30. Multiple Risk Factor Intervention Trial Research Group: Multiple risk factor intervention trial (MRFIT): risk factor changes and mortality results. JAMA 248: 1465–1477 (1982).
31. Stallones, R. A.: Mortality and the multiple risk factor intervention trial. Am J Epidemiol 117: 647–650 (1983).
32. Goor, D.: Open heart surgery—present, past and future. Harefuah 99: 380–382 (1980) [in Hebrew].
33. Weddell, J. M., and Beresford, S. A. A.: Planning for stroke patients: a four-year descriptive study of home and hospital care. Her Majesty's Stationary Office, London, 1979.
34. Dever, G. E. A.: Community health analysis—a holistic approach. Aspen Systems Corporation, Germantown, Md., 1980.

Epidemiologic Evidence for Cardiovascular Disease Initiatives in Israel and the United States

MANNING FEINLEIB, MD, DrPH

This paper is based on Dr. Feinleib's presentation at the Second Binational Symposium: United States-Israel: Interrelations of Epidemiology and Health Policy, held October 17–19, 1983, in Bethesda, Md.

Tearsheet requests to Manning Feinleib, MD, DrPH, Director, National Center for Health Statistics, Rm. 2–19, Center Bldg., Hyattsville, Md. 20782.

Synopsis

There seems to be much epidemiologic evidence implicating a variety of modifiable risk factors in the occurrence of coronary artery disease. Although "common sense" would imply modification of each of these risk factors, on both an individual and a national basis, in order to prevent the occurrence of coronary artery disease in middle and later life, the direct evidence for a beneficial effect from such modifications is, at present, quite meager. Nevertheless, there seems to be a growing awareness and also a growing change in lifestyle and health behaviors that will tend to accomplish the "common sense" recommendations. It is important that monitoring systems be put in place to document the extent of these lifestyle changes and to evaluate their effect on the continuing trends in coronary artery disease incidence and mortality. Joint efforts in the United States, Israel, and other countries will go far to quantitate these effects in these naturally occurring experiments.

CORONARY ARTERY DISEASE HAS BEEN DESCRIBED as one of the major public health epidemics of the 20th century. First described as a clinical entity in 1912, it was recognized with increasing frequency as being a major health problem, particularly among affluent white males in urban areas of industrialized countries of North America and Europe. By 1940 it was the leading cause of death in the United States, and its frequency continued to rise through the 1950s, reaching a peak in the mid-1960s. During the last 20 years the mortality from coronary heart disease has decreased markedly in the United States and in several other countries, such as Canada, Australia, and Israel, but the rates have remained level in most West European countries and have increased dramatically in Eastern Europe and some countries of the Third World. Although hundreds of millions of dollars have been spent investigating the origins and natural history of this disease, it is far from clear why heart disease has become such a major problem in the 20th century, why it now seems to be waning in some countries, and, indeed, whether the decline in mortality is due to an amelioration of the disease itself or a manifestation of improvements in medical care and improved survival.

During the 20th century there were also dramatic changes in the occurrence of the other major manifestation of cardiovascular disease, namely, cerebral vascular accidents or stroke. Stroke has been the third leading cause of death in the United States for about 50 years, being particularly important in the older age groups. Since at least 1940, however, the age-specific death rates for stroke have been declining steadily in both men and women in the United States. In many areas of the world where coronary heart disease is relatively rare, such as Japan, stroke is often one of the most important causes of death. As with coronary heart disease, it is not yet clear why the patterns of stroke incidence and mortality have varied as they have during this century.

During the last 30 years several epidemiologic studies of free-living populations have been conducted in the United States, Israel, and many other nations to investigate the factors associated with the occurrence of coronary heart disease and its natural history. Some of the factors that are found to affect the incidence of coronary

heart disease are listed in the box of page 251. In this report I will briefly review the evidence for factors that lend themselves most readily to prevention initiatives.

Several recent reviews summarized the body of information available from epidemiologic studies implicating each of the risk factors listed in the incidence of coronary heart disease (*1–4*). Before discussing individual risk factors, it may be worthwhile to summarize some of the sources of data and analytic techniques used in investigating the role of these factors in cardiovascular disease occurrence.

U.S. and Israeli Vital Statistics Systems

Both Israel and the United States have modern national vital statistics systems which allow detailed enumeration of deaths by specific causes and various demographic factors, such as age, sex, and ethnic group, that can be related to the denominators obtained from national censuses. Thus, each country can provide reliable, up-to-date information on the death rates from the various cardiovascular diseases. However, in the way morbidity data are collected for assessing the rates of occurrence of these diseases, including nonfatal events, the data bases of the two countries differ.

