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ANN ARBOR, MICHIGAN

DEPARTMENT OF EPIDEMIOLOGY

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

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 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 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!)?

It would be presumptious 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,

Frederick H. Epstein, M.D. Professor

FHE/jr

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

Klausstrasse 4 CH 8008 Zürich

12 September 1989

Dear Margaret and dear Ancel,

It must be quite wonderful to have been married for fifty years: It must be even more wonderful to be able to look back on so many good and creative years. Doris and I will be with you in our thoughts ten days from to-day and it will be our heartfelt wish that fate may continue to be kind to you in the years to come. It is a good thing, after all, that life expectancy is so much better now than it used to be since, on the whole, this has added life to years rather than on the reverse (I heard this motto first from Dr. Boas some 35 years The older one gets - I speak also of myself - the more grateful one becomes for all the kindnesses of fate. In your case, one thinks first of all of your illness, Margaret, which worried us all so much and which has become a thing of the past. - and one thinks of your recent encounter, Ancel, with clouds on well-being, clouds that will hopefully keep on passing. I can't help thinking that all that hard work in the garden has created beautiful flowers, plants and trees but has also made a healthier man of the gardener. Of course, such work contributes to happiness, too, but your happiness together will have mostly other roots. I shall not say anymore of kind fate because, beyond health, the good things in your life have not come from fate, it seems to me, but from faith, honesty and hard work. These are virtues which, though uncommon, you share with some others but, to achieve what you did, a special touch and genius were needed. Surely, what has come to be known as the "cholesterol theory" was put on the map by you and no single man has contributed more to it than you, adding the later to the initial contributions. The Minnesota Businessmen Study was started before all other longitudinal investigations, and you provided the vision and theoretical basis for it in your historical, if forgotten, paper on the biology of man in the Federation Proceedings. Who can measure the impact which the "Keys equation" had over the years? Without the Seven Countries Study, one of the cornerstones of the cholesterol theory would be missing, - the critical cornerstone, - quite apart from the other creative contributions of this inspired study. I won I tontinue along these lines, even though there would be much more to say. I just didn $^{ullet}$ t want to stop after I talked about the kindness of fate...

Your life and work, Margaret and Ancel, has also been an example to your friends and professional colleagues, - and your friends who happen to be both. When one sees you together, you make one feel good and one realizes what being together means, - or should mean. Thus, it is not really surprising that you have been married for fifty years... Your children and their families are, of course, a part of all this. A part is also your home which has a spiritual and physical aspect to it. I have seen two of your homes, - the house on the lake (on the occasion of the party you gave prior to the World Congress in New Delhi in 1966) and the house in Pioppi with its own beauty and its eternally and unforgettably beautiful view. When I thought of these houses the other day, thinking about

this letter ahead of writing it, it occurred to me suddenly that the word "lifestyle" which came to have such a tremendous influence was, I believe, also one of your inspired creations, Ancel. Perhaps, seeing your homes, one should not be surprised that the term should have come from you. Only, the term is so often used to convey "health engineering" (which is why it often doesn't work as well as it should) while, at the Keys', one becomes aware of all that is implied in "style".

Lastly, I would like to talk about what you meant to me, Ancel, and you, Margaret, too, once I became aware of the continuity between you. I talk about myself because Doris came over the horizon, as it were, only later, although we've also been married for 17 years by now. It has always made me most happy that you accepted Doris as a part of me and, as you got to know her, for what she is, me as a part of her. We talked a number of times about our first meeting, Ancel, when Dr. Boas asked you to talk at Mount Sinai. You invited me to speak at Stadium Gate 27 as I was on the way to Ann Arbor which became decisive to me. Then, it was you who asked me if I would accept nomination as chairman of the Council on Epidemiology which was, in many ways, the high point of my career. There were many other memorable occasions which I will not enumerate now, except for the recent one when I could sit next to you both at the opening of the Conference on Preventive Cardiology, - a long moment of pride and happiness when time stood still. I am deeply grateful for all Ilearned from you along the way and at the crossroads and for all your signs of friendship and sympathy over the years. You once said something to me many years ago, Ancel, though we left most things unsaid in our relationship, - that I had too thin a skin for my own good... It shows how well you know me and that you cared. Actually, the remark helped me a lot and I have recalled it to myself a good many times.

Doris and I wish you a most happy day with your family and, most probably, a number of friends, and much more of the good life, as far as the eye can see. As ever,

Most cordially,

Freel and Donis.

P.S.: I meant to write, too, that the photo you sent a year or two ago, Margaret and Ancel, at Xmas time, of the two of you in Pioppi, is almost the only photo, apart from my family, which I have in my study.

"Minnelea", 84060 Pioppi (SA) Italy 19 September 1989

Dr. Fred Epstein Klausstrasse, 4 8008 Zurich Switzerland B D P Y

Dear Fred,

We have just received your letter posted September 5 (showing the common slow delivery of mail here). And I must tell you how happy we are to hear from you, recalling the long years of our association. Alas, too many years have gone between!

We arrived here a few days ago to stay until late November when we must leave for me to give a talk at Key West. Thence to Minneapolis to celebrate Christmas with children and grandchildren before we return here. I had sworn off accepting invitations to give talks but I thought I would politely escape when I stipulated my requirements -- Travel first class from Italy for Margaret and me I got a prompt reply, adding to the provision for all costs at a fancy hotel and payment of \$1,500 for a manuscript!

Your letter reminds me of some of the busy and happily productive years after Margaret and I were married. I well remember how the cardiologists questioned my views in the early 50s and the time of my lecture in New York with you one of the small audience. I take great pride in the fact that the lecture converted you to embark on your most useful career. I have long admired what you did for the epidemiology of heart disease in spite of the handicap of your position in Zurich. Still we rejoice in your happy 17 years with Doris and the beauty of your home, and its contents in Zurich. May all those good things continue long into the future after we are gone.

Currently I am at long last finishing my manuscript on fatnees in middle age and longevity. I am sure, and I hope to convince others, that body fatness has been greatly maligned. The literature is full of biased rubbish on this matter. Actually, the data of almost all prospective studies agree that body fatness, short of "morbid obesity" (body msss index of 135 or so) is not the risk factor proclaimed by some. And in old age it seems it is better to be fat than thin.

But the years take their toll. I am still not back to where I was before my bouts with TIA and pneumonia.

Physical work is beyond me but I can still work the computers with Margaret correcting my mistakes as they appear on the screen. She does much else besides and continues to be well with no transverse colon. How lucky I have been with marriage and family. Any time we give way to discontent we quickly rejoice in our children and grandchildren. We are too far from them too much of the time. And we are happy to have the Karvonens and the Stamlers as close neighbors a good part of the year.

Margaret joins in sending all love and good wishes. Asever.

Ance Keys