Hemorrhagic Shock:

The Effect of Prolonged Low Flow on the Regional Distribution of Blood and its Modification by Hypothermia

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THE STUDY of irreversible hemorrhagic shock in the experimental animal is complicated by the number of vascular components involved. The heart,[7] arterioles,[24] capillary beds,[28] capacitance beds,[15] great veins[1] and sympathetic nervous system[5] and adrenal medullary secretions[13] are all concerned with the initial adjustment of hemorrhage and all may be implicated as conspirators in the final catastrophe of circulatory failure. The development of an oxygen debt[8] and the increase in fixed acids in the circulating blood[9] in dogs in hemorrhagic shock indicate some degree of tissue hypoxia. Hypothermia, which reduces the total body oxygen consumption,[14] has been shown to prolong the period of tolerance to severe hemorrhage[12] and to increase survival rate.[10]

Irreversible hemorrhagic shock in which blood pressure and cardiac output fall after restoration of blood loss has often been discussed in terms of falling total peripheral resistance. However, enough evidence has accumulated to show that total peripheral resistance is an inadequate indicator because the response of each vascular bed to a particular stimulus is individual.[18] The peripheral vasculature represents a number of resistances to blood flow placed in parallel and alterations in total peripheral resistance will be the result of changes in any or all vascular beds; such changes may oppose or assist each other. Since all vascular beds share the same pressure head the flow in each reflects its resistance and any alteration in flow in one bed will affect that of the rest.

In irreversible hemorrhagic shock, most authors agree that there is some rise in resistance to blood flow through both the splanchnic and renal vascular beds[3, 11, 27] and the site of the decreasing vascular resistance has not been determined although several studies have directed interest to the musculo-skeletal beds.[11, 16, 22] In those studies in which more than one regional flow has been measured interpretation of the findings has been complicated by decreases in cardiac output which several have suggested to be the principal factor in irreversible hemorrhagic shock.[7, 23]

These problems have been examined in these experiments with a preparation which permits changes in resistance to be inferred from blood pressure and blood flow measurements and allows separation of changes in action of the heart and large veins from those of peripheral circulation. It also permits division of systemic circulation into six convenient regions for measurement of flow while total body flow is kept constant. It permits the influence of prolonged low flow on circulation and its modification by hypothermia to be assessed.

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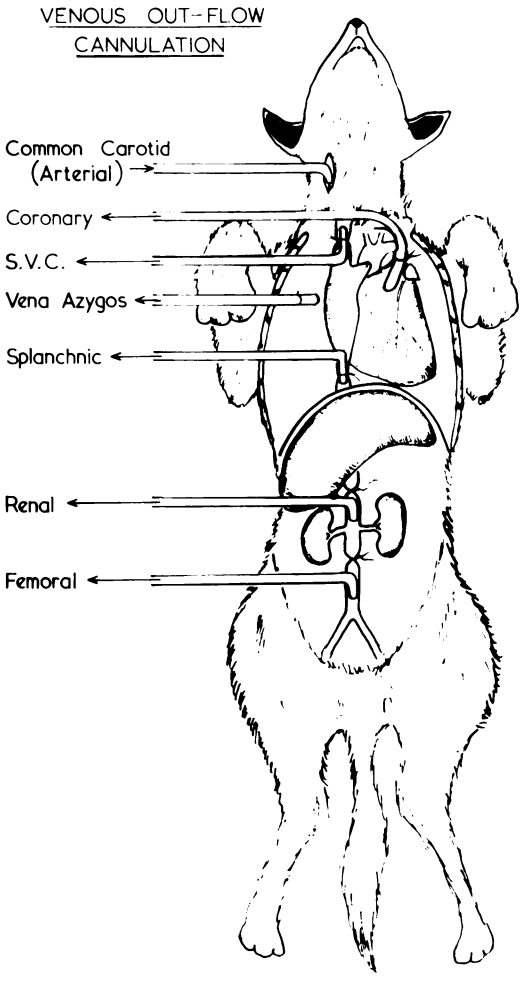

FIG. 1. Schematic diagram of cannulations used for measurement of venous drainage from each region.

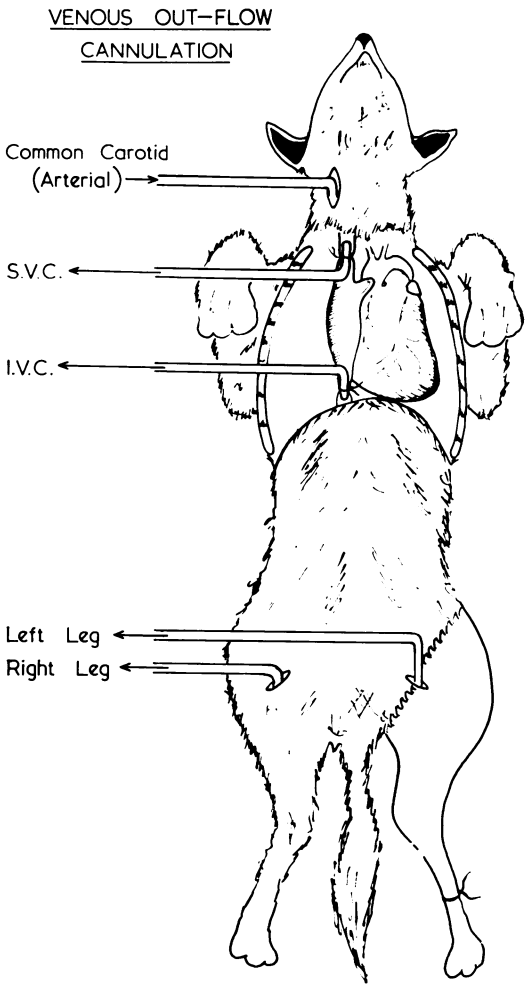

FIG. 2. Schematic diagram of cannulations used for measurement of venous drainage from each hind limb.

