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JOHN RODMAN PAUL

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A Biographical Memoir by
DOROTHY M. HORSTMANN AND PAUL B. BEESON

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JOHN PAUL was born in Philadelphia, Pennsylvania, the third child in a family of eight. His father was Henry Neill Paul, and his mother had been Margaret Crosby Butler of Yonkers, New York. The Pauls trace their ancestry to Joseph Paull of Illminster, England, who emigrated to this country in 1685, settling with William Penn's Quakers in Philadelphia. On his mother's side, John was a descendant of Theophilus Eaton, the first governor of Connecticut, and of Benjamin F. Butler, Andrew Jackson's attorney general. His maternal grandfather was William Allen Butler, an eminent lawyer and poet.

John's father was also a lawyer and a man of broad scholarly interests. He loved Shakespeare and Elizabethan drama, was Dean of the Philadelphia Shakespeare Society for many years, and published a number of Shakespeare commentaries as well as *The Royal Play of Macbeth,* a scholarly analysis of the origins of the play. His interests were also in natural history. In the 1880s, while at Princeton, he had taken part in expeditions to Montana for geological and paleontological explorations. His accounts of these trips fascinated John, who later counted them as a major factor in awakening his interest in science at a very early age.

This interest was further encouraged when the Paul family settled in Chestnut Hill, then an open suburb of Philadelphia,

with woods, streams, and fields where the Paul children could roam and bring home to their family museum minerals, butterflies, birds eggs, and even Indian arrowheads. Summers were spent at Beach Haven on the New Jersey shore, and shells and sea specimens were also added to their collections. A love of the out-of-doors was a deep and sustaining influence throughout John Paul's life, as well as the source of many of his hobbies—bird watching, archeology, wood carving, building stone walls, watercoloring, and photography, etc. It was also responsible for his being an active and articulate conservationist as early as the 1930s, long before the need for preservation of the environment became a popular cause.

As a child, John is said to have been reserved, rather shy, but with a strong humorous streak. He had stamina and energy but was not robust, so to improve his health he was sent to New Hampshire at age eleven, where he was tutored and spent much time out-of-doors during the winter before entering St. George's School, in Newport, Rhode Island. The six years at St. George's were important and happy ones: he was an outstanding student and won many scholastic prizes in Latin, Greek, and history. He became editor of the school magazine, manager of the football team, and coxswain of the school crew.

In 1911 John entered Princeton. At first he led a relaxed and carefree life there without any particular scholarly focus—until he came under the influence of Edwin Grant Conklin, professor of biology. Conklin was the kind of professor who lit fires under his students; from then on John took off scientifically and spent as much time as possible in the laboratory. Still he lived a full life at Princeton: he was very popular in his class, was an editor of the Princeton *Tiger,* a member of the Ivy Club, and manager of the crew and sometimes its coxswain.

The decision to study medicine came about through association with Cecil Drinker, one of John's heroes at the time and subsequently Dean of the Harvard School of Public Health.

The Paul and Drinker families had been neighbors and close friends during summers at Beach Haven, where Cecil had taught John to sail the Drinker's yawl. Cecil's younger brother, Philip, and John were the same age and became fast friends. Later they roomed together all through St. George's School and Princeton. During the Princeton years, Cecil, Philip, and John sailed together in the summers and it was on these pleasant cruises that Cecil persuaded John that he should go to medical school. The advice was accepted, and after graduation from Princeton in 1915, he enrolled at the Johns Hopkins University School of Medicine. His goal, he said in later years, was "to be a medical scientist just like Cecil," rather than a practicing physician, the role his family had in mind for him. He never swerved from his commitment to a career as an investigator.

In 1917, when he was in his second year of medical school, the United States entered World War I. In June, along with thirty-one other medical students, Paul joined the Hopkins unit as an enlisted man and sailed from New York in the first U.S. convoy of World War I to head directly for France, carrying combat and other troops—the vanguard of Pershing's army. The major part of the army transport on which he found himself was occupied by seasoned soldiers, and (as he wrote later) the medical contingent "consisting of the Johns Hopkins Hospital Unit, a hastily assembled and motley group of raw recruits, occupied a place befitting their military experience—far astern and deep in the bowels of the ship." After eighteen long days at sea, often in submarine-infested waters, the overcrowded ships finally reached St. Nazaire, where the men received a warm welcome from the French. The Hopkins unit went on by train to Bazoille sur Meuse, where Base Hospital #18 was set up, well back of the front line. John's assignments were as bacteriological technician and substitute ambulance driver. The bacteriology laboratory was a valuable experience that apparently

had considerable influence in shaping his subsequent career. His first duty was to determine the effectiveness of a new method of treating wound infections by continuous irrigation with a sodium hypochlorite solution devised by Dakin, an English chemist. The mountainous task of doing daily smears and bacterial counts on swabs from the wounds of the many patients who had infections with gas-forming bacilli eventually proved dull work; and since the results did not prove to be helpful as indicators of the course of infection, the study was finally abandoned. Driving an ambulance turned out to have greater rewards, which involved a month at St. Nazaire assembling Ford ambulances (they arrived two in a box) and proudly driving the finished products back to Bazoille.

