Past, Present and Future of Cardiovascular Epidemiology and Prevention in the U.S.A.

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There have been remarkable developments in the epidemiology and prevention of cardiovascular diseases over the last fifty years as there have been in basic science, diagnosis, and management related to these conditions. I will discuss selected examples from past and present studies and approaches and comment on some of the likely future directions for cardiovascular epidemiology and prevention in the United States.

THE PAST. 1950'S TO 1980'S.

Concern about the "epidemic" of coronary heart disease manifest in the rising death rate and frequency of sudden death in middle aged men following the second world war stimulated efforts to find the causes, describe the natural history and develop preventive approaches for CHD. Clinicians knew that hypercholesterolemia, hypertension, diabetes and hypothyroidism were associated with CHD in their patients, but it was not until 1948 when the National Heart Institute was founded and the Framingham Heart Study was initiated that longitudinal population-based investigations were designed to test specific hypotheses related to potential causes, to measure incidence, estimate risk, and describe the course of CVD.

The initial hypotheses addressed by the Framingham Heart Study were that incidence of CHD was related to age, male sex, elevated levels of blood pressure, cholesterol and body weight, to tobacco smoking, diabetes mellitus, and gout. Physical activity and increased thyroid function were postulated to be protective. Early results demonstrated associations between CHD and blood pressure, cholesterol and smoking and showed that incidence rates increased as levels of these risk factors increased throughout the range, from the lowest to the highest levels. Early epidemiologic studies in the United
States collaborating in the Pooling project were in Albany, Chicago Western Electric Company, Chicago Peoples Gas Company, Framingham, Tecumseh, Los Angeles and Minnesota. The Pooling Project established the importance of cholesterol, blood pressure and smoking as risk factors for white middle aged men. Since the mid 1960's multiple regression analyses have provided estimates of the probability of developing CHD and stroke based on composite risk factor profiles which use information on sex, age, blood pressure, cholesterol, cigarette smoking, glucose intolerance, left ventricular hypertrophy, family history and prevalent heart disease. An important lesson was that several moderately elevated risk factors increase risk as much or more than a single high risk factor does.

International differences in death rates from heart disease and stroke had a major influence on the design and implementation of epidemiological studies in the 1950's and 1960's. The Seven Countries Study pioneered international comparisons of lifestyles, especially diet, and showed that fat content of diets and serum cholesterol levels were correlated with heart disease rates in men in ecologic analyses. Several other studies enrolled cohorts in countries with substantially different CVD death rates. The NI-HON-SAN study used the opportunity provided by migrants from Japan to Honolulu or San Francisco to explore behavioral and environmental factors related to heart disease and stroke in more genetically homogeneous populations. Details of this study are presented in this volume. Comparisons with the Japanese population and with the Framingham cohort were envisaged when the Honolulu Heart Program, the Puerto Rico and Yugoslavia studies were implemented, however, the latter two are no longer active. International comparisons showed that although the major risk factors were the same, they did not account completely for the differences in CVD morbidity and mortality among these populations.

While it was known by the late 1960's that incidence of CVD could be predicted for groups of people, it was not certain that incidence could be reduced by lowering risk factors that were amenable to change. Primary prevention trials to answer this question included the High Blood Pressure Detection and Follow-up Program (HDFP), the Multiple Risk Factor Intervention Trial (MRFIT) and the Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT). These randomized controlled trials enrolled thousands of middle-aged subjects; men and women in HDFP, men only in MRFIT and LRC-CPPT. Endpoints were total mortality, CVD and CHD deaths and nonfatal myocardial infarction. Follow-up over periods of 5 or more years showed that levels of blood pressure, cholesterol and rates of cigarette smoking could be reduced by hygienic measures or drug treatment, and that end points could be reduced. The positive results of these trials published in the 1970's and 1980's have been major and continuing influences on medical practice and on the behavior of individuals. Clinical guidelines for treating high blood pressure and elevated levels of cholesterol through hygienic and pharmacologic means have been disseminated and accompanied by national education programs.

The Conference on the Decline in Coronary Disease Mortality in 1978, established the reality of the downward trend which began in the mid 1960's, and concluded that reasons for the decline were unclear though both primary prevention and better medical care had contributed. The conference also pointed out the need for new knowledge and for monitoring trends in mortality, morbidity and risk factors. A working group on heart disease epidemiology subsequently set the direction for the next generation of studies which were implemented beginning in 1984.

