mouth in capsules, starting with 20 mg twice a day and, usually, increasing to 3 times a day in a few weeks. Measurement of the Gothlin Index was repeated every 3 or 4 weeks, not oftener, because Gothlin had pointed out that a negative test is only significant if an interval of at least 3 weeks had elapsed since the previous test. Two of the 14 subjects were receiving potassium thiocyanate by mouth at the time the study was begun, and this was continued.

Results. In no case did any toxic effect develop that could be attributed to the rutin. One patient died of a stroke 2 weeks after beginning the medication. Two other patients did not return for adequate follow-up. However, 11 patients were followed for a period varying between 12 and 16 months. Capillary fragility became normal in 8 of these within 2 months of beginning medication, while in 3 it remained increased. One of the subjects in whom the fragility remained high developed a hemiplegia 4 months after beginning medication, and is reported to have died. No complication developed during the period of observation in the remaining 10 subjects, nor was there any significant change in blood pressure. Two subjects stopped taking the rutin after the capillary fragility had returned to normal. Within 6 weeks the capillary fragility was again increased. Rutin was resumed, and when the capillary fragility was tested a month later, it was again normal.

Conclusion. At least in certain cases, rutin appears to have the property of decreasing capillary fragility in subjects in whom this fragility is initially increased. In this effect it resembles hesperidin.

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Further Observations upon the Protracted Effect of Alpha-tocopherol Administered to Nursing Rats.*

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In a previous paper,[1] it was shown that a single dose of 0.5-5.0 mg of alpha-tocopherol administered on the 15th day of life to rats born of mothers on an E-deficient diet, and maintained after weaning upon vitamin E low diet, produced a significant delay in postpubertal degeneration of the testis. Similar doses given on the 5th day, or on the 28-30th day, were less effective than when given on the 15th day.

This paper is concerned with the effect of larger single doses, either given to the young directly, or through the mother's milk.

Experiment I. The mother was a third generation rat on E-deficient diet, 10 mg of alpha-tocopherol acetate having been given at the beginning of each pregnancy. Litter H_2 was the second litter; the first litter of 7 young did not survive 4 days. The young of H_2 were given 1 drop (25.6 mg each) of alpha-tocopherol acetate on the 15th day of lactation. Semi-castration was performed when they were 107 days old, and they were killed on the 182nd day. Repeated fertility tests were made by mating the rats with females which had been kept on a stock diet. During the mating period, male and female had access only to vitamin E-deficient diet. The birth of a litter was considered a positive test.

Experiment II. Each suckling rat of a second litter was given 51.2 mg of alpha-tocopherol acetate on the 15th day. The mother was again a third generation rat on E-deficient diet. The results are summarized in Table II.

From previous data, it has been found that

* Aided by a grant from the John and Mary R. Markle Foundation.

1 Kaunitz, H., Pappenheimer, A. M., and Schogoleff, C., *Am. J. Path.*, 1944, **20**, 247.

TABLE I.
Effect, upon Testes, of 25.6 mg Alpha-tocopherol Acetate Administered on 15th Day.

Rat No.	Age (days)	Body weight (g)	Testicular weight (g)	Motile sperm	Age at last positive mating (days)	Histology of testis (Mason)[2]
H_2 (1)	107	370	1.478	+		0-I
	182	388	0.744	0	127	IV-V
H_2 (2)	107	405	1.382	+		0
	182	414	0.766	0	111	IV-V
H_2 (3)	107	388	1.385	+		0
	182	400	0.800	0	123	III-V
H_2 (4)	107	390	1.300	+		0
	182	394	0.870	0	150	III-IV

TABLE II.
Effect, upon Testes, of 51.2 mg Alpha-tocopherol Administered on 15th Day.

Rat No.	Age (days)	Body weight (g)	Testicular weight (g)	Motile sperm	Age at last positive mating (days)	Histology of testis (Mason)[2]
H51 (2)	202	430	1.538	+		0
	229	415	1.478	0	149	0-I
H51 (3)	202	418	1.460	+		0
	229	400	1.064	0	187	I-III
H51 (4)	202	340	1.400	—	134	0-I
H51 (5)	202	320	1.244	+		0
	229	344	1.134	—	187	0-I

the average weight of one testis in untreated animals under otherwise identical experimental conditions is as follows:

75 days—36 animals—0.930 g
95 " —26 " —0.657 "
110 " — 5 " —0.520 "
135 " —11 " —0.490 "

At 75 days, 2 of the 36 untreated control rats had motile sperm, but no positive mating was obtained. After this age, motility was invariably lost and the testis showed advanced degeneration in practically all cases.

It is apparent that the single dose received on the 15th day of life has exerted a prolonged delaying effect upon testicular degeneration. The degree and duration of protection is, with the dose used (0.5 to 51.2 mg), roughly proportional to the amount of tocopherol administered. (Chart 1.)

[2] Mason, K. F., *J. Exp. Zool.*, 1926, **45**, 159.

