

Dr. Boring, Dr. Boring, Fidanza and Dr. Boring wish to meet and work together. Manuscripts on some of the dietary survey results are being collected by Dr. Boring (for publication in AMERICAN JOURNAL OF CLINICAL NUTRITION) and by the end of August will be complete for Finland, Italy, Yugoslavia and the Netherlands. The Greek data are in hand and the material just now and I am currently unable to spare the

Parco Grifeo 30 (i)
Naples, Italy
June 22, 1964

Dr. William H. Goldwater
National Heart Institute
National Institutes of Health
Bethesda 14, Maryland
U.S.A.

In reference to HE 07381-03
and to HE 04697

Dear Bill:

I have read your letter dated June 12 and have referred back to previous correspondence and memos re this matter of year 03 of our project in the Diet-Heart Feasibility Study. At this distance, and being confined to generalities, the result of the negotiations seems to be reasonably satisfactory.

I have noted the specific limitations and do not propose to take any strong exceptions because I was not privy to the discussions you had with Drs. Fetcher, Taylor, and others on my staff. However, I believe it appropriate to record some reactions, at least for the record.

- 1) The provision for rental, instead of purchase, of the electric typewrite is acceptable.
 - 2) Reduction to one-third of the budget for the research assistant to work on triglyceride methodology seems to me to smack of poor economy if it is true that triglyceride values have important relevance to our long-run aim and that a satisfactory and practical methodology is not yet at hand.
 - 3) I trust that the further documentation required for permissions to make the expenditures listed under educational and social science services, etc. will not be too time consuming for our staff, more particularly Dr. Fetcher. I am impressed with the fact that time devoted to "bureaucracy" is obviously time lost to other activity.
- Here detailed arrangements are going forward for the 5-year re-examinations in Finland starting September 1st. Immediately preceeding, as you must know, will be the technical conference on physical activity organized by Dr. Karvonen under the sponsorship of the Research Committee of the I.S.C.. Thanks to help from the International Cardiology Foundation, it appears that outstanding world experts will participate. I think Dr. Fox, of U.S.P.H.S. will sit in on the sessions. At the same time (last week of August), the nutritional people in our international cooperative program -- Professors

Roine, den Hartog, Fidanza and Dr. Buzina--wish to meet and work together. Manuscripts on some of the dietary survey results are being collected by den Hartog (for publication in VOEDING) and by the end of August these mss. will be complete for Finland, Italy, Yugoslavia (Croatia) and the Netherlands. The Greek data are in hand but to write up the material just now and I am currently unable to spare the time myself.

I have advised my collaborators that they should request permission to use funds in their U.S.P.H.S. budgets for the necessary travel to Helsinki. I hope they have done so. You must know that it is often difficult for our collaborators abroad to understand the need for such documentation and permission when the scientific approved project is so clearly evident, at least to them and also who are really familiar with the program.

Prof. Fidanza and I have been planning for the 5-year re-examination program here in Italy which must be in the first half of 1965. Dr. Imbimbo recently completed the check-up on mortality and major morbidity in Crevalcore and Montegiorgio. This year, as before the cooperation was excellent and we can be sure of practically no refusals for the full re-examination. Also, it appears that very few of the men have moved away from those study areas, so the total number of men, aged 45-64 in 1965, who must be fully re-examined, will be close to 1600.

We believe this work cannot be done in less than 5-6 weeks at Crevalcore and 4-5 weeks at Montegiorgio. For those who will work throughout in both areas at least one week break between is essential and 3 or 4 days are needed to move and set up shop. For Fidanza, Imbimbo and the technicians, this means they will require 12 weeks away from all other obligations and about 75 days in the field.

For the work in Italy in 1965 I shall try to provide at least one "outside" electrocradiographer at all times, probably Dr. Kallio of Finland for one area and Dr. Mohacek of Yugoslavia for another, thereby guaranteeing strict comparability of technique and interpretation. Drs. Blackburn and Rautaharju should be able to apply the computer-tape program which we hope will be nearly completely free of "bugs" as a result of the extensive application of it planned for it in Finland this fall.

At Makarska you talked briefly with Fidanza and our Greek colleagues, Drs. Aravanis and Dontas, about the costs in the year that includes the 5-year complete re-examinations (you recall that this will be in the fall of 1965 for Crete). Dr. Fidanza has been working on the budgetary needs and he will shortly submit the supplementary request as advised. You will understand the absolute necessity for supplementary funds arises from two reasons: 1) the grant as currently approved makes no allowance for the much greater costs in a year when all the men must be fully re-studied, and 2) The amounts specified some years ago are no longer applicable because of rising costs for everything. Work in Italy

is still cheaper than in Finland or the Netherlands and far cheaper than in the U.S.A. but salaries wages, hotels, meals, etc., have gone up something like 25% in the last 3 to 4 years.

