Hepatic outflow resistance, sinusoid pressure, and the vascular waterfall

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The pressure-flow characteristics of the hepatic common outflow resistance were determined in five anesthetized dogs. These curves were shown to be nearly linear in the range of normal flows, but exhibited a moderate convexity toward the pressure axis at low flows. The estimated sinusoid pressure at zero hepatic flow was found to be higher than the outflow (hepatic venous) pressure. This "closing pressure" averaged 1.6 mmHg relative to the hepatic venous pressure. Because of this closing pressure, estimated hepatic sinusoid pressure was only slightly less than the portal pressure. For an average portal venous pressure of 7 mmHg, hepatic venous pressure of 1.6 mmHg, and portal venous and hepatic arterial flows of 16.4 and 12.6 ml/min-kg body wt, respectively, sinusoid pressure was estimated to be 6.1 mmHg. The significance of a closing pressure in the hepatic outflow tract and the interpretation of outflow resistance in light of this closing pressure are discussed in detail. Two possible models of the hepatic vasculature are presented.

The entire prehepatic splanchnic vasculature is represented by

\[ R_s = \left( P_s - P_{pv} \right) / F_{pv} \]

Morphologically, the beginning of the common outflow resistance depends entirely on the location of the junction of the arterial and venous inflows. Although there is still controversy on this matter, it appears that most of the arterial blood joins the portal circuit at or near the periphery of the classical liver lobule (15, 20, 30). A small fraction of the hepatic arterial flow supplies the gall bladder and gives rise to a peribiliary arterial plexus, and the venous flow from this area is via the portal venules; it is thereby added to the presinusoidal portal flow. There is also some evidence for the direct entrance of arterial blood into terminal portal venules (21) as well as into the more central parts of the lobule (9, 30). To locate the outflow resistance, one must spatially define the mean junctional pressure. I have defined this as the pressure at the very beginning of the hepatic sinusoids. Thus, the resistance to flow through the hepatic sinusoids is incorporated into the total outflow resistance.

The model in Fig. 1 shows the importance of the outflow resistance on sinusoid pressure. Since the total hepatic flow must pass through this common path, changes in its resistance will directly affect the sinusoid pressure. With the preparation to be described, it has been possible to estimate a normal value of sinusoid pressure (mean pressure at arterio-venous junction) as well as pressure-flow characteristics of the outflow resistance in the canine liver. The results indicate the limitations of such a representation as shown in Fig. 1 and more appropriate models are suggested.

**FIG. 1.** Simple resistive model of splanchnic vasculature. \( P_a \), aortic blood pressure; \( P_{pv} \), portal venous pressure. \( P_s \), presinusoidal portal flow. \( F_{pv} \), portal venous flow. \( F_{hs} \), hepatic arterial flow. \( R_v \), portal venular resistance. \( R_h \), hepatic arteriolar resistance. \( R_L \), liver outflow resistance. \( R_s \), prehepatic splanchnic resistance.
METHODS

Five anesthetized (25 mg/kg pentobarbital) spontaneously breathing dogs were studied. The procedure that was ultimately established is shown in Fig. 2. The abdomen was opened with a midline incision. To measure arterial pressure, the gastroduodenal artery (g.d.a.), a continuation of the common hepatic artery, was catheterized and the catheter tip was placed just distal to the branching of the proper hepatic arteries. The gastroduodenal vein (g.d.v.) was catheterized and the catheter was threaded toward the liver but kept in the portal vein. This measured \( P_{pv} \) when normal portal venous flow was directed toward the liver, but estimated the sinusoid pressure, \( P_{sv} \), when the portal vein was occluded upstream from the catheter tip. Another catheter was held with a purse-string suture in the left hepatic vein. This vein was accessible at the junction of the left and central lobes of the liver (29). Sideholes had been cut in the catheter near the tip which was inserted about 1 cm. This catheter measured the hepatic venous pressure, \( P_{hv} \). The value taken as the hepatic venous pressure was the mean end-expiratory pressure. Since the negative respiratory dips occurring with each inspiration were not averaged, the true mean hepatic venous pressure was less than that which was considered here. There is some evidence, however, that negative hepatic venous pressures are ineffectual in producing increased flow (6, 14), so that the end-expiratory value may in fact be a more functional estimate of the outflow pressure. As will be shown here, however, the normal hepatic venous pressure appears to have little influence on hepatic flows. All animals were tied on their backs and pressures were referenced to a level 6 cm anterior to the back, the estimated level of the right atrium. Extreme care was taken to insure equal sensitivities and zero base lines of the hepatic and portal venous pressure gauges. Measurement of venous pressures was accurate to 0.1 mmHg. Pressures and flows were recorded on a Grass model 7 polygraph.