In the United States, national estimates of morbidity from disease are obtained by a variety of special surveys conducted by the National Center for Health Statistics (*5*). These include the National Health Interview Survey (NHIS), the National Health and Nutrition Examination Survey (NHANES), and the National Hospital Discharge Survey (NHDS). Each of these surveys is based on a random probability sample representative of the country, but participation in each of them is voluntary.

NHIS is a household interview survey of a cross section of the noninstitutionalized civilian population of the United States (*6–10*). A two-stage sampling procedure is used. First, 376 primary sampling units are drawn from approximately 1,900 geographically defined primary sampling units that cover the 50 States and the District of Columbia. Then, within each primary sampling unit approximately 100 households are randomly selected, yielding an annual sample of approximately 40,000 households and about 110,000 persons.

The first National Health and Nutrition Examination Survey (NHANES I) was initiated in 1970. The second NHANES began in 1976 and ended in 1980. In 1983 and 1984, the Center is conducting a National Health and Nutrition Survey of the Hispanic population of the United States. A third National Health and Nutrition Examination Survey is planned to begin in 1987. These surveys are designed to collect data that can be obtained best or only by direct physical examination, clinical and laboratory tests, and related measurement procedures (*11–19*).

Each country can provide reliable, up-to-date information on death rates from the various cardiovascular diseases. However, the data bases of the two countries differ in the way morbidity data are collected.

The sampling procedure is designed to give an estimate for the total U.S. population and is based on a multistage, highly clustered probability sample. Approximately 100 stands or examination sites are selected, and approximately 300 persons are selected for examination at each stand, yielding a total sample of approximately 28,000 people for both NHANES I and NHANES II.

The National Hospital Discharge Survey (NHDS) is a principal source of information on inpatient utilization of short-stay hospitals in the United States (*20–22*). Data collection began in 1964 and has been continuous since then. Like the other surveys mentioned, the sample plan is basically a two-stage, stratified design. The primary stratification variables are the number of hospital beds and geographic regions. Hospitals are selected in direct proportion to size so that hospitals with 1,000 or more beds are selected with certainty, and hospitals with less than 50 beds are sampled with a probability of approximately 1 in 40. The second stage of the design is a systematic sample of discharges from the sample hospitals. In 1979 the sample consisted of 544 hospitals from a universe of approximately 8,000 short-stay hospitals. Of the 496 hospitals in the scope of the survey, information was collected from 416 participating hospitals—an 84 percent response rate—on approximately 216,000 discharges of patients.

NHIS, NHANES, and NHDS provide an extensive array of information about the acute and chronic health status of Americans, including data on cardiovascular diseases and risk factors that may be associated with cardiovascular conditions.

In Israel, there had not been any effort to conduct a national health examination survey or household interview survey, so far as I am aware, until 1977. In the last quarter of that year the Health Services Survey was conducted as part of the Labor Force Survey, with interviews of 6,000 Israeli families. A similar effort was undertaken in 1981. However, because many of the medical services are provided by government- or employee-sponsored health plans, there are considerably more data available about hospital utilization, similar to those in the U.S. National Hospital Discharge Survey. These Israeli

Although "common sense" would imply modification of these risk factors, the direct evidence for a beneficial effect from such modifications is, at present, quite meager.

data do not depend on the voluntary compliance of the patient and therefore may provide considerably more complete (and less biased) information about morbidity from cardiovascular conditions than that available for the United States.

These data systems are fundamental to assessment of the current status of the respective populations with regard to cardiovascular diseases and the risk factors that may contribute to them, and to monitoring the secular trends in both disease frequency and the level of risk factors. For the epidemiologic point of view, however, relations between various personal and environmental factors and the occurrence of cardiovascular diseases are being investigated in specialized studies in both Israel and the United States.

Epidemiologic Studies in Two Countries

As clinical and vital statistics observations of the occurrence of coronary artery disease accumulated during the first half of this century and led to an increasing number of hypotheses about the etiology of coronary artery disease, the need to use a more organized and better controlled approach became obvious. Long-term prospective population-based studies of individual persons were considered the optimal strategy to acquire the necessary data. It was recognized that representative samples of several thousand persons would be needed; that these people would have to be examined while they were ostensibly healthy; that carefully standardized examination procedures, questionnaires, and laboratory methods were required; and that diligent and careful surveillance of the entire group must be maintained for many years.

Using this general approach, numerous epidemiologic studies involving tens of thousands of people have been undertaken during the last three decades in a variety of populations, including those in the United States and Israel.

