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FRANK LAPPIN HORSFALL, JR.

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A Biographical Memoir by

GEORGE K. HIRST

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FRANK L. HORSFALL, JR. was a clinician and a virologist whose influential leadership came primarily through his perceptive scientific experimentation, both in the laboratory and in the clinic, and also through his vast administrative skill.

He was born December 14, 1906 in Seattle, Washington, where he spent all his formative years until he was twenty-one. His father, a native Vermonter, was a prominent surgeon who maintained a large house on Capitol Hill, and Frank, the first of four children, was a high-spirited youth whose interests led him into a wide range of activities. By the time he entered high school, he had decided to become an engineer, and he spent afternoons and evenings with a friend rigging up the family Victrola for radio reception. In the course of his four years at high school, he participated actively in the student council, the boys' athletic association, the glee club, and the radio press association. He was valedictorian of his class.

During four years of college at the University of Washington he lived in a fraternity house, and during the early part of this experience he was uncharacteristically erratic in the pursuit of his studies. It was during this period that he went out for crew, a major sport at Washington, and made the junior varsity. One of his outstanding characteristics was a tendency to throw himself headlong into every new activity, and it is reported that he

became a passionate oarsman, spending every moment of his spare time rowing or hanging around the boathouse. However, many years later, although he kept his oar on the wall, he completely disavowed any interest in rowing and for that matter in all other forms of athletics, either as a participant or as a spectator.

Midway through his college course he gave up the idea of becoming an engineer and decided to enter the medical profession. This involved some heroic scrambling to complete the course-work requirements, but in 1927 he followed in his father's footsteps by entering McGill University, in Montreal, Canada, and graduated in 1932, at which time he received the Holmes Gold Medal for having attained the highest scholastic record in his class.

After receiving his medical degree, he spent a year as a house officer in pathology at the Peter Bent Brigham Hospital in Boston. This was a common preliminary to a postgraduate education in surgery. It was during this year that he discovered that he was exquisitely sensitive to formaldehyde, a fact which markedly influenced later career decisions.

He responded characteristically to this disability by embarking at once on an extensive study of formaldehyde sensitivity in experimental animals and coupled this with a long series of experiments on himself. The result was two substantial papers on the subject, in which for the first time Horsfall was the sole or the senior author, and in them he acknowledged the assistance and advice of both H. Zinsser and S. B. Wolbach. This was the beginning of Horsfall's informal training in immunology, training which was to continue after another year at the Rockefeller Institute.

He returned to Montreal for a year's internship in medicine at the Royal Victoria Hospital and then signed up for a year in surgery, but shortly after starting the latter position he found that it was incompatible with his formaldehyde sensitivity, and

he promptly resigned. Immediately thereafter, in the fall of 1934, he went to the Rockefeller Institute in New York City, where he was to remain with only minor interruption for the next twenty-five years. On giving up a surgical career, for which he was eminently qualified, he showed no outward evidence of regret and quickly plunged off in another direction, which involved him in clinical research coupled with basic research.

Horsfall came to New York at a time when the Rockefeller Institute Hospital was at a peak of its reputation in the academic medical world. Although it was a very small unit, it had a very big reputation for pioneering in medical research. The staff members were both clinical and nonclinical, and there was a well-developed mystique among them concerning the catalytic effect which clinical contact had on basic research.

A majority of the young people there were like Horsfall in that they came from purely medical backgrounds and were to spend formative postdoctoral years in this very stimulating environment learning, in an informal manner, the basic disciplines such as bacteriology, virology, immunology, and physiology. Through these young people the Hospital provided excellent medical care, and at the time Horsfall was added to the staff the pneumonia service had nearly completed a large and successful series of cases in which type I pneumonia had been treated with specific antipneumococcal horse serum. These results had aroused widespread interest, and such sera were coming into general use.

In addition to the time spent on clinical responsibilities, all of the younger staff members were engaged in some basic research project. Those on the pneumonia service often worked on model infections in mice. Among the older staff members there were some who did no clinical work at all, and the most outstanding of these was Oswald T. Avery. The exceptional thing about the Avery school was that its immediate goals were so great and still far removed from any clinical application. His

very solid intellectual outlook set the tone for the whole department.

