NATIONAL ACADEMY OF SCIENCES

REBECCA CRAIGHILL LANCEFIELD

1895—1981

A Biographical Memoir by

MACLYN MCCARTY

Biographical Memoir

Rebecca C. Hancock

REBECCA CRAIGHILL LANCEFIELD

January 5, 1895–March 3, 1981

BY MACLYN McCARTY

REBECCA CRAIGHILL LANCEFIELD was born on January 5, 1895, in Fort Wadsworth, New York, where her father, Col. William E. Craighill, was stationed as an officer in the U.S. Army Engineer Corps. As a member of an Army family, she lived in many different communities during her early years. After graduating from Wellesley College, however, and spending one year teaching in a girls school in Vermont, she returned to New York City. Except for a year's sojourn at the University of Oregon, she spent the remainder of her life there.

Her first move toward a career in science apparently came at Wellesley. Stimulated by her roommate's course in zoology, she dropped her notion of majoring in French and English and concentrated her efforts on biology. By the time she graduated in 1916, she was eager to begin graduate training. But she was forced to compromise: funds were short because of the death of her father, and her mother needed her help in supporting her five sisters. She saved enough from her earnings as a teacher during the following year to enable her to accept a scholarship with graduate tuition at Teachers' College of Columbia University. Fortunately, although this scholarship (established by the Daughters of the Cincinnati for daughters of Army and Navy officers) specified Teachers'

College, it was not necessary for her to take her courses there. Thus she spent the year in Hans Zinsser's Department of Bacteriology at the College of Physicians and Surgeons of Columbia University. Here she was able to broaden substantially her knowledge and experience in the branch of biology that interested her most.

There were a series of notable events in Rebecca Craighill's life in the spring of 1918. She received her master's degree from Columbia University and shortly thereafter was married to Donald Lancefield, a fellow graduate student at Columbia who was in the famous Department of Genetics under T. H. Morgan. Even more significant from the point of view of her future career in research, her application for a position at the Rockefeller Institute for Medical Research was accepted. That June she became a technical assistant to O. T. Avery and A. R. Dochez.

The timing of her arrival at the Rockefeller Hospital was of considerable importance in shaping the course of her life's work. Until late in 1917, Avery and Dochez had concentrated their efforts on studies of the pneumococcus. At that time, however, they traveled to Texas as consultants to the Surgeon General of the Army to investigate an outbreak of serious streptococcal infections that had been superimposed on a measles epidemic in a number of military installations there. Returning to New York with a collection of streptococcal strains that had been isolated during the visit, they set about trying to determine whether, as in pneumococcus, there were separate and distinct types of streptococci involved in the epidemic rather than a single unvarying pathogen. Their approach was to use the serological procedures that had proved successful in delineating pneumococcal types: the agglutination reaction and the protection of mice with specific antisera.

Their progress in these efforts was reported at a confer-

ence on *Streptococcus hemolyticus* that was held at the Princeton laboratories of the Rockefeller Institute on June 1, 1918. The discussions at the conference dealt with various aspects of the problem of streptococcal infections, but much attention was focused on the recently isolated strains. Avery prefaced his comments with this statement: "It is rather difficult from a study of the strains that we have isolated to tell whether they are all alike, whether they constitute one or several types." Dochez later enlarged on this point, describing the difficulties they had encountered with agglutination reactions as well as with mouse protection experiments. He concluded: "Up to now, however, we have been unable to obtain immune serum which affords any considerable degree of protection for white mice against experimental infection. We are still working along this line and it is possible that the proper combination of immune serum and test animal may be obtained."