Perhaps the best known of these studies in the United States is the Framingham Heart Study; in Israel it is the Israel Ischemic Heart Disease Study. Major contributions have also been made by many others in a variety of countries. Both the Framingham (*23–32*) and the Israeli studies (*33–42*) have been described in detail elsewhere, so only a few salient features need be mentioned.

The Framingham study was launched in 1948 with a sample of approximately 6,660 people in the town of Framingham, Mass., 5,209 of whom came in for examination between 1949 and 1950. These individuals have been followed for the last 33 years, with physical examinations conducted every 2 years. Both men and women between the ages of 30 and 60 in 1950 were included in the sample.

The Israel Ischemic Heart Disease Study (IIHD) was a prospective study of 10,059 men ages 40 and older in 1963. Civil servants and municipal employees in the Jerusalem, Tel Aviv, and Haifa areas underwent three extensive examinations in 1963, 1965, and 1968. The study involved a varying ratio, stratified sampling of subjects from six geographic areas of birth.

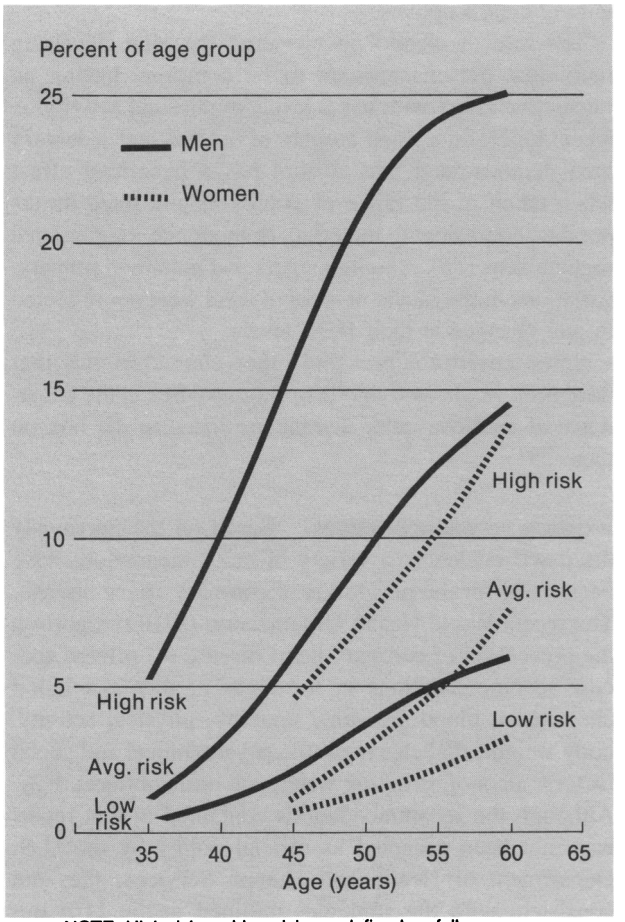
Both of these studies have provided data for a great number of reports on the relation of a wide variety of risk factors measured at the examination to the subsequent development of coronary heart disease and stroke. Throughout the period of active investigation of the IIHD there was active collaboration between the Israeli investigators and the investigators at Framingham and at the National Heart, Lung, and Blood Institute in Bethesda, Md. Thus, it is not surprising that many of the examination and laboratory techniques, as well as methods of analysis and presentation, in the two studies were highly comparable.

I turn now to evidence linking various risk factors to the occurrence of cardiovascular diseases by drawing on these two major studies for primary documentation of relationships.

Risk Factors

The five major risk factors for cardiovascular diseases are cholesterol, blood pressure, cigarette smoking, diabetes mellitius, and obesity. Their importance individually has been confirmed in virtually all major prospective studies. Four of these risk factors have also been shown in multivariate analyses to have independent, significant cumulative effects. An example of the cumulative effect of these variables in stratifying the population by risk of cardiovascular disease is shown in the chart, which is based on data from the Framingham Heart Study. Although obesity is a very important individual risk factor for coronary heart disease, indices of obesity have not been found to make any significant contribution to the multivariate model in many studies, presumably because the effects of obesity operate through its associations with the other risk factors in the box (*29*). Recent analyses of the Framingham data, however, have shown that when long-term risk is considered, obesity does have an effect independent of the other four risk factors (*43,44*).

Probability of developing coronary heart disease in 8 years by age, sex, and risk category (percent)



NOTE: High risk and low risk are defined as follows:

Risk factor	Low risk	High risk
Systolic blood pressure	105	150 (mm Hg)
Cholesterol level	185	285 (mg/d)
Smoke	No	Yes
Glucose intolerance	No	Yes

SOURCE: Framingham Heart Study (56).