THE PRESENT 1984 - 1996

Needs and opportunities for research identified by the working group included; community surveillance to monitor trends in incidence of fatal and nonfatal CHD and their relation to changing risk factors; longitudinal studies of the development of and trends in risk factors over the entire age range; and clinical trials of reduced salt intake and weight reduction. They commented on the need for better measurements or more information on physical activity, psychosocial characteristics, cigarette smoking, occupational exposures and water hardness. They also recommended studies of the quality of medical care, evaluation of interventions for CVD, as well as training programs for epidemiologists and biostatisticians.

Individual investigators initiated and continued epidemiological and prevention studies throughout the period and were responsible for many innovative approaches. A few examples in addition to those mentioned above and below are the Nurses Health Study, the Minnesota Heart Survey, the Bogalusa and Muscatine Studies, the Charleston, Evans County, Worcester, and San-Antonio Heart Studies, the College Alumni and the Physicians Health Studies.

The major new epidemiologic investigations initiated by the National Heart Lung and Blood Institute were; Coronary Artery Risk Development in Young Adults (CARDIA), Atherosclerosis Risk in Communities (ARIC), Cardiovascular Health Study (CHS) in people over 65 years of age, the National Growth and Health Study, the Strong Heart Study in American Indians, the Insulin Resistance Atherosclerosis Study (IRAS) and most recently the Family Heart Study and the Family Blood Pressure Program. These studies extend studies predominantly of middle aged white men, to include young adults, the elderly, minority populations and women. They, as well as studies continuing from the past, have broken new ground in detecting and confirming risk factors such as lipids and lipoproteins, clotting and fibrinolytic
factors, and the amount and distribution of body fat. Evidence on the role of low birth weight, insulin, hyperhomocysteinemia is accruing as is information on potential protective factors including vitamin E, flavonoids, other antioxidants, hormone replacement therapy and moderate alcohol consumption. The efficacy of aspirin for primary and secondary prevention has been demonstrated for men and is under investigation in women.

Current or recent primary prevention trials include Systolic Hypertension in the Elderly Program (SHEP), Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), Postmenopausal Estrogen/Progestin Interventions (PEPI), Trials of Hypertension Prevention (TOHP), Dietary Intervention Study in Children (DISC), Child and Adolescent Trial for Cardiovascular Health (CATCH), Obesity Prevention in American Indians (PATHWAYS), Dietary Approaches to Stop Hypertension (DASH), and the Women’s Health Initiative (WHI). Information from these and other ongoing clinical trials and epidemiologic studies has been or soon will be published in the medical literature. Three community-based prevention research demonstration studies were completed recently. In the Stanford Five City Project, the Minnesota and the Pawtucket Heart Health Programs, educational interventions were conducted using mass media, community organizations and environmental strategies. Changes in knowledge, risk factors, morbidity and mortality were the goals and evaluation of processes and results were essential components of these studies. Short-term benefits on CVD risk were detected in treatment compared with control communities and were in addition to those experienced by the U.S. population in general.

The earliest of the national education programs, Detection, Evaluation and Treatment of High Blood Pressure and the National Cholesterol Education Program were initiated in 1972 and 1985 respectively. Their continuing success guided the newer programs on Smoking, Obesity and Physical Activity, and the Heart Attack Alert Program which were initiated recently.

Major advances resulting from research in epidemiology and prevention in the present period include; increased understanding and recognition of new CVD risk factors in general, and in previously understudied populations; use of new non-invasive technologies to detect and measure pre-clinical atherosclerosis, silent ischemia, and cardiac dysfunction; development of community surveillance and intervention strategies; and demonstration of the efficacy of primary and secondary prevention approaches.

THE FUTURE

Recommendations for future research made in 1994 by the Epidemiology and Prevention Task Force include for epidemiology: clarifying relationships among subclinical atherosclerosis, CVD risk factors and clinical CVD; identifying precipitants of acute events; and monitoring and increasing knowledge of etiology and prevention of heart failure, cardiomyopathies and vascular disease of the kidney. The Task Force also recommended comparisons of CVD morbidity, disability and mortality in the U.S. and other countries, with assessment of lifestyles, geographic, socioeconomic, racial and ethnic characteristics as determinants of differences in CVD. The report states environmental and genetic factors influencing key risk factors should be identified; the interaction of genetic susceptibility and environmental determinants of CVD should be investigated; interrelationships of lifestyles, hormone metabolism and psychosocial factors should be studied in women, as should relationships of socio-economic status to CVD risk in men and women. Observations on blood pressure, amount and distribution of body fat are needed from childhood through adult ages to identify determinants and effects on CVD of levels and changes over the life span. Research is recommended on the determinants and precursors of CVD at older ages. Risk factors considered in need of further study include nutritional components, physical activity, diabetes, insulin, glucose metabolism, weight gain, obesity, thrombosis, platelet function, inflammation and psychosocial factors; relationships between these and other risk factors, atherosclerosis and CVD require elucidation.

