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THE EFFECT OF HAEMORRHAGE ON VENOUS RETURN AND REGIONAL BLOOD FLOW IN THE ANAESTHETIZED CAT

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SUMMARY

1. In cats under pentobarbitone anaesthesia, 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).

2. In these preparations, the mean venous return was 130 ml./kg. Of this 28 % came from the superior vena cava and 37 % from the hepatic, 23 % from the renal and 12 % from the iliac segments of the inferior vena cava.

3. After haemorrhage, the flows from all the venae cavae segments decreased. The quantitative changes varied with the particular cat, the degree and duration of the haemorrhage and whether the animal had been subjected to a previous haemorrhage.

4. The proportion of the reduced venous return draining from the superior vena cava and the hepatic segment increased, that draining from the renal and iliac segments decreased. Vasoconstriction occurred in all vascular beds, but was greatest in the kidney and hind limbs. Thus the blood flow through the head and liver was partially maintained at the expense of that through the kidneys and hind limbs.

5. Autoregulation of blood flow in the kidneys was usually seen immediately after the first removal of blood but with the onset of renal vasoconstriction it was reduced or abolished for the remainder of the experiment.

INTRODUCTION

Studies on blood flows during haemorrhage have usually been concerned with cardiac output or confined to single organs in the dog. It is difficult to assess from this type of experiment whether the distribution of the cardiac output is altered. Simultaneous measurements of regional blood flows and cardiac output or venous return are necessary.

These have been studied using a modification of the perfused cat preparation (Grundy & Howarth, 1957). The blood flows from the superior vena cava and from the hepatic, renal and iliac segments of the inferior vena cava were long-circuited through measuring cylinders and determined by direct timing. The sum of these flows was equal to the venous return (minus coronary and bronchial flows). The preparation was used to study venous return and regional blood flows in the anaesthetized cat and the effects of removal and restoration of blood.

METHODS

Extracorporeal circuit

The extracorporeal circuit was similar to, but smaller than, that described for the dog (Greenway & Howarth, 1963). Blood draining from the four segments of the venae cavae passed to outflow cylinders (*F*, Fig. 1) in which the flows could be timed. From these cylinders the blood drained into a glass reservoir (RES) and after passing through a glass wool filter (GW), it was lifted by a Sigmamotor pump to the annular space of the unit *R* supported above the animal. From this unit, blood returned by gravity to the right atrium via the input tube (*I*). The cardiac input was varied by adjusting the height of the unit *R* above the right atrium. Blood from the overflow of the annular space in unit *R* was returned to the reservoir through tube *O*. The venous pressures in the various segments of the venae cavae could be varied by raising or lowering the outflow cylinders. The blood was maintained at 38–39° C by means of a temperature-controlled water-bath around the reservoir and the temperature of the blood was measured by a thermometer (*T*) before it entered the animal.

Before each experiment the apparatus was cleaned, treated with Silicone MS Antifoam Emulsion RD (Hopkin and Williams Ltd.) and then sterilized with formalin as described for the dog. It was primed immediately before use with 100 ml. donor cat blood to which 20 mg (3400 u.) heparin (Boots) had been added.

Long-circuit technique

Cats were anaesthetized with sodium pentobarbitone (30 mg/kg, Abbott Laboratories) by intraperitoneal injection and additional doses of 5 mg were given intravenously whenever reflex limb movements occurred. In three cats, chloralose (70 mg/kg, British Drug Houses) was given intravenously after induction with ether. With careful haemostasis, the trachea was cannulated and loose ligatures placed round the following vessels: the right external jugular vein, the right femoral artery, the right femoral vein and the inferior vena cava both below the renal veins and above the lumboadrenal veins. Positive pressure artificial ventilation was then applied for the rest of the experiment and adjusted to almost suppress diaphragmatic movements. Loose ligatures were placed round the superior vena cava and azygos vein through the fourth intercostal space and the inferior vena cava through the seventh space. After allowing haemostasis to occur for a 30 min period during which the donor blood was obtained from another cat anaesthetized with ether, 10 mg heparin was given intravenously. At this stage the mean arterial and central venous pressures were recorded, using Hg and saline manometers respectively, from the right femoral artery and the right jugular and femoral veins.

The superior vena cava was then occluded. This caused a fall in arterial pressure of less than 10 mm Hg since the azygos vein was open. The input cannula from the unit *R* (Fig. 1) was inserted into the cardiac end of the superior vena cava (*I*, Fig. 2). The cranial end was then cannulated (SVC, Fig. 2), the blood drained to an outflow cylinder and returned through

the input cannula. The azygos vein was tied (*A*, Fig. 2). Thus the blood flow from the superior vena cava was long-circuited through the apparatus and returned to the right atrium.

