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Characteristics of the Mammary Tumor Milk Agent in Serial Dilution and Blood Studies.*

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The mammary tumor milk agent has been shown to be essential for the regular development of mammary cancer in mice.¹ It is usually transferred by nursing¹ and is present in various tissues³⁻⁶ as well as the milk. The infectious agent has the characteristics of a virus.⁷

This report gives data on the activity of the milk agent for mammary cancer in blood plasma, blood-cell suspensions, and serial dilution of extracts made from mammary tissue.

Blood was obtained from the hearts of mice known to harbor the agent. Either females of the A stock, 75 to 105 days of age, or females (A and C3H stocks and their hybrids) that had developed spontaneous mammary cancer were used. The blood was citrated to prevent coagulation but moderate hemolysis occurred. Separation of the cells and the plasma was by centrifugation (approximately 4,000 r.p.m. for 10 minutes) and the cells were washed with saline several times before they were used. The cells were suspended in saline and the plasma was injected either undiluted or diluted in saline (see table for details).

As test animals mice were used that were susceptible for mammary cancer and lacking

the milk agent. They were injected intraperitoneally when from 3 to 5 weeks of age. The incidence in control mice maintained as breeding females was approximately 1%.

The results for the blood studies are presented in Table I. Many of the mice in one series are living at 15 months of age.

The donors of the lactating mammary tissue were AZF₁ females that had had from 5 to 7 litters. The glands were macerated by means of a press, and serial dilutions were made with triple distilled water. Each animal received 1 cc of the suspension intraperitoneally and the surviving animals are 15 months of age. The preliminary results are tabulated in Table II.

Discussion. Woolley *et al.*¹¹ determined that the milk agent of mammary cancer could be obtained by the use of whole blood. The low incidence (19%) obtained in the experimental animals might have been influenced by the age of the test animals at the time of injection.^{7,8}

When blood was obtained from young donors 75 to 105 days of age, the results, based on small numbers, suggested that the agent might be either contained within or adsorbed on the blood cells.⁵ These results could not be confirmed in preliminary data secured after the testing of cell-suspension and plasma from mice that had developed spontaneous mammary cancer. In other experiments in which the mice received the agent by nursing, the data suggested that the agent might be more concentrated in older mice.⁷ Whether or not the differences observed in the studies on the blood components may be explained on the same basis must wait further investigations.

If the amount of the milk agent obtained by

* Assisted by grants from the Jane Coffin Childs Memorial Fund for Medical Research and the Graduate School Cancer Research Fund, University of Minnesota.

¹ Bittner, J. J., *Science*, 1936, **84**, 162.

² Bittner, J. J., *Cancer Research*, 1942, **2**, 710.

³ Bittner, J. J., *Proc. Soc. Exp. Biol. and Med.*, 1940, **45**, 805.

⁴ Bittner, J. J., *Bull. Minn. Med. Found.*, 1944, **4**, 94.

⁵ Bittner, J. J., Evans, C. A., and Green, R. G., *Science*, 1945, **101**, 95.

⁶ Woolley, G. W., Law, L. W., and Little, C. C., *Cancer Research*, 1941, **1**, 955.

⁷ Bittner, J. J., *Cancer Research*, 1942, **2**, 540.

⁸ Andervont, H. B., Shimkin, M. B., and Bryan, W. R., *J. Nat. Cancer Inst.*, 1942, **3**, 309.

TABLE I.

Material injected	Dilution	Amount, cc	No.	% cancerous
Plasma*	0	1	15	7
Cell-suspension*	1:2	1	10	60
Plasma†	1:2	1	10	50
Plasma†	1:2	0.5	11	36
Cell-suspension†	1:2	1	22	18
Cell-suspension†	1:2	0.5	13	46

† Donors—mice with spontaneous mammary cancer, preliminary data.
* Donors 75 to 105 days of age.

TABLE II.

Dilution	No. injected	% cancerous	No.	% cancerous
1:5000	22	41	41	46
1:1000	19	53		
1:100	18	28	18	28
1:10	19	11	50	8
1:5	31	7		

nursing influences the incidence and/or average cancer age, this may not be the case in older mice that receive injected material. When mice 3-5 weeks of age were injected intraperitoneally with extracts of mammary tissue containing the milk agent, more mammary tumors have been observed in the mice that received the more dilute suspensions. Although many of the animals are still under

observation, the data indicate that further work is essential to account for the results. There are several possibilities: (a) the presence of an inhibitory agent; (b) destructive effect by autolysing enzymes; (c) the development of active immunity with the injection of massive doses; (d) genetic differences between hosts and donors; etc.

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Dental Caries in the Cotton Rat. V. Influence of Strain Variation on the Caries Susceptibility.*

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The effect of diet on the extent of tooth decay in the cotton rat has been studied in a series of investigations.^{1,2,3,4} Considerable

variation was observed in the incidence and Elvehjem, C. A., and Phillips, P. H., *J. Nutrition*, 1944, **28**, 333.

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² Shaw, J. H., Schweigert, B. S., Elvehjem, C. A., and Phillips, P. H., *J. Dental Res.*, 1944, **23**, 417.
³ Schweigert, B. S., Shaw, J. H., Phillips, P. H., and Elvehjem, C. A., *J. Nutrition*, in press.
⁴ Shaw, J. H., Schweigert, B. S., Phillips, P. H., and Elvehjem, C. A., *PROC. SOC. EXP. BIOL. AND MED.*, in press.

¹ Shaw, J. H., Schweigert, B. S., McIntire, J. M.,