On entering this mixed atmosphere of clinical and academic science, Horsfall clearly and consistently showed his marked preference for those activities for which there appeared to be obvious relevant application to clinical work. Horsfall's emphasis on medical application would be demonstrated again and again throughout his career, even when he was not taking care of patients. He tackled his clinical responsibilities with enthusiasm. He was an eager therapist, and there are apocryphal reports about the strong restraints required to prevent him from testing in patients the enzyme capable of splitting the type III capsular carbohydrate, which had been developed by O. T. Avery and René Dubos. He was also an enthusiastic advocate of using type-specific serum in treating lobar pneumonia, and his influence was an important factor in switching the routine treatment at the Hospital from horse to rabbit antiserum.

This change in treatment was very successful and aroused wide interest. A large number of cases were treated with rabbit serum at the Hospital, and Horsfall and his colleagues published several extensive papers describing the clinical results. The use of this new method caught on generally. Commercial drug houses began producing rabbit antiserum, not only against types I and II, but also against a myriad of the rarer varieties.

Horsfall, working with Kenneth Goodner, accompanied this clinical work with a tremendous burst of laboratory activity in which they studied the comparative immunology of horse and rabbit sera in detail. These sera were found to differ from each other in a number of fundamental ways. In the space of a little more than a year, Horsfall and his colleagues published some twenty-three papers on these systems. Thirty or more immunological differences were highlighted, many of which were interpreted as suggesting distinct therapeutic advantages for the rabbit antibody.

Horsfall remained at the Hospital for three years and during his last year was Chief Resident Physician, a position which greatly increased his clinical responsibilities. Avery at the time was in the midst of his fascinating and fundamental work on the transforming principle. Horsfall was very familiar with all the current details of that work, which had been formalized by Avery into a series of personal lectures known as the Red Seal records. Frank Horsfall frequently sat at Avery's feet adsorbing the gospel, which he later was able to repeat in minute detail and often did so with great gusto. Yet he never did any research with Avery, much as he admired his whole approach. Their scientific style was entirely different, and Horsfall would have had a most difficult time adjusting to Avery's idiosyncrasies. For Horsfall, the transforming principle must have seemed far away from the world of patients.

Although the Rockefeller Hospital was at this time a prime source of candidates for academic positions in medical schools throughout the country, positions within the Hospital itself were at a premium. Nevertheless it became clear within a very short time that Horsfall's future would be in the Rockefeller Institute. It is difficult to assess the reasons for this early popularity which lay partly in his ability to see problems clearly, to apply himself to the problem with enormous energy, and then finally to present his results in a way which seemed simultaneously to be both conservative and expansive, romantic yet convincing. Thomas Rivers, who was a very influential person in American medicine at that time, was extremely devoted to Horsfall and played a large part later in promoting him as his own successor at the Rockefeller Institute Hospital.

It came as no surprise when in 1937 Horsfall resigned from the Hospital and accepted a staff position with the International Health Division of the Rockefeller Foundation. The change in employer was almost imperceptible. The principal Foundation laboratories were in fact housed at the Rockefeller Institute,

and Foundation scientists were treated as part of the family. Horsfall's daily contacts with staff members in the Hospital and the Institute continued as before, including his exceptionally close relationship with Rivers, a friendship which was now further cemented by the transformation of Horsfall into a virologist.

The Foundation had made a reputation for itself in virology through its pioneering work on yellow fever, and its leaders were anxious to continue this record of preeminence through an attack on the influenza problem. Horsfall became head of a laboratory section, previously organized by Thomas Francis, Jr., and the time seemed really ripe for developing a prophylactic agent against epidemic influenza. The virus of influenza had been isolated only four years before, and the Foundation offered Horsfall a very large technical staff, abundant laboratory space, generous financial support, and a sizeable professional staff that was equipped by experience to do large-scale fieldwork and to tackle epidemic problems on an international scale.