Factors affecting incidence of coronary heart disease

Five major risk factors	Cholesterol, blood pressure, smoking, diabetes mellitus, obesity
Personal factors	Exercise, psychology, society, behavior, genetics
Demographic	Age, sex, race, socioeconomic status
Dietary	Fats, carbohydrates, coffee, alcohol, salt, trace metals
Environmental	Carbon monoxide, weather, noise, water hardness, toxic substances
Biochemical	Lipoprotein profiles (high, low, and very low density lipoproteins and triglycerides), clotting factors, hormones
Other conditions	Respiratory diseases, gout, drugs

Four additional types of risk factors—exercise and psychological, societal, and behavioral factors—have been highlighted during the past decade. Physical exercise, during both work and leisure, is felt to affect the risk of coronary artery disease (*45*). Besides an evident conditioning effect on the myocardium and perhaps an ability to stimulate collateral arterial circulation to the heart, exercise is also felt to play a role by tending to induce an increase in the high density lipoprotein (HDL) fraction of the blood. Several studies, including the Framingham and the IIHD studies, have documented that individuals with high HDL tend to have a lower risk of developing coronary artery disease (*31,42*).

Psychological factors have also been suspected of playing a role in the incidence of coronary artery disease. Rosenman and Friedman popularized the concept of the type A–B personality, in which the type A person exhibits a behavior pattern characterized as achievement-striving, time-urgent, and hostile (*32*). Other psychological characteristics have also been implicated in recent studies. (*38,41*).

Sociological factors including occupation, economic level, and ethnicity, as measured by country of origin, have also been identified as risk factors for coronary artery disease. The Israeli experience has been particularly useful in documenting the marked differences of coronary artery disease rates among Jews who have come from different areas of the world to Israel (*35,39*). These differences cannot be accounted for by the traditional risk factors.

Diet. Many dietary factors have been suspected of playing a role in the etiology of heart disease and have become the focus for a number of prevention initiatives (*4*). Although major differences have been found in the rates of heart disease among populations having traditionally different diets, it has been more difficult to document the dietary contributors to heart disease within a single population. Because of the relative homogeneity of diets within a given population, the difficulty of accurately quantifying the differences that might exist among individual persons, and the tendency of dietary patterns to change somewhat over the long periods of followup necessary in these studies, it is difficult to know how much weight should be given to the sparse evidence linking heart disease and individual dietary components within populations. Another important factor that greatly complicates interpretation is the known genetic heterogeneity of populations, so that different persons will metabolize nutrients differently and have different regulatory mechanisms for controlling the levels of cholesterol and other factors in their bodies.

Despite these limitations, there is some evidence to implicate a variety of dietary components in an increased

'Throughout the period of active investigation of the Israel Ischemic Heart Disease Study there was active collaboration between the Israeli investigators and the investigators at Framingham and at the National Heart, Lung, and Blood Institute.'

risk of coronary heart disease. Populations that customarily consume diets high in saturated fat and cholesterol tend to have higher rates of heart disease than do populations with low intakes of these nutrients. Studies of patients in metabolic disease wards have clearly shown that elevating the intake of saturated fat and cholesterol will elevate the blood cholesterol levels. Thus, there is a plausible linkage of ecological data at the group level with a mechanism to explain a possible relationship at the individual level, although data from free-living individuals have not been clear cut for the reasons stated previously. Similar patterns seem to hold for data implicating sodium intake and the occurrence of hypertension.

Lipoproteins. Although hypercholesterolemia is a major risk factor for coronary heart disease, risk is even better defined when plasma cholesterol is measured in terms of the units of lipid transport known as the lipoproteins (*2*). The major lipoprotein families are very low density lipoproteins (VLDL), low density lipoproteins (LDL), and high density lipoproteins (HDL). Dr. Daniel Brunner and coworkers of the Donolo Government Hospital in Jaffa were among the first to point out, in 1958, that HDL (then known as the alpha cholesterol) was consistently low in coronary patients (*46,47*). Interest in HDL has been renewed in recent years because studies in Framingham and elsewhere have confirmed Brunner's early findings. In fact, these studies have shown that in both men and women older than age 50, HDL has the strongest relationship of any lipoprotein fraction to coronary heart disease (*31,42*).

On the other hand, persons with high levels of LDL are at increased risk of coronary heart disease, measured as either heart attacks or other events such as angina. LDL levels correlate closely with levels of total plasma cholesterol. Thus, higher levels of LDL carry greater risk of vascular disease, and higher levels of HDL appear to protect against the development of coronary heart disease. The biological mechanism involved in the inverse relationship of HDL and coronary heart disease remains unclear. What is known is that levels of HDL correlate positively with exercise, estrogens, and moderate ingestion of alcohol, and are inversely related to obesity, smoking, diabetes mellitus, and use of progestin-containing contraceptives.

