

the M.R.C. at this time had a lively personal interest in nutrition.

The War left Mellanby a tired man. It was therefore a happy idea on the part of Vanderbilt University to invite him to Nashville as a visiting lecturer. This visit he hugely enjoyed. He returned to Britain relaxed and benevolent, with all his war-time troubles shed. As he himself said to the present writer: "They taught me how to laugh again."

With his retirement from the M.R.C. in 1949, he devoted his time to his old love, re-

search. At the M.R.C. Nutrition Laboratory, Mill Hill, which he himself had done so much to create, he died suddenly on Sunday, January 30, having been engaged in an experiment an hour before.

He is survived by his wife, Lady May Mellanby, who herself has made important contributions to the study of nutrition, notably in connection with dental health.

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Scotland

Letter to the Editor

IN REPLY TO COMMENTS IN *Nutrition Reviews*

Dear Sir:

A recent report from this laboratory (J. CLIN. NUTRITION 1: 224, 1953) was the subject of comment¹ which, it seems to us, may lead to misunderstanding unless the points raised are specifically answered.

The writers of the review¹ infer that adequate nutrition in terms of good muscle mass, nitrogen equilibrium, or weight equilibrium, is impossible on diets containing only protein and fat. In Figure 1 is shown a long-term balance study in an elderly male who was maintained for more than six months on a formula diet in which the caloric sources were entirely protein and fat. Without any hormonal therapy, nitrogen and weight equilibrium were achieved, followed by weight gain and positive nitrogen balance during the administration of anabolic steroid hormones. These and other similar data are included in papers dealing with the evaluation of specific anabolic steroids and with pituitary growth hormone.^{2,3}

Regarding the statement in the review: "The palatability and the practicability of a high fat-high protein diet has been repeatedly examined with human subjects, and in each instance found unsatisfactory"—there is no question that a diet containing only protein and fat would have little to recommend it,

from the standpoint of palatability. Fortunately, the presence of amounts of carbohydrate sufficient to provide for palatability are still thoroughly compatible with major falls in serum cholesterol when suitable mixed diets are used. By way of illustration of this statement, in Figure 2 is shown the change in serum cholesterol and phospholipids in a severely diabetic patient maintained on a mixed diet containing large amounts of vegetable fat, who over a period of about one month had a decrease in serum cholesterol levels of approximately 400 mg per 100 ml.

It has been said that physical intolerance, with ketosis, rather than anorexia, prevents the success of this diet. In Figure 3 is shown a study designed specifically to bring out the "antiketotic effect of protein" under quantitatively controlled conditions on the metabolic ward. From this it is apparent, as one would expect in view of the relatively small amount of carbohydrate necessary to "turn the metabolic wheel," and the amount of carbohydrate which can be derived from protein, that protein would be a perfectly satisfactory substitute for carbohydrate in an antiketotic sense, so long as one has a proper balance of protein and fat.

Also not mentioned in the review was the fact that Ahrens *et al.* at the Rockefeller Institute have fully confirmed our observations regarding the profound decrease in serum cholesterol and phospholipids in patients maintained on high intake of vegetable fat.^{4,5}

More recently further confirmation has come from Beveridge *et al.*⁶ Whether the decrease in serum cholesterol, which one can obtain predictably with a high vegetable fat, nutri-

a fall in cholesterol as the formula diets, contain no added emulsifying agents of any sort. Further, in Figure 4 is a study in which precisely the same emulsifier was added to for-