It was to assist in this effort that Rebecca Lancefield was brought into the laboratory soon after. And although she had had no real opportunity before to display her special talents, it was clearly a case of bringing the right person to the right place at the right time. Within a year they had together identified four distinct serological types—as determined both by agglutination and mouse protection—that served to classify 70 percent of the 125 strains studied. The paper describing these results was submitted for publication on June 1, 1919, one year to the day after the conference. There can be little doubt that Rebecca Lancefield's native talent for solving this type of problem, perhaps accelerated in its development under the tutelage of two established masters, was a prime factor in the success of these studies. That she contributed much more than simply technical help was tacitly acknowledged by the inclusion of her name as a coauthor of the paper, a type of recognition seldom accorded to technical assistants in those days. It was a major publication, running

to some thirty-four pages and replete with tables that documented the findings in great detail. In addition to being the first account of specific types among the hemolytic streptococci, it also represented a record of the first encounter between these microorganisms and the investigator who was destined over the next five decades to become the master of their diversity.

At this point, however, the work with these streptococcal strains ended temporarily. The war was over and with it the Army support for the studies. Dochez went to Johns Hopkins; Avery returned to his first love, the pneumococcus; and Lancefield moved back to Columbia where she worked as a research assistant on problems of *Drosophila* genetics. Nevertheless, the streptococcal strains were not all simply discarded. Some of them remain today in the Lancefield collection as reference type strains of group A streptococci, still identified by the same letter and number designation that was assigned on their isolation in 1917.

In 1922, after her year at the University of Oregon, during which she and her husband Donald both taught, Lancefield came back to the Rockefeller Hospital for good. Mrs. L. (as she came to be affectionately known to her colleagues) was now associated with the rheumatic fever service of Dr. Homer Swift rather than with the pneumonia service. She was also enrolled again as a graduate student at Columbia, and most of the laboratory work for her Ph.D. thesis was carried out at Rockefeller on a problem concerned with the so-called "green" or viridans streptococci. These streptococci were erroneously suspected of having something to do with rheumatic fever; her studies, published in her thesis and in two papers in the *Journal of Experimental Medicine,* helped to dispel this notion. The viridans streptococci are an extraordinarily heterogeneous and protean group of microorganisms. It must have been of some relief to her—and of con-

siderable importance to science—that she was able before too long to resume her studies of hemolytic streptococci.

It is important to realize that the relationship of hemolytic streptococci to human disease was not well characterized in the period immediately following World War I. They were looked upon as important primarily as secondary invaders in such situations as puerperal fever, wound infections, and pneumonia that followed measles or influenza, as in the Army camp epidemics. The great prevalence of primary streptococcal sore throat did not appear to be clearly recognized, and the key role of streptococci in scarlet fever was yet to be discovered. There was even less of a clue with regard to their implication in the pathogenesis of rheumatic fever and glomerulonephritis. Thus Lancefield's early studies were initiated before the present picture of streptococcal disease had been formulated. The results that she obtained had much to do with originating and crystallizing these concepts and with providing a basis for understanding the clinical and epidemiological patterns of disease caused by these organisms.

Although Lancefield was no longer directly associated with Avery, their laboratories were in close proximity, and she continued to look to him for advice and counsel in the development of her research. As a great admirer of his scientific insights and approaches, she was well prepared to bring to her studies of the streptococci the same points of view that he had used so successfully in the case of pneumococci. Consequently, she considered the laborious and detailed serological analysis of the large family of streptococci as being primarily an essential means to a more significant end: that of determining the chemical nature and biological significance of the antigenic substances responsible for the serological reactions. The systematic classification that emerged from her serological grouping and typing of streptococci was not in

her mind the ultimate goal of her research. Rather, it was a needed step in identifying the most significant antigens and determining their role in the disease-producing capacity of the microorganisms.

In the mid-1920s she succeeded in obtaining two antigens in soluble form from hemolytic streptococci: one that was type specific and responsible for the distinction between the strains from the epidemic in 1918 and another that was species specific and present in all of the human strains that she examined. She soon encountered a surprising result in attempting to determine the nature of the type-specific antigen. Avery and Heidelberger had earlier established that the type-specific antigens of the pneumococcus were polysaccharides present in the capsule of the organism; subsequently, other pathogenic bacteria had been found to be similarly equipped with capsular polysaccharides that determined type specificity. Lancefield thus anticipated a similar situation in streptococci, but after careful studies was forced to conclude that this was not the case. Her soluble, type-specific antigen of streptococcus was clearly a protein, which she later designated as M-protein on the basis of the association of the antigen with the matt colony form of the organism when grown on an agar medium. The M-protein appeared to serve essentially the same function in determining the virulence of hemolytic streptococci that the capsular polysaccharide did in the pneumococcus.