The role of alcohol in elevating the HDL levels in individual persons appears to be complex, having an interactive effect with usual levels of physical activity. A recent report on a small number of runners and sedentary men demonstrated that alcohol has a beneficial effect when taken in the range of approximately three drinks per day, equivalent to the effect of moderate jogging on a regular basis (*48*). Among joggers and marathon runners, variations in the intake of alcohol level were not reflected in any changes in their HDL levels.

Some environmental and other characteristics that have been implicated in one or more studies in the occurrence of cardiovascular disease are listed in the box on page 251.

Existing recommendations. Based on the previously discussed evidence, a variety of recommendations have been made for the prevention of coronary artery disease. The recent World Health Organization (WHO) report on the prevention of coronary heart disease (*4*) offered specific recommendations in the areas of diet and blood cholesterol, blood pressure, smoking, physical activity, body weight, diabetes mellitus, psychological and social factors, alcohol, drinking water, and oral contraceptives. Although the recommendations contained in that report have not been accepted as official policy by the U.S. Department of Health and Human Services, they are consistent with the strategies outlined in the 11th Bethesda Conference on the Prevention of Coronary Heart Disease (*3*), which was sponsored by the American College of Cardiology, the American Heart Association, the Centers for Disease Control, and the National Heart, Lung, and Blood Institute.

Many of the recommendations are also reflected in the objectives for the nation for promoting health and preventing disease, which reflect the official policy of the Department of Health and Human Services (*49*). The objectives relevant to the prevention of coronary heart disease include those related to high blood pressure control, smoking, nutrition, physical fitness and exercise, and control of stress. The assessment of the degree of attainment of these national objectives will be based primarily on the U.S. data sets described previously.

Complexities of risk factors and intervention. Several recent studies have shed additional light on possible interactions and complexities of the risk factors and our ability to ameliorate their effects. For example, although cigarette smoking has been documented as an important risk factor for coronary heart disease in many studies, recent studies have shown that this effect seems to be

independent of the nicotine levels of cigarettes and the carbon monoxide levels of the inhaled smoke (*50,51*). This independence would imply that switching to a "safer cigarette" would not have any appreciable effect on the prevention of coronary artery disease. Cigarette smoking has a particularly profound effect on the occurrence of coronary artery disease prior to the age of 45. This disproportionate effect in younger persons may be the key reason why three recent prevention studies with randomized samples failed to show a beneficial effect on coronary artery disease rates in the groups assigned to smoking intervention (*52–54*). Additional speculations about these anomalous results recognized that most of the improvement in smoking behavior occurred among relatively light cigarette smokers, and those who smoked 25 or more cigarettes per day showed the least response to the intervention therapies. This evidence would strongly suggest that prevention initiatives should be aimed primarily at preventing the formation of the cigarette smoking habit in children and young adults rather than trying to change habits in those who have become addicted to cigarettes.

The efficacy of dietary modification to achieve reductions in blood cholesterol levels, and thereby a reduction in coronary artery disease rates, was demonstrated in the Oslo Study (*54*). Although these statistically significant results were not replicated in the Multiple Risk Factor Intervention Trial (MRFIT) (*53*) or the WHO factory study (*55*), the rationale for lowering cholesterol levels through modification of the fat content of the diet seems to be sound. It should be noted that the interactions of reduction of fat intake, weight control through regulation of caloric intake, and the effect of physical activity have not been adequately studied in either observational or intervention studies. A comparison of these factors in population groups in whom the rate of coronary artery disease is low compared with groups with a high rate, however, suggests that the triad of high fat diet, obesity, and physical inactivity are important risk factors that can be modified, albeit with difficulty, to enhance the cardiovascular fitness of high risk populations.

Conclusion

There seems to be much epidemiologic evidence implicating a variety of modifiable risk factors in the occurrence of coronary artery disease. Although "common sense" would imply modification of each of these risk factors on both an individual and a national basis in order to prevent the occurrence of coronary artery disease in middle and later life, the direct evidence for a beneficial effect from such modifications is, at present, quite meager. Nevertheless, there seems to be a growing awareness and also a growing change in lifestyle and health behaviors that will tend to accomplish the "common sense" recommendations. It is important that monitoring systems be put in place to document the extent of these lifestyle changes and to evaluate their effect on the continuing trends in coronary artery disease incidence and mortality. Joint efforts in the United States, Israel, and other countries will go far to quantitate these effects in these naturally occurring experiments.

