HB INTRO. TO
FIRST ANCEL KEYS LECTURE
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ANCEL KEYS: PIONEER

It is fine and it is fitting that the American Heart Association now has a lecture named Ancel Keys. Ancel Keys is a pioneer of cardiovascular disease research and founding father of cardiovascular disease epidemiology and prevention. He is a whole investigator; the consummate cardiovascular investigator. His first PhD thesis was on the arterial circulation of a elasmobranhs, at the Scripps Institute in 1928, in which he already used regressions to relate the weight to the length of fishes! He studied the oxygen disassociation curve of hemoglobin at 20,000 feet in the Andes, working out of the Harvard Fatigue Lab in 1935. His studies during WW II on metabolic and circulatory functions, and their deterioration under the stress of bed rest, heat, postural tilting, cold immersion, exercise, and semi-starvation, all culminated in a classic, The Biology of Human Starvation. In that series of studies, he demonstrated the remarkable change, due to experimental manipulation of environment, of factors previously considered constitutional, such as Sheldonian body types, work capacity, blood pressure and blood cholesterol levels. During the '40s and '50s he re-defined human biology and provided the normative distributions of most biological variables in healthy adult men. He authored classics that have directly affected our thinking, researches and daily lives, 40 and 50 years later.

If there is still an issue about intellectual priority of the concept of lifestyle and risk factors in causation and prevention of CVD, this issue should be settled by a 1948 manuscript, a presentation to the Chicago

Heart Association, entitled "Mode of life and the development of heart disease: research for a preventive hygiene"!

Dr. Keys probably knows more than anyone about body composition and the relationship between diet and physical activity and body compartments. He first established the intrinsic and presumably hereditary characteristics of blood lipid responses to diet, and followed up with a series of elegant isocaloric experimental substitutions of fats and fatty acids, leading to the Keys Equation. This is still the more valid mathematical construction of the relationship between change in dietary fat composition and blood total cholesterol level. This contribution over a decade is a body of work worthy of a lifetime of accomplishment by most productive investigators. Ancel Keys had the insights, the scientific rigor, the mathematical and computing savvy and the prodigious energy to tie these relationships into a regression equation that has stood the test of 30 years time. So much a part of our lives is the Keys Equation that even cartoonists today understand the non-linear relationship of dietary cholesterol to total serum cholesterol, shown in this picture showing the square root of an egg yolk!

Dr. Keys was the earliest to put forward hypotheses about the <u>population</u> causes of cardiovascular risk and disease. This seminal idea derived from his observations of population differences in diet, risk factors and disease, honed over a decade of peripatetic visits to exotic places with Paul Dudley White and other colleagues, including Martti Karvonen, Noboru Kimura, Christ Aravanis, Flaminio Fidanza and numerous other friends. These observations led to the formulation of the classic Seven Countries

Study that has so stimulated major researches and that provides the basis of the population strategy of coronary disease prevention through eating and behavioral patterns.

Dr. Keys initiated the methodology that led to the demonstration of large differences in coronary heart disease incidence, and the methodology and concepts that led to finding large differences in the composition of diet and to demonstration of a major phenomenon: population differences in the means and distributions of the risk factors. These findings indicate that we are dealing with mass cultural phenomena.

Dr. Keys first demonstrated the ecologic correlations between diet, lipids and disease. They were derided for many years. Now they are better understood for their importance in showing the population causes of disease and population effects of prevention, once causation is well established by congruent evidence.

He was the first to apply multiple logistic regressions developed in one population (in Europe) to another population (in the U.S.), showing that the risk factor concept is universal in its ability to discriminate individual risk within cultures, but that large differences in the force of risk factors exist according to the environmental setting.

Dr. Keys was a founding father of the cohort study in cardiovascular disease epidemiology, in a study initiated in the Fall of 1947 and variously called the Minnesota Business and Professional Men's Study, the CVD Study, and the Twin Cities Prospective Study.

He was a central member of the Diet-Heart Study, a "Club of Five", that produced another classic that, too, has led to major researches and to the 1970s decade of preventive trials, trials of everything, that is, but diet! In the Diet-Heart Study and other activities, he activated public recognition of the Diet-Heart hypothesis, and the Diet-Health relationship. He also picked up new and long-term colleagues including Jerry Stamler.

Ancel Keys basically "started it all". He forwarded it all: the clinical studies, the diet-laboratory experiments, the cohort studies, the population surveys and ecologic analyses, the clinical trials. And, he brought it all together, building a new biological, physiological, experimental and epidemiological science as he went along. This science he called Physiological Hygiene. Ancel Keys was central to the development of cardiovascular disease epidemiology and helped make it the important bridge it is today between biology, preventive practice and public health.

Few people in this country nowadays realize Dr. Keys' remarkable contribution to international cardiology through his teamwork with Paul Dudley White and other distinguished cardiologists around the world. The International Society of Cardiology, during the days of his early wanderings with Paul White, was an elite club that held meetings in pleasant places. It initiated the World Congresses of Cardiology, the first in Paris in 1950. The ISC was not really getting anywhere in stimulating research directions of the cardiovascular community, or any real collaborative research, or any international research or any research in

epidemiology and prevention. It had no systematic organization. Ancel's activities with Paul Dudley White and colleagues in the early ISC directly resulted in the formation of the Research Committee of the ISC and of the present structure of the ISFC.

The first major report and international visibility of CVD epidemiology occurred on center stage at the 2nd World Congress of Cardiology in Washington in 1954, headed by a panel of Ancel Keys, Paul Dudley White, Gunnar Björk, and Noboru Kimura. This was the real launching moment of international cardiovascular disease epidemiology and, along with developments in Framingham, Minnesota, Chicago and elsewhere, of the subsequent development of a new and recognized field.

Ancel and Paul White's efforts in the ISC Research Committee led to the coalescence at the 1966 Delhi 5th World Congress of Cardiology and formalization of the ISFC into Scientific Councils and a Lay Executive Board. The ISFC Council on Epidemiology was a direct outgrowth of these activities, and leads through a connected chain to the present leadership.

Dr. Keys' contribution to training in cardiovascular disease investigation was profound; not in formal courses, but rather in inviting younger colleagues of his distinguished investigator friends from around the world to come to Stadium Gate 27 at Minnesota for some months or years. This list of people is a part of a Who's Who of Cardiovascular Disease Epidemiology and Prevention. His work and thinking spawned hundreds of researches and dozens of careers. Most of those affected acknowledge the major influence of Ancel's writings, thinking and collaboration.

The American Heart Association Council of Epidemiology and Prevention, and the American Heart leadership present here today, are clearly to be commended for developming this lectureship which represents the field so well. They have established a new and fine tradition for the Council, and for the Heart Association, by the Ancel Keys Lecture. I am sure we all thank them, and we all thank Ancel Keys!

Henry Blackburn, MD
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