

JL Sept 1960



Notes from a Medical Journey

Fermo (Marche), Italy
7 April 1960

Dear Jay:

Letters intended from several medical journeys remain unwritten--days too crowded with work, evenings appropriated by gracious but demanding hosts, and nights overborne by fatigue or indolence. The time slips by on this trip too, but here at Fermo, overlooking the Adriatic sparkling 4 miles away and 1500 feet below, I am free until time to drive 20 miles to lunch with the research team at Montegiorgio, a still smaller town on a still higher hill. From my balcony, I can see part of the road, a white thread twisting up and down hills between a patchwork of fields of varied greens and the brown of newly ploughed earth. Beyond Montegiorgio, the snow-covered Sibilline Mountains stand sharply etched against the blue of the morning sky and all between sea and mountains are the smiling hills of Marche.

Here the Sabines came over two thousand years ago, fleeing from the Romans through the passes of the Appenines, building their hilltop fortresses against another rape and preying, no doubt, on the simple folk who were here before them. But soon they were all assimilated within the Empire, their levies marched with the Roman legions, and from Ancona the Roman navy set out to conquer Dalmatia across the Adriatic. Today, the great triumphal arch marking their success still stands on the water's edge at Ancona, and a vast remnant of the Roman city they built on the opposite shore forms the heart of Split, which the Italians call Spallato.

This is a region of small farms, each laid out in 5 sectors of different crops tended with loving care by all the family; 10 or 12 acres yield an astonishing produce, and both the people and their pairs of white oxen are sleek. The houses and villages are immaculate, the people are friendly and gay, the food is varied and plentiful, and only money is lacking. Wheat, sugar beets, and a few pigs and calves go to market. With the proceeds, they buy materials for clothing and farming implements and pay taxes and the "Mutua," which covers medical care. Somewhere, too, there must be enough to contribute to the Church and buy household furnish-

ings for the children when they marry. But, as in all the world today, some of the young people are not content, and more and more of them are leaving the farms.

Montegiorgio is a large agricultural village typical of a region where life is stable in spite of the migration of some of the youngsters, where there is no hunger, no serious problem of infectious disease, where contrasts between rich and poor are relatively small, and where we are sure of cordial cooperation now and in the five-year follow-up we plan. We want detailed medical data on all men aged 40 to 59 in the selected area. We cannot hope to examine every one of the 750 men on the roster, but the coverage should equal the 98% mark achieved in the study just finished at Crevalcore (near Modena).

Local doctors are helpful, but the real work is done by the team organized with the aid of Dr. Vittorio Puddu of Rome and Dr. Arrigo Poppi of Bologna. Colleagues from our research teams in Yugoslavia, Finland, and Greece come here for various periods to assure adherence to the standards adopted for all the areas in this international research program. Dr. Ivan Mohaček of Zagreb has been a constant member of the team both here and at Crevalcore and will come to Minnesota for the summer. Dr. Henry Blackburn of our staff in Minnesota spent a month at the outset at Crevalcore, and the good effects of his teaching are evident, especially in the objective recording of clinical and electrocardiographic findings.

This work, as in our other studies, is concentrated on relationships between the mode of life and the development of heart disease, especially coronary or "ischemic" heart disease, and how these may apply to prevention. We are concerned with cause and effect of course, but I have long since given over arguing about final causes. At present, it is enough to discover the sequence of events from health to disease and to be able to predict the statistical outcome in frequency of disease from the mode of life and the characteristics of the population in health. Already much has been learned.

From the data on the customary diet, we can make a fair estimate of the average concentration of cholesterol in the blood. Tell us the average concentration of cholesterol in the blood in the population, and it seems that we can predict, at least roughly, the relative frequency of coronary heart disease in the men of middle age. It is still pretty crude; the contributions of obesity, blood pressure, and activity are obscure, and the predictions are not much good for individuals. But, looking back a few years, the progress is impressive. Now we need much larger population groups in follow-up studies to be able to sort out details with more accuracy. This is a main feature of the programs at Crevalcore and at Montegiorgio; together, they cover about 1,500 men, aged 40 to 59 at the outset, who will be followed. Add the 600 Italians at Nicotera with whom we started this long-range program several years ago, the 1,500 men in rural Finland examined last year, the 1,500 in Yugoslavia studied in 1958, the 650 Greeks on the Island of Crete, and the 1,000 Netherlands soon to be studied at Zutphen, and we have nearly 7,000 men in Europe under surveillance.

Coverage in the United States is not nearly so good; in all surveys, many men refuse to cooperate and others are lost sight of because of changes in residence and occupation. But Dr. Henry Taylor now has nearly 3,000 railroad employees fully examined and for whom we think the prospect of follow-up is exceptionally good -- for the U. S., that is. The U. S. group provides one satisfaction: the "yield" of coronary heart disease so far is far richer than in any of the other groups.

Yesterday, we checked the local hospital at Montegiorgio and were impressed by both staff and facilities. About 80 of the 100 beds were occupied, and most of those were surgical; no coronary patients were to be found, and the Chief of Staff was hard put to remember when he had seen an infarct or a real case of disabling angina pectoris. This is typical of our experience in the rural areas in this part of the world. The local doctors know something about coronary heart disease because, several times a year, they go to medical meetings where coronary heart disease is a popular subject of discussion.

How much the diet has to do with the lack of coronaries here I should not like to say, though we already know that the average serum cholesterol is low. The dietary work has far to go, but certainly the usual diet here is calorically abundant and low in saturated fats. Dr. Flaminio Fidanza, who leads the Italian team, promises detailed data soon. We like the diet with its excellent bread, wonderful fresh vegetables and fruits, low-fat fresh cheese (ricotta, mozzarella, fior di latte), light, dry white wine ("verdicchio"), and meat and fish in small amounts but fine in flavor. Good soups and all kinds of pasta -- spaghetti, lasagna, fettuccini, etc. -- are a part of every main meal, of course.

Writing about food reminds me that Margaret and I should get on the road soon to be in time for lunch at Montegiorgio. She is busy on the Italian edition of our book, EAT WELL AND STAY WELL. The Finnish edition, which is well reviewed in Finland, was much easier. Incidentally, quite a few copies are being sent to Finns in Minnesota.

Anyway, it is time to think about food; we had only coffee and hot milk for breakfast, and that was five hours ago. Today, we shall lunch in the open air with blossoms overhead and wild flowers all about. Then we shall sit for a bit in the warm sun, lazily contemplating the rolling countryside, before getting back to work. The afternoon is long enough because we never dine until after eight.

With all good wishes to you and our friends at home,

As ever,



AK:ml



JL Oct. 1960

Notes from a Medical Journey

Palinuro, Italy
12 May 1960

Dear Jay:

At Naples, 100 miles north as the crow flies, a mountain of records, blood, and food samples from Montegiorgio is being processed and Dr. Joseph Anderson, arrived from Minnesota for the purpose, is checking chemical methods with Dr. Flaminio Fidanza and his assistants -- Drs. Mancini, Cioffi, Vitale, Imbimbo, and Matteoli. As a result of conferences at Brussels a few weeks ago, we are preparing for some years of blood studies on European insurance applicants. La Prevoyance Sociale of Belgium will cooperate, and other companies in England, Sweden, and Germany may join the program already represented in the United States by the Lincoln National Life and the Mutual Service Insurance companies. We expect blood samples from about 5,000 men in the first year, and this figure could well be tripled. Naples will be the laboratory headquarters for this work, but the control will remain in Minnesota.

