EFFECT UPON SERUM CHOLESTEROL *and* PHOSPHOLIPIDS *of* DIETS CONTAINING LARGE AMOUNTS OF VEGETABLE FAT

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The American Journal of Clinical Nutrition

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THE RELATIONSHIP of dietary constituents to the level of serum lipids and to the atherosclerotic process has been a subject of controversy for many years. It has been stated that not only dietary cholesterol *per se* is of importance in the determination of serum cholesterol levels, but that diets containing little or no cholesterol but large amounts of fat will also result in relative or absolute elevation of serum cholesterol.[1-3]

The present study reports the findings in a group of patients studied on the metabolic ward and maintained on chemically constant formula diets over a prolonged period. Excepting only the "pure fat" diets, the patients were maintained in weight equilibrium and excellent nutrition including a positive nitrogen balance.

METHODS

In each instance the diet was administered as a formula, usually through a tube, the tip of which lay in the stomach or duodenum. Dietary composition was constant in a quantitative sense. Salad oil composed of cottonseed oil alone, or of mixed soy and cottonseed served as the source of vegetable fat. Calcium caseinate* was the protein source. The formulae were fortified with adequate amounts of minerals and vitamins.

Free and total cholesterol were determined by a modification of the method of Schoenheimer and Sperry.[4] Phospholipids were assayed by the method of Youngburg and Youngburg.[5] In most instances, protein balance studies were carried out simultaneously.

FINDINGS

The first patient so studied (Fig. 1) was maintained on a diet in which, for a period of 30 days, all of the calories were supplied in the form of an emulsion of vegetable fat. The primary purpose of the study was to determine the effect of corticotropin and cortisone upon certain aspects of fat oxidation.[6] In the course of this study, it was noted that a rather profound fall occurred in the levels of serum cholesterol and phospholipids, the greater portion of the cholesterol fall being in the ester fraction. Initially, it was assumed that this fall was referable to the co-administration of hormonal therapy.[7]

A later study, carried out in a patient with combined acromegaly and diabetes and maintained on a formula diet containing only fat and protein (Fig. 2), revealed a fall in total cholesterol from approximately 300 to 200

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This work has been supported in part by grants from the National Institutes of Health and the Armour Laboratories.

* Furnished through the courtesy of Mead Johnson and Company.

