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OF

HANS ZINSSER

1878–1940

BY

SIMEON BURT WOLBACH

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Hans Zinsser was a compound of many talents, productive in science, education, literature, and poetry, and apparent in music, art, and sports. He had, moreover, an unusual capacity for making close and lasting friendships, a capacity arising no doubt from his own warm quality of friendliness and his generosity, tolerance, compassion, sense of fair play and courage. In any walk of life his alert, agile and able mind and splendid physique would have distinguished him. He was exceptionally fortunate in early educational advantages and home life, all quite different from those of most American-born scientists.

Outline of Dr. Zinsser's Life

Dr. Zinsser was born in New York City on November 17, 1878, into a German family of affluence and culture. On both sides his forebears were freedom-loving, independently thinking people. His father, August Zinsser, a manufacturing chemist, came from the Rhineland; his mother, Marie Theresa (Schmidt) from the Black Forest region which "had long been under the influence of French thought and political doctrine."

Dr. Zinsser was eight years younger than the next of three older brothers and because of this gap the attention and care he received was much like that given to an only child. The early environment provided him by highly educated and cultured parents who were devoted to each other was ideal. A country home in Westchester County, New York, gave out-of-doors pursuits and contact with domestic animals. Horses for driving and riding were at hand and he very soon acquired proficiency in horsemanship and a love of horses which lasted throughout his life. In later years he was a skilful and fearless rider to hounds. His early education, which included study of the violin and piano, was received at home from tutors and an uncle who was a physician and a musician as well. While an infant he

made his first trip abroad and travel in Europe was a yearly event until he was twenty years of age. On many of these excursions he was under the guidance of his cultured uncle and thus was thoroughly and tutorially exposed to the best in European art galleries and concert halls. Two early years were spent in school at Wiesbaden where this uncle lived. In Germany, France and Italy he also lived and travelled with his parents. At home, up to the age of ten, only German was spoken. At this age his first formal schooling began. The school, a private one in New York City, run by Julius Sachs, was highly esteemed by educated Germans. His training here was almost wholly in the liberal arts. At the age of seventeen (1895) he entered Columbia, imbued with a desire for the study of literature and for a career as a writer. At that time the elementary courses were given by the heads of the departments, so that he came into close contact with Professor George Edward Woodberry of the Department of Comparative Literature, from whom he acquired, through inspiration and criticism, invaluable facility and standards in composition of poetry and prose. In his junior year he took courses in biology under Edmund B. Wilson and Bashford Dean.

Up to this time the world of Hans Zinsser had been pretty much a world of things and thoughts created by the minds of men. He had been trained in the appraisal and appreciation of literary and artistic standards and opinions, sifted and accepted by the best intellects. Now, suddenly, a new world was exposed to him by Wilson and Dean whom he regarded as the ablest teachers he ever had. While not losing his literary aspirations, the biological sciences became his greatest interest. Ideas and convictions absorbed in earlier conversations with his agnostic father may well have fixed in him a naturalistic attitude which may in part account for this deviation of interests. Later he turned from general biology to medicine, a natural transition because Hans Zinsser was a practical-minded person who throughout his life aspired to useful results from his research.

The Spanish War led to his enlistment, during his third

year in college, in a cavalry unit (Squadron A) composed mostly of college men. After two years in this unit he got himself transferred to what he thought "was the toughest outfit in New York" and achieved thorough and revealing contacts with such American youth—offspring of many nationalities—as were mainly the product of city environment. He acknowledged the value of this experience in preparation for later adventures. At the end of his third year in college, three months spent on a paleontological expedition for Professor Osborn in the Southwest added to his scientific knowledge, gave him time for a thorough study of the Bible, and perhaps of greatest importance, added to his self-reliance because of the hardships and the variety of acquaintances incidental to a trip of this sort. It is a good guess that by this time his very carefully nurtured early education was well counterbalanced, and that his interest in people had spread to all levels.

During a college vacation when he was twenty, he took a walking trip through France and, according to Mrs. Zinsser, "his ardent admiration for things French and for France herself date from that time." He took no part in college athletics. He learned to fence in France when very young and fencing continued to be, with riding, one of his favorite exercises throughout his life.

