10545 P

Experimental Production of Congestive Splenomegaly.

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A variety of clinical studies on patients presenting the Banti syndrome have yielded much evidence to support the view that this syndrome is a secondary manifestation of a number of primary disturbances, resulting in chronic splenic vein hypertension.[1-6] These primary mechanisms, we believe, are obstructive in character within the portal bed, and may be intrahepatic (cirrhosis, Schistosomiasis, etc.) or extrahepatic (thrombophlebitis, external pressure on the vein, malformations, cavernomatous transformation of the splenic vein, etc.).

Over a period of several years we have tried to produce this syndrome experimentally by splenic vein constriction. The results have been uniformly disappointing, as either complete venous occlusion develops with splenic atrophy, or an adequate collateral promptly forms with no alteration in the size of the spleen.

The similarity between lesions produced by Schistosoma ova and small particles of silica suggested that a perivascular fibrosis within the liver, with progressive intrahepatic portal vein constriction, might be produced by injecting silica directly into the portal vein.

Five adult and 3 young dogs have been used and similarly studied. All animals have had several injections of a sterile saline suspension of silicon dioxide directly into the splenic vein.* Each injection is made at the time of an exploratory operation. The individual silicious particles are 1-3 micra in diameter. At the time of writing, 3 animals have progressed to a late enough stage of cirrhosis to produce splenic vein hypertension with splenomegaly. The latter occurred only when enough silica is given, in our cases 6.0 g, and only when sufficient time has elapsed to produce an advanced liver cirrhosis.

1 Klemperer, R., *Arch. Path.*, 1928, **6**, 353.

2 Larrabee, R. C., *Am. J. M. Sci.*, 1934, **188**, 745.

3 Campbell, H. E., *Chinese M. J.*, 1936, **50**, 1561.

4 Rousselot, L. M., *J. A. M. A.*, 1936, **107**, 1788.

5 Rousselot, L. M., *Bull. N. Y. Ac. Med.*, 1939, **15**, 188.

6 Thompson, W. P., Caughey, Whipple, Rousselot, *J. Clin. Invest.*, 1937, **16**, 571.

* The saline suspensions of silica were prepared for us by Dr. Leroy U. Gardner, director of the Saranac Laboratories, Saranac, N. Y.

This takes approximately 24 months. Of the remaining 5 animals, one (703) was sacrificed to study the early lesions of the sequence; another (708) was autopsied after developing "congestive splenomegaly"; one (287) died of postoperative hemorrhage from the site of the venipuncture wound following silica injection; 2 animals (285, 286) have received 6.0 and 5.0 g respectively of silica, but insufficient time has elapsed to develop to the stage of congestive splenomegaly.

During the first 6 months, no gross pathological changes can be detected in liver or spleen, and only a few early silicotic nodules are seen microscopically in the liver biopsy. This failure of the silica to settle in greater concentration in the liver has been a matter of extreme interest to us. After autopsy examination of the first animal in the early state (5.9 g of silica injected), it was found that greatly enlarged, hard lymph nodes were present in the hepatic chain draining the liver. Histologically these nodes proved to be completely replaced by silicotic nodules. This lymphatic lesion has consistently appeared in all our animals prior to the hepatic retention of the silica. The migration of inert particulate matter from the portal vein into the lymphatic vessels surrounding the veins in the portal spaces and thence to issue from the liver via the efferent lymphatics has been noted.[7, 8, 9] Such was the route taken by the silica in our animals. Only after the efferent lymphatics have been blocked, and this occurs after approximately 3.0 g of silica has been injected, does the silica accumulate in the liver in sufficient amounts to produce a progressive cirrhosis. Toward the end of the 2-year period the liver is enlarged, hard, and fibrotic. With this a splenomegaly is apparent and an associated rich venous collateral has developed. The spleens in the 3 completed experiments have reached very large proportions. (See Table I.)

At the end of the experiment in these same 3 animals a splenic vein hypertension has likewise been present as compared with normal venous pressures in the saphenous vein. (See table.) The readings as recorded are 2-3 times higher in the splenic vein than in the peripheral vein under the same conditions.

Microscopic examination of the liver at the stage of splenomegaly shows typical silicotic nodules of varying ages, located mainly in the periportal areas and occasionally in the mid-portion of the lobule. In the spleen a fine fibrosis is apparent. A few silica particles are found

[7] Herring, P. T., and Simpson, S., *Proc. Roy. Soc. Lond.*, 1906, **78**, 455.

[8] Kiernan, *Phil. Trans.*, 1833, 753, quoted by Herring.

[9] Schafer, *Proc. Roy. Soc. Edin.*, 1902, **24**, 65, quoted by Herring.

TABLE I.

Animal No.	Amount of silica, g	Duration followed, mo.	L—Living A—Autopsied	Liver	Spleen	Venous Pressure in mm of water	
708	6.0	26	A	Hard; cirrhotic	Large 19 x 5.5 x 3.5 cm	Splenic vein—295 Saphenous vein—63	
27	6.0	24	L	" "	Very large 31 x 7 x 3 cm	Splenic vein—230 Saphenous vein—35	
6	6.0	23	L	" "	Very large 25 x 8.5 x 3.5 cm	Splenic vein—260 Saphenous vein—60	
690	5.6	37	L	" "	Moderately enlarged	Splenic vein—225 Saphenous vein—140	Reading equivocal; technical difficulty
703	5.9	18	A	Normal size and consistency; early silicotic nodules	Not enlarged	—	
285	6.0	6	L	Firm; early cirrhosis	Moderately enlarged 16 x 5.5 x 1.5 cm	—	
286	5.0	7	L	Firm; early cirrhosis	Moderately enlarged	—	
287	6.0	8	A	Slightly enlarged; early cirrhosis	Very large 24 x 9.5 x 3.0 cm Weight 300 g	—	Size of spleen determined after death from hemorrhage

without any significant reaction. These particles occur in such small numbers that it is the opinion of Dr. Leroy Gardner and ourselves that they are insufficient to account for the marked enlargement of the spleen.

Summary. The injection of fine silicious particles directly into the splenic vein in the amounts described will produce a progressive cirrhosis of the liver. Secondary to this a state of splenic vein hypertension has been produced with a concomitant congestive splenomegaly.

10546 P

Reduction of Experimental Renal Hypertension by Pexis of Spleen or Omentum to the Kidney.

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The effect of the pexis between kidney and the spleen or omentum upon the blood pressure of dogs rendered hypertensive by Goldblatt's[1] method of renal constriction has been studied in this laboratory since 1936. Sixty-five dogs have been employed in the development of 2 suitable technics for establishing organ pexis to such ischemic kidneys. Seven animals survived the various surgical procedures for producing carotid loop,[2] hypertension[1] and the union of the organs.

Only 2 died as the result of the latter operation. Fifty-six dogs died or were discarded because of hemorrhage from the carotid loop employed for blood pressure determination, anesthetic deaths, uremia from infarction of the kidneys, distemper, and operative infection. Postoperative shock was insignificant following the pexis which was performed one to 3 months after the hypertension was established. Control operations in which the omentum and spleen were manipulated did not result in a significant prolonged fall in blood pressure.

The blood pressure of all of the 7 animals was lowered within 4 days following the union. Three of these, following the pexis of

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1 Goldblatt, Harry, *Experimental Hypertension Induced by Renal Ischemia,* The Harvey Lectures, 1937-38, Williams and Wilkins Co., Baltimore, 1938.

2 Van Leersum, E. C., *Arch. Ges. Physiol.,* 1911, **142**, 377.