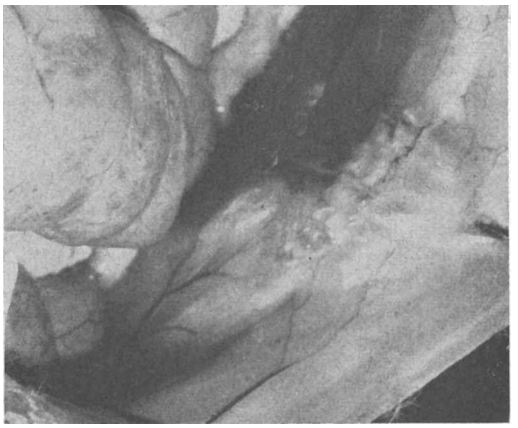

FIG. 2.
Treated animal showing no adhesions to site of scarification.

streptokinase and streptodornase for preventing postoperative intra-abdominal adhesions in rabbits due to trauma. It should be emphasized that in all of the treated animals with adhesions, the bands were adherent to the infected suture line, not to the area of scarification. The last series of experiments, in which no infection was found at the suture line, revealed no adhesions in the treated animals. Of the 10 treated rabbits with adhesions, 6 were closed with through and through sutures, and all of these animals had extensive infections at their suture lines. Inasmuch as the drug was administered only at the time of operation, it is conceivable that the enzymes were no longer active as the relatively slowly progressing infection extended from the suture line. It is interesting to note that wound cultures taken from infected suture lines revealed predominantly fecal organisms. In the present report, the optimum dosage was not determined. However, the results were found to be much better when the drug was placed in solution prior to use than when used in the dry form.

Conclusion. The results in this series of animals were sufficiently encouraging as to justify the further investigation of streptokinase-streptodornase in the prevention of experimental postoperative adhesions.

Addendum: Preliminary work in dogs has indicated so far that the drug does not prevent the formation of postoperative intra-abdominal adhesions in this animal. This may be due, however, to a variety of factors such as insufficient dosage, animal inactivators or inability of streptokinase and streptodornase to activate dog's serum. Kiser's(13) experiments have shown that *in vitro*, streptokinase and streptodornase fail to activate dog's serum except in very high dosage.

13. Kiser, J., personal communication.

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Effects of a Transient Vitamin A Deficiency on Subsequent Resistance to Cold.* (18279)

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It is becoming increasingly apparent that malnutrition may cause residual effects that persist long after dietary deficiencies have been corrected and the gross manifestations of nutritional disease have been ameliorated (1). Recent findings by Best and Hartroft (2) are pertinent in this regard. These work-

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1. Keys, A., *Science*, 1950, v112, 371.

ers found that less than a week of deficiency of choline or its precursors in the diets of young rats led to high blood pressure in 25% of the animals maintained on a good normal diet except for this short interval. Similar findings have been reported by others(3). The irreversible testicular degeneration of male rats fed a vit. E-deficient diet is another example of a residual effect of malnutrition. In the present communication data are presented concerning the residual effects of a transient vit. A deficiency in rats on the resistance of these animals to subsequent exposure to cold.

