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DONALD E. PARKER ("The Vestibular Apparatus") is professor of psychology at Miami University in Oxford, Ohio. He received his B.A. at DePauw University in 1958 and his Ph.D. in experimental psychology from Princeton University in 1961. In 1961 he was a postdoctoral research fellow in the Auditory Research Laboratory at Princeton. From 1962 to 1965 he was an experimental psychologist in the Aerospace Medical Research Laboratories of the Wright-Patterson Air Force Base. In 1965 he joined Hermann Schöne at the Max Planck Institute for Behavioral Physiology at Seewiesen in West Germany to study the psychophysiology of the vestibular system on a postdoctoral fellowship. Parker joined the faculty of Miami University in 1966. In addition to his research on the vestibular system he is investigating the influence of audio-frequency sound, infrasound and vibration on perception and performance. He is particularly interested in phenomena associated with temporary or permanent hearing loss. He writes: "I have a long-standing collaboration with a group of respiratory physiologists at the University of Kentucky concerning the perception of respiratory resistance. (How hard is it to breathe through a filter from a Coke bottle?)" Parker also writes: "My favorite entertainment is flying. I enjoy using the complex Air Traffic Control System—people, computers and radar—to ensure a safe flight in marginal weather conditions, particularly if a good ballet or opera company is performing at the destination."

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Established 1845 SCIENTIFIC AMERICAN November 1980 Volume 243 Number 5

The Rise and Fall of Ischemic Heart Disease

In the U.S. the death rates attributed to heart attack and other results of the obstruction of the arteries that nourish the heart have fallen since the 1960's. Why they have is not understood

by Reuel A. Stallones

Whenever a drastic difference is found in the frequency of a disease from one time to another or between disparate cultures or in different geographic areas, a special opportunity is created for research into the causes of the disease. Epidemiologists refer to these opportunities as natural experiments because they are untainted by the intervention of an experimenter. The recent history of heart attack and other conditions embraced by the term ischemic heart disease presents evidence that the inhabitants of the U.S. are all participants in just such an experiment, conducted on a grander scale than any experimenter could have devised. For more than 30 years ischemic heart disease has been the single greatest cause of death in the U.S. Of 1.9 million deaths in 1976, for example, some 650,000, or nearly a third of the total, were attributed to ischemic heart disease specifically. Without fanfare, however, the mortality rates for ischemic heart disease reached a peak in the mid-1960's and have steadily declined since then, for a total reduction that has exceeded 25 percent.

The terms ischemic heart disease, coronary heart disease and arteriosclerotic heart disease are more or less synonymous; they denote the clinical manifestations of atherosclerosis, the obstruction of the flow of blood through the arterial network, when the vessels that are obstructed are the coronary arteries, which nourish the muscle of the heart. Although the factors that determine the progression of atherosclerosis are not fully understood, the process is known to involve the growth of a mass called an atheroma in the inner layers of the arterial wall. In its early stages the mass contains smooth-muscle cells and cholesterol; later its structure is complicated by the growth of fibrous tissue and by deposits of calcium. Atherosclerosis may begin early in life, even in childhood. It progresses slowly over decades, thickening the walls of the arteries and restricting the flow of blood.

Eventually an atheroma may completely block a coronary artery, thereby depriving a segment of heart muscle of its supply of blood in the medical crisis known as a myocardial infarction, or heart attack. An atheroma also promotes the clotting of blood in an artery; hence a clot may produce a sudden myocardial infarction long before the atheroma is large enough to do so. The likelihood of a heart attack is therefore determined by two processes, the slow course of atherosclerosis and the rapid, unstable clotting of blood. Acute myocardial infarction is often fatal; in about a third of all the cases in the U.S. the afflicted person dies before receiving medical attention. Those who survive are at high risk of subsequent attacks; they may be permanently disabled, and ultimately they may die of congestive heart failure. In spite of advances both in knowledge of atherosclerosis and in medical care for the victims of ischemic heart disease, the brightest prospects for the future lie in the effective prevention of the disease. Plainly a sustained decline in the death rate for ischemic heart disease commands attention and calls for explanation.

Mortality data for the U.S. are derived from death certificates that have been coded for cause in accord with the International Classification of Diseases. Data in this form are available only since 1900, and for the first three decades of this century they are available only for states that had a registration method of sufficient quality to warrant admission to the system. The coding has been revised at approximately 10-year intervals to reflect the evolution of medical concepts of diseases and their causes. All these circumstances sharply limit the comparability of data over long periods of time, and so interpretations must be offered with more than the usual caution.