A shunt was established between the portal vein and abdominal interior vena cava (IVC) just downstream from the renal veins, as shown in Fig. 2. An electromagnetic flow probe (Statham M-4000) was incorporated into the shunt tubing and the shunt was secured into the respective vessels with purse-string sutures. Installation of the shunt necessitated total occlusion of the portal vein for periods up to 2-3 min. Excessive distension of the intestinal vasculature during this portal venous occlusion was minimized by simultaneously occluding the superior mesenteric artery during this period. Heparin, 300 U/kg, was administered just before the portal venous-IVC shunt was established.

Umbilical tape was placed around the portal vein between the gastroduodenal vein and the shunt, the ends of the tape were passed through a piece of glass tubing, and the tape was used as an occluder. The shunt could be occluded with a hemostat. With this arrangement, portal venous blood could be directed toward or away from the liver. Simultaneous occlusion of the portal vein and release of the shunt clamp channeled the blood through the flow probe to the IVC. After an initial transient of \( 1-10 \) s duration, the shunt blood flow stabilized at a constant level. This initial transient was a result of the lower resistance to blood flow through the shunt (50-100%) than through the liver. The value of shunt flow measured after this transient was assumed to be the same as the portal venous flow before shunting. In a few preliminary experiments a noncannulating probe was placed on the portal vein as well to test this assumption. The portal venous flow before diversion was found to be within 10% of the shunt flow after the initial transient. This portal venous probe was not used routinely because of the space limitation in the region.

The hepatic artery was connected to a Sigmamotor peristaltic pump or a Sarns roller pump. The Sigmamotor pump was used more frequently (four times), but the results were similar with the Sarns pump. Hepatic arterial flow rates could be varied over a wide range which was sufficient to encompass greater than normal total hepatic flow. With the portal flow diverted, the hepatic arterial flow was then the total hepatic flow, and the portal pressure measured at the liver was considered to be the sinusoidal pressure.

An occluder was also placed on the superior mesenteric artery, the source of more than half the portal venous flow. This vessel was occluded during the perfusion of the hepatic artery so that the availability of blood to the pump might be increased. If this were not done, the aortic pressure would fall greatly as the hepatic arterial flow rates were increased to the range of normal total hepatic flows.

To eliminate the possible effects of variations in arterial blood pressure initiating reflex activity in the hepatic vasculature via neural mechanisms, the hepatic plexus was severed early in the surgical procedure. Neural influences on the hepatic vasculature arriving via the vagus nerve are thought to be negligible (15, 17).

Estimation of the normal sinusoidal pressure was accomplished in the following manner. During a control period of about 15 min the portal flow was allowed to perfuse the liver normally. The hepatic artery flow was set to a nominal value of about 10 ml/min-kg body wt, and all pressures and flows were monitored. The portal flow was then diverted into the inferior vena cava. Sinusoidal pressure was estimated as the pressure in the portal vein with no portal inflow to the liver. The arterial flow was then set to zero and flow rates were increased in small steps, with each step being held for about 1 min. All pressures had stabilized by the end of this time. In one experiment decreasing steps were also employed, but no hysteresis was found. Either two or three series of increasing flow steps were performed on each ani-

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**FIG. 2. Experimental setup.**
mal. A pressure-flow curve ($P_s$ vs. $F_{ha}$) was thus determined. By reading from the curve the pressure at which the hepatic arterial flow equals the preshunt total normal liver blood flow, the sinusoid pressure with that normal flow was determined. Inherent in this estimation is the assumption that the pressure-flow characteristics of the hepatic outflow resistance are the same whether the hepatic blood arrives entirely through the hepatic artery or the total flow arrives properly split between the two input channels. There is no apparent way of investigating this assumption, but there does not seem to be any a priori reason for doubting its validity.

