mary cancer of Group 4 (on the diet supplemented with cholesterol and lard), which rarely developed lymphosarcomas.

In 15 years of inbreeding, mammary cancer rarely occurred in mice of the T.M. strain, and in our experiments none of the 47 breeding females of Group 1 (control) developed this malignancy. Consequently, the presence of the milk factor in the mice of this strain is unlikely. This question however, is being studied on mice of this strain, foster nursed by lactating females of the C57Bl strain.

It appears thus that there is more than one carcinogenic substance in eggs. One substance responsible for the development of lymphosarcoma and lung adenocarcinoma is present in both egg yolk and egg white, and the other substance stimulating mammary carcinogenesis would be present in the yolk only.

Summary. Mice of the T. M. strain were maintained from the age of 4 weeks on the Rockland rat diet (Group 1) supplemented with hard boiled egg white (Group 2), raw egg yolk (Group 3) or with cholesterol and lard (Group 4). In one series of experiments males and females were caged separately, while in the other one they were bred and their offspring maintained on the same diets. Each of the groups of the second series of experiments consisted of mice from 3 to 4 successive generations. The results were: The mice of Groups 2 and 3 developed a very high incidence of lymphosarcoma and lung adenocarcinoma. The mice of Group 3 developed, also, a relatively high incidence of mammary cancer (33% of the breeding females) which did not appear in the animals of Group 2 nor in the controls. Incidence of mammary cancer was particularly high in the mice of Group 4. From these results it appears that both egg white and egg yolk are carcinogenic, but that their carcinogenicity differs. A carcinogenic substance causing the development of lymphosarcomas and lung adenocarcinomas, would be present in both, while a mammary carcinogen, lipid in nature, is present in the yolk only.

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Blood Flow Rates in Small Vessels of the Hamster Cheek Pouch. (28255)

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Changes in blood flow rates have been used traditionally as criteria of small blood vessel activity, but methods of estimation have been largely subjective or indirect. Recently developed microcinematographic techniques, however, now provide the basis for direct quantitative determination of blood flow velocity and volume in individual microscopic vessels(1,2).

Materials and methods. A modification of the method of Hugues(1) was used in quantitative studies of blood flow in vessels of the cheek pouch of the golden hamster. Animals of 100 to 135 g body weight were anesthetized with 0.2 ml/100 g of sodium pentobarbitol (50 mg/ml). The cheek pouch was prepared for observation and immersed in mammalian Ringer's solution according to the technique of Lutz and Fulton(3). Single vessels, 14 to 80 μ in diameter, were viewed through a monocular microscope equipped with a water immersion objective at a magnification of 500X. A zirconium arc light source was used. A beam-splitter, attached to the body tube, projected the light-masked image of a straight segment of a vessel into a Grass 35 mm recording camera. The image was focused so that the direction of blood flow was

TABLE I. Blood Velocity and Volume Flow in Vessels (14 to 80 μ Diameter) of Hamster Cheek Pouch.

		Velocity, mm/sec			Vol flow, $mm^3 \times 10^{-3}$/sec			Diameter, μ		
Type of vessel	No.	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.	Range
Arterioles	75	4.4	2.39	.8-12.9	5.08	5.97	.19-35.83	34.3	15.10	14-80
Venules	57	2.6	1.42	.4- 6.6	4.10	3.87	.36-20.77	42.3	10.29	24-74

S.D. = Standard deviation.

at right angles to the direction of film movement. During the usual one-second exposure, with the film moving at a constant speed of 250 mm/sec, streaks formed by individual moving blood cells were superimposed on the film at an angle. The mean angle formed by the blood cells was then determined by taking an average of 5 direct measurements along the 25 cm strip of developed negative. Inside diameters of the vessels were measured before and after each exposure with an optical micrometer. The mean velocity (V) of the blood cells in mm/sec was calculated by the following formula, where θ is the mean angle formed by the blood cells, f is the film speed (250 mm/sec), and M, the magnification of the image on the film:

$$V = \frac{f \tan \theta}{M}$$

The mean blood cell volume flow rate (Q) in mm^3/sec was calculated from the formula $Q = V\pi r^2$ where r is the vessel radius.

Cheek pouch vessels were selected at random for measurement. It became apparent that the velocity of flow in individual vessels was closely related to the level of anesthesia. Therefore, a routine procedure was adopted to control for the anesthetic effect. For each vessel, one-second exposures together with diameter measurements were taken every 3 minutes during the entire period of anesthesia. The pattern of velocity change was essentially linear with the highest value occurring at the time when the animal showed the first signs of recovery. Further recordings could not be taken once reflex motion began and the experiment was terminated. The last measurement taken was considered to represent a reasonable estimate of the physiological value. Vessel diameter changes were infrequently noticed during the period of observation. A study of the effects of depth of anesthesia will be reported separately.

