THE INTOXICATION OF SPLENECTOMIZED MICE BY FEEDING FRESH SPLEEN AND OTHER ORGANS.

By PAUL A. LEWIS, M.D., and ARTHUR GEORGES MARGOT.

(From the Henry Phipps Institute of the University of Pennsylvania, Philadelphia.)

(Received for publication, June 23, 1915.)

As we have previously recorded,[1] splenectomized mice when fed with fresh sheep or mouse spleen frequently show signs of illness. Some animals die within a few hours after eating the organ, and of those that die some show hemorrhages into the peritoneal subserosa or peritoneal cavity. The mice that have been ill are apt to refuse to eat the fresh organ on several succeeding days. When they do eat again they may or may not show signs of illness once more. Splenectomized mice fed with fresh sheep muscle never showed any sign of acute illness. Intact mice fed with spleen also showed no sign of ill effect.

These experiments were made on animals from two weeks to four weeks after the removal of the spleen. The intoxicating effect was readily noticeable in animals infected with the tubercle bacillus. In the non-infected animals the result was definite, but somewhat irregular, so much so that it seemed impracticable to do systematic work which should include a consideration of the negative results.

Passing by the steps which led to a definite and decisive method of work we may say that we found that at four or five days after splenectomy the intoxication is more regular in its occurrence and is apt to be more severe than at later periods. Also, as we continued these observations, we became impressed with the fact that the hemorrhage into the serous membranes and especially into the peritoneum, which we had occasionally noticed, was really an integral part of the process. Following a natural train of thought from this point we were led to test the coagulation time of the blood. We have found that the most constant result, following the feeding of

[1] Lewis, P. A., and Margot, A. G., *Jour. Exper. Med.*, 1915, xxi, 84.

spleen to splenectomized mice, is a delayed coagulation time. With these facts as a basis for judgment, we have studied the nature of this intoxication as it relates to the time of its possible development after splenectomy, the rate of its development after feeding, its specificity both as to organ and as to species, the amount of fresh substance necessary to produce the intoxication, and finally the effect of the continuous feeding of less than the fatal amount of substance.

Methods.

The general methods of splenectomy and feeding have been stated in our previous papers. With regard to the feeding we may repeat that the animals are fed with the fresh organs before other food is given on that day. We have found that the change in coagulation time is apt to be somewhat more pronounced after the second day's feeding than on the first day. Therefore, in case the first feeding has given a negative result, we have always fed with the same substance on the next day. The coagulation time has been taken with Bogg's instrument, the blood being drawn from the tail. In the following experiments the first feeding was on the fourth day after splenectomy. The second feeding was on the following day. The coagulation time was taken before feeding and usually from three to four hours after feeding.

The results of these experiments may be summarized as follows:

Splenectomized mice fed on the fourth day and again on the fifth day show no change in the coagulation time of the blood when the following organs are used: lymph nodes, thymus gland, liver, kidney, skeletal muscle, lung, brain, pancreas, pituitary gland, testicle, adrenal, thyroid gland, salivary glands, and the mucosa of the large intestines.

When fed with the following tissues the mice show a delay in the coagulation time varying between two minutes and fifteen minutes: spleen of mouse, rat, guinea pig, rabbit, beef, sheep, cat, and man; gastric mucosa of mouse and cat; and mucosa of the upper small intestines of mouse and cat.

When fed with fresh human bone marrow and with dried sheep blood the mice also show a change in coagulation time. In the experiments so far done the change has been less pronounced than after the feeding of spleen or gastro-intestinal mucosa.

The mice which show the smaller changes in coagulation time seldom show any other evidence of the intoxication. When the delay in coagulation time is marked the animals are apt to be extremely sick, and a considerable number of the animals have died. Death when it occurs usually takes place before the eighth hour. In twenty hours the blood of the surviving animals has usually returned to the normal. Occasionally animals are encountered in which the return to normal is less rapid. In these instances the blood coagulates slowly and the animal is still sick at the end of twenty-four hours. These animals sometimes recover and sometimes die. The animals which die during the course of this intoxication reveal various changes at postmortem examination. In some no gross changes can be made out. In others there are found petechial hemorrhages of the serous membranes, particularly the visceral peritoneum. Some instances of hemorrhage into the intestine have been encountered. The most usual result is a diffuse, rather poorly marked reddening of the peritoneal serosa accompanied by a small amount of blood tinged peritoneal fluid. Occasionally extremely large hemorrhages into the peritoneal cavity have occurred. When this has happened the animal has died quite suddenly. No definite bleeding point has been discovered in any instance. An intense diarrhea accompanies some cases.

