There is no general agreement regarding the assessment of disease activity in CD. The clinical index most frequently used is the Crohn’s Disease Activity Index (CDAI), but its value is widely disputed. Most studies continue to use the CDAI because of the lack of a better index. Many complications of CD elevate the CDAI yet do not reflect active inflammation (4); this was illustrated by the increased stool frequency after small-bowel resection observed in our study. As we pointed out, all patients had stable body weights, no significant acute phase response (ie, normal C-reactive protein values), and no change in medication during the 3 mo preceding the study. This indicated that the patients included in the study were clinically in remission.

Capristo et al suggested that patients with and without small-bowel resection should not be pooled to study nutritional or metabolic changes. However, we were interested in the nutritional status of a representative sample of patients with long-standing CD. Exclusion of patients with small-bowel resections would have greatly impaired the clinical value of such a study. Second, in our opinion there is no essential metabolic difference in small-bowel function between patients with small-bowel resections and those in whom a small-bowel segment has been destroyed as the result of a previous inflammation. In both cases, small-bowel function is impaired, eventually resulting in malnutrition.

In our study, absolute daily fat intake was not significantly different between CD patients (35.1% of energy intake) and matched control subjects (33.6% of energy intake). Patients were clinically in remission and were not anorexic, in contrast with the patients in the study of Rigaud et al (5) who lost weight and reported decreased food intake. Although we did not measure energy metabolism directly, the patients in our study were presumably in energy balance because they all had stable body weights during the 3 mo preceding the study. This indicated that the energy expenditure in these patients because this may further our understanding of the pathophysiology of malnutrition in CD. Because of possible differences in daily total energy expenditure between patients and control subjects as a result of quantitative and qualitative differences in daily activities, the predictive value of resting energy expenditure measured by indirect calorimetry is limited. Hence, in this respect, the doubly labeled water technique seems to be the most adequate method (6).

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REFERENCES

My valedictory on the differences in biological potency between RRR-α-tocopherol and all-rac-α-tocopherol acetate

Dear Sir:

The paper by Burton et al (1), a collaborative study from 4 institutions, dealt with the relative biological values of RRR-α-tocopherol acetate and all-rac-α-tocopherol acetate, the 2 forms marketed in terms designated by the US Pharmacopoeia (2) as dl-α-tocopherol acetate and all-α-tocopherol acetate, respectively. On the basis of an assay in pregnant rats, 1 mg of the natural form RRR-α-tocopherol acetate is officially considered to have 1.36 times the activity of 1 mg of the synthetic product all-α-tocopherol acetate. The excellent studies by Burton et al make use of deuterium labeling to show that when RRR- and all-α-tocopherol acetate were fed, amounts of RRR-α-tocopherol in the tissues of human subjects were much higher than amounts of all-α-tocopherol. Burton et al concluded that the present official ratio of the biological activity of RRR-α-tocopherol acetate to all-α-tocopherol acetate of 1.36:1 is erroneous. The last sentence of their report reads, “It seems highly improbable that the official biopotency ratio is relevant to human needs, which might be better served by thinking in terms of a 2:1 ratio, as was first suggested 18 y ago in this Journal” (3).

The relative biopotency of RRR- and all-α-tocopherol acetate has been controversial for many years. Very little vitamin E is required by adults (<8 mg/d) to prevent nutritional deficiency, and nutritional deficiency is rare. As an antioxidant, however, much more tocopherol is recommended to inhibit undesirable free radical reactions in the tissues. The current conflict regarding the relative potency of tocopherol compounds has produced strong disagreement that makes an interesting story, which I will try to summarize.

The original protocol of the fourth Elgin Project (4) sponsored by the Food and Nutrition Board of the National Research Council [the first 3 projects (5) dealt with thiamine, riboflavin, and niacin-tryptophan] was designed to determine whether vitamin E was required by humans. No consideration was given in the original protocol to use all-rac-α-tocopherol acetate because almost pure RRR-α-tocopherol acetate was already available. After some of the subjects had been consuming a controlled diet that contained <4 mg total tocopherols/d for 54 mo, the sponsoring committee approved supplementation of the remaining subjects. Two members of the committee insisted, against my preference, that the effects of all-rac-α-tocopherol acetate as well as RRR-α-tocopherol acetate be included in the study. Unexpectedly, the data obtained during 138 d of supplementation (6) showed that 15 mg RRR-α-tocopherol acetate and all-rac-α-tocopherol acetate are not equal. When RRR-α-tocopherol acetate was administered to volunteers in a double-blind manner, significantly higher plasma RRR-α-tocopherol levels were observed than when all-rac-α-tocopherol acetate was used (7). As the quantities of the components of tocopherol acetate were the same in both forms, the differences in activity are due to the synthetic tocopherols.

