THE OUTFLOW OF BLOOD FROM THE LIVER AS AFFECTED BY VARIATIONS IN THE CONDITION OF THE PORTAL VEIN AND HEPATIC ARTERY

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The liver is the only gland in the animal body receiving both venous and arterial blood. The former is supplied to it at very low pressure by the way of the capacious portal vein, the latter, at very high pressure by the strikingly narrow hepatic arteries. Except for the relatively small amount which is supplied to the walls by the blood vessels and biliary ducts, none of the blood of the hepatic arteries mixes with that of the portal veins until the branches of the two vessels turn into the hepatic lobules. At the point where the two streams unite, that is to say, at the intrahepatic capillaries, their pressure must equal, which means that in its course in the interlobular connective tissue, the branches of the hepatic artery must offer an enormous resistance to the blood flowing through them. This frictional resistance resides in the arterioles and since these are richly supplied with active vasomotor nerves, great variations in hepatic inflow become possible.[1] On the other hand, although the portal venules are capable of active constriction and dilatation only to a slight degree,[2] it is possible that their caliber is very readily influenced by changes in the closely adjacent branches of the hepatic artery. In other words, it is possible that the flow through the interlobular portal venules is largely dependent upon the degree of turges-

[1] Burton-Optiz: Quarterly Journal of Experimental Physiology, 1910, iii, 297.
[2] Burton-Optiz: ibid., 1913, vii, 57.

cence of Glisson's capsule, which again will depend upon the caliber of the hepatic arterioles.

That the hepatic blood flow may influence that of the portal vein seems to have been first of all suggested by Gad. Burton-Optiz calls attention to this work, but he himself rather insists upon the opposite relationship, namely, "that the hepatic inflow may become a highly important compensatory factor whenever the portal inflow is lessened or entirely obstructed."[3] As we shall see later, however, certain of the results of this investigator could be explained on the above basis.

To put the hypothesis, that the pressure in the hepatic artery influences the portal flow, to the test was one of the objects of this research, the others being to supply futher data regarding the relative magnitude of the portal and hepatic moieties of blood supply. In the recent work of Burton-Optiz, which has furnished us with most valuable information on this latter point, the measurements were made by attaching stromuhrs to either the hepatic artery or the portal vein. Apart from the possible interference with blood flow or blood pressure produced by inserting the stromuhr, simultaneous measurements on both vessels cannot be made conveniently, and it is only by comparison of results independently taken on the two that conclusions can be drawn regarding the influence of the one blood flow on the other. In the present investigation, we have, therefore, measured not the inflow but the outflow of blood, and we have observed the effect produced on this by various experimental procedures which might furnish data relative to the above questions.

In choosing experimental procedures by which the flow in one vessel might alone be altered so that changes in the other could be observed, we are distinctly limited. Ligation of the hepatic artery will of itself fail to furnish us with the necessary information, because the sudden removal of the turgescence in the capsule of Glisson is likely to be followed by an immediate and maximal dilatation of the portal venules, so that the net effect on the outflow will be the difference between the withdrawal of the he-

[3] Burton-Optiz: ibid., 1911, iv, 93.

patic artery inflow and the compensatory increase in the portal inflow, if such should occur. Not knowing what proportion of the normal inflow is portal, one cannot, therefore, tell from outflow measurements whether it has undergone any increase. Obviously the only way to do this by measurement of inflow would be to compare the portal flow before and after ligation of the hepatic artery. So far as we are aware, this has not been done, but even if it had been, the results would be open to the criticism that the inflow of portal blood was more or less interfered with by the insertion of the stromuhr.

In the present research we have, therefore, studied the outflow of blood from the liver before and during stimulation of the hepatic plexus, in the hope that although the nerve influence is exerted on both groups of vessels, it would be so feebly on the portal venules, that these would undergo dilatation when the turgescence in the capsule of Glisson is lessened by diminished arterial inflow.

To control the results obtained by the above experiments, we have also studied the local influence of adrenalin on the liver outflow. This has proved a most difficult thing to do satisfactorily for reasons which will be set forth later on.

Observations have incidentally been made on the relative magnitude of the blood flow by way of the portal vein and hepatic artery respectively, and on several other points of general interest.