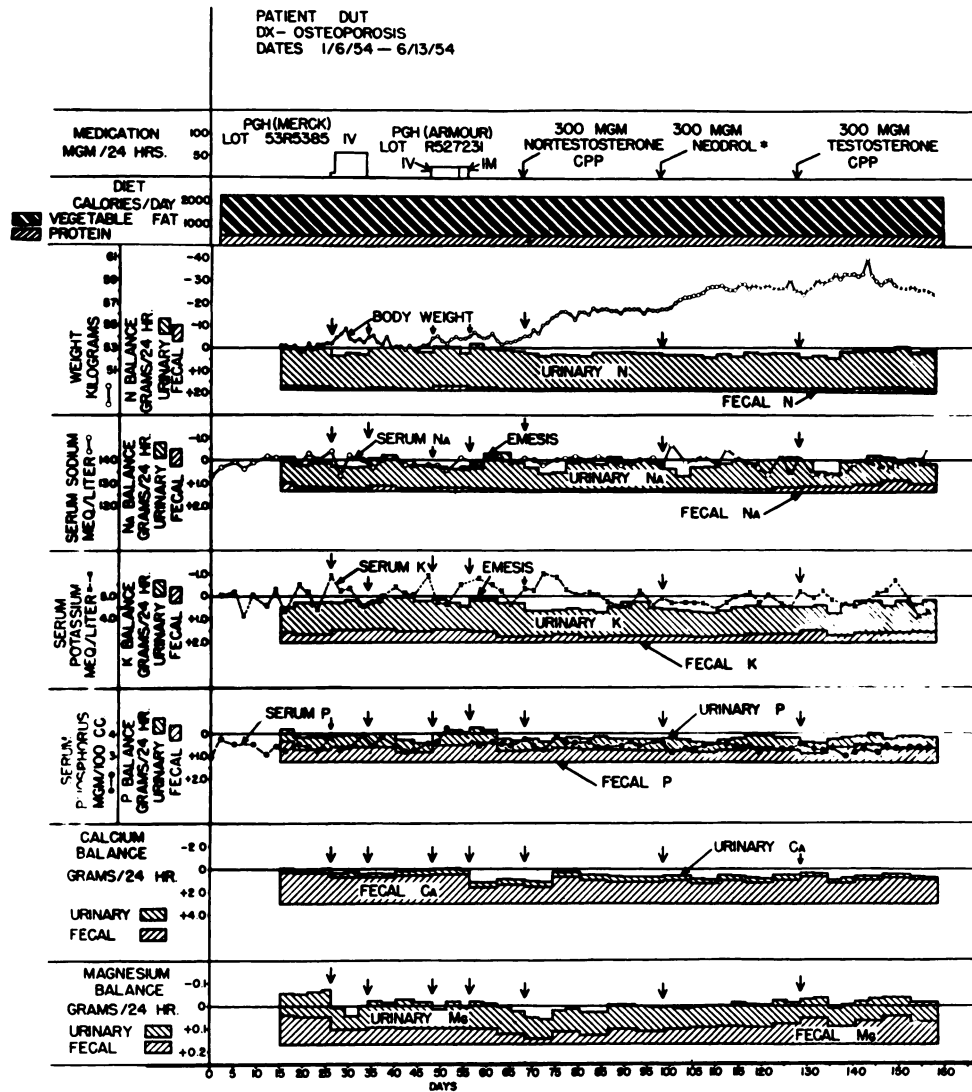


Fig. 1. Balance studies using formula diets containing only protein and fat (supplemented with essential vitamins and minerals).

tionally adequate diet, is good, bad, or indifferent for people with vascular disease, only a great amount of time and work will determine. We have been at some pains to point this out.

As to the comments in the review regarding Tween-80, cerebroside, etc., it is obvious that the mixed diets, which will produce as great

mulae containing identical amounts of protein, fat, and carbohydrate, the fat at different periods being of animal and vegetable origin, respectively. The differential effects produced by the two sources of fats, in regard to serum cholesterol, require no comment.

The method used for determination of plasma cholesterol is that of Michaels.⁷ In

Figure 5 are shown random plasma determinations compared with "classical" Schönheimer-Sperry determinations on the same plasmas. Except for the final colorimetry, the methods

metabolism. It is entirely possible that both factors may play a part.