Unlike Dr. John Gofman's atherogenic index service in California, this is strictly a cooperative research program. By follow-up studies on life insurance applicants, we propose to examine the predictive value for health and disease of blood cholesterol as well as the characteristics ordinarily recorded for insurance purposes. The data will not be used concurrently in underwriting and we, of course, derive only scientific profit. Within three years, we shall have at least 25,000 men in the follow-up study, including men in the population surveys such as that just finished at Montegiorgio.

So far, follow-up studies in the United States indicate that a single blood sample analyzed for cholesterol allows one to identify a group of men whose risk of coronary heart disease in succeeding years is more than 3 times that of the rest of the men of the same age. This seems to be more important than the information from blood pressure and a great deal more significant than the relative body weight. But what is the risk up and down the cholesterol scale and how is this variable related to other char-

acteristics? Follow-up studies on a much larger scale are essential, and that is where the insurance companies can contribute uniquely.

Our beginning with a few insurance companies has been made possible by the method we have developed for the estimation of the serum cholesterol concentration from a few drops of finger tip blood allowed to dry on a bit of paper and analyzed at leisure at a distant laboratory. The cholesterol in this dried form is stable for many months and is readily extracted and measured, as we discovered years ago. The "gimmick," however, is to use whole blood without any measure of the amount at the time it is drawn. Fortunately, the concentrations of cholesterol in the red cells and of the sodium in the plasma are remarkably constant, and the balance of these substances between cells and plasma is such that the ratio of cholesterol to sodium in whole blood allows a very satisfactory estimate, for our purposes, of the cholesterol concentration in the serum. The ratio of cholesterol to whole blood solids is almost as good in all but persons with major blood disorders.

So now for a couple of days here in the sun at Palinuro, Ernest Klepetar and I are discussing all these matters and making plans for the future. Ernest, who steals time from his responsibility as actuary and vice-president of the Mutual Service Insurance Companies to aid in our epidemiologic research, has played a major role in securing the cooperation of the insurance companies, and the efforts of his president, Felix Rondeau, stimulated the meeting at Brussels. Ernest and his wife, Edith, are with us and, as we both have new Kharmann-Ghia sport coupes, identical save in color, we create a minor sensation in the little villages where such cars are novelties. At the moment a crowd of men is examining our cars down in the street below this little hotel (officially "third category" but very comfortable).

Everyone in Italy has heard of Palinuro because it bears the name of Palinurus, the faithful helmsman of Aeneas who, according to Virgil, was lost overboard off this cliff-bound shore, a victim of the God of Sleep, who drugged him with the waters of Lethe. Later, when Aeneas visited the Underworld from Lake Avernus, a few miles north of Naples, he met the shade of Palinurus, who bewailed his unburied state. The prophetic Sibyl, Aeneas' guide in the Underworld, consoled him with the promise that a tomb would be erected for him, "and that place shall bear the name of Palinurus forever."

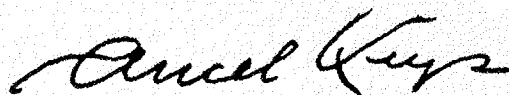
And so it is, except that Palinurus' tomb is not to be found unless, most fitting, it be the lighthouse on the jutting headland which controls the sea from here to Capri, 60 miles distant. It was a delightful walk winding up the sheep tracks above the little fishing harbor, wild flowers in profusion everywhere, to the lighthouse, blinding white in the spring sunshine and much bigger than it seemed from the village a couple of miles away. As we looked up, wondering whether photographs were allowed, we were hailed from a high window and invited to come in and inspect. Two families tend the light, and we saw all the workings, set the light itself in motion, and drank in the blue of the Tyrrhenian Sea. Supplies come by

mule along the crest of the ridge, and the older man said it is a tranquil life. "Perhaps too tranquil," remarked the younger man, as he turned to gaze at the mountain behind us.

Later, sitting on the terrace of our hotel in the evening glow, fragments of conversation from the road and from balcony to balcony were broken by dogs barking. A donkey brayed, and then we noticed that the lighthouse had begun its nightly vigil -- short and long flashes in unvarying rhythm -- and we pictured the slow descent of the timing weight as we had seen it in the morning. Somehow it called to mind the lonely Greek temples at Paestum, halfway between here and Naples, reminder of the city that flourished there long before Rome and vanished, perhaps because of the constant plague of malaria on those flat lands by the sea. That medical problem continued until a few decades ago but is now practically forgotten, and the new settlers in those reclaimed areas are worried about economics and politics rather than malaria. For that matter, they also seem to escape two of our modern plagues, dental caries and coronary heart disease, though they have at least their share of peptic ulcer, liver disorders, and valvular heart disease.

But now the hotel owner is coming to discuss the important matter of what we shall eat for dinner and it's time to write, "Best wishes to all."

As ever,



AK:ml

JL Jan 1961



Notes from a Medical Journey

Bucharest, Rumania
15 September 1960

Dear Jay:

Here at Bucharest I recall a trip from Vienna long ago, when I shared a train compartment with a swarthy fellow who plied me with chocolates, Turkish cigarets, and endless talk that revealed only familiarity with every corner of the Balkans and a great variety of "droll," that is, dirty, stories. His ticket read "Bucharest," but he left the train escorted by Hungarian officials who had slit open the lining of his suitcase to reveal packet after packet of Rumanian bank notes.

I never went beyond Budapest then, but thereafter it seemed that most tales of international adventure I read reached high points in Bucharest, where men in opera cloaks concealing lethal weapons were seduced by exotic beauties in transparent negligees who extracted state secrets in 6 languages. In short, Rumania was a mysterious unreality to me until a few days ago.

From Copenhagen last Sunday, I was the sole passenger in a plane labeled "Roumanian Airlines Special," rereading the page in my passport covered with a visa: "Official Invitation -- Roumanian Ministry of Health." I recalled, too, that my travel insurance does not cover nonscheduled flights. But the first leg of the flight was mostly dull, and I was delighted at East Berlin's dingy little airport when Drs. Paul D. White, E. Cowles Andrus, Michael deBakey, Luther Terry, and John Turner, a young protégé of Paul's, came aboard. We were going to Rumania to break some cardiologic ice, hoping to promote professional cooperation and exchange and to learn something about local medical affairs before going on to the European Congress of Cardiology in Rome.

We were cordially greeted at Bucharest Airport -- no customs inspection -- and big black Russian cars were waiting. Paul's bag was not to be found, and, as we stood around, we watched a plane-load of the return-

ing Rumanian Olympic Team go through customs -- every bag searched from top to bottom and magazines opened page by page. Still no bag (it hasn't been found yet, four days later), so off we went along wide, tree-lined boulevards into the brightly lighted city. The biggest and most ornate building (in the Stalin-Gothic style of Moscow University) we passed proved to be the Headquarters of the Government Press.

