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Supervitaminosis C in Tuberculosis.

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Although the effect of subvitaminosis C on the course of tuberculous infection in the guinea pig has been adequately studied, no extensive investigations deal with the possible influence of supervitaminosis. Mouriquand and co-workers,¹ Bieling,² Heymann,³ and Basu⁴ showed that the combination of a partial depletion of vitamin C and progressive tuberculous infection apparently shortened the life of guinea pigs. Greene and co-workers⁵ demonstrated clearly the effect of vitamin C deficiency on tuberculosis in guinea pigs. On the other hand Leichtentritt⁶ gave large amounts of orange juice to tuberculous guinea pigs on normal diets and found the survival period to be twice as long as that of tuberculous animals on a normal diet. Grant⁷ reported that increasing the amount of vitamin C seemed to decrease the severity and extent of the tuberculous lesions in the lungs of guinea pigs. Bella⁸ noted no increased resistance in tuberculous animals whose diet was supplemented by orange juice or cevitamic acid. Thus, although results reported to date show conclusively that a deficiency in vitamin C is an important factor in the progress of tuberculosis in the experimental animal, no agreement exists among the three authors reporting on the effects of increased amounts of the vitamin above a dosage ample for protection against scorbutic changes.

As none of them produced an extreme degree of supervitaminosis it seemed desirable to test the effect of massive doses of crystalline vitamin C.

Fifteen guinea pigs were maintained on a stock ration consisting of carrots, hay, lettuce and oats. Five of these animals were used

¹ Mouriquand, G., Dochaix, A., and Dosdat, L., *Compt. Rend. Soc. Biol.*, 1925, **93**, 901.

² Bieling, R., *Z. Hyg.*, 1923-24, **101**, 442.

³ Heymann, B., *Klin. Wchnschr.*, 1926, **5**, 59.

⁴ Basu, N., *Z. Vitaminforsch.*, 1934, **3**, 91.

⁵ Greene, M. R., Steiner, M., and Kramer, B., *Am. Rev. Tub.*, 1936, **33**, 585.

⁶ Leichtentritt, B., *Deutsche. Med. Wchnschr.*, 1924, **40**, 672.

⁷ Grant, A. H., *Am. Rev. Tub.*, 1930, **21**, 115.

⁸ Bella, G. B., *Bull. Soc. Ital. Biol. Sperm.*, 1935, **9**, 141.

as controls, and the others were given daily intraabdominal injections of 20 mg. of crystalline cevitamic acid. This amount is considered protective for man against the slightest prescorbutic alterations; it is a massive dose for the guinea pig. The preparation used (Cebione)* was a neutral crystalline product for intravenous administration. The use of more animals was impracticable, because an enormous quantity of Cebione was necessary to maintain even 10 animals over a period of 6 months, which is the length of time necessary to permit the disease to advance to a point at which a comparison can be made. After a 7-day period of treatment with cevitamic acid, both the control and experimental animals were infected by injecting 300,000 H_{37} tubercle bacilli into the groin. All animals showed positive cutaneous reactions to tuberculin 10 days after infection. Daily injection of Cebione was continued for 5 months from the date of infection, at the end of which time each animal had received 30 gm. of cevitamic acid. No detrimental effects of the daily injections were observed; the animals grew at a normal rate and behaved in every way just as the controls. When one of the controls died, all of the remaining animals were killed and necropsied.

Scoring the amount of tuberculosis on a basis of a possible 4 plus for each of 4 organs, lungs, spleen, liver and lymph nodes, averaging these values for each animal and subsequently averaging the values in each group, controls and experimentals, gave a value for controls of 3 plus, while for the experimental supervitaminosis C animals the value was 2.2 plus. No significant differences were observed. Both showed enlargement of inguinal glands, with marked caseation. The spleen, which appears to be the most vulnerable organ, was generally tremendously enlarged and thickly studded with tubercles. The liver was likewise severely affected, and peppered with yellowish necrotic tubercles. The lungs showed less involvement than the other organs.

Two criticisms of this work might be offered. The dose of tubercle bacilli may have been so large that slight influences of the vitamin were obscured. It is also possible that survival periods might have been a more suitable criterion but the limited supply of vitamin C did not permit the injection of a sufficient number of animals to use this basis for a protracted period.

Summary. Supervitaminosis C maintained for a period of 5 months does not protect guinea pigs against subcutaneous injection of 300,000 virulent human (H_{37}) tubercle bacilli.

* Merck & Co., Rahway, N. J., kindly supplied the Cebione used in this experiment.