by reducing thermal conductivity. They base this reasoning on work by Schoenheimer and Rittenberg(5) which showed that in the mouse the bulk of dietary fat is conveyed to fat depots before utilization. As a consequence, the superiority of fat over carbohydrate and protein in protecting against cold relates more to its effects on reducing heat loss than to increased heat production. Resolution of these 2 explanations utilizing heat-on time data awaits further study, particularly with high protein (high SDA) diets. Sufficient at present is the demonstration that regarding the total organism, utilizing a learned response, there is definite evidence that regulation of environmental temperature is a function of time of feeding.

Summary. Rats exposed to low ambient temperatures were trained to depress a response bar to obtain heat. Rats tested for heat reinforcement before feeding pressed for more heat than those tested after feeding.

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Carcinogenic Effect of Hens' Eggs as Part of the Diet in Mice. (25386)

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It has been shown that eggs are carcinogenic in chickens(1) and mice(2) and that their effect is not limited to a single organ or system. It appeared, however, that in "A" strain mice the systems most frequently affected by diet supplemented with eggs were respiratory and lymphoid. Out of 12 mice with malignancies, 10 had lung adenocarcinoma. Lymphoid organs (lymph nodes and spleen) were hypertrophied in majority of experimental mice. Three of them died of leukemia. The question is whether respiratory and lymphoid tissues are most susceptible systems to carcinogenesis in "A" strain or whether they are specifically affected by eggs in any strain of mice. To solve this problem more experiments of the same type were carried out upon "A" strain as well as other strains of mice. We report 3 series of experiments, 2 of which were carried out upon "A" strain and one upon "T.M." strain of mice. The latter is an inbred strain of mice developed in the School of Tropical Medicine (T.M.), from a pair of Swiss mice. During 10 years, according to Dr. C. Casas, no mice developed malignancies. It is considered a cancer resistant strain. This was the main reason for using it in present experiments. The series are referred to as second, third and fourth. The results of the first series have been described(2).

Methods. The second series consisted of 16 experimental mice (8 males and 8 females) and 16 controls (8 males and 8 females). The third series consisted of 16 experimental, 16 controls and 16 mice maintained on a Rockland rat diet supplemented with cottage cheese fed *ad lib.*, to find out whether a high protein diet had any effect upon carcinogenesis. Each of these 3 groups consisted of 8 males and 8 females. In above 2 series "A" strain mice were used. The fourth series was carried out upon "T.M." strain of mice, 16 experimental mice of 9 males and 7 females and 16 controls of 8 males and 8 females. In all 3 series controls were littermates, and males and females caged separately. Experimental mice were maintained on Rockland rat diet supplemented with hard boiled eggs at age of 4 weeks, immediately after weaning. Mice of second series received one egg daily during first month, 2 to 3 eggs daily thereafter. Mice

TABLE I. Time of Appearance, Location and Identity of Malignancies in Experimental Mice of Series 2.

Sex	Age in mo	Mo on diet	Primary tumors	Location	Identity of tumor
♂	10	9	3	lungs	adenocarcinoma
				liver	hepatoma
				lymphoid	leukemia
♂	11	10	1	liver	hepatoma
♂	12	11	1	"	"
♀	13	12	1	lymphoid	leukemia
♀	13	12	2	lungs	adenocarcinoma
				intestine	"
♂	17	16	1	liver	hepatoma
♀	18	17	2	lungs	adenocarcinoma
				lymphoid	leukemia
♂	19	18	1	"	"
♂	20	19	1	lungs	adenocarcinoma
♂	21	20		"	"
				liver	hepatoma
♀	23	22	1	lymphoid	leukemia

of third and fourth series received only one egg daily throughout experiment. As mentioned previously(2), mice eat preferably the yolk, and very little of the white. Controls were maintained on Rockland rat diet only, no eggs.