Our rooms at the Lido Hotel overlook a huge garden and terrace with dining tables around a blue-tiled swimming pool, the whole prettily illuminated. Hospitality was underscored in each of our rooms by plates of fancy cookies, bowls of fruit, flowers, and bottles of mineral water. After thirty-plus hours of travel, we would have been content to collapse, but of course there was a dinner with our friends Professor Iliescu, Dr. Ionescu, the assistant minister, and several others. Very pleasant, too many courses of good food and drink, but finally to bed with mounting hyperlipemia and too tired to care.

Professor Iliescu, director of a big, new cardiovascular center, ASCAR, was some years with Sir Thomas Lewis in London in the early twenties and, though now aged 70, he is full of charm and a great deal of energy. ASCAR has 120 beds and a big outpatient department, to which cardiac patients are referred from a dozen secondary centers in the city as well as from all over Rumania. Everything was spotless, and rooms and corridors were full of asters and chrysanthemums. The patients seemed well cared for and presented a full variety of cardiovascular disorders, including plenty of unquestionable myocardial infarctions and a man aged 34 so labeled but about whom we had much debate.

ASCAR is planned as a research as well as a diagnostic center and has a considerable group engaged in experimental work. Dr. Ionescu has much new equipment, including a big pump-oxygenator from the States now being tried with dogs before the expected application to man. The Rumanians are doing an increasing amount of cardiovascular surgery, using hypothermia at present.

The biggest show of equipment is at a center for work capacity evaluation and rehabilitation, where a vast battery of tests and examinations is applied to persons of all ages and disabilities -- circulatory, sensory, orthopedic, and so forth. This again is a center of centers, and we were told that subordinate units for such medical care for the workers are operating all over the country. "Social medicine," with stress on prevention and rehabilitation, is much emphasized here, though it is difficult to know how far hopeful theory and plans are actually put into practice.

Paul White has been keen to learn about the local attitude toward the claims of Dr. Anna Aslan for the value of procaine injections to retard aging and its associated disabilities. None of the local physicians could be induced to give more than noncommittal comments. Dr. Aslan is away at present, and we were discouraged from spending the time to pay a visit to her G.I. Parhon Geriatric Institute. But she must be officially in favor,

not only as evidenced by the support of the Institute but, perhaps more significant, by her frequent recent appearances in Congresses outside Rumania. Permission and provision of funds for travel to the capitalist countries are not available to many Rumanian doctors.

Our lectures, slowed by translation, were applauded by overflow audiences, and we have been kept busy here in Bucharest and on an auto trip to the Carpathian Mountains. We are not restricted, but we do have such a full program that there is no time for just wandering around. An evening in the marvelous new Symphony Hall was relaxing. The huge audience seemed to be both better dressed and more sophisticated in music than I recalled on similar occasions in the country of the Big Brother. Afterwards, yet another elaborate dinner tested our capacities. Our usual day's quota here seems to average 4,000 or more calories, not counting the contribution of alcohol which comes in at least 4 varieties at every meal. And we have 2 elegant multicourse meals every day. Such are the hazards of trying to promote international cooperation in medical research.

In a few hours (at 7 a.m.), I must be ready to take off for Rome via Vienna. The others go by way of Sophia for a day, but I am on the program of a preconvention Colloquium for Arteriosclerosis in Rome. As usual, "all roads lead to Rome."

As ever,



AK:mm



JL June 1961

Notes from a Medical Journey

Haarlem, The Netherlands
4 October 1960

Dear Jay:

Here in Holland, the lovely fall weather of Sunday faded yesterday, and now a soft drizzle portends the onset of the long season when leaden skies are the rule in the region around the North Sea. I hope for Indian summer when I get home tomorrow -- days when autumnal colors blaze red and gold in the sunshine and nights spectacular with Northern lights. Then, too soon, a morning will come when all the gardens have been blackened by a killing freeze. So with a sigh I look out at the neat flower beds here and say goodbye to summer.

I am staying at the home of Dr. F. S. P. van Buchem, who recently resigned his chair of medicine at Groningen for more leisurely scholarship. He is the leader of the Dutch team in the international collaborative program of heart research I try to coordinate. Between technical conferences at the Hague and Leiden and visits to great collections of paintings, we have gone over preliminary findings in the recently completed survey at Zutphen. Twenty cases of myocardial infarction among about 800 men aged 40 to 59 -- 85 per cent of all men in the total population roster -- give the lie to the idea that Holland is singularly spared from the coronary epidemic prevailing in countries that subsist on diets high in saturated fats.

Of course diet is not the whole story, but from our own direct observations, we now have 4 coronary-prone populations to contrast with 8 others more fortunate, and the parallel between saturated fats in the diets and cholesterol concentration in the blood still holds.

We are not sure of a continuous linear correlation between coronaries and blood cholesterol, but it is easy to make a demarcation between two categories. Populations in which middle-aged men average less than about 200 mg. of cholesterol per 100 cc. of serum are in one class. In another class, with much higher prevalence of the disease, are the

populations with higher average cholesterol values. Kimura's Japanese farmers and fishermen average only 140 to 160 mg. per 100 cc., while the rural men of Crete, southern Italy, and Dalmatia average 180 to 200. In all of these groups, the prevalence of coronary heart disease is really low, but we have not proved that the Japanese are much better off than the Greeks and the others. In the other class, too, we find it hard to prove that populations in which the middle-aged men average 235 mg. are much better off than in those with averages of 265 mg. Other factors at work? Or is it simply that our numbers are too small? Besides better methods, we probably need samples 5 times as big as those now being studied.

Since my last letter from Bucharest, the International Colloquium on Arteriosclerosis and the European Congress of Cardiology, both at Rome, have come and gone, and I have had a good visit with our team working on the island of Grete. The team on Crete -- doctors from Sweden, Italy, and England, as well as the very competent Greeks from Athens -- has put a fine-toothed comb to the villages, but coronaries are just as scarce as we found in our first survey there three years ago. In desperation, the team rounded up 100 men over 70 -- the "papoos" with great white mustaches and voluminous baggy pants, who abound there. Many of them were creaky and deaf and half blind, but the electrocardiograms were good.

From Greece, I hurried back to Rome to join a U. S. group made up of Paul White, E. Cowles Andrus, Luther Terry, and John Turner, a protégé of Paul's, in a meeting with the Russian delegation -- Myasnikov, Speransky, Vassilenko, and Khibshidsky -- to discuss cooperation in cardiovascular research. We got along fine personally, but too much time was given to talk about criteria based on recollections from clinical experience. This may be fun, but it is a poor substitute for actually working together or the analysis of objective data put into uniform classification systems. However, we agreed on some plans for more prolonged contacts, and we have increased hopes for real cooperation in the future.

