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THE EFFECTS OF ADRENALINE AND NORADRENALINE ON VENOUS RETURN AND REGIONAL BLOOD FLOWS IN THE ANAESTHETIZED CAT WITH SPECIAL REFERENCE TO INTESTINAL BLOOD FLOW

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SUMMARY

1. In cats, a venous long-circuit technique was used to measure the blood flows in the superior vena cava and the hepatic, renal and iliac segments of the inferior vena cava. The sum of these flows gave the venous return (minus coronary and bronchial flows). In further experiments using an electromagnetic flowmeter, flow in the portal vein and in the superior mesenteric and coeliac arteries was measured.

2. Approximately two-thirds of the hepatic blood flow is derived from the portal vein.

3. After block of conduction in the cervical region of the spinal cord, the proportions of the venous return coming from each region during the control periods were not significantly altered although the arterial pressure and total venous return were decreased.

4. Intravenous infusions of adrenaline caused an increase in venous return which was associated with a marked increase in hepatic blood flow. The increase in hepatic blood flow was due to an increase in flow in the superior mesenteric artery and portal vein. Flow in the coeliac artery remained unchanged. This response was unaffected by block of the cervical region of the spinal cord and by atropine or pentolinium.

5. Intravenous infusions of noradrenaline caused little change in venous return or regional blood flows. Small increases in superior mesenteric artery flow were occasionally seen and on cessation of the infusion a large but brief increase occurred. These facts suggest that noradrenaline has a similar action to adrenaline but this is masked by concomitant vasoconstriction.

INTRODUCTION

The effects of adrenaline and noradrenaline on cardiac output and on regional blood flows have been investigated many times but rarely simultaneously. It is therefore difficult to assess to what extent these sub-

stances cause a redistribution of the regional blood flows, although Barcroft & Swan (1953) attempted this on the basis of the results available for man. The problem has been re-investigated using a technique which allows measurement of the flows from four regions of the cat (Greenway & Lawson, 1966). To assess whether the responses to adrenaline and noradrenaline were modified by reflexes involving the brain, the infusions were repeated after the administration of a spinal anaesthetic into the cisterna magna.

These experiments confirmed that, as in man (Bearn, Billing & Sherlock, 1951; Bradley, Ingelfinger & Bradley, 1952), adrenaline increases the hepatic blood flow. Since variable effects on intestinal blood flow in animals have been reported (Folkow, Frost & Uvnäs, 1948; Green, Deal, Bardhanabaedya & Denison, 1955; Barer, 1961), it became of interest to determine whether this increase in hepatic flow was due to an increased flow in the hepatic artery, in the portal vein or in both.

METHODS

Long-circuit of the venae cavae

Twelve cats were anaesthetized by intraperitoneal injection of sodium pentobarbitone (30 mg/kg, Abbott Laboratories), while two were given 5% (w/v) urethane and 1% (w/v) chloralose (5–6 ml./kg, British Drug Houses) by the same route. The details of the technique have been described previously (Greenway & Lawson, 1966). The venae cavae were divided into four segments and the blood flow from each was separately long-circuited and measured by timing the collection of 10 ml. blood at 2 min intervals. The four segments comprised the superior vena cava and three regions of the inferior vena cava—the region receiving the hepatic veins, that receiving the adrenal, renal and ovarian or testicular veins, and that receiving the iliac veins. The sum of these flows gave the total venous return (minus coronary and bronchial flows). From these results, the proportions of the venous return coming from each region could be assessed by expressing each flow as a fraction of the venous return.

Stock solutions of (−)-noradrenaline tartrate (1 mg base/ml., British Drug Houses) in distilled water and (−)-adrenaline (1 mg base/ml., British Drug Houses) in 0·01 N-hydrochloric acid were diluted as required in Ringer Locke solution containing ascorbic acid (0·2 mg/ml.). Infusions were made for 15 min periods into the tube returning blood from the extracorporeal circuit to the right atrium.

To determine whether the responses to adrenaline and noradrenaline were influenced by reflexes involving the brain it was necessary to interrupt condution in the cervical region of the spinal cord. Surgical section proved unsatisfactory as complete haemostasis was difficult to achieve due to the heparin, and the position of the animal made access to the cervical vertebrae difficult. Therefore 5 mg cinchocaine HCl in 1 ml. 6% glucose (Ciba Laboratories) was injected into the cisterna magna. This procedure is referred to as cervical spinal anaesthesia. The block of the cervical spinal cord was assessed at intervals by noting the absence of diaphragmatic movements and of increases in blood pressure and heart rate when the artificial respiration pump was turned off for 1 min. The extent to which the spinal anaesthesia spread down the spinal cord was not assessed.

Portal vein flow

Twelve cats were anaesthetized with pentobarbitone and five with urethane and chloralose as described above. A tracheal cannula was inserted and the right femoral vein cannulated.

Two small branches of the left femoral vein were cannulated for the infusion of noradrenaline and adrenaline respectively. The abdomen was opened by a mid-line incision and the portal vein exposed. After the intravenous administration of 20 mg heparin (168 units/mg, Boots Pure Drug Co.), the mean arterial pressure was recorded from the right femoral artery and the mean right atrial pressure *via* a cannula in the right jugular vein. The portal vein was clamped and cut, and a cannula tied into each end. These cannulae were connected together through a 5 mm diameter extracorporeal probe from a Nycotron blood flowmeter type 372 and the clamps were removed. The portal vein flow was thus long-circuited via the flowmeter probe. The obstruction to flow in the vein during the cannulation procedure usually lasted 1–2 min. A side arm from the long-circuit was used to record mean portal vein pressure. All wounds were closed round the cannulae.

The various pressures were measured using Devices/C.E.C. pressure transducers and recorded, together with the output from the flowmeter, on a Devices pen recorder type M 8. Adrenaline and noradrenaline were infused intravenously for 5–8 min periods.