Methods

Thirty-five mongrel dogs weighing between 15 and 20 Kg. were anesthetized with thiopentone sodium * in doses of 20–30 mg./Kg. B.W. and placed on a positive pressure respirator delivering a mixture of oxygen and nitrous oxide (3:1). Additional supplements of thiopentone sodium were given as required to maintain a surgical level of anesthesia.

Measurement of Blood Flow. Two different preparations were used, both involving the use of total heart-lung bypass: (1) measurement of regional flow in six regions, the superior vena cava, the vena azygos, the coronary, the splanchnic (total hepatic venous return), the renal and the lower inferior vena cava (pelvis and hind limbs); and (2) measurement of blood flow from each hind limb.

(1) *Regional Flows.* This preparation has been fully described previously [18] (Fig. 1). Through a midline sternal splitting incision the heart was exposed and tapes were placed around the superior and inferior venae cavae and the pulmonary ar-

* Intraval. May & Baker Pty. Ltd., Dagenham, England.

TABLE 1. *Regional Flow (ml./min./Kg. B.W.) and Mean Arterial Blood Pressure Over a Period of 150 Minutes at Normal Temperature.* Mean ± S.E. n = 5

Vascular Region	Time in Minutes					
	0	30	60	90	120	150
Total flow	120 ± 4.0	120 ± 4.7	122 ± 5.6	124 ± 5.8	122 ± 5.1	124 ± 5.6
Splanchnic	46.1 ± 3.1	52.2 ± 5.9	51.7 ± 5.6	47.9 ± 4.9	43.1 ± 3.3	43.6 ± 2.8
Superior vena cava	25.9 ± 2.0	21.0 ± 1.8	24.0 ± 1.4	25.0 ± 1.6	27.7 ± 1.1	28.9 ± 1.6
Vena azygos	10.3 ± 2.8	10.4 ± 2.3	10.7 ± 2.1	11.8 ± 1.5	12.3 ± 1.0	11.9 ± 1.3
Renal	11.9 ± 2.1	13.7 ± 2.5	14.8 ± 2.8	13.9 ± 2.3	12.1 ± 1.9	12.7 ± 1.2
Coronary	13.6 ± 2.2	11.2 ± 1.0	12.5 ± 1.7	14.2 ± 1.7	15.3 ± 2.3	16.7 ± 2.7
Low inferior vena cava	16.7 ± 1.1	14.3 ± 1.3	13.0 ± 0.4	15.7 ± 1.3	18.8 ± 1.6	18.7 ± 2.4
Mean blood pressure (mm. Hg)	124 ± 7.4	117 ± 4.1	133 ± 6.7	139 ± 8.5	133 ± 10.0	135 ± 8.5

tery. Cannulae were placed (a) in the superior vena cava through the ligated proximal stump of the vena azygos; (b) in the inferior vena cava through the amputated stump of the right atrial appendage, and positioned so that its tip lay just proximal to the entrance of the hepatic veins; (c) into the distal stump of the vena azygos; and (d) through the right ventricular wall into its cavity.

Through a midline abdominal incision the inferior vena cava was exposed and cannulae placed in it above and below the entrance of the renal veins isolating each venous segment with ligatures. In this way the venous drainage from the superior vena cava, the vena azygos, the coronary sinus and Thebesian veins, the liver, the kidneys and the hind limb and pelvis could be collected and each measured separately.

Blood flow was measured by temporarily diverting the flow from each venous cannula to a measuring burette and determining the time taken to collect a known volume of blood. The blood then drained into the venous reservoir of a Kay-Cross spinning disc oxygenator from which it was pumped by a non-pulsatile pump † through a stainless-steel heat exchanger into the right common carotid artery.

Preliminary experiments showed that pressure in the cannulated venous segment did not change appreciably during timed collection of the blood in the measuring burette, so that changes in flow due to opposing pressure heads were considered to be negligible. Pressure in the cannulated venous segments was adjusted to atmospheric pressure during the experiment.

(2) *Hind Limb Preparation.* Through a right-sided thoracotomy (Fig. 2) the pericardium was opened and cannulae placed in the superior and inferior venae cavae as described above. Venous drainage from these two major segments of the circulation was measured in the same way as before and passed to the Kay-Cross disc oxygenator and returned to the right common carotid artery via a heart exchanger.

Using bilateral incisions below the inguinal ligaments the femoral vein of each leg was cannulated and the venous drainage measured before returning to the oxygenator. As before, pressure in each venous segment was adjusted to atmospheric pressure.

The left leg was skinned by using a longitudinal and circumferential incision

† Mono Pumps Pty. Ltd., Melbourne, Australia.