After the conference, several of us went to a small restaurant I know across the Tiber and dined at 9 P.M. on mussels, "ossobuco," fruit, and the golden Frascati wine made in the nearby Alban Hills. Later, we drove up to the Campodoglio, the official heart of Rome, stopping on the way to toss coins into the Trevi Fountain to assure another visit. From the parapet behind the Campodoglio, we looked down over the vast, floodlit Roman Forum and pondered the march of two thousand years of history since those white marble columns were new. Then the bells tolled midnight, the lights went out, and we went back to the hotel through deserted streets. I noted that it was just thirteen hours since Dr. Kimura and I had boarded the plane to Athens, and now he should have arrived at Boston, where he would be telling Ina White that Paul will be home shortly.

Then I was flying northeast, watching the clouds thicken as we left Italy and finally coming down through the mist to Zagreb, where auto traffic and parking are not yet a problem in the center of a city of 600,000. But Zagreb is not cut off from the West, and the Palace Hotel was full of chatter in Italian and German -- as well as of pictures of Tito in every room.

A few of us may meet again in Yugoslavia in the spring. Belgrade wants to embark on work parallel to that which we started in Dalmatia and Slavonia two years ago, and an outsider like myself may help cooperation between Zagreb (the Croats) and Belgrade (the Serbs). Anyway, while tempers flare in the U. N., it is increasingly possible to get on with the job of international cooperation in medical research. We may not yet know how to prevent coronary heart disease, but infarcts are just as unpopular in Moscow and Belgrade as they are in Minneapolis and Helsinki.

Now, in a couple of hours, I shall be standing around at the airport, waiting for plane departure, buying newspapers, drinking coffee, looking at counters full of stuff I don't want, and pondering my impression that Congresses are scientifically disappointing and emotionally (or only physically?) exhausting. In other words, this promises to be a typical ending of a fairly hard trip.

With best wishes to all in Minnesota,

As ever,

A handwritten signature in cursive script, reading "Ancel Keys".

AK:ml



October 1961

Notes from a Medical Journey

Opatija, Yugoslavia
24 April 1961

Dear Jay:

Time and distance have curious dimensions in this day of jet travel. The sombre buildings of Helsinki, half obscured by blowing snow, were surely more than three days away from my brief glimpse of the dogwood in flower in Atlanta, where I talked before the American Epidemiological Society. In between, there was the Research Committee of the American Heart Association at Atlantic City, three hours of television filming at New York, and a quiet evening with old friends at the home of Dr. Carl Johan Mollenbach in Copenhagen, after visiting the wonderful new hospital at Glostrup, where Danes, at the rate of several hundred a year, show that they, too, have no lack of myocardial infarctions.

At Helsinki Airport, Dr. Mariti Karvonen greeted me with the news of the Russian space flight. Can Gagarin really understand that he flew around the world in eighty-three minutes? I recall flying from Bangkok to Bombay through the night once, and, though I must have crossed all of Thailand, Burma, and India, it had no real meaning. And the only reality of Bombay was the fact that the airport was desolate and dusty, the coffee bad, and we piled back on the plane weary for the next leg to Teheran.

In the sauna bath (at 235 F.!) in Helsinki, I forgot about Gagarin when I learned about the findings to date in the experiment in two mental hospitals in Finland -- one with the diet unaltered, one with the diet changed by substituting vegetable oils for butterfat. The serum cholesterol decline in the second hospital was soon notable (and was reported in the Lancet last year). Now, with the dietary difference maintained for nearly two years, there is a remarkable difference in mortality, and this is accounted for by a sharp fall in deaths from circulatory diseases. However, we shall wait another year before Prof. Turpeinen and his colleagues bring out the story with all statistical details.

After the snow in Helsinki, Stockholm in the spring sunshine was a delight from the top floors of the new Folksam Company skyscraper. The Folksam Insurance officials are nearly ready to start the research program I proposed a year ago, and soon we shall add some 6,000 Swedes to our international collaborative follow-up study. Dr. Lars Carlson is keen on serum triglycerides, as well as cholesterol, as a possible prognosticator of coronary risk, so they propose to add this item -- which means that all subjects must report in the morning without breakfast.

The diet-heart disease question is hot in Scandinavia, with top-level committees charged to produce reports both in Sweden and in Norway. The chairman of the Norwegian Committee, Prof. Ragnar Nicolaysen, is all for government action to reduce the intake of saturated fats, including possible forcing price differentials against butterfat. The information is that the frequency of myocardial infarction is increasing at a phenomenal rate in Norway, and recent serum cholesterol surveys show values similar to those in Minnesota. But in a large rural area not far from Oslo, serum cholesterol values and the intake of saturated fat in the diet are much lower -- and the mortality rate at ages 40 through 60 is scarcely half that of Oslo.

After Oslo came hasty and, I hope, fruitful business in London, Brussels, and Amsterdam, a lunch in Zurich; then 7 of us -- 2 Swedes, 2 Dutchmen, a Dane, Dr. Henry Blackburn, and myself -- were in a Yugoslav plane en route to Zagreb and wondering, as we saw the white peaks of the Alps poking through the clouds below, how we were to go on to Opatija that night.

Two small cars and a bus were the answer for five hours of pitch-black night, driving rain, and many patches of fog, which made the winding road through the mountains that much more interesting! And so to bed at 3 a.m. and up early enough to arrange my slides for a lecture that morning ("Risk of Coronary Heart Disease") before several hundred doctors at the Yugoslav Congress on Cardiology. Heart disease is now proclaimed, officially, to be a major health problem in Yugoslavia.

That night I was host and chairman at a dinner for 24 of my collaborators from 9 countries who spoke English -- except at the end, when I called for short talks with the promise that any talk would be out of order if it was in a language that could be understood by more than 4 people present. So we cheered impassioned remarks we could not understand in Croatian, Finnish, Flemish, Hungarian, Greek, Swedish, Copenhagen Danish, Dutch, and Neapolitan Italian.

More seriously, we learned that the frequency of infarcts in Zutphen, the Netherlands, is similar to that in Minnesota, and the serum cholesterol averages in middle age are practically identical. We also learned more reasons to distrust the diagnosis of angina pectoris and to wonder about the meaning of inverted T waves.

Today the rain continues, palms sway in the wind, and the

lovely Dalmatian coast is visible only on the postcards at the hotel desk. Phooey! Shortly, Drs. Puddu, Fidanza, Imbimbo, and I shall drive to Trieste to catch the night train to Rome; while Henry Blackburn, Orma of Finland, and Dostas of Greece go with the Yugoslavs to Slavonia to check the health status of 800 men, first examined in 1958.

The calendar says it is Monday, and I have been away two weeks; my plane tickets say I shall be home in Minnesota on Sunday. A week ago Sunday I spent the day with the Dr. Clarence Dennis family in Stockholm, where he does surgery on a sabbatical, and the whole family have learned Swedish to the extent that daughter Jane is engaged to a Swedish medical student. For desperate infarct cases, Clarence is attempting a pump bypass of the heart, which cuts out 90 per cent of the oxygen need of the myocardium and maintains a good pressure in the aortic arch (hence in the coronaries). And I continue to say prevention is the only answer.