Coeliac and superior mesenteric artery flows

Four cats were anaesthetized with pentobarbitone as described above. A tracheal cannula was inserted and the right femoral vein cannulated. Arterial pressure was recorded from the right femoral artery. The abdomen was opened by a left subcostal incision and the coeliac and superior mesenteric arteries carefully exposed. It was unnecessary to administer heparin to these animals. A 2 mm diameter probe connected to the Nycotron flowmeter was placed on either artery as required and the flow recorded as before. In all the experiments described, the artery appeared in no way strained and the recorded flow was not affected by minor movements of the probe.

Adrenaline and noradrenaline were infused for 5–8 min periods via cannulae in small branches of the left femoral vein.

The electromagnetic flowmeter

The flowmeter was used to record mean flow only. When used with the extra corporeal probe to measure portal vein flow, zero flow was checked at frequent intervals by occluding the long-circuit tube for about 10 sec. At the end of each experiment the flowmeter was calibrated *in situ* according to the manufacturer's instructions, using the integrator which registers the flow regardless of flow velocity. In other experiments, using an extracorporeal circuit, the flowmeter was compared with direct measurement of the flow by timing the collection of 10 ml. blood. The two recordings did not differ by more than $\pm 5\%$ and usually agreed within $\pm 2\%$. The zero remained stable for at least several hours.

When used with the probe around the intact coeliac or superior mesenteric arteries the zero was checked between each infusion by occluding the artery distal to the probe. Any experiment where there appeared to be any possibility of movement of the probe or partial occlusion of the artery by the probe was discarded. At the end of each experiment the probe was calibrated *in situ* using the integrator according to the manufacturer's instructions.

RESULTS

Long-circuit of the venae cavae

Long-circuit of the venae cavae was carried out in fourteen animals. Table 1 shows the mean and range of the measured variables during a 15 min control period before any infusions were made. In addition to the measured flows, the relative regional blood flows are given by expressing the flow from each region as a proportion of the total venous return. These values fall within the same range as those previously reported (Greenway

& Lawson, 1966). Observations confirming the absence of venous shunts between the regions studied have also been given. In these experiments, clamping the hepatic artery and portal vein at the end of the experiment reduced the hepatic segment flow to less than 5% of its previous value, which confirmed that this segment flow is a valid measure of hepatic blood flow.

TABLE 1. The mean values and ranges of the measured variables recorded during the control periods in the fourteen cats

	Mean	Range
Cat weight (kg)	2·2	1·6–2·6
Mean arterial pressure (mm Hg)	129	109–159
Flows: (ml./min)		
Superior vena cava	86	56–105
Hepatic segment	92	61–125
Renal segment	53	39–73
Iliac segment	30	21–43
Venous return (ml./min)	261	186–314
Venous return/kg body wt. (ml./min)	117	101–136
Flows as proportion of the venous return:		
Superior vena cava	0·33	0·28–0·39
Hepatic segment	0·35	0·25–0·45
Renal segment	0·20	0·14–0·26
Iliac segment	0·12	0·08–0·17

A total of forty-four intravenous infusions of adrenaline and noradrenaline in doses of 1, 4 and 8 μg/min was made into these fourteen animals. Each infusion lasted for 15 min and was preceded and followed by control periods of 15 min each. No difference in the responses was apparent between animals anaesthetized with pentobarbitone or with urethane and chloralose. Typical responses to infusions of 1 μg/min are shown in Fig. 1, which shows the mean arterial pressure and the measured flows in an animal anaesthetized with urethane and chloralose. To illustrate the response to all the infusions, Fig. 2 shows the venous return and regional flows expressed as the changes from the control levels during each infusion.

Noradrenaline produced no consistent change in either the venous return or the regional flows in most of the experiments, even though the mean arterial pressure rose. Occasionally noradrenaline did increase the venous return and when this occurred all the regional flows increased slightly.

Adrenaline produced an increase in venous return during all except one infusion, even in doses of 1 μg/min which caused only a small rise (0–10 mm Hg) in mean arterial pressure. This increase in venous return was associated with a marked increase in flow from the hepatic segment of the inferior vena cava. The other regional flows were hardly changed although the superior vena cava flow sometimes decreased. No sustained increase in

flow from the iliac region of the inferior vena cava was seen, although in nineteen of the twenty-four infusions of adrenaline the iliac region flow increased during the first 2 min of the infusion, thereafter returning approximately to its control level. This rapid change could not be followed accurately due to the intermittent nature of the flow records.