Experiment III. A single dose of 13 or 26 mg alpha-tocopherol acetate was given to the mothers, either on the 5th or 15th day, so that the only source of vitamin E for the young was the mothers' milk. Again, definite retardation of testicular degeneration resulted, as is shown in Table III.

It is obvious without further analysis that the alpha-tocopherol excreted in the milk has delayed post-pubertal testicular degeneration. Comparing the groups in which the mothers received the single dose on the 5th or on the 15th day, one again notes a more prolonged and favorable effect in the latter group. The larger dose is also obviously more effective than the smaller one.

Reference to the chart suggests that the amount of protection afforded approximates that given by 0.5 to 1.0 mg, in the group where the mother received 13.0 mg on the 15th day, and 2.0 mg in the 26.0 mg group. Since there

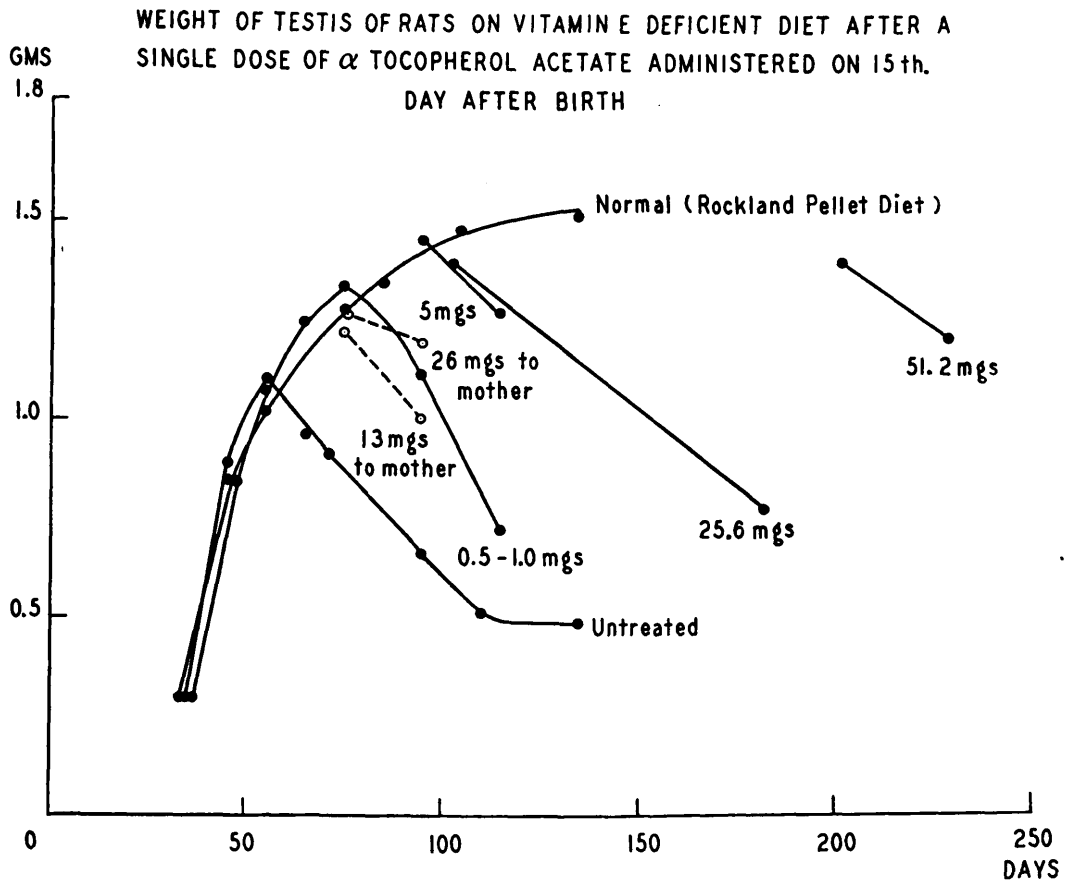

CHART 1.

TABLE III.
Effect, upon Testes of Offspring, of Alpha-tocopherol Administered to Mother.

α-tocopherol administered to mother		Testis examined	No. of	Average weight of testis	Motile sperm		Histology of testis (Mason)[2]		
Dose (mg)	Day	day	experiments	(g)	No.	%	0-I	II-III	IV-V
13	5	70-75	14	1.235	3	21	6	*8*	0
13	15	70-75	9	1.242	4	45	*5*	1	3
26	5	70-75	12	1.357	1	8	*10*	2	0
26	15	70-75	24	1.285	22	91	*24*	0	0
Control untreated		70-80	36	0.930	2	5.5	3	*20*	13
13	5	95	13	0.685	0	0	0	0	*13*
13	15	95	8	1.004	0	0	3	0	*5*
26	5	95	11	0.856	0	0	2	1	*8*
26	15	95	16	1.196	5	31	*10*	2	4
Control untreated		95	26	0.657	0	0	0	2	*24*