All experimental and control animals were autopsied and the organs affected fixed, sectioned, stained with hematoxylin and eosin and studied microscopically. In each series, the experiment terminated when last mouse on diet supplemented with eggs, died. All remaining controls were then killed and autopsied. When the last experimental mouse of second series died, 10 controls were still alive. When the last experimental mouse of third series died, 14 controls and 9 mice on diet supplemented with pressed cottage cheese were alive. Finally, when the last experimental mouse of fourth series died, 9 controls were alive and apparently in good health.

Results. Out of 16 controls of second series only 2 mice developed cancer. Both died at age of 21 months, one, male, of an adenocarcinoma of the lungs and the other, a female, of an ascites tumor. Out of 16 mice on diet supplemented with eggs 11 mice developed malignancies at the age of 10 to 23 months (Table I). Out of 16 controls of third series, 3 mice developed malignancies. They were all killed at the age of 19 months. One male had a hepatoma, another male and one female had adenocarcinoma of the lungs. Out of 16 mice on the diet supplemented with pressed cottage cheese, 3 developed malignancies. One male, which died at age of 14 months, had a carcinoma of the salivary glands. The 2 other mice, both females, were killed at age of 19 months; both had malignant hepatomas. Out of 16 experimental animals of the third series 14 developed malignancies (Table II). Four of these mice died before age of 18 months, 8 at 18 months and 2 at 19 months. Out of 16 controls of the fourth series, only one female developed an adenocarcinoma of the lungs. It was killed at age of 24 months. Out of 16 experimental mice 15 developed malignancies, and in 10 of them more than one primary tumor was found. In this series (Table III) only 2 mice

TABLE II. Time of Appearance, Location and Identity of Malignancies in Experimental Mice of Series 3.

Sex	Age in mo	Mo on diet	Primary tumors	Location	Identity of tumor
♂	11	10	1	lungs	adenocarcinoma
♀	14	13	2	"	"
				lymphoid	leukemia
♀	15	14	1	lungs	adenocarcinoma
♂	16	15	1	"	"
♀	18	17	1	oviduct	fibrosarcoma
♀	"	"	2	lungs	adenocarcinoma
				intestine	lymphosarcoma
♀	"	"	1	"	"
♀	"	"	1	"	"
♀	"	"	1	lungs	adenocarcinoma
♂	"	"	2	"	"
				intestine	lymphosarcoma
♂	"	"	2	lungs	adenocarcinoma
				lymphoid	leukemia
♂	"	"	3	lungs	adenocarcinoma
				liver	hepatoma
				lymphoid	leukemia
♂	19	18	1	lungs	adenocarcinoma
♀	"	"	1	"	"

TABLE III. Time of Appearance, Location and Identity of Malignancies in Experimental Mice of Series 4.

Sex	Age in mo	Mo on diet	Primary tumors	Location	Identity of tumor
♂	16	15	1	lungs	adenocarcinoma
♀	17	16	1	"	"
♂	20	19	1	"	"
♀	"	"	2	"	"
				"	peribronchial L-sarcoma
♂	21	20	2	"	adenocarcinoma
				peritoneum	lymphosarcoma
♂	"	"	1	intestine	"
				lungs	adenocarcinoma
				skin	squamous cell carcinoma
♂	22	21	1	lungs	adenocarcinoma
♀	"	"	4	"	"
				"	peribronchial L-sarcoma
				intestine	lymphosarcoma
				skin	squamous cell carcinoma
♂	"	"	1	peritoneum	lymphosarcoma
♂	"	"	3	lungs	adenocarcinoma
				intestine	lymphosarcoma
				skin	squamous cell carcinoma
♀	23	22	3	lungs	adenocarcinoma
				intestine	lymphosarcoma
				liver	anaplastic carcinoma
♀	24	23	2	lungs	adenocarcinoma
				mammary gland	"
♀	"	"	2	lungs	"
				"	peribronchial L-sarcoma
♀	"	"	3	"	adenocarcinoma
				"	peribronchial L-sarcoma
				intestine	lymphosarcoma
♂	"	"	2	lungs	adenocarcinoma
				"	peribronchial L-sarcoma

died before age of 18 months; all others died later.