Procedure and results. The animals employed in the present experiment were male rats of the University of Southern California strain in which the dietary regime of the mothers was such as to make the young rats satisfactory for bioassay studies for vit. A. The mother rats were maintained for at least 2 months previous to breeding and for 12 days after the birth of the litter on Sherman diet B (4) without addition of supplementary lettuce or meat. Litters were cut to 7 at 3 days of age, and on the 12th day mothers and litters were placed on a vit. A-low diet.† The young were weaned at 21-24 days of age and at a body weight of 40-50 g inclusive. At this time the young were divided into 3 groups. All animals were fed *ad lib.* a vit. A-free diet (U.S.P. XIII, to which were added 75 mg of mixed natural tocopherol esters per kg of diet), but they differed in the following respects. Group I received 6 days weekly a supplement of 50 U.S.P. units of vit. A.‡ These rats did not plateau in body weight and they showed no symptoms of vitamin A deficiency at any time during the experiment. Groups II and III were fed the same diet as Group I but the vitamin A supplement was withheld. These animals depleted of vit. A after 20 to 22 days of feeding at which time their body weight averaged approximately 105 g. The end of the depletion period was set as the 5th day on which rats on the vit. A-free diet showed stationary or decreasing weight. After depletion the animals in Group II received the same vitamin supplement as those in Group I (50 U.S.P. units of vit. A per day, 6 times weekly). Animals in this group gained weight rapidly following the vit. A administration, which was continued for a period of 12 weeks. Rats in Group III differed from those in Group II in the dosage of vit. A which was administered after depletion. For the first 28 days after depletion animals in Group III received 6 times weekly a supplement of 1.25 to 2.25 U.S.P. units of vit. A acetate per day. The average gain in body weight of rats in this group during this period was 47 g. Subsequent to the 28th day of feeding the above suboptimal dosage of vit. A, and for 8 weeks thereafter, animals in this group were administered the same vit. A supplement that was employed for Groups I and II. Twelve weeks after depletion rats in Groups II and III averaged 255 g and 241 g respectively in contrast to an average body weight of 269 g for animals of a similar age in Group I. No significant difference in gross appearance was observed between animals in any of the 3 groups.

After the 12-week refeeding period 24 rats each of Groups I and II and 22 rats of Group III were selected for further study. Experiments were conducted (1) with animals kept continuously in a large walk-in refrigerator at a temperature of 2 ± 1.5°C and (2) under standard laboratory conditions at an average temperature of approximately 23 ± 2°C. Six rats of each group were employed in the room temperature series; the balance in the cold room series. Animals were kept in individual metal cages with raised screen bottoms to prevent access to feces and were fed *ad lib.* the following purified diet: sucrose, 60%; casein,§

2. Best, C. H., and Hartroft, W. S., *Fed. Proc.*, 1949, v8, 610.

3. Handler, P., and Bernheim, F., *Am. J. Physiol.*, 1950, v162, 189.

4. Sherman, H. C., and Campbell, H. L., *J. Biol. Chem.*, 1924, v60, 5.

† Similar to U.S.P. XIII depletion diet except that commercial casein rather than extracted (vitamin A-free) casein was employed.

‡ Natural ester concentrate from Soupfin shark liver oil, prepared by Collett-Week-Nibecker, Ossining, N. Y. 50 U.S.P. units of Vit. A Natural Esters were dissolved in 0.1 ml of cottonseed oil containing 0.5% alpha-tocopherol as an antioxidant.

TABLE I. Effects of a Transient Vitamin A Deficiency on Subsequent Resistance to Cold.

Group	No. of animals	Initial wt, g	Change in body wt over 50-day period* g	% decedents	Avg survival time of decedents*
			Cold Room Series		
I	18	276.4	— 34.3 ± 3.6 (17)	5.6	38.0 ± 0.0
II	18	255.6	— 28.5 ± 5.2 (12)	33.3	21.3 ± 5.7
III	16	239.8	— 21.0 ± 5.4 (5)	68.8	28.8 ± 4.2
			Room temperature series		
I	6	254.1	+ 88.2 ± 10.9 (6)	0	—
II	6	254.8	+115.2 ± 8.6 (6)	0	—
III	6	247.6	+ 79.6 ± 9.7 (6)	0	—

The values in parentheses indicate the number of animals which survived and on which averages are based.

* Including standard error of the mean calculated as follows: $\sqrt{\frac{\Sigma d^2}{n}} / \sqrt{n}$ where "d" is the deviation from the mean and "n" is the number of observations.

25%; salt mixture, 5%; and cottonseed oil (Wesson), 10%. To each kg of the above were added the following synthetic vitamins: thiamine hydrochloride, 40 mg; riboflavin, 40 mg; pyridoxine hydrochloride, 40 mg; calcium pantothenate, 80 mg; nicotinic acid, 60 mg; ascorbic acid, 100 mg; biotin, 4 mg; folic acid, 10 mg; p-aminobenzoic acid, 400 mg; inositol, 800 mg; vit. B_{12},¶ 100 μg; 2-methyl-naphthoquinone, 10 mg; and choline chloride, 2 g. Each rat also received 6 times weekly a vit. A-D concentrate** containing 50 U.S.P. units of vit. A and 5 U.S.P. units of vit. D, and 3 times weekly a supplement of 1.5 mg alpha-tocopherol acetate. Feeding was continued for 50 days or until death, whichever occurred sooner.