These same considerations apply to the whole world, I suppose, but a greater extent in Italy and Greece than at home and in the other areas of our work. So some adjustment will be needed for the re-study in Crete in 1965 and in Corfu in 1966.

I believe that Prof van Buchem, Mr. Mulder and perhaps Prof. Dols have been in communication with someone at U.S.P.H.S. in regard to budget and finance and may have presented the picture of their needs for the 5-year re-examinations at Zutphen in the summer of 1965. As you know, the Dutch group has had more generous local support than the other teams and the U.S.P.H.S. grant covers only a third, or less, of the operating costs. But they too will need more money for the work in 1965.

Dear Bill: I enclose a separate letter, for convenience in filing, etc. concerning travel costs chargeable to HE-04697. Thank you for the greetings, including those to Drs. Puddu and Fidanza. I see Dr. Fidanza almost daily. Saturday afternoon Dr. Puddu came down this way to spend the weekend with a doctor friend who owns a fabulous place on the Amalfi Drive--six acres of cliff and crag plunging from the Drive some 500 feet down to the sea, including a 10th century fortress tower (walls 13 feet thick!). Both Puddu and Fidanza reciprocate your greetings.

I believe it is a good idea to record some reactions at large for the records.

Sincerely,

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Ancel Keys, Director.

3) I trust that the further communication regarding my permissions to make the expenditures listed under "other" and "special science services," etc. will not be too time consuming for our staff, more particularly Dr. Foucher. I am impressed with the fact that time devoted to "bureaucracy" is obviously time lost to other activity.

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At the same time (last week of August), the nutritional people in our international cooperative program -- Professors

TYÖTERVEYSLAITOS

INSTITUTE OF OCCUPATIONAL HEALTH - L'INSTITUT DE MÉDECINE DU TRAVAIL - INSTITUT FÜR ARBEITSMEDIZIN

HAARTMANINKATU 1 — HELSINKI — FINLAND

DIR. PROF. LEO NORO, M.D.

July 15, 1964

Dr. Henry Blackburn
Laboratory of Physiological Hygiene
Stadium, Gate 27
University of Minnesota
Minneapolis 14, Minn.
USA

Dear Henry:

Thank you very much for your wonderful recording of the traditional jazz. I will have it on tape at Ilomantsi. I got yesterday your letter of July 8, thank you.

I have, in fact, been writing a letter to you for a couple of weeks. I have a lot of questions, and every day more and more. As you perhaps know, I have some responsibility to arrange our study this fall. Martti is on vacation and will be back on August 5.

Some information and questions:

1. I agree with you that comparisons in history and clinical examination should be based on the individual items or their combinations. "Diagnostic impression" is not as such a poor characteristic, in many cases it is perhaps better than any individual item or their combination. But I feel that the variation in "diagnostic impression", perhaps systematic error, is much bigger than in individual items. I prefer to send you the microfilmed editions of our forms. I would like to know something about your reading machine. What reduction rate is good, do you prefer 35 mm film or 16 mm film? We can do microfilming in five days, but it costs about \$ 400. Where could we find this money? It seems that we in Finland are seriously running short of money because of the expenses of our study this fall.

It is possible, of course, to send the original forms to Minneapolis. But the transportation of the forms will take more than a month, coding of microfilmed forms is easier than that of the original forms. So I prefer microfilmed editions if we could find money for that purpose.

2. The exercise tests. Of course, all subjects should have our traditional single step test as we had in 1959. We just would like to add the bicycle exercise test to the program, if possible. This department has used Åstrand's bicycle exercise test for some years, with few technical modifications. As you know heart rate only is recorded in the original Åstrand's exercise test. The heart rate is recorded in the original Åstrand's exercise test. The heart rate is recorded in the original Åstrand's exercise test. The heart rate is recorded in the original Åstrand's exercise test.

same time we take ECG's during and after the exercise. Physical training has a remarkable effect on the results, and therefore the test seems to be valuable in the estimation of habitual physical activity. On the other hand, Dr. Hernberg and Karvonen have found a clear negative correlation between serum cholesterol and oxygen consumption estimated by this test, and I think the correlation might be biologically meaningful. Perhaps this is the main reason why we would like to add the bicycle exercise test to our program.

