The Epidemiology of

RHEUMATIC FEVER

and SOME OF ITS

PUBLIC HEALTH ASPECTS

BY

JOHN R. PAUL, M.D.

PROFESSOR OF PREVENTIVE
MEDICINE, YALE UNIVERSITY
SCHOOL OF MEDICINE

AND OTHER CONTRIBUTORS

Second Edition

for the

AMERICAN HEART
ASSOCIATION

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FOREWORD

In 1928, as a result of a request from the American Heart Association, the Metropolitan Life Insurance Company contributed a grant to the Association for the study of environmental factors in rheumatic fever and rheumatic heart disease. This work was done under a committee* of the Association and was published in 1931 under the title of *The Epidemiology of Rheumatic Fever—A Preliminary Report With Special Reference to Environmental Factors in Rheumatic Heart Disease and Recommendations for Future Investigations.* Ten years later the Association reviewed this subject in the light of many new developments which have transpired since the original work was published.

Consequently, another request was made by the American Heart Association to the Metropolitan Life Insurance Company, and a second grant was made by this Company for the purpose of bringing the work on the epidemiology of rheumatic fever up to date. This revision of the subject has again been done under the direction of a Committee of the American Heart Association, whose membership consists of T. Duckett Jones, Chairman; Louis I. Dublin, David D. Rutstein, and Homer F. Swift.

T. Duckett Jones, M.D., *Chairman*
Committee on the Epidemiology of Rheumatic Fever, American Heart Association.

*This original committee consisted of Robert H. Halsey, Chairman; Alfred E. Cohn, Louis I. Dublin, Haven Emerson, Homer F. Swift, and Edgar Sydenstricker.

INTRODUCTION

DURING the interim of more than 10 years (1930–1941) which has elapsed since the first edition of this book was prepared, great activity has taken place in research on rheumatic fever, and general interest in this disease has mounted. It is safe to say that the sum total of publications on rheumatic fever in this country during the past 12 years has exceeded the American work of all previous decades put together. Rheumatic fever has taken its place among the foremost medical problems in this country, ranking in importance (within the northern part, at least) close to tuberculosis and syphilis.

Appreciable strides have been made in the epidemiology of rheumatic fever; and notable contributions to our information about its local prevalence have been those of Hedley, of the United States Public Health Service, whose studies on rheumatic heart disease in Philadelphia hospitals represent a source of new data from which we have drawn quite heavily in this review. Furthermore, our appreciation of the pathogenesis of this disease has taken a new turn with the recognition of its close linkage to hemolytic streptococcal infections. This has been largely a result of Coburn's work, and has wrought a profound change in our concepts with regard to its nature.

Many of the definitions and explanations about rheumatic fever which were reviewed at some length in the earlier edition no longer seem necessary. In fact, general information about this disease has increased so much and the point of view has changed so radically that the present review is not in reality a second edition, but rather a new "monograph" with a new title to indicate that, in addition to embracing the subject of the epidemiology of rheumatic fever, the work also includes some of its public health aspects.

In this review, I have drawn almost entirely upon American and British and, to a lesser extent, Scandinavian sources of information. This results from the fact that most of the work dealing with the epidemiological and the statistical aspects of rheumatic fever to which we now have access, has primarily been carried out in these regions.

In conclusion, I wish to thank the Metropolitan Life Insurance Company for the generous grant which has again made this work possible, and at the same time to express my appreciation to the members of the supervisory committee of the American Heart Association—particularly to its chairman, DR. T. DUCKETT JONES, for without their suggestions the preparation of this review would have

been almost impossible. Thanks are also due to Dr. Ernest L. Stebbins for reviewing the entire manuscript, and also to Dr. T. D. Dublin. I am also indebted to Mr. Ralph D. Alley for drawing many of the charts, and to many others whose names are, unfortunately, too numerous to mention here.