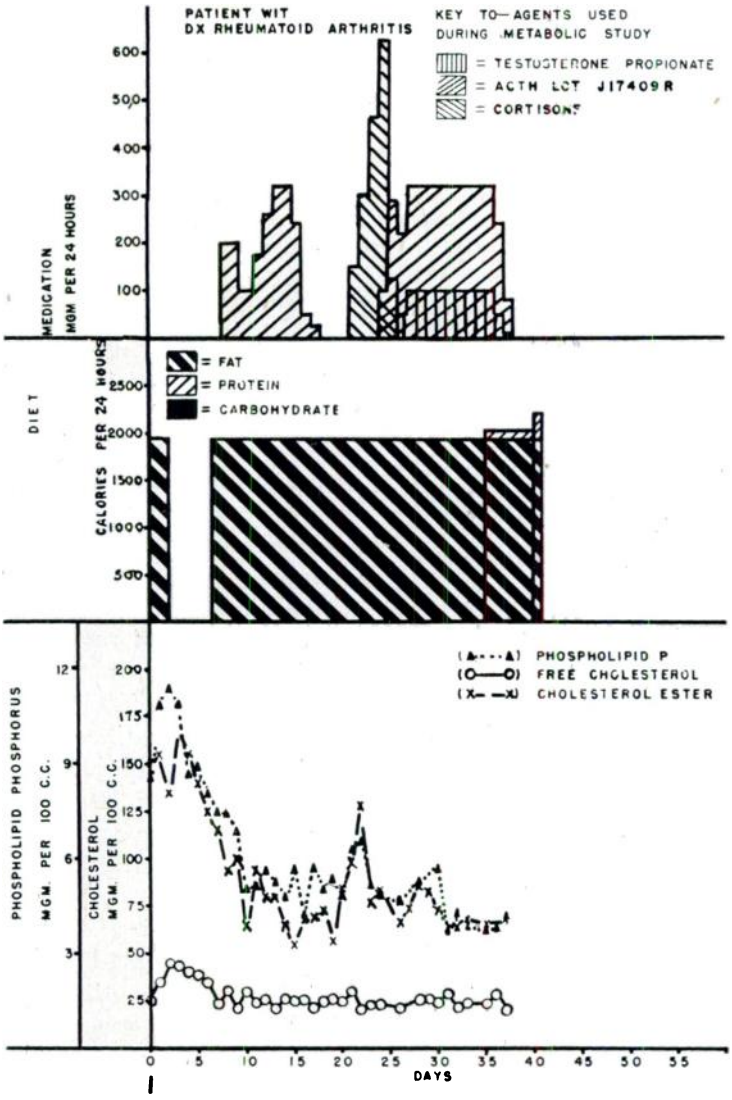


Fig. 1. Major fall in plasma cholesterol esters and phospholipids in a patient maintained on a "pure fat" formula intake. Initially it was assumed that ACTH therapy was responsible for this fall.

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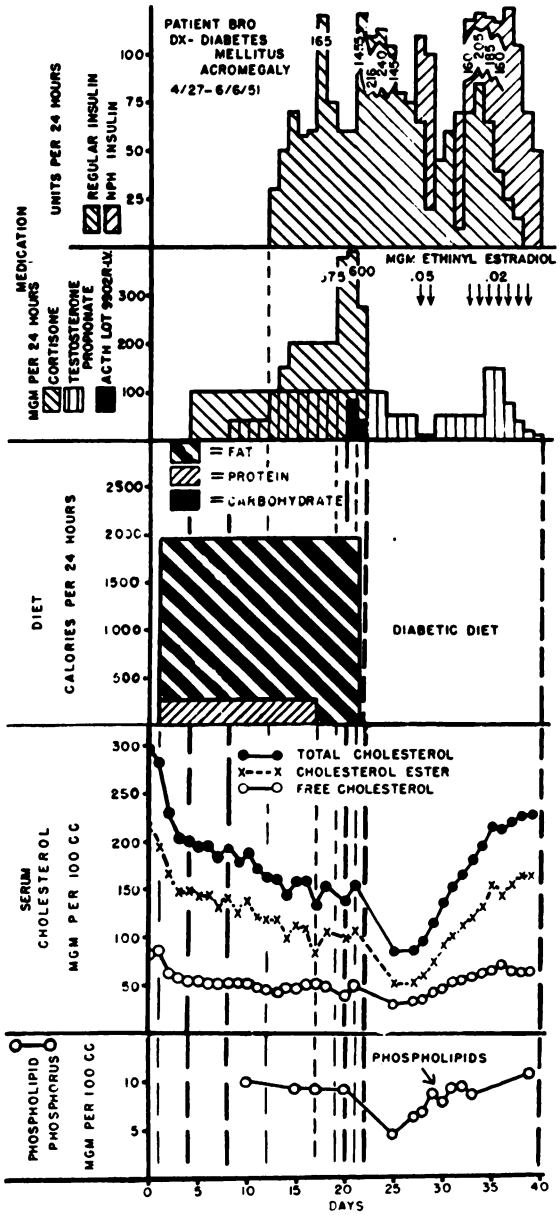


Fig. 2. Fall in plasma lipids during high vegetable fat intake. *The greater portion of the fall occurred prior to hormonal therapy.* A mixed diet resulted in return of lipids toward their previous levels.

mg. per cent in the space of four days, prior to the institution of any hormonal therapy. A further fall occurred with continuation of the diet and during the administration of hormonal therapy as noted in Figure 2. With resumption of a "standard" relatively high fat diabetic diet, and continuation of a portion of the hormonal therapy, the serum lipids rose toward the values which were obtained prior to the institution of the vegetable fat diet. This raised the question as to whether the formula diet *per se* might be responsible for the rather striking fall in cholesterol.

The next patient studied was maintained on an average mixed diet for a period of 15 days, after which the diet contained only fat and protein except for a brief period as shown (Fig. 3). With the institution of the high vegetable fat formula diet, her cholesterol levels fell from average values of 150 to average values of 75 mg. per 100 cc. The phospholipids behaved in a less constant fashion. The addition of as much as 60 Gm. daily of cholesterol to the diet resulted in no significant elevation of serum cholesterol, despite the absorption of approximately 50 per cent of the administered cholesterol (as indicated by determination of total digitonide precipitable sterols in the feces).