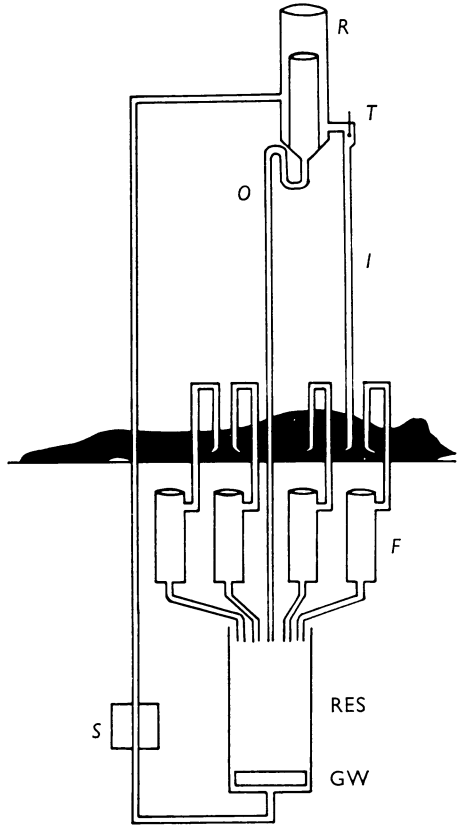

Fig. 1. The extracorporeal circuit. *F*, outflow cylinders; RES, reservoir; GW, glass wool filter; *S*, Sigmamotor pump; *R*, unit with annular space from which blood passed through input tube (*I*) to the right atrium or via the overflow (*O*) back to the reservoir; *T*, thermometer. The reservoir was enclosed in a temperature-controlled water-bath (not shown).

The inferior vena cava was occluded below the renal veins. The cannula recording venous pressure from the femoral vein was connected to the reservoir in order to drain the occluded segment. The inferior vena cava was cut below the renal veins and both ends were cannulated (RS and IS, Fig. 2). It was then tied above the diaphragm and the blood drained through the two cannulae into outflow cylinders. The input to the right atrium was correspondingly increased to keep the extracorporeal circuit volume constant. The femoral vein cannula was reconnected to record venous pressure.

The inferior vena cava was then cannulated (HS, Fig. 2) above the diaphragm on the caudal side of the tie and the blood drained to an outflow cylinder. The ligature round the vena cava above the lumboadrenal veins was tied (*T*, Fig. 2). Thus the vena cava was separated into three segments: the region draining the lower body (iliac segment), the region draining the renal and lumboadrenal veins (renal segment) and the region draining

the hepatic veins (hepatic segment). The blood flowing from these segments passed through three outflow cylinders into the reservoir from which it was returned to the right atrium.

After completion of the cannulations the wounds were closed and drainage tubes inserted. The preparation took 3 hr to set up from the time anaesthetic was administered and at no time was the flow from any vascular bed seriously obstructed for more than a few seconds. In two animals, the right renal vein was separately cannulated and drained through a fifth outflow cylinder.

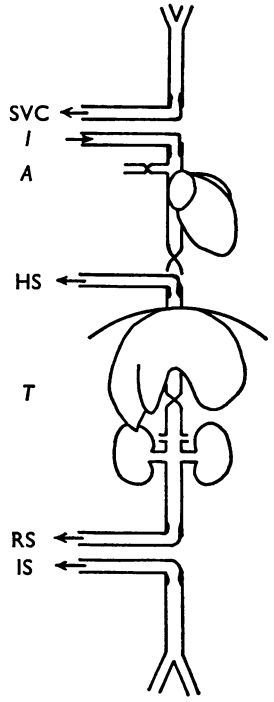

Fig. 2. The positions of the cannulae in the venae cavae. Blood was returned to the animal through input cannula (*I*), and drained through the cannulae in the superior vena cava (SVC), and the hepatic (HS), renal (RS) and iliac (IS) segments of the inferior vena cava. The azygos vein (*A*) was tied and the hepatic and renal segments of the inferior vena cava were separated by the tie *T*.

The pressures in the superior vena cava and iliac segment were measured through the right jugular and femoral vein cannulae and the outflow cylinders adjusted to restore these pressures to their pre-long-circuit values. In a few animals, the venous pressures in the hepatic and renal segments were recorded by small catheters inserted down the drainage cannulae. When this was not done, great care was taken to avoid obstruction at the cannula tip and the outflow cylinders were set at the same level as that of the iliac segment. The flows were measured by timing the collection of 10 ml. into each outflow cylinder in turn. These were repeated every 3 or 4 min. The small volumes of blood which oozed into the thorax and abdomen were returned to the reservoir. Post-mortem examinations were carried out in all experiments to verify the positions of the cannulae and ties.