It is somewhat ironic that Horsfall stepped out of the lobar pneumonia scene just as it was undergoing drastic change. The elaborate type-specific serotherapy routines which had been very painstakingly developed in the mid-thirties were briskly and permanently swept away with the advent of chemotherapy and antibiotics. This had little to do with Horsfall's change of employer at this time, but does reflect the sweeping pace of medical advances. During his three years on the pneumonia service, he had received excellent training in immunology. Plunging into virology was to be a new experience, and he quickly became a master of the fundamentals. Once again, he threw himself wholeheartedly into a new activity, which was to occupy his attention for several years.

Before leaving the Hospital, Horsfall married Norma Campagnari, who worked there as a nurse. It was a most successful marriage. She was a quick, merry, and very lively person and a

gracious hostess. Horsfall's domestic life was always important to him, and he devoted much time to it in spite of numerous external demands. They had three children, and he was very much attached to them all.

The Foundation provided a proper setting for an individual of Horsfall's brilliant and expansive outlook. In addition to his major projects, he was able to devote much of his time to some very fundamental biological problems, and one of these areas was quantitative biology. He became involved with and obviously enjoyed the design and execution of mechanical projects like a low-temperature storage cabinet or a complicated ventilation system for a single room containing a large number of ferrets that had to be individually housed. The latter project was so successful that it enabled him to conduct experiments on the highly contagious distemper virus without danger of spontaneous cross-infection.

The research was nearly all on influenza virus, and at that time it was necessary to measure virus concentration by intranasal inoculation of material into mice. To achieve any reasonable sort of accuracy required the infection of large numbers of animals, followed by individual isolation during the incubation period. Nevertheless, Horsfall did very large, highly quantitative experiments with influenza, in which he attempted to work out the amount of antibody required to neutralize different amounts of virus in the inoculum. This was the beginning of a long and complicated experimental series on neutralization, carried out with great care and repeated many times in the years which followed.

The idea of these experiments was to develop some conception of the mechanism of neutralization. He pushed the problem as hard as he could with the techniques at his command, but it was not until many years later that the mystery of neutralization began to unravel, and it was learned that much simpler host systems were essential to understand neutralization mechanisms.

Shortly after starting work with the Foundation, Horsfall took time out for a six-month sabbatical with Arne Tiselius at Uppsala. At that time Tiselius was carrying out his important pioneer work on the electrophoresis of macromolecules. Although Horsfall published a couple of papers with Tiselius in the field of physical chemistry, it is clear that he could not use this experience in virology without wandering far afield from his customary goals.

The main attraction of the Foundation position was the possibility of studying human influenza infection on a vast scale and attempting prophylaxis against the disease. The Foundation was well equipped for this sort of venture. With its previous experience in yellow fever research, it had developed numerous experienced epidemiologists and other fieldworkers whose value in executing the experiments that were planned in New York would be difficult to exaggerate. In his first years with the Foundation, Horsfall carried out some routine but straightforward investigations of influenza epidemics. This work, in a very new field, carried the mark of competence with it.

A ferret colony was an essential resource in carrying out influenza work at that time, and during the course of some early experiments, a spontaneous epidemic of distemper broke out in the Foundation's animal house and nearly all the animals were lost. To prevent a recurrence of this disaster, all new animals were immunized, in most cases using a formalinized spleen from a spontaneously infected animal. Later, some of these immunized animals were found to have mysteriously acquired high anti-influenza titers. It occurred to Horsfall at once that distemper virus infection might have some sort of cooperative effect in inducing high-level and persistent antibody responses to influenza virus.

It was a fascinating idea, and a "complex" vaccine containing both influenza and distemper virus was quickly developed for use in human beings. The Foundation provided large-scale pro-

duction facilities for the new product, which was made by growing both viruses in chick embryos and then freeze-drying a formalinized extract. With the threat of a widespread epidemic (1940–1941), there was no time to do a lot of testing on preparations before they could be used in human experiments. There were some feverishly performed experiments in laboratory animals and man, but they were not completed in time to modify the large-scale experiments which were being contemplated in the field.

Large amounts of vaccine were prepared and shipped to Great Britain, which was at war, just in case the epidemic became intolerable. The British examined the preparations in great detail, but did not utilize an opportunity to try them. In the United States, however, Horsfall conducted a large-scale demonstration, vaccinating, under well-controlled circumstances, volunteers in a large number of state prisons up and down the Eastern Seaboard.