789 Howard Avenue
New Haven, Conn.

December 1, 1941

*INTRODUCTION TO THE FIRST EDITION**

IT IS hardly necessary to emphasize the importance of rheumatic fever, now recognized as one of the major causes of human morbidity in this country, and one which easily ranks with other important diseases such as tuberculosis and syphilis. Many of the better-known manifestations of this disease appear in the form of heart disease, and have been thus labeled for generations, buried so to speak under the term heart disease; but it seems high time that increased effort should be made to single out rheumatic heart disease from the so-called cardiac group of diseases, and that the problem be attacked from the standpoint of a specific disease rather than from the standpoint of the organ which is affected.

Such a task is not easy, because of difficulty in defining the limits of rheumatic fever; but it demands consideration, for the statement has recently been made that among all the diseases, which logically fall into the infectious group, none offers a greater challenge to the medical profession than does rheumatic fever. In response to this challenge, interest in the disease is growing in many countries, and there is no dearth of work along clinical, pathologic, and bacteriologic lines. In spite of these efforts, however, many fundamental questions regarding this disease remain unanswered. We do not know definitely the causative agent of rheumatic fever, and hence we cannot be certain of the immunologic mechanisms involved. We probably have only a partial knowledge of its clinical course. From the practical standpoint, we are halted by the fact that no specific test has yet been devised to determine whether or not an individual has rheumatic fever; this means that there must be great gaps in our knowledge of its frequency and course.

As a valuable method of attack on some of the unsolved problems, students of the disease have long considered the possibilities of analyzing the situation from an epidemiologic standpoint. Studies in this field have, of course, already been made, but to a far more limited extent than with most other infectious diseases, largely because, as the disease is so poorly understood, data for analysis are simply not available. Pioneer efforts along these lines have already been initiated in England, but on a somewhat limited scale, whereas no really satisfactory epidemiologic work has been even attempted in this country. The American Heart Association has therefore suggested that this valuable method—the epidemiologic attack—be brought to bear on the problem; and so the following review has been assembled as a background for future work to be directed against some of the environmental problems which seem to be of importance in this disease.

New Haven, Conn. October 1, 1930

*Reprinted in part from the original, with omission of certain irrelevant details.

PART ONE

CHAPTER I

NOMENCLATURE—DEFINITIONS AND DISCUSSIONS

The term *rheumatic fever* is used throughout this review in preference to the terms: acute rheumatic fever, acute rheumatism, etc., which have been used by others to describe the same disease. *Rheumatic polyarthritis*, like the term *acute articular rheumatism*, is used only to designate a manifestation of rheumatic fever.

FROM the beginning we shall assume that rheumatic fever is a fairly definite clinical entity which is well described as such in modern textbooks of medicine. It is unnecessary, therefore, to repeat such descriptions here. But, although we may reaffirm here the belief that this disease still deserves to be regarded as a distinct clinical entity, we should recognize at the same time the existence of many nonspecific qualities about it, which are responsible for a nonspecific type of nomenclature. Undoubtedly one of the major difficulties which has confronted the epidemiologist who is anxious to investigate rheumatic fever is this nonspecificity, or lack of standardization of nomenclature. There is at present no satisfactory term for designating all the groups of conditions which include rheumatic fever, Sydenham's chorea, and rheumatic heart disease. As an example, let us take the adjective *rheumatic* or the term *rheumatic condition*, which in this review will be occasionally used to refer to conditions which we believe to be associated with rheumatic fever. This term rheumatic is a loose one, as Hedley[115] has pointed out. He says: "To the pathologist it implies conditions of the joint cavities unattended by destructive processes, in contradistinction to arthritic processes which are essentially destructive lesions. Even here is encountered the twilight zone of 'rheumatoid arthritis'. To the pediatrician, especially those in Great Britain, 'rheumatic' is limited to the description of rheumatic fever, rheumatic carditis, and Sydenham's chorea of childhood, the problem as a whole being referred to as juvenile rheumatism. To the student of arthritic diseases 'rheumatic' or 'rheumatism' is used to cover the entire problem of arthritic diseases, rheumatic fever, lumbago, and even gout. To the layman 'rheumatism' generally means any ache or pain involving muscles, joints, bones, and at times even the nervous system. The latter conception has at least the merits of clarity."