RESULTS

The preparation

Measurements during the control period. Twenty-nine female cats were prepared. At least 30 min were allowed for the flows to stabilize and during this period the cardiac input was adjusted to keep the volume of blood in the extracorporeal circuit constant. When the flows had become steady, measurements were made over 10–15 min to obtain the control values for each animal. The mean values and ranges for the twenty-nine animals are given in Table 1. To show the relative regional blood flows, the flow from each vena cava segment was expressed as a proportion of the total venous return (minus coronary and bronchial flows).

TABLE 1. The mean values and ranges of the measured variables recorded during the control periods in the twenty-nine animals

	Mean	Range
Cat weight (kg)	2·3	1·5–3·1
Mean arterial pressure (mm Hg)	119	79–160
Flows		
Superior vena cava (ml./min)	83	42–113
Hepatic segment (ml./min)	111	53–199
Renal segment (ml./min)	68	17–118
Iliac segment (ml./min)	35	19–55
Venous return (ml./min)	297	131–482
Venous return/kg body wt. (ml./kg.min)	129	68–217
Flows as proportion of the venous return		
Superior vena cava	0·28	0·20–0·35
Hepatic segment	0·37	0·29–0·47
Renal segment	0·23	0·13–0·36
Iliac segment	0·12	0·08–0·16
Duration of experiments from completion of long-circuits (min)	360	150–550

The general behaviour of the preparations confirmed the results of Howarth (1962). In some experiments there was a small loss of extracorporeal blood volume which was approximately accounted for by small quantities of blood oozing into the chest and abdomen which could not be drained. Administration of 5 mg pentobarbitone at any stage of the experiment caused small changes persisting for no more than 4 min and the ear flick and corneal reflexes were present throughout. The results obtained in the three animals under chloralose anaesthesia were similar to those in the animals under pentobarbitone anaesthesia.

Venous anastomoses. If the segmental flows were to be taken as measuring the blood flow through the tissues draining into each segment, it was necessary to show that shunting of blood did not occur from one segment to another through venous anastomoses. Howarth (1962) showed that, except in occasional animals, shunting of blood between superior and

inferior venae cavae did not occur. By measuring the flows while varying the venous pressures these results were confirmed and it was also found that shunting between the inferior vena cava segments was insignificant under normal venous pressure changes, although it could become significant if the venous pressure in a segment rose to a very high level. Such high venous pressures did not occur in these experiments.

Renal segment flow. The renal segment received the renal veins, the lumboadrenal veins and the left ovarian vein regularly and often the right ovarian vein. To assess the contribution by the kidneys to this flow, the right renal vein flow was measured in two animals. The flows during the control period are shown in Table 2. The right renal vein flow represented 9–10% of the venous return. Assuming equal blood flow through each kidney, the renal blood flow was 76 and 88% of the renal segment flow in the two animals. During the removal and restoration of blood, the right renal vein flow and the remainder of the renal segment flow varied in parallel. It is concluded that changes in the renal segment flow represent essentially changes in renal blood flow.

TABLE 2. Renal vein and renal segment flows during the control periods in two experiments

	Expt. 1	Expt. 2
Right renal vein flow (ml./min)	32	25
Remainder of renal segment flow (ml./min)	52	32
Total renal segment flow (ml./min)	84	57
Venous return (ml./min)	330	267

Effect of haemorrhage

Changes in the animal's blood volume were induced by removing blood from or adding it to the reservoir while, at the same time, the volume of blood in the reservoir was kept constant by adjusting the cardiac input. Thus the animal's blood volume was altered by the amount of blood added or removed. The removal of the blood was carried out at first rapidly then more slowly over 4 min, since this was found to result in a steady venous return for the subsequent period of 1–2 hr. No change in the packed cell volume of the blood occurred over this period.

The changes following the removal of blood were followed for 20 min in thirteen animals and for 1–2 hr in eight animals. In these animals the blood was removed in one step but in a further ten animals blood was removed in three steps at 20 min intervals. After return of the blood, measurements were continued for 1 hr, after which the removal of blood was repeated (second haemorrhage).

Venous return. Volumes of blood ranging from 5 to 85 ml. were removed. Although the removal of a large volume of blood usually resulted in a

larger decrease in venous return than the removal of a small volume (Fig. 3), no precise relation was found between the amount of blood removed and the resulting decrease in venous return. For example, in one animal the removal of 75 ml. blood decreased the venous return from 270 to 145 ml./min, while, in another, removal of 25 ml. blood decreased it from 270 to 120 ml./min.

