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TWIN CITIES

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TO: Henry Blackburn

FROM: Ancel Keys

RE: Memo from H.B. to A.K. dated 20 July 1982 and the copy of the Berlin manuscript

A. Berlin Manuscript:

1. General:

I have indicated that the Berlin manuscript seems to be of limited help to me in my consideration of the data on mortality and the risk factors, serum cholesterol and arterial blood pressure. Others may find it more helpful. The paper is much given over to speculation with little indication as to how those speculations can and will be put to definitive test. And I would like to see some consideration given to total mortality. Sole concentration on the incidence of coronary heart disease has dominated the field of our interests for a third of a century. I think it is overdue to look at the broader questions of untimely death. International vital statistics raise serious questions about diagnostic custom but not about age-standardized total death rates in the more developed countries. And the tiresome question of "trade off" and "competing causes" of death remains to plague us when only coronary "events" is the focus.

2. Particular:

Figure 2 of the manuscript reproduces the figure showing median cholesterol values and 10-year coronary death rates in the Seven Countries Study including the linear regression and the associated correlation. But the fact that the relationship is statistically highly significant by no means proves that the basic relationship is linear over the range 160 to 260 mg/dl. Consider the lower and the upper parts of the distribution; the slope in the lower part is not significantly different from zero while in the upper part of the distribution the slope is steeply upward. I would not emphasize apparent relationships dependent on so few points; I only say that we must not conclude very much from the results of solving a linear regression equation. The regression result shown in Figure 3 is perhaps more meaningful because the correlation is stronger and there is no suggestion that the relationship may differ in different parts of the distribution. Moreover, in the metabolic ward, experiments that produced the equation used for the ordinate there were no indication of anything but a linear trend over the wide range of the diets tested.

Figure 4 of the manuscript raises some questions because the curves shown are closer to the normal Gaussian than to the actual distributions. I have more serious questions about Figure 5.

Henry Blackburn
Page 2
July 30, 1982

B. MS "Cholesterol As Risk":

The suggestion of writing a paragraph on "implications" bothers me, partly because I am not at all sure what are or should be the implications, partly because unless such a paragraph is not cautiously worded the way would be opened for hot controversy that would becloud rather than clarify the scientific questions. If you wish to make a stab at an implications paragraph I would, of course, consider it. I would prefer, however, that you write more than a paragraph in an editorial separate from the scientific paper. If the manuscript of the paper is sent to The Lancet a suggestion for an editorial could be sent along with it. Perhaps you and Geoffrey Rose might join in an editorial or Letter to the Editor. I'd be glad to send Geoffrey a pre-publication copy of the manuscript.

I have indicated that the manuscript will not be in final form until I have the computer output noted in my memo of 28 July. Finally, we may consider other journals besides The Lancet, BMJ or the New England Journal.

/bg