Her soluble species-specific antigen did, however, prove to be carbohydrate in nature and was designated the C-carbohydrate. (The continuing close relationship with the Avery laboratory is illustrated by the fact that when Avery and his colleagues shortly thereafter found an analogous species-specific carbohydrate in pneumococcus, it was also called C-carbohydrate or C-substance.) The great importance of the streptococcal C-carbohydrate, however, proved

to be in the sorting out of the many different varieties of hemolytic streptococci that exist in nature. As she received more strains from numerous sources, it became apparent to Lancefield that her species-specific antigen was really group specific. It was common to strains isolated from strep throat and certain other human diseases, but a group of strains from bovine mastitis had a quite different group-specific carbohydrate and those from horses with strangles still a third. A continuation of this process established that there are several distinct serological groups of hemolytic streptococci in nature. Their differentiation proved of great importance in the study of streptococcal disease.

Lancefield designated the human strains that had been the object of her initial studies as group A and assigned letters of the alphabet to the others in sequence. Group A streptococci are responsible for most of the serious streptococcal infections of man, and it is infection with this group of organisms that leads to the poststreptococcal sequelae, rheumatic fever and glomerulonephritis. But the other groups of streptococci, regardless of their normal habitat, also occur in man and may be associated with disease. Group B streptococci, for example, which were initially encountered in cattle, are not uncommon in man and today are receiving much attention as the cause of septicemia and meningitis of the newborn. Lancefield carried out extensive studies of group B streptococci that laid the necessary groundwork for the present efforts to deal with this pediatric problem. In contrast to the situation in group A with its M-protein, she found that the type-specific antigens of group B streptococci are capsular polysaccharides, fully analogous to the pneumococcal polysaccharides. In working out the interrelationships between the several prevalent types of group B streptococci, she showed that specific antibodies to the capsular polysaccharide were highly protective against experimental infec-

tions. Many years later she returned to work on group B streptococci and initiated studies on their complex biochemical and antigenic structure that continue to be pursued in numerous laboratories throughout the world.

In company with many other experimentalists, Rebecca Lancefield's enthusiasm for working at the laboratory bench did not extend to the painful process of writing up the work for publication. She worked for nearly four years on the hemolytic streptococci without publishing any of her findings, but she quickly remedied the situation with a flurry of seven papers, all appearing in the *Journal of Experimental Medicine* in 1928. These papers included the first description of her M-protein and C-carbohydrate, with details of their chemical and immunological properties, and some information on their relationship to the bacterial cell. Her continuing work built on this base of new knowledge and led to the differentiation of serological groups of streptococci and delineation of the biological significance of the type-specific M-protein.

An interesting episode in the further sorting out of streptococcal diversity relates to Lancefield's exchanges with Fred Griffith, the noted British microbiologist. Griffith, after his famous work on the discovery of the transformation of pneumococcal types, had turned to studies of hemolytic streptococci. His technical approach differed significantly from that of Lancefield: he depended primarily on slide agglutination for serological differentiation of his strains, and she used a precipitin technique that depended on the property of her soluble antigens to give visible precipitates when mixed with antisera. Both workers used extensive adsorption of their antisera with heterologous strains to eliminate cross-reactions. Griffith examined a large number of human strains by his procedure and published his first extensive description of types of streptococci early in 1935.

On January 22, 1935, Lancefield wrote to Griffith requesting a reprint of his paper, and she included the following comment: "I have just read your paper in the current Journal of Hygiene with the greatest interest. I should not have supposed it possible to classify the majority of strains of *S. pyogenes* into so small a number of types as 27. It certainly makes a much more workable situation in this group if one can do that." Her interest had obviously been captured, and two months later she wrote requesting his cultures and samples of his antisera "to compare the types that I have encountered with yours." This began a long series of exchanges of strains, sera, and data that was prematurely terminated by Griffith's tragic death in the London Blitz in 1940.