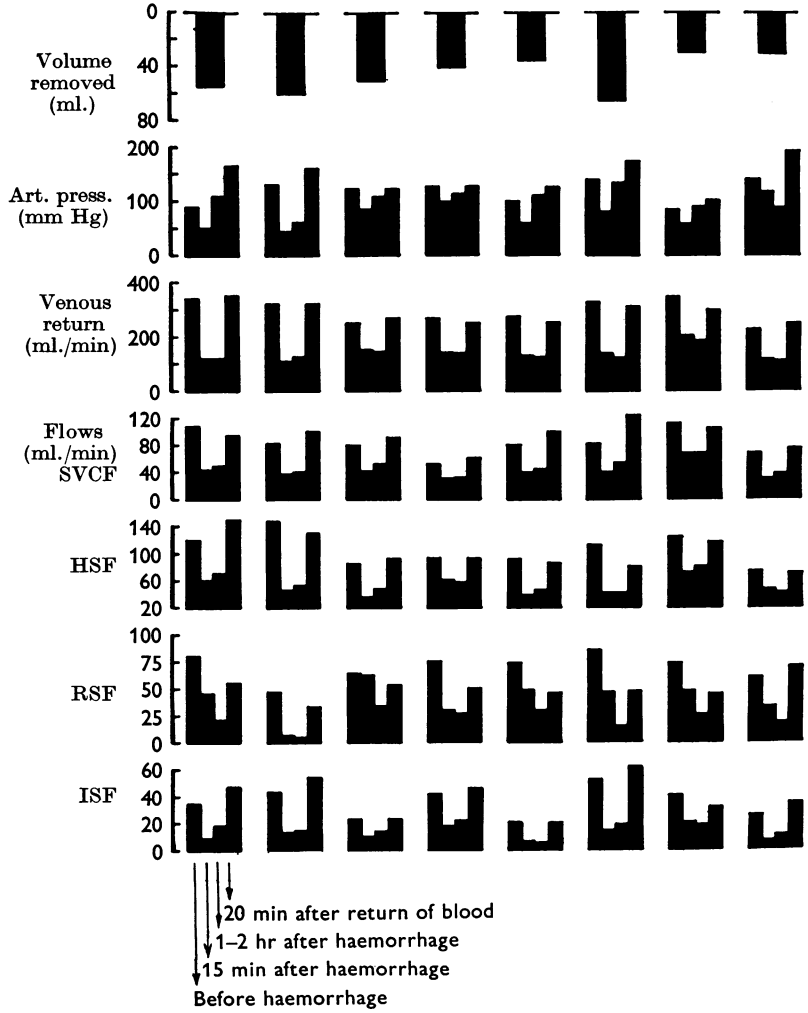

Fig. 3. The response in eight animals to the first haemorrhage. Ordinates, volume of blood removed, mean arterial pressure, venous return and the flows from the superior vena cava (SVCF) and the hepatic (HSF), renal (RSF) and iliac (ISF) segments of the inferior vena cava. Abscissa, each block shows the results in one animal before the haemorrhage, 15 min and 1–2 hr after it and 20 min after return of the blood.

When the removed blood was restored, the venous return rose to a level very similar to its pre-haemorrhage level (Fig. 3). When the same volume of blood was removed a second time, the fall in venous return was always greater than it had been on the first occasion.

Regional blood flows. Haemorrhage invariably resulted in a decrease in all the regional flows (Figs. 3 and 4). However, the extent of this decrease varied in the different regions studied. Such variations are difficult to see

