THE VITAMINS IN MEDICINE

by

FRANKLIN BICKNELL, D.M., M.R.C.P.

Honorary Physician, French Hospital, London

and

FREDERICK PRESCOTT, M.Sc., Ph.D., F.R.I.C., M.R.C.P.

Clinical Research Director, The Wellcome Foundation, London

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CHAPTER VIII

VITAMIN E

THE ANTISTERILITY OR ANTIDYSTROPHIC VITAMIN. ALPHA-, BETA-, GAMMA- OR DELTA-TOCOPHEROL

VITAMIN E is the name generally used when speaking of the vitamin in general or as it occurs in foods. Alpha-tocopherol is the most biologically active of several very similar substances, all of which have the properties of vitamin E. Thus while alpha-tocopherol means one distinct substance, vitamin E may mean either alpha-tocopherol, or a mixture of this and other similar substances. To avoid confusion vitamin E should be only used in the latter sense, and not as a synonym for alpha-tocopherol. The name tocopherol is derived from the Greek τόκος, childbirth, and φέρω, to bear.

HISTORY

Herbert McLean Evans, of California, will always have his name associated with vitamin E, partly because he and Bishop [1] in 1922 demonstrated the existence of an antisterility vitamin and partly because of the monograph on vitamin E written by himself and Burr [2] in 1927. This work remains to the present day the foundation of our knowledge of vitamin E. The authors showed that the foods richest in the vitamin were green leaves and the germ of seeds. Wheat germ and wheat-germ oil were found to have a remarkably high content of vitamin E, and remain to this day the best source. Rats were the experimental animals used, and for these animals it was proved that a deficiency of vitamin E leads to sterility in the male and abortion, though not failure to conceive, in the female.

The existence of the vitamin, however, had been foreshadowed in 1920 by Mattill and Conklin and confirmed in 1922 by Mattill and independently in 1923 by Sure. This early work is summarized by Evans and Burr [2].

Until 1928 vitamin E was thought to be entirely concerned with reproduction, but in this year Evans and Burr [3] reported that young rats suckled by vitamin E deficient mothers became paralysed, while Goettsch and Pappenheimer [4] in 1931 showed that guinea-pigs and rabbits when deprived of vitamin E developed a primary muscular dystrophy histologically identical with the progressive muscular dystrophies of man. From Denmark Ringsted [5], in 1935, and Einarson and Ringsted [6], in 1938, published careful and extensive research on the effects of lack of vitamin E on the central nervous system of adult rats. They pointed out that the neurological degenerations which were produced resembled those of amyotrophic lateral sclerosis and tabes dorsalis in man.

It is a depressing demonstration of the lack of co-ordination between research workers and clinicians that it was not until nine years after the discovery of vitamin E that Vogt-Möller [7] in Denmark first put it to any useful purpose by treating sterility in cows. In the same year he treated two women with habitual abortion with success [8], and six years later Young [13], in England, and Shute [14], in Canada, reported good results in the treatment of threatened abortion and pregnancy toxæmias.

Bicknell [9] in 1938, seven years after the possible value of vitamin E in human muscular dystrophy had been implied by animal research, started to treat cases of muscular dystrophy and neurological degeneration with vitamin E, or, rather, wheat germ. The improvement in his cases was

heart, a subject discussed on p. 657. In deficient cows (p. 606) sudden cardiac failure occurs, preceded by electrocardiographic changes, though there is little structural damage to the heart, while in dystrophic lambs (p. 606) there may be gross damage. In deficient monkeys there is virtually no damage [87] but there are changes in the electrocardiogram [86, 92] : the amplitude of the R and T waves is reduced with inversion of the latter [86], and also there is shortening of the time for the initiation of ventricular ejection [86]. The effect of vitamin E on the vascular system and blood is discussed on p. 622.

Changes in Metabolism. The metabolic changes brought about by lack of vitamin E are discussed on p. 594, so that here it is only necessary to draw attention to the way in which the creatine in the urine reflects the disturbed metabolism of the muscle. Just as dystrophic changes may be found in the muscles while the animal yet appears normal [103, 214], so may the creatine rise in the urine before any clinical change can be seen. Ni [182] was the first to apply to research in muscular dystrophy the well-known fact that urinary creatine is increased when the volume of functioning muscle is decreased [183]. He and Mackenzie and McCollum [29] noted the warning rise in the creatine of animals deprived of vitamin E. The latter authors have very fully investigated the subject and report that the best guide to the approach of muscular dystrophy is the rise in urinary creatine. This may occur while the increase in weight and the appetite are still satisfactory. The drop in creatine brought about by giving vitamin E is dramatic and precedes clinical improvement in strength, appetite and weight. It occurs in from twenty-four to forty-eight hours [29, 103]. There is increased destruction and increased formation of myoglobin, the former predominating [289] : this is of considerable interest as paralytic myoglobinuria in horses [130] has much in common with " stiff lamb disease " (p. 606), which is due to lack of vitamin E.

Rancid Fats : their Destruction of Vitamin E and their Relation to Muscular Dystrophy. Rancid fats rapidly destroy vitamin E by oxidation. This destruction is most liable to occur when vitamin E is in the form of the synthetic vitamin or concentrated preparations, since then it is no longer protected against oxidation by the anti-oxidants found associated with it in such natural sources as whole wheat germ [215].

It is important to realize that as vitamin E itself is an anti-oxidant it will be destroyed by fats before they become rancid through auto-oxidation. In other words a fat need not be rancid, certainly not smell rancid, before all its vitamin E is destroyed. Further, rancid fats can destroy vitamin E during digestion as long as both are fed together or within a short time of one another [50, 103, 216]. Claims that rancid fat given by mouth or by injection destroys vitamin E already absorbed into the body [217, 218] require further confirmation, probably being incorrect [99, 219]. If substantiated they are an argument against using ketogenic diets in any medical treatment.

The destruction of vitamin E by fats, due to their auto-oxidation, was investigated by Cummings and Mattill [220], who state that " the oxidation of unsaturated fats by atmospheric oxygen causes the formation of substances which impart to those fats a characteristic acrid odour, usually described as rancid." Rancidity, however, is difficult to define : some of its products (p. 671) are free fatty acids, aldehydes, ketones, and peroxides. Some substances having hydroxyl groups, such as wheat germ and other vegetable oils, retard rancidity and so protect vitamin E, but ultimately wheat germ oil itself becomes rancid. The fats commonly used in food are auto-oxidizable in the following order : cod-liver oil, lard, butter. Margarine is compounded of sundry fats and hydrogenated oils : far from destroying vitamin E it may even possibly be a good dietetic source, though it has many nutritional disadvantages.

From the point of view of the diets used to produce muscular dystrophy