaline (50 micrograms iv).

c. Failure to elicit reflex dilatation in the hind paw following coronary pressure elevation. Calibration of systemic manometer in steps of 50 mmHg.

d. Reflex dilatation as in "b" shortly after "c"

Time in figure 3 is indicated between vertical lines. Distance between two lines signifies 3 sec.

was without effect on systemic blood pressure, heart rate, and general peripheral resistance. In two experiments an interference of ineffective extrasystoles led to a drop in systemic pressure and could be mistaken for a depressor reflex elicited from coronary areas. In nine experiments, no changes of peripheral resistance were observed during elevation of coronary perfusion pressure, nor were any changes of arterial pressure and heart rate found, except in one experiment where the above-mentioned extrasystoles appeared. Figure 12 shows a typical experiment in which pressure elevations in the coronary perfusing system were produced from 170-200, 200-250 and 250-300 mmHg. The hind paw vascular resistance remains unchanged during these procedures, as can be seen from the constant blood flow of this region. The recording of coronary flow shows a proportional increase with perfusion pressure, proving that the cannula is successfully tied in.

Discussion

The results of the experiments described in section II seem to indicate that reflexogenic areas may exist within the coronary bed, which have similar functions as the classical systemic depressor areas, ie, peripheral vasodilation and bradycardia as a result of coronary perfusion pressure elevation (ref 2).

1. Nevertheless, in some cases simultaneous increases of systemic blood pressure could not be avoided. They must be considered as a contributing cause of the vascular reflex.

2. Increased perfusion of coronary vessels may cause a greater force of contraction of the heart. This would lead in turn to stimulation of tension receptors situated in the ventricular walls, an event that should cause a reflex dilation (ref 12).

3. Another error could be introduced if blood, during the high pressure period, squirted out from the coronary cannula into the aortic arch. Leakage of such blood may cause local pressure increases which cannot be detected by peripheral manometers and cause stimulation of aortic pressoreceptors. To exclude this objection in occasional tests the coronary cannula was introduced into the aortic root. With sudden increase of perfusion pressure up to 400 mmHg, no depressor reflexes were observed.

4. In two of our experiments no reflex dilation, during coronary pressure elevation, was observed in the paw, although depressor reflexes from the classical systemic areas could be elicited. If, however, as in these cases, the total depressor reflex action is weakened in the course of the experiment, it is feasible that the stimulation of the coronary areas--which admittedly must be only a small part of the total reflexogenic zones--might not lead to a detectable dilation.

5. The inconstancy of the depressor reflex observed in Experiment No. VIII is difficult to explain. Since the coronary cannula is not very rigidly fixed in position, it is possible that deep breathing or strong heart beats cause a shift of the cannula either deeper into the coronary artery or out of it. According to our experiments in section III, one could assume that the receptors are confined to the ostium; therefore, any deeper introduction of the cannula into the artery would exclude the receptor area from the perfusion

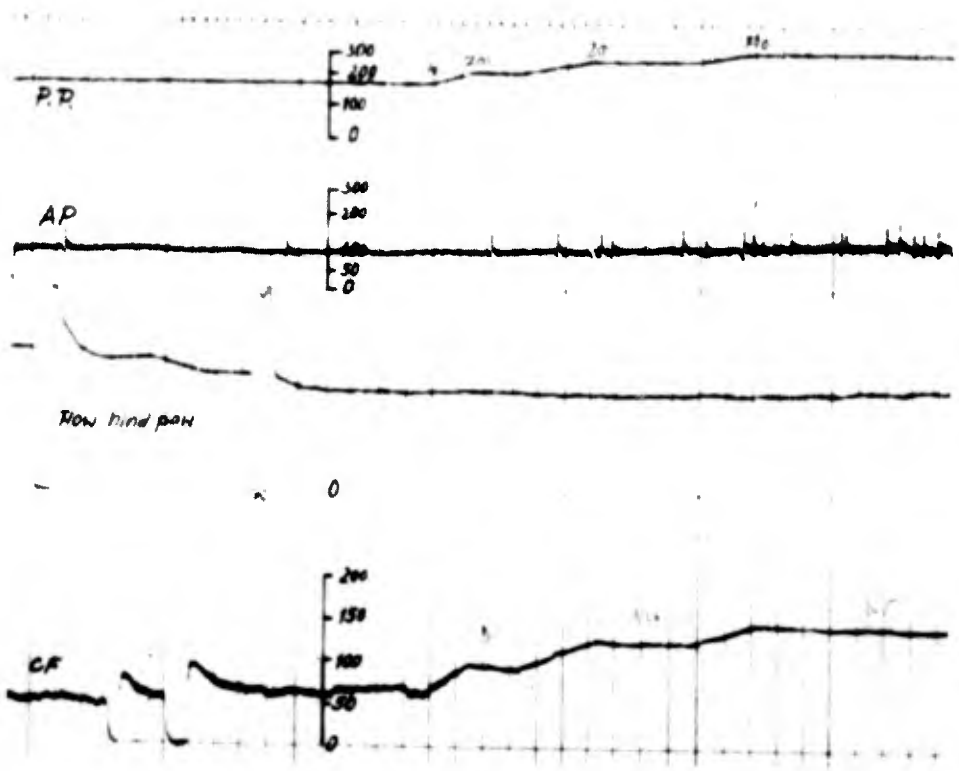

Figure 12: Effect of Increments in Coronary Perfusion Pressure From 170 - 300 mmHg on Flow in the Isolated (Nervous Pathways Intact) Paw.

Note constancy of flow in hind paw, indicating absence of vascular reflexes. This failure of response is to be contrasted with the effects observed using the indwelling cannula.

pressure action. The failure of earlier investigators, who never saw any depressor reflexes following pressure elevation in cannulated branches of the left coronary artery (ref 8), may arise from the fact that the ligatures they used blocked nerves and receptors near the cannulae. Finally, one may argue that the areas in question could vary in extent and responsiveness from animal to animal.

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13 ABSTRACT Pressoreceptor reflexes affecting coronary blood flow were investigated. No indication of reflexly induced changes of coronary vascular resistance has been found. Peripheral vegal stimulation resulted in a 25% increase in diastolic flow indicating vagal influence on the resistance of coronary vessels. Adrenaline injected into a coronary branch led to dilation prior to its effect on the contractile force of the heart. The effects of two representative catecholamines on coronary blood flow were investigated. Using a beta-receptor blocking agent, both constrictor and dilator effects have been observed following adrenergic stimuli. Separate pressure elevation in the main trunk of the left coronary artery caused peripheral dilation. Bradycardia was also observed. Although this is believed to be a part of a depressor reflex action, there is no evidence that there exists within the coronary vessels a separate reflexogenic area comparable in intensity to the aortic arch and carotid sinus. Moreover, branches from the aortic nerve must be assumed to be distributed as far as the coronary ostis. In such event, the coronary area must be considered to contribute a part of the systemic activation.

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