

# Cardiovascular Risk Factors in Children

The Early Natural History  
of Atherosclerosis  
and Essential Hypertension

GERALD S. BERENSON, M.D.



一九八三年六月卅日

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## Foreword

greater if started in youth, when lesions are beginning. Therefore, population studies to determine the characteristics of children destined to become high-risk adults are a key to the control of cardiovascular disease. The Bogalusa Heart Study is neither the first nor the only risk-factor study in children, but probably no other study of this kind is as equally community-based, as encompassing in the variables under investigation, and as promising in terms of the potential of looking at children in members of the whole family. Moreover, the breadth of interest of the town of Bogalusa makes it possible to gain insights into ethnic determinants of early risk. The Bogalusa Heart Study already has made its mark amongst its companion studies and will serve as a guide and reference for similar investigations around the world. The leadership by the World Health Organization in encouraging and coordinating risk-factor studies in the young underlines the significance of these investigations at the level of international health.

This monograph deals with susceptibility—the susceptibility of. There is every scientific reason to think that atherosclerosis has its origin early in life. Even though the lesions may develop at an accelerated pace only in adulthood when environmental conditions, especially nutritional and other living habits, are unfavorable, the formation of these very habits certainly begins in childhood and, once formed, they are difficult to change. Actually, pending further research, the odds are that even the earlier lesions are decisively under environmental control. Thus, whatever the eventual answer, the prevention of premature atherosclerosis must begin in youth.

This book on the findings of the Bogalusa Heart Study deals, of necessity, with risk factors—the precursors of coronary heart disease—or rather, the links between risk factors and the disease itself. The latter kind of study, the evolution of clinical disease, would have to encompass at least four or five decades. It should be remembered that the history of coronary heart disease epidemiology only started around 30 years ago, that its spectacular results relate mostly to “middle aged” adults, and that the need to include children in such investigations was actively recognized only at a later stage in the course of epidemiological research. But it is not necessary to conduct a “cradle-to-grave” study in order to provide evidence for a causal relationship between risk factors and disease. If such a relationship exists in middle age and beyond, the impact of risk-factor control is bound to be even

greater if started in youth, when lesions are beginning to form.

Therefore, population studies to determine the characteristics of children destined to become high-risk adults are a key to the control of cardiovascular disease. The Bogalusa Heart Study is neither the first nor the only risk-factor study in children, but probably no other study of this kind is as equally community-based, as encompassing in the variables under investigation, and as promising in terms of the potential of looking at children as members of the whole family. Moreover, the biracial character of the town of Bogalusa makes it possible to gain insights into ethnic determinants of early risk. The Bogalusa Heart Study already has made its mark amongst its companion studies and will serve as a guide and reference for similar investigations around the world. The lead taken by the World Health Organization in encouraging and coordinating risk-factor studies in the young underlines the significance of these investigations at the level of international health.

This monograph deals with susceptibility—the susceptibility of children to cardiovascular disease later in life, a model, incidentally, for the major chronic diseases in general. Why, it may be asked, are some investigators particularly “susceptible” to certain kinds of research? In this case, why did Dr. Berenson undertake the Bogalusa Heart Study? No doubt, as with the causes of coronary heart disease, there are many reasons. At Louisiana State University in New Orleans, where he studied and worked, the most decisive pathological groundwork for the belief that atherosclerosis starts in youth was convincingly laid. As a clinical and experimental investigator, Dr. Berenson had already made his name amongst atherosclerosis researchers. Finally, the choice of Bogalusa as the site for this new venture into epidemiology and preventive cardiology was not accidental. Dr. Berenson’s family helped found the town. Presumably Dr. Berenson himself would be able to tell the tale of his development into an epidemiologist and his deep commitment to preventive cardiology. However, creative ideas have a tendency to escape explanation!

Reading between the lines, one will possibly sense that this is not only a scientific report but the saga of a serious and exciting venture. Visiting Bogalusa and seeing the team in action is an unforgettable experience. The children in the study are received and treated with the now proverbial but not always practiced “TLC” (tender, loving care).



They feel good will and attention, but not the tightness of the statistical design and the rigorous quality control guiding the examination schedule. There is a quiet and matter-of-fact devotion and identification with the project on the part of all those involved, from the strictly professional staff to the volunteer health workers.

Research in community medicine is the pacesetter for community prevention programs. It is recognized more and more that motivation toward sensible patterns of everyday living is the prerequisite of success in reducing the risk factors predisposing to disease. The Bogalusa Heart Study, apart from its scientific merit, represents a statement of faith in disease prevention, a model for the creation of a working relationship between the people in the community and the "health team," and an action program true to the call, "from epidemiology to prevention."