The experiment was carried out in magnificent style. E. R. Rickard, who was Horsfall's chief field marshal, was a master at this type of human experiment. Not only was the distribution of inoculations carefully controlled, but a great deal of data was obtained on individuals through attempts at virus isolation and by determining pre- and post-infection antibody titers. Fortunately, the inoculations were completed a relatively short time before the onset of the epidemic, and the use of a large number of population groups proved valuable in the final analysis of the results.

In spite of the excellence of organization and the occurrence of a large-scale epidemic in the wake of vaccination, the results were very disappointing. Although antibody rises had been induced in many vaccine recipients, the rise in titer was small and evanescent, and the reduction in case rate was in most institutions negligible or at best marginal. Only in a couple of places was there as much as a 50 percent drop in incidence following

vaccination, and it turned out that in these places the batch of vaccine used had had the highest virus titer before formalinization.

When all the laboratory tests on the complex vaccine were finally in, the results explained in some degree the disappointing field tests. In general the virus content of the vaccine was low, and the initially promising effect of distemper virus in boosting antigenicity could never be reproduced. It is again rather ironic that, just as these results were being recorded, new methods of obtaining high virus titers, as well as high virus purity, were being developed. It wasn't until several years later that vaccines made with these improved reagents were tested and gave the first bona fide protection against influenza in the field. Even years later the secret of obtaining substantial and prolonged effects against epidemic influenza is still a formidable problem, and the earliest experiences with the "complex" vaccine were by no means unique.

Just as the episode of the vaccine trial was coming to a close, Horsfall was called back to the Rockefeller Institute Hospital, where he received a lifetime appointment as a full member. Essentially he took over Rivers' Department of Virology, but he peopled it with entirely new personnel, and in his new program he once again confined his attention to respiratory disease. Rivers, who was now Director of the Rockefeller Institute Hospital, played a very important role in shaping developments within that organization. The return of Horsfall, with the possibility that he might become the Hospital's next Director, brought Rivers' planning to a climax.

By now the United States had entered the war, and Rivers organized a naval unit at the Hospital, most of which later went to Guam under his command. The remainder of this unit stayed on at Rockefeller Institute with Horsfall as the commanding officer, and as a group they worked on respiratory diseases, especially those that they felt might have a virus etiology such as

atypical pneumonia. This naval unit continued right on into the post-war period with little change in its structure, problems, or personnel.

Thus in 1941 Horsfall began the main period in his scientific life, which was to last about twenty years, and during which he had magnificent resources, was able to devote his full time to science, and was free to determine his own course of action. In the latter part of this period, his duties would become more and more administrative, culminating finally in his move to Sloan-Kettering. In 1941, however, the Rockefeller Institute provided a most salubrious climate for research. The place was populated by a scientific elite, mainly oriented toward biology and completely involved in research activity in a life which was unencumbered by teaching or institutional politics, as might be the case in a university.

Horsfall had a widely recognized and well-justified reputation for fostering research activities in his department in such a way that the individual investigators enjoyed both great freedom and superb stimulation. By now Horsfall had received a thorough, although informal, education in the immunology, bacteriology, and virology of the day; and characteristically, as in the past, he continued to work in areas which were closely relevant to infections in man. Hospital beds were available, and the group took on as its main project the search for the etiology of a recently developed entity called atypical pneumonia. In the previous few years this affliction had replaced lobar pneumonia as the principal acute respiratory disease of man.

In this new situation Horsfall again threw all of his energy into the attack, and a multipronged effort was mounted. A putative agent was isolated in mice by serial passage of human lung material. An agent was isolated in the mongoose from a similar source. Still other investigations involved the use of cotton rats. A gram-positive bacillus was isolated from human cases of atypical pneumonia, and the relationship of this organism to

the disease was thoroughly explored. This led to the discovery of some rather nonspecific serological responses in the patients suffering from pneumonia. Some of the work suggested a relationship of PVM (pneumonia virus of mice) to the human disease. The volume and detail of their explorations were quite impressive, but none of these efforts led to any firm conclusions at the time regarding the etiology of atypical pneumonia.