3. We, in common with everyone else, are still unable to say with any certainty that a

PATIENT-FAW AGE- 37
 DX- DIABETES MELLITUS
 DATES 7/21/54 — 9/27/54

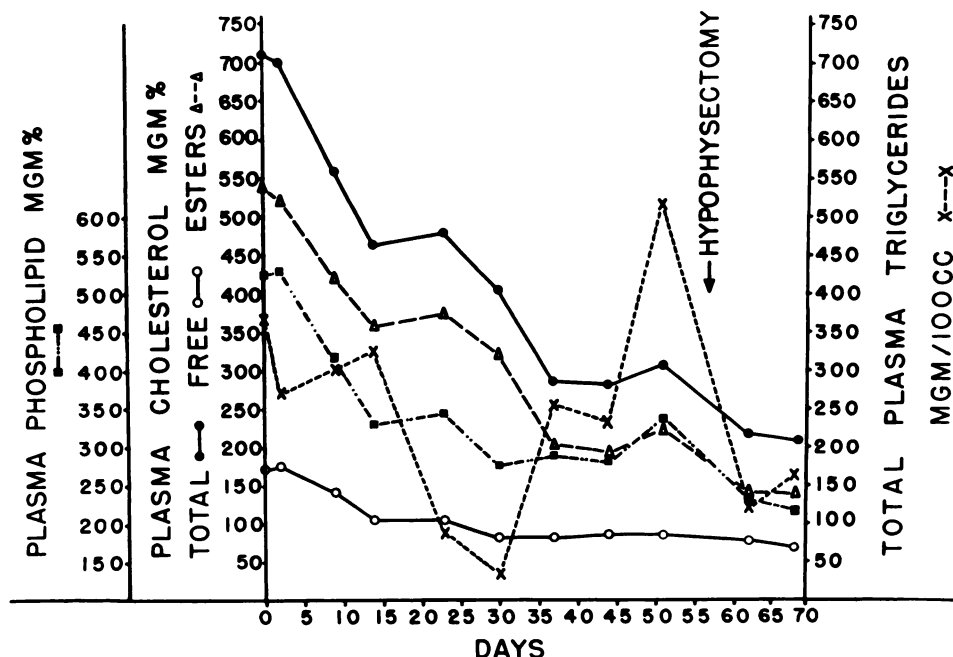


Fig. 2. Fall in serum lipids on non-formula, high vegetable lipid diet.

are essentially identical. The Michaels procedure in this regard appears to have certain advantages.

We wish to summarize our present views again.

1. Formula and mixed diets containing large amounts of vegetable fat consistently and predictably produce a profound fall in serum cholesterol and phospholipids, as compared to the levels obtained with diets containing equal amounts of fat of animal origin.

2. We are still unable to explain the mechanism of this differential effect. It is probable that the lack of cholesterol in vegetable fats is in a measure responsible. Some of the data, however, suggest the possibility that vegetable fats contain some substance(s) which have some specific effect upon cholesterol

low blood cholesterol is good, bad, or indifferent insofar as the production or progression of vascular disease in any given individual is concerned. Until we know more, however, it seems reasonable to us to accept the concept that a low or normal level is preferable to a high level.

4. On the basis of a rather vast number of observations, we can state without any hesitation that excellent nutrition can be maintained on formula diets containing only fat and protein (reinforced obviously with other essential nutrients, but free of carbohydrate), and with mixed diets which are high in fat and protein, and low in carbohydrate. We have yet to find a diet which can be considered in any sense of the word palatable which does not contain a reasonable amount