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## Preface

It is now clear from anatomic studies, necropsies on soldiers killed in Korea and Vietnam, and studies of coronary arteries from all age groups that atherosclerotic coronary artery disease exists early in life. Although it is considered that essential hypertension begins in the young, the early onset of this disease is not distinct. Determining the early phases of atherosclerosis and essential hypertension in children is a critical step in preventing the major cardiovascular diseases of our time.

Over the past 20 to 30 years, outstanding epidemiologic studies such as those in Framingham (Mass.), Tecumseh (Mich.), and Evans County (Ga.), have clearly shown the importance of relating risk factors to coronary heart disease and morbidity from hypertension. But this information has been obtained mostly from adult populations, and often from an age group in which advanced disease already exists.

The large epidemiologic studies of the past have been significant in that they outlined our attack on the major cardiovascular diseases occurring in the United States and many other Western countries. Our findings in the Bogalusa Heart Study on 5,000 children, reported in this text, begin a serious attempt to collect risk-factor data in childhood—a period when these diseases are developing. While developing, these diseases produce no pain or disability; young people are asymptomatic. These are aptly referred to as the “silent diseases.”

Major aspects of our study on children have followed the design of the epidemiologic programs on adults. With time, we will be able to link findings in children with those in adults, especially adults who have suffered heart attacks, strokes, and heart failure.

Although some risk-factor data, that is, levels of blood pressure and serum cholesterol, have been previously collected from children, carefully standardized techniques have not been followed, nor have those data been collected simultaneously to provide an opportunity to examine interrelationships of the variables, such as weight and cholesterol, or diet and lipids. The Bogalusa Heart Study has attempted to survey overall risk-factor data in a total community of children. This is different from studying selected children or individual patients seeing physicians and being admitted to hospitals for diagnosis and treatment. The Bogalusa Heart Study information is relevant to the general adult population—to the 10–20% who will develop hypertension, and ultimately suffer strokes and heart failure, and to the 50–75% who will develop arteriosclerotic heart disease.

We have described methods by which health personnel can obtain useful information on risk-factor variables in children, with the hope that the application of these methods in childhood will help to prevent cardiovascular diseases in adulthood.

One of the book's main purposes is to aid the physician in predicting a child's health care needs at a time when prevention can have optimum effects. The data will be particularly helpful to physicians interested in preventive health measures for the two major cardiovascular diseases: coronary artery disease and essential hypertension.

The Bogalusa Heart Study findings presented here will be a framework for future studies. The observations can be used for a single child under medical care or can serve as a comparison to observations from other populations of children. For such comparisons, the Appendix contains resource information in the form of grids on (1) growth and maturation, (2) blood pressure, and (3) lipids: cholesterol, triglycerides, and concentrations of  $\alpha$  (high density),  $\beta$  (low density), and pre- $\beta$  (very low density) lipoproteins.

Diet will be a main target in future efforts to alter a child's susceptibility to heart disease in adulthood. Nutrition studies and observations on eating behavior in Bogalusa children are presented here as a first approach in defining this major environmental factor.

Our last chapter is a summing up of general recommendations for



the care of children, and our impressions of the work being done on cardiovascular risk factors in children.

We know there are certain discrepancies and inconsistencies within the book—some because many of the chapters have been published earlier in somewhat different form, others because of our limitations. We hope they will not necessarily distort the information or the message.

G.S.B.

New Orleans

September 1979

## Acknowledgments

Obviously, our acknowledgments must first recognize the children of Bogalusa. They comprise this study.

The research which formed the basis for this book was supported by funds from the National Heart, Lung and Blood Institute of the U.S. Public Health Service (HL 02942) and Specialized Center of Research—Arteriosclerosis (SCOR-A) (HL 15103).

The implementation of an epidemiologic study such as the Bogalusa Heart Study involves the contribution of many persons. Some stand out significantly. Others involved in supporting services receive little or no recognition from the accomplishments of the study—for example, laboratory technicians, computer personnel, and secretarial staff. They are just as important, for without their help the daily implementation of our program would falter.

We have formally and informally drawn upon the experience and expertise of many consultants. The standards we set for the Bogalusa Heart Study were taken from previous epidemiologic programs such as Framingham, Tucumseh, and Evans County. Consultants from these programs and other professionals interested in cardiovascular epidemiology were used freely, and we appreciate their help in designing our studies.

