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FREDERICK GEORGE NOVY

1864—1957

A Biographical Memoir by

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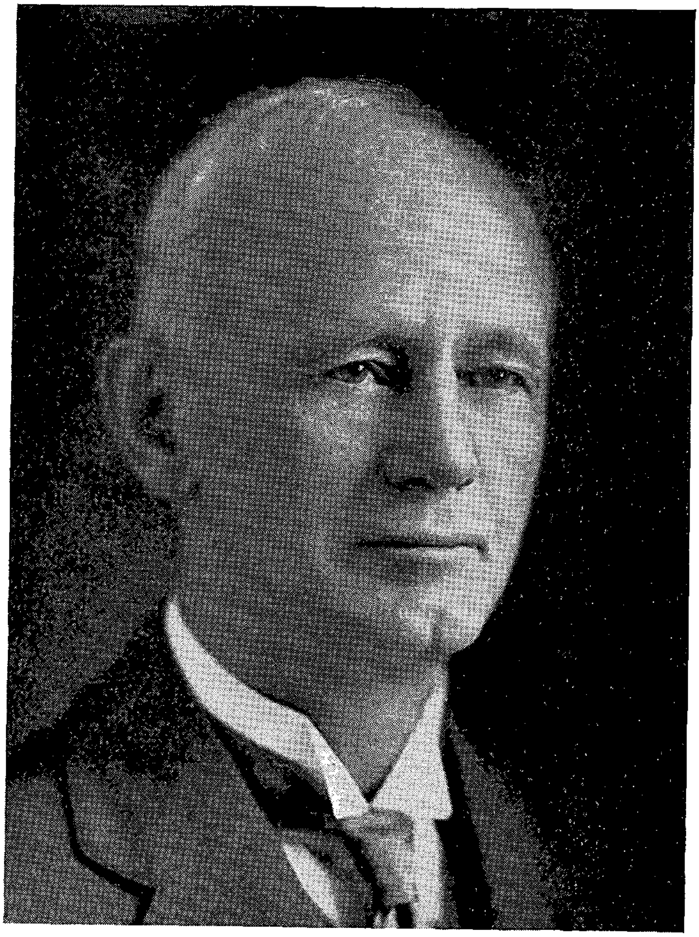
Biographical Memoir



F. G. Novy

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December 9, 1864–August 8, 1957

BY ESMOND R. LONG

FREDERICK GEORGE NOVY, pioneer teacher and investigator of bacteriology, died in Ann Arbor on August 8, 1957, at the age of ninety-two years and eight months. He was among the last survivors of that eager group of young American biologists and hygienists who journeyed to Europe in the 1880s to work in the laboratories of Louis Pasteur and Robert Koch and learn the fundamentals of the new science of bacteriology at first hand. In the succeeding seventy years Novy saw almost the entire development of modern microbiology as an academic discipline and field of research.

Novy was born in Chicago on December 9, 1864, the third son of Bohemian parents who had moved to America earlier that year. Novy's father had been a master tailor in the old country, and continued the occupation in this country. His mother had been a milliner; a heritage of property, which she sold, made possible their trip to America and establishment of a new home. Each of them had attended a village school in Bohemia; each had read intensively and had developed a desire to travel. Some light on Frederick Novy's longevity is seen in their long lives; his father died at eighty-four and his mother at eighty-three.

The first family home in Chicago was on the West Side, not far from the site of origin of the great Chicago fire of 1871, which Novy recalled vividly the rest of his life. Novy attended the public schools in Chicago after a year at the "Mission School," a primitive struc-

He began work immediately for a master's degree and attained this in June, 1887, with a thesis on cocaine and its derivatives. He followed up his first paper with a few additional short publications on cocaine and related compounds. These investigations were in the field of pure organic chemistry and represented exactly the type of professional effort that had attracted Novy to Ann Arbor in the first place. It was a short-lived occupation, however, for in the year in which he took his master's degree in chemistry Victor C. Vaughan, Professor of Hygiene and Physiological Chemistry in the university, persuaded him to take the position of instructor in his department.

