Although virus could not be reisolated from a number of specimens, this was true in both types of cells. Since most of the specimens from which virus could not be reisolated had been in storage at —20°C for at least 6 months, it seems probable that this failure was related to the conditions of freezing and storage rather than the cell system used.

Summary. A procedure for preparation of freezer-banked PMK cells has been described. Such cells provide a readily available source of SMK cell cultures of known characteristics in respect to growth and Simian viruses. The yield from one pair of monkey kidneys can provide seed for 5 to 7 thousand tubes of SMK cell cultures which may be made up and used as needed over a period of several months. The spectrum of viruses that will multiply and produce cytopathic changes or hemadsorption in such cell cultures appears to be similar to that in PMK cell cultures. In specific comparisons these cells appear to equal the sensitivity of PMK cells when used for the primary isolation of parainfluenza viruses types 1, 2, and 3.

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Venous-Arteriolar Response in the Canine Liver.* (30022)

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Increases in total vascular resistance as functions of elevated large vein pressures have been reported in the dog foreleg(1), kidney(2), and intestine(3,4), although decreases in resistance in certain vascular beds have been found(5-7).

Increases in resistance with elevated venous pressure have been explained in part on the basis of activated neural pathways(1), a myogenic response(4) and unknown factors (2). It was considered of interest to explore the influence of hepatic vein pressure on pressures and resistances in both hepatic artery and portal vein systems in the liver. These relationships were studied in the isolated, denervated, perfused dog liver with controlled perfusion rates of both inflow circuits. Results show a profound influence of hepatic vein pressure on hepatic artery resistance, suggesting the activation of a myogenic response.

Methods. Experiments were carried out on totally isolated, denervated dog-perfused livers. Adult mongrel dogs, intravenously anesthetized with sodium pentobarbital, 30 mg/kg, were used in all experiments. The liver was removed from the dog after being freed from all surrounding tissue with the exception of hepatic artery, portal vein and vena caval attachments. Inflow vessels were separately cannulated with plastic tubing following heparinization, 3 mg/kg. The liver was then freed and transferred to a strain gauge weighing device(8) and perfused at constant flow with Sigmamotor pumps. Flows were slowly increased until hepatic artery pressure and portal vein pressures were in the physiological range (4-11 mm Hg and 60-140 mm Hg, respectively), and the liver was maintained in the isogravimetric state. A large bore polyethylene cannula was then introduced into the orifice of the hepatic veins (a portion of distal and proximal inferior vena cava remained intact) and tied firmly in place. A small catheter (PE 150) was advanced through this orifice to monitor hepatic vein pressure within the liver sub-

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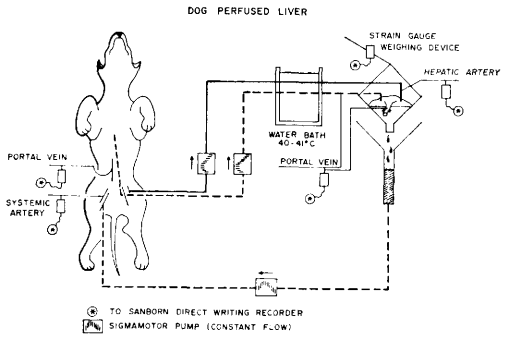

FIG. 1. Dog-perfused liver preparation.

stance. The distal end of the outflow cannula was adjusted so that hepatic vein pressure registered between 0 and —4 mm Hg and remained steady. Both hepatic artery and portal vein systems were very responsive to 0.1-0.2 μg injections of epinephrine (Suprarenin; Winthrop Laboratories) given into the inflow vessels.

The hepatic artery was perfused with blood from the aorta of a heparinized donor dog, anesthetized with intravenously administered sodium pentobarbital, 30 mg/kg. The portal vein was perfused with blood from the inferior vena cava of the dog. Fig. 1 is a diagrammatic presentation of the perfusion system. Blood flows were measured at the liver outflow and averaged 15 cc/min/kg body weight (range 10-23) and the liver blood temperature was maintained between 35°-38°C by means of an appropriately placed water bath in the perfusion circuit (Fig. 1). Hepatic artery, portal vein and hepatic vein pressures were measured on Statham pressure transducers and registered on a Sanborn direct writing recorder. The latter venous pressures were recorded alternately on a single pressure transducer in order to achieve greater accuracy of measurement. A zero catheter reference point was taken at the midpoint of the liver substance. Following a suitable equilibration period, hepatic vein pressure was elevated in steps by adjusting a screw clamp placed on the venous outflow cannula between its orifice and the site of pressure measurement. Following recovery from the partial venous obstruction, hepatic vein pressure and portal vein pressure returned rapidly to control values while recovery time for hepatic artery pressure was variable (2-12 minutes). At termination of each experiment, blood flows were separately measured through each inflow tubing and hepatic artery flow averaged 51% of total hepatic flow.