METHODS

The animals varied in size between about 10 and 20 kgm. After being anesthetized with ether and tracheal and carotid cannulae inserted, the abdomen was opened and the renal vessels ligated, including the adrenal (transverse lumbar) vein on the left side. The aorta was ligated well below the coeliac axis and a wide cannula inserted in the central end of the vena cava. The hepatic plexus was then carefully separated from the hepatic artery, and this was ligated beyond the point at which the hepatic branches leave it. The further preparation of the liver vessels, etc., depended on the nature of the experiment and requires no

special description here. A cut about 2 inches long was then made between the ninth and tenth ribs, and after prying these apart, a thread was placed around the vena cava just above the diaphragm. By pulling on this thread, the vein becomes entirely obliterated. Breathing was very slightly interfered with by these operations, but it became perfectly normal in a minute or so after the wound in the thoracic wall had been closed.

The operations being completed, a receiving vessel was attached to the cannula in the vena cava and connected by tubing with a volume recorder as described by one of us—R.G.P.—in a previous communication. To measure the blood flow a clamp placed on the tube of the recorder was removed at the same time that the ligature around the vena cava was pulled on. As soon as sufficient blood had collected in the receiver to operate the signals, the ligature around the vena cava was again loosened, and the receiver tilted up so that the blood flowed at low pressure back into the circulation. It was found that any attempt to accelerate the emptying of the receiver, by means of pressure, was likely to paralyze the right heart and cause a fatal lowering of blood pressure. Clotting was prevented usually by placing some leech extract in the receiver and by coating this with hard paraffin.

Because of the presence of minute inaccessible lumbar veins emptying into the vena cava just below the hepatic veins, some of the blood which collected in the receiver had not really traversed the liver. Being inconstant in amount, it has been impossible for us to allow for this in our experiments, but we believe that the error thus incurred does not affect the main conclusions which we have drawn

RESULTS

1. The magnitude of the combined flow

This may be taken as the average flow in cubic centimeters per second measured at the beginning of each experiment. The average of the three separate determinations which immediately precede whatever experimental condition was to be studied, is calculated. Of the observations suitable for such compilation, table I gives the results.

Omitting for the present experiment 17, the minimum flow was 4.16 c.c. per second to the maximum 8.9, the average for ten observations being 6.51. In several of the observations the liver was weighed after death and the flow calculated per 100 grams of liver substance, the average being 1.59, which is somewhat higher than that given by Burton-Opitz,[4] namely, 1.4. The figures from which this average is computed, however, vary considerable. The greater flow observed by us may be explained by the fact that the discharge of a few minute lumbar veins is included. But sometimes, and for no obvious reason, the flow may vary greatly from the above values; thus in experiments 14, 15 and 17, it

TABLE I

EXPERIMENT	AVERAGE FLOW PER SEC.	PER 100 GRAM LIVER	ARTERIAL BLOOD PRESSURE	WEIGHT OF DOG	WEIGHT OF LIVER
	cc.		*mm. per kgm.*	*kgm.*	*gram*
4	6.21		130–150		
6	7.63		130		
10	6.58	1.68	175	8.6	390
11	4.16	1.34	110	9.7	310
12	5.75	1.53	140		373
13	5.45	1.18	140	8.3	290
14	8.9	2.40	11	6.3	375
15	8.5	2.36	150	9.6	370
16	5.8	1.06	140	10.9	490
(17	12.5	2.27	160	14.2	550)
18	8.3	1.22	160	17.4	680

amounted to 8.9, 8.5, and 16.3 c.c. per second respectively. We are at a loss to explain these abnormally rapid flows. In one of them, viz., that of experiment 17, the vessels of the intestines were markedly dilated. This may have been the case in 14 and 15. In one or two experiments the flow was apparently much lower than above the minimum at the start, but its subsequent acceleration to about the normal probably indicated an incomplete obliteration of the vena cava in the thorax.[5]

[4] Burton-Optiz: ibid., 1911, iv, 113.

[5] A very marked increase in outflow often occurred when the arterial blood pressure became markedly depressed as a result of too much anaesthetic. We can at present offer no explanation for the result.

