The relations existing in man between plasma level and rate of excretion are entirely similar to those described in the dog by Shannon in the accompanying paper, except that at all plasma levels the phenol red clearance in man is relatively much greater than the inulin clearance. In man the maximal phenol red/inulin clearance ratio is 3.2 as compared to 1.7 in the dog. When one takes into account the fact that there is about twice as much free phenol red in dog's plasma as there is in man's, this difference becomes all the more significant in indicating a great difference in the capacity of the two kidneys to secrete this substance.

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Effect of Splenectomy on Bacterium Enteritidis Infection in White Mice.

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It has been well established that removal of the spleen in many species of animals depresses the natural resistance to certain bacterial, protozoan and spirochetal infections.* The rôle of the spleen in the maintenance of an acquired resistance to latent piroplasmidae and bacterial infections has been demonstrated in *Bartonella muris* infection in the rat, in *Bartonella canis* infection in the dog, in *Eperythrozoan coccoides* and *Bartonella muris* infection in the mouse, in infection with *Nuttalia equi* in the horse, Anaplasmosis in sheep and cattle and *Babesia bigeminum* in cattle.[3] Removal of the spleen converts a latent infection into manifest disease, often associated with a severe fatal anemia.

Morris and Bullock studied a spontaneous epizootic infection, with *Bacterium enteritidis* (Gaertner), in their rat colony and noted that splenectomy conspicuously lowers the resistance of the rat to this natural infection.[4] They were unaware, however, of the occurrence

* The relation of the spleen to resistance has been discussed in papers of Perla and Marmorston,[1] Marmorston[2], and in a recent monograph.[3]

[1] Perla, D., and Marmorston-Gottesman, J., *J. Exp. Med.*, 1930, **52**, 601; 1931, **53**, 869, 877.

[2] Marmorston, J., *J. Inf. Dis.*, in press.

[3] Perla, D., and Marmorston, J., *The Spleen and Resistance*, Williams and Wilkins, Baltimore, 1935.

[4] Morris, D., and Bullock, F., *Ann. Surg.*, 1919, **70**, 513.

of *Bartonella muris* anemia following removal of the spleen in almost all strains of rats.

In the experiments reported in this communication the effect of splenectomy on the course of a subsequently induced acute bacterial infection, *Bacterium enteritidis,* was studied in mice free of *Eperythrozoan coccoides* and *Bartonella muris,* since latent infections with these microorganisms may become active following removal of the spleen.[2]

All the mice used in these experiments were kindly furnished to us by Dr. Leslie T. Webster of the Rockefeller Institute for Medical Research. Two strains of mice were used. The animals of one strain were of a selected stock which had been found in the studies of Dr. Webster to be highly resistant (termed by him, "resistant") to spontaneous or induced infection with *Bacterium enteritidis* and pneumococcus. The mice of the other group (termed by him, "susceptible") were of a strain highly susceptible to these infections.[5] All of the mice were approximately 3 to 4 months of age. To confirm the absence of *Eperythrozoan coccoides* and of *Bartonella muris* in the mice, smears of the peripheral blood in the control and splenectomized mice were examined at intervals of one or 2 days during the entire experimental period of one month. These mice were found to be entirely free of these infections. At the end of the experiment all the mice were autopsied and microscopic sections of the kidneys were carefully examined for the presence of *Klossiella muris,* since the author had noted an increase in severity of *Klossiella muris* infection in young adult mice of certain strains following splenectomy. The strains of mice used in these studies were found to be free of this microorganism.

Effect of Splenectomy on the Course of Bacterium Enteritidis Infection in a Resistant Strain of Mice. The effect of splenectomy on a subsequently induced infection with *Bacterium enteritidis* in resistant mice was observed in 2 experiments. In the first experiment 45 mice were divided into 3 groups. Fifteen were splenectomized, in 15 a laparotomy was performed and 15 were used as controls. Six days after operation all were injected intraperitoneally with 0.3 cc. of an 18-hour broth culture of *Bacterium enteritidis.* Of the splenectomized mice 5 or 33% died within a week and only one control succumbed. (Table I.)