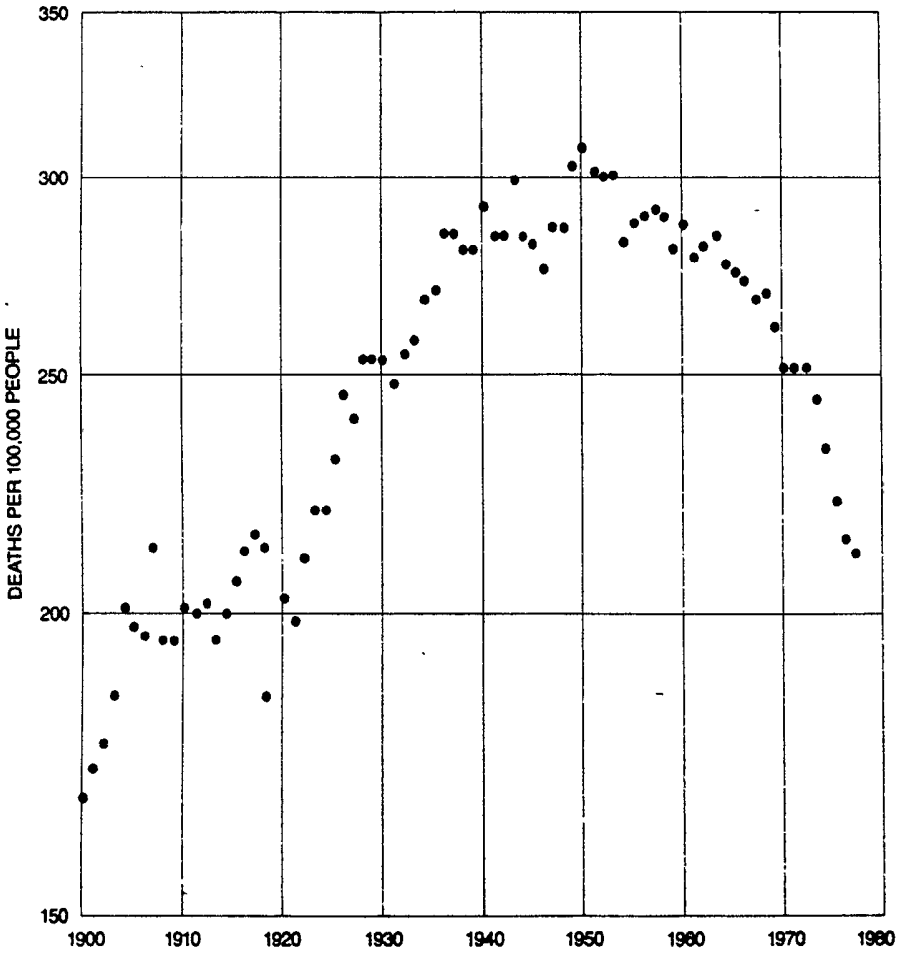
The changes in medical terminology preclude the direct examination of long-term trends in the mortality from ischemic heart disease, but the broader category "diseases of the heart" has reflected the changing patterns in spite of its lack of specificity. Between 1900 and 1920 the death rates attributed to diseases of the heart were relatively stable. An abrupt change came in 1920, when an upward trend was established that continued for 30 years. The abruptness of the change was accentuated by a deficit of deaths in 1919, the year that followed the excessive mortality of the influenza pandemic of that time. Moreover, a detailed analysis of heart-disease mortality by Theodore D. Woolsey and Iwao M. Moriyama of the U.S. Public Health Service demonstrates that in about 1920 the admission of southern and western states to the death-registration area added young people to the population base. This too accentuated the apparent break in the slope of the curve.

An examination of the deaths by 10-

year age groups shows, however, that the change in slope was characteristic of the mid-adult years. The death rates for diseases of the heart among people younger than 35 decreased steadily throughout the first half of the century, and the death rates increased steadily for people older than 75. If the change in slope were due to vagaries in the reporting or the classification of the deaths, then the reason for the change to be so highly selective for the age groups between 35 and 75 is obscure. Terence W. Anderson of the University of Toronto presented additional evidence that the change was not artifactual when he computed the ratios of the male to the female death rates attributed to diseases of the heart and showed that from 1920 onward the ratios increased sharply. To put it another way, the male and the female death rates diverged as they both increased between 1920 and 1950 because the death rates for males grew faster. A change in the rates by gender is no more likely to be adventitious than is a change in the rates for a particular age group.

Within the diversity of diseases that constitute the category of diseases of the heart, only one diagnosis, angina pectoris, showed an increase coincident in time with the one for the broader category. Angina pectoris means pain in the chest, and it results from the inadequate flow of blood to the heart. The pain itself is not considered now to be a likely cause of death, but in 1912, when James B. Herrick alerted the medical profession to a lethal disease marked by occlusion of the coronary arteries, he called the condition angina pectoris.

In 1930 a new rubric, diseases of the coronary arteries, was introduced. Apparently it replaced angina pectoris as the designation of choice for the lethal disease, which continued to rise rapidly through the 1930's and 1940's. In 1949 diseases of the coronary arteries disappeared from the classification system. It was absorbed into a more modern term, arteriosclerotic heart disease, which in turn gave way (in 1968) to ischemic heart disease. The time trends in this century for other forms of heart disease show no other plausible candidate to account for the overall increase in diseases of the heart. Ischemic heart disease can therefore be traced backward and downward in a logically consistent chain to the sudden change in mortality that marked the year 1920.