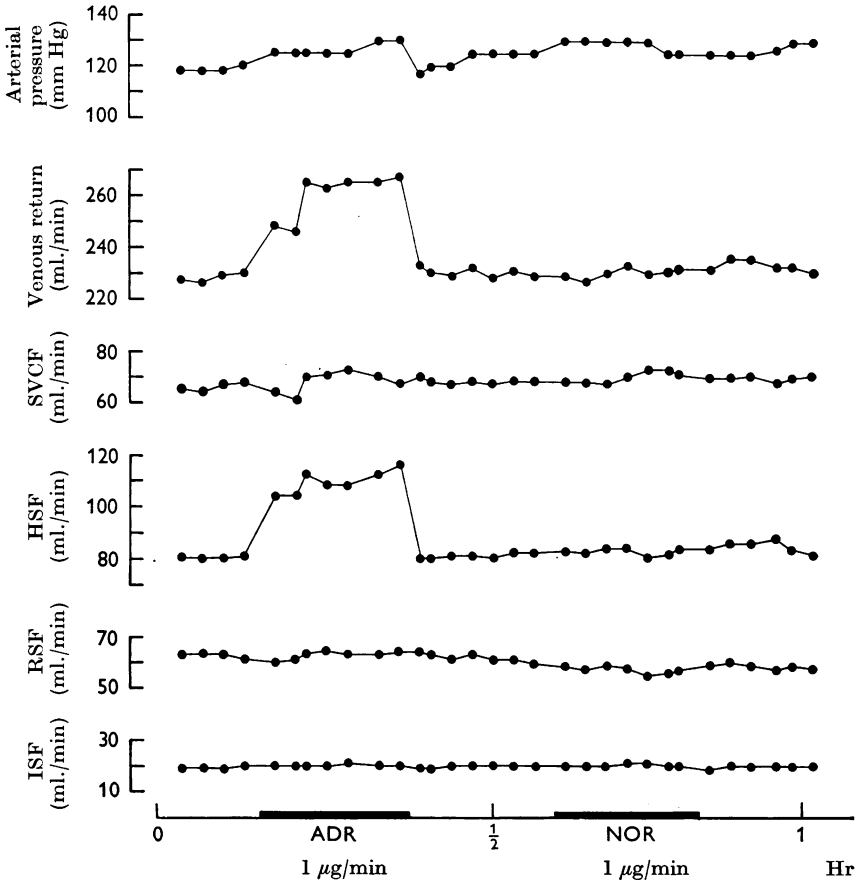

Fig. 1. The response to infusions of adrenaline and noradrenaline in one animal. Ordinates, mean arterial pressure, venous return and the flows from the superior vena cava (SVCF) and the hepatic (HSF), renal (RSF) and iliac (ISF) segments of the inferior vena cava. Abscissa, time in hr. Infusions of adrenaline (ADR) and noradrenaline (NOR) were given as shown.

The proportion of the total venous return coming from each of the four regions can be studied by expressing each regional flow as a fraction of the total. The proportions of the venous return draining from each region during the control periods are shown in Table 1, while Fig. 3 shows the changes from these control values which occurred during the forty-four infusions of adrenaline and noradrenaline.

Noradrenaline produced no consistent redistribution of the flows when it was infused in the doses studied, in spite of considerable rises in mean arterial pressure. On the other hand, adrenaline caused a marked increase in the proportion of the venous return coming from the hepatic segment of the inferior vena cava and a corresponding decrease in that coming from the other regions, especially the superior vena cava.

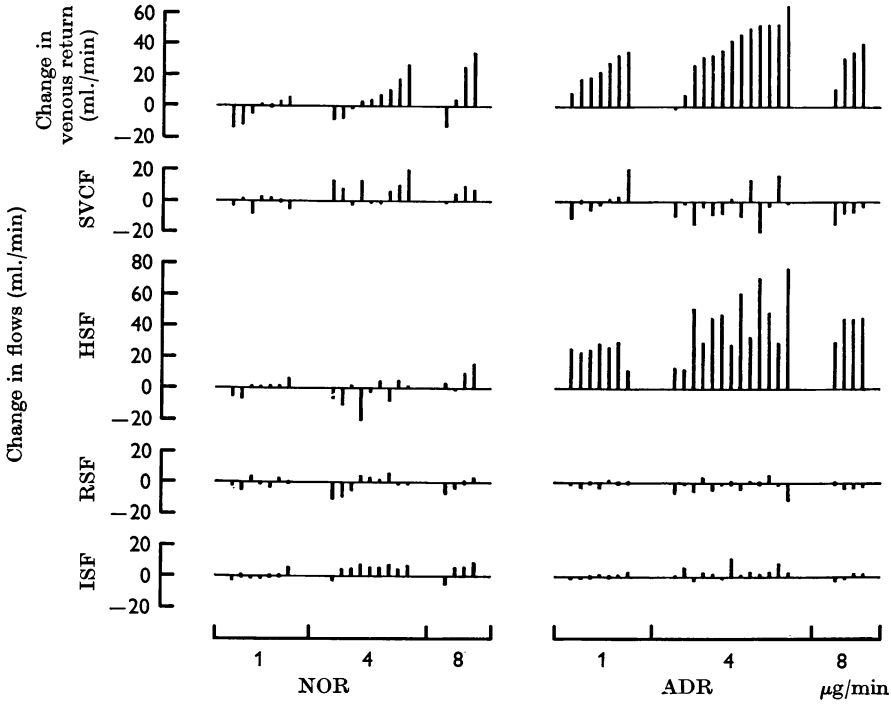

Fig. 2. The changes from the control levels in the flows during infusions of noradrenaline and adrenaline in all the experiments. Ordinates, change from the control level in the venous return and in the flows from the superior vena cava (SVCF) and the hepatic (HSF), renal (RSF) and iliac (ISF) segments of the inferior vena cava. Abscissa, the responses in all the experiments to 15 min infusion of noradrenaline (NOR) and adrenaline (ADR) in the doses shown.

Cervical spinal anaesthesia

To assess whether the changes occurring in response to the infusions of adrenaline and noradrenaline were modified by reflexes involving the brain, it was necessary to interrupt conduction in the cervical region of the spinal cord. After injection of a spinal anaesthetic agent into the cisterna magna in seven of the animals and after stability was reached, control values were obtained. The mean arterial pressure ranged from 35 to 83 mm Hg (mean 50 mm Hg) and the total venous return from 149 to

206 ml./min (mean 181 ml./min). All the regional flows were lower than before cervical spinal anaesthesia but the proportion of the total coming from each region was not changed in any marked or consistent manner. The proportion of the venous return coming from the superior vena cava ranged from 0·32 to 0·41 (mean 0·36), from the hepatic segment from 0·27 to 0·39 (mean 0·34), from the renal segment from 0·13 to 0·29 (mean 0·19) and from the iliac segment from 0·05 to 0·14 (mean 0·11). These values do not differ significantly from those during the control period before cervical spinal anaesthesia (Table 1).

