mental dogs with ascites, the splanchnic oxygen consumption was clearly decreased (Fig. 2).

The plasma proteins tend to be lowered in our subjects with congestive heart failure. Felder and coworkers found evidence of malnutrition paralleled to the duration and severity of the cardiac disease. This low plasma protein values may be occur in the patients having no appetite, being on a restricted diet, and with defective hepatic synthesis of protein. They also occur in most oedematous patients, in whom protein, particularly albumin, is lost into oedema and ascites. The malnutrition may also be a contributory factor in the production of the hepatic lesion.

CONCLUSION

In congestive heart failure, the influence of alterations of the systemic circulation on the liver was considerable, as following mechanism.

1) The hepatic blood flow in cardiac failure was moderately reduced in proportion to the reduction in total cardiac out-put. But, the former was more reduced than the latter particularly in the dogs with ascites.

2) The hepatic venous pressure was elevated in heart failure, reflecting to the rise in pressure in the vena cava, and this might conduct to the centrilobular necrosis and fibrosis. This histological changes in the liver leading also to hepatic blood flow was reduced due to increased hepatic resistance itself.

3) Ascitic fluid of the dogs with severe heart failure had a high protein content, and this phenomena was probably similar to that observed with the experimental hepatic venous obstruction.

4) The reduction in hepatic blood flow was compensated by an increase in arterial-hepatic venous oxygen difference which provided a normal splanchnic oxygen consumption. But, in the patients with severe congestive heart failure and dogs with ascites, splanchnic oxygen consumption was decreased.

5) The oxygen supply to the liver was decreased with diminishing cardiac output and hepatic blood flow. The anoxia may play a role in the production of hepatic lesion.

6) The malnutrition in congestive heart failure may be as have a similar importance as anoxia and hepatic venous hypertension.

REFERENCES


2. Hepatic Circulation and Ascites in Congestive Heart Failure†

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Liver cells are supplied their blood from two blood vessels i.e. hepatic artery and portal vein, and these two vessel systems are supposed to have each contribution to the liver cells; portal vein is thought to contribute more in supplying nutrition and hepatic artery more in supplying oxygen. Consequently I want to discuss the following problems in this treaty: What is the relationship between the blood flow to the hepatic artery and to the portal vein in

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congestive heart failure? If some definitive change is obtained in this respect, what does this change contribute to the production of ascites? and what is the meaning of ascites in congestive heart failure?

*Relationship between the blood flow to the hepatic artery and to the portal vein in right heart failure*  

To get the experimental right heart failure or strain severe enough to get the definitive trend in hemodynamic reactions, 85 dogs (weighing 10–12 kg) were given the intravenous injection of 1% lycopodium spores solution 3 times a week for 1–3 months. After moderate pulmonary hypertension had occurred, they were served to the experiments.

Hepatic blood flow and cardiac output were determined by the electric conductivity method. The principle was quite same as that of dye-dilution method. Instead of using dye, the salt concentration was measured electrically. In regard to the measurement of the ratio of hepatic arterial and portal flow, there are needs to say a few words, although the electric conductivity method was also employed. The principle of the measurement of this ratio is that when salt is injected into the aorta proximal to hepatic artery, the salt which travels through the hepatic artery reaches the hepatic vein earlier than that which passes over the portal vein because the latter must travel the longer distance (through intestinal and hepatic capillaries) than the former (through hepatic capillaries). Therefore when the former reaches the hepatic vein, it must be diluted by portal venous flow, and the degree of the dilution seemed to express the ratio which hepatic arterial flow contained in the total hepatic flow. As the concentration of the salt is quite same in hepatic artery as in femoral artery when salt is injected into the aorta, one can get the ratio of the hepatic arterial flow to total hepatic venous flow by comparing the salt dilution curve in hepatic vein and that in femoral artery, (Fig. 1). If one obtains this ratio, that of hepatic arterial and portal venous flow is easy to calculate.

In normal dogs total hepatic venous flow was about one-fourth of cardiac output and the ratio of the hepatic arterial to portal venous flow was about 1 to 4 (16.5 to 83.5%).

In pulmonary hypertension produced by the injection of lycopodium spores, total hepatic venous flow became about one-fifth of cardiac output and the ratio of hepatic arterial flow to portal venous one became 3 to 7; decrease of total hepatic flow and relative increase of hepatic arterial flow (and consequently relative decrease of portal venous flow) were demonstrated. It seems to be possible that hypoxia in liver cells due to the decreased hepatic flow is com-

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**Fig. 2.** Salt dilution curve in hepatic vein.