And so off on the road again, with all good wishes to Minnesota.

As ever,

A handwritten signature in cursive script, reading "Ancel Keys".

AK:ma



JL July 1962

Notes from a Medical Journey

Moscow, U.S.S.R.
11 September, 1961

Dear Jay:

Moscow shows many changes in five years. Driving in from the airport we went past miles of 8-story apartment buildings where there were only fields and log cabin farmhouses in 1956. Part of the way we drove on completed portions of the new superhighway to Leningrad, and in the center of the city it is obvious that Moscow has advanced to the point where it is easy to get killed by automobiles. Traffic is not really heavy by our standards, but it is fast and disorderly.

Dr. Myasnikov's Institute of Therapy is much changed too -- doubled in size and far better equipped than before. Today I gave an informal lecture to the staff with about a hundred doctors being assembled on short notice. And the atmosphere is different, less formal, and more relaxed; we actually discussed technical problems instead of being exposed to dogmatic statements. This is partly because of the fact that we know one another better from friendly meetings in Geneva, Stockholm, Brussels, and Rome in the last few years. And part of the change, I am sure, reflects the fact that the Russians now have more to offer in medical science and they know it.

One incident impressed me while going through the laboratories. Dr. Myasnikov waved at a bank of complicated equipment, said "stereovector electrocardiograph," and kept on walking. But we stopped and asked where it was made. "In Russia," said Myasnikov and started to go on. "But how do you like it?" we asked. He grinned and said, "It's no good. It doesn't work." Such an exchange would have been unthinkable in 1956.

Last night, we (Dr. Paul White, Margaret, and I) had dinner at Myasnikov's apartment with his wife, son, and daughter-in-law. The atmosphere was just like visiting friends in our own country. We talked about our colleagues, art (he has a fine collection of Russian paintings), food and drink, the complications of travel, and hunting for mushrooms.

We liked a kind of partly fermented sauerkraut, whereat the recipe was reconstructed with lively discussion and recourse to dictionaries and cook books. (You start with 50 pounds of cabbage and it is ready in 2 or 3 days.) It was that kind of an evening.

We arrived here by a Russian jet from Prague where we had attended the last two days of an International Congress on Angiology. The Czechs were most cordial and the social affairs were delightful, but we learned little from the scientific sessions. I was impressed with the Secretary General of the Congress, Prof. Z. Reinis, who seems to have an intelligent grasp of the epidemiologic approach to heart disease. Perhaps a fourth of the participants were from non-Communist countries but they were a very mixed bag, mostly men I had never heard of before (including those from the U.S.).

Prague used to be an impressive city and it is crowded enough (with pedestrians), but all seems rather down-at-heel. This last phrase comes to mind because I got to looking at shoes in shops and on the passers-by and could not believe that Czechoslovakia once had a high place in the ranks of producers of good shoes. All consumer goods seemed to be high in price and low in quality. There is no unemployment but a serious labor shortage. I would guess that part of this is the result of the great numbers of men in military service and in the police -- who are everywhere.

The current trip started ten days ago when Margaret and I flew to Ireland and got fouled up with an Irish Airlines jet that could not fly (eventually we were transferred to TWA) and bad weather. So we missed a night's sleep and had no real food from lunch on Saturday in New York until dinner late Sunday evening with Dr. Tim Counihan and his wife in Dublin.

Counihan is the new professor of medicine at University College, charming and able but so swamped with patients he will find it difficult to do any of the research in cardiology that interests him. He confirmed my suspicion that there are no reliable data on the frequency of heart disease in Ireland or on the average diet of the population. Dr. Fred Stare of Harvard has some kind of a cooperative research program going, comparing men in Ireland with their relatives in Boston, but nothing like an acceptable sample of the population has been set up.

Dublin was full of the International Congress on Surgery but we went on to Manchester the next day, after standing eight hours fogged in at the tiny airport. At Manchester, many hours late, we were met by the president of the Cooperative Insurance Society (which is building the largest skyscraper in England for its headquarters) and Prof. Jean Lequime, who had come over from Brussels to sit in on discussions about a research program which the Cooperative has agreed to sponsor. The purpose of the program is to determine the value of blood cholesterol measurements in predicting the risk of future heart attacks. We hope to get about 5,000 subjects a year, starting next spring. The big problem is to persuade 700 or so doctors to assist by putting a few drops of blood on filter paper for us. Pricking a finger is an "assault" that requires assent in England.


Manchester to Brussels is an easy direct flight and there we stayed at the Fondation Universitaire as Lequime's guests, since all hotels were full (conventions!). Lequime plans to set up a research program, under my coordination, which will cover thousands of employees of banks and other corporations in Brussels. La Prevoyance Sociale will underwrite most of the program. La Prevoyance is by far the largest insurance company in Belgium and, though a cooperative, is run as a benevolent dictatorship by our friends Henri and Raymond Lemaire. Instead of cutting insurance premiums, they believe in collecting what the traffic will bear and putting the profits into good works -- hospitals, preventoria, and now research.

At Brussels we inspected Lequime's new Institute of Cardiovascular Research which will be formally opened by the Queen on the 14th (but we could not stay so long). The Institute adjoins the Departments of Medicine and Surgery on either side and is admirably equipped. It will make a fine locus for our joint research in Belgium.

Finally, Dr. Paul White flew in from Boston. We had an elegant lunch (all varieties of fish and shellfish), an hour's rest and then we were on a Czech plane bound for Prague. We were cordially greeted at the airport, and Paul was soon whisked off to the hotel. Margaret and I lacked proper visas, so we had to wait in a dismal room until 2 a.m. when, finally, a phone call released us.

Such is the restful life of a traveler. With all the best,

As ever,



Ancel Keys

AK/ji

JL Oct. 1962



Notes from a Medical Journey

Corfu, Greece
24 September, 1961

Dear Jay:

This bedroom in the "Castello" near the town of Corfu is a far cry from the Tiflis-Moscow plane. I estimate the ceiling is 20 feet up and I paced the floor to yield an estimate of 25 feet square. Windows look out on pines and enormous pyramidal cypresses in gardens and then olive groves sloping down to the Ionian Sea, with a view across it of the desolate mountains of Albania only a couple of miles away.

By the time this letter is finished my colleagues should be returning from their work examining the men of the nearby villages. Then I'll put on bathing trunks and we'll walk down to the beach for a swim in crystal clear and very salty water. Margaret, Professor Noboru Kimura of Japan, Dr. Branca Tiefenbach of Zagreb, Yugoslavia, and a bright Greek doctor with the difficult name of Stamatoyannopoulos should join us too. They must finish the immunochemical measurements of beta lipoprotein in the day's batch of about 40 blood samples. This new method works with great dispatch -- we ran 72 samples, in duplicate, in our first routine afternoon's work with only half a dozen needing to be repeated because of poor checks.