After a year in France, Paul, his great friend John M. T. Finney, Jr., and others of the students at Base Hospital #18 were persuaded that they should return to Hopkins to complete their medical education. By a fortunate stroke of fate, Paul missed the ship on which he was scheduled to return—one that was torpedoed and lost—and came through on another, which sailed successfully from Brest to New York. Shortly after his arrival in Baltimore, the 1918 influenza epidemic erupted and the wards of the Johns Hopkins Hospital were filled with desperately ill patients, many of them professors and staff members. Apparently the wave of relatively mild respiratory illness that had swept France in 1917 was the forerunner of the more severe 1918 epidemic, and infection with the agent in France conferred immunity on those who had had experience with it, including John Paul. At that time he had had no clinical training but in the desperate situation was put to work on the wards as a substitute intern, to care for the patients as best he could. It was a harrowing ordeal, since the mortality rate was extremely high. The helplessness of the physicians made a deep impression on the young Paul. As he wrote years later:

"Many were the nights I passed, making do with a few hours

of uneasy sleep grabbed as best I could from a 20-hour day, tossing and twisting and deciding that it would have been better if the influenza patients had never come to the hospital. The lessons we learned in those days were not how to treat patients who had postinfluenza pneumonia with drugs, but rather how to save their lives by preventing exposure on the isolation wards by mixing them up with cases of tonsillitis and scarlet fever. If the patients with influenza were kept by themselves they had a far better chance of avoiding cross-infection with pathogenic bacteria, especially the hemolytic streptococcus. This was an *epidemiological* principle reminiscent of the days of Semmelweis and puerperal fever." *

Although his military experience caused him to miss his third year of medical school, Paul graduated with the class of 1919. He immediately joined W. G. McCallum, professor of pathology at Hopkins on a trip to Lima, Peru, where the summer was spent working on bartonellosis. The routine consisted of doing autopsies at the hospital in the mornings and exploring the city and its archeologic treasures in the afternoons.

On his return to Baltimore, John joined McCallum at Hopkins as an assistant in pathology. Two of his classmates, Arnold Rich and Leslie Webster, did the same, and the three had a lively and productive year in the laboratory. Paul's first contribution to medicine was made during that year—a paper on the histopathology of measles conjunctivitis. Thus his first work dealt with a virus infection—a prophetic note since he devoted most of the rest of his professional life to investigations in that field.

The next two years were spent as an intern at the Pennsylvania Hospital in Philadelphia. In 1922 he was appointed Director of the Ayer Clinical Laboratory of the Pennsylvania

* J. R. Paul, "A Clinician's Place in Academic Preventive Medicine: My Favorite Hobby," *Bulletin of the New York Academy of Medicine* 47(1971): 1264 (hereafter cited as "Clinician's Place").

Hospital, a post that had previously been held by Dr. Warfield T. Longcope. Activities during the six-year period at the Ayer Laboratory resulted in papers on a variety of subjects dealing with bacteriology and pathology, including the first ones on rheumatic fever, a disease that was to engage much of his attention in the ensuing years. In fact, it was when he presented a paper on the pleural and pulmonary lesions in rheumatic fever at the clinical meetings in Atlantic City in the spring of 1928 that he was invited by Francis Blake, professor of medicine at Yale, to join his department as an assistant professor. Thus began Paul's long association with Yale—one that continued until his death forty-three years later.

In the 1920s, the Yale Medical School was in the midst of a renaissance under the dynamic leadership of Dean Milton C. Winternitz. Winternitz had gathered together for the recently created full-time faculty a stellar group of young clinician–scientists, including among others Francis Blake, John P. Peters, Grover Powers, and James Trask. According to Dr. Paul, they were all "young, eager, and well trained men, imbued with the idea of making the fulltime system work." He himself fitted into this setting perfectly and within several years of his arrival in New Haven had launched into several major pieces of work that proved to be important landmarks in clinical investigation. Among these were the studies of rheumatic families, the discovery of the heterophile antibody (Paul–Bunnell) test for infectious mononucleosis, and the demonstration that the commonest clinical expression of infection with polioviruses is not paralysis, but the "minor illness" or "abortive" form of the disease that is often so mild as to go unrecognized.

The seeds of the scientific philosophy that characterized his later work at Yale, and in fact ran throughout his entire professional life, were planted early in John Paul's mind—when he was a second-year medical student. At that time he attended a meeting of the Federation of Biological Sciences in New York

City at which there was a lively discussion of the disastrous epidemic of poliomyelitis that had raged in New York and New England during the summer of 1916. In looking back on that occasion, he wrote:

"I must have been a singularly impressionable young man at the time, and I was certainly engrossed in watching and hearing the words of these great men, who were engaged in recounting their efforts to attempt to solve the problem of epidemic poliomyelitis, applying the very weapons which we had been taught to use in our first years at medical school. Dr. Simon Flexner was in the chair; Dr. Peyton Rous was at his side as secretary; and Hideyo Noguchi, who was there as a speaker, was introduced as a man of mystery, one who could almost turn lead into pure gold, or at least turn the virus of poliomyelitis into 'globoid bodies.'