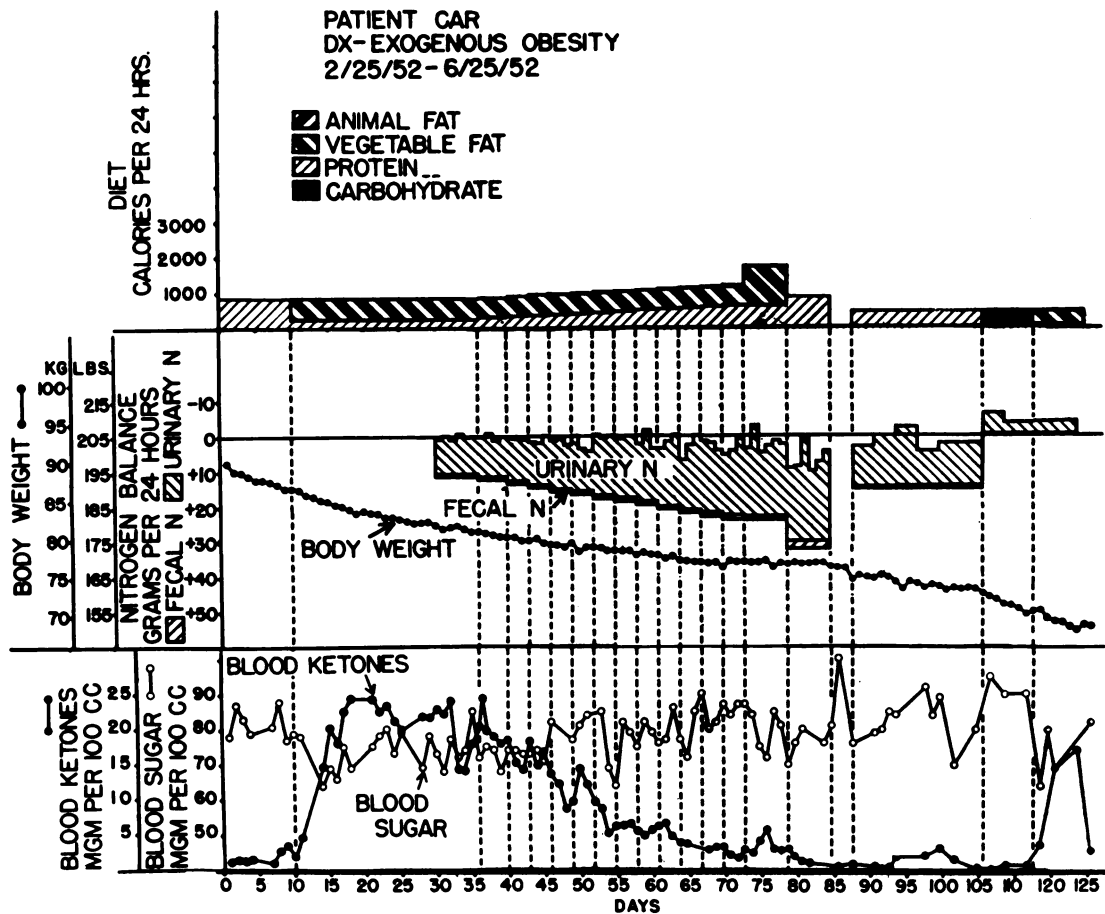


Fig. 3. Quantitative aspects of the antiketotic effects of protein. It appears in this patient (whose estimated daily caloric requirement was 1700 calories) that the amount of catabolized protein necessary to maintain a blood ketone level below 5 mg per 100 ml was of the magnitude of 125 g per day. This was so, essentially, regardless of the level of fat intake. However, when only protein was fed, less than 100 g of catabolized protein maintained comparable blood ketone levels.

This latter observation may indicate: (1) Greater efficiency of metabolism of endogenous as compared to dietary fat and/or, (2) Decreased total metabolism during the period of low calorie intake (days 87-106) with consequent decrease in the amount of fat catabolized; and, therefore, a decrease in the amount of non-fat calories necessary to "turn the metabolic wheel."



