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Effect of Carotene on Course of B. Tuberculosis Infection of Mice Fed on a Vitamin A Deficient Diet.*

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The importance of vitamin A as an anti-infective factor in diet has been comparatively well established. Green and Mellanby[1] have shown that rats fed on a diet deficient in vitamin A are very susceptible to pyogenic infection. The addition of carotene raised the resistance of the animals to this infection. While several workers have suspected that vitamin A deficiency plays an important rôle in the resistance of animals to *B. tuberculosis* infection, the exact relationship of this deficiency has not been well established experimentally, although the work of Smith[2] would appear to indicate that it may play some part in lowering resistance to the infection.

The author investigated the effect of addition of carotene to a vitamin A deficient diet used as food for animals infected with *B. tuberculosis*. Mice were selected as experimental animals. Browning[3] showed that histologically, tuberculous lesions in mice closely resemble those found in man and that the disease runs a subacute or chronic course in these animals.

Eighty adult mice from the same stock were fed on a modified Drummond-Watson diet which, with cod liver oil as a source of fat-soluble vitamins, maintained normal growth. The modified Drummond-Watson diet was constituted as follows:

Extracted Casein	1000
Rice Starch	2750
Marmite	250
McCollum's Salt Mixture	250
Cotton Seed Oil	500

Each animal received in addition a daily dose of 0.2 gm. ether extracted wheat germ.

Forty animals were inoculated intraperitoneally with 0.75 mg. of moist 21 days' culture of *B. tuberculosis* (bovine) and on the day of inoculation the animals were divided into 4 groups:

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1 Green, H. N., and Mellanby, E., *Brit. J. Exp. Path.*, 1930, **11**, 81.

2 Smith, M. T., *J. Lab. and Clin. Med.*, 1926, **11**, 8.

3 Browning, C. H., *Ed. Med. J.*, 1923.

Group 1 Infected with *B. tuberculosis*	Group 2 Uninfected	Group 3 Infected with *B. tuberculosis*	Group 4 Uninfected

Each group of mice was fed on a fat-soluble vitamin deficient diet. Groups 1 and 2 received a daily dose of 100 antirachitic units of irradiated ergosterol and 0.005 mg. of carotene. Groups 3 and 4 received the same daily dose of irradiated ergosterol as groups 1 and 2 but no carotene. Forty-four days after inoculation all the mice in group 3 had died. During this period the animals in group 4 showed no deaths but many animals showed xerophthalmia. Six deaths occurred in group 1 during the same period. None of the animals in group 2 died nor did they show any signs of vitamin A deficiency. The animals in group 1 all died within 74 days of infection.

In a second experiment 60 adult mice which had previously shown normal growth on Drummond-Watson diet with the addition of cod liver oil, were divided into 3 groups each containing 20 animals and placed on a fat-soluble vitamin deficient diet. Group 1 received a daily dose of 100 antirachitic units of irradiated ergosterol and 0.005 mg. or carotene. Group 2 received the same daily dose of irradiated ergosterol as group 1 but no carotene. Group 3 received no irradiated ergosterol but each animal received 0.005 mg. carotene.

After 60 days, 10 animals from each group were inoculated intraperitoneally with 0.75 mg. moist growth of a 21 days' culture of *B. tuberculosis* (bovine), and the carotene ration of group 3 was increased to 0.01 mg. per animal per day.

The results were as follows:

Group 1. 10 animals Irradiated ergosterol + carotene 0.005 mg.	Group 2. 10 animals Irradiated ergosterol	Group 3. 10 animals Carotene 0.01 mg.
10 animals dead within 11 days.	10 animals dead within 7 days.	10 animals dead within 17 days.

No deaths occurred in the non-infected mice.

All the dead mice in the above experiments were autopsied and cultures made from the spleen, heart blood and gut to detect any possible extraneous infection. No such infection was discovered.

Smears were made from the peritoneal exudate and spleen, and examined for *B. tuberculosis* infection. Numerous tubercle bacilli were found, also polymorphonuclear leucocytes and lymphocytes. Naked eye inspection showed enlarged spleens, tuberculous mesenteric glands, and large tuberculous masses in the lungs.

The above experiments would appear to indicate that *B. tuberculosis* infection in mice deprived of vitamin A and carotene runs a more acute course than in animals receiving 0.005 mg. of carotene per day. There appears to be some evidence that the acuteness of the course of infection varies quantitatively with the amount of carotene added to the vitamin A free diet and that vitamin D is of little importance in determining the course of *B. tuberculosis* infection in adult mice.

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Kidney Secretion in Reptiles.

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In birds there is now rather conclusive evidence that tubular secretion plays a major rôle in the excretion of uric acid by the kidney.[1, 2] Uric acid is the main nitrogenous urinary constituent of the arid-living reptiles (snakes and lizards) but no data are available as to its mode of excretion. The experiments reported here indicate that in the lizard, it is chiefly excreted by tubular secretion.

The urine/plasma ratio of uric acid has been compared with that of glucose after administration of phlorizin. Glucose is not secreted by the tubule[3] and phlorizin paralyzes the reabsorptive power of the tubule for glucose. Hence, the urine/plasma ratio for glucose should be a measure of the amount of glomerular filtrate if no glucose is reabsorbed under phlorizin. This error, if present, is probably small and would not affect appreciably the conclusions drawn from the present experiments.

The iguana *(Iguana iguana Shaw)* has been used as the experimental animal. Phlorizin was injected subcutaneously in dosage of 250 mg. per kilo 2 hours before the experiment or in 2 doses of 200 mg. per kilo the afternoon before and early on the morning of the experiment. The iguanas were anesthetized with urethane (5 cc. of a 25% solution per kilo), the cloaca opened with a small incision, cannulae tied into the ureteral papillae, and urine collected for a period of 10 to 30 minutes. The abdominal cavity was then

[1] Mayrs, E. B., *J. Physiol.*, 1924, **58**, 276.

[2] Gibbs, O. S., *Am. J. Physiol.*, 1929, **78**, 87.

[3] Marshall, E. K., *Am. J. Physiol.*, 1930, **94**, 1.