

DEPARTMENT OF EPIDEMIOLOGY

September 2, 1966

Dr. Ancel Keys, Director  
Laboratory of Physiological Hygiene  
University of Minnesota  
Stadium Gate 27  
Minneapolis, Minnesota

Dear Ancel,

I feel very badly and guilt stricken about not having responded earlier to your request which I much appreciated, to comment on the draft of your chapter "Exercise and Physical Activity". I suppose that the manuscript has by now gone to the printer so that whatever I say now or might have said before is all water under the bridges.

If one were to symbolize "Physical Activity Protects Against Coronary Heart Disease" as a chicken, it would look pathetically naked and completely plucked down to the skin after you finish with it in your chapter ....! What troubled me was not what you said - because all of it is, of course, factually correct - but rather the general tenor. As you know, Bob Bruce had asked me to review the epidemiological relation between physical activity and coronary disease at "Three Days in Cardiology" in Seattle last June and I had to make it my business, therefore, to go over the evidence. It is full of loopholes, as discussed in your chapter, but the reason for this is no so much, I think, that the hypothesis is faulty but that the relevant studies have so many flaws in basic design, methodology, or both. Moreover, it is not clear whether physical activity behaves as a graded characteristic or as a threshold value with regard to protection against coronary disease; nor are all these interrelationships necessarily the same at various levels of, say, blood pressure or serum cholesterol. In fact, if I remember correctly, Jerry Morris told me in London last spring that the striking excess ~~on~~ comparing drivers and conductors is concentrated among the drivers who are both overweight and hypertensive.

I don't want to prolong the argument which you know as well and, indeed, better than I do, except to say that the proper way to analyze the data would be by taking into account multiple and competing risk factors. This might show that there are, indeed, subgroups in the general population in whom physical activity does ~~not~~ matter. This relationship might be watered down if one looks at the whole population as one usually does because this is all there is, except for the data which begin to come from your own <sup>tail</sup> road workers study in Minneapolis. Finally, is not it perhaps true that we know so much more and with so much more certainty about diet because so much more work has been done in that area (largely thanks to you!)?

September 2, 1966

It would be presumptuous of me to quibble about sentences and words in your manuscript. All I am concerned about is that the indolent and slothful reader of this chapter in your book might find support from what you say to persevere in his ways. I have a feeling that this is the last thing you would wish. Certainly, you do not preach in this chapter what you practice yourself which is all to your credit! It seems to me that what you really want to drive home is this: don't you ever think that you can continue eating this noxious "average American diet" and counteract it by a little bit of trivial exercise. This message might be as or even more effective if you leave the door open more widely for the possibility that regular exercise might do good. Please forgive these barkings of a dog while the caravan passes on ...!

I do look forward to seeing you in New Delhi and perhaps, if only briefly, in Tel Aviv. Jerry and Rose Stamler told us what a most enjoyable time they had in your beautiful house in Italy.

With all good wishes and regards as always,

Yours very truly,

Fred.

Frederick H. Epstein, M.D.  
Professor

FHE/jr

September 7, 1966

Frederick H. Epstein, M. D.  
Department of Epidemiology  
School of Public Health  
University of Michigan  
Ann Arbor, Michigan

Dear Fred:

No, the ms. of the book has not gone to the publishers yet; I have done a lot of polishing and propose to do more when I have a little time. The big job still incomplete is to insert tables and figures and references in the text. Mostly these are ready--the 800+ references, complete with titles, are all typed--but I have to be sure where they go and I may throw some out and add others.

Thanks much for reading the draft of the physical activity chapter. I have already made some alterations, and will make more, in the effort to indicate clearly that the fact that the evidence is incredibly bad does not mean the hypothesis is wrong. But frankly, after critically analysing the many articles I was more than cross at the quality of the evidence and especially the bias and even distortion in the analyses and conclusions in many cases.

Even putting the best face on the picture, I shall lose friends and be damned because I insist on a critical analysis. On the other hand, if I had merely recited the conclusions of the various propagandists everyone would be happy!

Another book ms. is in press. "The Benevolent Bean" is in progress with Doubleday. Margaret did most of the work and the authors this time are Margaret and Ancel Keys. It will run about 200 pages printed, plus some illustrations, and will sell for \$4.00 to \$4.50.

We are off in a few days, first to Corfu for work and then some 3 weeks at Minnelea before going to Tel Aviv. We look forward to seeing you there and at New Delhi.

All good wishes,

Sincerely,

Ancel Keys, Director



INSTITUT FÜR  
SOZIAL- UND PRÄVENTIVMEDIZIN  
DER UNIVERSITÄT ZÜRICH

CH-8006 Zürich,  
Sumatrastrasse 30  
Telefon 01/257 66 11 25 December 1993  
Telefax 01/252 54 52

ADDRESS FOR CORRESPONDENCE: Klausstrasse 4, CH 8008 Zürich,  
Tel.: 01-3838236; Fax: 01-3836433

Professor and Mrs. Ancel Keys

Dear Margaret and dear Ancel,

It is Christmas day in the morning and it would not be a happy day if I were not going to start it by writing to you. Since we got back from Bethesda the day after Thanksgiving - which we spent with the "Bethesda children" - there has been a constant restlessness so that work and correspondence got into a chaotic state. Not a day passed without wanting to write to you but something always happened. Now, I can't stand it anymore and the only possible stress management, as one says nowadays, is to write! Please forgive me for having replied earlier to your letter of November 13 which awaited me on our return to Zürich. Therefore, obviously, I did not know you had written when I phoned you from Bethesda. In the meantime, we also received your wonderful Xmas card with the unforgettable group picture taken in Fukuoka. We loved it and we do thank you for it!