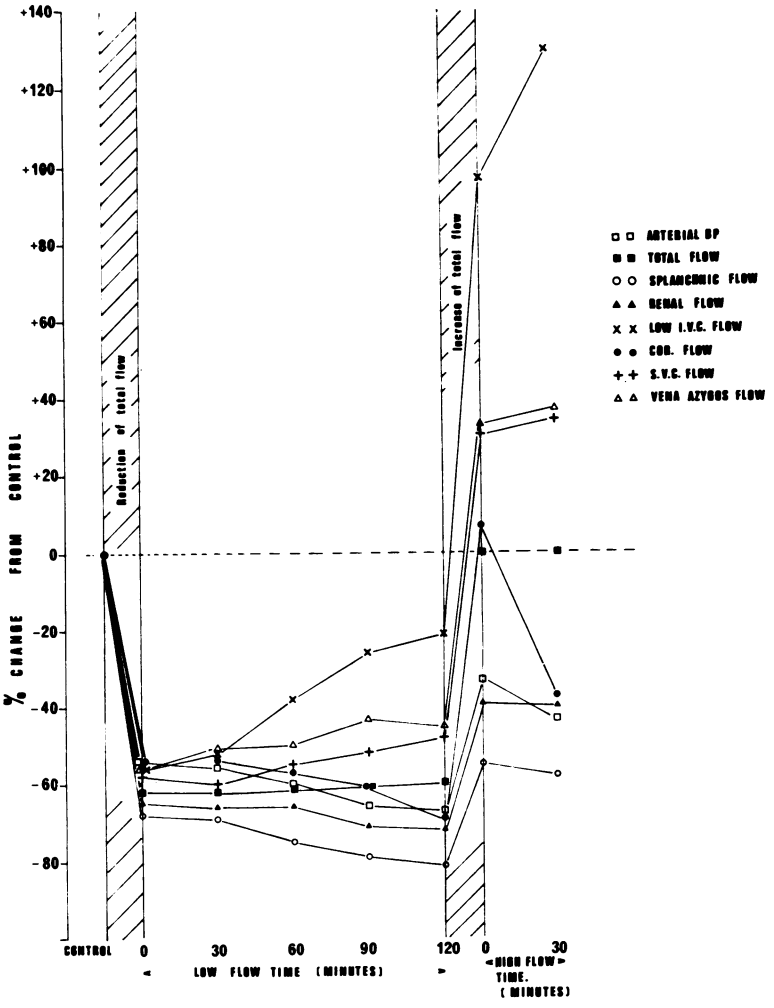

FIG. 3. The changes in total and regional blood flows and mean arterial blood pressure expressed as percentages of the control values, before, during and after the low flow period.

and progressive ligation of all vessels passing to the skin from the deep fascia as skin reflection proceeded. The skin was not detached at the paw but a stout ligature was placed around it at this level. The femoral and sciatic nerves were gently dissected free using a tissue plane separation technic, no muscle being either divided or ligated. The leg was then wrapped in a warm saline-soaked towel surrounded by a plastic sheet to minimize water and heat loss.

In all preparations heparin in doses of 2 mg./Kg. B.W. per hour was administered after all dissections were completed and before cannulation was performed. The oxygenator and extracorporeal circuit were primed with 1 liter of freshly drawn heparinized homologous blood and 500 ml. of 5% dextrose in water. The oxygenator was supplied with 100% oxygen.

Mean systemic arterial blood pressure was measured with a damped mercury manometer connected to a cannula placed in the left internal mammary artery. Venous segmental pressures were measured with a saline manometer. Zero pressure was set at the level of the mid-right atrium.

Esophageal temperature was measured with a thermometer probe * and the tem-

* Yellow Springs Instrument, Inc., Yellow Springs, Ohio, U. S. A.

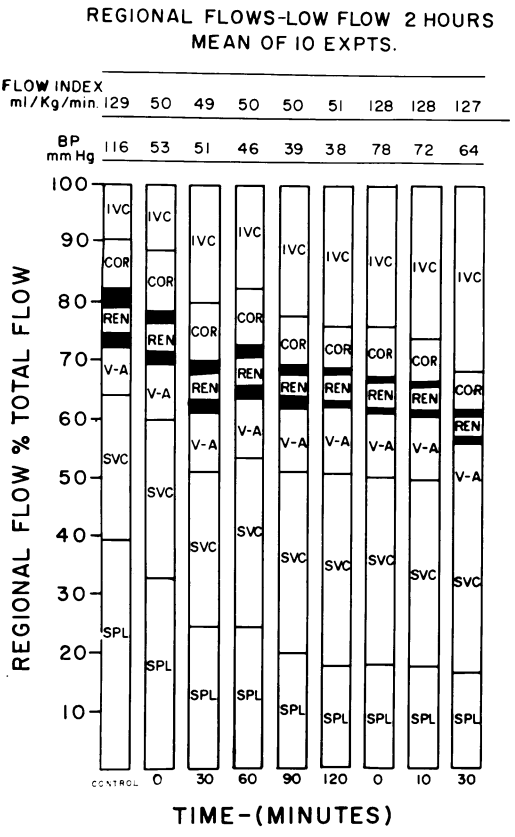

FIG. 4 (a). The proportions of total body flow (% total flow) distributed to each vascular region plotted against time (minutes) before and after the low flow period. Total body flow (ml./min./Kg. B.W.) and systemic arterial blood pressure are indicated.

perature of the water in the heat exchanger altered to maintain esophageal temperature at 37° C. in the normothermic experiments and at 25° C. in the hypothermic experiments.

Hemoglobin oxygen saturation of samples of arterial and venous blood was measured by the method of Roos and Rich.[21] Samples were collected anaerobically from each venous cannula and from the arterial line at intervals. Oxygen capacity of each set of samples was measured by the method of Peters and Van Slyke.[19]

The oxygen content of each sample was determined from the hemoglobin saturation and the oxygen capacity. Oxygen consumption of each region was then estimated by multiplying arteriovenous oxygen content difference by regional blood flow. Despite the use of 100% oxygen in the oxygenator, arterial hemoglobin saturation was never above 98%. Arterial blood P_{O_2} in the oxygenator was monitored with a Clarke electrode and did not exceed 120 mm. Hg.