2. The magnitude of the outflow with either the hepatic artery or the portal vein clamped

Comparisons between the outflow when one or other vessel is clamped, and the total outflow, give us approximately the relative contribution of either vessel. Partly on account of minute lumbar veins which open into the vena cava just below the hepatic veins and partly because of collateral circulation, a certain amount of blood continues to flow after clamping both vein and hepatic artery (Table II). Theoretically it should be possible to allow for this in our calculations, but practically it is impossible

TABLE II

Blood flow into vena cava in cc. per second after clamping the entire hepatic pedicle (Blood Pressure in brackets)

EXPERIMENT	BEFORE CLAMPING	DURING CLAMPING	REMARKS
9	8.75 [70]	1.2 [8]	Immediately preceding clamping of pedicle
	5.39 [70]	0.8 [80]	
	6.00 [70]	1.0 [70]	
		0.7 [60]	
16	5.6 [60]	0.504	Immediately preceding clamping of pedicle
	5.8	0.324	
		0.396	
17	12.1 [140]	1.80 [100]	Flow earlier in experiment
	13.3 [140]	1.08 [80]	
	12.1 [140]	0.297 [50]	

to do so because of its irregularity when measured under the above conditions. The shrinkage of the previously distended liver, thus allowing some outflow to continue after clamping, the fall of blood pressure due to stagnation in the splanchnic vessels, and the possibility that the same number of lumbar veins are not discharging into the cava in all the experiments, explain the irregularities. Although in many of the experiments attempts were made to obliterate the lumbar veins by mass ligation, it was found difficult to be certain that they were all obliterated.

(*a*) *The effect of clamping the hepatic artery.* After making several observations on the normal flow, the main branch of the hepatic artery central to the point from which the hepatic branches originate was obliterated either by applying a clamp or by

TABLE III

Blood flow from liver in c.c. per second as affected by clamping the hepatic artery (Blood Pressure in brackets)

EXPERIMENT	IMMEDIATELY PRECEDING OBLITERATION	DURING OBLITERATION	FOLLOWING OBLITERATION	AVERAGE DECREASE		REMARKS
				cc.	*per cent*	
3	10.00	6.64	6.2			Hep. art. not tied beyond liver
	10.00	7.3	9.13			
	9.3	6.05	6.2			
		6.95	8.1			
		5.84				
	Average. 9.75	6.55	7.4	3.2	33	Observation followed others made of effect of stim. of hep. plexus
5	9.53	8.20	11.25			Abnormally high rate of flow
	9.10	7.75	9.10			
		8.20	11.25			
	Average. 9.31	8.05	10.53	1.26	13.5	Observation made late in exp.
6	8.24	[7.94]				Late in experiment. Abnormally high rate of flow
	8.24	6.35	10.6			
	8.24	7.33	9.53			
	Average. 8.24	6.84	10.06	2.40	2.91	
11	4.28	3.07				Unusually slow rate of flow
	4.05	3.00				
		2.70				
		2.80				
	Average. 4.16	2.89		2.27	54	
12	5.75 [140]	[140]	4.5 [140]			
	5.75		4.5			
	5.75 [90]	[90]	4.5 [90]			
	Average. 5.75	3.94	4.5	1.81	31.4	
	Per 100 gram liver 1.53	1.02	1.20			

TABLE III—Continued

EXPERIMENT	IMMEDIATELY PRECEDING OBLITERATION		DURING* OBLITERATION		FOLLOWING OBLITERATION	AVERAGE DECREASE		REMARKS
						cc.	per cent	
12 Liver 5 minutes later	4.5	[140]	3.15					
	4.5							
	4.5	[90]	3.80					
12 Average.	4.5		3.32			1.18	26	
Per 100 gram liver	1.21		0.89					
12 Liver 10 minutes later	8.4	[100]	5.73					This increased flow late in exp. is a very common occurrence
	8.4		5.73					
	8.4	[60]						
Average.	8.4		5.73		7.97	2.67	31.7	
18	9.0	[160]	6.79	[160]				
	8.3		7.83					
	8.3		5.72					
			5.3					
Average.	8.5		5.9			2.6	30	

tightening a thread. In most of the experiments the main artery was also ligated beyond these branches.

The effect which obliteration of the hepatic artery has on the outflow seems to depend considerably on the condition of the animal at the time that the observation is made. In our earlier observations this particular experiment was not undertaken until after several others had been performed on the same animal, with the consequence, as already stated, that the flow was abnormally rapid and quite irregular. In two of these experiments (3 and 6), sufficiently constant results were, however, obtained, the hepatic artery moiety being respectively 33 and 29.1 per cent of the total flow. In another of this series, also showing a rapid flow, the hepatic moiety was only 13.5 per cent. In observations 12 and 18 the above experiment was the first one performed, and the results showed from 26 to 31.7 per cent of the blood to

be derived from the hepatic artery. In experiment 11, the diminution following clamping was 54 per cent, but the abnormally small initial flow in this case indicates a probable interference with the portal flow, although no cause for this could be discovered.