A study carried out in a patient with thyrotoxicosis, prior to the institution of any therapy and maintained on a formula diet which was compatible with excellent nutrition and weight equilibrium, resulted in a fall in serum cholesterol from average levels of approximately 120 mg. per 100 cc. to levels as low as 50 mg. per 100 cc. A proportional fall occurred in the phospholipids. With the resumption of a mixed diet, and despite continuation of hormonal therapy (which was instituted in the mid-portion of the study as shown in Fig. 4), the serum lipid levels rose to or above their initial value.

A similar study in a patient with untreated myxedema revealed a fall in serum total cholesterol from values averaging 220 mg. per cent to values below 100 mg. per cent. A comparable fall in phospholipids occurred (Fig. 5).

A later study in a patient maintained for a prolonged period of time on diets in which vegetable and animal fat were alternated in calorically equivalent amounts for specific periods, revealed findings comparable with the preceding, that is, a fall in cholesterol and phospholipids on the vegetable fat intake, and a rise to average levels on formula diets in

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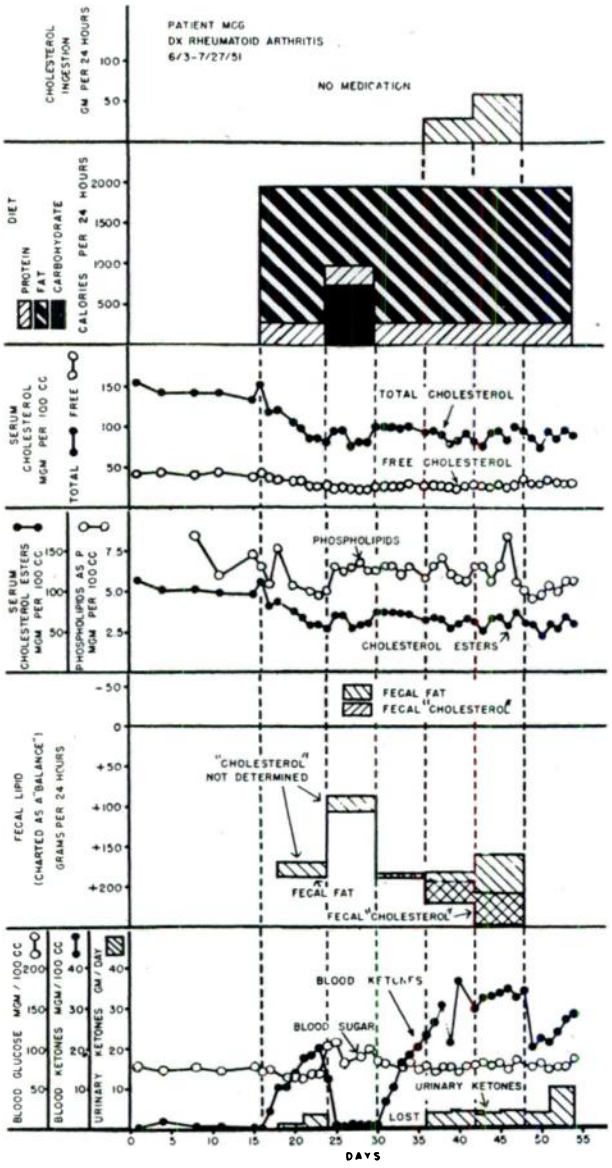


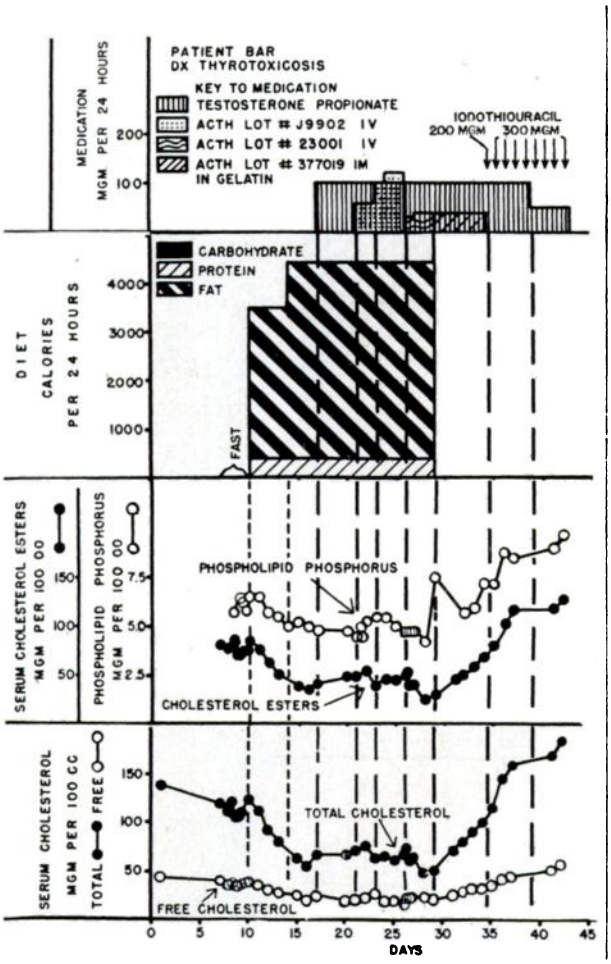
Fig. 3. Fall in serum lipids on high vegetable fat intake. Cholesterol administration caused no maintained elevation of lipids, despite evidence of absorption of approximately 50 per cent of the administered cholesterol (fecal "cholesterol" includes *all* digitonide precipitable lipids).

