Factors in Disease: A Project Summarized

The Framingham Study. The Epidemiology of Atherosclerotic Disease. THOMAS ROYLE DAWBER. Harvard University Press, Cambridge, Mass., 1980. xii, 258 pp., illus. $20. A Commonwealth Fund Book.

In this account of the 24-year epidemiological investigation known as the Framingham study Roy Dawber, who was director of the project for 16 years, has delightfully accomplished what he set out to do: to provide "a narrative that, without being too detailed, would give the reader reasonably complete knowledge of the overall project." Though the analyses are new, there are no new data. Rather, the importance of the work is as a summary: the Framingham results are finally presented in one place, in a consistent format, by one author.

I approached *The Framingham Study* with something of the anticipation and trepidation with which one approaches a movie made from a classic. I suspected that the original message would remain largely intact. But I hoped to find excitement in the new format. Indeed, excitement is to be found, partly between the lines, partly in the introductory chapters, and partly in Dawber's almost folksy interpretation. But throughout Dawber's fairness and benignity shine through. He will lose no friends and make no enemies with this volume. However, the powerful ferment, worldwide over three decades, in the field of cardiovascular disease epidemiology and prevention is alluded to only casually and only in generalities. Dawber speaks of what he knows best, Framingham.

Dawber begins by placing Framingham historically. Its origins can be traced back to the original thinking of Sir James MacKenzie about prognosis, prediction, and prevention of heart disease. These ideas affected Paul Dudley White, who, in turn, was an influential adviser to the fledgling National Heart Institute, whose first major undertaking was the Framingham study. Dawber acknowledges also the early conceptual and organizational contributions of Assistant Surgeon General Joseph Mountin, of David Rutstein of the Harvard School of Public Health, of the first NHI director, Cassius Van Slyke, and of Felix Moore, the statistician who put the Framingham population selection, sample size, and analyses on a firm base. Finally, he pays tribute to another pioneer in the epidemiology and prevention of cardiovascular disease, Ancel Keys.

Subsequent chapters are devoted to each of the cardiovascular risk factors: high blood pressure, blood lipid levels, tobacco smoking, obesity, physical activity, and diabetes. At the end of the volume a list of references cited and a chronological list of all Framingham publications between 1951 and 1978 are provided. Data are presented for men and women, by decade of age from 30 through 59, both as crude rates and corrected for dropout or development of a new cardiovascular event. Twenty-four-year incidence rates are given for all coronary disease and for myocardial infarction, angina pectoris, and brain infarction, according to the risk factor levels at entry among disease-free persons. An average annual incidence rate is also given for risk according to the most recent pre-disease measurement.

There are few surprises in the results presented or in Dawber's interpretation of them.

On hypertension, the conclusions are forthright: "The detection of elevated blood pressure in apparently well individuals long before any overt evidence of damage has become manifest appears highly desirable."

On blood lipids, Dawber opines that the data provide overwhelming evidence that the level of cholesterol in the blood is a powerful influence in development of coronary heart disease. "This evidence is so convincing that it is difficult to understand how any reasonable person can question the relationship."

On high-density lipoprotein cholesterol, there is none of the enthusiasm of Dawber's Framingham successors. Rather, "Prospective studies of HDL cholesterol in young individuals have not been conducted; the value of this measurement as a predictor is unknown except in older people. From the point of view of the physician interested in prevention, this added feature would not appear to be of much importance; it is unlikely that efforts to change blood lipids at advanced age would be worthwhile."

On diet, Dawber addresses the misinterpretation of findings about cholesterol intake as assessed through dietary questionnaires being unrelated to individual blood lipid levels. This finding has been used by investigators such as George Mann and by councils such as the Food and Nutrition Board of the National Research Council to downplay the importance of dietary cholesterol. In this regard Dawber states, "To conclude from the Framingham data that dietary intake is of no importance in determining the cholesterol level in human populations is not justified." He indicates that examination of such relationships is best carried out across a wider range of diet, serum cholesterol, and disease risk than is found in the Framingham study and, better still, by controlled experiments. Such experiments quantify the relationship between change in diet composition and change in blood lipid levels.

On smoking, Dawber has no uncertainties: "The physician is shrinking from his duty if he does not do his utmost to discourage the smoking habit."

On obesity and overweight, Dawber ignores others' different findings and perhaps even some of the Framingham results by these generalizations: "The conclusion of a minimal effect of obesity on the development of myocardial infarction drawn earlier in the Framingham study was not justified by the results of 24 years of follow-up. Myocardial infarction is importantly related to body weight." In fact, however, in figure 9-5, the principal figure displaying that relationship, there appears to be an insignificant *inverse* relationship between relative body weight and incidence of myocardial infarction in men ages 30 through 39 and a U-shaped curve for ages 50 and 59, with lower incidence of myocardial infarction in the overweight class of 100 to 119 percent relative weight than for lighter or heavier classes.

On multivariate prediction of coronary risk from the well-known Framingham multiple logistic regression model, one does not have to read deeply between the lines to discern Dawber's lack of enthusiasm for this effort, which has influenced analyses and interpretations in many other studies in addition to Framingham over the last decade: "Although estimation of risk on the basis of a combination of factors can be an interesting exercise, the use of this calculation to select those at higher risk, the top ten percent, may also be misleading. Because the approach to prevention must be made on an individual basis for each risk factor, no risk estimates are provided here for combinations of factors."

About the only sphere in which Dawber and other Framingham investigators may not be fully forthcoming is the assignment of disease diagnoses. The long, chatty chapter on clinical diagnosis of heart, brain, and peripheral artery manifestations never gives clear, unambiguous, quantitative criteria or discloses the effects of observer variation on diagnoses. These criteria and data on diagnostic performance have never been presented in any systematic form. Dawber has guessed correctly that the

clinical and scientific world would accept the credibility of experts. But impressionistic, "commonsense" diagnoses, however achieved, by however distinguished experts met together, are not enough. The Framingham reply is that sharpening the diagnosis would only serve to enhance the important relationships found.

