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*AK-Shekelle*  
*letter.*

Dear Rick,

"A history of activities and thought concerning the epidemiology and prevention of ischemic heart disease" would interest many persons in public health and, I hope, in cardiology and internal medicine. For me you pose difficult questions of when, what, why,, and judgment made harder by changing values and poor memory.

When we meet and talk about your questions I hope some answers will emerge but here I am making some notes to help as a starter. I follow your numbers.

In 1946 we had finished the semi-starvation work and I had to think of other research to undertake. My research on semi-starvation led to consideration of mortality in populations where starvation had been sll too common. I wondered about mortality after the war and was impressed by The U.S. statistics which showed the high rate of deaths from cardiovascular disease and indications of the increasing importance of coronary heart disease (CHD). Why? And why do some persons develop coronary heart disease and others do not. The answer could be found by recording many characteristics of persons in health and follwinig over time to find which would become victims of CHD. So I decided to try to answer the question. That meant examining persons in detail and follwing them over the years. I decided to use middle aged men because the incidence of CHD was considered to be high in such persons. My staff agreed and helped plan the research. No outside individuals were involved.

2) When we started there were no real areas of consesus about the cause or prevention of CHD beyond the idea that middle aged executive men are most common among patients. Associated was the idea that executive men are commonly overly stressed and over weight

3) The main lines of my research have been:

- a) the relation between the development of CHD and the pre-disease characteristics of persons when they were apparently "healthy".
- b) The effects of the diet on blood lipids.
- c) Differences in incidence, prevalence, and

mortality between populations and sub-populations.

d) Persons who have been most influential in my work include those who made my prospective studies possible and argued for or against theories. To name some: Paul White, of Harvard University, Gino Bergami in Naples, Italy, Jimenez Diaz in Madrid, Spain, Paul Soisalo in Helsinki, Finland, John Brock in Cape Town, South Africa, Noboru Kimura in Kuruma, Japan, Bozidar Djorgevic in Belgrade, Yugoslavia. Others I should name include Martti Karvonen (Finland), Jerry Stamler, (U.S.A.) Francisco Grande (Spain), Pierre Duchosal (Switzerland), Hugh Sinclair (England), Fred Epstein (Switzerland).

Unanswered questions include the long time effect of dietary changes on incidence of CHD; the importance of lipoprotein sub-fractions for CHD,

4) My thinking about CHD is indicated in item 1, above, The findings in my research of consequence seem to me to include:

a) The discovery and estimation of differences among populations in CHD.

b) The finding and measurement of effect of the diet on serum cholesterol.

c) The finding of characteristics related to longevity.

Margaret joins in sending best wishes to you and Sue.

As ever,

Ancel Keys