Production of Portal Hypertension and Esophageal Varices in the Mouse. (23952)

KENNETH S WARREN AND WILLIAM B. DEWITT
(Introducd by T. von Brand)
U. S. Dept. of Health, N.I.H., Nat. Inst. of Allergy and Infectious Diseases, Bethesda, Md.

Taylor(1) has recently reviewed the field of experimental portal hypertension. He stated, seconded by Child(2,3), that the "enigma of portal hypertension is at present complete." He further noted that, "It is likely to remain so until an acceptable experimental method of producing it can be found." His major criterion for portal hypertension was a significant and sustained rise of portal pressure. Esophageal varices, if present, would not only simulate the consequences of portal hypertension in humans, but would indicate a sustained rise in pressure.

The purpose of this communication is to report the occurrence of portal hypertension and esophageal varices in mice experimentally infected with *Schistosoma mansoni.*

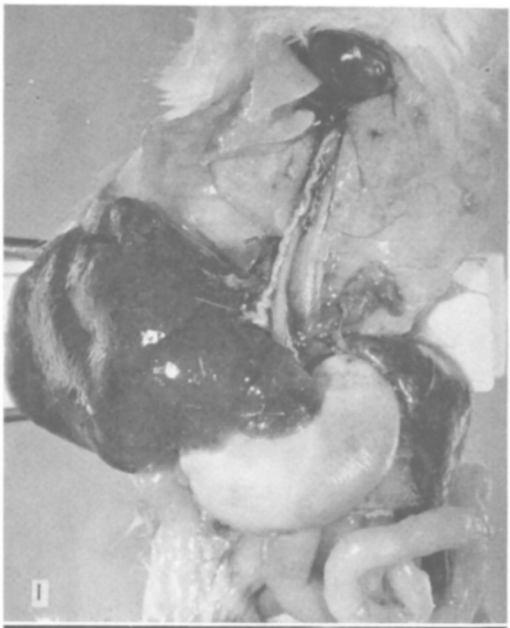
Materials and methods. Young adult Swiss albino mice were individually exposed to 100 cercariae of the Puerto Rican strain of *S. mansoni* according to the method of Olivier and Stirewalt(4). This produced an average of 24 worms in the portal circulatory system/mouse. The mice were sacrificed at two-week intervals from 6 to 16th week after infection. Portal pressure was measured by introducing a 22 gauge needle, connected to a strain gauge, into the portal vein. X-rays were obtained, under the same conditions, during injection of an opaque medium (50% Hypaque) into the portal vein. Although esophageal varices when present were readily apparent at autopsy, they were preserved for anatomic and photographic study by injection of a yellow latex medium into a mesenteric vein at uniform pressure of 200 mm of mercury.

Results. Esophageal varices were observed in 43% of the mice examined from 10 to 16 weeks after infection. No varices were seen in control animals or in animals infected for less than 10 weeks. The varices arose from the venous plexus about the stomach, spleen, and liver and joined the systemic circulation, usually *via* the inferior vena cava or pulmonary veins, as was shown in latex injected preparations (Fig. 1) and X-ray portagrams (Fig. 2). The varices were uniformly on the serosal surface of the esophagus and were never within the esophagus itself. The average portal pressure in control animals was 5 cm of water (range 2-8). In infected mice the portal pressure, as shown in Table I, rose to an average of 10.3 cm (range 6-18.5) from 8th through 16th week (biweekly differences were not significant). From the tenth week on, when varices were present, the average portal pressure in 23 infected mice without varices was 9 cm of water (range 6-13.5) as

TABLE I. Portal Hypertension and Esophageal Varices in Mice Infected with *Schistosoma mansoni.*

		Esophageal varices		Portal pressure			
	Wk after infection	No. examined	No. with varices	No. examined	Avg P.P.,* cm H_2O	No. with P.P. >10 cm H_2O	No. with varices
Varices not present	0	21	0	9	5.0 ± .7†	0	0
	6	19	0	9	6.3 ± .4	0	0
	8	20	0	10	9.4 ± .4	5	0
Total		60	0	28		5	0
Varices present	10	20	11	10	10.3 ± 1.1	5	4
	12	19	7	9	11.9 ± 1.2	7	3
	14	19	7	10	10.4 ± 1.0	4	3
	16	18	8	8	9.4 ± .8	3	3
Total		76	33(43%)	37		19(51%)	13

* Portal pressure. † Stand. error.



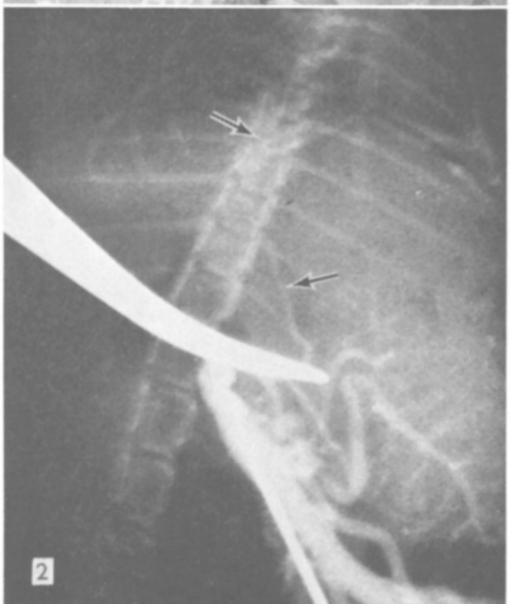


FIG. 1. 24 g mouse infected 14 wk—Yellow latex inj. of portal circulation. Note: hepatomegaly, splenomegaly, tortuous anterior and posterior periesophageal varices.