RESULTS

Figure 3A shows a pressure-flow curve from dog 4. The three curves were taken successively (curves 1, 2, and 3) with about 5 min between runs. The hepatic venous pressure in these runs was 2.2 in the first and 2.0 mmHg in the next two. The plot shows that the zero-flow pressure measured in the sinusoids is higher than the hepatic venous pressure observed at the same time. The former pressure will be termed closing pressure ($P_c$) hereafter. In this animal the closing pressure increased with time, while the hepatic venous pressure did not increase. The general shape of the individual pressure-flow curves is not greatly altered. In Fig. 3B, the calculated outflow resistance is plotted as a function of sinusoid pressure. These curves might be considered as being representative of a passive vascular bed, in which increases in intravascular pressure cause either passive elastic distension, or an increase in the number of open parallel channels, or both. In light of the finding of a closing pressure, however, the significance of the measured values of $R_L$ is questionable. This matter will be further discussed below.

This shifting of the curves with time was not always seen. Figure 4 shows the pressure-flow results from one animal in which there was no shifting (dog 3). A single curve could be drawn through all the points. This figure also indicates a typical calculation of the normal sinusoid pressure. The control $P_{pr}$ and $F_{ha}$ were 15.7 and 9.7 ml/min/kg body wt, respectively, and the portal pressure was 8.0 mmHg. This total hepatic flow of 25.4 ml/min/kg then corresponded to a sinusoid pressure of 6.6 mmHg in this animal. In the five animals analyzed in this manner the sinusoid pressure was always slightly less than the portal pressure. Table 1 presents the average results from these five animals. Where a shift of the curves was observed, only the results from the initial pressure-flow characteristics are presented. The average portal pressure was 7 mmHg and average sinusoid pressure was 6.1 mmHg. The corresponding average portal and arterial flows were 16.4 and 12.6 ml/min/kg, respectively. The mean hepatic venous pressure was 1.6 mmHg. The closing pressure, defined above, had a mean value of 3.2 mmHg. A closing pressure was found in all animals. The parameter $r_L$ is the inverse of the slope of the curve at the point of normal total flow. Its significance (and that of $P_c'$ and $R_L'$) will be discussed below.

The preparation also provided pressure-flow data on the hepatic arterial resistance. A moderate degree of hepatic arterial autoregulation (concavity of the pressure-flow curve)

![Fig. 3. A: pressure-flow characteristics of common hepatic outflow resistance from one animal (dog 4) with portal flow diverted. Three curves are taken successively in time. Units of flow are ml/min-kg body wt. B: outflow resistance for the 3 curves as a function of sinusoid pressure. See DISCUSSION.](http://ajplegacy.physiology.org/doi/abs/10.1152/jappl.1977.40.4.515)

![Fig. 4. Three successive determinations of pressure-flow characteristics of hepatic outflow resistance from dog 3. Preshunt total hepatic flow of 25.4 ml/min kg implies a control sinusoid pressure and outflow resistance of 6.6 mmHg and 0.22 RU, respectively. $m$, in equation, is slope of curve at normal total flow, and $r_L$ is incremental resistance (see text).](http://ajplegacy.physiology.org/doi/abs/10.1152/jappl.1977.40.4.515)
Toward the pressure axis) was seen in four of the five animals for pressures between 80 and 160 mmHg. In addition, a hepatic arterial closing pressure of 15–30 mmHg was consistently found. This pressure was taken to be the level to which the hepatic arterial pressure fell after the pump was stopped. Hepatic arterial closing pressures of this order were seen in four of the five animals isolated (28) perfused livers. Because there might have been some deleterious effects of the abnormally high arterial perfusion pressures (200–250 mmHg) at the maximal flow rates (about 3 × normal arterial flow), the complete results concerning the hepatic artery are not presented.