The two workers had great respect for one another—even though they did not see eye to eye on methodology and were never converted to each other's approaches. There was much in common between the types defined by the two different techniques, and Lancefield adopted the numbers that Griffith had assigned to his types in order to achieve uniformity. In a few cases discrepancies arose because Griffith was not grouping his strains on the basis of C-carbohydrate, and strains that did not belong to group A were included among his types. Another source of discrepancy led Lancefield to the discovery of a second surface protein antigen of group A streptococci, which she designated as T-antigen. T-antigen could take part in slide agglutination and thus be detected by Griffith, but it was not present in the soluble M-protein extracts. Subsequently, Lancefield and her colleagues were able to show that T-antigen—unlike M-protein—has no relation to virulence and, further, that the same or closely related T-antigen may be present on different M types. In the end, M types became the standard classification for bacteriological, clinical, and epidemiological studies, even though T

typing by slide agglutination remains an adjunct technique applicable to a number of situations in which M-protein is absent or difficult to detect.

As it turned out, the doubts that Lancefield expressed to Griffith about being able "to classify the majority of strains of *S. pyogenes* into so small a number of types as 27" proved to be well founded. The total number of recognized types has been added to by laboratories all over the world and is now well over sixty. She herself had little interest in the business of identifying new types, preferring to devote her energies to the biological properties of the organism and their bearing on disease-producing capacity. The most dramatic illustration of the fruits of this approach is the unfolding of the story of the central role of M-protein in streptococcal infections. This surface antigen not only determines the type specificity of the numerous strains of group A streptococci but also serves to protect the organism from host defenses. When M-protein is present, the white blood cells appear to be unable to engulf and destroy the organisms; in the presence of specific antibody, however, this protective effect of M-protein is neutralized and the white cells can do their job. These facts led to the concept that immunity to streptococcal disease is primarily type specific and that recovery from infection with one type does little to provide protection against the numerous other types of group A organisms. This served to explain why repeated strep throats were so common in childhood and why rheumatic fever is a notoriously recurrent disease. Thus her work on this antigen provided the basis for a better understanding of the epidemiology of the disease and a more rational approach to its control.

The work that she and her colleagues pursued during World War II continued with the sorting out of the various antigens, especially the relationships between M- and T-antigens. At the same time she supervised the large-scale pro-

duction of the grouping and typing sera that were provided to the military services for the first intensive studies of the epidemiology of streptococcal disease using the powerful tools that she had developed. In the postwar years she resumed her efforts to purify and characterize the properties of the important antigens. She carried out extensive studies of representative M- and T-antigens, a new surface protein that she designated as R-antigen, and the polysaccharide antigens of group B streptococci. In addition, in an illuminating study of the persistence of type-specific antibodies in man following group A streptococcal infections, she showed that lasting immunity to the M-antigen is commonly encountered.

Over the course of her work a vast number of streptococcal strains were sent to her; most of these are still preserved in the lyophilized state in her collection of some thousands of different strains. They were sent to her for identification, for a confirmation of identity, or because of some special feature of the situation in which they were obtained. They all received attention and analysis, resulting in a few dozen volumes of loose-leaf notebooks, in sturdy hard-cover binders, in which the data on each strain are recorded. Much of this information is written in her own hand, and it took some experience to be able to decipher her notes. But with persistence one could usually learn what he wanted to know about the strain in question. An equally large set of notebooks dealing with her research projects also exists, and these are even more difficult to decipher. (On occasion she even had trouble herself when trying to review experiments carried out two or three decades earlier.)

