

It is also known that polyunsaturated fatty acids, tocopherol and selenium have definite interrelationships in cellular metabolism. Polyunsaturated fatty acids, in general, increase the pathologic response to tocopherol deficiency. This is presumably owing to the oxidatively labile and antioxidant properties of the polyunsaturated fatty acids and tocopherol, respectively. Recently, Witting and Horwitt<sup>11</sup> have indicated that fatty acids containing more than four unsaturations, such as pentaenes and hexaenes, also will accentuate tocopherol deficiency states in the rat. Interestingly, the docosahexaenoic acid contained in cod liver oil may or may not be identical to the docosahexaenoic acid found in mammalian tissue.<sup>11,12</sup>

If muscular dystrophy is concerned with the inability to form the more unsaturated fatty acid(s) from arachidonic acid through the mediation of tocopherol, then unessential polyunsaturated fatty acids might be expected to augment tocopherol deficiency by a competitive mechanism even in the presence of adequate biological antioxidant activity other

<sup>11</sup> WITTING, L. A. and HORWITT, M. K. Effect of degree of fatty acid unsaturation in tocopherol deficiency-induced creatinuria. *J. Nutrition*, 82: 19, 1962.

<sup>12</sup> MARKLEY, K. S. Fatty acids. Their chemistry, properties, production and uses. New York, 1960. Interscience Publishers, Inc.

than vitamin E cofactor activity. Excessive intake of the essential fatty acids, linoleic and arachidonic acid, would cause utilization of tocopherol as an antioxidant in the absence of adequate biological antioxidant activity, thereby accentuating the tocopherol deficiency. Fatty acids of the hexaene and pentaene series, structurally different from those synthesized in mammalian tissues, could interfere with the further desaturation and chain lengthening of arachidonic acid to docosahexaenoic acid. Thus, the metabolic defect occurring in muscular dystrophy might be the inability of the tissue to convert arachidonic acid into the more highly polyunsaturated fatty acids such as  $\Delta$  4, 7, 10, 13, 16, 19-docosahexaenoic acid. In dystrophy cases of genetic origin, the enzyme may be incapable of performing its function adequately, whereas, in nutritional deficiency states, tocopherol or a derivative thereof becomes limiting for this specific system.

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## Chorionic Gonadotrophin in the Treatment of Obesity

Dear Sir:

May I refer to the article entitled "The Use of Chorionic Gonadotrophin in the Treatment of Obesity" by Capt. Barry W. Frank, MC, in your March 1964 issue.

This study shows that some obese patients (eight out of the author's series of forty-eight) can lose 20 to 30 pounds in fifty to sixty days on a 1,000 calorie diet with or without human chorionic gonadotrophin. This entirely negative result as regards the value of human chorionic gonadotrophin could have been predicted. The author's patients were kept on a

1,000 cal. diet (instead of 500 cal.) and 600 International Units of human chorionic gonadotrophin (instead of 875 I.U.) was given subcutaneously (instead of deep intragluteally) in doses of 200 I.U. three times a week (instead of daily doses of 125 I.U.). On such a regimen no action of human chorionic gonadotrophin on the reducing procedure can possibly be expected to appear.

For this there are two main reasons: (1) It is well known that about 80 per cent of injected human chorionic gonadotrophin is inactivated in the body within 24 hours; hence



the need for daily injections. This cannot be compensated by giving larger doses at longer intervals. Administering human chorionic gonadotrophin in such a staccato manner (Hormone Stoss) is extremely effective when used in gonadal disorders, particularly in hypogonadism, but this is quite unsuitable as a method of reproducing the uninterrupted physiological action of human chorionic gonadotrophin in pregnancy and it is just this action, as yet only vaguely understood, which I have found of greatest help in treating obesity.

(2) Most obese patients can get along comfortably on a 1,000 cal. diet without further assistance, but this is certainly not the case when the average obese patient going about his usual occupation is kept for periods of up to seven weeks on a diet of strictly 500 cal. only. Occasionally one does encounter a very determined patient who is able to do this, but only with considerable discomfort. Yet when human chorionic gonadotrophin in the correct dosage is added to this diet, there is not only no discomfort, but at least 80 per cent of patients who have been hardened crash dieters for many previous years spontaneously express enthusiasm over the unexpected ease and well being with which they can follow this regimen.