The search for an agent by Horsfall's group and others turned out to be far ahead of its time, and it was not until the mycoplasmas were delineated as a separate microbial group that investigators were able to determine the causative organism of this kind of pneumonia. In retrospect it was then shown that some of the earlier "virus isolates" (e.g., Eaton's lung passages from cotton rats) did in fact contain what we know now is the agent.

It is pertinent at this point to reemphasize the fact that Horsfall's training in basic disciplines was informal and that he approached his main problems, like atypical pneumonia, as a physician. This absence of formal scientific training was also true of the majority of students who came to work with Horsfall, many of whom settled into prominent academic clinical positions after leaving Rockefeller. This approach to viruses primarily as agents of disease was quite typical of the virology of the time, and as a result of this approach, the sum of the work done (on say atypical pneumonia) lacked the cohesion that came later, after the discipline had developed a more impressive internal structure. The biological revolution which was to gain momentum in the sixties completely changed the face of virology, which in the forties and fifties was dominated by clinical viewpoints and hence was somewhat amorphous.

During this period at Rockefeller, Horsfall's attention was not confined to the problem of atypical pneumonia. Some years before, while working on influenza with Richard Hahn, he was making some mouse-to-mouse passages of human lung material, and he isolated an agent which he called PVM. This virus was

normally latent in mouse colonies, but with passage its virulence could be enhanced so that it would cause pulmonary consolidation with a moderate mortality. This agent was to receive intensive study from time to time, in part because of its pneumotropism and also because it was thought to be related to the causative agent of some human pneumonias. The disease which it caused in mice was throughly studied in every aspect, including attempts at treatment and prophylaxis.

In the early stages of this work, it was found that the virus agglutinated red cells, and in addition it was shown that some substance in lung extracts also adsorbed to the virus. One of the most striking findings, however, was the discovery that certain high-molecular-weight carbohydrates had a distinct therapeutic effect on the pneumonia which the virus induced in mice. This unexpected finding came about when Horsfall, working with M. McCarty, was looking at the effects of the streptococcus MG (isolated from cases of atypical pneumonia) on PVM infection in mice. They found that a capsular polysaccharide from this bacillus had a profound therapeutic effect on the course of PVM infection in mice. The material was effective even after the disease had become well established and the intact macromolecule was necessary for therapeutic activity. Later on Horsfall and H. S. Ginsburg found that a similar polysaccharide from Friedländer's bacillus, group B, had an even greater therapeutic effect, and it also worked very well on mumps virus infection, in which the growth of virus was markedly suppressed.

All of the foregoing experiments were carried out on infections in complex organisms such as the developing embryo or the adolescent mouse. There never has been an adequate explanation of the curative mechanism at work, and the experiments have not been repeated with simpler host cell systems which became available later. Igor Tamm and Horsfall initiated a further series of chemotherapeutic experiments with the benzimidazoles and their derivatives on influenza virus infection, and thereafter the series was carried on by Tamm and others.

During this period Horsfall never forgot his early interest in influenza, and periodically he returned to influenza problems. It was a difficult virus to manage, but it had attractions which were then unknown for other agents; and Horsfall, always interested in quantitative biology, continued to study the relationship between hemagglutination inhibitors and virus-neutralizing antibodies. He was especially interested in the problem of antigenic strain differences between various influenza A isolates and did some very interesting work with I. Archetti showing that the antigenic profile of a number of influenza stocks could be quickly and permanently altered by *in ovo* passage in the presence of appropriate antibody. This type of experiment furnished the basic information through which the changes found in influenza virus from epidemic to epidemic could be explained, and this information is very fundamental to modern concepts of how the virus operates in nature.

Horsfall's interest extended briefly to other viruses from time to time, and his papers include reports on Coxsackie viruses, herpes simplex, mumps, and others. With some of these agents he was exploring the possibility of chemotherapeutic effects. He was also interested in the phenomenon of interference, in the effects of hormones (such as cortisone), and in metabolic inhibitors like fluoroacetate, which led eventually to the work with benzimidazoles.