"As a rapt listener, the idea first dawned on me that the religion of the true physician was incomplete without having the concepts of prevention thoroughly ingrained in him. This was particularly true when it came to the prevention of such a colossal tragedy as the 1916 epidemic. My immature reasoning, which I never lost, was that, together with attempts to cure this pestilence, there should be attempts to control it, and this should be done by clinicians who knew the disease best. In other words, this concept should radiate from the top physicians and pediatricians." *

Once these ideas had taken root, they were nourished by Paul's experience during the 1918 influenza epidemic and gradually flowered in the 1920s and 1930s as his concept of "Clinical Epidemiology" developed and took form. In his presidential address to the American Society for Clinical Investigation in 1938, he said:

"The term, Clinical Investigation in Preventive Medicine,

* Paul, "Clinician's Place," p. 1263.

is cumbersome and so I will not use it. . . . It presupposes the existence of a so-called sister science, Curative Medicine. . . . Clinical Investigation in Epidemiology is better for the purposes at hand; Clinical Epidemiology is best, and really what I mean. . . . It is a science concerned with circumstances, whether they are 'functional' or 'organic' under which human disease is prone to develop. It is a science concerned with the ecology of human disease. It must face the question of 'why' as well as 'how'. Clinical Epidemiology differs, therefore, from the orthodox science of Epidemiology, both in its aim, and its locale, as it were. The orthodox epidemiologist must of necessity deal dispassionately with large groups of people. It is the multiplication of observations which give him his results. The clinical epidemiologist, on the other hand, must of necessity deal with small groups of people; people whom he knows well and groups no larger than a family, or small community. The restriction of the size of the group rests on the fact that clinical judgment cannot be applied wholesale, without the risk of its being spread too thinly to be effective. . . . The clinical epidemiologist, . . . starts with a sick individual and cautiously branches out into the setting where that individual became sick, the home, the family, and the workshop. He is anxious to analyze the intimate details under which his patient became ill. He is also anxious to search for other members of the patient's family, or community group who are actually, or potentially, ill. It is his aim to thus place his patients in the pattern in which he belongs, rather than to regard him as a lone sick man who was suddenly popped out of a health setting; and it is also his aim to bring his judgment to bear upon the *situation,* as well as on the patient.

"Obviously there is nothing new to the family doctor about this concept of Medicine. It is the heart and soul of family practice and probably has been as long as family practice has existed. But now that the emphasis has shifted away from the

home and into the Hospital or Dispensary, clinical epidemiology will be practiced only if we take thought about it." *

Dr. Paul never cared for the term "Preventive Medicine," although eventually his professorship and his section at Yale used this terminology. He regarded it as "too boastful, too suggestive that great things might be just around the corner." † His belief was that the focus should be on the teaching of the underlying principles of prevention, i.e., epidemiology. In championing these concepts he was perhaps ahead of his time, but in the past decade his pioneering efforts have begun to bear fruit. The best possible support is provided by his own achievements in which he combined so successfully the study of certain diseases: at the bedside, in the laboratory, and in the natural setting in which they developed.

In the New Haven Hospital in 1928 rheumatic fever was a common disease. Paul took advantage of the opportunities this situation provided and turned his attention to unraveling the epidemiology of the disease. His focus was on rheumatic fever in families and the factors involved in its spread. Many of the social and environmental aspects were explored through intimate, long-term studies over an eight-year period of all members of 122 rheumatic families and suitable control families. When he began his studies, the role of the hemolytic streptococcus was not yet appreciated, but based on his observations Paul concluded that respiratory infection of some kind precipitated the acute attack. While not the first to suggest a relationship between the hemolytic streptococcus and rheumatic fever, it is fair to say that the book he published in 1930, *The Epidemiology of Rheumatic Fever,* and particularly the second edition in 1943, set forth the evidence for a causal relationship in such a way that there was never any further question about it.

* J. R. Paul, "Clinical Epidemiology," *Journal of Clinical Investigation* 17(1938):539–41.

† Paul, "Clinician's Place," p. 1267.

It was in the course of serologic investigations of patients with rheumatic fever that the heterophile antibody test for infectious mononucleosis was discovered. This came about when, having confirmed the observation made by Davidson in 1929 that agglutinins to sheep cells are present in the sera of patients with serum sickness, Paul raised the question whether such heterophile antibodies might not also be present in rheumatic fever since there were similarities between the symptoms of the two diseases. The results with sera of rheumatic patients were negative, but quite by accident, among the control specimens from patients with serum sickness and various other acute illnesses, there was one with an extraordinarily high titer—higher than had ever been described in serum sickness or any other clinical condition. The patient from whom the specimen came was a medical student with infectious mononucleosis. Gradually over the ensuing months several other patients with this disease were also found to have high heterophile antibody titers, while tests on some 275 controls gave consistently negative results. In 1932 Paul and Bunnell, a medical resident who collaborated on the project, published their findings. The test, which is still sometimes referred to as the Paul–Bunnell test, remains today as the chief laboratory method in the diagnosis of infectious mononucleosis.