Induction of "Hemorrhagic" Shock. After a control period of 15 to 45 minutes at a total body flow rate of 120 ml./minute/Kg. B.W. during which the regional flow stabilized, hemorrhagic shock was simulated by reducing total body flow rate to less than 50 ml./minute/Kg. B.W. This rate was maintained for 2 hours, during which regional flow was measured at 5-minute intervals. At the end of 2 hours total body flow rate was increased to control levels and further measurements of regional flow made. The low flow period was considered equivalent to the hemorrhage stage and the subsequent high flow period to that of reinfusion in the standard shock preparation.[3]

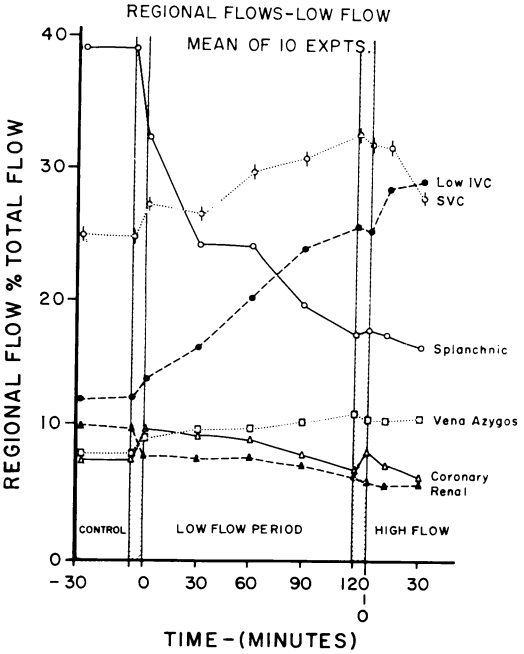

FIG. 4 (b). The proportions of total body flow distributed to each vascular region. The graded vertical bars indicate the beginning and ending of the 2-hour low flow period.

TABLE 2. *Regional Flow (ml./min./Kg. B. W.) and Mean Arterial Blood Pressure Before, During and After Two Hours of Low Flow.* Mean ± S.E. n = 10

Vascular Region	Control Period	Start of Low Flow Period	End of Low Flow Period	Start of High Flow Period	After 30′ High Flow
Total flow	129 ± 4.8	50 ± 2.6	51 ± 3.1	128 ± 6.0	129 ± 5.7
Splanchnic	49.1 ± 4.9	15.9 ± 1.6	9.3 ± 1.4	21.9 ± 4.1	20.6 ± 3.2
Superior vena cava	31.8 ± 4.5	13.4 ± 1.6	16.4 ± 1.4	41.1 ± 3.8	42.6 ± 4.0
Vena azygos	10.7 ± 0.7	4.8 ± 0.6	5.9 ± 0.8	14.2 ± 0.9	14.6 ± 1.0
Renal	13.0 ± 1.1	4.5 ± 0.3	3.6 ± 0.4	7.9 ± 0.8	7.8 ± 0.6
Coronary	10.5 ± 0.8	4.8 ± 0.4	3.4 ± 0.5	11.1 ± 1.6	7.7 ± 1.2
Low inferior (pelvis & hind limb)	16.3 ± 2.3	7.1 ± 1.0	12.8 ± 1.1	32.2 ± 3.1	37.5 ± 3.1
Mean blood pressure (mm. Hg)	116 ± 7.1	55 ± 2.6	38 ± 4.4	78 ± 7.2	66 ± 6.2

Hypothermia. In ten experiments hypothermia (esophageal temperature 25° C.) was induced by blood stream cooling (10° C.) after a control period at 37° C. and before the 2-hour low flow period. It was maintained until the end of the second period of high flow and then the animals were rewarmed to 37° C. Flow measurements were made as before during each of the five periods.

Results

Stability of the Preparation. In five dogs a constant rate of body flow of 120 ml./minute/Kg. B.W. and an esophageal temperature of 37° C. were maintained for a period between 150 and 180 minutes. The results of these experiments are summarized in Table 1.

From these data it can be seen that there were only small changes in systemic arterial blood pressure and regional flow over the period used in the subsequent experiments.

A. **Normothermia.** 1. *Regional blood flow.* The changes in regional flow which occurred when total body blood flow was reduced to less than 50 ml./minute/Kg. B.W. for 120 minutes are summarized in Table 2. There was an initial reduction in all blood flows and in systemic arterial blood pressure. After this however, blood flow in the splanchnic and renal vascular areas continued to fall significantly over the entire period of low total body flow. The fall in coronary blood flow was also marked and tended to follow the fall in mean arterial blood pressure. Musculoskeletal blood flow rose, particularly in the low inferior vena cava.

On restoration of high total body blood flow the splanchnic and renal blood flows rose but remained below control levels; coronary flow returned to and the musculoskeletal flow exceeded, control values, the greatest change being present in the region drained by the inferior vena cava (Fig. 3).

In Figure 4 are shown the proportions of total flow distributed to each vascular region. From this it can be seen that the initial reduction in flow caused little redistribution. However, during the period of low total body flow there was a progressive redistribution away from the splanchnic and renal vascular beds towards the musculo-skeletal areas. This was not reversed during the second high flow period.