Results. Fig. 2 presents data from 2 experiments, illustrating the profound influence of hepatic vein pressure elevation on hepatic artery pressure. It is noted in the upper frame that an increase in hepatic vein pressure from —1 to 10 mm Hg (Δ 11 mm Hg) produces an increase in hepatic artery pressure from 90 to 200 mm Hg (Δ 110 mm Hg), and an increase in portal vein pressure from only 6 to 13 mm Hg (Δ 7 mm Hg).

In the lower frame, an increase in hepatic vein pressure of approximately 9 mm Hg produces a rise in hepatic artery pressure of approximately 100 mm Hg and an elevation of portal vein pressure of only 9 mm Hg.

These data show a close correspondence of liver weight changes with alterations in hepatic artery pressures particularly in the upper frame. In the case of the experiment depicted in the lower frame, repeated elevations of hepatic vein pressure of the same magnitude were seen to produce identical results as that shown in the Figure. It was noted in several instances that hepatic artery pressure remained elevated in an oscillating unstable fashion for several minutes after release of hepatic vein partial occlusion.

Fig. 3 provides data from five dog perfused liver experiments showing the influence of elevated hepatic vein pressure on hepatic artery and portal vein pressures. A striking observation is the marked increase in hepatic artery pressure which greatly exceeds that of either hepatic vein or portal vein pressures in 3 of 5 experiments. Since blood flow rate is constant through the hepatic artery circuit, a large rise in vascular resistance occurs in this segment. The portal vein pressure response is a passive phenomenon since the ratio of hepatic vein pressure to portal vein pressure is decreased as a function of the rise in hepatic vein pressure.

Discussion. These findings suggest the operation of a venous-arteriolar response in the canine liver: a relatively small increase in hepatic vein pressure in 3 of 5 experi-

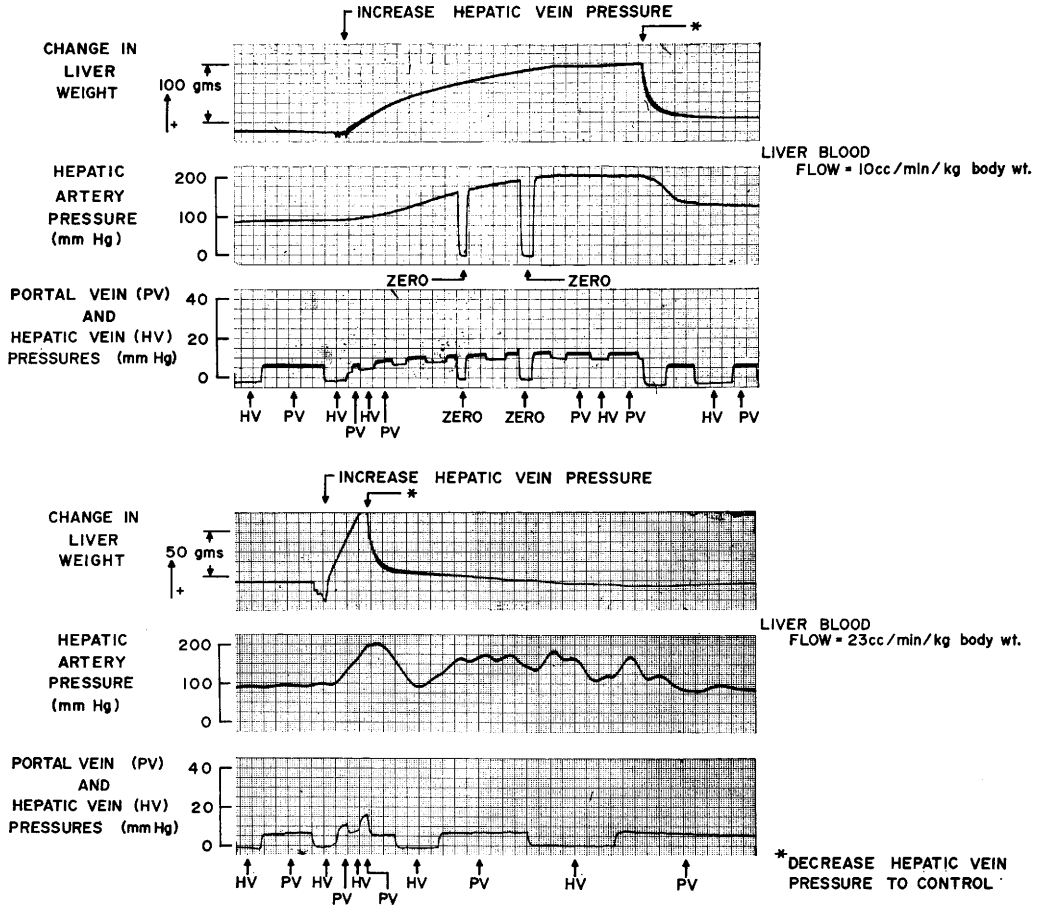

FIG. 2. Recordings from 2 experiments illustrating effects of increased hepatic vein pressure on portal vein and hepatic artery pressures and liver weight (blood flow rate constant).