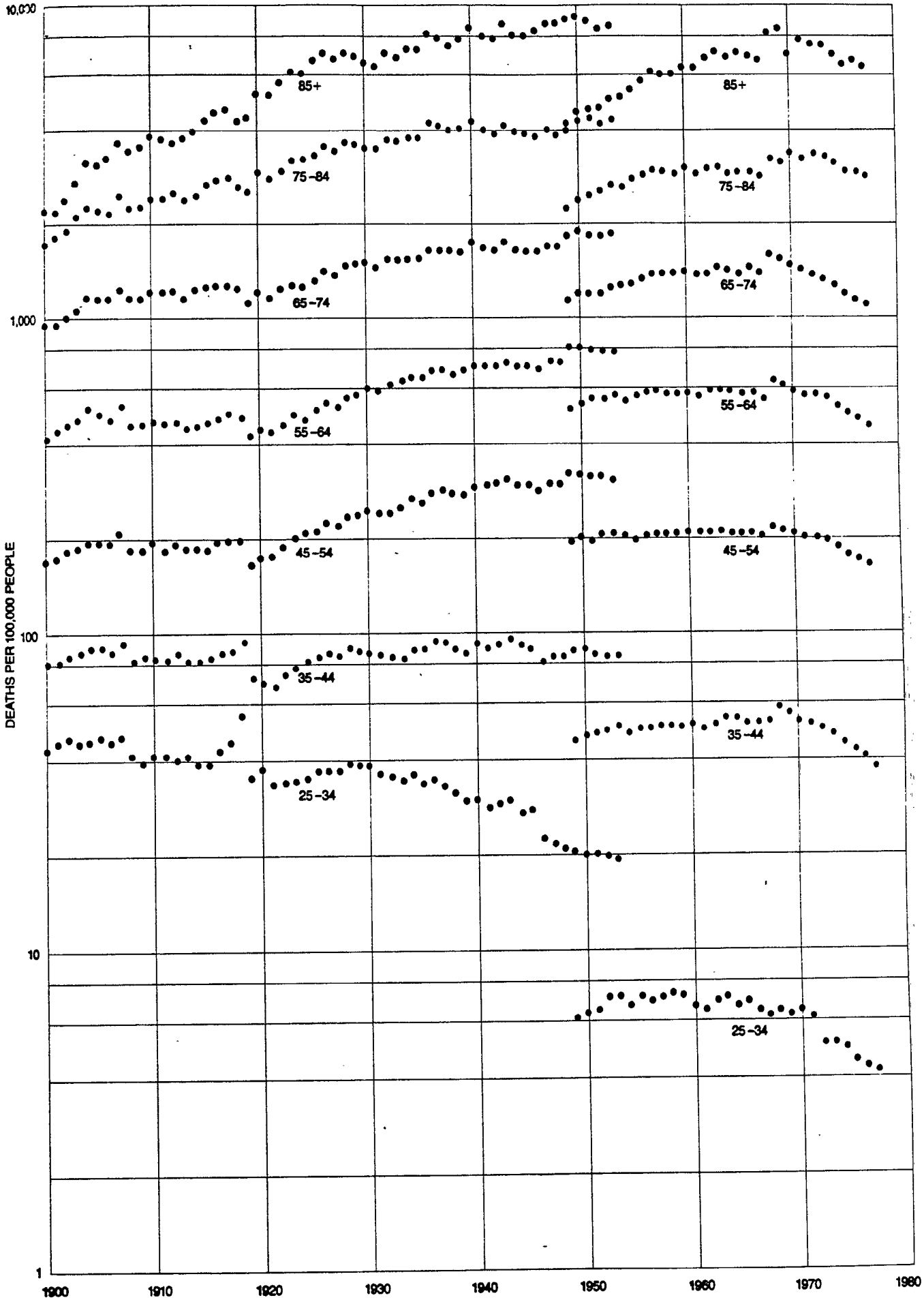
TIME TREND OF U.S. MORTALITY due to diseases of the heart shows a steep increase in the death rates from the 1920's to the 1950's and then an equally steep decrease that began in the 1960's. The rates have been scaled to fit the distribution of ages in the U.S. population according to the census of 1940. In this way the death rates for different years can be compared in spite of the changes in age structure in the past 80 years. The vertical scale is logarithmic.

The mortality rates for ischemic heart disease reached their peak in the mid-1960's, and by 1970 a declining trend was well established. The interpretation of the data for these years is mildly complicated by the 1968 revision of the system for coding the causes of death. One result of the revision was the transfer of a substantial number of deaths from hypertensive diseases into ischemic heart disease. Nevertheless, the decreasing trend of ischemic heart disease has continued through 1978, the most recent year for which information is available. Indeed, the rate of decrease appears to have accelerated since 1973. In the 1968 revision the category of ischemic heart disease was divided into two major subgroups, acute myocardial infarction and chronic ischemic heart disease, with remarkable results: acute myocardial infarction has fallen since 1968, whereas chronic ischemic heart disease has shown no consistent decline.

Parenthetically, the decrease in the risk of death from acute myocardial infarction for women is sharply at odds with the popular supposition that the redefinition of women's roles in American society (in particular their appearance in large number in executive offices around the country) will result in a redistribution in their pattern of illness. Increases in peptic ulcer and in myocardial infarction are projected, and sometimes cited. Since the mortality from peptic ulcer is decreasing as steeply as the mortality from myocardial infarction, the thesis appears to be contradicted by the observations.

The natural experiment involving the incidence of ischemic heart disease in the U.S. is signaled by marked variation in the geographic distribution of the disease as well as the changes over time. Before 1950 a geographic pattern for the mortality from ischemic heart disease was established in which the death rates were highest along the eastern and western seaboards (particularly toward the Northeast) and lowest on the Great Plains. A number of investigators sought to determine whether these differences were biologically genuine or were instead the result of variations in customs of diagnosis or in the availability and quality of medical care. The general conclusion was that although the data were shaky, the basic pattern could not be explained away as artifact.