Thus began a long association, marked by close collaboration and numerous joint publications, of which the best known was their book *Cellular Toxins* (1902; see appended bibliography), which started out as a smaller work in 1888, *Ptomaines and Leucomaines, or the Putrefactive and Physiological Alkaloids.* There can be no doubt that Novy's original interest in pure organic chemistry laid the background for these studies in bacteriological chemistry and developed a lasting sense of precision in his investigations. He retained that interest throughout life. He continued his membership in the Deutsche Chemische Gesellschaft, which he acquired in 1886, for nearly thirty years, relinquishing it during the First World War. His talent in chemistry led to his selection as a member of the Council on Pharmacy and Chemistry of the American Medical Association, a position he held for a quarter of a century (1905–1930).

A student always, Novy followed a graduate and medical curriculum as rapidly as he could in the midst of his academic responsibilities and received the Sc.D. degree in 1890 and the M.D. degree in 1891. In the latter year he was made Assistant Professor of Hygiene and Physiological Chemistry under Vaughan. The latter had just become Dean of the Medical School, so that much of the professional responsibility for the department devolved on Novy. This early obligation, imposed when he was less than thirty years of age, threw him into the midst of a highly stimulating group, vividly concerned with the development of medical instruction in the Mid-

dle West. The group included J. Playfair McMurrich and G. Carl Huber in anatomy, Henry Sewall and Warren P. Lombard in physiology, Arthur R. Cushny in pharmacology, Aldred Scott Warthin in pathology, and George Dock in medicine.

Shortly after the beginning of his association with Vaughan, young Novy, influenced by the rising tide of reports on the agents of communicable disease and already conscious of the coming importance of bacteriology for students of medicine, suggested to Vaughan that they use vacation time for a trip to Europe to learn facts and new methods of study in the rapidly developing science. Novy had been particularly impressed by Ferdinand Hueppe's *Die Methoden der Bakterien-Forschung,* which had just been published, and first suggested that they study with Hueppe in Wiesbaden. Vaughan acquiesced heartily in the idea of the trip, but proposed that they make their first objective the famous laboratory of Robert Koch in the Hygienic Institute in Berlin. This met with Novy's approval. In Berlin Novy worked primarily under Koch's assistant Carl Fraenkel, but listened to lectures by Koch himself. Novy wrote a short but picturesque account of the daily routine in Fraenkel's student laboratory, and its methods of intensive instruction, shortly after his return to the United States.

Back in Ann Arbor in the fall, he made preparations for a course in bacteriology, which was officially offered as a three-month elective in the university in January, 1889. Relatively few students took the course, but some of the faculty attended. Among these was the Professor of Physiology, Henry Sewall, a victim of tuberculosis, who wished to study his own case by the new bacteriological technics. Sewall was one of the first to appreciate Novy's talents and foresight. So successful was the course that in the fall of the next year, 1890, bacteriology became a requirement for students in the medical curriculum.

Novy made several subsequent trips to Europe to improve his understanding and acquaintance. He studied at the famous University of Prague, always a leading center for pathology, in 1894, and

at the Pasteur Institute in Paris in 1897, two years after Pasteur's death. He had, as a matter of fact, visited the Institute on his return from Berlin in 1888, but apparently without making the actual acquaintance of Pasteur. Although he missed an association with the French master, in subsequent years Novy knew the Pasteur Institute well and cultivated a warm and lasting friendship with an early successor of Pasteur, Emile Roux, one of the discoverers of diphtheria toxin. In his 1894 trip, again in company with Vaughan, he attended the International Congress of Hygiene and Demography held in Budapest that year, making the trip as a delegate from the Michigan State Board of Health. At this meeting he had the unique experience of hearing Alexandre Yersin describe his discovery of the plague bacillus and Roux and Emil von Behring report independently on their pioneer investigations on diphtheria antitoxin.