The data from the present study were not collected in the context of a clinical trial, and therefore lack the rigour to draw final conclusions. However, it is clear that the relative biopotency of tocopherol acetate is not a simple matter. Further research is needed to clarify the reasons for the differences in biological efficacy of the tocopherols.
pheryl acetate/d resulted in higher plasma concentrations than did 20 mg all-rac-a-tocopheryl acetate and that 50 mg RRR-\(\alpha\)-tocopheryl acetate/d had much greater biological potency than 80 mg all-rac-\(\alpha\)-tocopheryl acetate. To avoid controversy, I presented no analysis of these data in my summarizing presentation at a symposium on the role of vitamins in October 1959 (6). About 20 y later, when consumer use of vitamin E had grown considerably, I decided to report the data obtained after supplementation in greater detail (3).

To evaluate the conflicting evidence, a committee was organized by FT Perkins, who was then Chief of Biologists at the World Health Organization. We met in Geneva in April 1981. In this meeting, the animal assays were given preference over data obtained in humans and no agreement was reached. Convinced that the human data were different from the data derived from experiments in pregnant rats, Coy Fitch, I, and others conducted a definitive experiment in 1983 on 20 healthy men and women (7). The design of the experiment was such that each of 5 different vitamin E compounds in gelatin capsules was tested sequentially in each of the subjects. Briefly, the subjects ingested 800 IU of a tocopherol compound plus 100 mL whole milk and serum tocopherol concentrations were measured at 0, 8, 24, and 48 h. The total lipid content of each serum sample was also measured because lipid concentrations strongly affect tocopherol concentrations in the blood (8). The protocol was blinded as much as possible. An experienced technician performed the analyses in a different department. Tocopherol concentrations in the 24-h serum samples increased twice as much after ingestion of RRR-\(\alpha\)-tocopheryl acetate than after ingestion of all-rac-\(\alpha\)-tocopheryl acetate. The largest difference between the 2 compounds was found in samples obtained 8 h after ingestion. Incidentally, RRR-\(\alpha\)-tocopherol was absorbed faster than the acetates and higher concentrations were sustained in the serum, confirming previous studies in the literature.

The findings of Burton et al (1) should end the debate about the biological potency of the 2 vitamin E compounds most commonly purchased. Now in my 90th y, I doubt whether I will ever see the proper correction made in the official values of the tocopherols. Having introduced the term equivalent as used by committees of dietary allowance (9), I prefer that this designation be used to describe the potency of the tocopherols. In the recommended dietary allowances (10), 1 mg RRR-\(\alpha\)-tocopherol has a biological value of 1.0 \(\alpha\)-tocopherol equivalents. Accordingly, in modified US Pharmacopeia vitamin E units, RRR-\(\alpha\)-tocopherol should have a value of 1.0, all-rac-\(\alpha\)-tocopherol a value of 0.5, RRR-\(\alpha\)-tocopheryl acetate a value of 0.91, and all-rac-\(\alpha\)-tocopheryl acetate a value of 0.455.

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REFERENCES


Dietary determinants of iron homeostasis

Dear Sir:

A considerable amount of research over the past 50 y has contributed to our knowledge of iron bioavailability, particularly our understanding of the dietary determinants or variables that influence the iron status of individuals and populations. Studies of iron bioavailability have progressed from studies of single foods to studies of mixed meals and more recently of dietary intake over a given time period (1). The paper by Fleming et al (2), as stated in the accompanying editorial (3), is indeed a valuable contribution to this recent emphasis on the dietary determinants of iron homeostasis over prolonged time periods. Contrary to the findings of most earlier reports, dietary modulators of iron bioavailability influenced the serum ferritin concentration, one of the indexes of functional iron metabolism. The study, I suppose, brings to bear the concept of adaptive responses to iron absorption, metabolism, and balance. The subjects studied were a group of elderly, iron-replete persons whose dietary patterns varied. Iron homeostasis is known to be regulated by absorption from the gastrointestinal tract (4), in which absorption is inversely related to the stores of iron in the body. Consequently, iron bioavailability in humans can be adapted and regulated within a wide range of intakes to establish and maintain healthy iron status, particularly when the diet is varied. As adulthood is attained and in the elderly chosen for study, the physiologic demands for iron are minimal and adequate iron is absorbed to prevent iron deficiency (4) and maintain positive iron balance.

The authors stated 3 reasons that could account for the lack of correlation between dietary modulators and serum ferritin concentrations in previous studies: the need to take into account J) confounders of serum ferritin values, 2) supplemental iron intake, and 3) small sample sizes. The disparities in the duration of the studies might also account for the differences observed. Although the earlier studies were usually for periods of 4–6 mo (5), the study by Fleming et al (2) lasted \(\approx 2\) y. The effects of dietary factors might therefore be compensated for initially by adaptive responses in the gastrointestinal tract. After a period of adjustment, sustained variables in dietary composition could then exert influences on serum ferritin concentrations.