As a general average, we are probably safe in concluding that from 26 to 32 per cent of the blood which flows through the liver is derived from the hepatic artery. In other words, about one-third of the blood in the liver is arterial. Inasmuch as the hepatic artery is richly supplied with vasoconstrictor nerve fibers, the blood flow through it is subject to very considerable variations and consequently the ratio between the flow in it and in the portal vein may undergo alterations from time to time. It is probably on account of such changes that the unusual values, such as in experiments 5 and 11, are to be explained. To control this factor the observations should be repeated with the vasomotors paralyzed.

(*b*) *The effect of clamping the portal vein.*

These observations sufficiently corroborate those made by clamping the hepatic artery, for they show that the outflow is diminished by about two-thirds by clamping the portal vein. The unusually small decrease in the first observation of XVIII was probably due to faulty application of the clamp.

Although the above conclusion merely confirms that of Burton-Optiz, who found the hepatic artery to contribute from 24 to 44 per cent of the total flow, yet it seems to us important to have been able to confirm it by measurements which entail no sort of disturbance on the ingoing blood vessels. The minute size of those branches of the hepatic artery which actually enter the liver as compared with the enormous size of the portal vein would lead one to expect a much larger contribution of blood through the latter vessel even although the pressure differences in the two vessels are very great. The result explains why it is that deflection of the portal flow into the vena cava (Eck fistula) should ordinarily create no very marked metabolic disturbance. By still retaining from one-fourth to one-third of their normal flow (through the hepatic artery) the liver cells can perform their functions sufficiently to prevent a serious accumulation of such

TABLE IV

Blood flow from liver in c.c. per second as affected by clamping portal vein. (Blood Pressure in brackets)

EXPERIMENT	IMMEDIATELY PRECEDING OBLITERATION	DURING OBLITERATION	FOLLOWING OBLITERATION	AVERAGE CHANGE	
				cc.	*per cent*
IX	5.25 [100]	1.87 [100]	4.20 [80]		
	5.15	1.87 [80]	4.10 [80]		
			4.56		
Average.....	5.20	1.87	4.30	3.00	64
IX Continued	4.20 [80]	2.00 [70]	8.75 [60]		
	4.10 [70]	2.20 [70]	5.39 [70]		
	4.56 [80]	1.69 [60]	6.00 [70]		
Average.....	4.30	1.96		2.34	54
XVIII	8.30 [120]	4.60 [120]	[6.54]		
	8.30	6.70	7.2		
	8.25		8.25		
Average.....	8.30	5.56	7.70	2.74	33
XVIIa	7.20 [120]	2.50 [80]			
	8.25	2.76			
		2.88			
Average	7.7	2.70		5.00	64

substances as ammonia, monosaccharides, etc., in the systemic blood, unless excessive amounts of these substances are being absorbed from the intestine.

3. The effect of stimulation of the hepatic plexus on the outflow.

For purposes of stimulation the entire hepatic plexus was cut and the peripheral end carefully laid on guarded electrodes connected with a standard Rhumkorff coil of 10,000 windings, the secondary being placed either at 4 or 6 cm. from the primary. The stimulation did not have any effect on the respiratory movements; any slight effect which, as Burton-Opitz found, it might have on arterial blood pressure (with untied hepatic arteries) was

masked in our experiments by the slight fall which occlusion of the vena cava entailed.

The invariable result (cf. Table V) was an immediate acceleration in the blood flow, followed after a period of a few seconds by a return to the normal. The extent and duration of this increased flow were somewhat inconstant; the former varied from about five per cent in experiment 1, to sixty per cent in experiment 3, the latter, from 5 seconds (or less) in experiments 2, 4 and 6 to 15 seconds (or more) in experiments 8 and 10. This initial acceleration is no doubt to be attributed to a squeezing out of blood in the liver as a result of vasoconstriction. This constriction affects the branches of the hepatic artery much more than those of the portal vein, for it affects both the volume flow and the pressure in the hepatic artery, while the constriction of the portal venules, although it raises the portal pressure, causes no measureable change in portal flow.[6]

The subsequent return to the normal flow indicates either that the constriction does not last for long, or that it persists, but is accompanied by a compensatory increase in flow through the portal vein. In view of the fact that Burton-Opitz found constriction of the hepatic artery to persist at least as long as the hepatic plexus was stimulated, we are forced to accept the latter as the correct interpretation, namely, that a compensatory or reciprocal increase in portal flow occurs.