Incidentally, all the way from Minnesota we have carted 47 pounds of centrifuge, etc., plus 2 thermos flasks, for the lipoprotein method but it has been well worth it. Margaret demonstrated the method with great success in Brussels and in Russia before we got here. Doctors Myasnikov and Kipshidze were much interested and I hope to enable them to put the method to use in their institutes. The only technical snag was in Russia where we had to rig up alcohol lamps to seal the glass capillaries. Both in Moscow and in Tiflis we could not use Bunsen burners because "temporarily" there was no gas in the lines. Here in Corfu we use a little butane torch.

Now about Sukhumi in Georgia, on the eastern shore of the Black Sea. Sukhumi, Sochi, and a hundred miles of coast between are largely given over to resort hotels, where many thousands of Russians take their vaca-

tions, free or at small cost. The scenery is wonderful and the climate is mild all year. All over Russia people at every level of society try to get their reward of an annual trip to the Black Sea.

But our interest in Sukhumi was in the monkey colony and in the old men of the mountains. The monkey colony, as a center for research, goes back a long time but the present vigorous program began a dozen years ago. Various species are under study, but baboons, some being the eighth generation born there, are in the majority among the 1,300 monkeys in the colony. Deaths exceed births, but the population is kept up by imports from India and Africa.

Most of the research is done by the resident staff (Prof. Panin, director) but visiting researchers from other places in Russia are numerous. There are active programs in virology, endocrinology, and various diseases but of course we were most interested in the work on hypertension and atherosclerosis. Little or no work on nutrition has been done, and I was unable to get details of the chemical composition of the stock diet (which has been arrived at by trial and error) but it is clearly low in fat.

Baboons live in a family of a "head man," 20 to 30 females, and the offspring up to an age of about 2 years. At this age the young males must be segregated to prevent constant warfare. The most important experiment has been to "dethrone" the head man, putting him in a separate cage within his domain, and to introduce other adult males to take over. In a few weeks the dethroned male is apt to have constant hypertension, and in some cases, after months of this "stress," the electrocardiograph indicates coronary insufficiency or infarction. At autopsy, definite myocardial infarction was found in half a dozen cases.

Quantitative studies on the arteries are lacking, but the photos I saw of specimens did not show striking degrees of atherosclerosis. I did not see any data on the blood. I suggested that atherogenic diets be tried and was told that such experiments are planned.

Not far from Sukhumi is an area of farmer-shepherds, a sort of transition between pastoral and settled agricultural life. We were told that in this small region there are more than 300 men over 100 years of age. Anyway, we spent a hilarious afternoon at one of the farms with an old man of 117, his eighth wife, his "kid brother" of 96, his youngest son aged 23, and a flock of relatives and neighbors.

Ages are from church parish registries and tax records. It does seem that the old man has been around a long time; in 1884 he built his present farmhouse. Anyway, there was a great feast with innumerable toasts in wine. Dr. Paul White and his "older brother," as he called the old man, drank two "bottoms up" in vodka, whereupon old 117 tried to teach "younger brother" Paul (aged only 75) a Caucasian dance. Then the oldster called for his horse and trotted around making war whoops in the rain while we all howled with laughter.

The oldest man at the party was a neighbor, aged 126, who walks a mile and a half daily to call on his old pal. Old 126 was a bit creaky, slightly deaf, and probably half blind. At the long meal he went to sleep frequently, but only for a couple of minutes. Then, eyes closed, he would fish out tobacco and paper and roll a cigarette. Someone would give him a light and then he would reach out for a glass of wine. What a day!

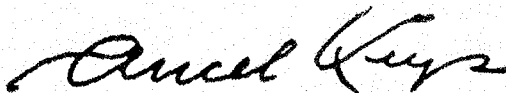
Dr. Kipshidze and colleagues want to organize a systematic study of people in these parts and have agreed to follow my protocols and methods, just as used here in Corfu. I suggested they study all the men over 90 and random samples of about 50 men in each decade from ages 20 to 90. There is a chance that we may go there again next July to help organize and standardize a survey. Also, I want to get more details about the diet which is obviously very low in animal fat. A main staple at every meal is a great dish of white corn meal mush. Where can I find a dietitian who speaks Georgian and Russian (unrelated)?

But now it is time to swim. Doctors C. Aravanis, A. S. Dontas, D. Lekos, and company have organized the job here so well that the main work of the day (starting before 8 a.m.) is finished by midafternoon, except for Miss Sdrin and her four dietitians who have no break checking the foods as eaten in the homes. After the swim and before dinner (usually about 9 p.m.) Dr. Ivan Mohacek (of Zagreb) and others will reread and classify the electrocardiograms of the day.

At this rate the whole job (700 subjects) will be done in less than a month. Margaret and I must leave tomorrow for Italy if we are to finish there and get home in ten days.

All the best,

As ever,



Ancel Keys

AK/j1

JL Nov. 1962



Notes from a Medical Journey

En route, Tbilisi (Tiflis)
to Moscow
18 September, 1961

Dear Jay:

Our Aeroflot jet drowns out talk (much noisier than our jets) as we fly north over the Caucasus after a fantastic week in Georgia. Dr. Paul White is writing notes in his journal and Margaret has curled up to sleep, so I'll start a thumbnail sketch of our stay in Tbilisi, travels through Georgia, and a weekend at Sukhumi on the Black Sea.

Today we had a big lunch with many toasts (the Georgians drink their local wine, the best in Russia) and then we started to worry about missing the plane. Roads were blocked for the arrival of the president of Cuba who was being given the works -- schools closed and Cuban flags everywhere. But our driver knew the back alleys and we were allowed to go on once we had slipped onto the airport road. As we were scrambling aboard the plane, a dozen of our Georgian friends arrived and then they stood around the plane on the ramp -- we standing at the open and unprotected forward door -- laughing and waving for half an hour while we waited for passengers who had been stuck in the Cuban "hero's" traffic snarl.

Last night we went by sleeper train from Sukhumi to Tiflis because weather canceled the evening plane. Margaret and I found ourselves in a 4-bed compartment with 2 Georgian men; but this was straightened out and eventually we were in a similar space with Dr. Paul White and Prof. Nodar Kipshidze, the Director of the new Institute of Therapy in Tiflis. Then the porter brought into the compartment a case of 12 bottles of Georgian wine, a present from our doctor friends in Sukhumi. We drank a bottle as the train started off and soon we were all sleeping as the train slid along on a remarkably smooth roadbed.

Morning brought its problems. The only "facilities" were a smelly W.C. at the end of the coach, and the idea is that each person is supposed to take the towel on his bunk to dry after a cold water wash.

Each of us, however, made the mistake of going to the little room early to respond to normal physiology, and by the time we got back to the compartment the porter (a husky middle-aged female) had departed with bed clothes -- and towels.

The purpose of our trip to Tiflis was to visit the new Institute of Therapy (patterned after that run by Dr. Myasnikov in Moscow) and to look into the question of the reputed great longevity of villagers in the Caucasus. The Institute is a 100-bed hospital and a laboratory building, the latter still in an early stage of construction. Dr. Kipshidze and his top staff of about 8 doctors seem to be competent and full of enthusiasm. They have decided to concentrate in 3 areas: cardiac diseases, liver disease, and bronchitis and emphysema. They already have the hospital operating, though research projects are not yet in full action.