Thus, when he began the study of medicine at the College of Physicians and Surgeons of Columbia University in the fall of 1899, he was proficient in German and French languages, thoroughly self-reliant and enthusiastic, probably more European than American in his point of view, yet possessed beyond most youths of attributes regarded as American—independence of thought, competency with horses and firearms, and in dealing with persons of all social levels.

While in the Medical School he completed his thesis for the M.A. degree on the early embryology of the mouse, and did extra work in bacteriology. His first scientific publication appeared in 1903, the year he received the degrees of M.A. and M.D. The years 1903 to 1905 were spent interning at the Roosevelt Hospital, after which he made a half-hearted

venture in the practice of medicine while remaining connected with the Roosevelt Hospital as Bacteriologist, and with Columbia University as Assistant in Bacteriology. In June 1905 he married Ruby Handforth Kunz of New York.

When in 1908 he received a full-time appointment at Columbia as Instructor in Bacteriology, he abandoned the practice of medicine with alacrity. This period in bacteriology at Columbia was a busy one. From 1907 to 1910 he was Assistant Pathologist at St. Luke's Hospital, New York. He was active in research, alone and in collaboration with Dr. Philip Hanson Hiss. With Dr. Hiss he also published the celebrated "Textbook of Bacteriology" now in its eighth edition. Most of the actual writing of this book was delegated to Dr. Zinsser because of his relish and facility for the task.

In 1910 he went to Leland Stanford University as Associate Professor of Bacteriology and Immunology. In 1911 he was appointed to the full professorship, which he held until 1913 when he was recalled to Columbia University as Professor of Bacteriology and Immunology.

A. W. Meyer, Professor of Anatomy Emeritus, has written a brief and entertaining account of "Zinsser at Stanford." From this source and from Mrs. Zinsser we learn that the years 1910-1913 at Palo Alto were very happy ones and, of course, very busy ones. After his arrival a laboratory was rapidly equipped for him in a building belonging to the Department of Anatomy. Some of his equipment was improvised and Mrs. Zinsser relates that she and Dr. Zinsser made many expeditions at night by horse and buggy when he was disturbed about the reliability of the bacteriological incubator. Dr. Zinsser himself helped build an animal house and an enclosure for goats, sheep and horses, animals necessary for his immunological research. Classes were small but composed of able students who gave gratifying response to Dr. Zinsser's enthusiastic and stimulating lectures. Professor Meyer describes him in 1910 as ". . . very youthful in appearance and the father of an engaging daughter of about two. He was slight of stature with light blond hair and scarcely evident eyelashes and eyebrows, frank

and exceptionally energetic and alert. His reactions not only were immediate, but sometimes surprising. Though full of life and mercurial in temperament, when serious he looks somewhat troubled. It soon became evident that President Jordan had surmised correctly that he was a 'live wire' and that he 'probably would go farther' than some others considered for the position." At Stanford Dr. Zinsser made many friends. He left them and his horses with regret when he took his family, his foils, and his violin back to New York. In his autobiography "As I Remember Him" he refers affectionately to "happy Stanford" and to his beloved friend, President Jordan.

Now followed ten productive years from 1913 to 1923 as Professor of Bacteriology and Immunology at Columbia University. During this decade he took part in the first World War as a member of the Red Cross Typhus Commission to Serbia in 1915 and in 1917-1919 as an officer in the Medical Corps of the United States Army. The Serbian expedition was scientifically unsuccessful but it brought Dr. Zinsser into close contact with "mass misery" and he characterized the typhus epidemic there as "as terrifying and tragic an episode as has occurred since the Middle Ages." Eight years later, in 1923, in Russia on a Sanitary Commission for the League of Red Cross Societies, he again encountered epidemic typhus. From these experiences he received the inspiration and material for his book "Rats, Lice and History" published in 1935, and out of them an objective which led him to concentrate on immunological research on typhus during the last ten years of his life.