In the second experiment 77 mice were divided into 3 groups: 32 were splenectomized, in 20 a laparotomy was performed, and 25 were used as normal controls. Forty-eight hours after the opera-

[5] Webster, L. T., *J. Exp. Med.,* 1933, **57**, 793.

TABLE I.
Effect of Splenectomy in Mice of a Resistant Strain on Course of a Subsequently Induced Infection with *Bacterium enteritidis*.

A. Intraperitoneal Injection.

	No. Mice	No. Died	% Died
Splenectomy	15	5	33
Laparotomy	15	0	0
Controls	15	1	6

B. Intrastomachal Injection.

	No. Mice	No. Died	% Died	Mice That Had Positive Blood Cultures and Survived	
				No.	%
Splenectomy	32	9	28	19	79
Laparotomy	20	0	0	9	45
Controls	25	2	8	12	52

tion all received 0.5 cc. of an 18-hour broth culture of *Bacterium enteritidis* administered directly into the stomach through a fine catheter.† Cultures on eosin-methylene-blue media of blood drawn from the tail vein were made daily during a period of one month. Colonies were identified by subcultural methods on Russell's triple sugar media and by subsequent agglutination tests with immune serum against *Bacterium enteritidis* for differentiation from *B. aertrycke* (mouse typhoid).

With the dosage of organisms employed less than 4% of normal control mice of this strain and those in which a laparotomy was performed, succumbed to the infection within a month. Only 2 of the normal controls died of the infection within the experimental period. This agrees with the previous findings of Webster.[5] Of the 32 splenectomized mice, 9 or 28% died within 2 weeks after introduction of the bacteria. None of the mice in which a laparotomy had been performed succumbed. (Table I.)

The greatest number of mice in which positive blood cultures were obtained occurred in the splenectomized group. Of 23 splenectomized mice that survived the injection about 80% had one or more positive blood cultures. Of the 20 mice in which a laparotomy was performed 45% had one or more positive blood cultures. Of the 23 mice in which no operation was done 52% had one or more positive blood cultures during the period of the experiment. (Table I.) The greatest number of positive blood cultures in all the groups occurred on the fifth day. However, in those mice that survived the infection, persistently positive blood cultures were found

†I am grateful to Dr. L. Webster of the Rockefeller Institute for carrying out this procedure.

during the 2nd and 3rd weeks, in the splenectomized mice in greater numbers than in the control mice. There is little difference in the curves (Fig. 1) of the normal controls and in those of the lapar-

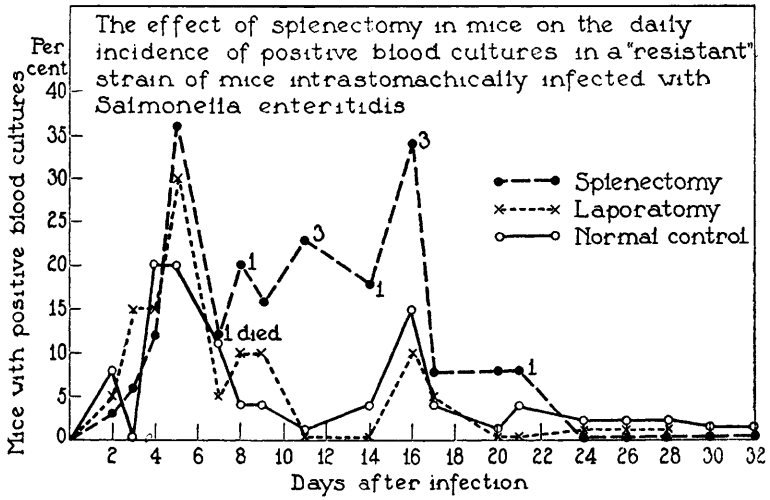

FIG. 1.

otomy controls. After the 21st day, the blood cultures of all the surviving mice were negative.

