TABLE SHOWING GLUCOSE, GLYCOGEN, AND LACTIC ACID LEVELS UNDER VARIOUS EXPERIMENTAL CONDITIONS

Series No.	No. cats used	Experimental conditions	Muscle glycogen average per cent.	Liver glycogen average per cent.	Blood sugar average per cent.	Blood lactic acid average per cent.
I	5	Normal, fasted 48 hours	.432	1.480	.112	.025
II	9	Adrenalectomized, untreated	.208	0.067	.048	.038
III	5	Adrenalectomized, adrenalin treated	.392	0.276	.051	.031
IV.	8	Adrenalectomized, extract treated	.585	1.305	.097	.026
V.	6	Normal, fasted 48 hours, glucose treated	.336	2.120	.137	.025
VI.	5	Adrenalectomized, glucose treated	.398	0.275	.206	.035

time. That the cortex in contrast to the medulla is of premier importance in the bodily economy has, nevertheless, been long appreciated.

The adrenal glands are indispensable in the maintenance of life processes. Considering their size they are possibly the most important chemical factories in the body. Extirpation of the organs brings about death in a few days. After pituitary, thyroid or parathyroid removal life may be maintained for many weeks or months, or even indefinitely in some cases. The remarkably rapid dissolution following adrenalectomy is due specifically to cortical loss.

Even in the severest conditions of inanition and exposure of animals to cold, in death from insulin or strychnine convulsions, and in experimental diabetes, the hepatic and muscle glycogen values are not often found to be reduced beyond the low levels which we have observed in adrenal insufficiency. The muscle glycogen and blood glucose in hepatectomy are not depleted more thoroughly than in the case of animals dying from adrenal extirpation. And in hepatectomy as well as pancreatectomy death is admitted to be due primarily to carbohydrate deficiency.

The results given herewith indicate that the severity of the carbohydrate changes in adrenalectomized animals is fully sufficient to produce death. This eventuality is readily averted by cortico-adrenal extract administration, which results in rapid restoration of the normal blood glucose and liver and muscle glycogen values. A serious incompetence in storing injected glucose has also been noted in animals without adrenal glands. The cortex is indispensably important in maintaining, in cooperation with other organs, the normal metabolism of carbohydrates. This apparently represents the prepotent function of the adrenal cortex in the organism.

Possibly the primary defect in adrenalectomy is to be found in failure to store liver glycogen. Adrenal insufficiency may perhaps be considered in synonymity with glycogen insufficiency.

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SOME EFFECTS OF OVARIECTOMY UPON BREEDING FEMALES

IT has previously been observed[1] that the secretions of the ovaries play an important part in the preparation of the mammary tissue of mice for the inception of the cancerous condition.

In a closely inbred strain of mice with a high incidence of breast cancer, it has been found that the age at which the appearance of the tumors was first noted follows a very regular unimodal curve which starts at four months, has its peak at eleven months and extends to the twenty-second month. The lower range of the standard deviation from the mean (11.6) of this curve falls in the 8th month. From this it is evident that the great majority (80–90 per cent.) of the females which are destined to develop cancer of the breast will do so between the seventh and fifteenth months.

The present experiment was conducted in an attempt to determine whether or not the high incidence of tumor in this strain is in any way controlled by ovarian activity.

Breeding females were separated from the males at seven months of age and were ovariectomized. They were then allowed to grow old under the same conditions as the control breeders. An equal number of breeding females were separated from the males at this same age and kept under similar conditions without operation, as controls.

There were then three distinct classes of animals in the experiment:

(1) Normal breeding females.

(2) Ovariectomized females which had been used as breeders for seven months.

(3) Females that were used as breeders for seven months and then separated from the males.

In the first class there were 1,938 females which

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[1] W. S. Murray, "Ovarian Secretion and Tumor Incidence," *The Journal of Cancer Research*, Vol. xii, No. 1, March, 1928.

lived to be over seven months of age. Of these, 1,275, or 65 per cent., died of cancer of the breast.

In the second class there were 195 animals. Of these 78, or 40 per cent., died of cancer.

In the third class there were 198 animals, 140 of which, or 70 per cent., died of cancer.

It is evident from the above that ovariectomy of breeding females at seven months reduces, markedly, the incidence of mammary cancer.

TABLE I

EXPECTATION OF LIFE

Age in months	Breeding females	Control females	Operated females
7–8	4.4	4.6	6.2
8–9	3.5	4.1	5.8
9–10	3.0	3.3	5.6
10–11	2.6	2.9	5.5
11–12	2.3	2.4	5.7
12–13	2.1	2.0	5.8
13–14	1.9	1.6	6.0
14–15	1.8	1.5	5.8
15–16	1.7	1.5	5.6
16–17	1.5	1.3	4.8
17–18	1.3	1.1	4.3
18–19	1.3	.7	4.5
19–20	1.2	.5	4.2
20–21	1.0		3.7
21–22			3.5
22–23	1.0		3.4
23–24			3.3
24–25			3.3
25–26			3.0
26–27			2.0
27–28			2.5
28–29			1.5
29–30			1.0
30–31			.5

If the expectation of life[2] (in months) is computed for the breeding females of this stock, regardless of the cause of death (Table I, Column 1), it is found to be 4.4 at seven months and falls in a steady curve to 1 when the mice are twenty-two months old.

If the expectation for the control females is computed in the same way, it is found that the curve closely approximates that of the breeding females but ends two months earlier.

The expectation curve for the operated animals is markedly different. Starting at 6.2 months, it falls off for four months, rises again until it reaches six at the thirteenth month, and then ranges gradually downward to .5 at the thirtieth month. This indicates that ovariectomy of breeding females during the seventh month not only prolongs the lives of some individuals in a marked degree but delays death among them so generally that at 17 months they have the same (or greater) expectation of life as do the breeding females at 7 months.

It appears from these data that ovariectomy of breeding females approaching the cancer age protects them to some extent against as early death as they would have had without operation.

That it also protects them in some degree against cancer of the breast may be seen from Table II.

TABLE II

PER CENT. OF THOSE DYING IN EACH AGE PERIOD, WHICH HAD MAMMARY CANCER

Age in months	Breeding females	Control females	Operated females
7–8	34	25	22
8–9	43	64	52
9–10	56	73	38
10–11	64	100	38
11–12	72	69	52
12–13	83	80	73
13–14	84	85	40
14–15	77	75	50
15–16	77	67	50
16–17	91	100	40
17–18	91	50	27
18–19	93	0	60
19–20	83		50
20–21	75		60
21–22			20
22–23	100		0
23–24			0
24–25			0
25–26			0
26–27			0
27–28			0
28–29			0
29–30			0

Here it is demonstrated that the percentage of those dying of cancer in each age period is appreciably higher in the breeding females and controls. It is shown that all the ovariectomized females in this experiment which live to be more than 22 months old are completely free from cancer.

To summarize: The influence of the ovary on the incidence of mammary cancer is, in this stock of mice, clearly established. It is sufficiently striking so that it may be demonstrated by removal of the ovary from breeding females seven months old. The removal of the ovaries greatly increases the expectation of life and decreases the incidence of mammary cancer.

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[2] Raymond Pearl, "Medical Biometry and Statistics," W. B. Saunders Co., Philadelphia, 1930.