EXPERIMENTAL STUDY ON THE ROLE OF THE SPLEEN IN PORTAL CIRCULATION IN THE EXCITEMENT OF SYMPATHETIC NERVES

by

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INTRODUCTION

BAYLISS and STARLING[2] (1894) reported the changes of portal pressure due to electric stimulation of vagal and splanchnic nerve, since then, a large body of research has been made regarding the effects of the stimulation of autonomic nerve or of various ageants upon portal circulation. Most of the investigations so far reported deal with the rôle of the liver in the circulation, but little have been studied on the rôle of the spleen.

However, the author feels it may be justified to assume the probable rôle of the spleen in the portal circulation in conformity with the studies as have been reported by other investigators. So, an experimental study was attempted to elucidate the rôle of the spleen in portal circulation in dogs.

The purpose of this communication is to describe the results of this investigation.

EXPERIMENTALS

METHODS and MATERIALS

1. Experimental Animal

Adult mongrel dogs weighing 5.5 to 15.0 kg were anesthetized with pentobarbital sodium solution by injecting intravenously 0.5cc per kg of body weight.

2. Methods

a) Measurement of Blood Pressure

A canula was inserted directly into a femoral artery. The canula was connected with a polyvinyl tube filled with heparinized saline solution. The polyvinyl tube was led to a Hg-manometer. Using this apparatus, the blood pressure of the dogs was kimographed.

b) Measurement of Portal Pressure

A polyvinyl tube was introduced into a mesenteric vein and was advanced to the root of portal vein. Portal pressure was recorded on the kimograph connecting the tube with HÜRTHLE's membrane manometer.

c) Measurement of Blood Flow

Blood flow was measused in splenic vein and superior mesenteric vein with air bubble flow meter.[7, 15, 41] For the measurement of the blood flow of splenic vein and of

superior mesenteric vein the vinyl tube of 4.0 mm in diameter and 39.8 cm in length (volume 5.0 cc), and the tube of 5.6 mm in diameter and 40.8 cm in length (volume 10.0cc), were used, respectively. As an anticoagulant, heparin was used in the present study.