It has become common practice to use the term *rheumatic heart disease* to indicate that the patient has or has had rheumatic fever, regardless as to whether it was clinically evident, and this usage will be followed in this review. It carries with it the implication that since heart disease is the most important and the most frequent single manifestation of rheumatic fever, it cannot be regarded as a complication but as an integral part of the usual disease picture.

Clinical Definitions. Definitions are badly needed in describing this disease, but they are not easy to give, partially because there are wide differences in the manner with which rheumatic fever is regarded clinically in different parts of this country. It is usual, for instance, to find in certain localities, and particularly in certain hospitals, that physicians can be very liberal with the diagnosis of rheumatic fever, designating all kinds of ill-defined chronic or subacute infections in childhood and adolescence, as rheumatic. In other places, as for instance in small American towns or rural communities, where there may be every indication that rheumatic fever is common, we hear physicians—usually older physicians—stoutly maintaining that they "hardly ever see a case of rheumatic fever among children," but they do recognize heart disease in childhood "due to tonsils, or tonsillitis" or "due to some focal infection."

In brief, then, one may well ask for a definition of the disease rheumatic fever. Is it a single disease; or is it perhaps a group of diseases? Is it merely a symptom complex like bronchial asthma, or a reaction to a variety of agents? Or is it a series of untoward, late reactions produced by Group A hemolytic streptococci? A few definitive criteria will be given in an attempt to answer these questions.

First, it is quite definite that this disease in some obscure way is associated with hemolytic streptococcal infections. The whole story of its pathogenesis does not necessarily begin and end with the *Streptococcus hemolyticus*, but one can say that the majority of cases of rheumatic fever appear under circumstances (whether they are clinical, bacteriological, immunological, or epidemiological) which point to the hemolytic streptococcus as one of the responsible agents. This feature will be given considerable discussion later in this review.

When it comes to *specific* attributes of this disease, we find that rheumatic fever owes its main claim to specificity to the *pathological picture* found at autopsy. Autopsy material furnishes us with characteristic lesions, of which the most striking are those in the heart, and to a lesser extent in and about the great vessels. The fact that blood vessels are affected indicates how widespread and varied may be the sets of clinical conditions which appear in this disease.

Clinical conceptions, on the other hand, are more difficult to define. But there are certain aspects of the clinical picture from which the disease may be visualized, and from them we have come to regard rheumatic fever as a common and serious form of illness, which occurs most frequently in young children or in young adults. In the majority of instances the active form of the disease is preceded by an upper respiratory infection due to the hemolytic streptococcus, although this situation is by no means invariable. Often the preceding acute infection is not clinically evident, and can only be detected by careful immunological investigation. The acute rheumatic attack may develop quickly into a fulminating form, and death may occur within a few days or weeks, but the usual course is prolonged, cover-

ing months or even years during which the course of the disease may be punctuated by periods of acute or subacute illness, frequently associated with tonsillitis, and marked by joint symptoms and heart disease; the latter being the most important and the most frequent single manifestation of rheumatic fever. Characteristically, this disease is very prone to recur, particularly in the first five or six years following the initial attack.

Symptomatologically, active rheumatic fever is recognized by a number of different manifestations, many of which seem to represent differing age expressions of the reaction of the host; thus we may find fever, acute and subacute arthritis, Sydenham's chorea, and carditis, with pericarditis, active myocarditis, or endocarditis. The endocardial lesions usually appear in the form of acute or subacute valvulitis, to which the mitral valve is singularly vulnerable. Also pleurisy and peritonitis, abdominal pain, epistaxis, torticollis, subcutaneous nodules, skin eruptions such as the marginatum form of erythema multiforme and erythema marginatum, are all listed among the manifestations of rheumatic fever. For years it was upon the acute and spectacular forms of the disease in which joint symptoms (particularly in young adults) played a prominent part that the interest of medicine was concentrated. Now we believe that the chronic or latent phases, which are particularly common in childhood, are of even greater importance.