From these results it appears clear that the organs most frequently affected by diet supplemented with eggs are lungs and those of the lymphoid system. Among experimental animals of the 3 series, 31 developed adenocarcinoma of lungs. Leukemia or lymphosarcoma was found in 22 mice. In many animals of fourth series, in addition to adenocarcinoma, a peribronchial lymphosarcoma invaded the lungs.

It is very difficult to distinguish between leukemia and lymphosarcoma. Only those with a very large number of white cells in the blood vessels were diagnosed as leukemia. In some mice with leukemia, a white cell count of 60,000 to 70,000 was found shortly before death. Animals which died of lymphosarcoma of the lungs did not reveal an increase in white blood count a short time before death, when they already presented symptoms of their disease, like dyspnea and cachexia. In mice with leukemia and in those with lymphosarcoma, spleen and lymph nodes were considerably enlarged, while the thymus remained unchanged.

It should be added that in almost all experimental females the ovaries were atrophic, while testes in males were very active. In 2 experimental mice nodular hypertrophy of the adrenals was found. The liver, as observed previously(2), appeared abnormal in all experimental mice.

Discussion. The nature of the carcinogenic substance and its localization in the 2 components of the egg, yolk or white, are still unknown. According to Arscott(3), Arscott,

Weswig and Schubert(4), Menge, Lillie and Denton(5) a growth substance, extractable with ethanol is present in the yolk of the egg. Hradek(6) found that this substance has the same characteristics as a substance extracted from tumors. From preliminary results of experiments, now being carried out, it appears that the carcinogenic substance in eggs is not limited to yolk only, but is also present in the white. The high protein of the diet does not seem to have any effect, since mice on the diet supplemented with cheese do not develop more malignancies than the controls.

Summary. It appears that there is no appreciable difference between "A" and "T.M." strains of mice in susceptibility to carcinogenic effect of eggs. In experimental mice of both strains the incidence of malignancies is very high, while among controls it is considerably lower in the "T.M." strain than in "A" strain. As in previous experiments(2), lungs and lymphoid tissue appear to be most susceptible to the carcinogenic effect of eggs. Malignancies of epidermal origin were not observed in "A" strain mice, while out of 16 experimental mice of "T.M." strain, 3 developed squamous cell carcinoma of the skin.

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Age of Donor and Host in Sex Histo-Incompatibility to Skin Isografts.* (25387)

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Sex histo-incompatibility to skin isografts among members of some inbred strains of mice, particularly in those of the A and $C_{57}Bl$ strains seems to be a well established phenomenon(1-7). These observations demonstrate that while skin isografts performed from female to female, male to male and female to male are in most cases successful, those performed from male to female result in a homograft-like rejection. The rejection of the male skin isograft by the female appears to be immunological in nature as has been suggested by Eichwald *et al.*(8), Hauschka(9) and Snell(10) who have interpreted this phenomenon as due to the recipient's lack of the donor's isoantigen which originates from a gene located on the Y chromosome. This view has been recently substantiated by the demonstration that tolerance of male skin could be achieved in female mice of the A and $C_{57}Bl$ strains, by injecting the females with isologous male spleen cells at birth(11-12) or during the post-neonatal period(13). Similar results were obtained by placing adult females with isologous males in parabiosis (13). However, recent observations made in our laboratories have indicated that while weanling female mice of the A strain not injected with isologous male spleen cells usually accept male skin isografts, older recipient females of the same strain similarly grafted with male skin reject this skin in most instances (14). This prompted us to further investigate this problem using female recipients of different ages which were grafted with skin from isologous donors of same approximate ages. Data are also presented from experiments designed to ascertain whether or not

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