d) Stimulation of Splanchnic Nerve

A paravertebral incision 5cm distant from the spinal column was made from just

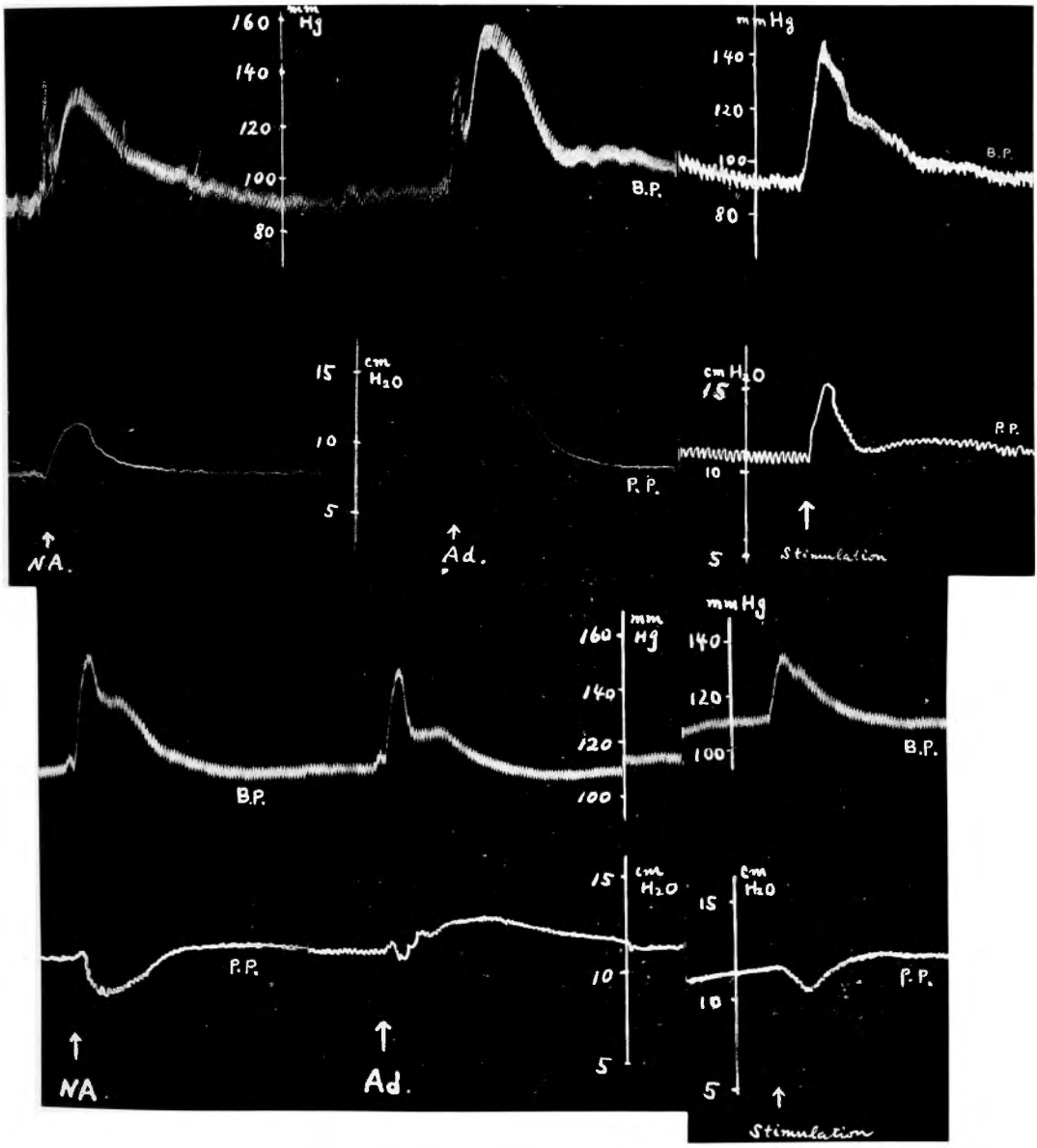

Fig. 1 Portal Pressure following the Injection of Adrenaline or Noradrenaline and following the Stimulation of Splanchnic Nerve

(upper; normal dogs
lower: splenectomized dogs)

beneath the left lowest rib to the pelvis, thus exposing splanchnic nerve without laparotomy. The exposed splanchnic nerve was cut and the peripheral segment of the cut nerve was electrically stimulated by square wave (10volt, 5 millisecond, 30 cps).

e) Determination of Blood Sugar Level

Blood sugar level was determined by the original method of HAGEDORN-JENSEN.

RESULTS

In order to investigate the significance of the rôle of the spleen, the observations were made in normal and splenectomized dogs.

As criteria to observe the rôle, portal pressure and blood sugar level were studied by intravenous injection of adrenaline or noradrenaline, and by electric stimulation of splanchnic nerve in the splenetomized dogs. Influences of the above-mentioned treatments on blood volume of splenic and superior mesenteric veins were investigated in normal dogs

1) Portal Pressure

In normal dogs, the injection of adrenaline or noradrenaline and electric stimulation of splanchnic nerve resulted in a rapid and marked rise of portal pressure, showing the maximum 30 seconds after the treatment, and returned to normal 2 minutes later (Fig. 1).

In the splenectomized dogs, similar rise was observed with adrenaline injection, but the rise of the portal pressure was less marked than in normal dogs; the maximum rise was seen 1 minute after the injection, and restored to normal in 3 minutes. On the contrary, the lowering of the portal pressure occurred immediately after the injection of noradrenaline or after the stimulation of splanchnic nerve in the splenectomized dogs; after 30 seconds, the lowering reached the maximum and it was gradually returned to normal in 2 minutes (Fig. 1).