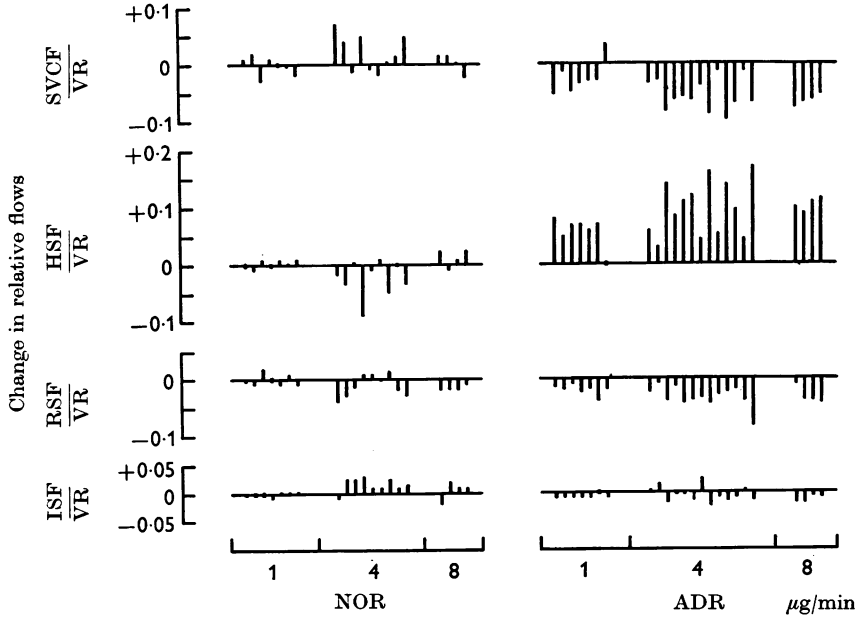

Fig. 3. The change from the control levels in the proportion of the venous return coming from the four regions during infusions of noradrenaline and adrenaline. Ordinates, the changes from the control levels of the relative flows expressed as the proportion of the venous return coming from the superior vena cava (SVCF/VR) and the hepatic (HSF/VR), renal (RSF/VR) and iliac (ISF/VR) segments of the inferior vena cava. Abscissa, the responses in all the experiments to 15 min infusions of noradrenaline (NOR) and adrenaline (ADR) in the doses stated.

Infusions of adrenaline and noradrenaline in doses of 1, 2, 4 or 8 μg base/min were carried out as before, 27 infusions being made in all. In every case, both noradrenaline and adrenaline increased the venous return, but in any one animal the increase caused by adrenaline was always greater than that caused by the same dose of noradrenaline. All the regional flows increased during each infusion but the extent of this increase varied in the different regions studied. These differences are most apparent when the regional flows are expressed as proportions of the total venous return.

Figure 4 shows the effects of these twenty-seven infusions. The increases from the control levels in the venous return are shown together with changes in the proportions of the total coming from each region. It can be seen that the effects of adrenaline were similar to those previously described: the proportion of the venous return coming from the hepatic

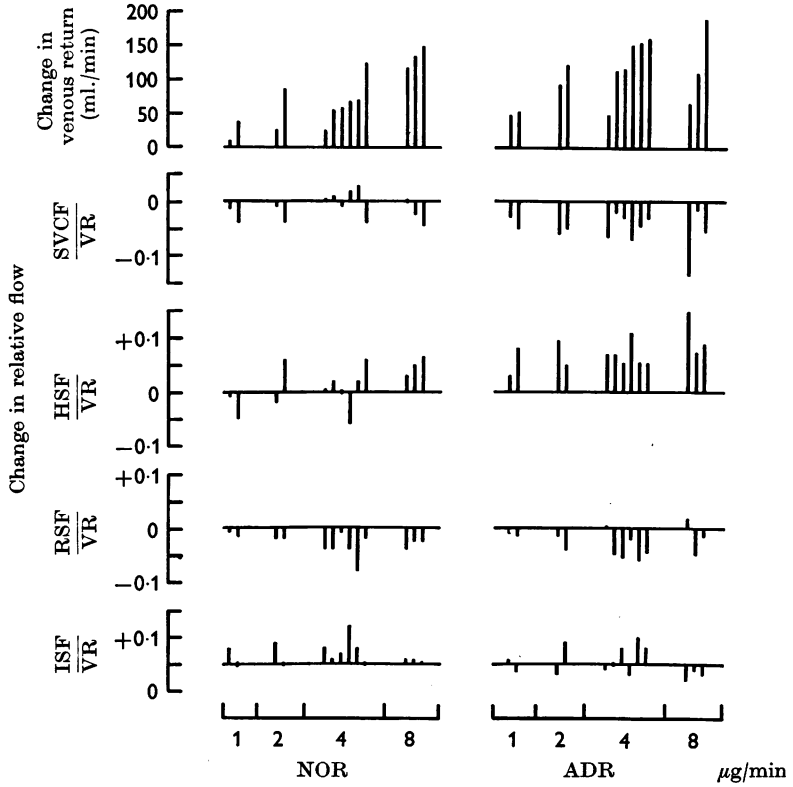

Fig. 4. After cervical spinal anaesthesia. The changes from the control levels in the venous return and relative regional flows during the infusions of adrenaline and noradrenaline. Ordinates, the changes from the control levels in the venous return and the relative flows expressed as the proportions of the venous return coming from the superior vena cava (SVCF/VR) and the hepatic (HSF/VR), renal (RSF/VR) and iliac (ISF/VR) segments of the inferior vena cava. Abscissa, the responses in all the experiments to 15 min infusions of noradrenaline (NOR) and adrenaline (ADR) in the doses stated.

segment of the inferior vena cava was always increased, while the proportions from the superior vena cava and renal segment of the inferior vena cava were decreased. Noradrenaline produced a more variable effect. In some cases the effect was similar to, but smaller than, the effect of adrenaline, while in others the proportion flowing from the hepatic segment

remained unchanged or fell. In every case there was a small decrease in the proportion coming from the renal segment.

The increase in hepatic blood flow caused by adrenaline infusions could result from an increased flow in the hepatic artery, in the portal vein or in both. Further experiments were carried out to investigate whether adrenaline caused an increase in portal vein flow.