In America Novy grew rapidly in stature as teacher and investigator. By 1900 his place as a foremost bacteriologist in this country was well established. He had published a textbook for students, collaborated with Vaughan in a widely read volume on ptomaines, taken part in local studies on typhoid fever, written authoritatively on the hog cholera bacillus, discovered one of the several etiological agents of malignant edema, developed apparatus and methods for investigating the biology of anaerobic bacteria, and written extensively on laboratory methods in general bacteriology.

In 1900, when a report from an officer of the U. S. Marine Hospital Service raised the suspicion that bubonic plague was smoldering in San Francisco's Chinatown, Novy's reputation was such that he was a logical choice for membership in a commission appointed by the Secretary of the Treasury—whose responsibilities then included what is now the Public Health Service—to ascertain if the disease really was rife. The commission, consisting of Simon Flexner of Philadelphia, Chairman, Llewellys F. Barker of Chicago, and Novy, located several cases of bubonic plague, proving conclusively that the disease was endemic, and opened the way for rigid measures for the prevention of its spread. Novy used his experience and the exhaustive back-

ground he accumulated through concurrent studies of plague to write instructional articles for both the medical and lay public on the subject and to indicate what provisions should be adopted if the disease escaped its confines and spread to other parts of the United States.

In the same year, 1900, Novy took part in the foundation of the Society of American Bacteriologists; in 1904 he became its fifth president, succeeding Theobald Smith in that influential position. Two years previously, in 1902, he had been made full Professor and head of the now well-established Department of Bacteriology in the University of Michigan, after passing through the lower academic grades in the Department of Hygiene and Physiological Chemistry.

At the time when Novy commenced his work in bacteriology and related microbiology, relatively little original work in the field had been done in this country. Theobald Smith and his associates had discovered the cause and mode of transmission of Texas fever in cattle. George M. Sternberg, an early investigator in many fields of bacteriology, a systematist and authoritative teacher, was one of the several discoverers of the pneumococcus and had written a *Manual of Bacteriology* which was a leading text in the field in this country for years. William H. Welch and T. Mitchell Prudden had brought German knowledge and methods to the United States and were training many young men who later assumed posts of importance. As a result of this and other stimulation, in the late eighteen eighties and early nineties embryo courses and investigative laboratories for bacteriology were appearing throughout the country. The course given by Novy in 1889 is commonly described as the first formal university course in the country. The practical applications of bacteriology were by that time widely recognized, however. It was rapidly taking its place as an indispensable auxiliary science in pathology and public health and had made its way into the teaching of medicine and surgery.

At the turn of the century numerous American journals were devoting all or much of their space to bacteriological developments;

these included the *Journal of Medical Research* (founded as the *Boston Journal of the Medical Sciences* in 1896), the *Journal of Experimental Medicine,* also founded in 1896, and the *Journal of Infectious Diseases,* founded in 1904. The *American Journal of Public Health,* which went through a series of transitions in name and format before its present stabilization, was from its earliest years a medium for publication of the applications of bacteriology to public health.

Novy was an early entrant in the field of bacteriological instruction. In 1894 he put out a short informal text on *Laboratory Work in Bacteriology,* which was elaborated, revised, and enlarged in a second edition in 1899. It came out through Novy's insistence, as noted in the preface of the book, that a thorough course of laboratory instruction in bacteriology was essential in the proper education of medical students. The text was based on the day-to-day work of the Hygienic Laboratory of the University of Michigan and represented the painstaking teaching that characterized all of Novy's efforts.