2) Blood Sugar

The injection of adrenaline[3, 12, 25] to normal dogs resulted a gradual rise of blood sugar level, whereas in the splenectomized dogs the injection gave a two-phasic rise to

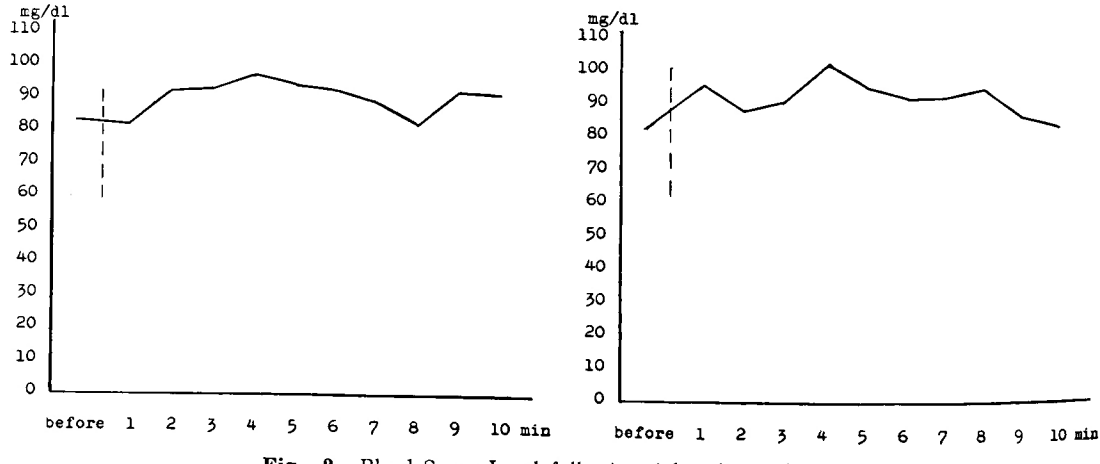

Fig. 2 Blood Sugar Level following Adrenaline Injection
(left : mean value of 5 normal dogs
right; mean value of 4 splenectomized dogs)

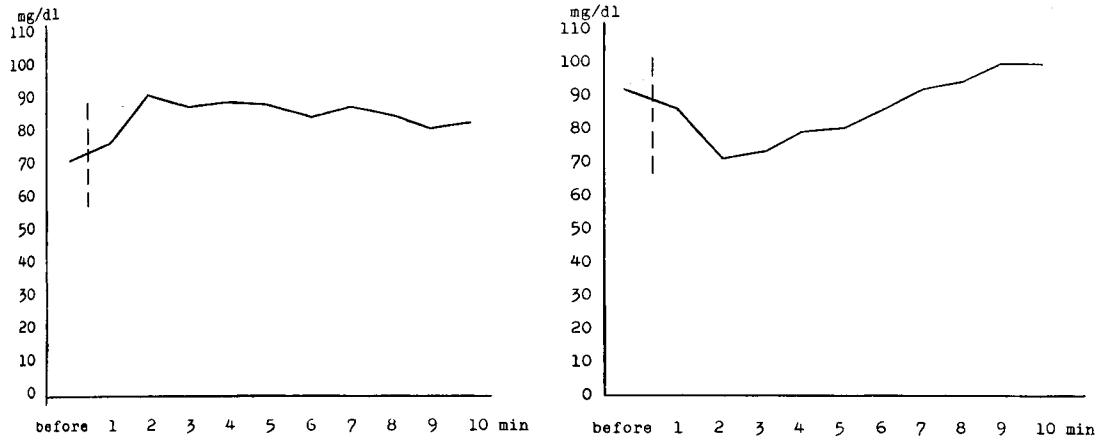

Fig. 3 Blood Sugar Level following Noradrenaline Injection
(left : mean value of 4 normal dogs
right : mean value of 4 splenectomized dogs)

show peaks 1 and 4 minutes after the injection (Fig. 2).

With the injection of noradrenaline,[3, 12] the level was rather raised in normal dogs, while, in the splenectomized dogs, it was lowered and became minimum 2 minutes after the injection, and gradually returned to normal (Fig. 3).

3) Volume of Blood Flow of Splenic and Superior Mesenteric Vein.

Volume of blood flow of splenic vein was exceedingly increased without exception either by the injection of adrenaline or noradrenaline or by the stimulation of splanchnic nerve.