His war record was distinguished. He was commissioned Major in 1917 and Colonel in 1918. He was with the A.E.F. in France for two years as Sanitary Inspector of the First Corps, and later of the Second Field Army. For a period he was Assistant Director of the Division of Laboratories and Infectious Diseases. Bayne-Jones has written: "The thoroughness of his inspection under conditions of danger and discomfort and his lashing condemnation of breaches of sanitary regulations are vividly remembered by all who saw him in action. With his usual comprehension he grasped the breadth of the problems

of military sanitation, understanding their relationship to the hygiene of the individual and to general public health. The orders issued on his recommendation in the Second Army became a treatise, published in 1919, entitled 'The Sanitation of a Field Army.'" After the war he was awarded the Distinguished Service Medal. In the accompanying citation are these statements: "For exceptionally meritorious and distinguished services. While acting as Sanitation Inspector of the Second Army he organized, perfected and administered with extraordinary and exceptional success a plan of military sanitation and epidemic-disease control." Interest in military sanitation persisted and his last publication, which appeared in 1940 just before his death, was "On the Medical Control of Mobilization." In this paper he advocated procedures which he believed would prevent the occurrence of disastrous epidemics.

At Columbia, as always, his research was chiefly in the field of immunology. The years 1914-1916 were largely given to the study of the *Treponema pallidum* by cultural methods and to problems of immunity to syphilis in animals.

The first edition of his textbook on immunity, now in its fifth edition, was published in 1914 with the title "Infection and Resistance." "A Laboratory Course in Serum Study" was published in 1916.

In 1923, at the age of 45, he came to Harvard University Medical School as Professor of Bacteriology and Immunology, and in 1925, on the retirement of Dr. Rosenau, received an added distinction at Harvard by having the Charles Wilder Professorship transferred to him.

At Harvard Dr. Zinsser flourished to his full capabilities. He became a University figure because his diverse interests and many talents brought him into contact with the outstanding intellects in many departments and all branches of biology, philosophy, social science, and education. He was a rapid and omnivorous reader. He acquired a reputation for his judgment of literature and, in Cambridge discussions, for his stimulating comments "in a bewildering variety of subjects." His first appearance as a speaker on non-technical subjects was his delivery

of the "Ether Day" address at the Massachusetts General Hospital—always a distinguished occasion—in 1924. In after years he was in considerable demand as a speaker for academic occasions and he gave numerous notable addresses on education, general and medical.

His department always presented a busy appearance. Pupils of many nationalities came to work with him. Research in immunological fields remained Zinsser's major interest until 1930, after which typhus fever absorbed completely his scientific endeavors. Superfluous intellectual energy went into writing of prose and poetry. He contributed articles frequently to the Atlantic Monthly, his first in 1927 entitled "The Perils of Magnanimity, a Problem in American Education" was admonitory in tone regarding "The Foundations" and in particular the Rockefeller Foundation. This short article is illustrative of Zinsser's self-reliance in judgment and courage in expression of convictions that characterized his academic activities at Harvard. Perhaps it illustrates his wisdom for, in the opinion of many, some of the perils he indicated have materialized.

Dr. Zinsser's bibliography indicates how he ripened at Harvard in literature and in science. His addresses on education reflect his own wide experience in teaching and give evidence of his erudition. Much that he wrote is epitomized and in some instances expanded in his autobiography "As I Remember Him." His continuous research on immunological problems was well qualified to make him appreciative of the complicated interplay of factors, those amenable to experimentation and those dependent upon human qualities, good and bad. He was as critical of premises obtained from observation of human affairs as from his laboratory work. His writings indicate that he was as much concerned over the evil operations of men's minds as was Mark Twain but he was cheerful about it and on the whole optimistic, at least never gloomy. In his books, "Rats, Lice and History" and his autobiography, his hopes and thoughts about humanity were revealed. What some of them were can be indicated best by quoting from Charles Sedgewick Minot (The Problem of Age, Growth and Death. Lowell Institute Lectures, delivered

March 1907). "The time will come, I hope, when it will be generally understood that the investigators and thinkers of the world are those upon whom the world chiefly depends. I should like, indeed, to live to a time when it will be universally recognized that the military man and the government makers are types which have survived from a previous condition of civilization, not ours; and when they will no longer be looked upon as the heroes of mankind. In that future time those persons who have really created our civilization will receive the recognition which is their due. Let these thoughts dwell long in your meditation, because it is a serious problem in all our civilization today, how to secure due recognition of the values of thought and how to encourage it."