The geographic pattern for 1950 persisted through 1960, but some important trends began to emerge. The states with the highest death rates in 1950 had the smallest increase in the decade that followed. The result was a relative shift of ischemic heart disease toward the Southeast. An analysis of the data for California by Nemat O. Borhani and H. H. Hechter of the University of California at Davis shows that between



U.S. MORTALITY BY AGE GROUP is plotted for diseases of the heart (1900–1953), arteriosclerotic heart disease (1949–67) and ischemic heart disease (1968–77). The last two diagnoses both signify the obstruction of the arteries that nourish the heart. Through 1950 the death rates increased steadily for the old and decreased steadily for the young. The change in the trend of the death rates that came in 1920 affected the people whose ages were in between. In contrast, the recent decline in the death rates has affected all age groups.

1950 and 1969 the death rates for ischemic heart disease in that state actually decreased by about 20 percent for white males and 25 percent for white females. The peak mortality in California came in about 1955.

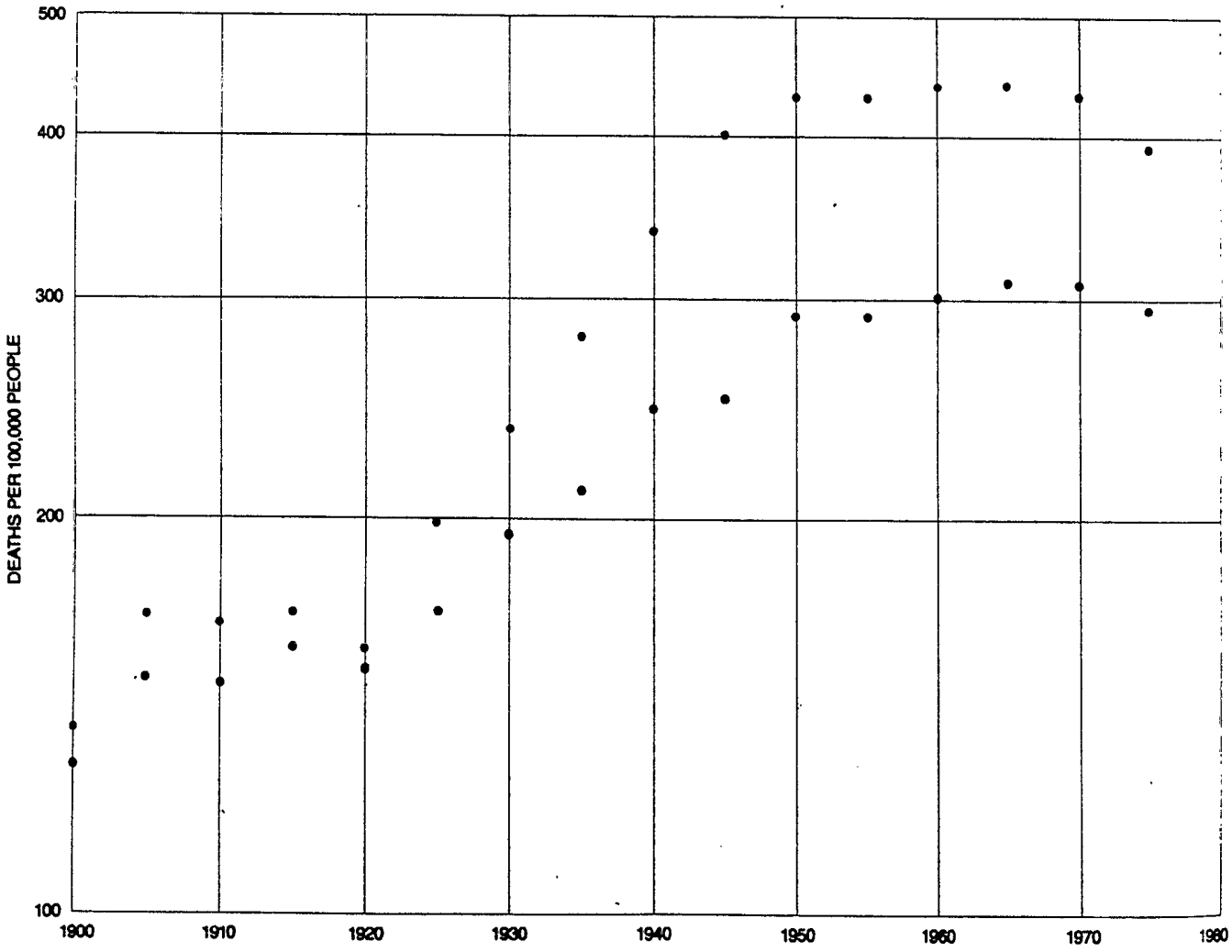
In retrospect, therefore, one can see that California gave the earliest manifestation of a decline in ischemic heart disease that extended to other parts of the U.S. in the 1960's and 1970's. By 1970 ischemic heart disease was heavily concentrated east of the Mississippi. This was primarily owing to the geographic distribution of acute myocardial infarction. Chronic ischemic heart disease was dissociated from acute myocardial infarction in geographic pattern as well as in the national time trend.