Since, as already mentioned, this author could not detect any change in portal flow when the peripheral end of the hepatic plexus was stimulated, although he was able to observe a rise in portal pressure, it follows that the compensatory increase in the outflow in our experiments cannot be due to an active vasodilation of the portal radicles, but to their passively opening up on account of a lower pressure in the neighboring arterioles. This tendency to open up which results from the removal of the arterial turgescence must be greater than the constriction of the vessels resulting from stimulation of the hepatic plexus. The tissues of the capsule of Glisson must act somewhat in the manner of

[6] Burton-Opitz: ibid., 1913, vii, 57.

TABLE V

The effect of stimulation of the hepatic plexus on the outflow of the liver. (*Blood pressure in brackets*)
Blood flow in cubic centimeters per second

EXPT.	NORMAL	DURING STIMULATION OF PLEXUS	NORMAL	DURING STIMULATION OF PLEXUS	NORMAL	DURING STIMULATION OF PLEXUS	NORMAL	DURING STIMULATION OF PLEXUS	REMARKS
2	3.38 [120]	3.38 [125]	3.38 [125]						Coil of 4 cm. No change in Blood pressure.
	3.75 [120]	4.82 [125]	3.75 [125]						
	3.95 [120]	3.75 [125]	3.59 [125]						
		3.75 [125]							
		3.38							
3	5.84 [134]	9.75 [134]	5.62 [150]	9.75 [150]	8.10 [110]	8.10 [130]	12.10 [130]	14.60 [80]	Coil 6 cm. A marked acceleration in the flow is noticeable later in the experiment.
	6.20 [140]	9.75 [134]	5.04 [150]	9.75 [150]	5.40 [110]	9.13 [130]	12.10 [130]	9.74 [100]	
	5.84 [140]	9.75 [140]	6.64 [150]	6.95 [150]	6.09 [110]	9.13 [130]	10.00 [130]	12.10 [100]	
		6.64 [150]	6.20 [150]	6.95 [116]	6.95 [122]	12.10 [130]	10.00 [130]	12.10 [100]	
		5.84 [160]	7.67 [150]	6.95 [110]	5.84 [120]	10.00 [130]	8.10 [130]		
		5.84 [150]		6.95 [110]	8.10 [130]	10.00 [130]	10.00 [100]		
					8.10 [134]		14.60 [100]		
							14.60 [100]		
							12.10 [100]		
4	6.84 [130]	9.83 [140]	7.15 [140]	7.49 [130]	6.20 [160]				Coil 4 cm.
	5.83 [140]	7.15 [150]	6.06 [120]	7.49 [140]	6.55 [120]				
	6.56 [140]	7.15 [150]	6.84 [140]	5.43 [150]	6.56 [130]				
				5.42 [160]					
5	12.70 [90]	14.70 [90]	12.70 [96]						
	13.60 [90]	14.70 [90]	8.65 [80]						
	12.00 [90]	12.70 [90]	12.70 [80]						
		13.60 [96]	12.00 [80]						
6	5.74 [60]	7.94 [60]	5.74 [65]						The hepatic a. had been temporarily clamped earlier in the experiment. Strength of stimulant not given.
	6.57 [60]	5.74 [60]	7.33 [66]						
	6.35 [60]	6.57 [60]	6.00 [66]						
		6.57 [60]							
8	2.60 [150]	3.30 [150]	2.70 [150]	3.20 [140]	2.60 [130]				
	2.50 [150]	4.50 [150]	2.40 [150]	3.00 [140]					
	2.50 [150]	3.60 [150]	2.10 [140]	3.00 [140]					
				2.50 [140]					
				2.30 [140]					
10	8.40 [160]	10.50 [180]	7.16 [170]	10.00 [170]	5.20 [170]	9.14 [180]	4.77 [170]		The marked irregularity in flow could not be explained.
	6.17 [180]	8.40 [180]	7.30 [170]	8.73 [180]	6.00 [170]	8.10 [180]	4.77 [170]		
	5.10*[180]	10.00 [180]	7.60 [170]	8.40 [180]	8.40 [180]	8.10 [180]	4.50 [170]		
		30 sec. rest		30 sec. rest					
		9.14 [170]		7.16 [170]		7.16 [180			
		7.16 [180]		8.72 [170]		8.72 [180]			
				8.72 [170]		6.20 [170]			
				7.16 [170]		5.10 [170]			