After Zinsser concentrated on typhus fever research, he made many visits to Charles Nicolle in Algiers. A friendship begun in 1928 in Tunis ripened into mutually great affectionate regard. These two men, both versatile in literature and science, had everything except years in common. Of Nicolle's death, Zinsser wrote: "It was the same order of sorrow as had been the death of my father."

Up to his death, Zinsser was active in the laboratory. His final goal was an effective vaccine against typhus fever. In 1935 he was sent by Harvard University to France as Exchange Professor. In 1938 he was an Exchange Professor at Peiping University Medical College.

Abounding in energy and seemingly physically and mentally tireless, life at Harvard was a full one. In addition to a house on Chestnut Street, Boston, the Zinssers had a farm at nearby Dover, where entertainment of a vigorous sort was provided for members of his department and for medical students. Until his last illness he rode to hounds with the Groton Hunt, and in spite of long working hours in the laboratory he kept lean, muscular and tanned. When perplexed or satiated with work he fiddled. Apparently as a minor side-issue he kept his textbooks up to date. There were always in his room, upon a stand-up desk built for his predecessor Dr. H. C. Ernst, high piles of great sheets of paper, large enough to provide for foot-wide margins around the

printed pages of text which he pasted upon them as soon as a new edition was printed. The wide margins provided ample room for recording instantly the changes and additions suggested by publications as they appeared.

Dr. Zinsser's Scientific Work

Dr. Zinsser's two textbooks must be included as part of his scientific work. His "Textbook of Bacteriology," first published in 1910 with Philip Hanson Hiss, Jr. and finally with Stanhope Bayne-Jones, has gone through eight editions and thirty-eight printings, and has been translated into several languages, including Chinese.

"Infection and Resistance" which was published in 1914, went through three editions; a fourth edition in 1931 was published under the title "Resistance to Infectious Diseases" and in 1939 the fifth edition, written in collaboration with John F. Enders and LeRoy D. Fothergill, appeared with the title "Immunity: Principles and Application in Medicine and Public Health."

Both these books and particularly the one on immunology are examples of what textbooks should be because they present in an integrated and clear manner that which is known or believed and stimulate interest and curiosity by revealing the problems still unsolved.

Although Dr. Zinsser made contributions of etiological significance for syphilis, rheumatic fever, and typhus fever, he worked consistently throughout his career in the field of immunology. In a list (perhaps incomplete) of 106 papers recording actual research, 70 deal with subjects in immunology; over half of these (43) are concerned with fundamental aspects of immunity; the remainder with immunological problems of pyogenic diseases, tuberculosis, syphilis, typhus and virus diseases.

Dr. Zinsser's first paper, in 1903, was upon the effects of radium on bacteria. During the next five years his publications dealt with laboratory methods and interesting examples of infection in man. From 1908 to 1911 he collaborated in research with Dr. Hiss on the preparation of extracts of leucocytes and on the application of these extracts of leucocytes to the treat-

ment of infections in man. They showed that the extracts did not promote phagocytosis and that their moderate bactericidal activity could not account for their effectiveness. In reviewing this work, Dr. Zinsser wrote in 1940 that he was "inclined to believe that the beneficial effects are to be attributed to those obscure factors which account for the not infrequent successes of so-called nonspecific protein therapy, which consists in the injection of almost any bacterial or other protein."

