cortex since adrenal insufficiency is frequently accompanied by achlorhydria, and therapy with ACTH is accompanied by hyperchlorhydria. Finally, the development of peripheral neuropathy is similar to that in swine described by Wintrobe.

Summary. 1. An abnormal metabolic state has been induced in 4 human volunteers through combined use of a diet deficient in pantothenic acid and a metabolic antagonist, (omega-methyl pantothenic acid). 2. This abnormal state was accompanied by clinical and biochemical abnormalities suggesting adrenal cortical insufficiency, and by a peripheral neuropathy. 3. Administration of pantothenic acid alone did not immediately reverse the abnormal state. A good diet of natural foods and multiple vitamins resulted in rapid complete recovery.

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Sensitivity of Females of the C Stock to Male Infection with the Mammary Tumor Agent.* (21205)

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The mammary tumor agent (MTA), one of the factors usually required for the development of a high incidence of spontaneous mammary cancer in mice(8,9), may be administered by the injection of extracts of either normal or cancerous tissues from infected animals(10), including seminal vesicles(4) and cauda epididymis(15). Following the mating of agent-free females of some strains, which are either susceptible or resistant to the development of this type of cancer, with males of cancerous stocks, the appearance of mammary cancer in either the females or their progeny has been explained as resulting from the transmission of the MTA by the male at the time of coitus(3,7,11-17). Differences have been found in the sensitivity of agent-free females of various strains to become "infected," as well as the ability of males possessing the agent to infect females of either the same, or other stocks(12).

Females of the C (Bagg albino) stock have been found to be susceptible to the development of mammary cancer, as determined by a high incidence in mice which possessed the MTA, obtained by nursing females of a cancerous strain(1).

This report considers the sensitivity of

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agent-free females of the C stock to become infected with the agent after being mated with males of different cancerous stocks, as determined by the incidence of mammary cancer in the C females. As controls agent-free males were tested with C females in 2 studies.

Materials and methods. Males of the cancerous A, C_3H, and dilute brown stocks, possessing the MTA, were used in the present investigations. Males of the Andervont(1-7, 15) subline of the C_3H stock, maintained in this laboratory since 1948, will be referred to as the C_3H/An line, while our subline has been called the Z(C_3H) line(10-12). Other Z males were used which were descended from females which had been nursed on a female of the cancerous A stock. These will be called Za (Z with the agent from the A stock) males, to distinguish them from the typical Z animals. The Za males were of the second generation, since fostering. The Zb males were from the fostered subline of the Z stock, and were free of the MTA. The mice of the cancerous dilute brown stock were of the D_8 subline(10). In most instances, when females of the C strain were mated with males of other strains, 5 females were mated with each male, and they were permitted to have as many litters as they would before they either developed cancer or died of other causes. The females were usually separated from the males, except in force breeding experiments, before their litters were born. The mice received Purina fox chow and tap water.

Results and discussion. The incidences of mammary cancer, with the average cancer ages given in days, for females of the different inbred stocks are recorded in Table I. The data are for mice observed during the same periods as represented in Table II, except for the control C stock.

The observations for the C stock were for breeding females born between 1943 and 1951, and included only the mice which were continued for at least 300 days. Of the total, 71% lived for more than 450 days, and 35% were maintained for longer than 600 days; the average ages at death for mice of the 2 later groups were 593 and 720 days, respectively. Of the C females which survived for longer than 600 days, all had at least 5 litters, 82% had 7 or more litters, and 28% had at least 9 litters each. All C females which had been mated with their brothers, to continue the inbred stock, died without mammary cancer.

TABLE I. Observations on Development of Mammary Cancer in Inbred Strains Maintained during Period of the Experimental Studies.

	Data for breeding females			Data for virgin females		
Stock	No.	Cancer (%)	Ca. age	No.	Cancer (%)	Ca. age
A	352	90	302	—		
Z(C_3H)	589	97	273	37	86	399
Za	75	92	316	27	67	390
C_3H/An	127	98	229	117	94	354
D_8	150	76	458	—		
C	252	0	—	—		

Virgin females of the A strain were not observed during the course of the present study, but the incidence of mammary cancer was determined at previous periods and found to be no higher than 5%(8-10). Several of the females of the Za group are still living and the data for mammary cancer are for mice of litters in which all animals are now dead. While the same percentage of the breeding females of the D_8 stock developed mammary cancer as reported previously(10), the cancer age for the present series was later (405 vs. 458 days, respectively). The D_8 virgins in the group observed earlier showed an incidence of 66%, with an average age of 459 days.

The C females which were mated with males of other stocks are tabulated in Table II, by experiments. Mice of Groups 2 and 6, and 4 and 5 were litter mates, separated so that approximately the same number from each litter was placed in each series. The females of Group 2 were maintained as force breeders, and those of Groups 4 and 6 were force bred part of the time. Other females (Group 5) had their uterine horns amputated at the junction with the body of the uterus, leaving the ovaries *in situ* and intact. These females were housed with the same males as their intact litter-mate controls (Group 4). The C females mated with males of the Z(C_3H) stock were born between 1947 and 1951; the others between 1949 and 1951.

TABLE II. Incidence of Mammary Cancer in Females of the C Stock when Mated with Males of Other Stocks.