On the other hand, there is no lack of forthrightness in Dawber's opinions on collecting, managing, and collaborating in the analysis of epidemiological data. He has clearly been stung by a world in which Framingham data, collected under a highly visible government contract, involving many Public Health Service officers and staff and long-term government funding, are considered the property of the institution that commissioned and sponsored the study:

> The separation of the investigators collecting the data from those directly responsible for its analyses became a real problem. In spite of frequent meetings of all concerned, I found that as Principal Investigator, I had less and less control over the analysis. In addition, the staff at the National Institutes of Health became increasingly possessive of the data, ostensibly to preserve the confidentiality of medical records. The question of ownership of the data still has not been completely resolved and has arisen in other studies financially supported by NIH. My own insistence was that the data collected by an investigator in a study under his personal direction are primarily his. They must be available to him for analysis and reporting. The National Heart, Lung, and Blood Institute authorities took the view that the data were theirs, and were not to be released to anyone. Fortunately, we arrived at reasonably amicable arrangements whereby earlier data were made available to me. The lesson I learned was that under no circumstances should any scientific investigator allow his work to be controlled by others who act not strictly as co-investigators but as analysts of the findings of the research.

This is an understandable view. Perhaps a more appropriate view today would be that, after initial publications and major contributions are made, the principal investigator would then best encourage, consult, supervise, and share with others the exploitation of data obtained collaboratively.

The book contains many other pithy statements of the author's views, based on 30 years of experience. All of Framingham can be found here. The saltily seasoned judgment of the original and senior Framingham investigator is lagniappe.

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Bacterial Cell Surfaces

Microbial Cell Walls and Membranes. H. J. ROGERS, H. R. PERKINS, and J. B. WARD. Chapman and Hall, London, 1980 (U.S. distributor, Methuen, New York). x, 564 pp., illus. $75.

This book comes at an appropriate time, for different disciplinary approaches are now converging on the study of the microbial cell wall. The book is a sequel to the highly successful *Cell Walls and Membranes* by Rogers and Perkins. A comparison of that book with the present volume reveals the many advances that have occurred over the past decade.

These authors together with Ward have completely rewritten their book. The new volume emphasizes the ultrastructure of bacterial envelopes, membrane composition and function, the structure and biosynthesis of peptidoglycan, additional polymers of the wall, autolysins, and the cell wall in growth and division. The mechanisms of antibiotics that inhibit the assembly of the wall receive major emphasis. In addition, the structure and biosynthesis of yeast and fungal walls are described.

The majority of the chapters give an intensive, thorough review of their topics. The mechanism of penicillin action is described with an in-depth, objective analysis. This topic, the biosynthesis of peptidoglycan, other antibiotics affecting bacterial wall synthesis, and the biosynthesis of teichoic acids receive extensive treatment and provide some of the highlights of the book.

The authors have omitted a number of topics that might have contributed to the central focus of the book. For example, there is no description of the relationship of any of the surface appendages, such as pili and flagella, with the membrane and the wall. Wall polysaccharides in Gram-positive organisms are given only a cursory view. This is surprising in light of the current interest in such bacteria as *Streptococcus mutans*, one of the cariogenic organisms. In addition, the role of the envelope in chemotaxis and bacterial adherence is not discussed. In one or two chapters some of the more recent information has not been included. For example, the important contribution of Schwarz and his co-workers (1978) concerning the arrangement of glycan chains in the sacculus of *Escherichia coli* is not described in the chapter on the structure of peptidoglycan even though the chapter contains references from 1979.

Scientists in a number of disciplines, including pharmaceutical chemistry, will be attracted to this book. With supplementation, it would make a useful textbook for an advanced course in bacterial cell surfaces.

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Regional Tectonics

Sedimentation in Oblique-Slip Mobile Zones. Papers from a symposium, Auckland, New Zealand, Jan. 1979. PETER F. BALLANCE and HAROLD G. READING, Eds. Blackwell Scientific, Oxford, 1980 (U.S. distributor, Halsted [Wiley], New York). vi, 266 pp., illus. Paper, $37.50. International Association of Sedimentologists Special Publication No. 4.

Strike-slip tectonic regimes have received considerable attention during the past five years, as witness a number of significant conferences and volumes on the topic. This is largely because intracontinental transforms, in particular, are spectacularly developed systems, are susceptible to relatively easy study, and are increasingly recognized as important in the search for hydrocarbons.

Not surprisingly, because the stratigraphic record associated with an oblique-slip fault is only properly preserved in fault-offstepping pull-apart basins, such basins feature in several papers in this symposium volume. The volume contains some papers, particularly those of Bluck on the late Devonian of the Midland Valley of Scotland, Steel and Gloppen on the early Devonian of western Norway, and van der Lingen and Pettinga on the Makara Basin in New Zealand, that are valuable additions to the literature in providing definitive and well-interpreted data sets. A sequence of papers (Spörli, Lewis, van der Lingen and Pettinga, Prebble, Ballance, and Norris and Carter) on basins associated with the Alpine Fault System of New Zealand and its terminations gives an excellent insight into the Cenozoic evolution of the New Zealand plate boundary system, although greater emphasis on basins of the Marlborough area would have been more useful in a volume on oblique-slip zones. Papers by Heward and Reading on the Carboniferous of Cantabria and Robertson and Woodcock on Cretaceous-Paleogene sediments associated with the Antalya Complex in Turkey are fine but seem a little out of place in this volume in that neither makes a convincing case for