We have been unable to distinguish in any way between the intoxication resulting from feeding spleen and that following the feeding of gastro-intestinal mucosa.

The tabulated results of the work on which the foregoing statements are based, together with the necessary control experiments, follow (Experiments I to XXX, Tables I to VIII).

TABLE I.

Experiment I. Rate of Development of the Intoxication after Feeding with Fresh Sheep Spleen.

Mouse No.	Coagulation time.					Remarks.
	Before feeding.	After feeding.				
		30 min.	1 hr.	2 hrs.	3 hrs.	
187	5 min., 10 sec.	5 min., 0 sec.	5 min., 20 sec.	7 min., 10 sec.	9 min., 20 sec.	Died.
188	6 " 10 "	6 " 30 "	6 " 20 "	8 " 0 "	8 " 10 "	Ill.

TABLE II.

Experiment II. Amount of Fresh Spleen (Human) Necessary To Produce Delayed Coagulation.

Mouse No.	Amount eaten.	Coagulation time.		Remarks.
		Before feeding.	After feeding.	
	mg.			
317	100	5 min., 10 sec.	8 min., 10 sec.	Ill.
318	100	4 " 0 "	8 " 20 "	Died.
319	50	6 " 0 "	10 " 10 "	"
320	25	4 " 20 "	6 " 20 "	Ill.
321	10	4 " 40 "	6 " 10 "	"
322	10	5 " 0 "	6 " 20 "	Well.
323	5	6 " 10 "	6 " 0 "	"

TABLE III.

Experiments III to VII. Effect of Feeding Spleen of Other Animals to Splenectomized Mice.

Organ fed.	Mouse No.	Coagulation time.					
		First day feeding.			Second day feeding.		
		Before.	After	Remarks.	Before.	After.	Remarks.
Experiment III.	158	4 min., 30 sec.	4 min., 20 sec.		4 min., 20 sec.	7 min., 10 sec.	Very ill.
Spleen (cat).	159	4 " 20 "	4 " 10 "		4 " 40 "	6 " 20 "	Ill.
	160	5 " 20 "	5 " 30 "		5 " 10 "	5 " 10 "	
	161	5 " 30 "	5 " 40 "		5 " 20 "	8 " 30 "	Died.
Experiment IV.	119	6 " 10 "	6 " 10 "		6 " 0 "	6 " 10 "	
Spleen (beef).	120	5 " 30 "	7 " 30 "	Ill	7 " 20 "	11 " 30 "	"
	121	4 " 20 "	4 " 30 "		4 " 20 "	10 " 10 "	"
	122	4 " 30 "	4 " 20 "		4 " 40 "	6 " 30 "	Ill.
Experiment V.	178	6 " 0 "	6 " 10 "		6 " 30 "	6 " 30 "	
Spleen	179	4 " 10 "	7 " 20 "	"	7 " 0 "	8 " 10 "	Very ill.
(guinea pig).	180	4 " 20 "	4 " 30 "		4 " 20 "	4 " 10 "	
	181	5 " 10 "	5 " 20 "		5 " 0 "	5 " 20 "	
Experiment VI.	174	4 " 10 "	4 " 20 "		4 " 30 "	6 " 10 "	
Spleen	175	4 " 20 "	4 " 20 "		4 " 10 "	7 " 40 "	Ill.
(rabbit).	176	5 " 10 "	5 " 0 "		5 " 30 "	7 " 10 "	"
	177	4 " 30 "	4 " 25 "		5 " 0 "	6 " 30 "	
Experiment VII.	170	5 " 30 "	7 " 10 "	"	6 " 10 "	7 " 20 "	
Spleen (rat).	171	6 " 0 "	6 " 20 "		6 " 10 "	6 " 20 "	
	172	6 " 10 "	6 " 30 "		5 " 40 "	6 " 0 "	
	173	5 " 20 "	8 " 30 "	Very ill	8 " 10 "	8 " 40 "	Did not eat. Died.

TABLE IV.

Experiments VIII to XI. Effect of Feeding Gastro-Intestinal Mucosa to Splenectomized Mice.

