The frequency of degenerating spermatogonia increased notably in the period from 8 to 20 hours. Emphasis is attached to the observation that a decline in incidence of resting spermatogonia follows the 20-hour interval. This suggests that some of the spermatogonia are actually undergoing degeneration and not proceeding into spermatocytes. The reticulated or prophase-like spermatogonia also show increased degeneration 6 to 20 hours after irradiation but without the consequent effect noted above for resting spermatogonia. This suggests that these spermatogonia-like cells are reacting to irradiation more like spermatocytes than spermatogonia.

In the 24-hour interval there was no lowering of incidence of spermatocytes although evidences of degeneration were present.

It is recognized that degeneration does occur in the testes of untreated animals. The frequency appears to be of the order of 1 to 6 in 100 tubules. These degenerating cells are few in number in any given tubule.

Summary. Quantitative data are presented to show incidence of spermatogonia and spermatocytes in normal mouse testicles at stated intervals in a 24-hour period, and compared with data for testicles of mice killed at hourly intervals the 24 hours post-irradiation. Testicles were exposed to a single dose of 1440 r for 18 min. 40 sec.

The data indicate that within the 24 hours a pattern of response can be demonstrated which is limited to the spermatogonia. Active mitosis is inhibited for at least the first 24 hours and resting spermatogonia decrease in incidence after 20 hours. Reticulated spermatogonial cells, resting and meiotic spermatocytes do not decrease during the interval studied. Supplementary effects of irradiation are noted by a tabulation of the frequency of degenerating cells, confirming the belief that mitotic spermatogonia and resting spermatogonia are the most sensitive germinal cells. Degeneration of the reticulated spermatogonial cells does not result in a lowered incidence of these cells at any time in the 24-hour period.

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Effect of Methylcellulose on Growth Response of Rats to Low Vitamin Intakes. (19283)

R. C. ELLINGSON AND O. N. MASSENGALE. (Introduced by Warren M. Cox, Jr.)
From the Research Laboratories, Mead Johnson and Co. Evansville, Ind.

With increasing use of methylcellulose as a laxative in the treatment of chronic constipation(1-4), the question naturally arises—will continued ingestion significantly decrease the intestinal absorption of certain essential nutrients? Perhaps the question has already been answered in the negative by the fact that no clinical symptoms of vitamin deficiencies have been reported in patients who have ingested methylcellulose for long periods of time. Musick(1) cites the unpublished work of Shapiro, who showed that daily ingestion of methylcellulose did not interfere with the absorption of vit. K. However, for more

direct evidence we have studied the effect of ingestion of methylcellulose on the growth response of normal and depleted animals to minimal dosages of thiamine or vit. A. Thiamine and vit. A were chosen as representative of the water-soluble and oil-soluble vitamins, respectively.

Experimental. The given vitamin was dissolved or dispersed in a solution of methylcellulose of such concentration that daily administration by stomach tube of 2.0 cc supplied to each rat the desired quantities of the vitamin and methylcellulose. For the groups receiving no methylcellulose the daily dose of the vitamin was dissolved or suspended in 2.0 cc of water, if water-soluble, or in 0.5 cc of cottonseed oil, if oil-soluble. All dilutions were freshly prepared each day from assayed stock preparations of the vitamins. The experiments were of 28-day duration, during which time the weight responses of the experimental animals were observed. Each group consisted of 5 male and 5 female rats. In all instances, when methylcellulose was administered, a dosage of 50 mg per rat was employed. *Thiamine.* Both normal stock rats and thiamine-depleted animals were used. The depletion period was 18 days. The rats were on a thiamine-free diet* and were fed 6 μg of thiamine hydrochloride daily by stomach tube, with or without simultaneous administration of methylcellulose.† The thiamine was supplied as either crystalline vit. B_1 or thiamine in admixture with other vitamins.‡ *Vit. A.* Stock rats were depleted of vit. A according to the procedure in the U. S. Pharmacopoeia XIV, page 789. Each deficient rat was given 3 units of vit. A daily as either an aqueous vitamin preparation‡ or a fish liver oil concentrate,§ with or without simultaneous administration of methylcellulose.

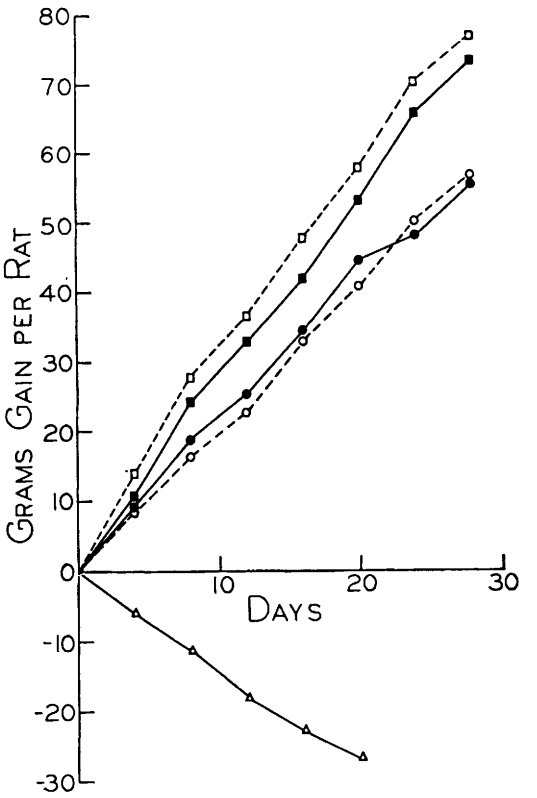

FIG. 1. Weight response curves of B_1-depleted rats given 6 μg of thiamine daily for 28 days with and without 50 mg of methylcellulose. Legend: △——△ control, ●——● cryst. B_1 and methylcellulose, ○- - -○ cryst. B_1, ■——■ B_1 as aq. vit. preparation and methylcellulose, and □- - -□ B_1 as aq. vit. preparation.