2. *Regional oxygen consumption.* The values of average oxygen consumption of each region are set out in Table 3. At the

TABLE 3. *Regional Oxygen Consumption (ml./min./Kg. B. W.) Before, During and After the Two Hour Low Flow Period.* Mean ± S.E. n = 6

Vascular Region	Control Period	Start of Low Flow Period	End of Low Flow Period	Start of High Flow Period
Total O_2 consumption	3.53 ± 0.54	3.41 ± 0.33	3.03 ± 0.42	4.28 ± 0.80
Splanchnic	1.38 ± 0.25	1.34 ± 0.16	0.97 ± 0.11	1.59 ± 0.34
Superior vena cava	0.78 ± 0.15	0.81 ± 0.10	0.86 ± 0.27	1.02 ± 0.34
Vena azygos	0.37 ± 0.07	0.38 ± 0.04	0.35 ± 0.08	0.42 ± 0.17
Renal	0.31 ± 0.13	0.20 ± 0.04	0.19 ± 0.03	0.31 ± 0.06
Coronary	0.31 ± 0.04	0.25 ± 0.03	0.08 ± 0.05	0.17 ± 0.03
Low inferior vena cava	0.53 ± 0.10	0.50 ± 0.04	0.63 ± 0.07	0.84 ± 0.25

start of the low flow period, despite a fall in all regional blood flows, there was no significant change in oxygen consumption of any vascular bed. However, by the end of the period, splanchnic oxygen consumption had decreased by 30%, coronary oxygen consumption by 73% and the vascular bed drained by the low inferior vena cava had increased by 21%. On restoring the total body flow to the control level, splanchnic oxygen consumption returned to control levels, coronary oxygen consumption remained depressed and the low inferior vena cava increased over control levels by 60% and superior vena cava by 40%.

3. *Hind limb preparation.* Intact and skinned hind limb average blood flows are set out in Table 4. There were no significant differences between the means of blood flows from each limb before, during and after the 2-hour low flow period. These results show that the large increase in low inferior vena caval blood flow noted in the previous experiments was due primarily to changes in the hind limb muscle vascular beds. Section of the sciatic and femoral nerves of the skinned hind limb produced little change in blood flow.

In Figure 5 are plotted the proportion of total body blood flow distributed to each hind limb. On lowering total body blood flow here was a temporary redistribution away from the hind limbs but within 30 minutes blood flow had returned to control levels and thereafter continued to rise.

The mean oxygen consumptions of each limb are set out in Table 5. The changes are similar to those reported for the low inferior vena cava.

B. **Hypothermia.** 1. *Regional blood flow.* In Table 6 are set out the mean regional blood flows resulting from cooling of the animal to 25° C. esophageal temperature before, during and after a two hour period of low total body flow.

The induction of hypothermia caused a redistribution of blood flow away from the splanchnic and renal areas and towards the remaining musculo-skeletal vascular beds. In Figure 6 the changes expressed as a percentage of control values at 37° C. are plotted.

During the low flow period, there were no further changes in regional blood flow apart from the overall reduction seen at the start of this period. On returning to a high total body flow rate and maintaining the hypothermia, regional blood flows returned to those values existing before the start of the low flow period. Rewarming to 37° C. esophageal temperature restored all regional blood flows, with the exception of the renal and vena azygos, to control lev-

els. The distribution of blood flow during each of these stages are shown in Figure 7.

2. *Regional oxygen consumption.* The oxygen consumption data for this series of experiments are set out in Table 7. Hypothermia produced falls in oxygen consumption ranging from 71% for the splanchnic region to 90% for the region drained by the vena azygos. At the start of the low flow period there were slight rises in total body and regional oxygen consumptions of the musculo-skeletal beds which persisted unchanged for the duration of the low flow period. After the restoration of high total body flow, total body and regional oxygen consumptions fell to levels below those recorded before the low flow period.

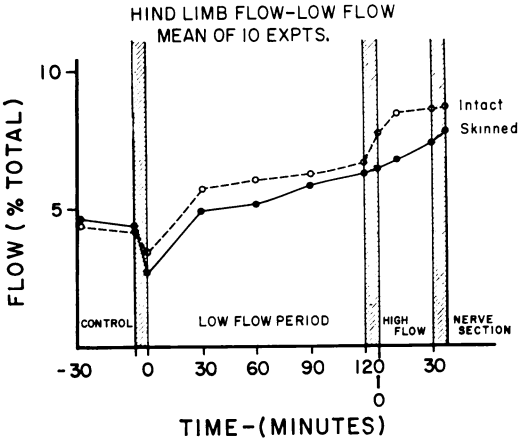

FIG. 5. The proportions of total body flow distributed to each hind limb plotted against time. The vertical shaded bars indicate the beginning and ending of the low flow period.

Discussion

This preparation has allowed the simultaneous measurement of blood flow in those regions considered to be important in the response of the body to prolonged hemorrhage and has also permitted the separation of the changes arising from functional alteration of the heart [7] and great veins [1, 23] from those arising from the peripheral vascular beds.

Following hemorrhage of small volumes it has been reported [20, 25] that the cardiac output initially falls and then spontaneously returns towards control levels over a variable period of time. In our experiments such compensation could not occur, and this, in association with the effects of extensive operative surgery [11] may account for the comparatively rapid appearance of the continuing fall of systemic arterial blood pressure (equivalent to circulatory failure), during the low flow and the following high flow periods.