FIG. 2. 23 g mouse infected 14 wk. X-ray portagram—50% Hypaque inj. into portal vein with distal portion of vein clamped. Note: dilatation of portal vessels, tortuous esophageal varix (arrows).

compared to an average of 13.3 cm (range 8-18.5) in 13 mice with varices. Portal hypertension was considered to be present when pressure rose above 10 cm of water. This occurred in 51% of the infected mice examined from tenth week of infection on.

Discussion. *S. mansoni* infection not only produces a significant rise in portal pressure in mice, but also causes development of esophageal varices. This provides a relatively rapid method for reproducing portal hypertension in the small laboratory animal. Studies are being planned in larger animals, keeping one particular limitation in mind, that of finding a good host for the particular species of schistosome utilized.

Many different methods (surgical, toxic and dietary) have been used in the past in unsuccessful attempts to produce consistent portal hypertension in experimental animals (1,3). One method frequently attempted has been to reproduce Laennec's cirrhosis, by either dietary or toxic means. It is of interest therefore that portal hypertension has been reported to occur in only 30% of human cases of Laennec's cirrhosis(3,5) while it has been estimated to be present in 40-70% of those with hepato-splenic schistosomiasis(5,6).

Another approach frequently employed in attempts to produce portal hypertension has been the introduction into the portal circulation of relatively inert substances of different particle sizes to create a mechanical block(1). The production of eggs in large quantities by the parasite simulates this method, but the eggs have one further unique ability. They excite a localized fibrotic reaction which effectively obliterates the entire portal area(7). This may be the final factor for the development of portal hypertension in mice infected with *Schistosoma mansoni.*

Summary. A useful technic for producing portal hypertension and esophageal varices in the laboratory animal has been described. Ten weeks following infection of mice with *S. mansoni,* there was a significant increase in portal pressure in 51% of our animals, and the development of esophageal varices in 43%.

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Geographic Variation in Plasma Protein Patterns of Snakes. (23953)

HERBERT C. DESSAUER AND WADE FOX

Departments of Biochemistry and Anatomy, Louisiana State University School of Medicine, New Orleans

We have reported(1) that electrophoretic patterns of plasma proteins of a number of species of reptiles and amphibians show distinct geographic variation. Some of these protein differences occur between currently recognized geographic races, whereas other differences appear to be independent of morphological variation. To our knowledge only 3 other examples of intraspecific variations in the pattern of plasma proteins have been reported. Deutsch and McShan(2) found distinct differences between patterns of the channel catfish and the white catfish which were considered at that time to be of the same species. Later studies, however, suggest that these two forms should be classified as different species(3). Smithies(4) demonstrated the presence of genetically determined differences between patterns of Caucasian and African races of man. Recently, Zweig and Crenshaw(5) have shown that 2 races of the turtle, *Pseudemys floridana,* can be differentiated by their plasma patterns. The present paper describes the nature of geographic variations found in plasma patterns of several species of snakes (common kingsnakes, racers, common water snakes, and common garter snakes).

Materials and methods. Snakes were either collected personally or obtained from naturalists in other sections of the United States. Locality of capture and scientific and common names(6) were recorded as exactly as possible for each animal. After a fast of one week, specimens were anesthetized with ether and bled from a cardiac puncture. The condition of the primary and secondary sex organs was noted; animals were fixed in formalin, catalogued, and saved for deposit in the La. State Univ. Museum of Zoology. Blood was collected in heparinized tubes and centrifuged at 4°C. Plasma was separated immediately from cells and an aliquot of plasma was subjected to paper-electrophoresis on the same day that the animals were bled. In each electrophoretic run, a sample of human plasma served as a standard reference. Two-hundredths ml of plasma was applied across a 1 inch strip of Muncktells 20 S filter paper and fractionated in barbital buffer (pH 8.6, ionic strength 0.05, 15% glycerol v/v) for 17 hrs at 170 v with an LKB paper-electrophoresis unit operating at 26 to 28°C. Details of the electrophoretic procedure have been published(1). After electrophoresis, each strip was dried and stained with bromphenol blue. The stained strips were made translucent with mineral oil and scanned at 590 mμ with Beckman DU spectrophotometer. Optical densities were plotted against distance along the strip, and the area under the resulting curves was used to calculate percentages of protein fractions. In order to eliminate possible variabilities due to the apparatus, samples of all populations being compared were rerun simultaneously on parallel strips. Fresh samples were not always available on the same day and frozen plasma (stored at −20°C), which produced patterns nearly identical to the fresh, was substituted.

Results. Plasma protein patterns of snakes characteristically exhibit 2 distinct groups of anodal fractions which are separated by an