Portal vein flow

Portal vein flow was measured in seventeen animals. The results obtained in the five animals anaesthetized with urethane and chloralose lay within the ranges obtained in the twelve animals anaesthetized with

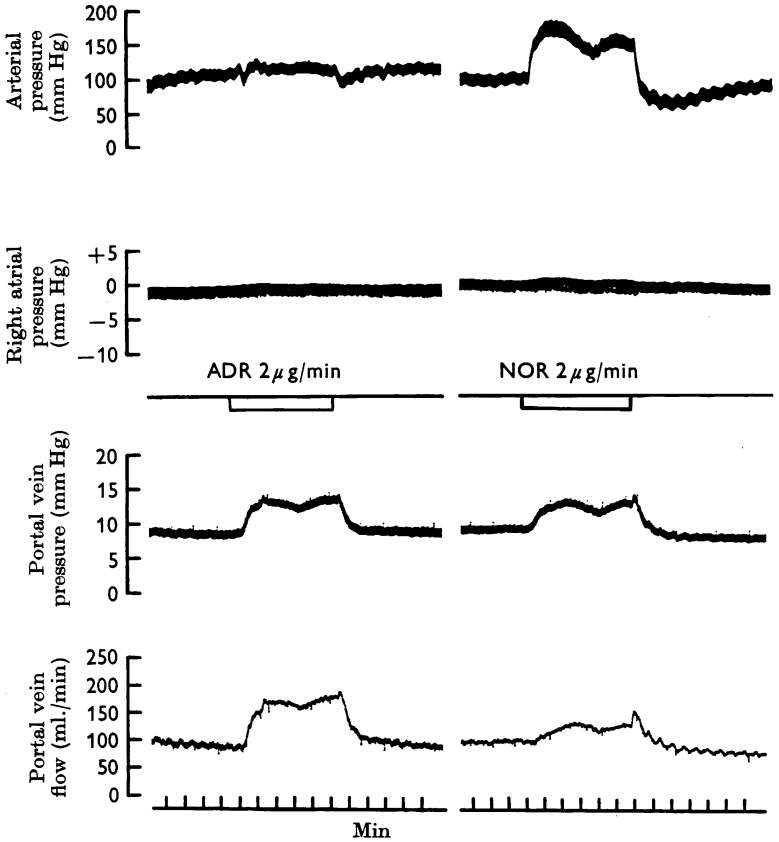

Fig. 5. The portal vein flow response to infusions of 2 μg/min of noradrenaline and adrenaline in one animal. Ordinates, mean arterial pressure, mean right atrial pressure, mean portal vein pressure, mean portal vein flow. Abscissa, time in min. Noradrenaline (NOR) and adrenaline (ADR) were infused during the periods shown.

pentobarbitone, in regard to both the control flows and the responses to adrenaline and noradrenaline. The values during the 15 min control period, after stability was reached but before any infusions were carried out, were as follows. The mean arterial pressures ranged from 100 to 160 mm Hg (mean 129 mm Hg), the portal vein pressures from 6·5 to 14 mm Hg (mean 9·5 mm Hg) and the portal vein flows from 31 to 146 ml./min (mean 61 ml./min). The cats weighed 1·3–4·0 kg and the portal vein flow ranged from 11·4 to 52 ml. min^{-1} kg^{-1} (mean 25 ml. min^{-1} kg^{-1}).

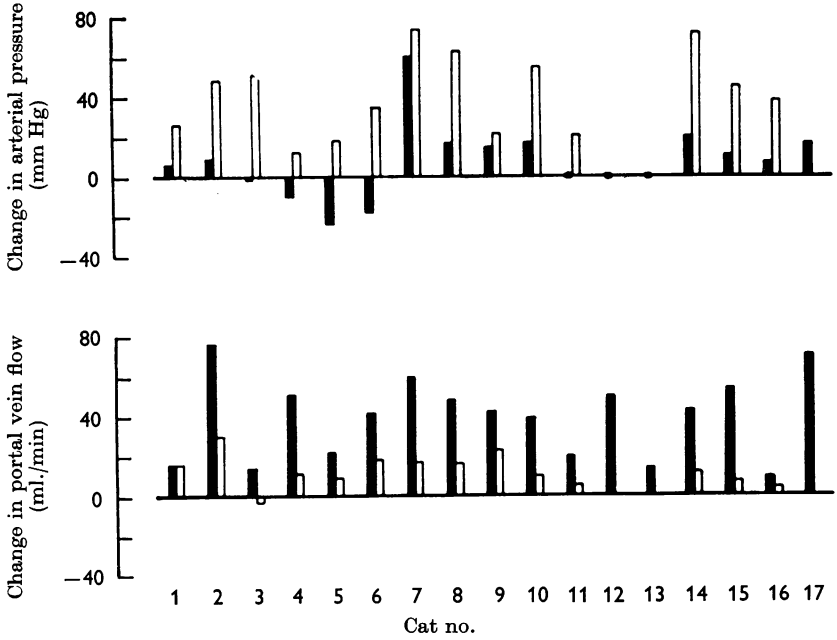

Fig. 6. The portal vein flow responses to the first infusion of adrenaline and noradrenaline in all the cats. Ordinates, the change from the control levels in the mean arterial pressure and in the portal vein flow. Abscissa, the solid blocks represent the responses to adrenaline, the open blocks the responses to noradrenaline, in each of the seventeen animals. The doses were 1 μg base/min in cat 1, 2 μg base/min in cats 2–13 and 4 μg base/min in cats 14–17. In cats 12, 13 and 17, adrenaline only was given.

Adrenaline was infused on fifty-three occasions and noradrenaline on twenty-eight occasions in doses of 0·5–4 μg/min for periods of 5–10 min. Figure 5 shows the responses obtained in one animal to infusions of adrenaline and noradrenaline in doses of 2 μg/min. The mean arterial pressure, portal vein pressure and portal vein flow are shown.

To illustrate the variation from animal to animal, Fig. 6 shows the changes from the control level in mean arterial pressure and in portal vein flow during the infusions of adrenaline and noradrenaline. The blocks

show the responses in each of the seventeen cats to infusions of adrenaline and noradrenaline given in the manner shown in Fig. 5. The values were read off at 1 min intervals for the period of each infusion and the mean taken. These particular responses were the first pair in each animal and the first infusion in the three animals in which only adrenaline was given. On repetition of the infusions, the change in portal flow usually remained similar although in some animals it progressively decreased. This decrease was associated with a decrease in the control flow and the response was restored on infusion of 10–20 ml. 10% Rheomacrodex in 0·9% NaCl (Pharmacia Ltd). In these animals some haemorrhage occurred into the abdomen.