Organ fed.	Mouse No.	Coagulation time. First day feeding. Before.	After.	Remarks.	Second day feeding. Before.	After.	Remarks.
Experiment VIII. Stomach (mouse).	34	4 min., 30 sec.	4 min., 20 sec.		4 min., 20 sec.	7 min., 10 sec.	
	35	5 " 0 "	6 " 10 "		5 " 10 "	7 " 20 "	
	36	4 " 10 "	10 " 20 "		4 " 30 "	10 " 30 "	
	37	6 " 0 "	6 " 10 "		6 " 0 "	9 " 20 "	
Experiment IX. Small intestine (mouse).	30	6 " 20 "	7 " 0 "		5 " 20 "	9 " 0 "	
	31	4 " 40 "	6 " 5 "		5 " 0 "	8 " 20 "	Died.
	32	6 " 10 "	6 " 20 "		5 " 30 "	6 " 40 "	
	33	5 " 5 "	5 " 20 "		5 " 5 "	7 " 30 "	
Experiment X. Stomach (cat).	154	5 " 40 "	7 " 10 "	Ill	6 " 0 "	9 " 10 "	Ill.
	155	6 " 20 "	6 " 10 "		6 " 10 "	7 " 20 "	
	156	6 " 10 "	6 " 30 "		6 " 20 "	6 " 20 "	
	157	5 " 10 "	5 " 10 "		5 " 20 "	10 " 40 "	Died.
Experiment XI. Small intestine (cat).	150	4 " 20 "	6 " 10 "		5 " 0 "	8 " 20 "	Very ill.
	151	6 " 0 "	6 " 10 "		6 " 10 "	6 " 20 "	
	152	5 " 30 "	5 " 20 "		5 " 20 "	11 " 10 "	Died.
	153	5 " 20 "	5 " 30 "		5 " 20 "	7 " 30 "	Ill.

TABLE V.

Experiments XII and XIII (a). Effect of Feeding Dried Whole Blood and Bone Marrow to Splenectomized Mice.

Substance fed.	Mouse No.	Coagulation time. First day feeding. Before.	After.	Remarks.	Second day feeding. Before.	After.	Remarks.
Experiment XII. Dried whole blood (sheep).	182	5 min., 30 sec.	5 min., 20 sec.		5 min., 30 sec.	6 min., 0 sec.	
	183	4 " 10 "	7 " 10 "	Ill	7 " 0 "	7 " 40 "	Ill.
	184	6 " 0 "	6 " 20 "		6 " 10 "	6 " 10 "	
	185	5 " 20 "	6 " 0 "		5 " 0 "	6 " 40 "	"
Experiment XIII (a). Bone marrow (man).	327	4 " 10 "	6 " 20 "				
	328	4 " 30 "	5 " 20 "				
	329	5 " 0 "	7 " 0 "	"			
	340	4 " 20 "	6 " 10 "				

TABLE VI.

Experiments XIII (b) to XX. Effect of Feeding Various Organs to Splenectomized Mice.