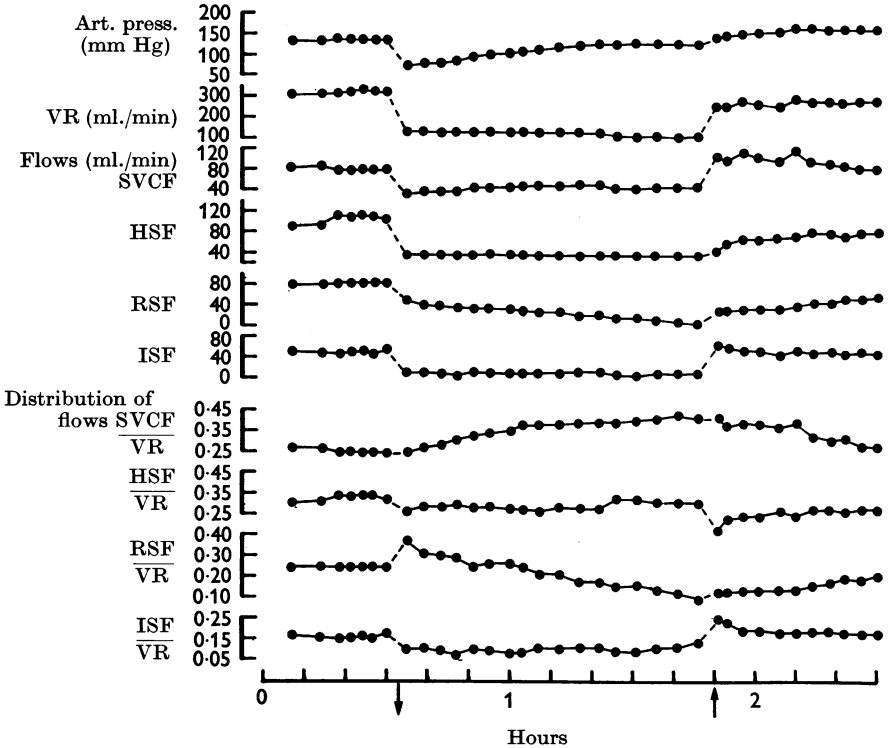

Fig. 4. The response in one animal to the first haemorrhage. Ordinates, mean arterial pressure, venous return (VR), the flows from the superior vena cava (SVCF) and the hepatic (HSF), renal (RSF) and iliac (ISF) segments of the inferior vena cava, and the relative flows expressed as the ratio of each flow to the venous return. Abscissa, time in hours from completion of the preparation. Blood (63 ml.) was removed at the first arrow and returned at the second arrow.

when the actual flows are studied since the levels of each flow and of the total venous return vary widely in different animals. If the regional flows are expressed as proportions of the total venous return, the redistribution of the flows following haemorrhage becomes more apparent. The results in one animal are shown in Fig. 4. After the initial fall following haemorrhage, the flow from the superior vena cava recovered slowly while the renal

segment flow progressively fell over 1–2 hr. The importance of these apparently small changes is shown when the flows are expressed as proportions of the venous return, for example, the superior vena cava flow rose from one quarter to almost one half of the venous return over 1–2 hr. The redistribution of the regional flows 1–2 hr after the haemorrhage in all the experiments is shown in Fig. 5.

The pattern of the redistribution after the first haemorrhage was quite variable but there was usually an increase in the proportion of the venous

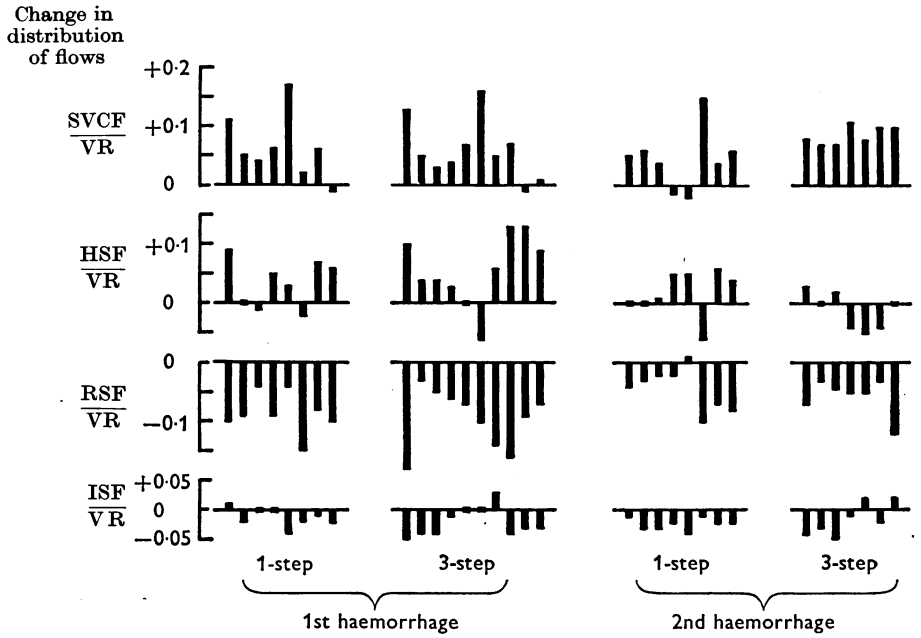

Fig. 5. The change in the distribution of the regional flows 1–2 hr after haemorrhage. Ordinates, the change from the prehaemorrhage level to that observed 1–2 hr after haemorrhage in the proportion of the venous return coming from the superior vena cava (SVCF/VR) and the hepatic (HSF/VR), renal (RSF/VR) and iliac (ISF/VR) segments of the inferior vena cava. Abscissa, the response in the different animals after removal of blood in one step or in three steps at 20 min intervals, on the first and second occasions that it was carried out.

return coming from the superior vena cava and a marked decrease in that coming from the renal segment of the inferior vena cava. The proportion of the venous return coming from the hepatic segment was usually increased while that from the iliac segment was often decreased but these were more variable.

The redistribution found 1–2 hr after the second haemorrhage was similar though the changes were smaller in many animals.