As a control procedure, flow measurements were made in 5 hamsters to determine whether or not the Ringer's solution should be maintained at body temperature in preference to room temperature. Recordings were taken at 3-minute intervals during an initial period of about 30 minutes with the cheek pouch immersed at room temperature (26 to 27°C). The solution was then removed and Ringer's solution at 37°C was applied by drip for a 15-minute period during which measurements were continued. After this time, the drip was stopped and solution at room temperature was reapplied for an additional 30 minutes. No significant alterations were discerned in either the pattern of velocity change with time or in vessel diameters. In subsequent experiments, Ringer's solution at room temperature was used.

Results. Table I summarizes data obtained from 75 small arterial vessels ranging in diameter from 14 to 80 μ and from 57 small venous vessels with diameters of from 24 to 74 μ. Further analysis of the data by grouping vessels of similar size revealed no apparent relationship between vessel diameter and blood velocity.

For purposes of comparing groups of arterioles and venules more similar in size, Table II summarizes the results obtained from vessels 30 to 38 μ in diameter. Of all the vessels observed, 18 arterioles and 18 venules fell into this intermediate size range. The similarity in mean velocities and ranges between the more homogeneous groups of vessels (Table II) and the heterogeneous group (Table I) further suggests the lack of relationship between vessel size and blood velocity.

Discussion. Hugues(1) found mean velo-

TABLE II. Blood Velocity and Volume Flow in Vessels (30 to 38 μ Diameter) of Hamster Cheek Pouch.

		Velocity, mm/sec			Vol flow, $mm^3 \times 10^{-3}$/sec			Diameter, μ		
Type of vessel	No.	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.	Range
Arterioles	18	4.8	2.78	1.2-12.9	4.08	2.22	.85-10.37	33.3	2.66	30-38
Venules	18	2 2	1.65	.4- 6.6	1.86	1.23	.10- 4.67	33.8	2.90	30-38

S.D. = Standard deviation.

cities in 82 arterioles (30 to 70 μ diam) and in 76 venules (30 to 70 μ diam) of the rabbit mesentery to be 6.0 and 3.6 mm/sec respectively. The results reported here (Table I) for vessels of the hamster cheek pouch are 4.4 mm/sec in arterioles and 2.6 mm/sec in venules comparable in size to those studied by Hugues. While the velocities in vessels of the cheek pouch appear to be somewhat lower than those in the rabbit mesentery, the ratios of mean velocity in venules to that in arterioles are approximately the same, 1:1.7, in both cases. If cheek pouch vessels of essentially the same size range are compared (Table II), the mean velocity in venules is 2.2 mm/sec and in arterioles, 4.8 mm/sec with a ratio of 1:2.2.

Neither these studies nor those of Hugues show any significant correlation between vessel size and blood velocity within the size ranges studied. However, it is possible that more refined high-speed microcinematographic techniques which permit measurement of velocity of individual blood cells within vessels at the capillary level(4) may reveal such relationships.

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Conversion of Phenylalanine to Phenethylamine in Patients with Phenylketonuria. (28256)

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In phenylketonuria there is a 20-40 fold increase in the blood levels of phenylalanine. Recent studies in this laboratory have shown that L-phenylalanine is decarboxylated by mammalian aromatic L-amino acid decarboxylase, an enzyme which is also present in brain(1). Since normal blood levels of phenylalanine are of the order of 10^{-4}M and the Michaelis constant for phenylalanine decarboxylation is greater than 10^{-2}M, one would expect to find an increased synthesis of phenethylamine in phenylketonurics.

In this investigation it was possible to show that production of phenethylamine is indeed markedly increased in patients with phenylketonuria. Also, it was found that synthesis can be appreciably reduced by administering the decarboxylase inhibitor, α-methyl-dopa*(1,2). The possible implications of increased synthesis of this biologically active amine in the brain are discussed.

Methods. The principal subjects of this investigation were 2 phenylketonuric patients (J.R., a 28 year old woman and D.P., a 22 year old man), hospitalized in the Clinical Center. In addition to clinical stigmata characteristic of the disease, the diagnosis had been confirmed by elevated fasting levels of plasma phenylalanine and by positive ferric

* α-Methyl-3,4-dihydroxy-DL-phenylalanine.