We saw valvular and hypertensive heart disease patients but no clear-cut recent infarcts, though we were told that coronary heart disease is fairly common. One man in his 30's carried a tentative diagnosis of coronary heart disease with which we could not concur. He had a history of spells of atypical chest pains, lasting hours at a time, not associated with exercise, and not relieved by nitroglycerine. Blood pressure, electrocardiogram, blood studies, and chest roentgenogram were perfectly normal. After our discussion the doctors stopped talking about him as a "probable coronary."

The Institute of Therapy takes referred patients, presumably in the area of their interests, though the patient population was not greatly different from that of any medical department in a general hospital. Patient facilities are comfortable and the equipment is not bad as far as it goes; presumably it will be much more complete when the lab building is finished. An open-heart surgery unit is planned, but we learned no details. They do no surgery now, but mitral valve and patent ductus operations are done at another hospital in town.

En route to Sukhumi we stopped at Saltubo, a mineral water spa with a dozen hotel-like units, each with a capacity of 300 to 400 ambulant patients or people sent there for a rest with some medical attention. Bedrooms, some for couples with sitting room attached, are cheerful and look out over a great park-like area with views of the mountains. Each building has pleasant dining rooms, a theater (movies and concerts alternate), recreation rooms, verandas for taking the sun, physical therapy facilities, and a dental clinic. Patients come from all over Russia and it is completely free for those sent by medical referral; others pay the equivalent of a dollar or two daily for the three-week "cure." Saltubo is always full and several large new units are in construction.

On admission each patient has medical and dental examinations. Some bring documentation from their referring physicians, but mostly this is pretty scanty. A dietitian prescribes one or another diet (the food looked pretty good), everyone has a schedule for the bath, and some have additional physical therapy of a simple kind. The dentists are busy. With a three-week stay each dentist has an average of only about 20 minutes for each patient.

The doctors at Saltubo attribute wonderful things, especially for rheumatic patients, to the radioactive mineral water. The whole atmosphere, including the decor, resembles the old spas of Central Europe before World War II. The Tiflis doctors with us smiled about the Saltubo water, but they and we agreed that the rest and change in pleasant surroundings help many people.

This letter threatens to be too long so I'll try to continue about the monkey colony and the old men when I have time in the next few days. A bit ago, we passed up the Aeroflot tray dinner in hope of something better to eat in Moscow. Incidentally, the air hostesses are amiable but obviously not selected for youth and beauty. The fact that they have no uniforms and seem to shop in bargain basements does not help.

Now we are apparently power-diving (Russian style) for the Moscow Domestic Airport; the seat belt sign is on but people are walking in the aisles and pushing toward the exit.

All the best,

As ever,

A handwritten signature in cursive script, reading "Ancel Keys".

Ancel Keys

AK/ji

JL Feb 1963



Notes from a Medical Journey

Barcroft Laboratory
White Mountain, California

23 July, 1962

Dear Jay:

You have had many letters from me from unusual places abroad. Here is one from an unusual spot, too, but this time in the U.S.A., only some 300 miles from my old home in Berkeley, California. The Barcroft Laboratory is the main station of the University of California High Altitude Facility. Here we are at about 12,500 ft. up on White Mountain.

On the 20th, at 10 p.m., Dr. John H. Talbott (editor of the J.A.M.A., formerly head of medicine at the University of Buffalo) and I squeezed into a stifling Greyhound bus at Las Vegas and at 1:45 a.m. dismounted at a desolate fork in the road near Goldfield. As planned, an old Navy ambulance was waiting to drive us to our first destination at 10,200 ft. But we blew a tire so it was nearly 6 a.m. when we lurched up to the untidy clutter of huts that is Crooked Creek Station.

Drs. D. E. Dill and F. G. Hall rolled out of their bunks to put us down for an hour's rest before starting basal metabolism and respiratory tests. Bruce Dill, long time head of the Harvard Fatigue Laboratory, recently retired from his job as chief of medical research of chemical warfare, U. S. Army, and "Greg" Hall is professor of physiology at Duke University. After arterial punctures and more respiratory tests, we came up here to "Barcroft" the next day, and day after tomorrow we go to the summit for final testing.

The reason for all this goes back to 1935 when we spent some months in the Andes on the border of Chile and Bolivia studying acclimatization to high altitude. Recently, Bruce dug out the old data from altitudes up to 20,140 ft., where Brian (now Sir Brian) Matthews and I spent a week suffering more from sleeping in a hole in the snow (50° below at night) than from arterial oxygen saturation of 70 per cent.

So Bruce got the idea, and money for it, of repeating the tests and measurements made when we were twenty-seven years younger. Drs.

W. H. Forbes and Ross McFarland, still on the Harvard faculty, were also on our Andean expedition and have just left after their tests here on White Mountain. Unfortunately, Matthews can't get away from England. E. Hohwü Christensen, also with us in the Andes, is on loan to the Indian government from his professorship at Stockholm; I saw him in Bombay in February. The remaining 2 men on the Andean expedition were Harold Edwards, who had a fatal coronary many years ago, and Dr. E. S. Guzman Barron, of the University of Chicago, who died more recently. Still, this repeat on the 6 of us should show what nearly thirty years of aging can do to the complex functions involved in the response to altitude.

This University of California High Altitude Facility, supported by federal grants and from fees, caters to many kinds of visiting scientists. For example, 2 anesthesiologists, who were testing their theory of the importance of the spinal fluid pH and pCO_2 in the control of respiration, left this morning; this afternoon a group of astrophysicists arrived. There is a fair amount of laboratory gear here and investigators bring special equipment with them according to their needs. The dormitory has 18 double-decker bunks, there is hot and cold water, and a cook provides the kind of abundant, "wholesome grub" characteristic of a Boy Scout camp (we take turns with the dishes). When time permits, we contemplate a tremendous view of these weathered, barren White Mountains (only small patches of snow in July) and to the west, across Owen's Valley far below, the jagged range of the Sierra Nevada. Straggling up White Mountain to around 11,000 feet are the unique bristle-cone pine trees, the oldest living things in the world, ancient when the present patriarchs of the sequoias were seedlings.

So far the tests show that we have indeed deteriorated since the days in the Andes but perhaps less than we had feared. One change, in myself at least, is less joyful acceptance than in 1935 of the discomforts of dreary high places where the likelihood of crushing headaches and Cheyne-Stokes respiration at night increases with age. And, while I still like exercise, I find exercising to exhaustion is no longer so attractive.

Barren heights, cold, and low arterial oxygen saturation do not engender ebullient spirits. I remember the somber Indians on the Altiplano of Chile, Peru, and Bolivia. Even if they do sleep without literally gasping for breath at 12,000 to 17,000 ft., they rarely laugh except when they get drunk--which is as often as possible. I gather the same is true in Tibet.

I'll append a note after the work on the summit. Here I have autographed a couple of copies of "Eat Well and Stay Well" but for once you have a letter that is not full of talk about atherosclerosis, cholesterol, and dietary fats.