References

1. Feinleib, M.: Risk assessment, environmental factors, and coronary heart disease. J Am Coll Toxicol 2: 91–104 (1983).
2. Levy, R. I., and Feinleib, M.: Coronary artery disease: risk factors and their management. *In* Heart Disease, edited by E. Braunwald. W. B. Saunders Co., Philadelphia, 1980, pp. 1246–1278.
3. Bethesda conference report: eleventh Bethesda conference. Prevention of coronary heart disease. Am J Cardiol 47: 713–776 (1981).
4. WHO Expert Committee: Prevention of coronary heart disease. WHO Technical Report Series 678. World Health Organization, Geneva, 1982.
5. Pearce, N. D.: Data systems of the National Center for Health Statistics. Vital and Health Statistics, Series 1, No. 16. DHHS Publication No. (PHS) 82–1318. National Center for Health Statistics, Hyattsville, Md., December 1981.
6. Health survey procedure: concepts, questionnaire development, and definitions in the Health Interview Survey. Vital and Health Statistics, Series 1, No. 2. PHS Publication No. 1000. National Center for Health Statistics, Washington, D. C., May 1964.
7. Health Interview Survey procedure, 1957–74. Vital and Health Statistics, Series 1, No. 11. DHEW Publication No. (HRA) 75–1311. National Center for Health Statistics, Washington, D. C., April 1975.
8. Simmons, W. R.: U.S. National Health Survey: the statistical design of the health Household Interview Survey. Health statistics. PHS Publication No. 584–A2. Public Health Service. U. S. Government Printing Office, Washington, D. C., July 1958.
9. Feller, B. A.: Health characteristics of persons with chronic activity limitation: United States, 1979. Vital and Health Statistics, Series 10, No. 137. DHHS Publication No. (PHS) 82–1565. National Center for Health Statistics, Hyattsville, Md., December 1981.
10. Wilder, C.: Prevalence of chronic circulatory conditions, United States, 1972. Vital and Health Statistics, Series 10, No. 94. DHEW Publication No. (HRA) 75–1521. National Center for Health Statistics, Rockville, Md., September 1974.
11. Plan and initial program of the Health Examination Survey. Vital and Health Statistics, Series 1, No. 4. PHS Publication No. 1000. National Center for Health Statistics, Washington, D. C., July 1965.
12. Plan, operation and response results of a program of children's examinations. Vital and Health Statistics, Series 1, No. 5. PHS Publication No. 1000. National Center for Health Statistics, Washington, D. C., October 1967.
13. Plan and operation of a health examination survey of U. S. youths, 12–17 years of age. Vital and Health Statistics,

Series 1, No. 8. PHS Publication No. 1000. National Center for Health Statistics, Washington, D. C., September 1969.

