

April 11, 1972

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Donald T. Fredrickson, M.D.
Inter-Society Commission for
Heart Disease Resources
Suite 204
44 East 23rd Street
New York, New York 10010

Dear Doctor Fredrickson:

Thank you for sending me a copy of Dr. Oster's critique of the Report of the Inter-Society Commission for Heart Disease Resources.

I find Dr. Oster's critique to be specious, ill-informed, and tendentious. 1) He has chosen to ignore the fact that the general results at Framingham have been confirmed in other studies in the United States, notably in the Pooling Project, and in my own studies on some 10,000 men in Europe. 2) He chooses to make discrete classes out of the continuously distributed variable cholesterol. 3) He ignores studies on repeated blood samplings that number many-fold the 48 persons he studied twice. 4) He ignores or misunderstands analyses with multivariate methods. 5) He concludes that because there is uncertainty as to the precise value of the exponent in the exponential equation (where the value 2.66 was one approximation), there is no exponential relationship.

I am surprised at some of the discussion by Stephen Bauman, the consulting mathematician. Apparently he is unaware of the fact that the Walker-Duncan method to solve the multiple logistic gives almost identical results to those from the Truett-Cornfield method. But the Walker-Duncan method does not involve the assumptions that Bauman finds so alarming. I am also surprised at both Oster and Bauman in their efforts to reduce to an absurdity a descriptive equation because it looks wild at zero or infinite levels.

It is interesting that neither Oster nor Bauman comment on the critical point, normally that when cholesterol is reduced in mid or late life the relationship of the new cholesterol level to future risk may not be similar to the relationship that existed before the cholesterol level was altered. And no mention was made of the numerous dietary trials that have been reported over the last twenty years.


Dr. Oster notwithstanding there can no longer be any doubt that serum cholesterol, like arterial blood pressure, is an extremely important risk factor in the development of coronary heart disease. There is no indication that there is a critical level of "abnormal" versus "normal"; in all analyses the risk rises steadily and steeply with the cholesterol level. The perfect model for the relationship may not be the simple exponential with an exponent between 2 and 3 but the exponential is the best yet studied.

It should be mentioned, too, that everyone knows about intra-individual variability in serum cholesterol. So it is agreed that a single sample of blood is a shaky guide to the true average for the individual. What Dr. Oster fails to realize, however, is that the relationship found between coronary incidence and this rather poor estimate of the cholesterol must be an under-estimate of the true relationship.

Finally, Dr. Oster chooses to ignore the many well-controlled experiments on the effect of dietary changes on the serum cholesterol level in man. We do know the average cholesterol response to specified dietary changes though we do not know with certainty the effects of such dietary changes on life expectancy. Dr. Oster's statement in the next-to-last paragraph on p. 18 is grossly erroneous and misleading.

Medical Counterpoint has given space to an irresponsible article.

Sincerely,


Ancel Keys, Director

cao

cc H. Blackburn

May 20, 1974

Donald T. Fredrickson, M.D.
Inter-Society Commission for
Heart Disease Resources
Suite 316
44 East 23rd Street
New York, New York 10010

Dear Dr. Fredrickson:

I am enclosing a copy of the paper I presented at the Federation meetings and data on the trans fatty acid content of margarines. Various members of the margarine industry have been in contact with me since the Federation meetings and have pointed out that margarine contains varying amounts of linoleic acid which they believe may counteract the influence of the trans fatty acids in margarine base stock. The L/O ratio of the red blood cells indicates that the swine fed margarine base stock were not deficient in linoleic acid. However, it is possible that the presence of trans fatty acids in hydrogenated fats requires the presence of more linoleic acid than fats devoid of trans fatty acids. I tried to bring this out when I served on the sub-committee on dietary fats of the American Heart Association in 1968.

W. H. Schmidt, Director of Product and Development Division of Lever Brothers Company, told me that his company would be glad to provide a trans-free margarine fat. However, they would need to add palm kernel oil or coconut oil as a "hardening stock" and both oils carry a 10¢/pound duty. Fred Mattson told me that the industry doesn't have enough PUFA available to hydrogenate soybean oil completely and rearrange with corn or cottonseed oil. The reluctance of the industry to provide trans-free margarine is, therefore, complicated by political and economic factors.

Data of the ISC Report on Finland (Table 3) is of interest. I spent ten days with Drs Miettinen and Nikkila after the Third International Symposium on Atherosclerosis in Berlin last October and visited the Lever Brothers plant in Helsinki with Dr. Miettinen. Consumption data indicates that the people consume approximately one-half of their visible fat as margarine which has a very high trans and low linoleic acid content. This margarine is prepared from hydrogenated fish oil and rapeseed oil. I brought back five samples of blood for analysis; you will note that this blood contains C20:3 ω 9 and some samples approximately 5% trans fatty acids.

Donald T. Fredrickson, M.D.
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The Fleischmann corn oil margarine is prepared under contract as Standard Brands does not have a hydrogenation or margarine plant. It is high in trans fatty acids and low in C18:2 ω 6. I believe the industry will now take a serious look at trans fatty acids and help to determine whether a high level of linoleic acid will prevent completely the elongation and incorporation of trans fatty acids into cell membranes. I believe that the level of PUFA in margarines, shortenings and salad oils can and should be increased. It is unfortunate that some segments of the industry have taken advantage of incomplete data. One director of research told me that the industry was trying to provide high PUFA because the medical profession demanded it and the industry couldn't comply without increasing the trans fatty acid content of the margarine base stock. It is unfortunate that the relationship between PUFA and trans fatty acids was not thoroughly explored. However, I believe that the industry is now willing to consider another approach to the need for a high level of PUFA in dietary fats. In the meantime, I suggest that you contact Dr. Schmidt at Lever Brothers, Edgewater, New Jersey, and ask him to prepare a special high PUFA trans-free margarine for your study. Promise margarine is not as satisfactory as the Becel trans-free margarines that Lever has available in Europe.

Sincerely yours,



F. A. Kummerow, Director
The Burnside Research Laboratory

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