Recommendations for research on prevention of CVD include research on methods for translating knowledge about modifying lifestyles and management of risk factors into public awareness, policy and practice. Specifically the Task Force recommended developing more effective methods for modifying blood lipids, preventing high blood pressure, obesity and diabetes mellitus and eliminating smoking. Ways should be found to reduce CVD-related limitations on function and quality of life by influencing social settings and psychological variables. Approaches to secondary prevention that were suggested involve physician education, clinical research and dissemination of information about effective strategies against disease progression and death. The Task Force recommended evaluation of interventions in older people, in women, minorities, groups with low socio-economic status, children and adolescents. They also cited needs for better understanding of etiology and prevention of congenital heart disease, for more effective methods for preventing rheumatic heart disease and for treating Kawasaki disease.

Many of these investigations are underway in ongoing observational and intervention studies which will be presenting results in the next several years. Longitudinal population based research studies continue to be necessary along with surveillance to monitor trends in prevalence, incidence and risk factors, as well as mortality, case fatality and medical care. The dramatic changes over time in death rates for CHD in the U.S.
Reduce coronary heart disease deaths to no more than 100 per 100,000 people.
Reduce stroke deaths to no more than 20 per 100,000 people.
Increase to at least 50 percent the proportion of people with high blood pressure whose blood pressure is under control.
Increase to at least 90 percent the proportion of people with high blood pressure who are taking action to help control their blood pressure.
Reduce the mean serum cholesterol level among adults to no more than 200 mg/dL.
Reduce the prevalence of blood cholesterol levels of 240 mg/dL or greater to no more than 20 percent among adults.
Increase to at least 60 percent the proportion of adults with high blood cholesterol who are aware of their condition and are taking action to reduce their blood cholesterol to recommended levels.
Reduce dietary fat intake to an average of 30 percent of calories or less and average saturated fat intake to less than 10 percent of calories among people aged 2 and older.
Reduce overweight to a prevalence of no more than 20 percent among people aged 20 and older and no more than 15 percent among adolescents aged 12 through 19.
Increase to at least 30 percent the proportion of people aged 6 and older who engage regularly, preferably daily, in light to moderate physical activity for at least 30 minutes per day.
Reduce cigarette smoking to a prevalence of no more than 15 percent among people aged 20 and older.
Source: Healthy People 2000.
are shown in Figure 1. Comparable information on morbidity and a wider range of CVD is needed for the future. Studies of economic costs, quality and availability of care are relatively new directions in epidemiology and ones requiring development and testing of methods.

Randomised clinical trials are needed to provide definitive answers about promising new preventive and therapeutic approaches such as preventing hypertension, raising HDL-cholesterol and lowering homocysteine levels, and also to identify any adverse effects of interventions which may otherwise escape detection. Populations participating in clinical trials and community interventions will be more diverse and research is needed to enhance participation and retention of those who are hard to recruit.

On the national level, specific goals have been set in "Healthy People 2000" National Health Promotion and Disease Prevention Objectives 10. The challenge for CHD is to reduce the death rate to no more than 100 per 100,000 people, and for stroke to reduce the death rate to no more than 20 per 100,000 people. Assuming recent rates of decline continue, the goal for CHD should be attainable but the decline in stroke mortality appears to be slowing down. Approaches to reaching the objectives for CVD are indicated by the goals for reducing cholesterol, controlling high blood pressure, reducing the prevalence and initiation of cigarette smoking and reducing the prevalence of overweight by reducing dietary fat intake and increasing physical activity. The targets for these risk factors are shown in Figure 2. Although trends are generally encouraging, obesity is increasing. Improvements in other risk factors have been less in some subgroups than in others 13.

This brief overview of accomplishments, opportunities and challenges for epidemiology and prevention of CVD in the U.S.A. indicates that future improvements in cardiovascular and general health are necessary and possible if current knowledge and proven strategies are combined with unprecedented opportunities to develop and apply new knowledge for the benefit of individual patients, families and populations.

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