Rebecca Lancefield's devotion to her streptococcal studies was just as durable and persistent as the type-specific antibodies that she had described, and she maintained her laboratory activity until a few months before her death. In June 1979, sixty years after her arrival at the Rockefeller Hospital

to work with Avery and Dochez, she was still coming in regularly, driving her own car back and forth from Douglaston, Queens, as she had since before the war. Although the annoying infirmities of age began to make it impossible for her to maintain her customary schedule, she did not abandon the effort until Thanksgiving Day, 1980, when she fell at home and broke her hip. She never regained full mobility, and she died on March 3, 1981.

Many of her colleagues feel that there was an inexplicable delay in general recognition and appreciation of her great scientific contributions. There is certainly some truth in this, but it must also be noted that among microbiologists she had long ago attained international stature as the outstanding authority on streptococci. Both the national and international organizations devoted to streptococcal problems have renamed their groups "The Lancefield Society," the former while she was still active. As further evidence of her recognition within the general field, she was elected president of the Society of American Bacteriologists in 1943 and of the American Association of Immunologists in 1961. Even though they may have been somewhat delayed in arriving, a number of other honors also came to her. She received the T. Duckett Jones Award of the Helen Hay Whitney Foundation in 1960, the American Heart Association Achievement Award in 1964, and the Medal of the New York Academy of Medicine in 1973. Rockefeller University recognized her contributions and long service to the institution with an honorary D.Sc. in 1973; her alma mater Wellesley College followed suit with a similar honor on the occasion of the sixtieth anniversary of her graduation in 1976.

She was elected to the National Academy of Sciences in 1970. Regrettably, this came too late for the Lancefields to enjoy the fellowship of the annual meetings with their longtime friends, the A. H. Sturtevants. "Sturt" and his wife,

Phoebe, had regaled them for years with tales of the Academy meetings during their shared summer holidays at Woods Hole. Rebecca attended a few meetings, but I am sure that she missed the special flavor that might have been contributed by the presence of her friends. She always spent the summer at Woods Hole, a place that was second in her heart only to her laboratory. For the most part she did not engage in laboratory work or writing there, the stay being reserved for renewal and recreation. In fact, a major aim was to escape the hot, humid weather of a New York City summer, which she detested; and in any event, throughout her early decades at Rockefeller it was impractical to try to do bacteriological or immunological work where neither the laboratories nor the animal quarters were air conditioned. She found Woods Hole ideal for relaxation, tennis, and especially swimming, an activity that she pursued to her final summer.

The description of Lancefield's scientific contributions gives an incomplete picture of her life in the laboratory. As single-minded as she was in the pursuit of her research goals, she could always find time to provide advice and assistance to other workers, both within and outside the laboratory. A visitor with an interest in streptococcal problems would leave with a thorough indoctrination and with most of his questions answered—as well as with a collection of cultures of reference streptococcal strains and samples of the relevant antisera. Streptococcal strains and antisera, together with directions for their use, were freely supplied to laboratories all over the world. The younger associates and postdoctoral fellows in our group found that she was not only ready to help whenever needed but that she expected to participate fully in all of the activities of the laboratory, including the parties and informal get-togethers. The pre-Thanksgiving eggnog party that she initiated is still carried on today, using her recipe.

Since I became the head of the rheumatic fever service after Dr. Swift's retirement in 1946, my own direct association with Rebecca Lancefield extended over more than half of her career at Rockefeller. Many of her major contributions had been completed and the groundwork already laid for others by this time, but I had ample opportunity to observe her working methods at first hand and to collaborate with her in more than one research project. Out of this came some insight into the qualities that were responsible for her success as an investigator. Because of her intuitive recognition of the great complexity of hemolytic streptococci, she was fully aware of the inherent danger of drawing premature conclusions from limited data. Accordingly, she could never be satisfied with the results obtained with one or two strains exhibiting a given characteristic after analysis with one or two antisera. It was always necessary to examine *all* available strains with each of many antisera, a procedure that greatly increased the burden of the analysis because of the diversity of the organisms and the heterogeneity of the antibody response of different rabbits to the multiple antigens involved. Such careful investigations, however, prevented her from drawing misleading and oversimplistic conclusions, and her meticulous approach is responsible, I believe, for the great durability and reproducibility of her published findings.