The first investigations of poliomyelitis, the disease on which Paul's main work was subsequently concentrated, also began early in the 1930s. In Middletown, Connecticut, twenty-six miles from New Haven, a small epidemic occurred in 1930. Paul and his colleague James Trask were struck by the wide range in severity of the disease. Some suspected cases not only did not have paralysis, but had little or no neck stiffness. Were these also infections with the virus of poliomyelitis? The following year, New Haven experienced a sharp epidemic and the opportunity to answer this question by attempting to isolate the virus presented itself. Characteristically, Paul and Trask

went into the homes of patients hospitalized with paralysis and visited others in the neighborhoods where the cases were coming from. They took histories, did physical examinations, and collected throat washings from siblings and contacts who had minor illnesses—brief episodes of headache, vomiting, and sore throat, commonly labelled "summer grippe." Family after family, through which waves of such illnesses passed, were studied. The throat washings were duly tested by intracerebral inoculation of monkeys, and from two children, polioviruses were recovered. These were the first isolations of the virus from living patients in over thirteen years, and they added significantly to the handful of such successful isolations reported in the world literature up to that time. In describing these important results, Dr. Paul later pointed out that the work had been undertaken against the advice of several well-known senior investigators in the field who considered the approach "one which was expensive and would not yield valuable results. . . . Monkeys cost from 6 to 8 dollars each. This was regarded as an expensive laboratory animal, and it was deemed unwise for amateurs to spend so much money on this type of research, particularly when it was their initial piece of work in this field and there were many more orthodox things to be done." * The successful outcome in the face of such discouraging pronouncements bolstered the confidence of the two young investigators, and Paul and Trask continued their "unorthodox" studies. Using recently isolated human strains of the virus, they soon made another major contribution by demonstrating that polioviruses exist in at least two and possibly three serologic types. A preliminary report of similar findings by Burnet and McNamara in Australia had appeared in 1931, but it had been greeted with incredulity by most U.S. workers.

* J. R. Paul, "From the Notebook of John Rodman Paul," *Yale Journal of Biology and Medicine* 34(1961–62):164.

These early and highly productive investigations by the Yale Poliomyelitis Study Unit, founded in 1931 and led for many years by Paul and Trask, were supported by small grants of several thousand dollars from various sources; but in 1936, the unit received the first research grant ever given by the President's Birthday Ball Commission, which eventually became the National Foundation for Infantile Paralysis and finally the National Foundation. The Foundation continued its support of the unit through Grant #1 until 1968.

In the mid-1930s, Paul's work was interrupted by illness. He developed severe pulmonary tuberculosis, and after a brief hospitalization in New Haven went to The Desert Sanitorium in Tucson, Arizona, where he remained for two years. The time spent there, far from being a fallow period, was full of activity of quite a different sort. Leita Paul accompanied her husband and took advantage of the opportunity to study the archeology of the Indians of the Southwest at the University of Arizona. She reported to John on lectures and seminars, and he took an equal interest in the subject. The experience was a source of lasting fascination with Indian culture for the Pauls. As he improved, John joined Leita in digging expeditions that yielded many fine pieces of pottery. During the summers—when Tucson was unbearably hot—they stayed in Tyrone, New Mexico. There they became particularly interested in the Mimbreño tribe, whose pottery designs were unusual in that they were zoomorphic. Paul collected and photographed many rare specimens; his interest culminated in a fine exhibition of Mimbreño pottery, which he displayed in 1956 at the Yale Art Gallery, working with art students in gathering materials and preparing and illustrating the catalogue with his own drawings.

Several other major hobbies also flourished in Arizona: photography, ornithology, and painting. During the first year, largely spent in bed on an open-air porch, a camera rigged to the foot of the bed allowed photography of western birds—a

whole world of new species to learn about. Later, many of these were portrayed in delicate watercolors of great precision and charm.

Throughout the Arizona period there was regular communication with the laboratory in New Haven. In fact, a letter went out to Dr. Paul from Dr. Trask every single day during the two years. Plans for experiments were discussed, results were reported and analyzed, and at one point Dr. Trask came out for a visit. As convalescence progressed, Paul was able to undertake some work in the laboratory at The Desert Sanitorium and also to serve as a consultant on rheumatic fever cases. His interest in this disease was as lively as ever, so he decided to take advantage of his situation by investigating the effects of climate on its occurrence by determining the prevalence of rheumatic heart disease among Indian children living in reservations from the edge of Mexico to the Canadian border. Since the social and environmental aspects of life on the various reservations were similar, any differences in rates might be attributed to climate. With Dr. George Dixon, Dr. Paul started off in the family Ford and systematically examined approximately 1000 Indian school children in Montana, Wyoming, New Mexico, and Arizona, representing latitudes of 45°, 43°, 37°, and 33°. The results indicated that rheumatic heart disease was ten times more prevalent in those living close to Canada than in children living on the Mexican border.