Las Vegas Airport
27 July, 1962

Writing a letter is difficult in a crowded shack of an airport at 95° F. (it is 109° outside), especially in the din of a hundred slot

machines being fed by sloppy, half-naked morons. But I am sustained by anticipation of leaving soon for more civilized parts and by relief at getting here safely.

My last stage from White Mountain was a chartered single-engine Cessna plane from Bishop, California. Over the middle of a lunar landscape the engine quit. The pilot got it going again quickly and then said, "Doc, I don't think we have enough gas to make it. What'll we do?"

By the time radiophone checks assured us that we had no place to refuel, we had passed the point of no return and there was nothing to do but cut the fuel injection pressure to the near-stall level, which meant the engine quit every few minutes, and hang on. Both tanks were dry when we finally coasted down to Las Vegas at noon.

The stay at the summit (14,246 feet), where we started the final tests at 3 o'clock this morning, seems very long ago, even though my hematoma, from an unlucky arterial puncture, is still fresh and my respiration is far from back to normal. Apparently I hyperventilated at a great rate for several days, ending with an arterial pH of 7.57 to 7.61, which may account for the severe headache that is only now subsiding.

So ends another adventure. It will be interesting to remember some day but not to repeat. See you soon, I hope.

As ever,



Ancel Keys

AK/j1



JL Mar '63

Notes from a Medical Journey

Velika Krsna (Serbia)
Yugoslavia
18 September, 1962

Dear Jay:

In the courtyard of the Community Hall of this Serbian village of 5,000, a dozen women, heads covered with kerchiefs, split and de-stone tiny peaches amid a litter of piles of boxes and barrels of fruit destined for a jam factory some miles away. In the entry hall are stacked scores of crates of blue plums from which slivovitz (plum brandy) will be made, while along the dusty road come little horse-drawn carts bringing more fruit to this co-operative center. But the farmers, too, are converging here, for this is the headquarters of a new epidemiologic study on cardiovascular disease, identical in methods and criteria with parallel programs that I am co-ordinating in 10 other areas in Finland, Italy, Greece, Holland, and Croatia.

The 14-man team here, under Prof. Bozidar Djordjevic and his able lieutenants, Drs. Vladan Josipovic and Thomas Strasser, began field work on September 10 and as of tonight will have covered about 500 men, aged 40 to 59, in detailed medical examinations, 12-lead electrocardiograms before and after fixed exercise (step) test using 2-channel Eliam jet writers from Sweden, respiratory function tests, etc. At least 98 per cent of all the 750 men of these ages in the prescribed area will be covered (carefully!) in barely two weeks -- a prodigious effort made possible by good preparation, competent personnel, and the example of Prof. Djordjevic, himself, who sets the pace in overlong days of intensive work. We shall analyze the bloods for cholesterol in Minneapolis.

Upstairs, in "Laboratorium II", the internists take histories and do physicals in one room and, in another, Dr. Petar Milutinovic and his associates carry out a study, new in this Serbian program, on thyroid function. The twenty-four-hour uptake of radioactive iodine (I^{131}) by the thyroid is measured in every man. This goes so smoothly that I shall propose its inclusion in the five-year follow-up studies in other areas, beginning with Dalmatia and Slavonia (in Croatia) next year.

The rest of the work is done in the big auditorium, with whitewashed walls and rough cement floors, of the Community Hall. The chemical lab, and place for bleeding (needles without syringes and without stasis), is the stage, raised 3 feet above the main level. On a bench outside the door wait the men who have come ahead of appointment, and, now and then, a woman, usually with a child, comes in to ask for medical advice. This is an extra job for the team, which, in an area with no doctor in this or in neighboring villages, inevitably must act as a sort of polyclinic -- thereby doing a service and developing good will for the program. Belgrade, with its big hospitals and medical school, is only 50 miles to the north, but rural medical service here, as elsewhere in the world, is a problem.

At the end of the month, detailed dietary studies will start here under the direction of Dr. Bozidar Simic. I hope to arrange for Dr. D. Galanos of Athens (on our Greek team) and Dr. Kurt Loebl (in Dr. Daniel Brunner's medical department in Jaffa, Israel) to observe this work, Galanos to give the benefit of his experience, Loebl to learn with an eye to application in Israel.

Everyone is working so hard, maintaining high standards but with no pause to compare the accumulating data, that it is not yet possible to say much about the local picture of disease. The team has turned up a couple of cases of previously undiagnosed diabetes and several cases of tuberculosis and nephritis. As in all our population studies, hypertension (e.g., B.P. of 160/95) is common and some rheumatic hearts are found, but heart disease is not common among these middle-aged men. However, so far, 3 definite old myocardial infarcts and several cases of angina pectoris have been found, so we may guess that the prevalence of coronary heart disease will prove to be intermediate between the high rates we find in the U.S.A., Holland, and Finland and the rarity of the condition observed in our studies in Italy, Japan, the Greek islands, and Dalmatia.

The outstanding surprise is the large number of cases of chronic bronchitis and emphysema among these farmers. We look forward to the analysis of the respiratory function tests. There is no clue as to the cause, so here is a new problem to be studied. Asthma is conspicuous by its absence. This is in contrast to some other rural areas near Belgrade.

This operation is being supported entirely by the Yugoslavs. I have contributed protocols, skinfold calipers, and E.C.G. paper and, to help at the start of the field operations, I sent here Dr. Gunnar Blomqvist of Stockholm and Dr. Henry Blackburn of our senior staff at the University of Minnesota. We shall do the cholesterol analyses and put all the data through the punch card-electronic computer mill.

Like the paralleled epidemiologic researches in other areas in this co-ordinated program, it is hoped that this cross-sectional survey in Serbia can be extended into a follow-up study for at least five years. Incidence is more important than prevalence, and the follow-up will show what characteristics of men in health are significant for future disease

development. All of this should contribute to the long-range goal of prevention of heart disease. So this present work should be only the beginning.

Accordingly, we are most interested in the reaction of the men from Belgrade who visited the field operation yesterday. The delegation was headed by the Yugoslav Minister of Health, Noma Markovic, and included the former minister, currently Director of the National Health Institute, Dr. Herbert Kraus, and Dr. Radivoje Berovic, Dean of the Medical Faculty. Their good will is essential for long-term support. Also, in the future I hope help will come from the U.S. Public Health Service.

Tonight there will be a dinner, with speeches no doubt, in a small hotel at Topola where Kara George ("Black George"), the founder of the dynasty that preceded Tito, and his descendants are buried in a mosaic-encrusted Byzantine-style church (built 1930). And tomorrow I leave for home via Vienna. A couple of days ago I 'phoned Margaret from Belgrade and she said rain and cold weather continue in the Twin Cities. I hope it brightens by the 30th when we are to receive 20 of my cardiologic colleagues from Finland, Holland, Belgium, Israel, Italy, Japan, Egypt, and Russia who will stay three days before we all go on to the World Congress on Cardiology in Mexico. In the meantime, I'd like to clean off the desk and get some rest, but that is a forlorn hope.

All best wishes,

As ever,

A handwritten signature in cursive script, reading "Ancel Keys".

Ancel Keys