At this point some of the conundrums that have appeared repeatedly in research on the epidemiology of ischemic heart disease should be mentioned. In a number of population-based studies the factors most consistently predictive of ischemic heart disease have been blood pressure, the blood-serum concentration of cholesterol and cigarette smoking, together with a strong selection for males and an increased risk with increasing age. In the U.S., however, the associations with cigarette smoking, serum cholesterol and male gender fade among people over 65 years old. Moreover, in countries with a very low mortality rate from ischemic heart disease a male preponderance is not evident at any age. Related to this point are the international comparisons of morbidity and mortality directed by Ancel Keys of the University of Minnesota, which failed to show an association of ischemic heart disease with cigarette smoking or with serum cholesterol in those communities where the frequency of the disease was low.

These epidemiological observations are consistent with the hypothesis that occlusive disease of the coronary arteries is resolvable into two components that are partially differentiated in the current system of disease classification as acute myocardial infarction and chronic ischemic heart disease. According to this hypothesis, the rise and fall of the mortality for ischemic heart disease and the marked differences in the incidence of the disease in different regions of the U.S. are best understood as being primarily due to trends in the incidence of acute myocardial infarction, a condition strongly associated with both cigarette smoking and serum cholesterol and having a special affinity for males. Chronic ischemic heart disease may have varied to a lesser degree, but its history cannot be traced clearly through the confusion of diagnoses applied to the deaths due to chronic heart disease.

The rise and fall of ischemic heart disease affords a special opportunity to link changes in the factors that appear to determine the risk of the disease in individuals to the sweeping changes in the frequency of the disease in the population at large. For any single factor to account neatly for the overall trend it should meet certain well-defined conditions.

If its effect was immediate, it should have appeared in about 1920, increased through the 1930's and 1940's and then begun to disappear in the mid-1960's. An immediate link is likely only if the causative factor affects the most labile component of the occlusive process, namely clot formation. If the causative factor is presumed to stimulate the de-



U.S. MORTALITY BY GENDER is plotted for diseases of the heart. The death rates for males are in color and those for females are in black. The upward trend that began in 1920 was markedly greater for males. This is evidence that the increase was not fortuitous.

velopment of atherosclerosis, then a latent period of at least 20 years must be subtracted from the critical years in the trend of mortality in order to derive the trend of the causative factor.

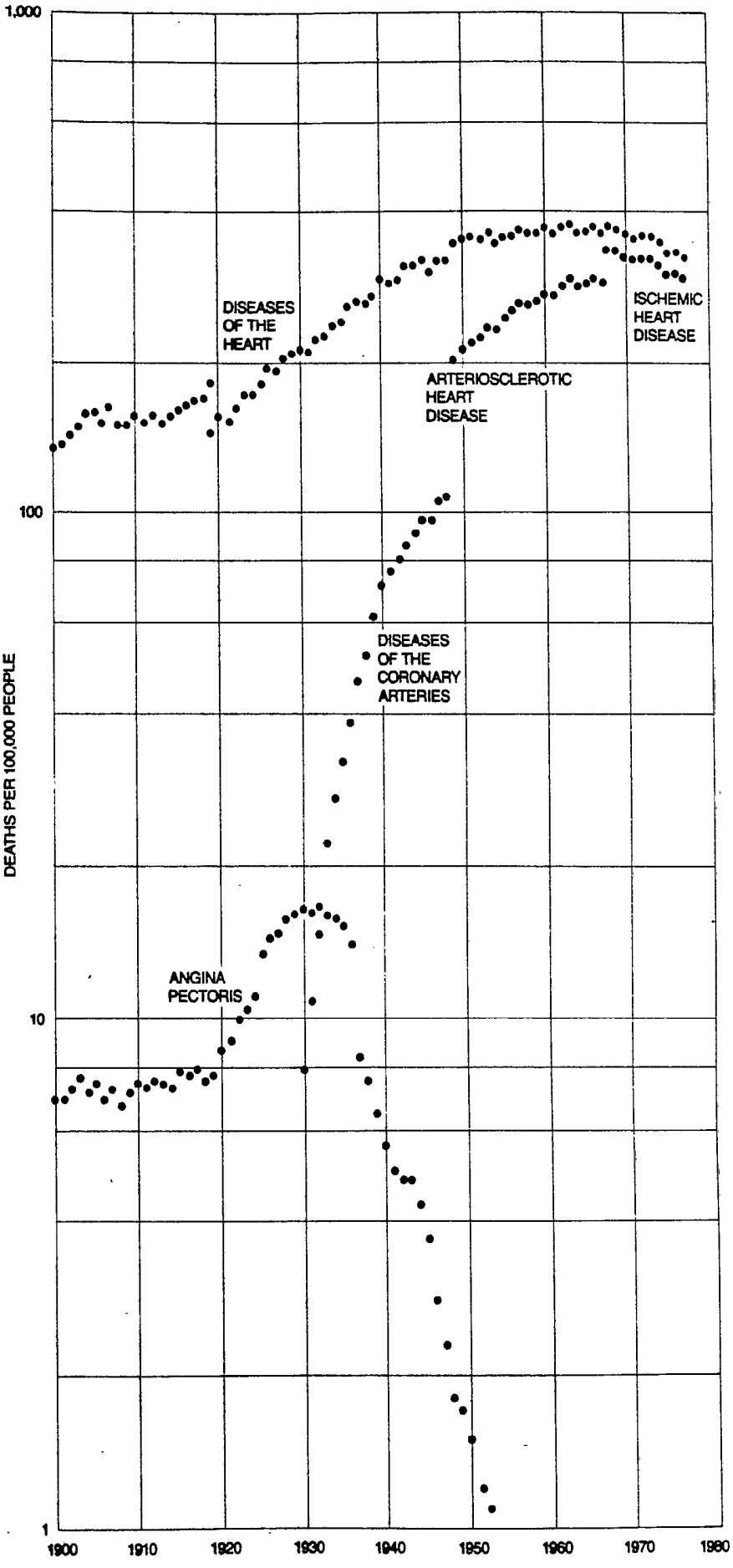
At its inception the causative factor should have affected men and women at about the same time, but the effect on men should have been notably greater, and it should have been greatest on people in their mid-adult years. After 1968 the death rates for acute myocardial infarction declined in equal proportion for men and women and also for younger and older adults; that is, the force of mortality has been constant for these age- and gender-specific categories. The implication is plain: if the decrease in mortality in one of these groups is due to the decrease in the intensity of some single causative factor, that factor should show an equal decrease for each of the other groups.