14. Miller, H. W.: Plan and operation of the Health and Nutrition Examination Survey, United States, 1971–1973. Vital and Health Statistics, Series 1, Nos. 10a, 10b. PHS Publication No. 1000. National Center for Health Statistics, Washington, D. C., January 1977.
15. Plan and operation of the HANES I Augmentation Survey of adults 25–74 years, United States, 1974–75. Vital and Health Statistics, Series 1, No. 14. PHS Publication No. 1000. National Center for Health Statistics, Hyattsville, Md., June 1978.
16. McDowell, A., Engle, A., Massey, J., and Maurer, K.: Plan and operation of the Second National Health and Nutrition Examination Survey, 1976–1980. Vital and Health Statistics, Series 1, No. 15. DHEW Publication (PHS) 81–1317. National Center for Health Statistics, Hyattsville, Md., July 1981.
17. Roberts, J., and Rowland, M.: Hypertension in adults 25–74 years of age, United States, 1971–1975. Vital and Health Statistics, Series 11, No. 221. DHHS Publication No. (PHS) 81–1671. National Center for Health Statistics, Hyattsville, Md., April 1981.
18. Fulwood, R., Abraham, S., and Johnson, C. L.: Serum cholesterol levels of persons 4–74 years of age by socioeconomic characteristics, United States, 1971–74. Vital and Health Statistics, Series 11, No. 217. DHEW Publication No. (PHS) 80–1667. National Center for Health Statistics, Hyattsville, Md., March 1980.
19. Fulwood, R., et al.: Hematological and nutritional biochemistry reference data for persons 6 months-74 years of age, United States, 1976–80. Vital and Health Statistics, Series 11, No. 232. DHHS Publication No. (PHS) 83–1682. National Center for Health Statistics, Hyattsville, Md., December 1982.
20. Simmons, W. R.: Development of the design of the NCHS Hospital Discharge Survey. Vital and Health Statistics, Series 1, No. 39. PHS Publication No. 1000. National Center for Health Statistics, Rockville, Md., September 1970.
21. Haupt, B. J.: Utilization of short-stay hospitals, annual summary for the United States, 1980. Vital and Health Statistics, Series 13, No. 64. DHHS Publication No. (PHS) 82–1725. National Center for Health Statistics, Hyattsville, Md., March 1982.
22. McCarthy, E.: Inpatient utilization of short-stay hospitals, by diagnosis, United States, 1979. Vital and Health Statistics, Series 13, No. 69. DHHS Publication No. (PHS) 83–1730. National Center for Health Statistics, Hyattsville, Md., December 1982.
23. Dawber, T. R., Kannel, W. B., Revotskie, N., and Kagan, A.: The epidemiology of coronary heart disease. The Framingham enquiry. Proc R Soc Med 55: 265–271 (1962).
24. Kannel, W. B., Castelli, W. P., Gordon, T., and McNamara, P.: Serum cholesterol, lipoprotein and the risk of coronary heart disease. The Framingham Study. Ann Intern Med 74: 1–12 (1971).
25. Ashley, F. W., and Kannel, W. B.: Relation of weight change to changes in atherogenic traits: the Framingham study. J Chronic Dis 27: 103–114 (1974).
26. Kannel, W. B.: Role of blood pressure in cardiovascular disease: the Framingham study. Angiology 26: 1–14 (1975).
27. Kannel, W. B., and McGee, D., and Gordon, T.: A general cardiovascular risk profile: the Framingham study. Am J Cardiol 38: 46–51 (1976).
28. Kannel, W. B., Hjortland, M. C., McNamara, P. M., and Gordon, T.: Menopause and risk of cardiovascular disease: the Framingham study. Ann Intern Med 85: 447–452 (1976).
29. Gordon, T., and Kannel, W. B.: Obesity and cardiovascular disease: the Framingham study. Clin Endocrinol Metab 5: 367–375 (1976).
30. Gordon T., et al.: Diabetes, blood lipids and the role of obesity in coronary heart disease risk for women. The Framingham study. Ann Intern Med 87: 393–397 (1977).
31. Castelli, W. P., et al.: HDL cholesterol and other lipids in coronary heart disease. The Cooperative Lipoprotein Phenotyping Study. Circulation 55: 767–772 (1977).
32. Haynes, S. G., Feinleib, M., and Kannel, W. B.. The relationship of psychosocial factors to coronary heart disease in the Framingham study. III. Eight-year incidence of coronary heart disease. Am J Epidemiol 111: 37–58 (1980).
33. Medalie, J. H., et al.: Blood groups, myocardial infarction and angina pectoris among 10,000 adult males. N Engl J Med 285: 1348–1353 (1971).
34. Kahn, A. H., et al.: The incidence of hypertension and associated factors: the Israel Ischemic Heart Disease Study. Am Heart J 84: 171–182 (1972).
35. Medalie, H. J., et al.: Myocardial infarction over a five-year period—I. Prevalence, incidence and mortality experience. J Chron Dis 26: 63–84 (1973).
36. Medalie, H. J., et al.: Five-year myocardial infarction incidence—II. Association of single variables to age and birthplace. J Chron Dis 26: 329–349 (1973).
37. Medalie, H. J., et al.: Angina pectoris among 10,000 men; 5 year incidence and univariate analysis. Am J Med 55: 583–594 (1973).
38. Goldbourt, U., and Medalie, H. J.: Characteristics of smokers, nonsmokers and ex-smokers among 10,000 adult males in Israel: I. Distribution of selected socio-demographic and behavioral variables and the prevalence of disease. Isr J Med Sci 11: 1079–1101 (1975).
39. Medalie, H., Papier, C., Goldbourt, U., and Herman, B. J.: Major factors in the development of diabetes mellitus in 10,000 men. Arch Intern Med 135: 811–817 (1975).
40. Goldbourt, U., Medalie, H. J. and Neufeld, N. H.: Clinical myocardial infarction over a five-year period—III. A multivariate analysis of incidence, the Israel Ischemic Heart Disease Study. J Chron Dis 28: 217–237 (1975).
41. Medalie, H. J., and Goldbourt, U.: Angina pectoris among 10,000 men: II. Psychosocial and other risk factors as evidenced by a multivariate analysis of a five year incidence study. Am J Med 60: 910–921 (1976).
42. Goldbourt, U., and Medalie, H. J.: High density lipoprotein cholesterol and incidence of coronary heart disease—the Israel Ischemic Heart Disease Study. Am J Epidemiol 109: 296–308 (1979).
43. Garrison, R. J., Feinleib, M., Castelli, W. P., and McNamara, P. M.: Cigarette smoking as a confounder of the relationship between relative weight and long-term mortality. JAMA 249: 2199–2203 (1983).
44. Hubert, H., Feinleib, M., McNamara, P. M., and Castelli, W. P.: Obesity as an independent risk factor for cardiovascular disease: a 26-year followup of participants in the Framingham Heart Study. Circulation 67: 968–977 (1983).
45. Morris, J. N., et al.: Vigorous exercise in leisure-time: protection against coronary heart disease. Lancet No. 8206: 1207–1210, Dec. 6, 1980.