which the fat was entirely of animal origin. During a portion of this study the fat was derived entirely from egg yolk in an amount equivalent to 36 egg yolks daily. Normal but not supernormal levels of cholesterol occurred during the egg yolk feeding (Fig. 6).

More than twenty studies of the type noted above have been carried out on the metabolic ward in this institution. Included among the patients are relatively normal individuals, patients of the types noted above, and others with initial hypercholesterolemia in association with severe diabetes and with the nephrotic syndrome. A study in one such nephrotic is shown in Figure 7. A major fall in the cholesterol and phospholipids occurred on diet

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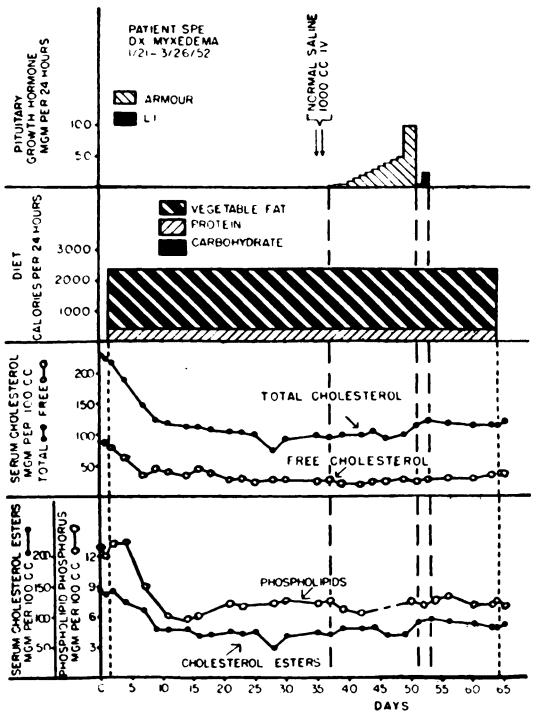


Fig. 4. (left). High fat diet-induced fall in plasma lipids in a hyperthyroid patient.

Fig. 5. (above). Fall in plasma lipids in a myxedematous patient during intake of a high vegetable fat diet.