In the experiments in which the haemorrhage was produced in three steps by removing blood at 20 min intervals, the distribution 1 hr after the final removal was similar to that described for the one step removal experiments (Fig. 5). These 3-step haemorrhages demonstrated that the size of the changes in the flows and in the relative distribution depended on the severity of the fall in venous return. This in turn depended on the

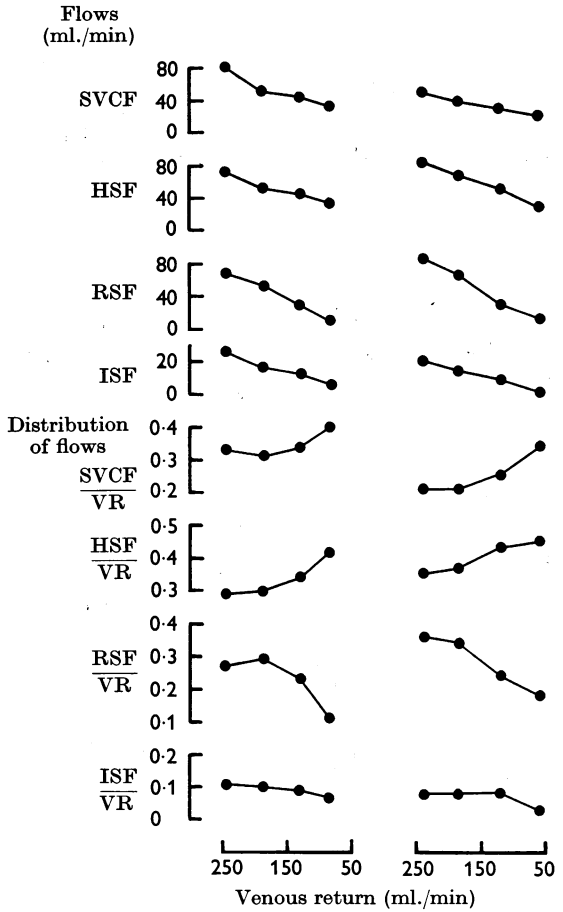

Fig. 6. The effects in two animals of removing blood in steps at 20 min intervals. Ordinates, the flows from the superior vena cava (SVCF) and the hepatic (HSF), renal (RSF) and iliac (ISF) segments of the inferior vena cava and the relative flows expressed as a ratio of each flow to the venous return (VR). Abscissa, venous return in each animal.

volume of blood removed though not in any precise way. The results for two animals are shown in Fig. 6.

Time course of the response. Progressive changes in the flows occurred

from the moment the blood was removed until it was restored. These are shown for one animal in Fig. 4. The changes in the regional flows occurring 15 min after the first haemorrhage in eight animals are shown in Fig. 3. The redistribution of the flows at this time after both the first and second haemorrhages is shown in Fig. 7.

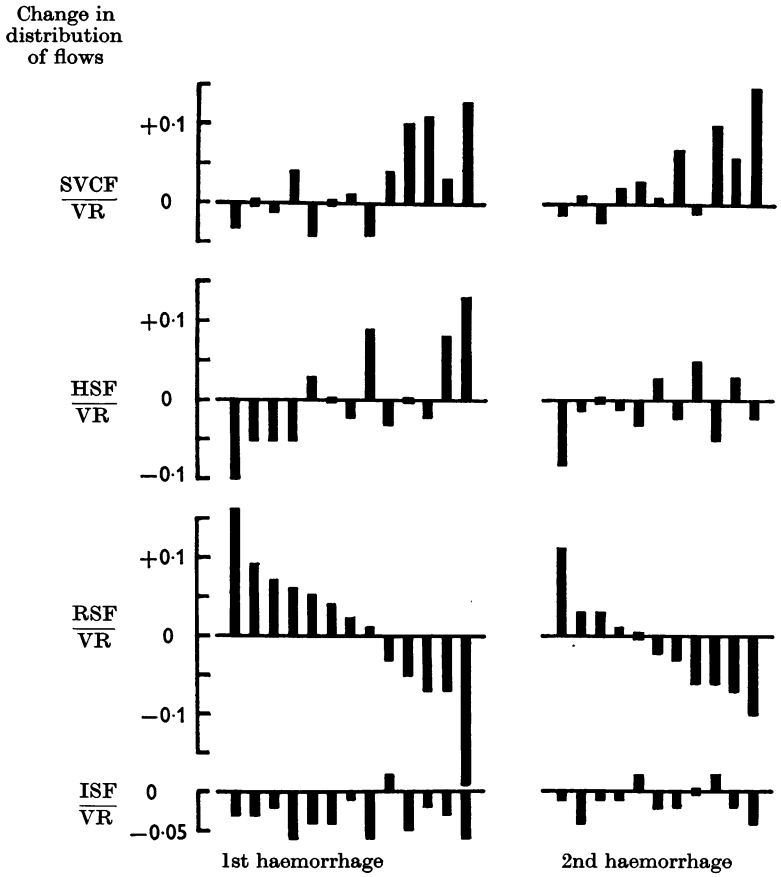

Fig. 7. The changes in the distribution of the regional flows 15 min after haemorrhage. Ordinates, change from the prehaemorrhage level in the proportion of the venous return coming from the superior vena cava (SVCF/VR) and the hepatic (HSF/VR), renal (RSF/VR) and iliac (ISF/VR) segments of the inferior vena cava. Abscissa, response in the different animals 15 min after haemorrhage on the first and second occasions it was carried out. The order is re-arranged to show the continuous series discussed in the text.

