

Ahrens E H, Jr., Hirsch J, Insull W, Jr., Tsaltas T T, Blomstrand R & Peterson M L. The influence of dietary fats on serum-lipid levels in man. *Lancet* 1:943-53, 1957.
[Rockefeller Institute, New York, NY]

This paper reported the first long-term metabolic-ward studies in which precisely controlled exchanges of various fats demonstrated that serum cholesterol levels could be lowered significantly by fats rich in polyunsaturated fatty acids and raised by saturated fats. [The *SCI*[®] indicates that this paper has been cited in over 445 publications since 1957.]

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It was with great surprise that I read, in the spring of 1952, a short letter to the editor of the *Journal of Clinical Endocrinology* from L.W. Kinsell¹ in which he showed that cholesterol levels were markedly and rapidly lowered by substituting vegetable fat for animal fat in the tube-fed diet of a patient with splenomegaly. Older and more experienced colleagues (who shall now be nameless) doubted the wisdom of my troubling to explore this clue. Nevertheless, we took the gamble and in 1954 reported a full confirmation of Kinsell's finding: for six months we studied six patients on the metabolic ward and on solid-food diets. Their cholesterol levels were down on vegetable fats and up on animal fats when these were isocalorically exchanged.²

Our 1957 paper was a much more detailed description of novel methods as well as results: metabolic-ward techniques, patient selection, oral formula feeding, attainment of the metabolic steady state, dissection of methodologic from physiologic factors in analysis of serum lipid levels, and compositional data not then available in standard

texts on the 28 dietary fats we exchanged. Our laboratory was a busy place with the capability to cope with 6 to 10 metabolic-ward patients simultaneously. The development of new insights was sufficiently rapid to make our weekly research rounds very exciting.

This report, with confirmation from the laboratories of Beveridge, Bronte-Stewart, Kinsell, and Keys, sparked the undertaking of a series of prospective large-scale controlled trials at various other sites. Their goal was to test a proposition called the Lipid Hypothesis: that is, if the level of serum cholesterol is lowered, the incidence of new events of coronary heart disease will be reduced. The inconclusive results of these many trials did not disprove the hypothesis; rather, the designs of these studies are now considered to have been inadequate to the purpose.³

I recall with great pleasure the keen interest in this work of *The Lancet's* editor, Sir Theodore Fox; he not only tolerated, he encouraged the publication of an unusually long report heavy in chemical detail, in which the individual responses to 52 dietary fat exchanges in 40 patients were spelled out. Although we noted in 1957 that "these data show clearly the unpredictability of responses in individual patients to a given dietary fat intake," we failed at that time to see the full significance of that sentence, and only came to recognize its real implications 14 years later in studies of the several types of responses of patients to cholesterol feeding.⁴ Sadly, the importance of individual heterogeneity in the human species has been overlooked by those now recommending a single dietary approach (the AHA Prudent Diet) for the entire US population over the age of two years.⁵ The myopia of that recommendation is grounded in the tendency of many workers to focus on mean changes in study cohorts of whatever size, thus concealing the wide variations that individuals manifest to changes in regimen, be they pharmacologic or dietary.

1. Kinsell L W, Partridge J, Boling L, Margen S & Michaels G. Dietary modification of serum cholesterol and phospholipid levels. (Letter to the editor.) *J. Clin. Endocrinol.* 12:909-13, 1952. (Cited 300 times since 1955.)
2. Ahrens E H, Jr., Blankenhorn D H & Tsaltas T T. Effects on human serum lipids of substituting plant for animal fat in diet. *Proc. Soc. Exp. Biol. Med.* 86:872-8, 1954. (Cited 195 times since 1955.)
3. Ahrens E H, Jr. The management of hyperlipidemia: whether, rather than how. *Ann. Intern. Med.* 85:87-93, 1976. (Cited 85 times.)
4. Quintao E, Grundy S M & Ahrens E H, Jr. Effects of dietary cholesterol on the regulation of total body cholesterol in man. *J. Lipid Res.* 12:233-47, 1971. (Cited 160 times.)
5. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial Results. I. Reduction in incidence of coronary heart disease. *JAMA—J. Am. Med. Assn.* 251:351-64, 1984.