However, volume of blood flow of superior mesenteric vein was different from agent used, or to the stimulation. That is, the injection of adrenaline resulted a slight increase of that volume (Fig. 4), while that of noradrenaline caused a marked decrease of the volume (Fig. 5). In case of the stimulation

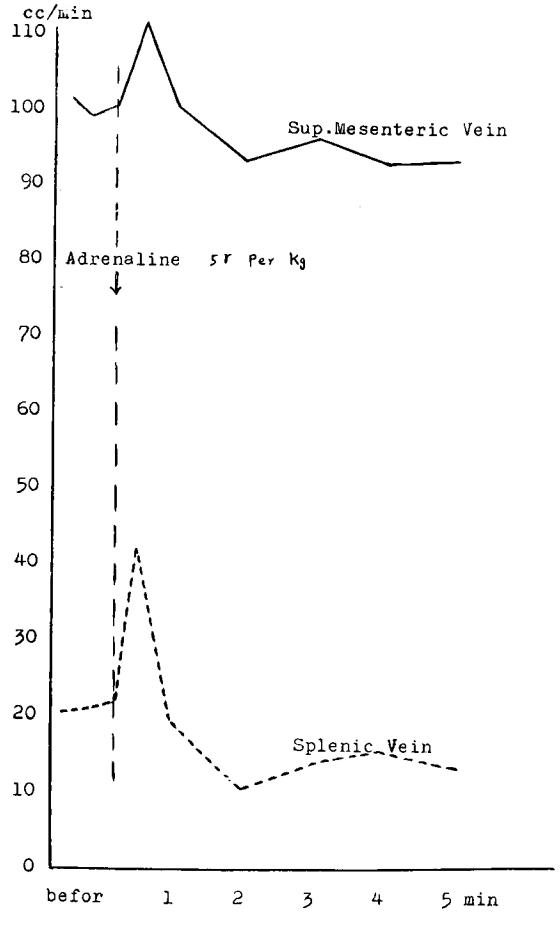

Fig. 4 Blood Flow in Splenic and Superior Mesenteric Veins following Adrenaline Injection

to splanchnic nerve too, a considerable decrease of that volume of the superior mesenteric vein was observed (Fig.6).

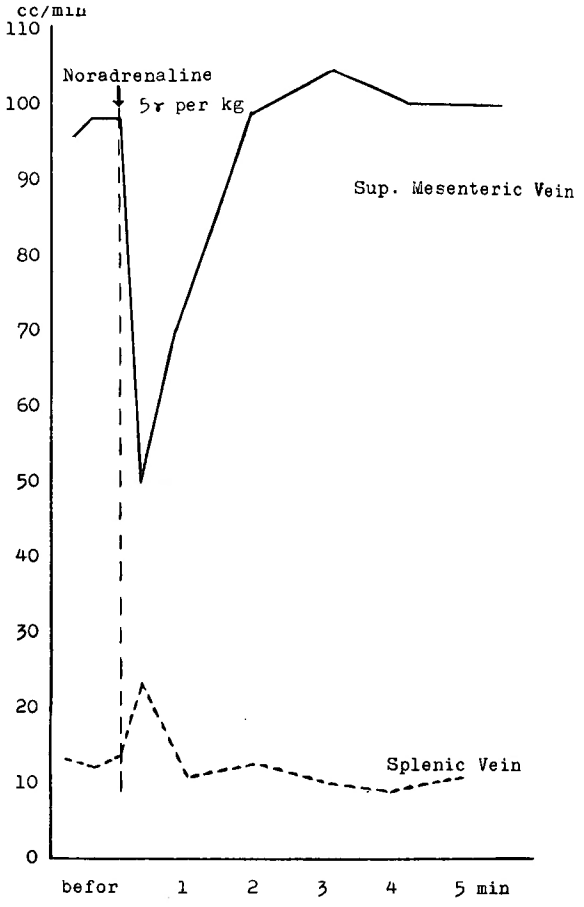

Fig. 5 Blood flow in Suplenic and Superior Mesenteric Veins following Noradrenaline Injection

DISCUSSION

It is generally believed that 20 % to 40 % of the blood circulating in the portal vein comes from splenic vein in man and dogs.[4, 8, 14, 18, 26, 28] Views concerning the relation between splenectomy and portal pressure vary from investigator to investigator. Some investigator reported the drop of portal pressure after the splenectomy[39] and others, insignificant changes of the pressure due to the splenectomy.[13, 14, 29, 37] The study here reported showed no significant difference in portal pressure between the normal and splenectomized dogs.