Glancing over the author's charts one notices that of his forty-eight patients twenty-seven (56 per cent) lost less than his mean of 12 pounds, and that among these patients ten (20.8 per cent) lost less than 5 pounds. This suggests that his relatively high mean loss is due to the eight cases (16 per cent) in which the loss was exceptionally high (20 to 30 pounds). I think that most workers in the field of obesity would agree with me that obese patients strictly observing a 1,000 cal. diet for fifty to sixty days can be expected to lose more than a mean of 12 pounds.

The conclusion must then be that in the majority of cases in the series the diet was not strictly maintained. (See also my Letter to the Editor criticizing the article by Craig et al., *Am. J. Clin. Nutrition*, 12: 230, 1963, in the September 1963 issue of the *Journal*, p. 197.) If the twenty-seven cases in which loss was minimal, presumably due to faulty dieting, are excluded from the author's charts, the mean

loss for the remaining ten cases in which placebos were given works out to 19.4 pounds, and for the eleven remaining cases in which human chorionic gonadotrophin was given to the almost identical figure of 19.3 pounds. This can be considered a reasonable mean loss in patients dieting rather carefully on 1,000 cal. for fifty to sixty days.

For the purposes of comparing these figures with our own results, we picked from a card index in which all patients treated for obesity are arranged alphabetically by surnames, the first 500 consecutive cases in which there was at least twenty days of treatment. On analyzing the case sheets we found that the group was composed of 122 males and 378 females who ranged in age from eleven to seventy-eight years. The mean age was forty-one years. The degree of overweight above statistical norms ranged from 4.5 to 234 pounds. The mean overweight was 42 pounds. On the twentieth day of treatment the loss of weight ranged from 2.3 to 35 pounds and the mean loss was 16.94 pounds. Only seven patients lost less than 10 pounds (1.4 per cent) and only fifteen (3 per cent) lost more than 25 pounds, showing that the remaining 478 patients (95.6 per cent) clustered very closely around the mean loss of 16.94 pounds in twenty days.

Obviously we have extensively checked our results against patients receiving a placebo but only few were able to adhere to the diet for twenty days and in these cases we always found wide variations in the observance of the diet, producing results quite comparable to those of Capt. Frank. Never were we able to produce uniformity of weight loss.

We share the author's regret that we have so far been reluctant to report blood chemical studies. This is because—as more and more workers are pointing out—our present knowledge of metabolic processes in obese subjects and their reaction to underfeeding is still scanty. We have found it impossible to draw any useful conclusions for or against human chorionic gonadotrophin from such studies. For the moment, therefore, we must content ourselves with hard clinical evidence and plausible hypotheses. What has, however, been



accomplished (Politzer et al. Biochemical changes resulting from drastic weight loss. *South African M. J.*, 37: 151, 1963) is to show that a 500 cal. diet with or without human chorionic gonadotrophin does not bring about any significant biochemical changes.

To what extent the psychologic effect of seeing the treating physician, being weighed and having an injection daily plays a role in our procedure is difficult to assess, because the suggestability of patients varies so widely. On the other hand, since our results are so uniform, we have not, in many years and in close cooperation with a clinical psychiatrist, been able to convince ourselves that the daily visit is an important therapeutic factor in patients receiving human chorionic gonadotrophin, although it may have some deterrent effect on a few patients who cannot resist the temptation occasionally to transgress. However, we do find that such patients cheerfully

confess a *lapsus linguae* when confronted with a gain of a few ounces. If further studies should prove us to be wrong in this view, the extra work involved would then be most rewarding.

Our results are decidedly better than any we have hitherto found published elsewhere. Since obesity is a major health problem, we look for the day that a qualified and unbiased observer, who is experienced in the management of obesity, will come to Rome (perhaps under the auspices of your Society?) to check our figures, to study our cases and to familiarize himself with our technic and all its details. This knowledge could then be applied to his own cases, without introducing arbitrary deviations of his own invention. Only when this is accomplished in a large series of cases can the value of our method be definitely established.

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