Organ fed.	Mouse No.	Coagulation time. First day feeding. Before.	First day feeding. After.	Second day feeding. Before.	Second day feeding. After.	Remarks.
Experiment XIII(b). Lymph nodes (sheep).	83	6 min., 40 sec.	6 min., 20 sec.	6 min., 30 sec.	6 min., 20 sec.	
	84	5 " 30 "	5 " 30 "	5 " 30 "	6 " 0 "	
	85	4 " 20 "	4 " 30 "	5 " 10 "	5 " 30 "	
	86	5 " 10 "	5 " 20 "	5 " 10 "	5 " 10 "	
Experiment XIV. Thymus (sheep).	87	6 " 10 "	6 " 0 "	6 " 0 "	6 " 30 "	
	88	5 " 30 "	5 " 20 "	5 " 10 "	5 " 20 "	
	89	6 " 0 "	6 " 10 "	6 " 20 "	6 " 10 "	
	90	5 " 0 "	5 " 20 "	5 " 10 "	5 " 30 "	
Experiment XV. Large intestine (mouse).	162	6 " 20 "	6 " 40 "	6 " 30 "	6 " 30 "	
	163	6 " 10 "	6 " 10 "	6 " 20 "	6 " 10 "	
	164	5 " 30 "	5 " 20 "	5 " 20 "	5 " 30 "	
	165	5 " 40 "	5 " 30 "	5 " 30 "	5 " 30 "	
Experiment XVI. Liver (sheep).	108	5 " 20 "	5 " 30 "	5 " 10 "	5 " 30 "	
	109	4 " 20 "	5 " 10 "	5 " 10 "	5 " 10 "	
	110	5 " 10 "	5 " 20 "	5 " 20 "	5 " 10 "	
	111	5 " 30 "	5 " 30 "	6 " 0 "	6 " 20 "	
Experiment XVII. Pancreas (sheep).	75	5 " 20 "	5 " 10 "	5 " 30 "	5 " 30 "	Note slight decrease in coagulation time. Compare with salivary gland (Experiment XXV).
	76	4 " 10 "	4 " 30 "	5 " 20 "	4 " 0 "	
	77	5 " 20 "	5 " 20 "	6 " 20 "	4 " 10 "	
	78	5 " 10 "	4 " 40 "	6 " 10 "	4 " 20 "	
Experiment XVIII. Pituitary body (sheep).	100	6 " 20 "	6 " 10 "	6 " 20 "	6 " 20 "	
	101	6 " 10 "	6 " 10 "	6 " 30 "	6 " 10 "	
	102	5 " 10 "	5 " 0 "	5 " 20 "	5 " 30 "	
	103	6 " 15 "	6 " 10 "	6 " 0 "	6 " 0 "	
Experiment XIX. Brain (sheep).	104	6 " 0 "	6 " 10 "	5 " 20 "	5 " 30 "	
	105	6 " 10 "	6 " 0 "	6 " 0 "	6 " 0 "	
	106	5 " 20 "	5 " 10 "	4 " 40 "	5 " 0 "	
	107	6 " 20 "	6 " 30 "	6 " 10 "	6 " 30 "	
Experiment XX. Kidney (mouse).	112	6 " 0 "	6 " 10 "	6 " 10 "	6 " 30 "	
	113	6 " 0 "	6 " 30 "	5 " 30 "	5 " 20 "	
	114	5 " 20 "	5 " 10 "	5 " 10 "	6 " 0 "	
	115	4 " 30 "	4 " 40 "	4 " 40 "	5 " 0 "	

TABLE VII.

Experiments XXI to XXVI. Effect of Feeding Various Organs to Splenectomized Mice.

Organ fed.	Mouse No.	Coagulation time. First day feeding. Before.	First day feeding. After.	First day feeding. Remarks.	Second day feeding. Before.	Second day feeding. After.	Second day feeding. Remarks.
Experiment XXI.	127	6 min., 10 sec.	6 min., 0 sec.		6 min., 0 sec.	6 min., 0 sec.	
Lung tissue	128	5 " 0 "	5 " 20 "		5 " 10 "	5 " 20 "	
(mouse).	129	6 " 10 "	6 " 10 "		6 " 10 "	6 " 20 "	
	130	6 " 20 "	6 " 10 "		6 " 30 "	6 " 30 "	
Experiment XXII.	123	5 " 0 "	5 " 10 "		5 " 15 "	5 " 10 "	
Muscle (sheep).	124	4 " 30 "	4 " 20 "		4 " 20 "	4 " 20 "	
	125	5 " 10 "	5 " 30 "		5 " 20 "	5 " 10 "	
	126	6 " 0 "	6 " 10 "		6 " 10 "	6 " 10 "	
Experiment XXIII.	79	4 " 50 "	4 " 30 "		4 " 30 "	4 " 40 "	
Thyroid (sheep).	80	5 " 10 "	5 " 0 "		5 " 20 "	5 " 30 "	
	81	5 " 10 "	5 " 20 "		5 " 10 "	5 " 30 "	
	82	6 " 30 "	6 " 10 "		6 " 10 "	6 " 10 "	
Experiment XXIV.	115	6 " 10 "	4 " 10 "	Ill } Second reading at 6 hrs.	5 " 10 "	5 " 30 "	} Second reading at 6 hrs.
Adrenals (man).	116	5 " 30 "	5 " 30 "	"	5 " 20 "	4 " 10 "	Ill.
	117	5 " 30 "	3 " 10 "	"	5 " 40 "	6 " 10 "	"
	118	5 " 20 "	4 " 0 "	"	5 " 0 "	5 " 10 "	"
Experiment XXV.	313	5 " 10 "	2 " 30 "	Died, 18 hrs.			} Second reading at 2 hrs.
Salivary gland	314	6 " 20 "	3 " 10 "	" 10 "			
(mouse).	315			Did not eat	5 " 30 "	2 " 10 "	Died, 4 hrs.
	316			" " "	5 " 40 "	3 " 30 "	" 2½ "
Experiment XXVI.	330	5 " 20 "	5 " 30 "		5 " 30 "	5 " 30 "	
Testicle (rabbit).	331	5 " 10 "	5 " 0 "		5 " 0 "	5 " 20 "	
	332	6 " 10 "	6 " 30 "		6 " 0 "	6 " 0 "	
	333	4 " 30 "	5 " 0 "		5 " 0 "	5 " 0 "	