You will help me a lot by testing which is the shortest time period needed between the preceding single step test and the bicycle exercise test. According to Åstrand all heavy exercise is forbidden for few hours before the test. My impression, based on nothing, is that perhaps one hour would be enough. If you will find in your studies that the interval have to be 2 hrs or more, we cannot use the bicycle exercise test. Or, perhaps we could divide the subjects randomly into two groups, one having the single step test and the second one the bicycle test. By random sampling we would not loose very much information. Although the bicycle exercise test might be better, we have to use in this study, so much as possible, the same methods we used in the initial study, among them the traditional single step test. But perhaps the random sampling is not so foolish idea.

In the field study a single load only will be used. The load for male subjects aged 44-63 is 900 kilobong meters per min., for young student boys with some physical activity 1200. In our system "speed" is 50 cycles per min. The exercise lasts for 6 (or at least 4) min. and the heart rate is followed for 5 min. after the exercise. Heart rate is recorded before the exercise, and at the end of each minute during the exercise and the recovery period. ECG's are, by the way, technically reasonable good. I hope you could use in the study subjects of "our age", from 44 to 63.

In the bicycle exercise test we should have a telemetric system with small tape recorder, first of all to record the heart rate, and ECG too, if you consider it important. Our telemetric system is not suitable for this type of recording, and our two Elemas are needed in ordinary ECG's. I hope you could find machines needed and have them in our study during those two months.

3. Who will pay the expenses of "computer"-ECG's, transportation, tapes, etc. If all or part of expenses will be paid from our funds, please let me know how much.

4. I have a list of over 10 foreign persons who are going to work with us. Well, I suppose most of them are tourists. In any case, I have not got any information about how long they will work with us. You understand that we should have the same team in the East and the West, so much as possible. If you know more about these foreign fellows (how long?, what they are going to do?), please let me know. Please do not forget yourself and Pentti.

5. I am afraid that Ilomantsi will be crowded by tourists during the first week of our study. Please let me know the dates Ancel, Henry Taylor, or perhaps some other friends from Keys' Lab. will be at Ilomantsi. I try to arrange them some place to sleep.

Just now, this is quite enough for me. In few days more. The forms arrived.

Best regards to Nelly and my friends in the Lab. 1964

Dr. Henry Blackburn
Laboratory of Physiological Hygiene
Stadium Gate 27
University of Minnesota
Minneapolis 14, Minn.
USA

Regards,



E. Orma, M.D.

P.S. I have understood that you will travel a lot in Europa in August. Please let me know your addresses, if I have to contact you in some emergency matter.

Thank you very much for your wonderful recording of the traditional jazz. I will have it on tape at Ilomantsi. I got yesterday your letter of July 8, thank you.

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INSTITUTE OF OCCUPATIONAL HEALTH - L'INSTITUT DE MÉDECINE DU TRAVAIL - INSTITUT FÜR ARBEITSMEDIZIN

HAARTMANINKATU 1 — HELSINKI — FINLAND

DIR. PROF. LEO NORO, M.D.

July 22, 1964

Dr. Henry Blackburn
Laboratory of Physiological Hygiene
University of Minnesota
Stadium, Gate 27, Minneapolis 14
Minnesota, USA

Deftbrillaber

Dear Henry,

Martti mentioned that you perhaps want to study anaemia problem in our study and that you perhaps will bring for us a machine which either measure hemoglobin cell count or/and the size of the cells, ^{as} you know an epidemiological ^{anaemia} ~~cells~~ study in these areas was carried out by Dr. Antila: sideropenia very common and a lot of cases of anemia.

My opinion is that this problem has been studied very well. But if you want to correlate individual ^{workers} ~~workers~~ with some other characteristics, Dr. Antila's work does not help.

So for as anemia are concerned, sideropenia and sideropenic anaemia seems to be here the most important and surprisingly common. The method which count the red cells, perhaps measure their diameter is insensitive. We should measure serum iron, iron ^{binding capacity,} ~~binding capacity,~~ I am afraid that our lab. ^{facilities} ~~facilities~~ are not capable for that.

If you are going to bring with you, or to send to us, some kind of "hemocytometer" which for me seems to have not much value in our study, please let me know. It means some extra work ⁱⁿ ~~on~~ the field laboratory, perhaps a extra lab. technician. And it is very difficult in Finland to find nurses or lab. technicians willing to work in field studies. We have a shortage of them and the few we have prefer to work in more comfortable ^{conditions} ~~conditions~~, e.g. at hospitals at Helsinki.