Active rheumatic fever implies that the process which maintains this disease is proceeding, in that it is going on more or less in the same sense that a case of tuberculosis is progressive when it is said to be clinically active. Some of the signs of this activity have just been mentioned, but activity in this disease is also often estimated by the amount of fever and from certain nonspecific tests such as leukocytosis, and elevation of the erythrocyte sedimentation rate. It may exist in the absence of clinical symptoms. *Inactive rheumatic fever* implies that activity has for the time being ceased, and yet there is enough evidence in the clinical picture or in the patient's history to indicate that he had had one or more attacks of the disease.

From these descriptions one can easily see how many features of rheumatic fever are essentially nonspecific in character, and how difficult the task of diagnosis may be for the clinician, who sees what are said to be examples of rheumatic heart disease in both the adult and the child in which "no history of rheumatic fever" is available. He also sees what may be examples of the disease in childhood with no symptoms other than occasional fever and mild pains in the limbs, and he is not alone among those who have encountered difficulty in trying to interpret their significance. He sees the disease following close upon the heels of tonsillitis and scarlet fever, but he also sees it after what appear to be nonstreptococcal diseases. In fact, he often sees the development of rheumatic heart disease without any antecedent evidence or history of rheumatic fever. In the adult he sees

borderline cases, which may be either rheumatic fever or rheumatoid arthritis. He is dismayed by the difficulty of determining when the disease is active or old. To many physicians, therefore, the idea of a "rheumatic state" or diathesis has been and still is even more appealing than that of a specific disease. It certainly is easier from a "diagnostic" standpoint, but it is not the view which we will follow in this report.

Rheumatic Heart Disease. Although, according to Wilson,[312] the heart is suspected of being involved in all juvenile cases of rheumatic fever, the term rheumatic heart disease is not used here in that sense. In this review it is used to indicate that *clinical evidences* of lesions of rheumatic fever are present in the heart. This involvement may take the form of myocarditis, cardiac enlargement, pericarditis, or endocarditis. Of these one of the most distinctive lesions clinically is a particular form of chronic valvular disease—mitral stenosis. The other clinical evidences of rheumatic cardiac lesions are almost too numerous and too complex to list here, and it goes without saying that this is a feature which has made for some confusion. Much of this confusion lies in the fact that clinically it is often difficult to distinguish rheumatic heart disease from other forms of heart disease.* Perhaps the greatest difficulty which confronts the clinician in this respect is his interpretation of a systolic murmur, not only in children and adolescents, but in young and old adults. Is it a functional (or physiological) murmur? Is it due to a congenital defect? Is it caused by rheumatic heart disease? Or is it a sign of arteriosclerotic heart disease? These decisions must be made whenever possible through the development of clinical knowledge and clinical judgment if we are to progress in the field of rheumatic fever; and the terms mitral insufficiency or organic heart disease, etc., should always be supplemented by an etiological qualification if it is possible to do so.

Sydenham's Chorea. In most recent reviews on rheumatic fever, Sydenham's chorea has been accepted as one of the manifestations of this disease, and only during the past few years has doubt been again expressed as to its relationship to rheumatic fever and rheumatic heart disease. This question has been raised by Jones and Bland,[138] Coburn and Moore,[34] and others.[301, 91] One of the major reasons for discounting chorea (that is, chorea without other evidences of rheumatic fever) has been that it is less apt to be accompanied by carditis,[202, 273, 254, 3] and, when carditis does occur, there are almost invariably other signs of rheumatic fever, such as joint pains, fever, and leukocytosis. Exact agreement on this point has not been

*Progress, however, has been made in this direction, first by the American Heart Association[196] and later by the work of Hedley,[108] but the situation still demands an appreciation of the fact that the broad term *heart disease* is still too widely used, and the time has come for it to be supplanted by more concise definitive terms. Similar broad terms applying to other important diseases have been discarded—we no longer hear of lung disease, liver disease, etc., although kidney disease is a term which does, however, still survive. Different kinds of heart disease have long been classified on an *anatomical* basis, *i.e.*, as myocarditis, aortic and mitral endocarditis, but time has proved that while this type of division supplies certain important concepts of disease, a proper diagnosis requires etiological (as well as anatomical) qualifications when possible.