Results. In Fig. 1 and 2 are plotted the growth response curves of the various groups of animals. Since the response of the groups of normal rats was almost identical with that of the groups of thiamine-depleted rats, curves for the latter animals only are plotted in Fig. 1. Examination of the figures reveals that daily ingestion of methylcellulose by the rat does not significantly change the growth response to minimal doses of vit. A or B_1.

Discussion. Dutcher and coworkers(5) demonstrated, in the rat, that administration of mineral oil with varying amounts of carotene decreases the intestinal absorption of

* Thiamine-free diet: 18% casein (vit.-free), 4% salt mixture, 8% cottonseed oil, 5% autoclaved yeast, 2.5% Ruffex, 60.5% starch, 1% wheat germ oil and 1% cod liver oil.

† Dow Chemical Co. Methocel, 400 cps., Pharmaceutical grade.

‡ Known under the trade name of Poly-Vi-Sol. It contains, in addition to vit. A palmitate, irradiated ergosterol, ascorbic acid, thiamine hydrochloride, riboflavin, niacinamide and small amounts of inert ingredients.

§ Known under the trade name of Mead's Oleum Percomorphum. Consists of liver oils of percomorph fishes, Viosterol and other fish liver oils.

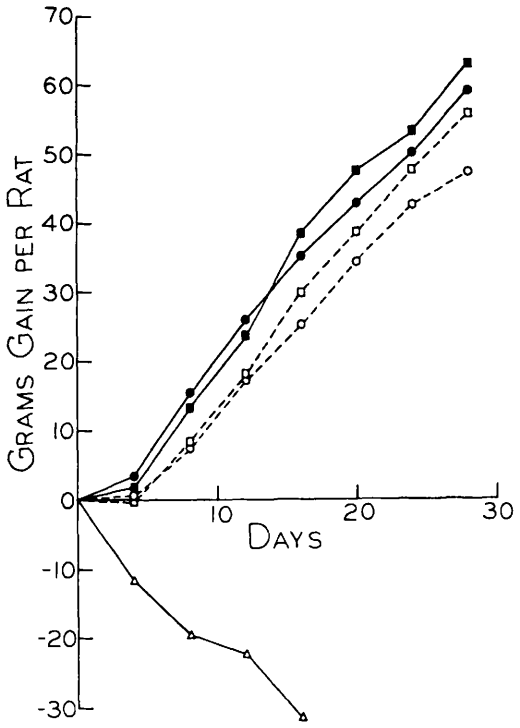

FIG. 2. Weight response curves of A-depleted rats given 3 units of vit. A daily for 28 days with and without 50 mg of methylcellulose. Legend: △——△ control, ●——● A as aq. vit. preparation and methylcellulose, ○- - -○ A as aq. vit. preparation, ■——■ A as fish oil and methylcellulose, and □- - -□ A as fish oil.

carotene, but that mineral oil has little effect on the absorption of vit. A administered in cod liver oil or as a vit. A concentrate. The explanation proposed for the different effects of mineral oil was the greater solubility of carotene in mineral oil than in the intestinal fluids and the greater solubility of vit. A in the intestinal secretions than in mineral oil. More recently, however, Paul, Ellis, and Paul (6) propose that the decreased effectiveness of β-carotene administered in mineral oil may be the result of partial isomerization of active β-carotene to stereoisomers of lower biological activity and that stereoisomerization of vit. A in mineral oil does not result in decreased biological activity. Whatever the true explanation may be for the effect of mineral oil on the utilization of carotene and of vit. A by the rat, these studies emphasize the possibility that ingestion of methylcellulose might decrease the effectiveness of the oil-soluble vitamins in the animal.

In order to learn whether ingestion of methylcellulose might decrease absorption of water-soluble or oil-soluble vitamins, low dosages of vit B_1 or A were fed to normal stock animals or depleted rats, and the growth responses were observed. Earlier work with vit. A(7) indicates that if decreased absorption were significant it would be reflected in decreased growth of the rats. The dosage of methylcellulose employed was 0.7 to 1.0 g per kg body weight which is approximately equivalent to 10 times the dosage ordinarily given to man.

From the weight gain of the thiamine-depleted and normal animals given 6 μg of thiamine daily for 28 days with and without simultaneous administration of methylcellulose, it is evident that the latter agent does not reduce the effectiveness of the low thiamine dosage and, therefore, does not decrease the intestinal absorption of the water-soluble vitamin. Similarly, the weight gains of the A-depleted rats show that the simultaneous administration of methylcellulose with 3 units of vit. A does not decrease absorption of the oil-soluble vitamin.

Conclusion. Daily ingestion of methylcellulose does not significantly decrease the effectiveness of (1) thiamine hydrochloride in the depleted or normal rat, or (2) vit. A in the A-depleted rat. These data are interpreted to mean that daily ingestion by the rat of large amounts of methylcellulose does not decrease the absorption of water-soluble or oil-soluble vitamins, and therefore does not increase the daily requirement of the rat for these factors.

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