Best regards, *Sincerely*

August 12, 1964

Dr. Esko Orma
Institute of Occupational Health
Haartmaninkatu 1
Helsinki, FINLAND

Dear Esko:

Things move fairly well from here. Ancel is back for 10 days and says he has written Martti about the Ilomantsi visitors. Presumably the whole Helsinki conference (20 - 30?) will want to come to Ilomantsi for a day or so and Ancel suggests they be lodged in Joensu and driven up. The burden of this socialization at the opening of the field work is regrettable but politic. If any of us can help in the routine (anthropometry, blood, etc.) to free up your people for the social guide work, we will certainly do it. Ancel says that besides Dontas and Pentti who will stay for Karelia and myself who will stay about 2 weeks, there will be one working observer, Dr. Lamm from Hungary and possible the assistant of Dr. Lukl of Prague.

Mohacek with one technician, can operate the conventional ECG procedure through Karelia. I will do tape-telemetry pulse rate at the bicycle station and teach it to the technician of that station and Pentti will take orthogonal leads before, during, and after the work load you prescribe, (Forget the treadmill. We won't be bringing it) but only on every 5th or 6th man.

Will you have a defibrillator and cardiac drugs available on the rare chance of an accident?

We will discuss the microfilming when we come. I still feel we must have the step test in everyone, not random sampling. I believe 45 - 60' will be sufficient interval before the bicycle, but for intra-group comparisons it is not so important if everyone has the preceding step test. I regret we have not been able to explore this question further but will still try to get some older men in the next 10 days.

We, if Goldwater approves, will pay the expenses of the tape operation.

Page 2
Dr. Esko Orma
August 12, 1964

The technician for blood could easily do the hematocrit with our little electronic meter. I will see how interested Ancel is in this. A blood drop from the syringe is placed on parafin paper and pipetted into a standard cell pipette and hematocrit read directly (a function of electrical resistance across a standard blood column).

I leave here tomorrow and can be reached Tuesday, 18th, c/o Hotel Palace, Prague. I will fly to Helsinki on the 24th or else be driving in with Gunnar.

Best regards,

Henry Blackburn, M. D.

HB/cjh

September 30, 1964

Dr. Esko Orma
Institute of Occupational Health
Haartmaninkatu 1
Helsinki, Finland

Dear Esko:

Hope all goes well! Enough magnetic tape and telectrodes for W. Finland went off last week to you.

For the return shipment of the equipment I will send details later. It is possible we would like to keep the Mnemotron tape recorder stored with you for use next spring. At any rate the material to be returned should be well packed by a professional packer, shipped air freight COLLECT, consigned to Norman Jensen, Inc., 324 Fourth Avenue So., Mpls. with myself to be notified.

I've just got back and haven't yet cleared my desk but I will continue to think of possible publications to involve Kallio. One of these, including all our interests, could be the survival rate by age and area of men with clinical coronary disease 5 years ago. This has a "clinical and epidemiological" flavor of interest. Another is the question we discussed of comparing questionnaire responses to clinical impression. In this regard, I'd like to send you my breakdown of the first few days work, but need for this soon the total number of men examined through September 9, just the number.

I hope plans are being made to photocopy all the clinical forms of 1959 and 1964 as soon as possible.

Best regards to Martti, Kallio, Pirko, Nedeljkovic and all,

Henry Blackburn, M.D.

HB/cjh

cc: Dr. Keys

October 5, 1964

Dr. Esko Orma
Institute of Occupational Health
Haartmaninkatu 1
Helsinki, Finland

Dear Esko

Do you think you could dig up the letter you wrote and never sent me about the follow-up forms or compose a new one? Assuming we agree on continued use of the Rose and MRC questions, and on recording of blood pressure, I need your suggestions for other items.

The object of other questions, including those about medical visits and a system review is simply to avoid omissions of data relevant to a new morbid event by giving certain stimuli (a la Barry) to the memory. They are not for analysis individually.

The object of information on physical signs, especially murmurs, is an attempt to eliminate valvular heart disease from the coronary and ECG classes.

Please also let me know and send me copies of examples of your follow-up questionnaires on mortality. We did not discuss this adequately and I didn't see your clinicians actually involved in questioning relatives about circumstances of death. I would be most grateful to get your opinions about this, and if possible before mid-November.

Best regards to all, especially Pirko!

Sincerely

Henry Blackburn, M.D.

HB:r