TABLE 4. *Regional Flow (ml./min./Kg. B. W.) and Mean Arterial Blood Pressure Before, During and After Two Hours if Low Flow.* Mean ± S.E. n = 10

Vascular Region	Control Period	Start of Low Flow Period	End of Low Flow Period	Start of High Flow Period	After 30′ High Flow	After Nerve Section of Skinned Limb
Total flow	119 ± 3.8	29 ± 2.4	29 ± 2.5	115 ± 4.9	114 ± 4.9	113 ± 6.6
Superior vena cava	36.7 ± 3.8	11.2 ± 1.4	11.8 ± 1.1	37.9 ± 4.3	34.2 ± 4.6	38.7 ± 6.3
Abdomen (IVC)	71.9 ± 3.5	16.1 ± 1.2	13.5 ± 1.6	61.0 ± 4.4	61.8 ± 5.3	58.2 ± 3.4
Skinned limb	5.4 ± 0.8	0.8 ± 0.2	1.7 ± 0.1	7.4 ± 0.7	8.4 ± 1.0	7.9 ± 0.9
Intact limb	5.5 ± 0.8	0.9 ± 0.2	1.8 ± 0.2	8.9 ± 0.9	10.3 ± 1.4	7.6 ± 1.6
Mean blood pressure (mm. Hg)	110 ± 7.1	37 ± 4.0	27 ± 3.5	71 ± 6.3	74 ± 6.6	78 ± 8.9

TABLE 5. *Regional Oxygen Consumption (ml./min./Kg. B. W.) Before, During and After the Two Hour Low Flow Period. Hind limb preparation.* Mean ± S.E. n = 5

Vascular Region	Control Period	Start of Low Flow Period	End of Low Flow Period	Start of High Flow Period
Total O_2 consumption	3.05 ± 0.32	1.35 ± 0.30	1.77 ± 0.18	3.04 ± 0.35
Skinned limb	0.083 ± 0.022	0.052 ± 0.010	0.119 ± 0.011	0.171 ± 0.047
Intact limb	0.089 ± 0.021	0.081 ± 0.021	0.131 ± 0.017	0.158 ± 0.052

TABLE 6. *Regional Flows (ml./min./Kg. B. W.) and Mean Arterial Blood Pressure Before Cooling, After Cooling to 25° C. (Esophageal Temperature) During and After the Two Hour Low Flow Period and After Rewarming to 37° C.* Mean ± S.E. n = 10

Vascular Region	Control Period at 37° C.	Control Period at 25° C.	Start of Low Flow Period 25° C.	End of Low Flow Period 25° C.	Start of High Flow Period 25° C.	End of High Flow Period 37° C.
Total flow	140 ± 6.2	133 ± 8.4	40 ± 4.9	44 ± 5.5	135 ± 6.9	140 ± 5.6
Splanchnic	43.8 ± 2.2	29.2 ± 2.6	10.6 ± 1.6	10.3 ± 1.7	28 ± 2.4	47.9 ± 4.7
Superior vena cava	30.0 ± 2.6	36.7 ± 3.8	10.5 ± 1.5	12.9 ± 1.8	38.7 ± 2.6	31.2 ± 4.2
Vena azygos	17.3 ± 1.9	20.8 ± 2.2	6.3 ± 1.0	6.0 ± 1.3	16.5 ± 1.6	13.1 ± 2.0
Renal	17.4 ± 2.5	8.6 ± 1.5	2.6 ± 0.6	3.6 ± 0.9	7.4 ± 1.3	10.9 ± 1.6
Coronary	10.3 ± 0.9	9.9 ± 1.4	3.7 ± 0.8	4.5 ± 1.0	13.1 ± 2.1	12.3 ± 1.5
Low inferior vena cava	21.6 ± 2.4	28.1 ± 3.5	6.7 ± 1.2	6.9 ± 1.2	31.3 ± 3.8	25.1 ± 6.2
Mean blood pressure (mm. Hg)	123 ± 5.4	91 ± 7.5	50 ± 4.3	69 ± 8.0	104 ± 7.9	87 ± 10.3

In the present study although initial changes were proportional to the fall in total body flow rate, later, the magnitude, direction and onset of subsequent changes were different in each vascular bed. After 30 minutes the splanchnic blood flow began to fall and continued to fall throughout the remainder of the 2-hour low flow period. Renal blood flow remained constant for 60 minutes after its initial fall and then began to fall at a rate which was not as marked as in the splanchnic region. Coronary blood flow fell throughout the low flow period at about the same rate as the fall in mean arterial blood pressure. In contrast, blood flow through the low inferior vena cava began to increase after 30 minutes and had almost returned to control levels despite the falling arterial blood pressure and the low total body flow at the end of 120 minutes. The experiments in which hind limb flow was measured indicate that the marked increase in low inferior vena cava flow was due primarily to flow through muscle and that once established it was maintained after section of the femoral and sciatic nerves which carry the bulk of autonomic innervation to the hind limb.[4]

The temporary loss of neurally induced vascular tone in the hind limbs of animals subjected to hemorrhagic hypotension has been reported previously. Mellander and Lewis[16] in experiments on the vascularly