Results are summarized in Table I. Findings indicate that a transient sub-lethal deficiency of vit. A markedly impaired the rats' ability to withstand subsequent exposure to a low environmental temperature. In the room temperature series all animals survived the experimental period of 50 days; in the cold room series, however, a significant difference was observed between the various groups in the ability of rats to withstand prolonged exposure to cold. Whereas only 1 out of 18 rats which had received vitamin A continuously from weaning on succumbed under cold room conditions, 17 out of 34 rats which had previously been depleted of vit. A (Groups II and III) and subsequently refed with this vitamin died under similar conditions. The mortality rate was particularly marked for animals in group III which had been depleted of vit. A and fed for 28 days thereafter a suboptimal amount of this vitamin. Values for Group II were intermediate between those for Groups I and III. After the third week of cold exposure necrotic changes were observed on the paws and tip of the tail of virtually all rats in the cold room series. Amputation of part or all of the tail occurred in approximately one-fourth of the series. A number of animals developed priapism. At autopsy kidney, adrenal and ventricular weights were sig-

§ Vitamin Test Casein, General Biochemicals, Chagrin Falls, O.

‖ Hubbel, Mendel and Wakeman Salt Mixture, General Biochemicals, Chagrin Falls, O.

¶ Vit. B_{12} Oral Grade Solids, Chas. Pfizer & Co., Brooklyn, N. Y.

** Nopco Fish Oil Concentrate, assaying 800,000 U.S.P. units of vit. A and 80,000 U.S.P. units of vit. D per g.

nificantly increased and testes weight significantly reduced over that of room temperature controls. In general, however, no significant difference in body weight or gross appearance was observed between the various groups either under cold room or room temperature conditions.

Discussion. Available data indicate that requirements for a number of nutrients are markedly increased under conditions of low environmental temperature. This is particularly true for some of the water-soluble vitamins. An increased requirement for thiamine(5,6), pyridoxine(7), and ascorbic acid (8) has been demonstrated following prolonged exposure to low environmental temperatures. Requirements are also increased for vit. A(9). Previous findings indicate that the survival time of vit. A-deficient rats is markedly reduced under conditions of low environmental temperature(9). Results of the present experiment indicate that a transient pre-test deficiency of vit. A (apparently corrected by the administration of relatively high doses of vit. A) may also impair the ability of rats to withstand subsequent exposure to cold. Available data, however, do not indicate what factors are responsible for the lowered resistance.

Findings of the present experiment suggest that transient nutritional deficiencies may leave residual effects in the organism which normally are not readily apparent but which may become manifest under conditions of stress. Further experiments are indicated to determine the residual effects of transient nutritional deficiencies (of other nutrients as well as vitamin A) and the aggravating effect of stress factors thereon.

Summary. A transient deficiency of vit. A, apparently corrected by the administration of relatively high doses of this vitamin, markedly impaired the ability of rats to withstand subsequent exposure to cold.

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Effects of Atropine on Brain Respiration.* (18280)

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The pronounced central nervous disturbances of atropine poisoning and the use of the drug in the treatment of postencephalitic Parkinsonism suggest the desirability of an examination of its metabolic action on central nervous tissues. It has been shown *in vivo*(1) that atropine depresses the oxygen consumption of brain. *In vitro* experiments on the effects of atropine on other tissues, *e.g.* muscle(2), have produced negative results. However, data on the effects of the alkaloid on the *in vitro* respiration of brain homogenates are lacking. This paper describes some effects of atropine on the respiration of rat brain homogenates.

Methods. Rats of mixed strains were used. After decapitation the brains were removed, weighed and homogenized in glass homogenizers(3). The homogenates were made directly in the complete medium used, the only

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