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The Effect of Nephrectomy and Suprarenalectomy in the Rat on Resistance.

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There is abundant evidence that the suprarenal gland, in some manner still unknown, plays an important rôle in the defensive mechanism of the body against poisons. Lewis[1, 2, 3] in 1921, established the fact that suprarenalectomized rats are killed by much smaller doses of a variety of poisons than are normal animals. These experiments have been confirmed by Scott,[4, 5] Marine and his co-workers,[6, 7] Belding and Wyman,[8] and more recently Jaffe.[9] Stewart and Rogoff,[10] and Rogoff and his co-workers,[11, 12] while clearly showing in their experiments that suprarenalectomized animals have lowered resistance, believe that this is not specifically due to loss of suprarenal substance. They[10, 11] argue as follows: Since the general mortality following double suprarenalectomy in rats obtained by various workers, is about 50 per cent, and since approximately 90 per cent of this mortality occurs between the 5th and 15th day following the operation, therefore any increased sensitiveness found between the 5th and 15th day is due to the moribund state of the animal. This conclusion ignores the well established fact that while 50 per cent of rats survive indefinitely the removal of both suprarenals, practically 100 per cent are killed by a dose of poison (typhoid vaccine), far below the minimum lethal dose for normal animals, and that no other operative procedure has so far been found in which a comparable lowering of resistance follows.

It is our purpose to report further experiments in support of the view that doubly suprarenalectomized rats while still surviving in good condition, have markedly lowered resistance, and also to report experiments showing that rats made truly moribund by nephrectomy do not show a comparable lowered resistance. We, therefore, have studied the resistance of nephrectomized rats to small doses of standard typhoid vaccine. The principal data of these experiments are given in Table I.

TABLE I.
Resistance of Doubly Nephrectomized Rats to Typhoid Vaccine.

Number of rats	Average weight	Interval between removal 1st and 2nd kidney	Amount vaccaine	Duration of Life		
				Min.	Max.	Average
	gm.	days	cc.	hrs.	hrs.	hrs.
5	221	7	—*	72	104	89
6	261 1/2	30	—*	72	102	91 2/3
6	197	7	.4†	80	97	90

*Controls.
†Injected 48 hours after removal of second kidney.

The right and left kidneys were removed at intervals of 7 and 30 days. Forty-eight hours after removal of the second kidney all the rats were semi-comatose and in a moribund state. In spite of this fact the duration of life of the animals injected with 4 cc. typhoid vaccine did not differ in any way from the non-injected rats.

A parallel series of rats of the same stock and age were suprarenalectomized and their resistance tested with small doses of the same standard typhoid vaccine. The principal data of these experiments are given in Table II.

The data of Table II show that doubly suprarenalectomized rats, injected with 0.4 and 1 cc. of typhoid vaccine at 48 hours, 72 hours, 82 hours, and 96 hours after suprarenalectomy are not killed. On the other hand beginning about 144 hours after suprarenalectomy all rats injected were killed by 0.4 to 1 cc. of the poison, whereas the mortality from control suprarenalectomized rats in our series has been approximately 30 per cent. These results clearly indicate that the lowering of resistance following suprarenalectomy is delayed at least 4 days, and that the rather abrupt fall in resistance after this time is due to the exhaustion of the influence normally exerted by the suprarenals. This sharp change in resistance after 96 hours can be interpreted as indicating that the suprarenal influence persists and is effective in the tissues for at least 96 hours. In this respect the suprarenal gland appears to be comparable to the thyroid and parathyroid glands. Thus it is well known that following thyroidectomy no significant change in heat production ordinarily occurs for 4 or 5 days, at which time the decrease is abrupt.[13] A similar factor of safety has been noted in the case of the parathyroid gland. In

animals deprived of a normal calcium intake, fatal tetany may occur within a few hours, whereas in dogs fed with bone meal prior to parathyroidectomy, the onset of tetany may be delayed for more than 48 hours.[14]

TABLE II.
Resistance of Doubly Suprarenalectomized Rats to Typhoid Vaccine.

Number of rats	Average weight	Interval* between operation and injection	Amount vaccine	Duration of life after injection.
3	gm. 238	hrs. 48	cc. .4	No immediate effect. Lived 64, 66, 51 *days* respectively.
4	115	72	.4	No immediate effect. Alive after 5, 5, 5, 5 *days* respectively.
4	165	82	.4	No immediate effect. Lived 27, 28, 8, 23 *days* respectively.
2	125	96	1	No immediate effect. Alive after 5, 5 *days* respectively.
4	180	96	.4	No immediate effect. Alive after 5, 5, 5, 5 *days* respectively.
4	172	144	.4	Severe reaction. Dead after 9, 5½, 7, 8 *hours* respectively.
3	122	147	1	Severe reaction. Dead after 6, 9, 12 *hours* respectively.
3	93	168	1	Severe reaction. Dead after 8, 12, 22 *hours* respectively.
4	148	168	.4	Severe reaction. Dead after 6, 13½, 9, 12 *hours* respectively.
2	111	192	.4	Severe reaction. Dead after 10, 20 *hours* respectively.

*Both suprarenals removed at once.
Normal animals withstand 20 cc. of single intraperitoneal injections of standard typhoid vaccine.

While suprarenalectomized animals show a marked lowering of resistance to various poisons, it is known that such animals (rabbits, rats) are capable of producing more antibodies (hemolysins, agglutinins) from the same doses of antigen than are normal animals,[6, 7] and also that such animals show a notable regeneration at the thymus and lymphoid tissues. These striking biological facts, we believe, furnish additional evidence, opposed to the view that the lowered resistance is due to a moribund state of the animal.

SUMMARY.

It has been shown that the duration of life of nephrectomized rats is not affected by injections of the same typhoid vaccine which regularly shortens the life of suprarenalectomized rats. It has also been shown that suprarenalectomized rats have a refractory period of approximately four days before any marked drop in resistance is manifest. These findings, together with the fact that the suprarenalectomized animals fully retain their ability to form antibodies and to regenerate the thymus and lymph tissues, suggest that suprarenalectomy exerts a specific physiologic influence on resistance.

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Fractionation of Irradiated Cholesterol: Chemical Observations.

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One of us recently reported[1] that cholesterol, as a result of exposure in air to light from the mercury-vapor quartz lamp, reacted differently from the untreated cholesterol towards a reagent consisting of aniline and concentrated hydrochloric acid. With the aid of this color reaction, fractionation of irradiated