Although Novy began his professional life, as we have seen, as a chemist and published a chemical text for medical students (*Directions for Laboratory Work in Urine Analysis,* 1892, entitled *Laboratory Work in Physiological Chemistry* in its second edition, in 1898), his early responsibilities in hygiene and public health, fostered by Victor Vaughan, and his own self-acquired training in microscopic zoology led him inevitably into a career in microbiology. His association with Vaughan and his own interest in chemistry rapidly carried him on to a search for toxic products of bacterial growth. In these early studies, and partly under the influence of Vaughan, Novy was convinced that within the bodies of microorganisms, or among the products of their metabolism, substances of definable composition could be discovered, whose action could be correlated with the symptoms of disease. This was the view of a number of German bacteriological chemists, particularly Ludwig Brieger of Berlin, and so it is not surprising that Novy's discovery of certain free bases in the bacterial products of the hog cholera bacillus led him to identify

them tentatively as specifically active products in hog cholera. His more mature considerations of a protein product in the microorganism, against which some immunological response could be built up, was more in line with modern thinking.

Investigations of much greater importance, carried out some years later and published in 1894, led to his discovery and isolation of an anaerobic bacillus causing fatal septicemia in animals, with characteristic "malignant edema." Such organisms had been known as far back as the researches of Pasteur in the 1870s and August Gaertner of Jena identified a similar organism, which was soon designated generally as Gaertner's bacillus. In the succeeding years Novy's organism came to be recognized as a significant one, distinguishable from Gaertner's, and clearly one of the several agents capable of causing malignant edema.

The study of this and similar organisms led Novy into ingenious developments of apparatus for the cultivation of anaerobic bacteria. These investigations were reflected in equipment invented years later for studies on bacterial respiration. In the meantime the "Novy jar" had become standard bacteriological equipment. It was but one of many useful pieces of apparatus he devised during his period of intensive laboratory investigations. So well-recognized were his accomplishments in bacteriological technic that he was chosen for responsibility in this field in the authoritative statements published from time to time in the *Reference Handbook of the Medical Sciences.*

His activities were extra- as well as intramural, and he proved an expert in the now deeply cultivated field of public relations. Throughout the 1890s he was vigorously engaged in acquainting the Michigan public with facts on the germ theory of disease, on the nature of diphtheria, typhoid fever, and tuberculosis, on food poisoning, on disinfection, and on many similar matters of significance for public health. He maintained close relations with the Department of Health of the state of Michigan all his life; his steadfast

service and his own achievements were recognized by the Michigan legislature by a special testimonial in 1931.

Shortly after the turn of the century he began the work for which he is best known, the study of trypanosomes and spirochetes. The investigations on spirochetes were published a little later than those on trypanosomes, but the studies were closely related, and for convenience the spirochetal studies will be considered first. So intense was Novy's devotion to this field, and so well known in the medical school were his studies that he acquired the nickname "Spi," and Spi Novy he remained to students and friends the rest of his life.

Among his first investigations of spirochetes were studies directed toward the etiological agents of relapsing fevers, of which the best known was the *Spirocheta obermeieri* described by Otto Obermeier about 1870. One natural habitat of the organism was the blood of the rat, and it was customary to maintain strains of the spirochetes in the laboratory by successive transfers to rats; attempts at artificial cultivation in the laboratory had consistently failed. Novy and his associate, R. E. Knapp, succeeded in cultivating the rat spirochetes in blood-filled collodion sacs in the rat peritoneal cavity and thus broke the long stalemate in cultivation methods. Their investigations, supplementing those of others, made it clear that several different strains of spirochetes were concerned in the relapsing fevers of different geographic regions. The strain with which Novy and Knapp did most of their work, which had been received from a colleague in New York, later came to be known as *Spirocheta novyi.*

The investigations furnished the basis for a controversy with the distinguished German protozoologist Fritz Schaudinn, the discoverer of the microbic cause of syphilis. Schaudinn believed in an interrelationship of spirochetes and trypanosomes, the former being considered a transitional stage in the life cycle. Novy's studies showed that they were independent forms of life, and Schaudinn admitted the fact in later years.