*Irregular flow makes magnitude of increase somewhat uncertain.

erectile tissue; with a normal inflow through the hepatic artery this tissue must exercise a certain compression on the portal radicles, but when the arterial inflow is cut down, the latter vessels must open up and permit more blood to flow through them. That this passive dilatation of the portal radicles does not entail an initial fall in total outflow—because of a temporary stagnation in the (portal) blood flow—is to be explained by the fact that the blood, which has already gained the hepatic lobule itself is not affected by the diminution in turgescence in the interlobular tissues; it flows on, but has added to it the blood which has been pressed out of the hepatic arterioles as a result of their constriction.

Although there is at present no other evidence than the above that such a compensatory increase in the portal venules does occur, it is of interest to note that Burton-Opitz has found the hepatic artery to be become dilated when the portal blood flow is made to cease by deflecting it into the renal vein.

There are, however, certain observations of this author[7] which although interpreted by him in another way may yet as well be attributed to a passive dilatation of the portal venules. Thus it was found that the portal flow became greater when the hepatic plexus was stimulated. Since this increased flow was much more marked when the plexus was uncut, it was attributed to the reflex rise in the arterial blood pressure, which under these conditions is quite distinct. Such an explanation cannot account for the increase which, although much less marked, is stated to have occurred when the peripheral end of the cut plexus was stimulated. Burton-Opitz attributes this also to a general rise in blood pressure resulting from constriction of the hepatic artery in the liver. It may, however, be due to a passive dilatation of the portal venules.

We have also studied the change which is produced in the outflow when the hepatic plexus is stimulated after ligation of the hepatic artery. Table VI gives the results.

It is seen that a very slight, if any, increase in outflow occurred when the plexus was stimulated with ligated arteries. Where

[7] Burton-Optiz: ibid., 1911, iv, 113.

present it was very transient, and is no doubt to be explained by a squeezing out of the blood in the hepatic arteries, or possibly in the portal venules. That there is no permanency in the increased outflow in the experiment as compared with those of the previous group indicates that the portal venules were fully dilated from the beginning, the arterial tension being low because the arteries were ligated.

TABLE VI

The effect of stimulation of the hepatic plexus on the outflow of blood from the liver after ligation of the hepatic arteries. (Figures represent c.c. per second, mean arterial blood pressure in mm. Hg in brackets)

EXPERIMENT	BEFORE STIMULATION	DURING STIMULATION	AFTER STIMULATION
VIII	8.10 [100]	7.10 [100]	4.00 [90]
	7.20 [100]	7.10 [100]	4.40 [90]
		5.00 [90]	5.50 [90]
			5.20 [90]
VIIIa	5.50 [90]	5.00 [80]	
	6.30 [90]	6.80 [80]	
	5.20 [90]	5.00 [80]	
XI	3.07 [110]	3.40 [110]	2.73 [100]
	3.00 [110]	3.00 [110]	2.36 [100]
	2.70 [110]	2.85 [110]	
	2.80]110]	3.00 [110]	
IXa	2.73 [100]	3.20 [100]	2.80 [100]
	2.63 [100]	3.00 [100]	2.50 [100]

The action of adrenalin on the hepatic blood flow

These experiments were undertaken partly to furnish further evidences for or against the above hypothesis concerning the effects of stimulation of the hepatic plexus, and partly to find out to what extent constriction of the portal venules might curtail the outflow of blood. The adrenalin was injected in quantities of 2 cc. of either 1-10,000 or 1-5,000 in the pancreatic duodenal vein, it having been shown that this amount of saline does not by itself cause any appreciable change in the outflow. Larger amounts of saline were found to increase the outflow, probably because of diminution in the viscosity of the blood. Any changes in the blood flow due to the rise in general arterial blood pressure are

discounted in our experiments because the outflowing blood was either collected in a large receiver and not permitted to enter the heart until several measurements had been taken, or the small receiver was used but quickly emptied and another measurement made before the adrenalin had affected the arterial blood pressure. The observations were made with and without ligation of the hepatic arteries. Table VII gives the results.