TABLE VIII.

Experiments XXVII to XXX. Control Experiments Relating to Figures Previously Presented. Intact Mice Fed with Various Organs.

Organ fed.	Mouse No.	Coagulation time.					
		First day feeding.				Second day feeding.			
		Before.	After.	Remarks.		Before.	After.	Remarks.	
Experiment XXVII. Spleen (sheep).	42	5 min., 20 sec.	5 min., 10 sec.	Amount eaten 0.0 gm.		5 min., 5 sec.	5 min., 0 sec.	Amount eaten 0.340 gm.	
	43	4 " 10 "	4 " 40 "	" " 0.065 "		4 " 40 "	5 " 10 "	" " 0.185 "	
	44	5 " 30 "	5 " 40 "	" " 0.185 "		5 " 10 "	5 " 10 "	" " 0.08 "	
	45	5 " 40 "	5 " 10 "	" " 0.08 "		6 " 5 "	5 " 20 "	" " 0.225 "	
	46	5 " 30 "	6 " 0 "	" " 0.06 "		6 " 10 "	6 " 20 "	" " 0.068 "	
	47	6 " 0 "	6 " 5 "	" " 0.095 "		6 " 20 "	6 " 10 "	" " 0.275 "	
Experiment XXVIII. Small intestine (mouse).	45	5 " 5 "	5 " 0 "			5 " 20 "	5 " 10 "		
	46	4 " 20 "	4 " 30 "			5 " 0 "	5 " 10 "		
	47	5 " 0 "	5 " 10 "			5 " 30 "	5 " 40 "		
Experiment XXIX. Stomach (mouse).	42	5 " 30 "	5 " 5 "			5 " 10 "	5 " 30 "		
	43	5 " 30 "	6 " 0 "			5 " 20 "	5 " 30 "		
	44	6 " 30 "	6 " 20 "			6 " 10 "	6 " 0 "		
Experiment XXX. Salivary gland (mouse).	328	6 " 0 "	4 " 30 "	Ill } Readings at					
	329	5 " 30 "	3 " 0 "	Died } 2 hrs.					
	330	6 " 30 "	5 " 10 "	"					

Other experiments were made to determine the effect of feeding the regular diet of oats and bread on the coagulation time of the blood. Neither the intact nor the splenectomized animals showed any change after eating this food.

The intoxication as described bears a certain general resemblance to peptone poisoning. The fact that it is developed from the intestinal tract likewise suggested that the effects might be due to imperfectly detoxicated digestion products. In following up these suggestions we have studied the reaction of mice to Witte's peptone. We have been unable to poison mice by feeding this substance. When intraperitoneal injections of this peptone are given, an intoxication is produced which causes a delay in the coagulation of the blood and which may lead to death. The change in coagulation time develops more slowly. It is not apparent in six hours but is well developed at eighteen hours. No difference could be detected between the reaction of intact and splenectomized mice to Witte's peptone.

If those splenectomized mice, which, having been fed with either spleen or gastro-intestinal mucosa, survive, are fed continuously with the same substance, a certain number of them will die at later feedings. The remainder after ten days or two weeks no longer develop the evidence of illness, even though they may eat large quantities of material. They do not become sick and the coagulation time of the blood remains normal.

Many important questions raised by the demonstration of this tolerance have not as yet been clearly answered in our experiments. We have much reason for considering that this is an acquired tolerance or immunity produced by the repeated feedings in the susceptible animal. Our figures show certain instances in which animals definitely ill with a definitely delayed coagulation time fail to show reactions at subsequent feedings. These instances are, however, small in number and up to the present time few of our observations have been made with this point sufficiently in view. On the other hand, we know that mice immediately after splenectomy differ considerably in their susceptibility to the intoxication. After a number of weeks they become less susceptible spontaneously. In just what degree the natural process operates and in how far we

influence it by repeated feedings we are unable to decide at present. When we speak of this tolerance as acquired we express our present belief but recognize it as possible that the repeated feedings may have served chiefly to select the resistant animals.