Back in New Haven in 1937, work on poliomyelitis went forward rapidly. The thrust was still toward exploring the clinical epidemiology of the infection as a clue to how the virus was spread and how the disease might be prevented. Having previously demonstrated the presence of the agent in the throats of individuals with the minor illness, or the "abortive" form of poliomyelitis, Paul and Trask again went into the homes, this time to collect fecal material from siblings of paralytic cases. Previous tests of such specimens had been unsuccessful, largely

because of the problem of bacterial contamination and resulting brain abscesses in intracerebrally inoculated animals. From a fecal specimen collected in 1937, however, poliovirus was isolated, by switching to intraperitoneal inoculation of the monkeys. The recovery of virus from feces had actually been reported some twenty years earlier by Swedish workers, but their results had been challenged by Dr. Flexner of the Rockefeller Institute and that was enough to cause the subject to be dropped.

Paul and Trask's confirmation of the presence of virus in the intestinal tract opened a whole new era in research on poliomyelitis: it turned investigators away from the unfruitful experiments with laboratory-adapted strains that had led to false conclusions and an incorrect characterization of poliovirus as a strictly neurotropic agent. The swing of the pendulum back to clinical investigation and field epidemiology led rapidly to the demonstration by the Yale group that during epidemics the virus is shed not only from the throat and intestinal tract, but is also present in sewage and in flies that feed on feces.

During the 1930s, every summer brought large epidemics of poliomyelitis somewhere in the United States, and Paul and Trask were called upon as consultants to aid the harassed and frustrated health officers who were helpless in the face of mounting numbers of cases. At least the presence of "experts" gave the appearance that *something* was being done. Thus opportunities were provided to engage in a series of clinical epidemiological studies. Investigations were carried out in Philadelphia; Los Angeles; Charleston, South Carolina; Detroit; Buffalo, New York; Florida; Toronto, Ontario; and Winnipeg, Manitoba; to name but a few.

In the early 1940s, with the outbreak of World War II, new problems and new responsibilities arose. Dr. Paul was appointed Director of the Commission on Neurotropic Virus Diseases of the Army Epidemiological Board. The Commission

was set up to study arthropod-borne virus diseases and poliomyelitis in members of the U.S. Armed Forces. In 1943, Dr. Paul headed a small group known as the Virus Commission, which included besides himself, Maj. Albert Sabin and Lt. Col. Cornelius Philip. The team was dispatched to North Africa to study hepatitis, sandfly fever, and poliomyelitis. Dr. Paul's diaries vividly describe Cairo at the time as unbelievably crowded, teeming with British and American military personnel and allied and axis civilians. The laboratory was finally set up outside the city in the desert, close to the 38th General Hospital, which was staffed by the Jefferson Medical College Unit. One of the first problems to be dealt with was the occurrence of increasing numbers of cases of suspected poliomyelitis among U.S. troops. The British army had reported cases of myelitis and encephalitis some months earlier, and a strain of poliovirus had been recovered at the Rockefeller Institute in New York from nervous tissue of a fatal case. But the U.S. medical officers, particularly the neurologists, were very skeptical about the diagnosis of poliomyelitis in U.S. troops in Egypt and accepted it only after the virus was repeatedly isolated from various patients. Obtaining monkeys to carry out the tests was a problem, and Paul had to visit Ethiopia to trap his own animals and bring them back to Cairo.

These results confirming the occurrence of poliomyelitis among adult "immigrants" to the area were of particular importance to Paul because of their implications concerning the epidemiology of the infection. Paralytic poliomyelitis was considered a rare disease in Egypt—not more than five or six cases were reported yearly in a population of 16 million, and all were in young children, none in adults. Paul concluded that the paucity of cases among the local inhabitants did not denote absence of the virus, but quite the opposite. The presence of *infantile* paralysis denoted probable wide dissemination of the agent in a population living in a poor sanitary environment:

circulation of the virus was confined to susceptible young children who acquired their infections in the first few years of life and subsequently remained immune for the rest of their lives. However, when susceptible adults, such as soldiers from England and the United States who had never met the virus before, were introduced into such an area of high endemicity, they were exposed, infected, and contracted paralytic poliomyelitis at a surprising rate. Several years later Paul provided further confirmation of this hypothesis in studies that he conducted among U.S. troops in other parts of the world, including the Pacific and the Far East. Shortly after the war he obtained the final proof in the course of serologic investigations conducted in Egypt. By means of these he showed that a high percent of children in the area had experienced poliovirus infections and had acquired specific antibodies by two years of age, and by four virtually all were immune. It was in connection with these efforts that he coined the term "serological epidemiology" to describe an approach that in his hands had yielded discoveries of fundamental importance.