ments resulted in a marked increase in hepatic artery pressure. Since blood flow rates were held constant through both hepatic artery and portal vein systems, the marked increase in hepatic artery pressure indicated an increase in vascular resistance in the arterial segment. As hepatic vein pressure was increased, the pressure difference from portal to hepatic vein remained relatively constant or declined slightly, indicating a purely passive response in this segment. The data strongly suggest that an increase in transmural pressure in the terminal hepatic arteriolar segment stimulates the smooth muscle of this segment to contract in a typical myogenic (Bayliss) fashion(4,9). Johnson(4) has shown that an increase in venous pressure in an intestinal segment elicited an increase in total vascular resistance in the segment from 30 to 50%. The data in the present study are compatible with his findings except that the liver response appears to be much more intense than that of the intestine.

The influence of localized compression forces on the arterial segment as a result of accumulation of blood and extravascular fluid following hepatic vein pressure elevation, cannot be completely excluded from the results of the present study. In one experiment, liver weight, however, had essentially returned to the control value following release of hepatic vein partial obstruction, and yet hepatic artery pressure remained above its control value for several minutes.

Our findings support those of Shoemaker (10), in that a large fraction of the total liver blood flow was found to proceed through

the hepatic artery segment.

These results are in agreement with those reported in the kidney(2), and in the mesenteric bed(3,4). Recent studies on the perfused and *in situ* dog kidneys(6,7) and in the lung(5) show that a rise in venous pressure results in a decrease in total resistance, thereby signifying passive vascular beds in these regions.

It is of interest that the most prominent examples of a myogenic response elicited by increased venous pressure are found in the hepato-splanchnic bed. It is interesting to speculate on the significance of these findings: since the liver of the dog characteristically shows hepatic vein constriction and liver pooling in a variety of shock or anaphylactic states, a myogenic response in the arterial segment would serve to limit blood flow to the liver thus influencing the volume of blood pooled in this critical region.

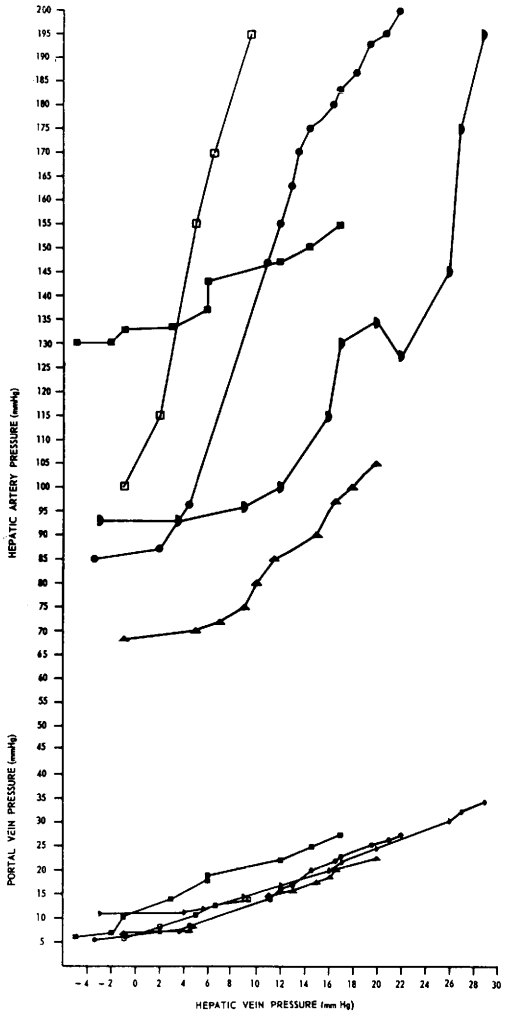

FIG. 3. Effect of increased hepatic vein pressure on portal vein and hepatic artery pressures (blood flow rate constant) (5 perfused liver experiments).

Summary. A series of experiments has been carried out on the dog-perfused liver. The liver was continuously weighed and perfused at constant flow with arterial blood through the hepatic artery, and venous blood through the portal vein. Hepatic vein pressure was increased in steps by means of partial outflow obstruction with a screw clamp adjustment. Hepatic artery pressure was seen to increase in a profound fashion as a function of elevated hepatic vein pressure in 3 of 5 experiments. An increase in hepatic artery segment resistance occurred, presumably on the basis of a venous arteriolar (myogenic) response. The vascular segment between hepatic and portal veins exhibited only passive changes as a result of increased venous transmural pressure. The peculiar arterial response would serve to decrease flow through the hepatic arterial system in the face of liver pooling in ceratin stress states previously observed in the canine species.

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