Before I come to professional matters, may I tell you a little bit about ourselves. We are staying in Zürich for the holidays, having decided not to go up to the Engadin because it would be too uncomfortable for Doris and too hazardous with ice, snow and the rather steep steps up to the house. As a matter of fact, it turns out that Doris needs another operation, this time for a total hip replacement. We had already seen Dr. Stauffer, the head of orthopedic surgery, at Hopkins who thought that the continuing and continuous pain in the leg was caused by the prothesis being loose. This was confirmed by Professor Schreiber (who also operated on Silvia Mancini) in Zürich and he will do the new operation early in February. In the circumstances, we are really very glad about this because there is now hope to remedy a situation which has made life quite difficult these last two years. We'll keep you posted. Perhaps, Doris will be well enough to come with me to the Seven Countries symposium which Daan Kromhout has organized in Venice, as you well know. Is it conceivable that you will be there, too? That would be truly wonderful. Of course, Jerry will talk in Venice, too. I am still unhappy that Doris could not come to Fukuoka after all because it was such a marvellous occasion. Still, we are grateful that we could be in Atlanta together. As I said already on the phone, I am so very grateful that the Keys Lecture was so well received. Incidentally, my son Andy listened to it, too, and he was very pleased with his father which made me happy as well. Andy is Professor of Medicine now in Birmingham, with his research interest in arrhythmias, - he is chairman of the subcommittee on sudden death of the AHA Council of Clinical Cardiology; he is also a "supporter of the faith" as far as prevention is concerned. His brother Tony, by the way, who lives in Bethesda with his family, is a partner of Jenner and Block at their Washington office, - the same Mr. Jenner who

defended Jerry in his case against the Committee on Unamerican Activities,- small world...

To come back to your good letter of November 13, I did ever so much appreciate the manuscript on the Mediterranean diet (and your mention of me) and the ode, so to speak, on cheese. As regards the latter, we also like cheese and don't worry too much over eating it -whether or not serum cholesterol matters as one gets older - because we always get the quarter-fat variety. There are a few low-fat cheeses which are good if one looks for them but I am distressed how little effort is made by the dairy industry to produce tasty low-fat cheeses. Some of them, like the Appenzeller here, have such a strong smell that it turns one off. I think that there is a lot more that could be done on that front. You ask for the manuscripts on the Fukuoka and Atlanta talks. I will send them early in January to Pioppi. The Fukuoka paper was ready for printing, as you know, subject to Henry's editing. The Keys Lecture was written to be given as a talk. For the paper to be published in Circulation, I will have to re-write it and add to it. I only had 40minutes which is not much for a major lecture; Russ only wanted to give me 35 minutes but finally agreed to 40 to which I adhered. It had essentially three parts: a look on the history of CVD epidemiology, especially the beginnings, a look at your original views on cholesterol in the light of present knowledge and my hobby-horse on CHD prevention having an impact on other chronic diseases, protecting health on a broad front. I wanted to pay particular attention to the evolution of your concept as you first presented it at this historic small meeting at Sinai to which Dr. Boas had invited you and where we first met. I thought this was not only timely in view of the current attacks on the cholesterol theory but because none of the previous Keys Lectures had addressed specific major aspects of your work. Needless to say, I concluded that your basic tenets had stood the test of time. I think this message and others got across well.

It was good to talk to you, if only in writing. Doris and I think of you both most fondly and send our warmest greetings, as ever,

Yours. Fred.

410 Groveland Avenue, no.802  
Minneapolis, MN 55403  
16 July 1994

Prof. Dr. F.H. Epstein  
Klausstrasse 4  
CH-8008 Zurich  
Switzerland

Dear Fred,


At last I respond to the talk you gave in Venice. I had to wait for Margaret to read it to me. I can no longer read ordinary typescript or newsprint. Happily, I can read the monitors on my computers, especially my big 20-inch monitor; the usual 12-inch monitor is very difficult for me, even with a magnifying glass.

Half an hour ago Margaret finished reading to me your Venice talk and I am overwhelmed; firstly, the masterful review and evaluation of the literature; then my sense of wonder about what you wrote about me. Do I really deserve all that praise? Yes, I was the first with some ideas and action about what seemed to be a new frequency of heart attacks, the new problem. I was lucky in escaping some clinical persuasions and having to think about what next as I was getting free from my work as a Special Assistant to the Secretary of War. Also I was fortunate in the offer of a professorship in the School of Public Health - no more giving 50 lectures a year in physiology to the medical students. I could set up a new department and be free to explore new ideas.

Now I have an enormous amount of Seven Countries data in the memory of my computers. I keep busy finding and analysing new facts and relationships, some of them important in my opinion. Several reports are on the way, Margaret checking my mistakes she sees on the monitors.

Many thanks for your letters and manuscripts. We hope to be back at Minnelea by mid-September. In the meantime all our best wishes for you and Doris.

As ever,

  
Ancel Keys