Perhaps the most notable thing about this period of Horsfall's life was the long series of collaborators who worked with him in the New York laboratory, many of whom subsequently went out into key positions in the medical–academic world. The list includes such individuals as Lewis Thomas, Edward Curnen, Harry Ginsberg, D. A. J. Tyrrell, M. R. Hilleman, E. D. Kilbourne, Igor Tamm, F. M. Davenport, G. S. Mirick, and Maclyn McCarty. It would be impossible to find a more outstanding group of microbiologists who were connected with any other single laboratory. Because of the way in which Horsfall operated, these individuals often contributed as much

as they received, and each one in his way left his mark on the group. It was part of Horsfall's genius that he could at the same time exert a strong influence over the events occurring in his laboratory and also allow great freedom of expression.

In 1953 Herbert Gasser retired as Director of the Rockefeller Institute, and the accession of Detlev Bronk to this post foreshadowed great changes for the organization and all who were connected with it. Within a couple of years, Bronk converted the Institute into a University of Science, took in students, enlarged the faculty, added to the physical plant, and severely shook up its reserved character. During this period of rapid change, Bronk was preoccupied with plans for expansion, and in addition he played a very active role as President of the National Academy of Sciences.

As Vice-President and Physician-in-Chief to the Hospital, Horsfall was now second in command. He assumed the responsibility for many of the day-to-day tasks in running such an institution, and during this period he was especially appreciated by the older members from Institute days and often devoted a great deal of time and attention to their special problems. He became further and further separated from the laboratory, where, fortunately, Igor Tamm was present to assist in carrying on the old tradition. Prior to this time almost all of Horsfall's papers were published under joint authorship, but thereafter he published alone, mainly reviews on such topics as chemotherapy of virus infections and others with which he was familiar. He never gave anyone the impression that he was unhappy with this change, as he slid almost imperceptibly into a totally different kind of existence.

Being second in command and defender of the old tradition under Bronk was not entirely easy, and when in 1959 the directorship of the Sloan-Kettering Institute became available, the trustees (including a Rockefeller brother as chairman) offered the post to Horsfall, who accepted and made the move just across York Avenue.

Replacing Cornelius Rhoades was difficult, for Sloan-Kettering at the time was virtually the single-handed creation of Rhoades, who had built it up in the course of some twenty years. He made many of the staff appointments and followed many individual research programs in a very personal way. Horsfall's style was entirely different. He made few immediate changes, but in time he developed his own very loyal staff. Previously the emphasis at Sloan-Kettering was on studies of the chemical carcinogens and on cancer chemotherapy. This slant was not changed at once, and much of this kind of activity was preserved. Naturally the new emphasis was on the viral etiology of cancer and on molecular biology, both of which were just coming into prominence elsewhere. Horsfall was a staunch advocate of basic research in biology, and he was eclectic in his approach toward the tumor problem. He was conservative in his estimates of future progress in the cancer field and was unwilling to make superficial and encouraging predictions. This attitude was repeatedly expressed in the numerous reviews on the cancer problem which he began writing at this time.

When Horsfall came to Sloan-Kettering there was already a large building program under way, which he saw to completion. He also played the most important role in added staffing. In regard to the latter, he was also very reserved and relied heavily on a board of scientific consultants, with whom he met several times a year and went over many of the details of ongoing scientific programs. In the ensuing discussions of scientific merit, he was forthright and outspoken and used the highest standards of judgment, but he also listened intently to advice that was given. Because of his conservative attitude, things changed slowly, and his effect on the institution became evident only in his latest years.

Outside of the institutions in which he worked, Horsfall's life was a continuous flurry of activity. He was especially well known for his leading role on various boards of both local and national character. On the federal level he was at various times

a member of the President's Commission on Heart Disease, Cancer, and Stroke and of the Defense Science Board of the Department of Defense. In the years immediately after the war, he served as consultant to the Surgeon General of the U.S. Army and was on the Commission on Immunization of the Army Epidemiological Board. Outside of the government he was active in the National Foundation for Infantile Paralysis for many years, both before the vaccination campaign for poliomyelitis and after the focus of attention was switched to congenital diseases. He was a member of many scientific advisory bodies for such organizations as the Institute of Microbiology at Rutgers, the Oklahoma Research Foundation, and the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine.

Even more impressive was his devotion to the affairs of New York City, where he was a member of the Board of Directors of the Public Health Research Institute from 1955 on and was chairman of its Research Council for a large part of that time. In addition he was a very important influence in the organization and development of the Health Research Council of New York City, which for many years played a very important role in public health research.