In practically every instance, whether with or without ligation of the hepatic arteries the adrenalin produced a definite diminution in outflow. We have already alluded to the fact that although Burton-Opitz succeeded in showing that a rise in portal blood pressure occurred after the injection of adrenalin into the portal vein, yet he could not make out, by stromuhr measurements of the portal inflow, that this had suffered any curtailment. The present results are therefore mainly of interest in that they supply such evidence. Apart from the difference in technique of our experiments as compared with those of Burton-Opitz, it is important to note that we injected about twice as much adrenalin as this author. We believe that similar results would be obtained with smaller injections. It will be noted that a few of our observations (viz., XII, XVIa and XVIIa) show a slight increase in outflow as the first effect of the adrenalin injection. This increase in outflow is probably due to a squeezing out of blood from the venules, but it is too inconstant, and, when present, too insignificant to make its presence or absence a distinguishing feature between adrenalin constriction of the venules and nervous constriction of the arterioles, where the initial acceleration is so marked a feature.

It will be noted that the diminution in outflow, both absolutely and relatively, was usually much more decided when the hepatic arteries were intact than when the only blood supply to the liver was through the portal vein. The observations were divided into these two groups in the hope that some clue might be furnished indicating the exact locus of action of adrenalin, i.e., whether on the portal venules central to their union with the branches of the hepatic artery, or beyond this point. In the former case, we should expect the relative diminution in outflow, as a

TABLE VII

The local effect of the injection of adrenalin (2 cc. of 1 to 10,000) on the outflow of blood from the liver. (Figures represent cc. blood per second; mean arterial blood pressure in brackets)

A. With intact hepatic arteries

EXPERIMENT	BEFORE ADRENALIN	DURING ACTION OF ADRENALIN	CHANGE IN FLOW	
			cc.	*per cent*
XIV	9.30 [110 mm.]	8.80 [110 mm.]		
	8.80 [110 mm.]	5.56 [130 mm.]		
	8.80 [110 mm.]	6.00 [130 mm.]		
Average.....	8.9	6.80	−2.10	−25.0
XIVa	8.00 [60 mm.]	7.50 [60 mm.]		
	9.30 [60 mm.]	5.00 [80 mm.]		
		3.50 [80 mm.]		
Average.....	8.65	5.30	−3.35	−38.0
XV	8.55 [150 mm.]	4.16 [150 mm.]		
	8.55 [150 mm.]	3.60 [150 mm.]		
		3.24 [150 mm.]		
Average.....	8.35	3.66	−4.89	−57.0
XVa	6.84 [150 mm.]	3.96 [150 mm.]		
		3.60 [150 mm.]		
		4.95 [150 mm.]		
Average.....	6.84	4.17	−2.67	−39.0
XVI	5.85 [140 mm.]	5.94 [140 mm.]		
	4.77 [140 mm.]	6.93 [140 mm.]		
	5.13 [140 mm.]	6.75 [140 mm.]		
Average.....	5.25	6.54	−1.29	−24.0
XVIa	7.38 (140 mm.]	9.00		
	7.38 [140 mm.]	6.30 [140 mm.]		
	7.65 [140 mm.]	6.90		
Average.....	7.45	7.40	−0.06	
XVIb	6.12 [140 mm.]	5.49 [140 mm.]		
	5.67	4.68		
	5.67	6.12		
Average.....	5.82	5.42	−0.40	−6.0

TABLE VII—Continued

EXPERIMENT	BEFORE ADRENALIN	DURING ACTION OF ADRENALIN	CHANGE IN FLOW	
			cc.	*per cent*
XVII	10.20 [160 mm.]	11.20		
	11.20 [160 mm.]	8.10 [160 mm.]		
	11.20 [160 mm.]	6.50 [160 mm.]		
Average.....	10.90	8.61	−2.29	−22.0
XVIIIa	10.90 [140 mm.]	11.25 [140 mm.]		
	12.00 [140 mm.]	9.72 [140 mm.]		
	10.90 [140 mm.]	8.50 [155 mm.]		
		7.60 [155 mm.]		
Average.....	11.20	9.29	−1.91	−17.0
B. With ligated hepatic arteries				
XII	7.90 [100 mm.]	8.40 [120 mm.]		
	7.00 [100 mm.]	6.30 [120 mm.]		
	6.00 [60 mm.]	5.10 [100 mm.]		
		(15 sec. interval)		
		5.73 [120 mm.]		
		5.73 [100 mm.]		
Average.....	7.00	6.60	+0.40	−5.6
XIV	3.75 [60 mm.]	4.69 [60 mm.]		
		4.20 [60 mm.]		
		4.30 [60 mm.]		
Average.....	3.75	4.39	+0.64	+17.0
XVI	4.59 [120 mm.]	3.69 [120 mm.]		
	4.59 [120 mm.]	4.59 [120 mm.]		
		4.14 [120 mm.]		
		4.05 [120 mm.]		
Average.....	4.59	4.12	−0.47	−10.0
XVIa	6.04 [120 mm.]	3.33 [100 mm.]		
	4.77 [120 mm.]	4.50 [100 mm.]		
		3.87 [100 mm.]		
		4.78 [100 mm.]		
Average.....	5.40	4.12	−1.28	−23.0