**DISCUSSION**

A sinusoid pressure only slightly less (average about 1 mmHg) than the portal pressure was found in the canine hepatic bed. Thus, the portal venular resistance was only about one-third of the calculated liver outflow resistance. Comparative data from consideration of intrahepatic resistances and pressures as indicated in Fig. 1 are given infrequently in the literature. Shoemaker (28) gives some discussion of the model, but his experimental methods were not sensitive enough to provide usable data about $R_L$.

Bradley (5) discusses this representation and also presents calculations of the resistances. For these calculations he has utilized the work of Friedman and Weiner (11) who estimated sinusoid pressure by averaging the portal and hepatic venous-wedged pressures. In their studies, however, they frequently found hepatic venous-wedged pressure to be higher than the portal pressure. This finding casts some doubt on the meaning of their estimate. They found a sinusoid pressure of 8.5 mmHg with a portal pressure of 9.6 mmHg. Surprisingly, this is very similar to the results reported here using a more direct technique. Price and associates (27) have successfully estimated canine sinusoid pressure with a wedged hepatic venous catheter. They reported a pressure which was much closer to the portal than the hepatic venous pressure, typically within 2 mmHg.

There is also some evidence suggesting that the pressure drop across the portal venules (presinusoid) is small in man. Balfour and associates (3) have measured the hepatic venous-wedged pressure in a cirrhotic patient. They found a pressure drop across the portal venules of 2–3 mmHg with a control pressure of about 20 mmHg. Moreno and associates (22) estimated sinusoid pressure also in cirrhotic patients by transiently occluding the portal vein and measuring downstream pressure. They found the sinusoid pressure to be 4–5 mmHg less than the control portal pressures of about 30 mmHg.

Nakata and his colleagues (23), however, provide contradictory evidence. Using a micropuncture technique, they were able to measure directly pressures in the hepatic vasculature of the rat. They found greater than half the pressure drop across the hepatic vasculature to occur presinusoidally. Unfortunately, the margin of the rat liver which they examined does not have an arterial input to the terminal (less than 100 μm) portal venules. Thus they were basically working with a single-input, single-output vasculature. Nevertheless, there does not seem to be a closing pressure in the rat, or if there is, it must be very close to the hepatic venous pressure.

Closing pressures have been demonstrated in several other vascular beds (8, 13, 24, 25, 28), and the entire arterial bed also appears to show an effective closing pressure. Price's group (27) has also reported a closing pressure in the hepatic vasculature. They present results from one animal showing a zero-flow estimated sinusoid pressure (hepatic venous-wedged pressure) of 5 mmHg with a hepatic venous pressure of 1.5 mmHg. The existence of a closing pressure in the liver may result from the action of the sinusoidal endothelial (Kupffer) cells. These cells have been shown to be capable of bulging into the lumen of the sinusoid to completely stop flow (4, 19, 20). These bulging endothelial cells exist in all sinusoids, but are most prominent at the juncture of sinusoid to central vein. That their “tension” is variable is apparent from the fact that increasing depth of anesthesia is associated with an increasing number of blocked channels (4). McCuskey (20), in an extensive investigation, was able to show constriction of the endothelial sphincters on administration of epinephrine. There is also the possibility that the closure occurs in the larger hepatic veins. That these veins in the dog have significant amounts of smooth muscle is well known (1, 2, 10), and there is thus the potential for sphincteric action in these vessels.

The hepatic closing pressure averaged 1.6 mmHg higher than the hepatic venous pressure. Considering the thickness of the liver (which may provide a hydrostatic pressure gradient of 5–10 mmHg), one might question the functional significance of this closing pressure. However, the hydrostatic pressure head exists not only within the vessels, but also surrounding them. Thus, for vessels in the lower region, the increased pressure within the vessels is balanced by a similarly increased extravascular pressure. An equivalent situation obtains for the decreased pressures in the upper regions. Since the two venous pressure gauges were referenced to the same zero-pressure reference level, the measured closing pressure represents the lowest closing pressure for the entire hepatic vasculature regardless of hydrostatic level. Slight variation in either the balance of intra- and extravascular hydrostatic pressure heads or the intensity of the contractile region responsible for the closure may result