To this sort of managerial responsibility Horsfall brought a very special talent. He was always completely familiar with the underlying structure in any organization that he served, and he always came to meetings fully briefed and with all of his homework well in hand. In the meetings themselves he played an especially important role in presenting and analyzing difficult problems, a role which he performed with such remarkable clarity that the problems would be understood by all, including the lay people who were present. Both in official and in private discussions, he made frequent use of hyperbole to drive home his point. His exaggerations were sometimes outrageous and were frequently coupled with a puckish manner. Even with long experience it was difficult to tell if he was serious.

Mention was made earlier of his overriding interest in

clinical medicine, an interest which became obvious in a number of ways. In addition to devoting a large portion of his scientific time to problems which had clinical application, he also devoted a great deal of time and effort to writing and speaking, very often on clinical topics. He contributed a great many articles to some of the best-known medical textbooks, and these dealt generally but not exclusively with virus diseases and their treatment. He edited (with Igor Tamm) and wrote extensively for the third edition of the widely used textbook, *Virus and Rickettsial Diseases of Man.* He also wrote a large number of reviews on chemotherapy in which the emphasis was frequently on agents of potential use in man.

During his lifetime he received many honors, dating from the time of his graduation from Medical School. He was given the Eli Lilly Award in Bacteriology and Immunology in 1937, the Casgrain and Charbonneau Award in Medicine from McGill in 1942, the John Lewis Prize from the American Philosophical Society in 1959, and the 50th Anniversary Gold Medal Award of Peter Bent Brigham Hospital in 1963.

Horsfall was elected to the Academy in 1948 and served on its Committee of Science and Public Policy (COSPUP) from 1963 to 1966. He became a member of the American Philosophical Society in 1956 and of the American Academy of Arts and Sciences in 1967. He had memberships in many professional societies, including the American Society for Clinical Investigation and the Association of American Physicians, to which he was elected in 1937 and 1942, respectively. He was a member of the Harvey Society and served as its President in 1956, and he was a lifelong member of the American Association of Immunologists and its President in 1967. A long list of other societies includes the Royal College of Physicians and Surgeons of Canada and the Royal Society of Medicine of Great Britain. He received honorary degrees from the University of Alberta, McGill University, and Uppsala University.

Horsfall served on the editorial boards of a number of professional journals, including the *Journal of Experimental Medicine*, the *American Journal of Public Health, Virology, Excerpta Medica,* and the *Journal of Immunology.*

During his years at Sloan-Kettering, Horsfall lived on the top floor of the Hospital–Institute complex, but since he found life in city apartments to be unbearably stifling, he also maintained a home in upper Westchester County, New York, where he frequently spent long weekends. It was here that he enjoyed the pleasures of working with his hands. He was quite skillful as a carpenter and this and cultivation of the soil gave him relief from the strenuous tensions of administrative duties. It was here that he enjoyed the intimacy of family life. He is survived by his wife, Norma, who resides in Silver Spring, Maryland; a son Frank L. Horsfall III, a microbiologist and director of research in an organization concerned with environmental science; and two daughters—Susan Shahmanesh who lives in Brooklyn, New York, and Mary Sullivan who lives in Leesburg, Virginia. There are three grandchildren.

During the fall of 1970 Horsfall felt himself beginning to fail. He had decided to retire just before it was discovered that he had cancer, of which he died on February 19, 1971. His death left a void which was widely felt, not only among his colleagues and staff, but also in the entire scientific community.

IT IS A PLEASURE to acknowledge the considerable assistance of Mrs. Norma Horsfall and also of Marilyn Moor of the Memorial Sloan-Kettering Cancer Center in furnishing important information and a bibliography. I am also indebted to several previous biographers, especially an extended account by Colin McLeod, published in the *Yearbook of the American Philosophical Society* (1971, pp. 127–32). Informal short biographies by Igor Tamm, Alexander Bearn, and Chester Southam were also available. I am indebted to the *University of Washington Alumni Bulletin* for information collected at the time Dr. Horsfall received recognition as a distinguished alumnus.

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