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Differences Between High and Low Breast Tumor Strains of Mice When Ovariectomized at Birth.*

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The following differences were noted between 2 high and one low breast tumor strains of mice when ovariectomized at birth. The high breast tumor strains were the Jackson Laboratory dilute brown "JAX" (dba) and "JAX" C3H strains. These 2 strains have a high incidence of mammary tumors both as breeding and as virgin animals. The low tumor strain was the Jackson Laboratory "JAX" C57 black strain. The observations are based on a group of 125 JAX dba, 20 JAX C3H and 30 JAX C57 black mice. The results for each strain as reported in Table I have been uniform, and we believe deserve preliminary presentation, although not all of the above animals are dead up to the present time.

Easily noticed differences concerned the vagina. The vagina of the ovariectomized JAX dba and JAX C3H mice did not present the classic castrate picture but became much more stimulated than might have been expected. With both strains the vagina opened only a few days later than that of non-castrated littermate females. Progress to obvious mucification and to distinct cyclic cornification is much

TABLE I.
Findings for Animals Ovariectomized at Birth and Observed When Beyond One Year of Age.

	High tumor		Low tumor
	JAX dba	JAX C3H	JAX C57
Vaginal orifice	Open	Open	Closed or small pore
Cyclic vaginal cornification	Yes	Yes	No
Uterine stimulation	”	”	”
Mammary gland	Extensive growth, marked development	Extensive growth, marked development	Variable growth, slight development
Mammary adenocarcinoma†	26	2	0
Nodular hyperplasia of adrenal cortex	Extensive	Extensive	Slight
Mating with male	No	No	No

†The dba and C57 Black strains have reached an older average age than the C3H strain at the present time and, therefore, no estimation of the final percentage of tumors can be attempted.

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slower than with normal females. The vaginas of some of the JAX C57 black females failed entirely to open although observed from birth up to 20 months of age. Usually, however, a small pore appeared and remained more or less open.

The uterus of the JAX dba and JAX C3H mice after remaining small up to about 6 months of age began to enlarge and attained a size as large, and much larger in most cases, than those of virgin females of a comparable age. The uterine glands were enlarged and sometimes cystic. The JAX C57 black uterus was small and similar to that of a pre-puberty female throughout life.

The mammary glands of the high cancer strain females developed extensively and mammary adenocarcinomas appeared in ovariectomized females of both strains. With the low cancer strain some of the mammary glands remained rudimentary and comparable to those of normal male mice, while others, sometimes in the same mouse developed systems with long but slender ducts. No mammary adenocarcinomas were observed. Even so-called pre-cancerous changes were not present although frequent in the glands of the high tumor females.

The adrenal glands of the JAX dba and JAX C3H mice began to show grossly noticeable areas of nodular hyperplasia[1] in a few cells in the outer edge of the adrenal cortex around 3 months of age.† A number of these areas eventually appeared and enlarged until the adrenal was uneven in contour and several times normal size. All animals had abnormal adrenals. In a few cases cortical carcinomas occurred and attained a size of one centimeter or more in diameter. In the JAX C57 black females very small areas of nodular hyperplasia also occurred in the adrenal cortex and in one case, at least, at around 3 months of age. Few of these areas appeared, however, and but little enlargement of them occurred in later life. The contour and size of the adrenal gland remained quite normal.

Males were experimentally placed with the females but so far no vaginal plugs have been found indicating that normal mating reactions were not attained.

Although the above differences were first noted with mice ovariectomized at birth, they have no necessary connection with early castration in itself. Marked similar strain differences appeared when the ovaries were removed at one month and at 6 months of age.

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[1] Woolley, G. W., Fekete, Elizabeth, and Little, C. C., *Proc. Nat. Acad. Sci.*, 1939, **25**, 277.

† Some of the early stages were found by William Daughaday, a holder of a Harvard University National Scholarship and a summer student at the Roscoe B. Jackson Memorial Laboratory.

Conclusion. Marked differences appeared in strains of mice when they were ovariectomized at birth and then examined in later life. The high tumor JAX dba and JAX C3H strains showed stimulated uterus, vagina and mammary glands. The adrenal glands exhibited extensive nodular, hyperplastic areas. All of these organs of the low tumor JAX C57 black strain remained essentially unstimulated. To ascertain whether the above differences are characteristic of all high and low tumor strains, other strains are being studied.

11841

Observations on Sensitization of Guinea Pigs with Alum-Precipitated Ragweed Extract.

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Alum-precipitated ragweed pollen extract is a potent antigen for producing anaphylactic sensitization in guinea pigs,[1-4] whereas the watery extract is by comparison a poor one. Alum-precipitated extracts have been successfully applied in sensitizing guinea pigs to house dust[5-8] and cotton linters[5, 6, 9] and in sensitizing dogs to horse serum.[10] The enhanced antigenic response of the alum-precipitated extract is generally attributed to two factors: first, retention of the antigenic substance by the precipitate so that it is only slowly liberated into the system, thus producing a continuous stimulation for the production of antibodies; and second, the local tissue response to the precipitate at the site of injection is said to delay absorption of the antigen. Thus diphtheria toxoid has been detected at the site of injection from a few days to several weeks after administration

1 Harrison, W. T., *U. S. Public Health Reports*, 1934, **49**, 462.
2 Caulfeild, A. H. W., Brown, M. H., and Waters, E. T., *J. Allergy*, 1936, **7**, 451.
3 Zoss, A. R., Koch, C. A., and Hirose, R. S., *J. Allergy*, 1937, **8**, 329.
4 Sherman, W. B., Stull, A., and Hampton, S. F., *J. Immunol.*, 1939, **36**, 447.
5 Coulson, E. J., and Stevens, H., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 457.
6 Coulson, E. J., and Stevens, H., *J. Allergy*, 1940, **11**, 537.
7 Friedman, H. J., *J. Allergy*, 1939, **10**, 479.
8 Hampton, S. F., and Stull, A., *J. Allergy*, 1940, **11**, 109.
9 Cohen, M. B., Cohen, S., and Hawver, K., *J. Allergy*, 1939, **10**, 561.
10 Waters, E. T., Markowitz, J., and Jaques, L. B., *Science*, 1938, **87**, 582.