Adrenaline infusions produced a small rise in mean arterial pressure, a large rise in portal vein flow and a rise in portal vein pressure. The range of the increases in the portal vein flow in these experiments (Fig. 6) was similar to the range of the increases in the flow from the hepatic region of the inferior vena cava (Fig. 2). The effect of noradrenaline was small but more variable. On two occasions the flow decreased slightly, on two it remained unchanged and on the remaining twenty-four occasions it rose slightly. On cessation of the infusion, while the mean arterial pressure was falling, the portal vein flow often increased before returning to the control level. This effect was similar to that illustrated in Fig. 7. This effect on cessation of the infusion was occasionally seen following adrenaline, but when present it was invariably smaller than that following noradrenaline.

In two animals, the effect of adrenaline on portal vein flow was unaffected by the administration of atropine sulphate (1 mg/kg, B.P.) or pentolinium tartrate (1 mg/kg, May and Baker).

These results suggest that at least part of the increase in liver blood flow caused by adrenaline infusions is due to an increase in portal vein flow. The size of the increase is similar in the two cases, but, since they were studied in different animals and the range is wide, participation of the hepatic artery in the response could not be excluded. In an attempt to investigate this further, a series of experiments was carried out in which a probe of the electromagnetic flowmeter was placed first on the superior mesenteric artery and then on the coeliac artery. Infusions of adrenaline and noradrenaline were carried out while it was on each site.

Flows in the superior mesenteric and coeliac arteries

In the four animals weighing 2·8–3·7 kg (mean 3·3 kg), during the control period the flows in the superior mesenteric artery ranged from 33 to 77 ml./min (mean 53 ml./min) and in the coeliac artery from 31 to 88 ml./min (mean 62 ml./min). The sum of these flows in each animal lay within the range of values described for the hepatic segment flow (Table 1). Slow

oscillations in the flows were often seen, especially in the coeliac artery flow (Fig. 7).

A total of twenty-one intravenous infusions of adrenaline and noradrenaline in doses of 1 and 2 μg/min were made while the flow in each artery was recorded. Typical responses in one animal in which adrenaline

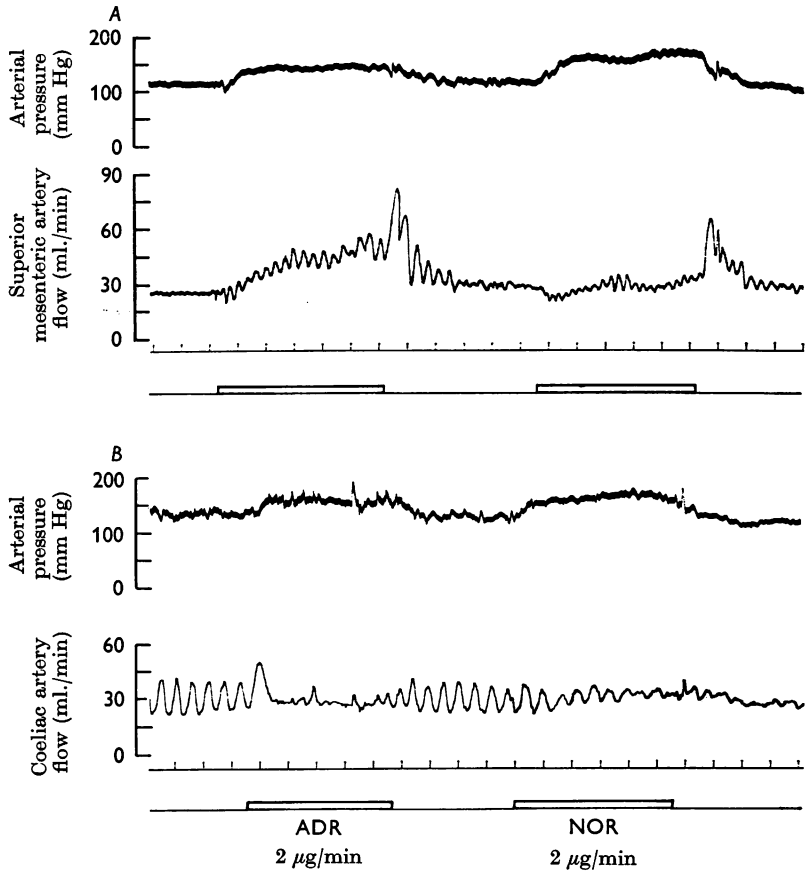

Fig. 7. The responses in one animal to infusions of adrenaline and noradrenaline in doses of 2 μg base/min while recording the flow in the superior mesenteric artery (*A*) and subsequently in the coeliac artery (*B*). Ordinates, the mean arterial pressure and the arterial flow. Abscissa, time in min. Adrenaline (ADR) and noradrenaline (NOR) were infused during the periods shown.

and noradrenaline were infused in a dose of 2 μg base/min are shown in Fig. 7. The difference in the response to the intravenous infusions of adrenaline was clear-cut: the superior mesenteric artery flow showed a marked increase while the coeliac artery showed little change. The changes in arterial pressure and in coeliac and superior mesenteric artery flows in response to all the infusions are shown in Fig. 8. Again, the values were

read off at 1 min intervals for the period of each infusion and the mean taken. The increase in superior mesenteric artery flow was often preceded during the first minute of the infusion by a small decrease in flow and on cessation of the infusion a brief increase was usually seen before the flow returned to its control level. The slow oscillations in coeliac artery flow seen during the control period usually disappeared during the adrenaline infusions but the mean flow remained unchanged. Occasionally, a brief increase in coeliac artery flow occurred when the infusion was begun (Fig. 7).