The other two diseases that the Virus Commission was assigned to investigate, hepatitis and sandfly fever, were both continuous sources of enormous morbidity in the U.S. Army, seriously interfering with the conduct of military operations. An amicable arrangement was worked out in which Sabin and Philip took on sandfly fever, and Paul chose to study hepatitis. In these studies he was joined by Maj. W. P. Havens of the 38th General (Jefferson) Hospital Unit. Epidemiologic features of cases in British and American troops in North Africa and in Sicily during the epidemic of 1943 were investigated, and sera and stool specimens were obtained from patients in the acute phase of the infection. These materials were kept frozen until some months later, when, having recovered from a severe bout of hepatitis, Paul returned to New Haven, where he was joined by Major Havens. Together they set about testing the speci-

mens collected in Egypt in volunteers in order to identify virus positive pools that might be used in attempts to transmit the infection to some experimental animal. These studies in volunteers constituted the first demonstration in the United States of the enteric–oral transmission of infectious hepatitis; similar results were obtained simultaneously in England by MacCallum and Bradley. Paul and Havens later went on to define the times at which hepatitis virus was present in blood and feces both before and after the appearance of jaundice. They also conducted cross-protection studies in volunteers and showed a lack of cross immunity between serum and infectious hepatitis. This work, along with studies by others, formed the basis of the differentiation of the two hepatitis viruses and the diseases they cause, a classification that still holds today.

After World War II, with the return to peacetime activities, Paul turned his attention to building the Section of Preventive Medicine into an active teaching, training, and research unit. The Section had been established in the Department of Internal Medicine at Yale in 1941, with Dr. Paul as professor and chairman. He preferred this arrangement to having a separate department because he viewed his territory as an integral part of medicine and pediatrics rather than a separate discipline allied to public health. The focus was to be on "the epidemiology of disease in families, in the local community, . . . clinical and environmental virology, including the role of insects and animals as vectors of human disease, etc." *

Paul struggled in the not too favorable climate of the 1940s and 1950s to bring his concepts of clinical epidemiology to medical students, house staff, fellows, and faculty. He championed the home visit as a teaching exercise in which a student, accompanied by a faculty member, could gain some idea of the role played by family and environmental and social deter-

* Paul, "Clinician's Place," p. 1268.

minants in influencing the patient's disease, whether it was an acute infection or a chronic or recurrent malady. He strongly supported J. N. Morris's contention that "epidemiology . . . helps to complete the clinical picture and to clarify the natural history of disease." * His efforts to bring his philosophy to students and colleagues also took form in his book, *Clinical Epidemiology,* published in 1958 "to introduce this subject to doctors or students of medicine, biology, or sociology in nontechnical language and with examples they might use." † The book went through several editions and has been the text for students in courses given in many departments of preventive medicine in the United States.

To the Section of Preventive Medicine—later Epidemiology and Preventive Medicine—over the years came a stream of postdoctoral fellows from the United States and other parts of the world. Many of them subsequently went on to distinguish careers in virology and epidemiology in Europe, South America, and the United States. At Yale they absorbed the philosophy of clinical epidemiology that permeated Paul's laboratory, while participating in ongoing studies on rheumatic fever, arthritis, streptococcal infections, measles, infectious mononucleosis, hepatitis, and particularly poliomyelitis.

Work on poliomyelitis was in full swing in the Yale laboratory in the 1940s and 1950s, and some of Dr. Paul's most telling contributions were made during this period. One came about in the course of a serological survey of poliovirus antibodies among north Alaskan Eskimos that he conducted in 1949. There was no evidence that poliomyelitis had occurred in the Point Barrow area since 1930, when illnesses suggestive of the paralytic form of the disease had been recorded. In those

* J. N. Morris, *Uses of Epidemiology,* 2d ed. (Baltimore: Williams & Wilkins, 1964), p. 277.

† J. R. Paul, *Clinical Epidemiology* (Chicago: Univ. of Chicago Press, 1958; rev. ed., 1966), p. xiii.

pre-tissue-culture days the only feasible technique for large-scale serum surveys was the mouse neutralization test, which could be used to detect only Type II poliovirus antibodies. Remarkably, Paul and his colleagues found that virtually none of the Eskimos under the age of twenty years had Type II antibodies, whereas these were almost universally present in persons over that age, i.e., those who had been alive in 1930 when poliomyelitis was known to have visited the area. Clearly the 1930 epidemic had been due to Type II—an extraordinary piece of luck for the investigators. Some of the Eskimo sera were also tested for antibodies to Types I and III polioviruses by the more cumbersome and restricted technique of neutralization tests in monkeys. The results were unexpected and extremely provocative: antibodies to these two types were present only in persons over thirty-five and forty-five years, respectively, indicating that Types I and III had been absent for very long periods. The import of these findings, the "moment of truth" as Paul put it, was that a single exposure to a poliovirus type could convey lifelong immunity. From that time on, he held the belief that the way to provide permanent immunity against poliomyelitis was to induce inapparent infection with attenuated virus strains. He therefore aligned himself early with the approach championed by Sabin, and by Koprowski, which eventually led to the development of the currently used oral poliovirus vaccines.

In the 1950s Paul and his colleagues conducted small and large field trials of the Sabin strains in the United States and in Central America, with special emphasis on the unique opportunity that the live virus vaccine afforded to do experimental epidemiology in humans. These studies contributed not only to establishing the safety and effectiveness of the vaccines, but they also provided precise information about the incubation period of the infection, the capacity of polioviruses to spread among susceptible contacts, the prevalence and interfering ef-

fect of infection with other enteroviruses on oral vaccine "takes," and the dissemination of vaccine strains in the environment—in flies and in sewage.