Effect of Splenectomy on the Course of Bacterium Enteritidis Infection in a "Susceptible" Strain of Mice. Twenty-three mice of stock highly "susceptible" to *Bacterium enteritidis* were divided into 3 groups (Table II). Splenectomy was done in 9, a laparotomy in 5, and 9 were used as controls. They were all infected by injection into the stomach, as in the previous experiments, 48 hours after operation. All animals, in which a laparotomy was performed, died. In the susceptible group the unoperated infected animals all developed bacteremia (see Fig. II) and 7 of 9 succumbed. There was a slightly higher mortality in the splenectomized than in the normal mice, but the experiment shows no significant difference between splenectomized and the 2 control groups.

In mice that are highly resistant to *Bacterium enteritidis* infec-

TABLE II.

Effect of Splenectomy in Mice of a Susceptible Strain on Course of a Subsequently Induced Infection with *Bacterium enteritidis.*

Operation	No. Mice	No. Died	% Died
Splenectomy	9	8	89
Laparotomy	5	5	100
Controls	9	7	77

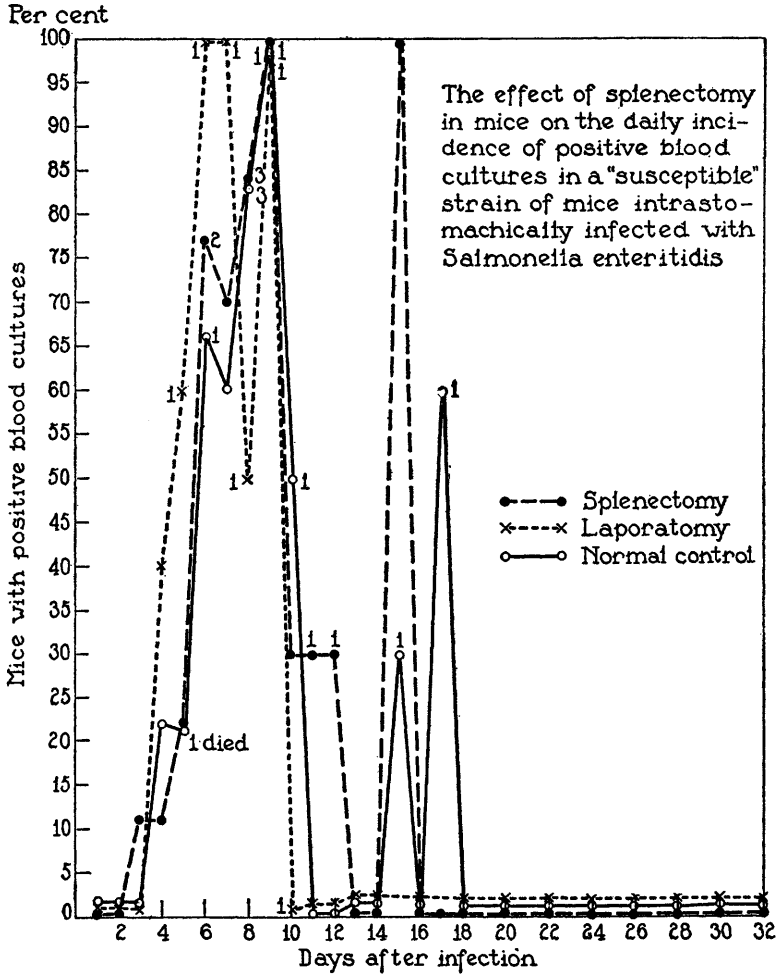

FIG. 2.

tion, the spleen has an important part in the maintenance of natural resistance to the acute infection. In mice of susceptible strains, which normally succumb in high percentages to enteritidis infection, the spleen offers little protection against the infection.

Summary. 1. In a strain of mice highly resistant to bacterial infection the removal of the spleen depresses the natural resistance to a subsequently induced infection with *Bacterium enteritidis.* 2. In a strain of mice highly susceptible to bacterial infection the removal of the spleen does not affect the natural resistance to a subsequently induced infection with *Bacterium enteritidis.*