Rebecca Lancefield never developed very much sympathy for the modern feminist's point of view on women in science. She was not enthusiastic about honors that recognized her as the "first woman" to do this or that and preferred those that came without reference to her sex. She had no illusions about the difficulties of having both a scientific career and a family, but she felt that with determination and hard work it was possible without special treatment. In the case of her own small family, her efforts to provide a rewarding home life along with her scientific pursuits were notably successful,

even though there must have been problems at times in adapting. She commuted by car from Douglaston, Long Island, for over forty years, which by itself was something of a triumph, considering bad weather, gasoline shortages, and the like.

Donald Lancefield survived Rebecca by only a few months. Their daughter, Jane Hersey, did not follow her parents into a career in biology and received her education in the classics. She has not managed to avoid science altogether, however; for some time, she served as a book review editor for *The American Scientist.* She and her husband, George Hersey, have two sons, Donald and James.

MUCH OF THE MATERIAL on which I drew for this memoir came from my own files. I am indebted, however, to the Rockefeller University Archives for the opportunity to reread some of Rebecca Lancefield's correspondence and for access to the annual reports to the Board of Scientific Directors of the Rockefeller Institute, which were helpful in piecing together the early history of her work.

SELECTED BIBLIOGRAPHY

1919

With O. T. Avery and A. R. Dochez. Studies on the biology of streptococcus. I. Antigenic relationship between strains of streptococcus haemolyticus. J. Exp. Med., 30:179–213.

1921

With C. W. Metz. Non-disjunction and the chromosome relationship of *Drosophila willistoni*. Proc. Natl. Acad. Sci. USA, 7:225–29.

1922

With C. W. Metz. The sex-linked group of mutant characters in *Drosophila willistoni*. Am. Nat., 36:211–41.

1924

Antigenic relationships of the nucleo-proteins from the Gram-positive cocci. Proc. Soc. Exp. Biol. Med., 22:109–11.

1925

The immunological relationships of streptococcus viridans and certain of its chemical fractions. I. Serological reactions obtained with antibacterial sera. J. Exp. Med., 42:377–95.

The immunological relationships of streptococcus viridans and certain of its chemical fractions. II. Serological reactions obtained with antinucleoprotein sera. J. Exp. Med., 42:397–412.

1928

The antigenic complex of *Streptococcus haemolyticus*. I. Demonstration of a type-specific substance in extracts of *Streptococcus haemolyticus*. J. Exp. Med., 47:91–103; II. Chemical and immunological properties of the protein fractions, 469–80; III. Chemical and immunological properties of the species-specific substance, 481–91; IV. Anaphylaxis with two non-type specific fractions, 843–55; V. Anaphylaxis with the type-specific substance, 857–75.

With E. W. Todd. Variants of hemolytic streptococci; their relation

to type-specific substance, virulence, and toxin. J. Exp. Med., 48:751–67.

With E. W. Todd. Antigenic differences between matt hemolytic streptococci and their glossy variants. J. Exp. Med., 48:769–90.

1933

A serological differentiation of human and other groups of hemolytic streptococci. J. Exp. Med., 57:571–95.

1934

A serological differentiation of specific types of bovine hemolytic streptococci. J. Exp. Med., 59:441–58.

Loss of the properties of hemolysin and pigment formation without change in immunological specificity in a strain of *Streptococcus haemolyticus*. J. Exp. Med., 59:459–69.

1935

With K. Goodner and H. F. Swift. The serological classification of hemolytic streptococci in relation to epidemiological problems. Am. J. Med. Sci., 190:445–53.

With R. Hare. The serological differentiation of pathogenic and nonpathogenic strains of hemolytic streptococci from parturient women. J. Exp. Med., 61:335–49.

1938

Two serological types of group B hemolytic streptococci with related, but not identical, type-specific substances. J. Exp. Med., 67:25–40.

A micro precipitin-technic for classifying hemolytic streptococci, and improved methods for producing antisera. Proc. Soc. Exp. Biol. Med., 38:473–78.