### Table 1. Results from all animals

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Avg ± SEM</th>
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<tbody>
<tr>
<td>1</td>
<td>12.3 ± 1.6</td>
</tr>
<tr>
<td>2</td>
<td>12.4 ± 1.6</td>
</tr>
<tr>
<td>3</td>
<td>9.7 ± 1.6</td>
</tr>
<tr>
<td>4</td>
<td>9.3 ± 1.6</td>
</tr>
<tr>
<td>5</td>
<td>13.6 ± 1.6</td>
</tr>
</tbody>
</table>

Flows are normalized to body weight. 1 resistance unit, $R_U = 1$ mmHg/(ml/min-kg body wt).
in a distribution of closing pressures within the liver. This matter is discussed in detail below.

It was also shown here that the hepatic closing pressure can change without significantly altering the shape of the pressure-flow curve (Fig. 34). This increasing closing pressure might have been the result of an increased level of circulating catecholamines. As the hepatic arterial flow rates were increased to and above normal total hepatic flows, there was an inevitable fall in systemic arterial blood pressure which should have caused catecholamine release. Direct sympathetic stimulation has been shown to increase the closing pressure in the vascular bed of the rabbit ear (13) and indirect stimulation of the sympathetic system by cold has been shown to increase the closing pressure in the vessels of the human forearm (8). More pertinent are some preliminary results from a dog with a right-heart bypass whose atrial pressure was controlled by the level of a collapsible tube. It was found that elevation of right atrial pressure to about 3 cm H₂O had little effect on portal venous pressure. During a continuous intravenous infusion of epinephrine, however, the portal pressure was not affected until the atrial pressure was elevated to about 10 cm H₂O (S. Permutt, personal communication). This suggests that the hepatic closing pressure is elevated by circulating catecholamines.

The phenomenon of a zero-flow intercept greater than the hepatic venous pressure on the pressure-flow characteristics adds another dimension to the interpretation and meaning of outflow resistance. R_L is the inverse slope of the line drawn between the hepatic venous pressure on the pressure axis and the point along the curve that represents normal flow and pressure (see Fig. 5). Since the pressure-flow curves are nonlinear, perhaps one should be equally concerned with the actual slope of the pressure-flow characteristic specific to the normal range of sinusoid pressure and hepatic flow. The inverse of this slope has units of resistance and it is designated by r_L, signifying an incremental resistance. From the shape of the experimentally determined curves (Figs. 3A and 4) it is clear that r_L is much smaller than R_L (i.e., steeper slope). Table 1 shows the average values of R_L and r_L to be 0.16 and 0.07 resistance units (RU), respectively. (1 RU = 1 mmHg/(ml/min-kg body wt)).

One may also calculate the resistance defined as R_L' = (P_ha - P_v)/F_liver (Fig. 5). The existence of a closing pressure implies that R_L' is a better estimate of the frictional (Poiseuille) resistance than R_L (so long as P_v ≤ P_ha). As sinusoid pressure is increased above the closing pressure, the vessels open. Further increases in pressure may distend the vessels, thereby decreasing resistance and producing a curvilinear pressure-flow graph convex toward the pressure axis. Table 1 shows the average value of R_L' at normal flow to be 0.10 RU, a value between r_L and R_L. Were the pressure-flow curve linear, R_L' would be equal to r_L at all flows.

The curvilinear nature of the pressure-flow curve at low flows might also be a result of a distribution of closing pressures in parallel channels. As sinusoid pressure is increased above P_ha, additional parallel pathways are recruited, and increments in pressure will cause disproportional increments in flow. When all channels are open additional increments in pressure generate a more linear pressure-flow curve with slope 1/R_L. If the linear portion of the pressure-flow curve is extrapolated down to the pressure axis, the point of intersection (P' in Fig. 5) will be between the zero-flow closing pressure, P_e, and the highest closing pressure in the bed (i.e., the pressure above which the pressure-flow curve becomes linear). It can be shown mathematically that in a bed with a distribution of closing pressures, P_e' is a weighted arithmetic mean of all closing pressures, where the weighting factor for each closing pressure is the conductance, G (1/resistance), through each respective channel. For n parallel channels, the extrapolated closing pressure, P_e', can be calculated from the following equation:

\[ P_e' = \frac{\sum_{i=1}^{n} P_{e,i} \cdot G_i}{\sum_{i=1}^{n} G_i} \]