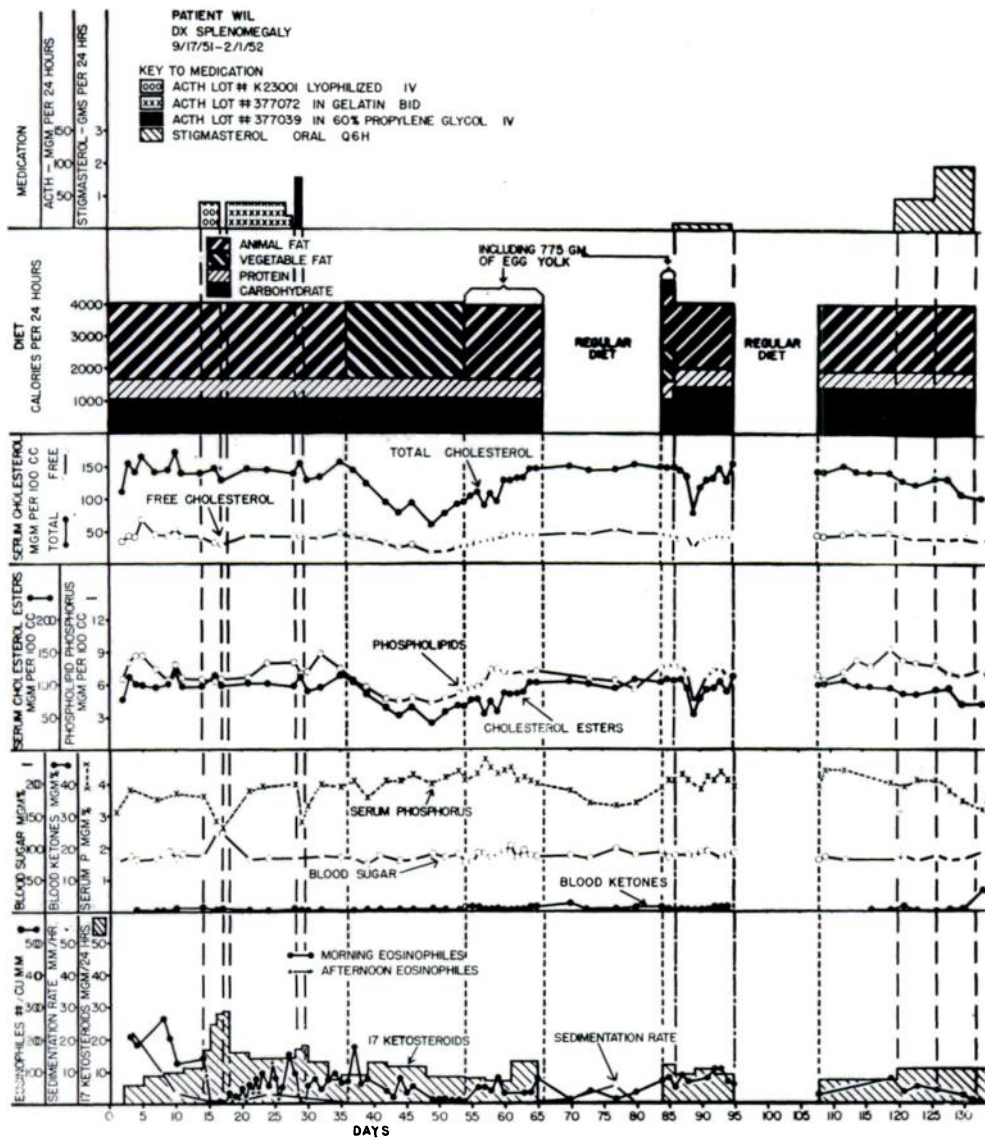


Fig. 4. Comparative effects of calorically equal amounts of animal and vegetable fat. The emulsifying agents were identical in each instance.