**Fig. 3.** Relationship between the blood flow of the hepatic artery and to the portal vein in right heart failure.
pensated by the relative increase of oxygenated hepatic arterial flow.

As symptoms of congestive heart failure have been often discussed on the basis of the hypoxia or the excessive accumulation of blood in various organs, these results need to be compared with those of hypoxic and hypervolemic conditions.

Hypoxic condition was produced by the simple apparatus connected to the trachea of the dog, which consisted of a long glass tube containing the sodalime and contributed to increase the dead space and resistance to the respiration of the dog. By means of this one can get the low oxygen saturation in the blood as low as 50\% or lower. This experiment demonstrated that in severe hypoxic condition the total hepatic venous flow less increased than the cardiac output and the ratio of the arterial hepatic flow to portal one became 1 to 9. Relative decrease of hepatic arterial flow (i.e. relative increase of portal flow) was demonstrated.

In contrast to the hypoxic conditions, rapid infusion of polyvinyl-pyrolidone (Pereston N, 2000 cc/hour) demonstrated the relative increase of hepatic arterial flow to portal one i.e. the result similar to pulmonary hypertension produced by the intravenous injection of lycopodium spores. However, those results are not specific for the rapid infusion of the fluid, but was also obtained even in the opposite condition e.g. that of acute blood loss, which was performed in our experiments by withdrawing the various amount of blood (10\%–30\% of the supposed total blood volume) from the femoral vein. In the latter condition one may suppose that when whole body needs more blood than it has, shorter distance is more employed than longer and consequently the whole body can compensate the decrease of blood volume by shortening the mean circulation time.

From these experiments it is at least impossible to assume the behavior of hepatic circulation and consequently hepatic cellular change observed in right heart failure only due to anoxia or hypoxia, because change in distribution of hepatic blood flow in our experimental pulmonary hypertension is less similar to that of hypoxic condition than that of the rapid infusion of the fluid or the blood loss.

Then, what is the meaning of such a change in distribution of hepatic blood flow in the pulmonary hypertension for the appearance of the symptoms or the signs of the right heart failure and the modification of the metabolism of liver cell itself? If such change in distribution of hepatic blood flow persists for fairly long time, nutrition, which comes from intestinal tract and is distributed to the liver and the whole organism via portal vein, must be insufficient for the whole body and the liver, though the hypoxic conditions of the liver cells due to decreased hepatic blood flow may be fairly well compensated. Consequently one might see the resemblance of these symptoms between liver cirrhosis and right heart failure in regard to the nutritional deficiency, which is, of course, less severe in degree.

**Change in distribution of blood flow and the production of ascites**

As rapid infusion of the polyvinylpyrrolidone-solution is often accompanied by the production of ascites, attempts were also made to study the conditions of ascites formation in comparison with the hemodynamic changes in rapid and slow infusion of the fluid. The rapid infusion was performed by the intravenous injection of the fluid at the rate of 1000 ml./hr. and the slow infusion at the rate of 500 ml./hr. Measurements were performed not only on the change in distribution of hepatic blood flow but hepatic wedge, hepatic venous and inferior caval pressure by venous catheterization. In these experiments it was demonstrated that the rapid infusion caused the increased resistance in postsinusoidal hepatic vein, presinusoidal portal vein, and with the decrease of portal flow ascites formation resulted, though the slow infusion caused the portal blood flow increase without ascites formation. It seems possible that when the overload to the right ventricle is not so severe, it is relieved by the circulation employing the longer distance, but when the overload become more severe, it tends to be relieved by the formation of ascites accompanied by the increased resistance in presinusoidal portal as well as postsinu-
soidal hepatic vein.

Then attempt was made to see whether or not similar relationship between the acites formation and distributional change of hepatic flow could be obtained with the injection of smaller and larger amount of lycopodium solution, but it has been failed, though various hemodynamic changes (i.e. increased resistance in presinusoidal portal vein and postsinusoidal hepatic vein and decreased portal flow) suggested that ascites might be produced with these conditions.

While the precise mechanism of the production of the ascites was not fully understood in these experiments, the question arose whether or not the discrepancy between the results of the infusion of lycopodium spores and the polyvinylpyrroldidon solution was due to the difference of the rate of transfer of produced ascites into the systemic circulation. Accordingly it is necessary to study what conditions modify the transfer rate of ascites into the systemic circulation.

Transfer rate of ascites into the systemic circulation

What conditions accelerate or delay the transfer rate of ascites into the systemic circulation? And does the right heart failure accelerate or inhibit the transfer rate of the ascites into the blood?