Finally, the causative factor should have begun to decrease in California a decade before it decreased in the northeastern states, and a decade after that it should still be strong in the southeastern states. If a single factor fails to meet all these criteria, some combinations of factors might be considered, although the argument must thereby be weakened and made more complex.

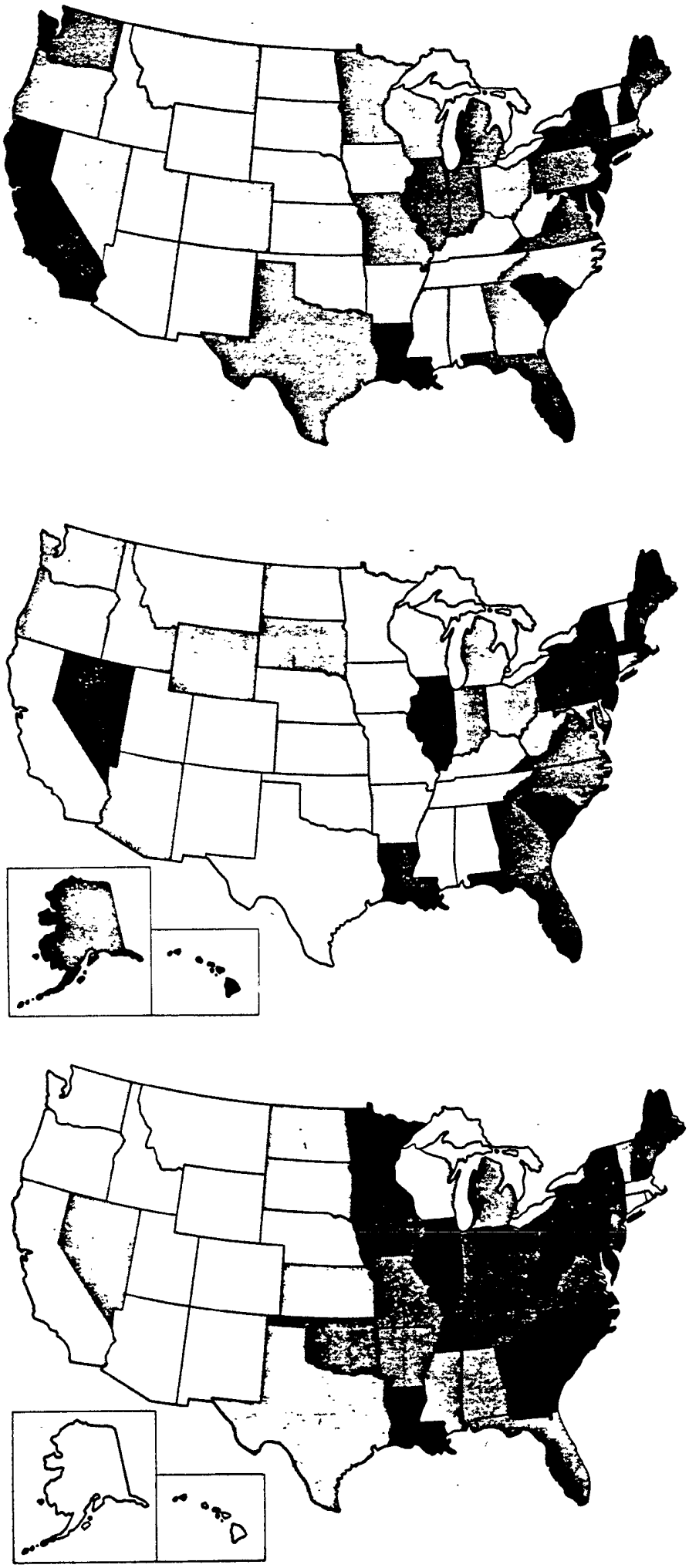
The evidence is strong that a diet high in fat, and particularly saturated fat, increases the concentration of serum cholesterol. In the controlled environment of the hospital the intentional alteration of serum cholesterol by manipulation of the diet has been fully documented, and epidemiological observations in many environments around the world have related low-fat diets to low mean cholesterol levels with comfortable consistency. (Low-fat diets in those communities, however, are usually found to be linked with strenuous physical activity.)