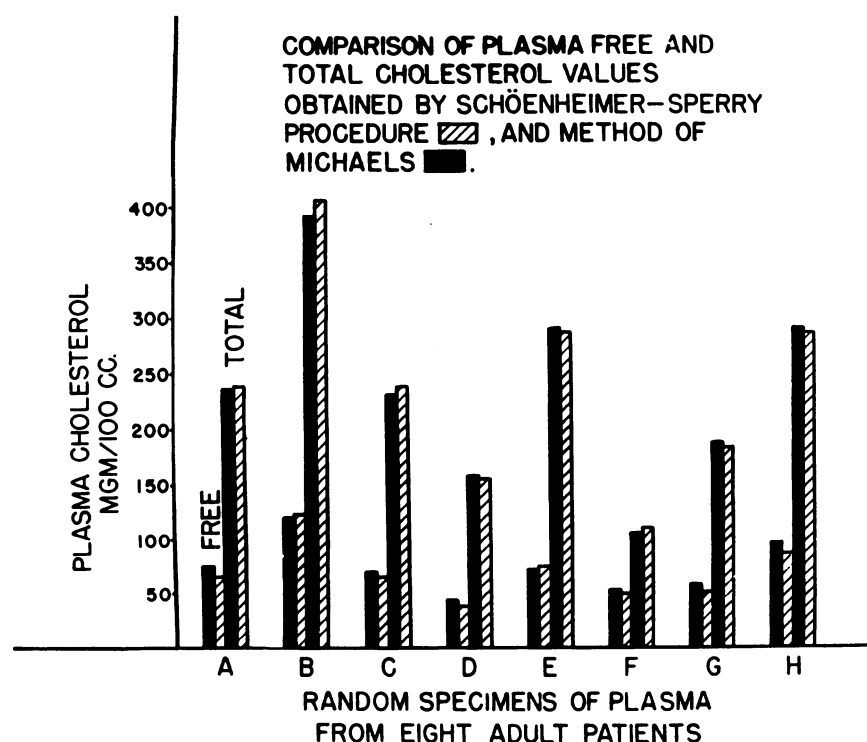


Fig. 5. Comparative free and total plasma cholesterol values, as determined by the Schönheimer-Sperry, and Michaels methods.

of carbohydrate. We do not expect to find such a diet, nor do we see any major reason to search for one.

5. Depending upon the amount of protein in the diet, patients may be maintained with little or no hyperketonemia on formulae containing only fat and protein as sources of calories. In other words, protein in sufficient amount is quite as efficient an antiketotic agent as is carbohydrate. In this connection, it may be well to point out that levels of blood ketones as high as 20 to 25 mg/100 ml are apparently compatible with excellent health. In the mixed high vegetable lipid diets used clinically in this institution, the blood ketone levels rarely exceed two mg/100 ml.

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ADDENDUM

A recent report by Best, Duncan, Wathen, VanLoon, and Shipley,⁸ as well as other previous reports, indicates that β -sitosterol will produce a fall in serum cholesterol, presumably by its inhibiting effect upon cholesterol absorption or re-absorption from the intestinal tract. In our hands, sitosterol as well as some other derivatives of vegetable fat have on occasion produced such an effect. Such changes, however, have not been consistent, and have never been of the magnitude noted during the administration of large amounts of vegetable fat.

Until recently, all of the vegetable fats which we have used have been high iodine number fats, e.g. soy, corn, and peanut oil. To determine whether the unsaturated fatty acid content of vegetable fat might have any bearing upon the lowering of plasma cholesterol and phospholipids, a comparative evaluation of vegetable fats of high, medium, and low iodine numbers has been carried out. As

shown in Figure 6, the effect upon the level of serum cholesterol and phospholipids appears to be related directly to the unsaturated fatty

acid content of the fat. Studies to determine the mechanism of this effect are now being undertaken.

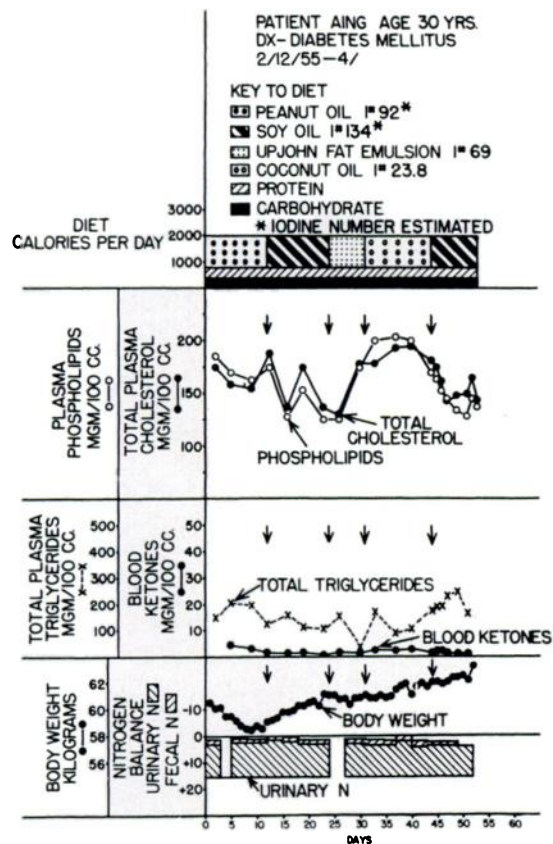


Fig. 6. Comparative effects of different vegetable fats upon the plasma cholesterol and phospholipids. From this study, it appears that the ability of vegetable fat to lower plasma cholesterol is associated with its unsaturated fatty acid content.

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