Opinions differ on what were Novy's most fruitful contributions to science. To many of his colleagues his work on trypanosomes has

had the most influence. His first object in the field was the development of methods for their artificial cultivation. In this, in association with Ward J. MacNeal, he was eminently successful. For their investigations they used strains of the common rat trypanosome, *T. lewisi* and the virulent organism *T. brucei,* the etiological agent of nagana, or the tsetse fly disease of South Africa. Novy and MacNeal devised a procedure for growing the trypanosomes in pure culture in the condensation water of slanted tubes of blood agar. This appears to have been the first cultivation of a pathogenic protozoon.

Their results aroused prompt interest and early confirmation from abroad. The distinguished Charles Nicolle, Director of the Pasteur Institute of Tunis, introduced a modification of their blood agar medium which became known as the "N:N:N medium" (after Novy, MacNeal, and Nicolle, on the mistaken assumption abroad that MacNeal's last name was Neal).

Characteristically Novy carried his investigations into the field of artificial stimulation of resistance to trypanosome infections. He and his associates found that they could build up some immunity. An important outgrowth of the studies was a deep interest in the problem of anaphylaxis. Novy and Paul H. de Kruif of the Department of Bacteriology, with others in the department, including two of Novy's sons, Robert L. Novy and Frank O. Novy, followed up certain observations made in the course of their efforts to immunize animals against the virulent trypanosomes of nagana (*T. brucei*) and surra (*T. evansi*). They noted an extraordinary drop in temperature and acute collapse in some of the inoculated animals, and chronic intoxication and ultimate fatality in others. It appeared that some specific poison was being introduced, or induced in formation, in the blood. The postulated poison, as far as could be deduced from the symptoms, apparently had something in common with the anaphylatoxin hypothecated by others as an explanation of the symptoms of anaphylaxis, which had been a puzzle ever since the phenomenon had been brought to the attention of the medical world by the French physiologist Charles Richet.

The speed of the acute reaction in the inoculated animals, and the minuteness of amount of trypanosomal poison capable of eliciting it, convinced Novy that the toxic substance was of extraordinary potency. The finding that it, or a toxic substance of similar potentiality, could be generated by mere contact of rat serum with the trypanosomal antigen, appeared to furnish a lead for determining its real nature. It was soon learned that incubation of the serum with other colloids, particularly comminuted agar, resulted in a similar development of toxicity. This increased the lines of attack but complicated the problem, since a characteristic feature of anaphylaxis is its high degree of specificity.

Chemical studies indicated that anaphylatoxin production was not the result of protein cleavage, but some reason was uncovered to indicate that changes of the fibrinogen of the blood were concerned. Additional studies, carried out by others of Novy's staff, indicated that the alkali reserve of the blood was not modified. No firm conclusions were reached, but studies by de Kruif and other associates linked the phenomenon of anaphylaxis with the globulin fraction of the serum and particularly the euglobulin. The essential nature of the potent substance remained undisclosed, however. In the meantime, investigators in many other laboratories were baffled in a similar way, and the general trend seemed to be to await a riper time for solution of the anaphylatoxin problem.

A later generation at the University of Michigan looked upon Novy's studies in microbic respiration as the climax of his work. These investigations, carried out in the mid 1920s when Novy was in his early sixties, formed another of the several well conceived and broadly executed programs conducted by Novy and other members of his staff. Novy's genius in devising and adapting apparatus was instrumental in the precision of attack on the problem. As in the case of the trypanosomes and anaphylatoxin, a lengthy series of publications resulted.

Certain of the pathogenic protozoa, including *Trypanosoma lewisi,* with which he had had signal success in the past, were among

the microorganisms used in the study. The best-known results, however, were those secured in association with Malcolm H. Soule, on the respiration of tubercle bacilli. Their studies gave a clear picture of all of the important features of gas exchange during the growth of tubercle bacilli, and indicated that the slow growth of these organisms in the body could be explained on the basis of respiration and multiplication under conditions of low oxygen tension. Today such studies are carried out with standardized equipment, such as the Warburg apparatus, with which minute amounts of oxygen and carbon dioxide can be measured, but no greater accuracy in uncovering the major aspects of growth is achieved than was attained by Novy and Soule with the more cumbersome but effective devices of Novy and his associates.