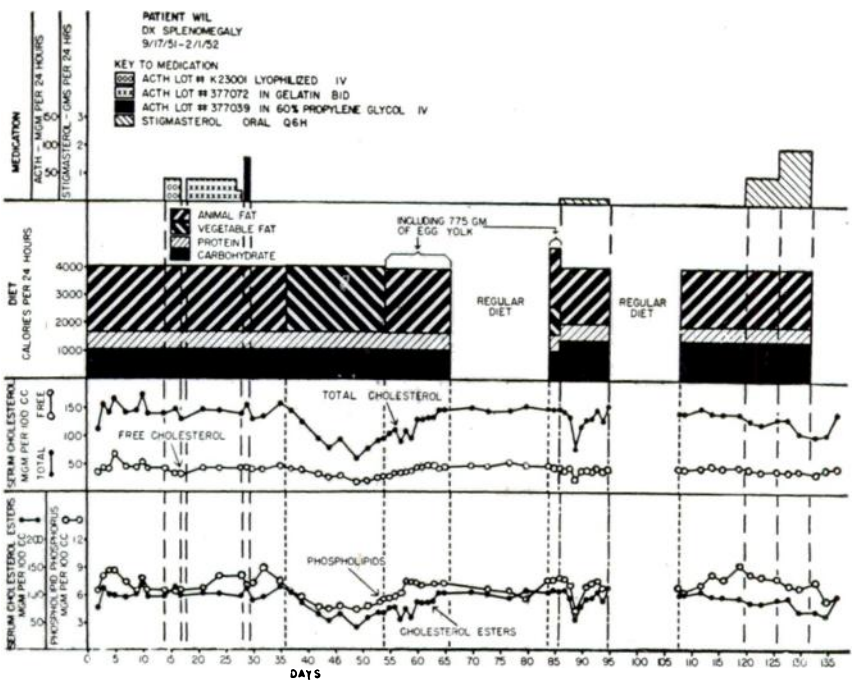


Fig. 6. Effects of calorically equivalent amounts of animal and vegetable fat upon plasma lipids. Egg yolk equivalent to 36 eggs daily did not result in "hypernormal" cholesterol levels. The effect of stigmasterol may or may not be significant.

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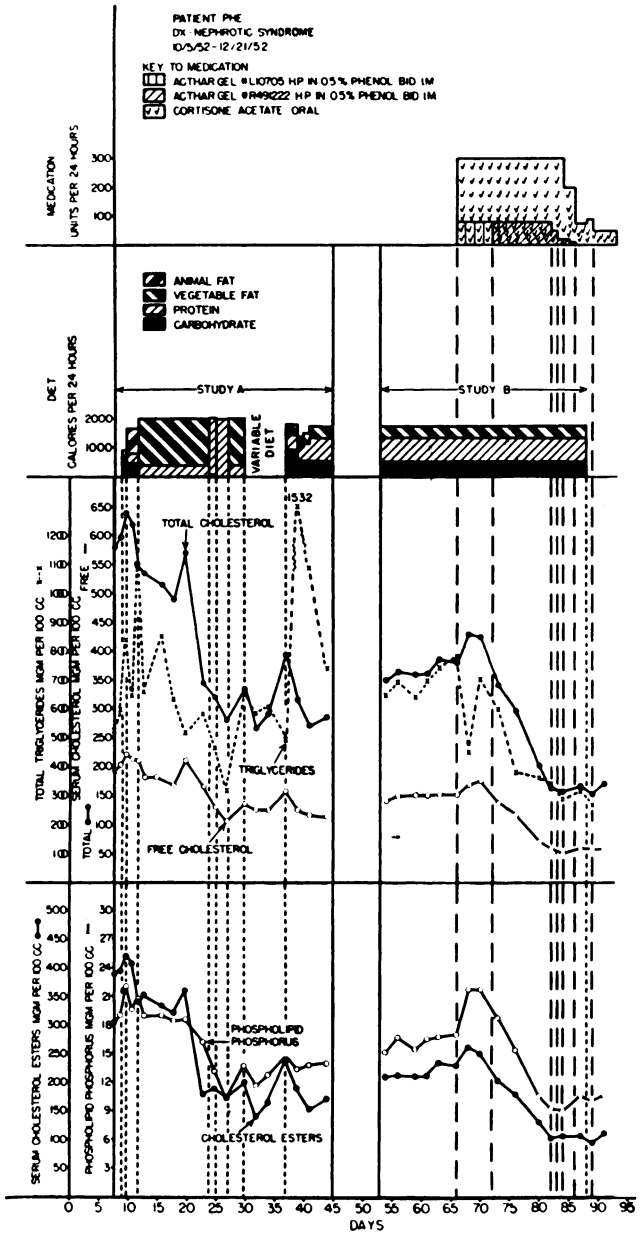


Fig. 7. Effect of a high vegetable fat diet upon a nephrotic patient with marked elevation of serum lipids. Because of the onset of nausea and vomiting, it was impossible to continue the high fat formula. It is of interest that during the diet-induced fall in serum lipids, no change in serum protein occurred; whereas, during the ACTH-cortisone-induced remission of the disease, a rise in serum albumin and a fall in serum globulin occurred in association with the decrease of serum lipids to normal levels.

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alone. Because of the appearance of nausea and vomiting, it was impossible to continue the high vegetable fat diet in this patient. The serum lipid values did not return completely to normal until the nephrotic syndrome was completely controlled with ACTH and cortisone therapy.

The findings in the severe diabetics with elevated serum lipids will be reported in detail in a separate communication. In all instances, the institution of diet high in vegetable fat and in protein has resulted in a major fall in cholesterol and phospholipids. The fall in the two entities has usually been proportional, although occasional exceptions to this have been noted.