Studies were performed to see the rate of transfer of ascites into the systemic circulation by the injection of the ascites fluid of human patients or Ringer's solution stained with dye T1824 into the peritoneal cavity of the rabbits.

The appearance time and concentration of the dye in the venous blood were examined in the following manners. The dye appeared earlier and in larger amount in the systemic circulation when the rabbits were injected the solution of lycopodium spores and developed the moderate pulmonary hypertension. This was also noted in the case of the anoxic conditions. However, infusion of Ringer's solution into the vein delayed the appearance of the dye into the systemic circulation. Therefore the difficulty mentioned in previous chapter is supposed to be partially understood, because it was shown that

in the condition of pulmonary hypertension produced by the injection of the lycopodium spores, ascites was able to disappear quickly even if it might be produced.

Same sort of study was also performed by use of radioisotope $^{131}$I in the patients with congestive heart failure with liver enlargement with or without ascites. The experiments demonstrated that in congestive heart failure transfer rate of ascites into the systemic circulation was markedly accelerated when compared with normal subjects. It was also shown, however, that when congestive heart failure advanced and death was near, transfer rate of ascites into the systemic circulation decreased in rate and volume.

As the ascites is thought to be transferring to the blood vessels mainly via lymphatic systems, one could say from these experiment that when hepatic blood flow decreases, the increased production and transfer rate of ascites into the systemic circulation have appeared, which compensates the decreased hepatic venous flow in congestive heart failure, but this compensatory mechanism tends to fail if right heart failure has far advanced.

Summary

Though our experiments are still on the way and have much to be done, tentative conclusion may be as follows:

1) In experimental right heart failure with dogs produced by the injection of lycopodium spores, total hepatic blood flow was shown to decrease with the distributional change of relative increase of hepatic arterial flow (and consequently relative decrease of portal venous one).
2) Such change in distribution of hepatic blood flow as this may bring out the insufficient nutritional supply for the whole body, though it compensates the supposed anoxic conditions of the liver cells due to the decreased blood flow.

3) This change in distribution and other hemodynamic conditions tend to accelerate the production of ascites, but if it is produced, it is able to transfer rapidly into the systemic circulation in the experimental pulmonary hypertension.

4) In congestive heart failure of man, ascites transfers rapidly from peritoneal cavity to systemic circulation, and this rapid transfer of ascites is thought to compensate the decreased hepatic blood flow, though this compensatory mechanism tends to fail if right heart failure is far advanced.

3. Liver Function Tests in Congestive Heart Failure with Special Reference to Enzymatic Activities

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It is reported by Chavez that one of the organs that suffer most in heart failure is undoubtedly the liver. Hepatic disturbances in cases of congestive heart failure have been studied on the basis of liver function tests including BSP, bilirubin excretion and colloidal reaction as well as of histological findings of hepatic tissue. But few reports seem to have been made of an enzymatic approach.

In the present study cases of congestive heart failure were subjected to various liver function tests and additionally by enzymatic tests, in an attempt to pursue the hepatic disturbances developed. Chronological observations were made of the constrictive pericarditis experimentally induced in rabbits as to the animal's hepatic function with an emphasis on enzymatic activities of serum and hepatic tissue in reference to histological findings.

Clinical Observations

Material:

Those observed during April 1962 and March 1963 were 96 cases of congestive heart failure consisting of 28 males and 68 females of 15–79 years of age. The causative diseases for congestive heart failure were 39 cases of rheumatic heart disease, 19 cases of arteriosclerotic heart disease, 13 cases of rheumatoid valvular disease, 9 cases of chronic cor pulmonale, 7 cases of syphilitic heart disease, 5 cases of hypertensive heart disease and 4 cases of endocrine heart disease.

The severity of the above cases was classified by the New York Heart Association standards (NYHA). The cases were divided on the basis of onset into two categories, acute failure which referred to a rapid progress during the two weeks prior to the present study and chronic failure which showed no progress during the same period. The acute category included cases with initial onset and those with acute exacerbation of previously controlled failure. The present cases were divided into a right sided group, a left sided group and a combined group on the basis of venous pressure and clinical findings. Liver function tests and serum enzymatic activity tests were performed (Table I).

Clinical Symptoms:

The incidence of hepatomegaly, splenomegaly, pleural effusion, ascites, edema, elevated venous pressure and a prolonged circulation time observed in the cases belonged mostly to IV stage, according to NYHA. The above incidence was also observed in high percentage in an acute failure group as well as in a combined group (Table II).

Liver Function in Cases of Congestive Heart Failure:

The results of the tests were analysed in terms...