Novy's last scientific article, which appeared in 1953 when Novy was nearly ninety years of age, was one with a storybook background. More than forty years previously he had developed an interest in ultramicroscopic life and filterable agents of disease, i.e., the viruses which occupy the attention of a large proportion of all microbiologists today. In the course of his studies with other members of his department on trypanosomes, Novy had obtained evidence of a filterable agent accompanying the trypanosomes in rats' blood and responsible for an encephalitis that accompanied the trypanosomal manifestations of disease on inoculation of the blood in experimental animals. Much was learned of the nature of the agent, but all work had to be stopped when the stock material containing the virus was unaccountably lost. Fortunately the records of the experiments were meticulously kept. Thirty-five years later, during the cleaning of an old laboratory preparatory to a move, workers found a set of tubes of dried blood, which were promptly identified as the long missing virus culture. Appropriate tests showed that, in spite of long storage and desiccation, the original virus in the tubes, although attenuated, was still viable. The original notes were brought out and the significant data were published, Novy being as excited and eager as any one of the active staff. Students of Novy

(Walter J. Nungester and Harry E. Morton), casting up the total on known viruses, calculated that this virus was actually among the earliest discovered, a feat ensuring Novy a place among the pioneer virologists.

Novy's students and associates have left abundant testimony to his unique talents as investigator and teacher. His insistence on adequate control in research, and his industry and logic in teaching, earned for him a reputation as a strict disciplinarian. It is commonly accepted that Novy was the original model for the scientifically uncompromising Dr. Gottlieb in Sinclair Lewis' *Arrowsmith,* although Novy himself could not reconcile the picture of Dr. Gottlieb's guttural, broken English with his own facility of expression and polished style, of which he was not a little proud. But his role as a taskmaster was tempered. Novy's many students, who are carrying on with the precepts he taught, remember his humor when they recall his mannerisms and always note the generous interest behind his sharp comments. His biographer, Ruth Good, wrote that although he was a master of the barbed tongue his wit was on the kindly side and often used to lessen the pain of his caustic criticisms.

In the late years of his academic life, as with so many men who have proven their organizing ability by success in research, increasing administrative responsibilities were thrust upon him. His scientific investigations, of course, were correspondingly curtailed. From 1930 to 1933 he was intensively occupied with duties as chairman of the Executive Committee of the Medical School. In 1933 he was elected Dean of the school. It was a perfectly natural course for a teacher and investigator with his broad perspective in medical education. He had written much on the subject in its widest aspects, and had an intimate understanding of the necessities in keeping up with the progress of medical science. He continued as Dean, as well as head of the Department of Bacteriology, until he reached the age of retirement in 1935.

Many honors were conferred on Novy, some of which have already been noted in this memoir. He was elected to the National

Academy of Sciences in 1924 and to the American Philosophical Society in 1934. He was elected to the Association of American Physicians at the early date of 1900. He was Henry L. Russell Lecturer at the University of Michigan in 1927 and George M. Kober Lecturer at Georgetown University in 1931. His name was selected for enduring distinction in the Welch-Novy-Russell lectures of the Society of American Bacteriologists. He was gold medalist of the American Medical Association in 1930. In 1931 he received a citation from the Legislature of the State of Michigan for his long and tireless service to the state's Department of Health. Abroad he was made a Chevalier of the Legion d'Honneur and a member of the Order of the White Lion of Czecho-Slovakia, the native land of his parents.