Group	Stock of males	No.	Cancer (%)	Avg age in days		Avg No. litters		Females born
				Cancer	Nonca.	Cancer	Nonca.	
1	Z(C_3H)	8	50	544	686	9.0	10.3	1947
2	Z(C_3H)	14	64	483	688	9.9	9.6	1949
3	Z(C_3H)	5	60	558	533	8.0	7.5	1950
4	Z(C_3H)	14	50	495	720	8.0	6.5	1951
5	Z(C_3H)	17	53	551	666	—	—	1951
1–5	Z(C_3H)	58	55	520	678			
6	A	15	33	554	599	10.4	9.2	1949
7	C_3H/An	10	10	636	616	8.0	7.0	1950
8	C_3H/An	8	25	684	597	9.5	6.0	1951
9	D_8	10	0	—	676	—	8.3	1951
10	Za	9	22	482	646	8.5	9.0	1952
11	Zb	14	0	—	671	—	8.4	1949 & 51

Five to 17 C females, in 5 separate studies, were mated with males of the cancerous Z(C_3H) stock, and in each series from 50% to 64% developed mammary cancer (Table II). The average cancer age for the total was 520 days, and the cancerous females average from 8 to 10 litters. Whereas Muhlbock(16) did not observe the development of mammary cancer in sterilized females of 2 groups of hybrids which had been mated with males possessing the MTA, in the present study the same incidence was found in those with amputated uterine horns (Group 5) as in unoperated, litter-mate controls (Group 4).

When Z males possessing the agent from the A stock were tested, 2 of the 9 C females mated with these Za males had mammary cancer (Group 10). The noncancerous females lived to an average age in excess of 21 months and cast an average number of litters equal to those which showed higher incidences of cancer.

Fifteen females of the C stock were mated with males of the cancerous A strain (Group 6), 18 with C_3H/An males (Groups 7 and 8), and 10 with D_8 males (Group 9); the respective incidences of mammary tumors were 33%, 17%, and 0%.

Two series of C females, totaling 14 mice, were housed with agent-free males of the Zb subline and all died without mammary cancer, after giving birth to an average of 8.4 litters (Group 11, Table II). This incidence was the same as that noted in the control C females (Table I).

In previous reports(11-12), data were presented on the development of mammary cancer in the hybrids derived by mating females of the C stock with males of the cancerous Z(C_3H) stock. These observations have been corroborated in the present series. Also, by observing the incidence and age of development of tumors in the hybrids, the time of infection of the females by the males could be ascertained. The few mammary tumors which appeared in the progeny prior to this time occurred in old mice, but after the C mothers became infected, the incidence in their CZF_1 progeny was in excess of 90% and the average cancer age was approximately 8 months. The data indicate that the C females might become infected between the birth of their third and eighth litters, and that the females need not develop mammary cancer to become infected with the MTA by males of the cancerous stock. Several mammary tumors, from C females and their CZF_1 progeny, were tested by biological assay and found to carry the MTA.

To obtain some material on the time relationship between the administration of the MTA and when it might be transferred in the milk, C females which were 4 to 6 months of age were injected with extracts containing the agent. The progeny born in their first litters showed a high incidence of mammary cancer. Other preliminary data demonstrate that if C females become infected with the agent from males of the cancerous Z stock, their progeny born in later litters but sired by agent-free Zb males continued to have a high incidence of mammary cancer.

Only preliminary data may be presented for the hybrids obtained from the other crosses, since many of them are still under observation, with the youngest animals being approximately 20 months of age.

Confirming the observations of Andervont and Dunn(1-4,6,7), in hybrids obtained by mating C females with the C_3H/An males more mammary tumors are being found among mice born in early litters than was seen in any other cross. Of those which have died, 40% have had mammary cancer at an average age of 580 days. When Za males were tested, the hybrids cast by C females after they became infected have shown an incidence of 86% at an average age of 275 days, with 6 of the 49 mice still living. No evidence that the D_8 males infected any of the C females was obtained. Of their 126 CD_8F_1 progeny which have died, 4% have had tumors at an average of 538 days. This compares with an incidence of 3% at 572 days in 102 $CZbF_1$ hybrids, all of which are now dead.

Summary. Females of the agent-free, but susceptible, C (Bagg albino) stock remained free of mammary cancer after they were bred with males of the C strain and with males of another stock lacking the mammary tumor agent (MTA). However, when they were mated with males of high cancerous strains, differences were noted in the ability of the males of these strains to transfer the agent and infect the C females. After C females were mated with males of the cancerous $Z(C_3H)$ strain, over 50% of the females developed mammary cancer, and the same incidence was observed in females with amputated uterine horns as in intact litter-mate controls. The source of the agent may be of some significance in male transmission experiments. In some crosses, only preliminary data could be reported in the hybrids.

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Effects of Ethionine upon Hepatic Glycogen Formation from Glucose in Intact Rats.* (21206)

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Ethionine (S-ethyl homocysteine), an analogue of methionine, has been found to induce a fatty liver in fasting female rats(1,2). Male rats and females pretreated with testosterone fail to develop this fatty change in the liver (3). Ethionine also inhibits, in female rats, the incorporation of labeled DL-methionine and glycine into liver protein *in vivo*(4) as well as the incorporation of L-cystine, DL-leucine, L-valine, and L-lysine into liver protein and plasma protein(5). This inhibition

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