By the 1950s, Paul had become a recognized international figure in virology and epidemiology. Inevitably, with his great knowledge and almost unique perspective, he was constantly being asked to serve on committees for the United States Armed Forces, the National Institutes of Health, the World Health Organization (WHO), and others. For fifteen years he was Director of the Commission on Viral and Rickettsial Infections of the Armed Forces Epidemiologic Board, and for twenty years, a member of several of the WHO Expert Committees on Viral Diseases. In 1956 he also served as the leader of the first medical mission under governmental auspices to visit the Soviet Union. As a member of numerous U.S. Public Health Service Committees during the years 1955–1962, he was in the thick of controversies over the licensing of the Salk and Sabin-type poliovirus vaccines and the subsequent problems associated with them. In this period he served as a senior statesman, helping to guide a national policy.

Many honors came to Paul over the years. Among these were the Medal of Freedom of the U.S. Government (1946), the Howard T. Ricketts Award of the University of Chicago (1954), and an Honorary D.Sc. from the same university (1956). He was elected to the National Academy of Sciences in 1945. In 1950 he was elected an honorary member of the Royal Society of Medicine, London, and was also a Fellow of the Royal College of Physicians and of the Royal Society of Health of Great Britain. The list of professional societies in which he was active is a long one, and he served as president of several: the American Society for Clinical Investigation (1938), the American Epidemiological Society (1950), and the Association of American Physicians (1956). In 1963 he was awarded the Kober Medal of the latter—an honor that he particularly cherished.

He was also a member of the Society of American Archeologists, the American Geographical Society, the American Academy of Arts and Sciences, and the Century Association of New York.

Dr. Paul retired from the chair of Epidemiology and Preventive Medicine in 1961. His research activities continued undiminished, however, for he immediately became the first Director of the World Health Organization Reference Serum Bank at Yale, one of three established by WHO in different countries. He led this laboratory through its early development and undertook among other projects a nationwide serologic survey of U.S. military recruits, measuring their immune status with respect to a variety of viral and bacterial diseases.

Infectious mononucleosis had been one of Paul's continuing interests since the chance discovery of the heterophile antibody test in 1931. Over the years unsuccessful attempts were made in his laboratory to isolate the etiologic agent, using materials collected from students at Yale, Smith, and the University of Connecticut. While the search was a frustrating one, the prospective serological study of the disease at Yale, which was undertaken by Niederman and Paul beginning in the late 1950s, eventually paid off handsomely. Thus when a technician in the laboratories of Werner and Gertrude Henle in Philadelphia developed infectious mononucleosis and was found to have acquired antibodies to the recently discovered Epstein–Barr virus (EBV) in the course of her illness, the Henles and their colleagues were quick to explore a possible etiologic role for EBV in infectious mononucleosis. They turned to the Yale Laboratory, and serologic tests on the collection of sera obtained from Yale students on entry to college, together with serial specimens from those who developed the disease during the ensuing four years, provided strong confirmatory evidence of the role of EBV in infectious mononucleosis. Although at this time he was not immediately involved in the work, Dr. Paul took great satisfaction in seeing his foresight rewarded and the potential of sero-

logical epidemiology as a research tool so productively exploited by his younger colleagues.

An episode in connection with the first publication of serological studies on the Yale students, which represented a collaboration between Niederman and McCollum at Yale and the Henles at the University of Pennsylvania, illustrates one strong aspect of John Paul's character—his uncompromising honesty. A reporter for the *New York Times* had published an article in the Sunday science section hailing the Yale authors and the Henles for the remarkable discovery that EBV is probably the etiologic agent of infectious mononucleosis. Dr. Paul was aghast at this misstatement and immediately sent a letter to the editor (published the following Sunday) pointing out that it was the Henles and their colleague Diehl who were responsible for the discovery, not the Yale group, whose contribution was merely confirmatory. The editor was so astonished that he telephoned Dr. Paul to tell him that never before in his long experience had he received such a letter denying credit for an accomplishment.

Chronic heart disease imposed the necessity for less and less physical activity, and in 1966 Dr. Paul retired from the directorship of the WHO Serum Bank. The increasing discomfort and restrictions due to his cardiac problems never elicited a complaint from him, however. He suffered no decline in intellectual vigor, and with typical determination and fortitude he spent the last five years of his life in a concentrated period of writing. He accepted an appointment of the Department of History of Science and Medicine and set about preparing three books and a number of papers on historical subjects. His most important contribution during this period was his magnificent book, *A History of Poliomyelitis,* published by the Yale University Press in 1971—a few months before his death. This has been widely acclaimed as a classic in medical history: it not only tells the story of a dramatic disease, but also reveals the way

scientific discoveries are actually made—how backward steps as well as forward ones are part of the slow process and how the personalities and foibles of scientists inevitably affect the course of events.