Discussion

From the foregoing, it appears that patients maintained on chemically constant diets containing very large amounts of fat of vegetable origin, without exception have striking falls in plasma cholesterol and usually in phospholipids. The precise metabolic and clinical interpretation of these findings is by no means clear, but the following statements appear to be in order:

1. Formula diets containing large amounts of fat in which all of the fat is of vegetable origin (that is, essentially free of cholesterol) are associated with a profound fall in the serum lipids above noted. This would appear to refute the statements which appear in the literature that high dietary fat *per se* is always associated with relative or absolute elevation of serum cholesterol.

2. The reason for the fall in cholesterol and phospholipids under the conditions above reported is unknown. The following possibilities must be considered:

(a) The findings are referable merely to the lack of dietary cholesterol and phospholipids.

(b) Some component of the vegetable fat, possibly one or more of the vegetable sterols, has some direct or indirect effect upon cholesterol and/or phospholipid metabolism. Peterson has reported that the administration of soybean sterols has such an effect, but feels that the mechanism is largely one of interference with absorption.[8]

(c) Some other component of the fat formula is responsible for the observed effect. In this connection it should be noted that the formula diets have been emulsified with either a cerebroside preparation,* or Tween 80® (polyoxyethylene (20) sorbitan monoöleate).† The effects observed, however, do not appear to depend upon the emulsifier which is used.

The above possibilities are currently under investigation.

Summary

The use of formula diets containing large amounts of vegetable fat has resulted consistently in a major fall in serum cholesterol and in phospholipids. Whatever the meaning of this observation, it is apparent that high dietary fat *per se* does not result in elevation of serum cholesterol.

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Resumen

Efecto de dietas ricas en grasas vegetales sobre el colesterol y los fosfolípidos séricos

El empleo de fórmulas dietéticas ricas en grasas vegetales ha resultado constantemente en un descenso importante de los niveles del colesterol y los fosfolípidos séricos. Cualquiera sea el significado de esta observación, es evidente que las dietas ricas en grasa no conducen por sí mismas a una elevación del colesterol sérico.

Cocktails and Calories

"Cider, wine, gin and cocktails must be forbidden: even a dull cocktail party may provide about three quarters of the entire day's ration of calories. For those whose business leads them to bars and dinners, tomato juice—that most repellent of all drinks—seems to be accepted as a 'good fellow' drink. While at parties beer surreptitiously used to replace sherry in a sherry glass can camouflage the social solecism of sobriety."
—F. Bicknell. *The Medical Press* 228: 493, 1952.

Meat Exonerated

"The conviction is more widespread than one might think that meat causes vascular diseases, arterial hypertension, intoxications and uremia.

"This is at variance with scientific reality: the newer concepts of the pathogenesis of arteriosclerosis, in fact, attribute much greater importance to lipid metabolism, especially to cholesterol levels, than to protein metabolism. It may be recalled here that the much vaunted vegetarian diet is no protection against vascular sclerosis, to judge from the diffusion of this disease among the Hindu population which lives solely on milk, eggs and cereals, and among herbivorous animals like the horse.

"Nor is it true that meat, in proper proportions, is any more responsible for intoxications than other animal proteins may be, and the treatment of arterial hypertension today depends more on a diet low in sodium than in proteins. It thus remains inexplicable that meat, and not fish, should be blamed for damage through an excess of uric acid, when both contain approximately the same amount of uric acid; sardines, in fact, are richer in it."
—D. Jasonni. *Archivio Italiano delle Malattie dell'Apparato Digerente* 18: 294–295, 1952.

The Original Description of Rickets

The Signs which belong to the disproportioned nourishment of the parts.
First, there is an unusual Bigness of the Head.
Second, the fleshy parts are daily more and more worn away.
Third, certain swellings and knotty excrescences are observed about some of the joynts.
These are chiefly conspicuous in the wrists, and somewhat less in the ankles. The like tumors also are in the tops of the Ribs, where they are enjoyned in the gristles in the Breast.
Fourthly, some bones wax crooked, especially the bone called the shank bone, and the Fibula or small bone of the leg.
Fifthly, the Teeth come forth both slowly and with trouble.
Sixthly, the Breast in the higher progression of the disease becomes narrow on the sides.

—Francis Glisson (from *De Rachitide*, Batavia, 1650)

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