Certainly dietary customs in the U.S. have changed in important ways. In recent years saturated fats have been replaced to a considerable degree by unsaturated fats, and data are available to support the contention that serum-cholesterol values for large population groups decreased from the 1960's to the 1970's. And yet if recent dietary changes have caused the mortality rates to fall, surely the deprivations of the depression years should have left a similar mark on the curve. Moreover, the concentration of serum cholesterol is not associated with the risk of ischemic heart disease in older people, yet people over 65 have shown the same proportional decrease in the death rate as younger adults.

There the matter rests for now. Some evidence supports the argument that the decline in the death rates for ischemic heart disease could be due, at least in part, to decreasing cholesterol, and this could be due, at least in part, to changes



SUCCESSION OF DIAGNOSTIC TERMS within "diseases of the heart" includes four whose death rates (*black dots*) appear to form a sequence. Beginning in 1920 the attribution of deaths to the first term, angina pectoris (literally "pain in the chest"), increased notably. The newest term in the sequence is ischemic heart disease. The death rates have not been adjusted for age.



in fat ingestion. Diet, however, does not provide a satisfactory explanation for the rise in ischemic heart disease in 1920. The death rates for ischemic heart disease did not track dietary changes in the ensuing 40 years, and the recent decline in mortality is not fully consonant with the changes in diet or in serum cholesterol.

Cigarette smoking spread through American culture after World War I, coinciding with the increase in ischemic heart disease, and during the past 15 years or so smoking has decreased. On the assumption that a major portion of the harmful effects of cigarette smoking has little or no latency, so that the risk of ischemic heart disease rises and falls almost immediately with changes in cigarette consumption, the correlation looks quite good.

The decline in cigarette smoking has been much more pronounced, however, in middle-aged men than in middle-aged women, a difference that is not at all in accord with the equivalence in the decline in mortality for the genders. Moreover, the lack of association for older people between ischemic heart disease and smoking as well as serum cholesterol raises the question of how a reduction in smoking could effect a decrease in risk for this age group. Little information is available about regional variations in cigarette smoking, but a concordance between such variation and the geographic pattern of the mortality from ischemic heart disease also does not seem likely.

Even though high blood pressure is known to be associated with an increased risk of myocardial infarction, the death rates for hypertensive disease have decreased in log-linear fashion since 1950, whereas those for ischemic heart disease increased, reached a peak and then began to decline. Programs for the detection and treatment of hypertension have become far more effective in the past decade, but the forces responsible for the rise and fall of ischemic heart disease must be operating quite independently, and with much greater effect.

In an interval of about 20 years Americans changed from a nation of walkers

GEOGRAPHIC PATTERNS in the death rates for ischemic heart disease are demonstrated by maps of the U.S. for 1950 (*top*), 1960 (*middle*) and 1969–71 (*bottom*). In each map the 10 states in which the death rates for white males 55 through 64 years old were greatest are shown in dark color, the 10 states in which the death rates were smallest in white. States with intermediate death rates are shown in three intermediate shades of color. California's drop in death rates from 1950 to 1960 antedated by a decade the trend that spread through the nation. By 1971 ischemic heart disease was concentrated in the eastern U.S.