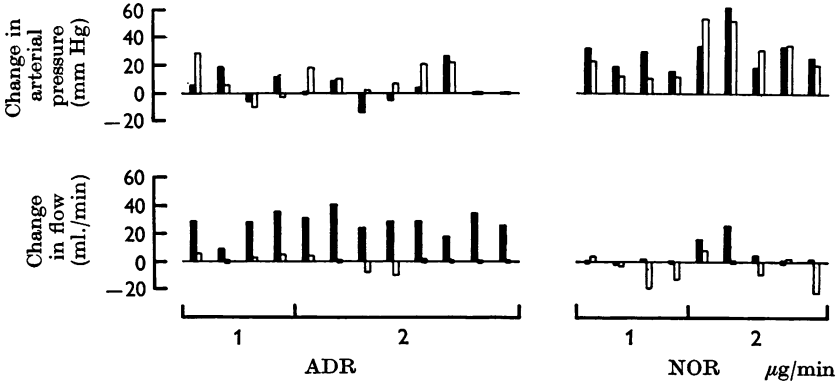

Fig. 8. The responses to all the infusions of adrenaline and noradrenaline. Ordinates, the change from the control levels in the mean arterial pressure and in the arterial flow. Abscissa, the solid blocks represent the changes from the control levels in the superior mesenteric artery flow, the open blocks the changes in coeliac artery flow, in response to infusions of adrenaline (ADR) and noradrenaline (NOR) in the doses shown.

Intravenous noradrenaline infusions caused little change or a decrease in the flow in the coeliac artery, although the slow oscillations were often modified. There was little change in superior mesenteric artery flow during the noradrenaline infusions but a marked feature was the brief but large increase in flow which occurred when the infusion was ended. This was similar to the brief increase in portal vein flow previously noted.

It is concluded from these experiments that the increase in hepatic blood flow caused by adrenaline is due to an increased flow in the superior mesenteric artery and portal vein. Flow in the coeliac artery is not increased.

DISCUSSION

The regional blood flows and venous returns, recorded in these experiments by long-circuit of the venae cavae, lie within the ranges previously described and discussed (Greenway & Lawson, 1966). The mean hepatic segment flow was 92 ml./min. In the separate series of animals in which

portal vein flow was measured, the mean portal vein flow was 61 ml./min. If these experiments are comparable, then two-thirds of the hepatic blood flow is derived from the portal vein and one-third from the hepatic artery. This estimate is in reasonable agreement with data for other animals reviewed by Grayson & Mendel (1965). The sum of the flows in the coeliac and superior mesenteric arteries lies within the range of values for hepatic flow. However, the number of animals studied is small and flow in the inferior mesenteric artery was not measured.

The administration of a spinal anaesthetic agent into the cisterna magna caused a fall in mean arterial pressure and a decrease in venous return. Surprisingly, the proportion of the venous return coming from each of the four regions studied was hardly altered. This suggests that during the control periods during which these measurements were made, when one factor affecting the regional blood flows is removed, the remaining factors are re-adjusted in such a way that the distribution remains unchanged. This does not exclude the possibility that changes in blood flows occurred through small vascular areas. Such changes may not result in a significant change in the gross regional flows measured.

In these experiments, noradrenaline caused little change in the venous return or in the regional flows studied, even though the mean arterial pressure was increased. Our results are consistent with other work which shows that noradrenaline causes vasoconstriction in all regions studied in man (Bearn *et al.* 1951; Barcroft & Swan, 1953) and animals (e.g. Folkow *et al.* 1948). Thus noradrenaline appears to cause no gross redistribution of the regional blood flows. However, small changes are apparent when flow from smaller regions is studied and in some animals noradrenaline caused a small increase in portal vein and superior mesenteric artery flows and a decrease in coeliac artery flow. The occurrence of a brief increase in flow on cessation of the infusion may indicate that noradrenaline has a similar action to adrenaline but this is masked by a concomitant vasoconstriction. After cervical spinal anaesthesia, a small effect qualitatively similar to that of adrenaline was seen in some animals.

Our results confirm the observations in man (Bearn *et al.* 1951; Bradley *et al.* 1952) that adrenaline administration resulted in a marked increase in hepatic blood flow. The proportion of the venous return coming from the liver increased from about 35 % to 45–50 % in most of our experiments. This effect was marked even with infusions which did not raise the mean arterial pressure by more than 5 mm Hg. There have been few studies on the effects of adrenaline on hepatic blood flow in anaesthetized animals. Grayson & Johnson (1953) and Ginsburg & Grayson (1954), using internal calorimetry in the rat and rabbit, showed that adrenaline increased hepatic blood flow and suggested that a baroreceptor reflex was involved. In our

experiments in the cat, adrenaline caused an increase in hepatic blood flow after cervical spinal anaesthesia and an increase in portal blood flow after atropine and pentolinium. A baroreceptor reflex does not therefore appear to be involved in this species.

The results of the experiments, in which the blood flow in the portal vein, the superior mesenteric artery and the coeliac artery was recorded, suggest that the increase in hepatic flow was due to an increase in flow in the superior mesenteric artery and portal vein. Since the coeliac artery flow was unchanged by the infusion of adrenaline, it seems unlikely that the hepatic artery played any part in the increase in hepatic blood flow. These conclusions are at variance with reports in the literature that adrenaline decreases portal vein flow (Clarke, 1933; Folkow *et al.* 1948) although Green *et al.* (1955) showed a brief decrease followed by an increase in superior mesenteric artery flow in the dog, and Barer (1961) obtained variable changes, but usually an increase, in mesenteric vein flow in the cat. However, all these studies employed single injections of adrenaline rather than infusions. In our studies, the superior mesenteric artery and portal vein flows often showed little change or a slight decrease during the first minute of the infusion and then rose progressively. The occurrence of a slight overshoot in the superior mesenteric artery and portal vein flows on cessation of the infusion in some animals suggests adrenaline may have a small vasoconstrictor action which partly offsets its vasodilator action. In the experiments involving long-circuit of the venae cavae, adrenaline infusions increased the venous return and caused at least a slight rise in mean arterial pressure. Since this did not cause a sustained increase in the other regional flows, some vasoconstriction must have occurred. Therefore it appears that, due to vasodilation of the intestinal blood vessels and some vasoconstriction elsewhere, most of the increase in cardiac output passes through the superior mesenteric artery, portal vein and hepatic vein. Such an increase would also change the relative contribution of the hepatic artery and portal vein to hepatic blood flow. The significance of such a change is not clear at present.