Zinsser's studies of fundamental problems in immune phenomena began at about the time he went to Leland Stanford University in 1910 and studies of the precipitin reaction made him realize that antigen-antibody reactions should be amenable to elucidation by physical-chemical methods particularly as applied to colloidal chemistry. This led to a close association with Stewart Young, the professor of Physical Chemistry and the publication of important papers by them on the precipitin reaction. At this period Zinsser " . . . often expressed a very strong belief that physical chemistry would ultimately explain a great many things in the field of immunology" and, aware of his inadequate knowledge of mathematics, he plunged into the study of algebra and trigonometry in preparation for the mastery of calculus because, as he said, "If I am ever able to do anything with bacteriology I have got to be able to handle my physical chemistry like a man, not like a . . . fool." Unfortunately, Zinsser did not devote enough time to become greatly competent in physical chemistry, which may be explained in part by his return to Columbia and new interests in problems presenting practical objectives. As a result of this excursion into physical chemistry he became one of the earliest proponents of the "unitarian view" concerning the essential identity of the antibodies, a subject which he has succinctly dealt with in historical perspective in his textbook on immunity. In 1919, his interest in the physical-chemical aspects of immunity also led to the addition of a biochemist to his department at Columbia. The appointee, J. Howard Mueller, remained with Dr. Zinsser until the latter's death, and succeeded to the Professorship of Bacteriology and Immunology at Harvard. Years later Zinsser was able to apply successfully his

earlier acquired physical-chemical knowledge to the determination of the size of virus particles by filtration through membranes of graded porosities and to methods for determining the metabolic activity of cells in tissue cultures most favorable for the cultivation of viruses and rickettsiae.

An objective of Dr. Zinsser on returning to Columbia was the achievement of a method of active immunization against syphilis, apparently a possible goal because of "Noguchi's success in cultivating spirochetes and his observations on reactions produced by the injection of luetin. . . ." "A series of papers was published during the years 1914 to 1916 on the cultivation of Spirochaeta *(Treponema pallidum)* pallida, on fluctuations on the virulence of these organisms, on spirochetocidal antibodies and on phenomena of immunity to syphilis in animals." He did not succeed in his objective, a method for immunization against syphilis, but he added to the knowledge of spirochetes and disclosed problems presented by the differences between the properties of spirochetes in cultures and virulent ones from human lesions that are still unresolved, including the question that prevails to this day—actual proof of the cultivation of *Treponema pallidum*.

Dr. Zinsser, in 1914, was one of the first investigators to study the effects of heat upon the behavior of proteins used to immunize animals, and to show that a heat-resistant fraction was concerned with the specific nature of the resulting immune body. His later tuberculin studies led to a generalization of first importance, applicable to responses in bacterial infection in general. This generalization can be expressed by quoting from his 1921 paper. "It would appear that certain non-coaguable substances of uncertain chemical constitution are being constantly elaborated in the course of bacterial growth and passed into the circulation of infected animals. As a result of this, infected animals become sensitized to the heat and acid-resistant materials. Early in the course of infection the animal becomes sensitized and subsequently the further elaboration and distribution of these materials from the bacterial focus play a fundamental part in the injury of the animal. These proteose-like substances, like tuber-

culin, possessing but slight toxicity for the normal animal, become highly toxic to the sensitized one. Thus these substances, while not being true exotoxins in the ordinary sense, would still represent a highly toxic bacterial product comparable in its injurious effect to toxins when produced in the body of an animal thus sensitized. . . ." "If there is any value in these deductions, the attention of bacteriologists should be turned to the nonprotein constituents of bacterial cells in their further immunological studies, as well as to the protein materials."

This generalization of Hans Zinsser's is perhaps his greatest in the field of immunology. It reflects his knowledge of pathology and his broad understanding of the sequences that compose a disease entity. "Residue antigens" was the name he gave to these "heat and acid-resistant materials." He and his associates and many others confirmed and extended his observations, now of very great theoretical and practical importance in the elucidation and serum treatment of bacterial diseases. Through the work of Heidelberger and Avery we know now that at least certain of Zinsser's "residue antigens" are polysaccharides.