TAKENAKA[38] stated that the presence or absence of the spleen had nothing to do with the rise of portal pressure following adrenaline injection to the rabbits, since he could not observe any evidences of the difference in the rise of the pressure between normal and splenectomized rabbits. SOEJIMA[35, 36] reported that the spleen does not necessarily participate in the mechanism of raising the portal pressure in dogs. The present author is incapable of accepting TAKENAKA's and SOEJIMA's opinions.

Meanwhile, AOKI[1] stated that the removal of the spleen gave effects on the change of the reactions of portal circulation to various drugs injected, in view of the fact that the changes of portal pressure following the administration of the drugs were relatively little in the splenectomized dogs as compared with the normal dogs. The present author accepts his view. The author feels it may be justified to assume that the spleen plays a rôle in the rise of portal pressure, since marked differences were observed in the changes of portal pressure following the injection of adrenaline or noradrenaline or following the electric stimulation of the splanchnic nerve between normal and splenectomized dogs.

It is quite probable that a number of factors participates in the rise of portal pressure in complicated way.[34, 35, 36] Suppose that the rise of portal pressure depends exclusively

upon the increase in the amount of the blood entering the portal vein, it would be able to assume that the amount of the blood circulating in the splenic vein influences much more on the rise of the pressure rather than that circulating in the mesenteric vein. As a matter of fact, as was observed in this investigation, when noradrenaline was injected or splanchnic nerve was electrically stimulated, the portal pressure was reduced in the splenectomized dogs, whereas it was raised in the normal dogs. The spleen is contracted following the injection of adrenaline or noradrenaline or electric stimulation of splanchnic nerve[19, 24, 32] and thereby the output of the blood from the reservoir in the spleen occurs. The above mentioned increase of the blood in the splenic vein may be due to the output of the blood from the spleen which is resulted from the striking contraction of this organ. In other words, the spleen possibly regulate the portal pressure by temporary output of the blood which is stored in this organ.

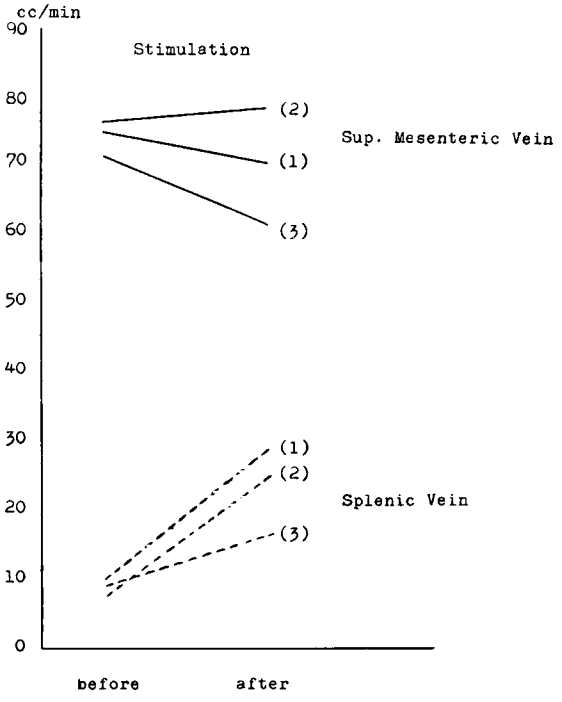

Fig. 6 Blood Flow in Splenic and Superior Mesenteric Veins before and after the Stimulation of Splanchnic Nerve