He was a constituent member of numerous societies and, in the course of his professional life, president of many of them. Among his presidencies were those of the Society of American Bacteriologists (1904), the American Society for Experimental Pathology (1921), and the American Association of Immunologists (1924). He served as vice-president for the Section on Pathology and Bacteriology in the International Congress on Tuberculosis in Washington in 1908, and for the section on tropical medicine in the International Congress on Hygiene and Demography in Washington in 1912. He was a vice-president of the International Congress on Microbiology in London in 1936 and honorary president of this Congress in New York in 1939. He was a charter member of the American Academy of Tropical Medicine and its vice-president in 1936. He held a series of administrative offices in the scientific and medical societies of his own state of Michigan. His interest in medical student affairs led to a long and close association with the medical fraternity Nu Sigma Nu, of which he was honorary president in 1932 and secretary of the corporation for the long period 1897 to 1947. Many societies graced their own records by electing him an honorary member. He was a life member of the American Associa-

tion for the Advancement of Science and one of its vice-presidents in 1910.

A nonogenarian in 1954, and mentally alert if not physically active, Novy had many years to look back upon the science he had helped create. He considered himself an old-time bacteriologist and always listed himself as such. The fields of his greatest achievement were not strictly in bacteriology, however, but rather in the broader domain of microbiology. As we have seen, his work encompassed several of its recognized major branches: true bacteriology, protozoology, virology, and immunology. In his fifty years of intense professional activity he had seen remarkable developments in understanding in all of these fields. In the twenty-two years of retirement, he remained a recognized authority and wise counselor, whose advice and assistance were constantly in demand.

ACKNOWLEDGMENTS

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KEY TO ABBREVIATIONS

Amer. Chem. J.=American Chemical Journal
Amer. J. Med. Sci.=American Journal of the Medical Sciences
Amer. J. Roentg. Rad. Therap.=American Journal of Roentgenology and Radium Therapy
Amer. Med.=American Medicine
Ann. Int. Med.=Annals of Internal Medicine
Ann. Rep. Surg. Gen. U.S.M.H.S.=Annual Report of the Surgeon General of the United States Marine Hospital Service
Bol. Asoc. Med. Puerto Rico=Boletin de la Asociacion Médica de Puerto Rico
Centralbl. Bakt.=Centralblatt für Bakteriologie und Parasitenkunde
J.A.M.A.=Journal of the American Medical Association
J. Anal. Chem.=Journal of Analytical Chemistry
J. Appl. Micros.=Journal of Applied Microscopy
J. Exper. Med.=Journal of Experimental Medicine
J. Hyg.=Journal of Hygiene
J. Infect. Dis.=Journal of Infectious Diseases
J. Lab. Clin. Med.=Journal of Laboratory and Clinical Medicine
J. Mich. State Med. Soc.=Journal of the Michigan State Medical Society
Med. News=Medical News
Med. Surg. Reporter=Medical and Surgical Reporter
Mich. Alumnus=Michigan Alumnus
Pharm. Era=Pharmaceutical Era
Pharm. Rundsch.=Pharmaceutische Rundschau
Proc. Amer. Assn. Adv. Sci.=Proceedings of the American Association for the Advancement of Science
Proc. Ann. Conf. Health Officers=Proceedings of Annual Conference of Health Officers in Michigan
Proc. Soc. Exper. Biol. Med.=Proceedings of the Society for Experimental Biology and Medicine
Rep. Counc. Pharm. Chem.=Reports of the Council on Pharmacy and Chemistry of the American Medical Association
Rep. Mich. Acad. Sci.=Report of the Michigan Academy of Science
Rep. State Board Health=Report, Secretary of the State Board of Health, Michigan
Trans. Assn. Amer. Physicians=Transactions of the Association of American Physicians
Trans. Clin. Soc. Univ. Mich.=Transactions of the Clinical Society of the University of Michigan
Trans. Internat. Congr. Hyg. Demog.=Transactions of the International Congress on Hygiene and Demography

Trans. Mich. State Med. Soc. = Transactions of the Michigan State Medical Society
Trans. Pan-Amer. Med. Congr. = Transactions of the Pan-American Medical Congress
Ztschr. Hyg. = Zeitschrift für Hygiene und Infektionskrankheiten

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