Published after his death was "An Account of The American Epidemiological Society" and *Serological Epidemiology,* which he edited with Dr. Colin White. He also wrote histories of several Commissions for the Archives of the Armed Forces Epidemiologic Board (AFEB). These included *A History of the Virus and Rickettsial (V & R) Commission, A History of the Early Years of the Virus Infections Commission,* and *Addendum to the History of the Neurotropic Virus Commission,* which completed his earlier account written shortly after World War II, when military censorship was still in effect. In addition he left several incomplete manuscripts, including one on influenza in World War I.

Throughout his seventy-eight years, Paul was a person of enormous energy, imagination, and inner strength. These traits were concealed in a gentle exterior that often belied the toughness beneath. He had the essential qualities of a leader: all who came in contact with him respected him and recognized his integrity, judgment, and wisdom. Despite his eminence and many honors, he retained a certain shyness; modesty and humility were strong in his character. His professional manner was rather formal and reserved, and it was not easy to get to know him well. But with friends he was a wonderful companion—lively, warm hearted, and possessed of a delightful sense of humor, understated humor. He was a stimulating conversationalist and took immense pleasure in good talk in the company of friends over dinner and a bottle of his favorite Mosel wine, of which he was a connoisseur. He had a particular gift for friendship and kept up with a host of devoted friends around the world who had entered his life beginning in his school days.

Paul travelled widely over the years; an unquenchable wanderlust was one of his main characteristics. His foreign travels began early, when as a medical student he spent a summer working at the Grenfell Mission in Labrador. Curiosity about the behavior of disease in different geographic areas, cultures, macro-, and microclimates took him to many parts of the globe. Besides his early expedition to Peru with W. G. McCallum and assignment during World War II in North Africa and the Middle East, his later research activities involved fieldwork in Costa Rica, Cuba, Puerto Rico, Iceland, Germany, Czechoslovakia, Morocco, Israel, Korea, and Japan. Whatever the country, his interest in the culture and art of the people—and always the birdlife—led him to devote as much time as possible to exploring these aspects. He kept a diary during most of his life, and his war journals and various travel journals are filled with perceptive and witty observations on people and places. Not surprisingly, descriptions of birds and many skillful sketches of them dot the pages.

John Paul's life has been described by John Enders as a "splendid edifice." * It was indeed rich in all of its facets—in family, friends, career, and by no means least in the devoted companionship of his wife, Leita, during their forty-nine years of marriage. In summing up, one of his Yale colleagues has said: "Armed with a quiet zest and a pocketful of hobbies that stretched from Aves to Zunis, he was courteous and reserved on the surface, delightful and gracious beneath and with a generosity of spirit and adventurousness of mind few have commanded. There is an old pre-Socratic saying that 'Character is Man's Destiny.' Dr. Paul richly fulfilled that vision—as a physician and teacher, as a scientist, and most of all, as a person." †

* J. F. Enders, "Book Review: A History of Poliomyelitis: Yale Studies in the History of Science and Medicine—6. By John R. Paul," *New England Journal of Medicine* 285(1971):359.

† E. Atkins, "John Rodman Paul, M.D.," *Yale Medicine* (Fall/Winter 1971), p. 9.

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KEY TO ABBREVIATIONS

Am. J. Hyg. = American Journal of Hygiene
Am. J. Med. = American Journal of Medicine
Am. J. Med. Sci. = American Journal of the Medical Sciences
Am. J. Public Health = American Journal of Public Health
Ann. Intern. Med. = Annals of Internal Medicine
Arch. Pathol. = Archives of Pathology
Bull. Ayer Clin. Lab. = Bulletin of the Ayer Clinical Laboratory of the Pennsylvania Hospital
Bull. N.Y. Acad. Med. = Bulletin of the New York Academy of Medicine
Bull. U.S. Army Med. Dep. = Bulletin of the United States Army Medical Department
Bull. WHO = Bulletin of the World Health Organization
Conn. Med. = Connecticut Medicine
Conn. State Med. J. = Connecticut State Medical Journal
Int. Assoc. Med. Mus. Bull. = International Association of Medical Museums Bulletin
Johns Hopkins Hosp. Bull. = Johns Hopkins Hospital Bulletin
J. Am. Med. Assoc. = Journal of the American Medical Association
J. Bacteriol. = Journal of Bacteriology
J. Biol. Chem. = Journal of Biological Chemistry
J. Clin. Invest. = Journal of Clinical Investigation
J. Exp. Med. = Journal of Experimental Medicine
Med. Clin. North Am. = Medical Clinics of North America
Milbank Mem. Fund Q. = Milbank Memorial Fund Quarterly
Newsl. Assoc. Teach. Prev. Med. = Newsletter of the Association of Teachers of Preventive Medicine
Pan Am. Health Organ. Sci. Publ. = Pan American Health Organization Scientific Publication
Proc. Pathol. Soc. Phila. = Proceedings of the Pathological Society of Philadelphia
Proc. Soc. Exp. Biol. Med. = Proceedings of the Society for Experimental Biology and Medicine
R.I. Med. J. = Rhode Island Medical Journal
Trans. Am. Clin. Climatol. Assoc. = Transactions of the American Clinical and Climatological Association
Trans. Assoc. Am. Physicians = Transactions of the Association of American Physicians
Yale J. Biol. Med. = Yale Journal of Biology and Medicine

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