A number of individuals at Tulane and LSU Medical Schools have helped through their encouragement, frequent consultations, and sup-

port of the program. Dr. Jack P. Strong has been a continual advisor to the program. One colleague deserves particular mention. Although not a coauthor in the clinical research, Dr. Bhandaru Radhakrishnamurthy has been a coinvestigator in all of our laboratory work for many years. He served as a daily contributor, not only to the biology of the program but to the administrative decisions we faced. His patience and reassuring guidance are a continual support to this research.

Mr. Edward R. Dalferes, Jr. has also been part of our family for many years. He is the first person we turn to for everything. Dr. Ralph R. Frerichs was an epidemiologist with our program and we owe him a great deal of thanks for his help in conducting the first phase of our study and publication of much of the material in this text. Recognition must also go to Dr. John L. Harris (deceased) and Dr. Lawrence J. Cohen, our first pediatricians.

In Bogalusa, appreciation is given to the field staff. Not only has this group performed as a closely knit team, responsible in their research and training duties, but their dedication to the program and faith in our leadership has been inspiring. They and the many volunteers who helped with the screening really represented this program to Bogalusa. The staff's direction has come from Mrs. Imogene W. Talley, but we cannot appropriately fit her role to the title we have given her—community coordinator. Her patience and dedication molded the program into part of Bogalusa itself. Without her tireless efforts and mature insight into the needs of the study, our degree of success could not have been accomplished. Imagine finding someone with Mrs. Talley's capability (along with eleven nurses and other staff, all of whom volunteered to join the group), in a small community like Bogalusa and transforming them into a well-trained group to collect research data! We refer to our research team as "ordinary" nurses (but nothing is ordinary about a good nurse). Their willingness to be monitored and repeatedly trained according to the same protocol reflects their desire that the study be conducted properly and their commitment to the program's importance. What blessings were given to this study from such a mixture of talent—people within a small community who accepted an unproven program on a trial basis, worked part-time, and struggled to do something that seemed worthwhile.

From a personal standpoint, thanks must be given to my parents, who lived in Bogalusa over many years. Respect for them in Bogalusa made our task easier. The acceptance shown to us by Bogalusa con-

vinces me that the community had that respect, and that we chose the right place for the study.

In every investigator's career there are those who help shape his approach to research. First, I must thank Dr. George E. Burch, who helped excite within me an interest in research and who emphasized the importance of research in clinical medicine. I am grateful to Dr. Albert Dorfman and his team, Martin B. Mathews, John A. Cifonelli, and Saul Roseman, who showed me the unlimited horizons of applying biochemistry and biochemical research to medicine, and who supported and encouraged me over many years to continue in academic medicine. And, I am also grateful to Dr. C. A. McMahan, whose insight into clinical research design guided me in conducting research involving large numbers of people and helped me understand the necessary methods involved in obtaining reliable information in an epidemiologic study. His penetrating comments, "The award of a grant only provides a hunting license," "the importance of standing on the shoulders of others," "the need for development of protocols," "the Director has to set the standards," and "when you stand in front of the scientific public," have served as guidelines for the conduct of this program.

Finally, we are especially grateful to the Bogalusa children and their parents, who have had such tremendous faith in the Heart Study. Their unusually high participation has made our program a success. Without them and their support this study would not have been possible. This contribution will be to children all over the world.

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# I. Introduction to studies on the early natural history of arteriosclerosis

## 1. Cardiovascular risk factors in children

For thy children we shall have visions.

Although coronary atherosclerosis was recognized much earlier, it was just 60 years ago that James Herrick related myocardial infarction to the anatomic obstruction of a major coronary artery and alerted the medical profession to this clinical syndrome (Herrick, 1912; Lie, 1978). From that time our understanding of the clinical features of coronary heart disease and the underlying arterial lesions has advanced considerably. Although the precise phenomena accounting for the complete occlusion of coronary vessels are still being debated, there is little doubt that in Western countries the fat-laden, raised, intimal fibrous plaque of atherosclerosis occludes most of the lumen of coronary arteries. Despite the need for further study, our understanding of coronary artery disease has now provided insight into ways of approaching the clinical problems and their prevention. Studies of children are just beginning to show directions for prevention at an optimum time. Clearly, it is at the early stages of disease that efforts to limit the ravages of atherosclerosis and primary hypertension have potential to be most fruitful.

It hardly seems necessary to emphasize the significance of the major cardiovascular diseases that occur in adults in this country. Coronary heart disease, essential hypertension, and diabetes mellitus are so common that we almost accept them as expected morbidity in the middle aged and in the elderly. Even though recent national health