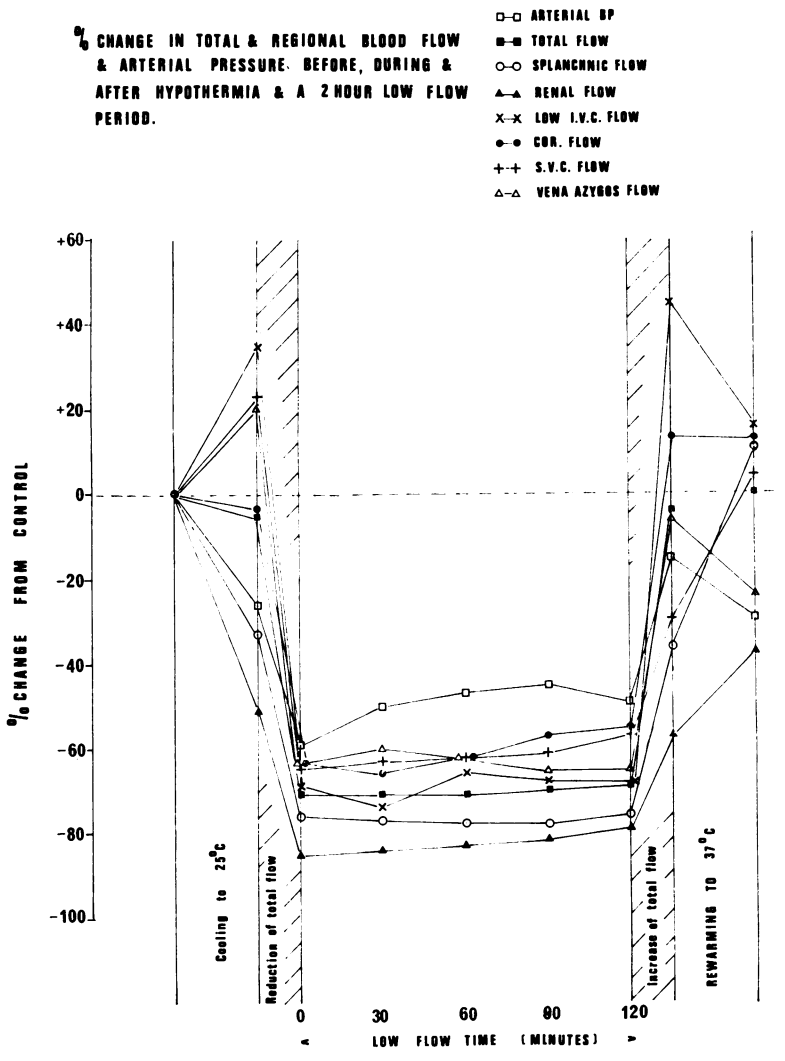

FIG. 6. The changes in total and regional blood flows and mean arterial blood pressure expressed as percentages of control values before and after cooling to 25° C., and before, during and after the low flow period.

intact but neurally isolated hind limb of the cat demonstrated the loss of arteriolar constriction to both sympathetic nerve stimulation and circulating catecholamines during the hypovolemic stage, and then its restoration after transfusion. Rothe *et al.*[22] in the neurally intact but vascularly isolated hind limb (its blood supply being provided by a healthy donor animal) of dogs subjected to hemorrhagic hypotension showed a loss of sympathetic nerve activity during the hypotensive phase, which reappeared with the transfusion and disappeared again only as a terminal event. They concluded that irreversibility was not due to loss of neural activity, and that central nervous system failure occurred terminally. Mellander and Lewis[16] concluded that the temporary loss during hypovolemia was due to the dominant action of vasodilator metabolites. Fell[11] found a relative decrease in femoral artery vascular resistance in dogs during hemorrhagic hypotension which remained below control levels after reinfusion.

In this series of experiments, on restoration of control total body flow rate the changes already present in the regional vascular beds persisted. Splanchnic and renal blood flows remained below control

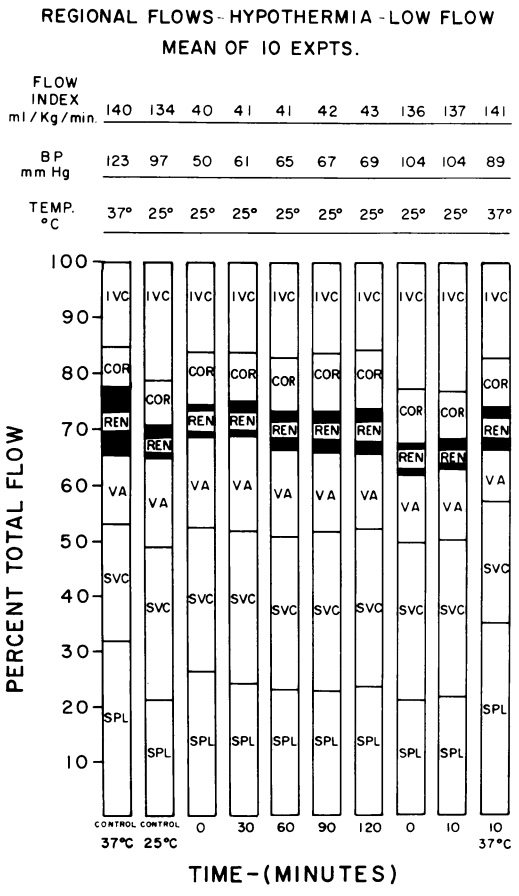

FIG. 7 (a). The proportions of total body flow distributed to each vascular region (% total flow) plotted against time (minutes). Total body flow (ml./min./Kg. B.W.), systemic arterial blood pressure and esophageal temperature (°C.) are also shown.

levels; coronary blood flow returned to, and musculo-skeletal regional flows exceeded control levels, despite the mean arterial blood pressure remaining below control levels. These discrepancies between regions suggest that any loss of a resistance-maintaining factor (e.g., neurogenic activity) is not general. Interpretation of the results is however difficult, for McGiff[17] has shown that the late increase in renal vascular resistance is due to humoral influences.