Folkow, Lewis, Lundgren, Mellander & Wallentin (1964) have suggested that stimulation of the sympathetic vasoconstrictor fibres to the intestine causes a redistribution of the blood flow. There was a profound vasoconstriction of the mucosa with little reduction in total intestinal blood flow which seemed to imply some fairly wide bore vessels actually became opened up in deeper layers of the intestinal wall. The responses to noradrenaline in our experiments suggest that it may have a very similar effect while adrenaline could produce the increase in flow by opening the wide bore vessels while constricting the mucosal vascular bed to a much smaller extent. Further work is necessary to test this hypothesis.

The slow oscillations in the flow in the coeliac artery and, to a lesser extent, in the superior mesenteric artery during the control period may have been due either to active changes in vasomotor tone or to passive changes resulting from rhythmic contractions of intestinal smooth muscle. They were abolished by both adrenaline and noradrenaline which relax intestinal smooth muscle, a finding which may support the second possibility.

The increase in intestinal blood flow during the infusion of adrenaline became progressively less during the course of experiments in which some haemorrhage occurred. The response appeared to be markedly reduced by the loss of only a small volume of blood (5–10 ml.) and restored by infusion of a small volume of dextran.

In most experiments, during the infusion of adrenaline the blood flow through the iliac segment showed a brief increase followed by a return to the control values. Thus, of the changes observed in man (Allen, Barcroft & Edholm, 1946), the rapid increase in flow during the first 2 min of the infusion was seen but could not be studied with our technique, while the smaller sustained increase did not occur. It may have been masked by a concomitant cutaneous vasoconstriction. Other workers have observed an increase in skeletal muscle flow in cats when single injections of adrenaline were given (e.g. Folkow *et al.* 1948; Celander, 1954; Barer, 1961).

The smallest doses of adrenaline employed in these experiments appear to lie at the upper end of the range which might be secreted by the adrenal medulla (Kaindl & von Euler, 1961; Celander, 1954; Marley & Paton, 1961; Feldberg & Lewis, 1964). It remains to be shown whether endogenous release of adrenaline results in an increase in intestinal blood flow. It is not clear whether the time course of endogenous release would be comparable to a single injection or to a constant infusion. The responses to adrenaline may be modified by anaesthesia although the increase in hepatic blood flow was described in conscious man. Further elucidation of these problems awaits the measurement of the responses to both exogenous and endogenous adrenaline in the conscious unrestrained animal.

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REFERENCES

Allen, W. J., Barcroft, H. & Edholm, O. G. (1946). On the action of adrenaline on the blood vessels in human skeletal muscle. *J. Physiol.* **105**, 255–267.

Barcroft, H. & Swan, H. J. C. (1953). *Sympathetic Control of Human Blood Vessels*, p. 93. London: Edward Arnold.

Barer, G. R. (1961). A comparison of the circulatory effects of angiotensin, vasopressin and adrenaline in the anaesthetized cat. *J. Physiol.* **156**, 49–66.

BEARN, A. G., BILLING, B. & SHERLOCK, S. (1951). The effect of adrenaline and noradrenaline on hepatic blood flow and splanchnic carbohydrate metabolism in man. *J. Physiol.* **115**, 430–441.

BRADLEY, S. E., INGELFINGER, F. J. & BRADLEY, G. P. (1952). Determinants of hepatic haemodynamics. In *Visceral Circulation.* Ciba Foundation Symp., p. 219. London: Churchill.

CELANDER, O. (1954). The range of control exercised by the sympathico-adrenal system. *Acta physiol. scand.* **32**, Suppl. 116.

CLARK, G. A. (1933). The vaso-dilator action of adrenaline. *J. Physiol.* **80**, 429–440.

FELDBERG, W. & LEWIS, G. P. (1964). The action of peptides on the adrenal medulla. Release of adrenaline by bradykinin and angiotensin. *J. Physiol.* **171**, 98–108.

FOLKOW, B., FROST, J. & UVNÄS, B. (1948). Action of adrenaline, noradrenaline and some other sympathomimetic drugs on the muscular, cutaneous and splanchnic vessels of the cat. *Acta physiol. scand.* **15**, 412–420.

FOLKOW, B., LEWIS, D. H., LUNDGREN, O., MELLANDER, S. & WALLENTIN, I. (1964). The effect of the sympathetic vasoconstrictor fibres on the distribution of capillary blood flow in the intestine. *Acta physiol. scand.* **61**, 458–466.

GINSBURG, M. & GRAYSON, J. (1954). Factors controlling liver blood flow in the rat. *J. Physiol.* **123**, 574–602.

GRAYSON, J. & JOHNSON, D. H. (1953). The effect of adrenaline and noradrenaline on the liver blood flow. *J. Physiol.* **120**, 73–94.

GRAYSON, J. & MENDEL, D. (1965). *Physiology of the Splanchnic Circulation*, p. 106. London: Edward Arnold.

GREEN, H. D., DEAL, C. P., BARDHANABAEDYA, S. & DENISON, A. B. (1955). The effects of adrenergic substances and ischaemia on the blood flow and peripheral resistance of the canine mesenteric vascular bed before and during adrenergic blockade. *J. Pharmac. exp. Ther.* **113**, 115–123.

GREENWAY, C. V. & LAWSON, A. E. (1966). The effect of haemorrhage on venous return and regional blood flow in the anaesthetized cat. *J. Physiol.* **184**, 856–871.

KAINDL, F. & VON EULER, U. S. (1951). Liberation of noradrenaline and adrenaline from the suprarenals of the cat during carotid occlusion. *Am. J. Physiol.* **166**, 284–288.

MARLEY, E. & PATON, W. D. M. (1961). The output of sympathetic amines from the cat's adrenal gland in response to splanchnic nerve activity. *J. Physiol.* **155**, 1–27.