History of Vitamin D

Historical Review

Man is reported to have been aware since early antiquity of the substance we now know as vitamin D. The first scientific description of a vitamin D-deficiency, namely rickets, was provided in the 17th century by both Dr. Daniel Whistler (1645) and Professor Francis Glisson (1650). The major breakthrough in understanding the causative factors of rickets was the development in the period 1910 - 1930 of nutrition as an experimental science and the appreciation of the existence of vitamins.

Considering the fact that now we accept that the biologically active form of vitamin D is a steroid hormone, it is somewhat ironic that vitamin D, through a historical accident, became classified as a vitamin. It was in 1919/20 that Sir Edward Mellanby, working with dogs raised exclusively indoors (in the absence of sunlight or ultraviolet light), devised a diet that allowed him to unequivocally establish that the bone disease, rickets was caused by a deficiency of a trace component present in the diet. In 1921 he wrote, "The action of fats in rickets is due to a vitamin or accessory food factor which they contain, probably identical with the fat-soluble vitamin." Furthermore, he established that cod liver oil was an excellent antirachitic agent.

Shortly thereafter E.V. McCollum and associates observed that by bubbling oxygen through a preparation of the "fat-soluble vitamin" they were able to distinguish between vitamin A (which was inactivated) and vitamin D (which retained activity). In 1923 Goldblatt and Soames clearly identified that when a precursor of vitamin D in the skin (7-dehydrocholesterol) was irradiated with sunlight or ultraviolet light, a substance equivalent to the fat-soluble vitamin was produced. Hess and Weinstock confirmed the dictum that "light equals vitamin D". They excised a small portion of skin, irradiated it with ultraviolet light, and

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then fed it to groups of rachitic rats. The skin that had been irradiated provided an absolute protection against rickets, whereas the unirradiated skin provided no protection whatsoever; clearly, these animals were able to produce adequate quantities of "the fat-soluble vitamin", suggesting that it was not an essential dietary trace constituent. In parallel studies, Steenbock and Black found that rat food which was irradiated with ultra violet light also acquired the property of being antirachitic. However, because of the rapid rise of the science of nutrition -- and the discovery of the families of water-soluble and fat-soluble vitamins -- it rapidly became firmly established that the antirachitic factor was to be classified as a vitamin.

The chemical structures of the vitamins D were determined in the 1930s in the laboratory of Professor A. Windaus at the University of Göttingen in Germany. Vitamin D$_2$ which could be produced by ultraviolet irradiation of ergosterol was chemically characterized in 1932. Vitamin D$_3$ was not chemically characterized until 1936 when it was shown to result from the ultraviolet irradiation of 7-dehydrocholesterol. Virtually simultaneously, the elusive antirachitic component of cod liver oil was shown to be identical to the newly characterized vitamin D$_3$. These results clearly established that the antirachitic substance vitamin D was chemically a steroid, more specifically a seco-steroid.

**Key reference citations:**


Glisson, F. *De Rachitide sive morbo puerili, qui vulgo The Rickets diciteur*, London 1-416 (1650).


McCollum, E.V., Simmonds, N., Becker, J.E. and Shipley, P.G. Studies on experimental rickets. XXI. An experimental demonstration of the existence of a vitamin which promotes calcium deposition. J. Biol. Chem. 53:293-312 (1922).


