used because in man the virus is usually present in high concentration before the diagnosis is made and therapy instituted. Ten mice received aspergillic acid in the amount of 50 mg per kilogram intraperitoneally immediately following the inoculation of the virus and twice daily thereafter. All mice died within 3 days, the treatment thus being completely ineffective.

Conclusion. Aspergillic acid in high concentration had no effect *in vitro* on the infectivity of the Western type of equine encephalomyelitis virus. There was also no effect on the course of the infection in mice.

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Relation of the Milk Influence to the Carcinogenic Induction of Mammary Cancer in Mice.*

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The administration of carcinogens to mice of inbred strains may result in the appearance of epitheliomas, sarcomas or other tumors to which the animals show no spontaneous susceptibility. In certain strains in which lung tumors, hepatomas, leukemia, or mammary cancer appear spontaneously carcinogens have accelerated their onset.[1,2,3,4] This suggests that the synthetic carcinogen might, in these instances, potentiate the spontaneous mechanism of carcinogenesis.

Three known influences are of etiologic significance in the development of mammary cancer of the "genetic" type which occurs in high incidence in certain strains of mice.[5] These factors are (1) a genetic susceptibility, (2) an hormonal influence, and (3) a milk influence, which is a substance contained in the breast milk of high mammary cancer strains.

The relationship of the carcinogen-induced to the spontaneous neoplasm can be studied in the case of mammary cancer by using the dba strain, in which mammary cancer appears spontaneously and can also be induced by the administration of one of the carcinogenic hydrocarbons, methylcholanthrene.[6] The present experiments were designed to test the role of the milk influence in governing the response of the mammary tissue to carcinogens. Previous experiments with these mice demonstrated that the mammary gland stimulation coincidental with forced breeding was an important factor in conditioning the neoplastic response to methylcholanthrene.[7]

Strain dba males† were crossed with C3H females possessing the milk influence (Z stock) and with C3H females lacking the milk influence (ZB stock). The F_1 hybrid animals so obtained were observed as either virgin or as forced-bred females during treatment with methylcholanthrene. Breeding females of the genetic constitution (ZB♀ × dba♂)♀ × dba♂ were also skin-painted with methylcholanthrene. Of the factors necessary for the development of spontaneous mammary cancer,

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TABLE I.
Table Summarizing Data on Induction of Mammary Cancer in Mice With and Without Milk-Influence.

Genetic type	Milk-influence No.	Negative	Mammary cancer	Nodules	No milk-influence No.	Negative	Mammary cancer	Nodules
			Breeding ♀'s.					
C3H♀ × dba♂	6	0	5*	1*	16	10	1†	5†
dba	27	0	27	—				
(C3H♀ × dba♂)♀ × dba♂					15	5	5†	5†
			Virgin ♀'s.					
C3H♀ × dba♂	7	6	1	0	28	28	0	0
dba	31	27	4	0				
C3H	12	0	0	0				

* Latent period of carcinogenic induction 110-145 days for mammary cancer; 0.25% solution of methylcholanthrene in benzene used. Tumors were large and grew to the same size as spontaneous tumors in dba mice. Carcinogen was applied to the skin two to three times weekly.

† Latent period of carcinogenesis always in excess of 200 days. All tumors except one were smaller than those seen in test animals possessing the milk influence.

these backcross animals lacked only the milk-influence. Virgin females of the C3H stock, which develops mammary cancer spontaneously as virgins, were similarly treated with methylcholanthrene.

The results are recorded in Table I. "Nodules" were early cancerous lesions histologically, and were always multiple. Any lesion less than 3 mm in diameter was termed a "nodule" rather than a cancer. In contrast to the more or less uniform histologic appearance of adenocarcinoma in the dba strain, the induced mammary cancers exhibited a variety of histologic patterns. Squamous metaplasia within both "nodules" and larger carcinomas was characteristic of carcinogen-induced mammary cancer. In two instances the stromal tissue of a carcinoma showed sarcomatous change.

Mammary cancer or cancerous nodules were induced in the absence of the milk-influence. Carcinogenic induction of mammary cancer in low cancer strains has been reported,[8,9,10] but in these experiments the milk-influence was not a controlled factor.

In genetically identical mice (212-dba) the histologic pattern of induced mammary cancer differed in certain respects from that of the spontaneous neoplasm, suggesting a difference in the spontaneous and induced diseases. However, if breeding females treated with methylcholanthrene possessed the milk-influence, they developed mammary cancer earlier, in greater frequency, and with more vigorous growth of the cancer than in genetically identical animals lacking this influence. This would suggest a relationship between the spontaneous and induced diseases.

Preliminary data suggest that susceptibility to the carcinogenic induction of mammary cancer may be strain specific; positive correlation with susceptibility to spontaneous mammary cancer may or may not exist. Preliminary observations indicate that breeding females of one high mammary cancer strain exhibited a precocious appearance of mammary cancer under the influence of methylcholanthrene, whereas breeding females of one other high cancer strain proved resistant to the accelerated onset of the same neoplasm.

The incidence of carcinogen-induced mammary cancer in strain dba females and in hybrid females, resulting from crossing strains dba and C3H, was greatly reduced if the test animals were not permitted to breed.

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