Total body oxygen consumption, which was only slightly below control levels, did not change significantly during the low flow period but increased during the second high flow period. However, at the start of the low flow period both renal and coronary oxygen consumptions were below control values and although renal oxygen consumption was unchanged, coronary oxygen consumption, which was at control values at the start of the low flow period, fell during this period and rose rapidly to exceed control levels early in the high flow period. Oxygen consumption of the musculo-skeletal regions was little changed by the low flow period but exceeded control levels at the start of the high flow period. It is possible that hypoxia may have been present in the vascular beds of the renal, splanchnic and coronary beds, but of these in only the renal vascular bed has it been established[26] that hypoxia will cause an increase in vascular resistance. In the musculo-skeletal areas it is unlikely that hypoxia was present since oxygen consumption exceeded control levels.

No general action by nervous or humoral

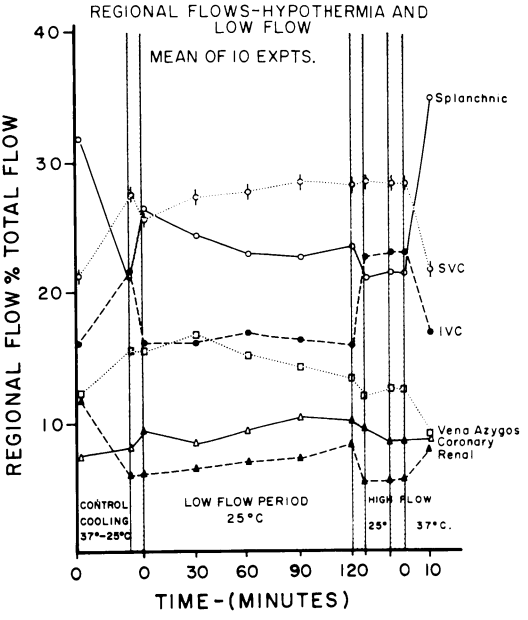

FIG. 7 (b). The proportions of total body flow distributed to each region before and after cooling to 25° C., and before and after the low flow period (indicated by the vertical shaded bars).

TABLE 7. *Regional Oxygen Consumption (ml./min./Kg. B. W.) Before and After Induction of Hypothermia and During and After Two Hour Low Flow Period at 25° C.*
Mean ± S.E. n = 5

Vascular Region	Control Period at 37° C.	Control Period at 25° C.	Start of Low Flow Period 25° C.	End of Low Flow Period 25° C.	Start of High Flow Period 25° C.
Total O_2 consumption	4.39 ± 0.39	0.92 ± 0.11	1.12 ± 0.08	1.13 ± 0.12	0.45 ± 0.07
Splanchnic	1.92 ± 0.16	0.56 ± 0.08	0.55 ± 0.07	0.56 ± 0.07	0.30 ± 0.05
Superior vena cava	0.76 ± 0.09	0.15 ± 0.06	0.21 ± 0.03	0.21 ± 0.04	0.06 ± 0.03
Vena azygos	0.52 ± 0.09	0.05 ± 0.02	0.15 ± 0.01	0.12 ± 0.07	0.01 ± 0.01
Renal	0.20 ± 0.04	0.03 ± 0.01	0.05 ± 0.01	0.05 ± 0.01	0.03 ± 0.01
Coronary	0.34 ± 0.05	0.05 ± 0.01	0.06 ± 0.01	0.03 ± 0.01	0.02 ± 0.01
Inferior vena cava	0.53 ± 0.08	0.08 ± 0.04	0.16 ± 0.03	0.14 ± 0.04	0.02 ± 0.01

factors known to be present during hemorrhagic shock can explain the paradoxes in regional vascular behavior unless they are combined with additional factors with specific actions on each region. The abolition by hypothermia in the low flow period of most specific changes reviewed above suggests that some metabolic product could be the additional factor. However, evidence of disturbance in the oxidative systems is lacking since oxygen consumption remained at or near control levels throughout the normothermic experiments. Although hypothermia reduced oxygen consumption markedly in all vascular regions, the effect was not maintained after the onset of low flow. It is possible that the rising oxygen consumption at the end of this period and its fall when high flow was restored was the result of variation in temperature of organs following the reduction of flow.

Since hypothermia with normal flow rates produced changes in blood flow distribution similar to the introduction of low total flow at normothermia, low flow itself is not the determinant of the changes observed.

Other studies [6] using low total body flows in extracorporeal heart-lung bypass at normothermia have shown that irreversible circulatory deterioration does not occur if the perfusion is not prolonged, suggesting a time dependent mechanism is present. The factors concerned in the appearance of irreversibility may be of a local metabolic nature, not necessarily associated with oxidative systems, concentration dependent and directed not at the splanchnic, renal and coronary vasoconstriction but at the musculo-skeletal vasodilatation.

Skeletal muscle vascular beds are the largest blood flow regions in the body and their importance in determining the distribution of blood flow in the normal animal [2] and the response of the body to hemorrhage is emphasized by these experiments. In the intact animal the imbalance in regional blood flow in hemorrhagic shock, in conjunction with the myocardial failure [7, 23] may lead to a situation where the limited and falling cardiac output is inadequate to maintain nutritive blood flow to all regions.

Conclusion

In this study it has been demonstrated that each vascular region behaves in an individual fashion in response to prolonged low total body flow. It has been suggested that such a state simulates that of hemorrhagic shock and that the changes observed after hemorrhage. The variation of behavior in different vascular regions in-

validates the use of total peripheral resistance as an indication of the circulatory changes in shock.

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