During the period 1926 to 1930 he published a number of papers on the virus of herpes and on immunologic studies of the herpesencephalitis problem. The results, together with those of others, are summarized in a paper entitled "An Immunological Consideration of the Virus Problem" published in 1936. While working with the virus of herpes he became interested in the sizes of virus particles. "Finding no precise information on this subject in the literature, he undertook with Tang to make the necessary determinations by measuring viruses against the permeability of graded filters made of collodion by a method more or less analagous to that which Bechold used in an attempt to establish a scale of sizes for various substances ranging from crystalloids to Prussian blue." "The results were published in 1927. He estimated that herpes virus, Rous sarcoma virus and bacteriophage 'were of a magnitude larger than casein and collargol and smaller than colloidal arsenic.' This range of sizes was from 20 to 100 millimicrons. Considering the difficulties and uncertainties, these determinations are amazingly close to

the value accepted at present, namely: for bacteriophage, 75 millimicrons, for the Rous sarcoma virus, 70 millimicrons, for herpes virus approximately 130 millimicrons. In this original work Dr. Zinsser was the first to determine the approximate size of virus particles by filtration through membranes of graded porosities." [1]

It is not advisable to attempt to outline systematically Zinsser's numerous papers pertaining to anaphylaxis and allergy. He was, however, the first to formulate a clear distinction between the tuberculin type of allergic response and classical anaphylactic shock as seen in animals. He pointed out that the tuberculin reaction—also allergic in nature—could be elicited only after a primary tissue reaction induced by the presence of the tubercle bacillus itself, in the animal. With the late Dr. Francis Grinnell he showed how a similar type of reaction could be produced with the unaltered proteins of other bacteria, such as the pneumococcus. He was convinced that allergic reactions were responsible for the lesions of some diseases and specifically, as a result of sensitization by the streptococcus, for those of rheumatic fever. Although not yet proved, this conception of the etiology of rheumatic fever still appears to many investigators as the most probable mechanism whereby the characteristic lesions of this disease are established.

Section I of his textbook with Enders and Fothergill is probably the best exposition of the "Principles and Theory" of immunity that can be found in a single volume in English. The five chapters devoted to "hypersensitiveness" illustrate Dr. Zinsser's absorption in this field and contain his own contributions fairly and appropriately presented and appraised in relation to the present day knowledge.

Dr. Zinsser's name and scientific reputation today are associated perhaps too largely with typhus fever. Substantial and serviceable as were the original contributions in this field by him and his associates, the writer appraises more highly the earlier products of his research. His fascinating books, "Rats,

[1] Biographical sketch by Professor S. Bayne-Jones in the Archives of Pathology, Vol. 31, p. 269, 1941.

Lice and History" published in 1935, and his autobiography, "As I Remember Him" published in 1940 compel emphasis upon lay and medical readers of his typhus work. Of his Serbian experiences as a member of the American Red Cross Sanitary Commission, organized by Richard P. Strong, he wrote in his autobiography: "My work at this hospital led to little immediate discovery. I gathered a great deal of information about the clinical aspects of the disease, did a great many autopsies, and learned the things that one can learn about typhus by living in an epidemic region. But scientific studies were hampered, not by any lack of opportunity or equipment, but rather by the fact that in typhus investigations at that time there was much underbrush to be cleared away. Before the true causes of the disease were uncovered, almost every known microorganism had, at some time or other, been implicated."

Apparently in Serbia in 1915, Zinsser elected to follow wrong trails. Nicolle, Comte and Conseil in 1909 had established that epidemic typhus was louse-borne and in 1910 Ricketts and Wilder proved that Mexican typhus or tabardillo could be transmitted from man to man in the same manner. They also found, in the bodies of infected lice, microorganisms which they regarded as the cause of typhus and which by their description were in all probability *Rickettsia prowazeki*. In 1911, Nicolle, Conseil and Conor showed that guinea pigs were susceptible to typhus.

In 1930, when Zinsser returned to typhus fever, *Rickettsia prowazeki* was the proved cause of typhus and had been grown in tissue cultures. Typhus unassociated with lice had been revealed in the United States and early in 1931 the virus was found in rats trapped in Baltimore and later in the year the rat flea was proved to be the carrier. Differences in animal reactions to European or epidemic typhus on the one hand and to murine typhus and tabardillo on the other had been described by Mooser. Mexican typhus and murine typhus produced in guinea pigs a much more severe inflammatory reaction in the tunica vaginalis after intraperitoneal inoculation than did European typhus. Also in contrast to European typhus, Mexican and murine typhus

infected guinea pigs showed great numbers of rickettsiae in the inflammatory exudate. Indeed, by 1930 there was an extensive literature dealing with the two diseases in which rickettsiae had been shown to be the pathogenic agents, Rocky Mountain spotted fever and typhus, and with rickettsiae in general, pathogenic and non-pathogenic alike. An effective vaccine containing rickettsiae obtained from the ground viscera of infected ticks and killed by phenol, for immunization against Rocky Mountain spotted fever, was in use.