In the meantime, another possible rôle of the spleen in the regulation of the portal pressure should be taken into consideration. SUGITANI[37] pointed out the rôle of the spleen in this mechanism by liberating catecholamine, on a basis of the fact that blood level of catecholamine in the portal vein was increased in normal dogs when the portal pressure was experimentally reduced, while it remained unchanged in the splenectomized dogs. MANN and WEST,[27] PEART,[33] and BROWN and GILLESPIE[5, 6] reported that catecholamine ("sympathin" as termed by themselves) was liberated from the spleen into the splenic vein by electric stimulation of splenic nerve of cats. Investigations reported by EULER[9, 10] or MORI[30] revealed that catecholamine-like substances were stored in greater amounts in the spleen. In view of these investigations, the homeostatic rôle of the spleen through the liberation of catecholamine in the regulation of the portal pressure appears to be probable as well.[22, 23, 24, 31]

For further study of the effect of catecholamine on blood sugar level in the presence or absence of the spleen, blood sugar level was measured in normal and splenectomized dogs following the injection of adrenaline or noradrenaline, since it is reasonably assumed that catecholamine liberted from the spleen may give rise to the increase of blood sugar level which is caused from glycogen stored in the liver. As a result, the level was found

to be decreased in the splenectomized dogs following noradrenaline injection, while it was increased in normal dogs. Thus, it was suggested that the spleen plays significant rôle in the regulation of blood sugar. However, the injection of adrenaline did not result any significant difference in the aspect of blood sugar between normal and splenectmized dogs, in contrast to noradrenaline. Thus, the data presents the possibility that the spleen may not participate in the regulation of blood sugar level when adrenaline was increased in the blood.

Thus, the present author was led to the following conclusions that the spleen plays a significant rôle in the regulation of portal pressure and blood sugar level.

SUMMARY

For the purpose of investigating the significant rôle, if any, of the spleen in portal circulation, an animal experiment was carried out in the normal and splenectomized dogs by the aid of the stimulation of sympathetic nerve. Results obtained are as follows:

1) In the normal dogs, a marked rise of the portal pressure resulted either from the injection of adrenaline or noradrenaline or from the electric stimulation of splanchnic nerve. In the splenectomized dogs, however, a drop of the pressure occurred follewing the injection of noradrenaline or the stimulation of the same nerve, though i nadrenaline injection a slight increase of the pressure was observed. It was assumed that the spleen plays a rôle in the regulation of the portal pressure by the increased output of the blood due to the mechanic contraction of the organ as well as by a homeostatic action with the liberation of catecholamine from the spleen.

2) An increase in blood sugar level resulted from the injection of noradrenaline in the normal dogs. On the contrary, in the splenectomized dogs, the injection resulted a decrease of the level. This difference could possibly be accounted for by the action of catecholamine liberated from the spleen. Thus, the spleen possibly participates in the regulation of the blood sugar level.

The general conclusion drawn from these results is that the spleen plays an important rôle in the regulation of portal presssure and blood sugar level in dogs.

Acknowledgement

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和文抄録

交感神経興奮状態時の門脈循環に於ける脾臓の役割について

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交感神経興奮状態時の門脈循環に於ける脾臓の役割を追求するために，正常犬と脾剔犬を用いて動物実験を行つた結果，次の結論を得た．

1) 正常犬では，アドレナリン注射，ノルアドレナリン注射，内臓神経電気刺戟の何れの場合でも門脈圧は急速且著明な上昇を示した．併し脾剔犬では，アドレナリン注射の場合門脈圧は軽度の上昇を示したが，ノルアドレナリン注射，内臓神経電気刺戟の場合には逆に門脈圧は低下した．

一方正常犬の脾静脈の血流量は，アドレナリン注射，ノルアドレナリン注射，内臓神経電気刺戟の何れの場合でも著明に増加したが，上腸間膜静脈の血流量は，アドレナリン注射の場合は軽度の増加を示し，ノルアドレナリン注射，内臓神経電気刺戟の場合は著しく減少した．

この事実から脾臓は門脈圧の維持に重要な役割を演じているものと考えられる．

2) 正常犬にノルアドレナリンを注射した場合には血糖値の増加を示したが，脾剔犬にノルアドレナリンを注射した場合には逆に血糖値は減少した．

この事実から脾臓は血糖値の調節にも重要な役割を演じているものと考えられる．

以上総括して脾臓は，そこに貯蔵されている血液並にカテコールアミンを放出することによつて，門脈圧の調節・血糖値の調節に重要な役割を演じていることが考えられる．