1939

With G. K. Hirst. Antigenic properties of the type-specific substance derived from group A hemolytic streptococci. J. Exp. Med., 69:425–45.

1940

Type-specific antigens, M and T, of matt and glossy variants of group A hemolytic streptococci. J. Exp. Med., 71:521–37.

The significance of M and T antigens in the cross reactions between certain types of group A hemolytic streptococci. J. Exp. Med., 71:539–50.

1941

Specific relationship of cell composition to biological activity of hemolytic streptococci. Harvey Lect., 36:251–90.

1943

With H. F. Swift and A. T. Wilson. Typing group A hemolytic streptococci by M precipitin reactions in capillary pipettes. J. Exp. Med., 78:127–33.

Studies on the antigenic composition of group A hemolytic streptococci. I. Effects of proteolytic enzymes on streptococcal cells. J. Exp. Med., 78:465–76.

1944

With W. A. Stewart. Studies on the antigenic composition of group A hemolytic streptococci. II. The occurrence of strains of a given type containing M but no T antigen. J. Exp. Med., 79:79–88.

With R. F. Watson. Studies on the antigenic composition of group A hemolytic streptococci. III. Types with serologically identical M but distinct T antigens: Types 10 and 12. J. Exp. Med., 79:89–98.

With W. A. Stewart, A. T. Wilson, and H. F. Swift. Studies on the antigenic composition of group A hemolytic streptococci. IV. Related T but distinct M antigens in types 15, 17, 19, 30, and in types 4, 24, 26, 28, 29, 46. Identification by slide agglutination. J. Exp. Med., 79:99–114.

1946

With V. P. Dole. The properties of T antigens extracted from group A hemolytic streptococci. J. Exp. Med., 84:449–70.

1952

With G. E. Perlmann. Preparation and properties of type-specific M antigen isolated from a group A, type 1, hemolytic streptococcus. J. Exp. Med., 96:72–82.

With G. E. Perlmann. Preparation and properties of a protein (R antigen) occurring in streptococci of group A, type 28, and in certain streptococci of other serological groups. J. Exp. Med., 96:83–97.

1954

Cellular constituents of group A streptococci concerned in antigenicity and virulence. In: *Streptococcal Infections*, ed. M. McCarty, pp. 3–18. New York: Columbia University Press.

1955

With M. McCarty. Variation in the group specific carbohydrate of group A streptococci. I. Immunochemical studies on the carbohydrates of various strains. J. Exp. Med., 102:11–28.

1957

Differentiation of group A streptococci with a common R antigen into three serological types, with special reference to the bactericidal test. J. Exp. Med., 106:525–44.

1958

Occurrence of R antigen specific for group A type 3 streptococci. J. Exp. Med., 108:329–41.

1959

Persistence of type-specific antibodies in man following infection with group A streptococci. J. Exp. Med., 110:271–92.

1960

With E. W. Hook and R. R. Wagner. An epizootic in Swiss mice caused by a group A streptococcus, newly designated type 50. Am. J. Hyg., 72:111–19.

1962

Current knowledge of type-specific M antigens of group A streptococci. J. Immunol., 89:307–13.

1964

With E. H. Freimer. Type-specific polysaccharide antigens of group B streptococci. J. Hyg., 64:191–202.

1971

With J. Rotta, R. M. Krause, W. Everly, and H. Lackland. New approaches for the laboratory recognition of M types of group A streptococci. J. Exp. Med., 134:1298–315.

1975

With M. McCarty and W. Everly. Multiple mouse-protective antibodies directed against group B streptococci. Special reference to antibodies effective against protein antigens. J. Exp. Med., 142:165–79.

1977

With S. D. Elliott and M. McCarty. Teichoic acids of group D streptococci with special reference to strains from pig meningitis (Streptococcus suis). J. Exp. Med., 145:490–99.

1979

With J. Y. Tai and E. C. Gotschlich. Isolation of type-specific polysaccharide antigen from group B type Ib streptococci. J. Exp. Med., 149:58–66.