(see the APPENDIX). The average value of P_e' for the five dogs (extrapolated from the control point of normal P_ha and total flow) was found to be 4.1 mmHg. If there is in fact such a distribution of closing pressures, then P_e' may be considered to be the effective back pressure for the bed, whose total resistance is r_L. There are thus two explanations consistent with the shape of the empirical pressure-flow curve, the first postulating resistance changes due to elastic changes in vessel diameter, and the second postulating resistance changes due to recruitment of parallel inelastic collapsible vessels. Indeed, both mechanisms probably exist.

The incremental resistance, r_L, has additional significance insofar as it determines the extent to which flow variations through the sinusoids cause pressure changes in the same. Knowing r_L at any point should enable one to predict the effect of finite changes in pressure from finite changes in flow (or vice versa). Hepatic arterial flow variations will also produce portal venous pressure variations via r_L. The fact that the normal r_L is so small may explain why total hepatic arterial occlusion causes such small changes in portal pressure in the normal vasculature (18, 31, 32). Indeed, considering the average value for r_L found here of 0.07 RU and a typical P_ha of 10 mmHg, one would expect total occlusion of the hepatic artery to produce less than 1 mmHg
change in the portal pressure, with everything else unchanged. This is in good agreement with the present observations and the results of others (18, 31, 32). If the magnitude of this drop in $P_{hv}$ following hepatic arterial occlusion increases, as it does after chronic carbon tetrachloride toxicity (31), a change is implied in the shape of the outflow characteristics at the operating point ($r_L$), whether or not the calculated values of $R_L$ or $R_{L'}$ are changed.

Figure 6 shows two models which summarize the two explanations of the results found here. For the outflow resistance, the model in Fig. 6A assumes a single closing pressure, $P_c$, and a resistance $R_{L'}$ which must decrease as $P_c$ increases (Fig. 5). In the model the closing pressure is represented by a battery symbol of magnitude $P_c - P_{hv}$ and is in series with $R_{L'}$. As long as $P_{hv} < P_c$, there must exist a “vascular waterfall” of this magnitude. For $P_{hv} \geq P_c$, the magnitude of the waterfall is zero (26).

The model of Fig. 6B assumes a constant resistance, $r_L$, with a distribution of closing pressures providing an effective back pressure to flow of $P_{c'}$ (Fig. 5). This average closing pressure generates a vascular waterfall of mean magnitude $P_{c'} - P_{hv}$, for $P_{hv} < P_{c'}$. For hepatic venous pressures between $P_c$ and the highest individual closing pressure in the bed, there will be a varying number of individual waterfalls, but the representation of Fig. 6B will no longer hold. For $P_{hv}$ greater than the highest individual closing pressure all waterfalls are zero. A model to represent the outflow resistance of $P_{hv} > P_c$ would consist of two distributions of pathways, one with a back pressure of $P_{hv}$ and the other with effective back pressures consisting of the individual closing pressures higher than $P_{hv}$. Such a model would be somewhat more complex and will not be pursued here.

Also included in the model of Fig. 6 are battery symbols representing a closing pressure and vascular waterfall (of magnitude $P_{c} - P_{hv}$) for the hepatic artery. The hepatic arterial pressure-flow characteristics have been studied elsewhere (18, 28, 32) and these investigations as well present observations all indicate the existence of a zero-flow closing pressure in the hepatic artery bed much higher than that which could be accounted for by the closing pressure in the outflow bed alone.

The use of the electrical battery symbol of varying magnitude to represent the closing pressure and vascular waterfall must be taken with caution. It is only valid for flow in the normal direction. The pressure-flow characteristics in the reverse direction may be quite different. Indeed, it has been shown that reverse perfusion of the hepatic artery is virtually impossible, whereas reverse perfusion from hepatic to portal vein is relatively free flowing (12). This would seem to suggest an infinitely high waterfall for reverse perfusion of the hepatic artery and a small one, perhaps similar to the one found here, for reverse perfusion of the portal vein.