The results form a continuous series ranging from those in which the proportion of the venous return coming from the renal segment was increased to those in which it fell. In the latter the distribution of the flows was similar to that 1–2 hr later and progressive changes were small. In

the former, the increased proportion of the venous return coming from the renal segment was often associated with a decreased proportion from the hepatic segment and little change in that from the superior vena cava. In these animals (e.g. Fig. 4), the renal segment flow progressively fell and the hepatic segment and superior vena cava flows rose, resulting after 1–2 hr in the distribution already discussed.

The response to the second haemorrhage was somewhat different. In animals where the renal segment proportion of the venous return was increased 15 min after the first haemorrhage, the change after the second haemorrhage was either much smaller or abolished (Fig. 7). Such an increased proportion was never seen in any animal subjected to a third or subsequent haemorrhage.

Restoration of the blood. When the removed blood was restored to the animal, the venous return came back promptly to its control level. The regional flows all increased but did not return to their original levels (Fig. 4). Twenty minutes after restoration of the blood, the renal segment flow was usually still below the control level, while one or all of the others were above their control levels (Fig. 3). Thus the proportions of the venous return coming from the different regions had only partly returned towards the pre-haemorrhage levels at this time. In many animals the renal flow was still low 1 hr after restoration. This altered base line may account for the smaller response 1–2 hr after the second haemorrhage (Fig. 5).

Arterial pressure. Although the mean arterial pressure fell at the first haemorrhage, it usually recovered rapidly (Figs. 3 and 8). One hour after the haemorrhage it was sometimes as high as or higher than the pre-haemorrhage level. This recovery of the arterial pressure did not correlate with the venous return which remained more or less steady. On restoration of the blood it returned to or above the pre-haemorrhage level. After the second haemorrhage, recovery of the blood pressure was small or absent and in some animals it fell progressively. On restoration of the blood it recovered to the control level in less than half the animals (Fig. 8).

DISCUSSION

The technique of long-circuiting the venae cavae in the cat and dog has been used by several workers and the method was discussed critically by Greenway & Howarth (1963). It provides a useful and inexpensive means of studying venous return and regional blood flows. Although the surgery involved is extensive, it is no more than would be needed to measure the same variables in acute experiments using other instruments, e.g. electromagnetic flowmeters. The technique has the advantage that the flow measurements are direct and accurate and no calibration is needed but it can be used to study only steady or slowly changing flows.

In these experiments, the basic preparation in the cat (Grundy & Howarth, 1957; Howarth, 1962) has been modified to allow separate measurement of the blood draining from four areas into the venae cavae. The superior vena cava flow is predominantly from brain and skeletal muscle, the hepatic segment flow from liver and the iliac segment flow from skeletal muscle. Although the renal segment flow is contaminated by the blood draining from the adrenal glands, lumbar muscle and uterus, we

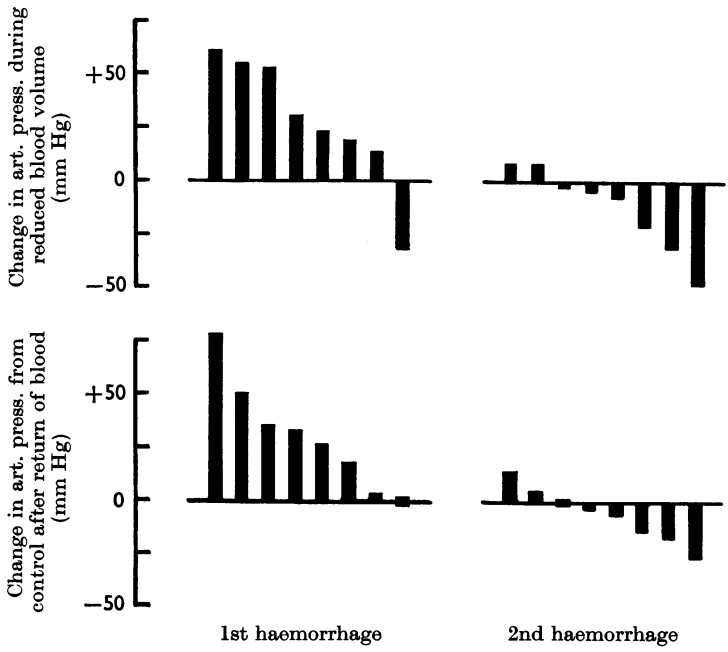

Fig. 8. The changes in mean arterial pressure during and after the period of reduced blood volume. Ordinates, upper curve, the change in arterial pressure between 5 min and 1–2 hr after the haemorrhage, lower curve, the difference between the arterial pressure before the haemorrhage and at 20 min after restoration of the blood. Abscissa, the responses in the different animals to the first and second haemorrhages.

have shown that changes in this segment flow do accurately reflect changes in renal vein flow. Under the conditions of these experiments, shunting of blood between these segments through venous anastomoses does not occur.