46. Brunner, D., and Lobl, K.: Serum cholesterol, electrophoretic lipid pattern, diet and coronary artery disease: a study in coronary patients and in healthy men of different origin and occupations in Israel. Ann Intern Med 49: 732–750 (1958).
47. Brunner, D., Altman, S., Loebl, K., and Schwartz, S.: Cholesterol percentages in coronary patients with and without increased total serum cholesterol levels and in healthy controls. J Atheroscler Res 2: 424–437 (1962).
48. Hartung, G. H., et al.: Effect of alcohol intake on high-density lipoprotein cholesterol levels in runners and inactive men. JAMA 249: 747–750 (1983).
49. Promoting health/preventing disease: objectives for the nation. U.S. Department of Health and Human Services, Government Printing Office, Washington, D. C., 1980.
50. Castelli, W. P., et al.: The filter cigarette and coronary heart disease: the Framingham study. Lancet No. 8238: 109–113, July 18, 1981.
51. Kaufman, D. W., et al.: Nicotine and carbon monoxide content of cigarette smoke and the risk of myocardial infarction in young men. N Engl J Med 308: 409–413 (1983).
52. Rose, G., Hamilton, P. J. S., Colwell, L., and Shipley, M. J.: A randomised controlled trial of anti-smoking advice: 10-year results. J Epidemiol Community Health 36: 102–108 (1982).
53. Multiple Risk Factor Intervention Trial Research Group: Multiple Risk Factor Intervention Trial. JAMA 248: 1465–1477 (1982).
54. Hjermann, I., Holme, I., Velve Byre, K., and Leren, P.: Effect of diet and smoking intervention on the incidence of coronary heart disease. Lancet No. 8259: 1301–1310, Dec. 12, 1981.
55. World Health Organization European Collaborative Group (G. Rose, chairman): Multifactorial trial in the prevention of coronary heart disease: 3. Incidence and mortality results. Eur Heart J 4: 141–147 (1983).
56. Feinleib, M.: Discussion of "Epidemiology of cardiovascular diseases: current perspectives." Am J Epidemiol 104: 457–462 (1976).

The Pertussis Vaccine Controversy

ALAN R. HINMAN, MD

This article is based on the author's presentation at the Second Binational Symposium: United States-Israel, held in Bethesda, Md., October 17–19, 1983.

Tearsheet requests to Alan R. Hinman, MD, Director, Division of Immunization, Center for Prevention Services, Centers for Disease Control, Atlanta, Ga. 30333.

Synopsis

Over the past few years, there has been continuing controversy about whether the benefits of routine vaccination for pertussis outweigh the potential risks. Some of the epidemiologic and technical issues include ascertainment and reporting of cases, case definition and laboratory confirmation, identification and purification of antigens, vaccine potency measurement, vaccine efficacy, and vaccine safety. Other factors include legal and economic issues, ethical concerns, emotional overlays, and the role of the media. Much of the evidence for the benefits of pertussis vaccination arises from epidemiologic studies regarding the incidence of the disease and the effectiveness of the vaccine in preventing it. The very nature of epidemiologic data has contributed to the controversy, since there is virtually no epidemiologic study with absolutely incontrovertible results that allow only one interpretation. Nonetheless, available evidence indicates that the benefits of pertussis vaccination far outweigh the risks.

OVER THE PAST FEW YEARS, there has been continuing controversy about whether the benefits of routine vaccination for pertussis outweigh the potential risks. The controversy involves not only the interface among epidemiology, politics, and policy, but also legal and economic issues, ethical concerns, emotional overlays, and the role of the media. In this paper I will first describe some of the epidemiologic and technical issues involved in the pertussis vaccine controversy and then discuss the impact these issues have had on the development and implementation of public policy.

Epidemiologic and Technical Issues

Ascertainment and reporting of cases. It is widely felt that the diagnosis of pertussis is not considered in all circumstances where it might be appropriate and that there is substantial underreporting of cases in this country. One indication of the degree of undernotification is the fact that the number of pertussis hospitalizations in the United States reported through the National Hospital Discharge Survey exceeds the number of cases reported to the Centers for Disease Control through the routine