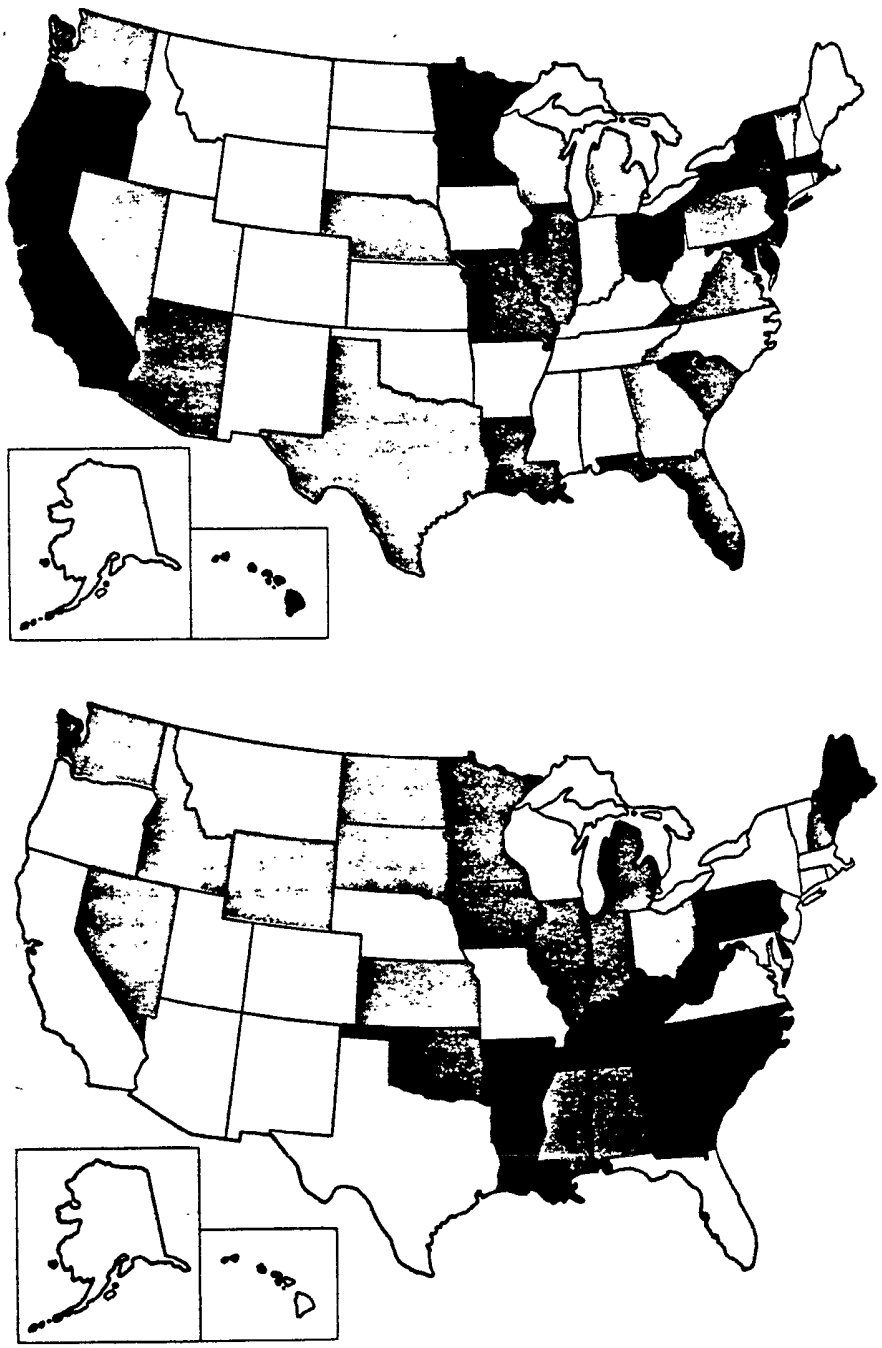
to a culture dependent on automobiles, and the beginning of that interval coincides well with the rise in ischemic heart disease. Concurrently the flow of cheap fuel reduced the caloric expenditure of people at work to some small fraction of its previous value. Almost no one now spends his life at hard labor as our grandparents understood it; we are taller, heavier and probably stronger, but we are not inured to the daylong expenditure of effort in walking and working that was expected of most people in the 19th century. Yet if an increasingly sedentary way of life is invoked to account for the increase in ischemic heart disease, the decrease is left unexplained. The national mania for recreational jogging has not spread to large numbers of upper-middle-aged men and women, both black and white, whose death rates are falling as rapidly as those of younger people.

Although arguments are heard about the effectiveness of specialized treatment facilities for ischemic heart disease, it is unlikely that these treatments have had a major effect on population mortality data, because the mortality rates for a large population are quite insensitive to such influences. It is just as unlikely that the benefits of a treatment would accrue nearly equally to males and females and whites and nonwhites across a broad age span, or that an effective treatment would have been introduced in California 10 years before it appeared in states such as New York and Massachusetts. Any residual doubt on this issue could be laid to rest if the morbidity rates for ischemic heart disease in a large population were known. Stated quite simply, if the incidence of the disease is declining in parallel with the mortality, the treatment of the disease is of no consequence in explaining the decline. Unfortunately, but almost predictably, the evidence is equivocal.

In summary, four major variables are known to be associated with the risk of ischemic heart disease in individuals. Among the four, hypertension does not fit the trend of the mortality from ischemic heart disease at all; physical activity fits only the rising curve, serum cholesterol fits only the falling curve and only cigarette smoking fits both. In no case is the fit as precise as one would like. This raises doubt that any of the factors is a fully satisfactory explanation for the variation in mortality.

Much more could be clarified by the use of existing data. The nomenclature for diseases has been relatively stable since 1949, a period that includes a significant part of the increase in ischemic heart disease and all of its decline. Samples of death certificates for this period should be recoded according to the classification system adopted in 1968 in order to delineate the apparent dissociation between acute myocardial infarction and chronic ischemic heart disease. In the same set of data, attention to occupation and other indexes of social status would provide important information, and detailed analyses of the shifting geographic patterns would be particularly useful.

We now have strong assurance that programs based on our present knowledge can reduce the risk of death from ischemic heart disease. Unfortunately these programs require people to stop doing certain things they like to do, such as smoking cigarettes or eating whatever they want to, or to do things they do not want to do, such as taking antihypertensive drugs or exercising strenuously. If the individual characteristics and habits now known to influence the frequency of the disease do not contain sufficient information to fully explain the epidemiological patterns in time and in space, and the evidence presented here suggests that they do not, then we may direct our attention to more general environmental factors in a search for more effective and more acceptable means of prevention.



GEOGRAPHIC PATTERNS FOR TWO COMPONENTS of ischemic heart disease are shown for 1969–71. The upper map displays the death rates for chronic ischemic heart disease. The lower map displays the death rates for acute myocardial infarction: the sudden blockage of a coronary artery. Again dark color marks the 10 states in which death rates were greatest for white males from 55 through 64, and white marks the 10 states in which rates were smallest. Acute myocardial infarcts account for southeastern concentration of ischemic heart disease.