Our values for the venous return (minus coronary and bronchial flows) are in good agreement with cardiac output determinations in the cat reported in the literature (Baxter, Cunningham & Pearce, 1952; Cross, Groom, Mottram & Rowlands, 1957; Grundy & Howarth, 1957). As in the dog (Greenway & Howarth, 1963), comparison between different animals

and different species is difficult, due to the lack of a close correlation between cardiac output and body weight or surface area, the varying effects of the anaesthetic agents and the varying durations for which the animal has been anaesthetized. Data on regional blood flows in the cat are very few. The proportion of the venous return draining from the superior vena cava in our experiments is in close agreement with other work in both cat and dog (Greenway & Howarth, 1963). Our mean hepatic blood flow of 48 ml./kg.min is close to values for the dog considered to be reliable by Bradley (1963) but it is higher than most of the values reviewed by Grayson & Mendel (1965).

In the intact anaesthetized animal, a rapid haemorrhage lasting 1 min usually results in an immediate fall in cardiac output, followed by a small increase over the following 4 min. Thereafter it remains approximately steady for some minutes (Guyton, 1959). We observed similar changes in venous return in two early experiments where a rapid haemorrhage was used. In our later experiments, we preferred to use a rapid then slower removal of blood over 4 min since this resulted in a steady venous return over the following 1–2 hr. This period was too short for significant haemodilution to occur and the packed cell volume remained constant, confirming the results of Guyton, Batson & Smith (1951).

The variation from animal to animal in the response to haemorrhage is very great and probably depends on the interaction of many factors including the activity of the vasomotor centre and the blood gas tensions and pH. The effect of these factors on the regional blood flows during haemorrhage needs to be studied.

In most experiments, the proportion of the venous return coming from the superior vena cava increased during the period of reduced blood volume. This confirms the findings of Coleridge & Hemingway (1958) and Howarth (1962). Howarth showed that this response was attributable, at least in part, to cerebral vasodilation. The variability in extent and time course may reflect different responses to haemorrhage in the tissues whose blood drains into the superior vena cava.

The proportion of the venous return coming from the hepatic segment changed little in some experiments and rose in others. Thus these results for the anaesthetized cat support the growing body of evidence reviewed by Grayson & Mendel (1965) and expressed clearly by Sapirstein, Sapirstein & Bredemayer (1960), that the blood flow through the liver is not disproportionately reduced after haemorrhage. Our results relate only to hepatic flow and further work is needed to investigate the relative changes in portal vein and hepatic artery flow.

The reduction in the proportion of the venous return from the kidneys 1–2 hr after haemorrhage was most consistent. A striking feature was the

variation in the response 15 min after the first haemorrhage. The proportion of the venous return coming from the kidneys increased in more than half of the animals. This type of response has been clearly seen in isolated kidneys and is referred to as autoregulation of blood flow. Possible mechanisms are discussed by Selkurt (1963). After 20 min, this autoregulation was replaced by a progressive decrease in the renal blood flow. When this occurred, the autoregulation was not merely masked, it was reduced or abolished for the remainder of the experiment and the renal blood flow remained low for more than 1 hr after restoration of the blood. De Wardener & Miles (1952) reported similar changes in renal blood flow after haemorrhage in the dog. In some animals, no autoregulation was apparent during the first haemorrhage, even though there had been no obvious technical difficulties during the preparation of these animals.

Generally haemorrhage caused a decrease in the proportion of the venous return coming from the iliac segment but considerable variation was observed. This variation may reflect the competitive effects of sympathetic nerve fibre activity and tissue metabolites shown by Lewis & Mellander (1962).

Since, in some experiments, the arterial pressure at the end of the first period of haemorrhage had risen to the control level, the relative blood flows at this time reflect the relative changes in the peripheral resistance of tissues draining into the various venae cavae segments. In all cases the peripheral resistance was increased but the increase was much greater in the kidney and hind limbs than in the liver and head. It is clear from our experiments that the arterial pressure of an anaesthetized cat is no guide to the venous return or regional blood flows.

After restoration of the blood following the first period of haemorrhage, in some animals the arterial pressure showed a steady rise to very high levels at which it then remained. The cause of this rising pressure is not clear and requires further investigation.

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