TABLE VII—Continued

EXPERIMENT	BEFORE ADRENALIN	DURING ACTION OF ADRENALIN	CHANGE IN FLOW	
			cc.	*per cent*
XVIb	5.13 [60 mm.]	2.97		
	4.50	3.33		
	4.41	5.04		
Average.....	4.68	3.76	−0.92	−20.0
XVII	8.10 [140 mm.]	5.67 [140 mm.]		
	9.70 [140 mm.]	5.94 [140 mm.]		
	7.20 [140 mm.]	4.86 [140 mm.]		
Average.....	8.30	5.82	−2.48	−30.0
XVIIa	4.86	6.39		
	6.66	6.21		
		4.50		
		6.84		
Average.....	5.76	5.96	+0.20	+4.0

Average decrease in blood flow on injection of adrenalin into portal vein with intact hepatic arteries, 22.0 per cent.

Average decrease in blood flow on injection of adrenalin into portal vein with hepatic arteries ligated, 10.5 per cent.

result of adrenalin injection, to be greater when the hepatic artery is tied than when it is patent. That the opposite should actually be the case probably means that the adrenalin, although injected into the vein, acted most strongly on the hepatic arterioles, with which it was brought in contact by eddying of blood into them. Being very richly supplied with vasomotor nerves, the arterioles are so sensitive to adrenalin that the smallest trace can cause them to constrict to a relatively greater degree than a much larger dose acting directly on the portal venules.

On account of the irregularity in our results in this regard, we do not desire to insist on the above differences between the groups of observations as of much significance. We think, however, that we are warranted in the conclusion that the constriction cannot be confined to the portal venules before they join with the hepatic arterioles.

That adrenalin should cause a diminution in liver outflow, and stimulation of the hepatic nerves should not do so, when the hepatic artery is ligated (cf. Table VI) indicates that the vasomotor supply to the venules must be very feeble.

CONCLUSIONS

1. The total outflow of blood from the liver of the dog varies between 1.06 and 2.40 cc. per second and 100 grams of liver. There is only a very general relationship between the magnitude of the flow and the mean arterial blood pressure.

2. Even after the vessels of the hepatic pedicle have been clamped, blood still collects in the vena cava. Part of this comes from minute lumbar veins; the remainder may be due to collateral circulation.

3. Occlusion of the hepatic artery usually causes the outflow to diminish by about 30 per cent, but since the exact ratio between the flow in the portal vein and the hepatic artery will depend on the extent to which these vessels are under vasomotor control at the time of observation, the diminution may be considerably greater or less than 30 per cent.

4. Occlusion of the portal vein usually diminishes the outflow by about 60 per cent.

5. Stimulation of the peripheral end of the cut hepatic plexus, with both artery and vein intact, causes an immediate increase in the outflow, after which this returns approximately to its original amount. This return to the normal flow is explained as due to a passive dilatation of the interlobular portal venules resulting from a lowering of the arterial tension in the capsule of Glisson.

6. The changes in outflow following stimulation of the hepatic plexus are very much less marked, or absent altogether, when the hepatic artery is ligated.

7. Injection of adrenalin (2 cc. of 1 in 10,000) into the portal vein causes an immediate decrease in the outflow. This result is practically the same with unligated as with ligated hepatic arteries. It indicates that the ramifications of the portal vein in the liver are supplied with vasoconstrictor nerve fibers. Since a similar diminution did not occur when the hepatic plexus was stimulated, the portal vasomotor nerve fibers must be very feeble.