Confidential

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JEREMIAH STAMLER, M.D.
PROFESSOR AND CHAIRMAN
DINGMAN PROFESSOR OF CARDIOLOGY

August 24, 1976

Dr. Henry Blackburn
School of Public Health
Laboratory of Physiological Hygiene
University of Minnesota
Stadium Gate 27
Minneapolis, Minn. 55455

Dear Henry:

The attached is self-explanatory. Please regard this as confidential.

I hope we can work carefully with Dr. Weidman on the further evolution of his knowledge and concepts in this area.

Kindest regards.

Cordially,

Jeremiah Stamler, M.D.

JS/mh

attach.

P.S. Deliberately, I read your letter to Dr. Weidman only after I dictated all my comments. Let me try to make a quick point or two with regard to your critically important paragraph 3: First of all, I believe based on the standard deviations for saturated fat intake and for dietary cholesterol intake for men all of us have studied in the U.S.A. that there is enough non-homogeneity even within our population theoretically to test the hypothesis that diet plays a role in accounting for the inter-individual differences around the population mean. Correspondingly, I further believe that if a study were designed properly, a proper test could be done, and the result would indicate an association -- in keeping with all the other findings -- across populations, in the metabolic ward, in intervention studies, in experimental animals. In the comments I sent Dr. Weidman, you will note I spelled out several criteria for proper accomplishment of the test of the hypothesis, beginning with use of diet as the pivotal independent variable, preferably at least three components (cholesterol, saturated fat, poly fat), and not one. If this is the pivot of the design, and if reported differences in diet among individuals are both valid and unbiased, and if the sample size is adequate, then the hypothesis is testable and the answer is almost certainly going to be positive -- provided that genetic metabolic factors do not somehow themselves influence diet (e.g., to put forth the "wildest" notion, persons with

poor genetic mechanisms leading to hypercholesterolemia somehow are "programmed" to eat less saturated fat and cholesterol). All my clinical impressions about how people with different serum cholesterol levels eat -- and I believe our CPEP, National Diet Heart Study, Minnesota Business Men and Professional Men Study, MRFIT Study data would be consistent with this -- suggest that such a far-out hypothesis is wrong. If it is wrong, then that kind of bias could not creep in, and then -- I repeat -- a positive association should be demonstrable. Several years ago, when we applied for an LRC contract for Northwestern, I proposed to do a thorough re-study of this question as one of the aspects of our special local effort. We were never awarded a contract. Nowadays given all the problems of bias based on widespread knowledge in the population about serum cholesterol levels and diet, the study is of course extremely difficult to do properly in the U.S.A. As you suggest in your letter to Weidman, it really is not a very important study, far less important for example than using the same energy to study in the metabolic ward the basis for inter-individual differences in serum cholesterol on any given uniform diet -- assuming that some people have reasonable specific hypotheses to explore in that area.

Let me make one additional thought explicit, be it implicit in the above: Presumably sampling on the basis of diet differences -- i.e., from the upper and lower ends of the diet distribution -- should wash out genetic factors, if it is reasonable to assume that they do not influence diet by some subtle metabolic mechanism, and if the data are unbiased in the sense that people's knowledge about their serum cholesterol has led them to change their diet. Thus, to touch on a matter in your letter I believe the genetic component can be "washed out" or controlled in a properly designed study of the role of diet in inter-individual differences around a group mean -- if it is worth the trouble to do it at all! One reason I doubt its worth is that the lower standard deviation of the mean serum cholesterol for men on identical diets in the metabolic ward, compared to free-living men or eaters of a house diet with free choice, values of $\pm$ 35 mg./dl. vs. $\pm$ 45 mg./dl. as reasonable examples, is by itself proof that even the modest inter-individual diet differences within a free-living more or less homogeneous population account in part for the degree of dispersion around the group mean. Given all the other data, what further proof is needed?

Aside from the above, I am in fundamental agreement with the points you make in your letter to Dr. Weidman.

Dictated by Dr. Stamler and mailed in his absence

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August 24, 1976

Dr. William H. Weidman
Pediatric Cardiology
Mayo Clinic
Rochester, Minnesota 55901

Corresp.

Dear Dr. Weidman:

This is a belated response to yours of May 3rd, for which I apologize. The communication arrived at our office in Chicago during the most intense teaching period we experienced during the year, and I did not get to read it until I went abroad for meetings and a working vacation. I hope that the attached comments are useful at this juncture.

I look forward to discussing this whole matter with you at an early date, after our return to the States on August 17th. (This is being dictated from abroad, at the IXth Ten Day International Teaching Seminar on Cardiovascular Epidemiology in Denmark.)

Kindest regards.

Cordially,

J Stamler mh

Jeremiah Stamler, M.D.

JS/mh

P.S. Please forgive the length of the attached comments and their repetitiveness, largely due to the dictation method used to get all the ideas down -- and my load of work upon return, precluding detailed cutting.

P.P.S. One other thought, on the general question -- something to ponder pending our having an opportunity to exchange personally on it: For those concerned about modifying present diet of American children, it is worth considering the diet of children in countries like Japan, where life expectancy at birth, one year, five years, ten years, and fifteen years of age, is at least as good as ours (and Japan is not the only country like this), yet the diet of children is quite different. There is really no solid reason to enshrine the diet of our children today as optimal, to be left alone -- particularly since it is evolving all the time anyway, under a variety of influences, including that of our advertising industry, the commercial firms linked to it, McDonald hamburger

stands, Dairy Queen, etc., etc., plus -- I like to believe -- some of the influences from many of us in the scientific community (positive influences, I am convinced).

Dictated by Dr. Stamler and mailed in his absence