We also have certain evidence that this tolerance is in considerable degree specific in the sense that the animals tolerant to spleen following repeated feedings with this organ are still susceptible to intoxication with gastro-intestinal mucosa and *vice versa.* We hope to extend our observations in this direction in the near future.

In most of the experiments tabulated above the result has been decisive. Certain instances when this has not been entirely the case require comment.

1. Thyroid feeding gives no change in the coagulation time of the blood. The animals may, however, become ill and some may die with an acute intoxication.

2. Suprarenal gland when fed to mice gives rise in most instances to an acute or subacute intoxication with some peculiar characteristics. The coagulation time of the blood is not slowed. It may possibly in some instances be hastened.

3. Administration of pancreas seems to shorten the coagulation time of the blood appreciably. In no instance have we been able to see evidence of illness.

4. The salivary gland of the mouse when fed to mice causes a violent fatal intoxication. The mice do not behave exactly as in the case of the spleen-fed mice and the coagulation time of the blood is also shortened.

These intoxications with thyroid, suprarenal, and salivary gland are important in this connection, as they might be confusing to one who was not aware of the possibility of their occurrence. We feel justified in putting them to one side as having no connection with the subject at hand for the reasons, first, that splenectomized mice are no more susceptible than normal mice in either instance; secondly, that the animals which die do not show the hemorrhagic lesion so frequently found in animals dying after eating spleen or gastro-intestinal mucosa; and, finally, because the coagulation time of the blood either is not altered or is diminished. The intoxications with thyroid and suprarenal glands bear some resemblance to

the picture of such a poisoning which could be drawn on the basis of the well known properties of these organs. That with salivary gland was entirely unforeseen and seems to offer an entirely new subject for consideration.

The experiments presented in which an intoxication of definite character is shown to result from feeding splenectomized mice with either fresh spleen or the mucous membrane of the stomach and upper small intestine are of course difficult if not impossible of interpretation at present.[2] The reaction being so closely limited to these organs, together with the fact that no direct distinction can be made between the intoxication developed in either case, makes it seem reasonable to suppose that there is some close interaction between the spleen and the upper gastro-intestinal mucosa with respect to some function or functions. It is interesting that such an interrelationship has been put forward in the interpretation of experiments of a very different nature.

Luciani[3] reviews the observations of a number of workers in this connection. It is stated to have been shown that an extract of the spleen taken at the height of digestion is capable of activating the zymogens extracted from the pancreas. *In vivo* experiments are said to have rendered it probable that this activation is not only possible but is an important factor in proteolytic digestion. A similar form of interactivity has been supposed to exist between spleen and stomach, but has not been demonstrated experimentally.

Except for the meager suggestion which may be offered by these physiological writings we know of nothing in the literature which is in any way related to the facts as we have observed them. Until more observations are at hand a hypothetical discussion of the subject would be without profit.

SUMMARY.

The intoxication which is developed when splenectomized mice are fed with fresh spleen is more regular in occurrence when the feeding experiment is carried out four or five days after splenectomy than when it is done at later periods. The intoxication is easily recognizable even in its less severe forms by a lengthening of the coagulation time of the blood.

[2] The experiments with dried blood and with bone marrow should in the future receive equal consideration with those in which spleen is used. Up to the present, extraneous circumstances have prevented our giving much attention to the reaction to these substances.

[3] Luciani, L., Physiologie des Menschen, Jena, 1906, ii, 80, 101.

An intoxication of the same character is produced when splenectomized mice are fed with the mucous membrane of the stomach and upper small intestine. Bone marrow and dried blood probably give the same reaction in a somewhat milder form. The other organs either give no intoxication at all when fed, or in certain instances the thyroid, adrenal, and salivary gland (mouse) give intoxications of a different character which affect intact mice and splenectomized animals equally.

The spleen or the gastro-intestinal mucosa is equally effective in producing the intoxication, whether it be derived from heterologous or homologous species.

Certain experiments, not reported in detail, indicate that the susceptibility to the intoxication disappears in time and that this time may be shortened by repeated feedings with sublethal amounts of organ substance.