7131 C

A Note on the Mode of Action and Administration of Vitamin D.

CORNELIUS DALY.* (Introduced by A. Knudson.)

From the Department of Biochemistry, Union University Medical Department, Albany Medical College.

Lewis and Zotterman[1] have suggested that ultraviolet light forms in the skin a histamine-like substance which, presumably, would increase the gastric secretions. Also, various investigators have reported a decreased alkalinity in the intestinal contents during exposure to ultraviolet light. Furthermore, it has already been demonstrated that acidity in the gastrointestinal tract, by making calcium salts more soluble, has a healing effect on rickets. Therefore, we thought that vitamin D might increase the absorption of calcium and phosphorus by stimulating the secretion of gastric juice.

Standard rachitic rats were given from 0.005 to 0.5 mg. of histamine subcutaneously, twice each day for 21 days. The smaller doses of the drug caused no noticeable change in the appearance and general behavior of the animals. On the other hand, the larger doses increased the respiration, heart rate and especially the secretions from the eyes so that these rats appeared "watery-eyed" throughout the experimental period. Roentgenograms of the different groups of rats, taken at the end of treatment, showed no evidence of healing when compared with the controls. Thus it is apparent that vitamin D does not cure rickets by acting on the gastric juice.

These experiments support the findings of Bauer *et al*[2] and Hottinger,[3] who were unable to explain the healing action of vitamin D on the basis of an increased formation of acid in the gastrointestinal tract.

We also made a comparative study of oral and subcutaneous administration of vitamin D. Although Kramer and his associates[4] have cured rickets by subcutaneous injection of cod liver oil in ether solution, the relative efficiency of the 2 methods of treatment

* George Alexander Research Fellow in Biochemistry, 1930-32, sponsored by The Leopold Schepp Foundation, New York.

[1] Lewis, T., and Zotterman, Y., *Heart*, 1926, **13**, 203.

[2] Bauer, W., Maddock, S. J., and Wood, J. C., *Am. J. Med. Sci.*, 1931, **181**, 399.

[3] Hottinger, A., *Strahlentherapie*, 1929, **34**, 637.

[4] Kramer, B., Kramer, S. D., Shelling, D. H., and Shear, M. J., *J. Biol. Chem.*, 1927, **71**, 699.

was not compared. We found that both procedures were equally efficient in healing rickets when 0.1 to 0.2 mg. of viosterol were given to rachitic rats daily for 21 days. However, when the equivalent of 21 doses of vitamin D was administered in one dose on the first day, or a third of the total amount on each of the first, seventh, and tenth days, it was observed that the subcutaneous method of treatment brought about a complete cure while oral administration resulted only in moderate or advanced healing. This was true even when the viosterol for a particular day was given in 3 portions of 0.1 cc. each in order to insure a more accurate dosage.

These observations indicate either incomplete absorption of vitamin D from the intestine, when given in large amounts by mouth, or a mechanism less efficient for storage than that formed when the vitamin is administered subcutaneously in ether solution.

Wilkins and Kramer[5] have already shown that the injection technique is practical, and our results demonstrate further that it is possible to inject large doses of viosterol without loss of effectiveness. Therefore, it seems evident that subcutaneous administration would be advantageous in clinical treatment where difficulty is experienced with oral administration. Using a highly concentrated preparation of viosterol or cod liver oil, sufficient vitamin D could be given in 2 or 3 injections to either cure or prevent rickets.

Fifty-three rats were used in the 2 series of experiments. Rats 28 days old weighing from 40 to 60 gm. were kept on the Steenbock rachitic diet for 21 days, at the end of which time a marked degree of rickets developed. The rats were then weighed, X-ray pictures taken, and the experimental period started. After 21 days the final weight was recorded and X-ray pictures were again taken. In doubtful cases the line test was used as a check on the roentgenograms. Only those rats gaining, or at least maintaining their weight during the experimental period were considered in our studies.

[5] Wilkins, L., and Kramer, B., *Bull. Johns Hopkins Hosp.*, 1927, **40**, 52.