From a functional point of view, the significance of an effective closing pressure in the hepatic sinusoids may be profound. Since there appears to be no osmotic gradient across the endothelium, sinusoid filtration is extremely sensitive to sinusoid pressure (6, 14). Thus, precise control of sinusoid pressure is essential if filtration is to be controlled. The existence of a closing pressure may provide the mechanism for this degree of precision. Indeed, a shift of closing pressure(s) will change the sinusoid pressure at constant flow. This can be accomplished with no change in $r_L$ (curve shape), so that interactions between the venous and arterial circuits (via $r_L$) remain the same.

The existence of a closing pressure by itself should provide some degree of isolation of sinusoid pressure from changes in central venous pressure. If either model of Fig. 6 holds, then $P_c = P_{hv} + (P_{hv} - r_L)$ or $P_c = P_{hv} + (P_{hv} - r_L)$, and hepatic venous pressure has no influence on $P_c$ as long as $P_{hv} < P_c$. In this preparation hepatic venous pressure was not controlled, so the actual degree of isolation is not certain. However, $P_c$ and $P_{hv}$ can vary independently of each other since increases in $P_{hv}$ were observed with no change or a decrease in $P_{hv}$. Further support is apparent from the fact that the negative respiratory dips observed in the hepatic vein do not appear in the portal pressure. Since $P_{hv} - P_{hv} + (P_{hv} - r_L)$, it is clear that they should also be absent from the sinusoid pressure as well.

Greenway and Lautt (14) have shown, however, that in the anesthetized cat increases in hepatic venous pressure are at least partially reflected back to the portal venous pressure. For hepatic venous pressures greater than $P_c$, this would be expected, but they found about 50% of the increase in $P_{hv}$ to occur in $P_{hv}$ below the mean closing pressure (relative to hepatic venous pressure) of 1.6 mmHg found here. Negative hepatic venous pressures, however, were not reflected in the portal venous pressure. There is no apparent explanation for this discrepancy except to suggest that the cat has a smaller closing pressure than the dog. Similarly, in the rat (18, 28, 32) and Leong (6) have shown $P_{hv}$ (at constant hepatic flow) to be independent of $P_{hv}$ for $P_{hv}$ less than zero. Changes in $P_{hv}$ greater than zero cause almost equivalent changes in $P_{hv}$. In the dog, Hanson and Johnson (18) have shown that an increase in $P_{hv}$ from 0 to 3 mmHg causes an increase in $P_{hv}$ from 9 to 10 mmHg; at higher levels of $P_{hv}$ further increases cause similar increases in $P_{hv}$.

Control of the sinusoid pressure is also important in the consideration of systemic vascular volumes and compliances. The blood-storage function of the liver has been the subject of much discussion and experimentation over the past...
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Recent quantitative work has shown that the liver may store a relatively large fraction of the total blood volume and impart it to the systemic circulation (7, 16). The amount of volume stored must be closely related to the intrahepatic sinusoid pressure, and the above discussion with respect to control of filtration and sinusoid pressure also pertains to the regulation of stored volume.

Appendix

Consider $n$ parallel channels each with a distinct closing pressure. For an inflow pressure $P_i$, the flow through the $i$th channel, $F_i$, with conductance $(1/resistance) \cdot G_i$ and closing pressure $P_{ci}$ is found as:

$$F_i = (P_i - P_{ci}) / G_i$$

Summing over all channels, one has

$$F = \sum_{i=1}^{n} (P_i - P_{ci}) \cdot G_i = P_{es} \sum_{i=1}^{n} C_i - \sum_{i=1}^{n} P_{ci} \cdot C_i$$

Extrapolating to zero flow, one can calculate the extrapolated closing pressure ($P_e'$ in Fig. 5). For $F = 0$

$$P_e = P_e' = \frac{\sum_{i=1}^{n} P_{ci} \cdot G_i}{\sum_{i=1}^{n} G_i}$$

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