There existed the problem of identity or non-identity of Old World or louse-borne epidemic typhus and the New World non-louse-borne endemic typhus, and the relation of epidemic louse-borne typhus in Mexico to both. Also, there was the problem of Brill's disease, sporadic typhus, apparently not louse-borne, which existed in cities in Northeastern United States, but restricted to emigrants from typhus regions of Europe.

The great objective of Dr. Zinsser and his numerous associates was the production of an effective vaccine for the prevention of typhus. In 1931, shortly after Dyer and others of the United States Public Health Service found typhus virus in Baltimore rats he, with Castaneda, proved the presence of the virus of Mexican Typhus in rats in Mexico City. Also in 1931, with Mooser and Castaneda, he showed that the rat louse, *Polyplax spinulosus*, could, as well as the rat flea, transmit the infection in rats. By reasoning based on epidemiologic data and by direct isolation of rickettsiae from patients with the disease, he showed that Brill's disease was typhus of the European type and came to the conclusion that it represented a recrudescence of typhus infection acquired in Europe prior to emigration.[2] His studies indicate, therefore, that man may very well be an epidemic reservoir of typhus for a period of ten to thirty years following infection. The implications of this conclusion are of very great importance.

Zinsser and Castaneda began studies in 1930 directed toward

[2]Recent investigations by Plotz employing the differential technique of complement fixation to distinguish between epidemic and murine typhus have confirmed Dr. Zinsser's important and pioneering observations.

the production of a vaccine against typhus. For this purpose great numbers of rickettsiae would have to be made readily available. The only vaccine then in use (since 1920) was that of Weigl, prepared from lice artificially infected by injection of rickettsia into the gut by means of a fine pipette introduced through the anal aperture. These lice then had to be nurtured for a week or more upon typhus-immune persons. Since it required from 50 to 100 lice to produce vaccine sufficient for the immunization of one person, the method obviously was not practicable for large scale use.

By subjecting rats to injurious procedures in order to reduce their "resistance" to typhus, Zinsser and Castaneda succeeded in 1933-34 in obtaining huge numbers of rickettsiae in the peritoneal exudates following inoculation with murine typhus but not with European typhus. Vitamin deficient diets, benzene poisoning and exposure to x-rays were used to decrease "resistance"; the last method proved most efficacious. The rickettsiae thus obtained, killed with formaldehyde, met the experimental tests for an efficient vaccine. This type of vaccine was used in human beings by Castaneda in Mexico and by Veintemillas in Bolivia. Zinsser and Castaneda also used formaldehyde-killed rickettsia obtained in the same manner for the production in a horse of an immune serum which was later used in Mexico "with a fair degree of success in preventive and therapeutic trials." Because this serum, though giving protection to guinea pigs inoculated with murine typhus gave only partial protection against the European strain, no beneficial effect was expected in patients with European typhus.[3]

Because the method of x-ray radiation failed to provide suspensions of European rickettsiae sufficient for the preparation of vaccine, tissue culture methods for the growth of rickettsiae were the next recourse of Dr. Zinsser. With Fitzpatrick and

[3] Recent results of the treatment of rickettsial diseases, Rocky Mountain spotted fever and typhus, with "hyperimmune" sera obtained from rabbits produced by repeated injections of rickettsiae, indicate that such sera are of value only in very early stages of the disease and that only in exceptional instances is diagnosis established sufficiently early for their use.

Wei, a medium was devised (1937-38) which was superior to those hitherto employed. This medium was essentially a modification of the Nigg-Landsteiner modification of Maitland's medium; the essentials of which were Tyrode's solution, blood serum and appropriate minced tissue devised for the cultivation of vaccinia virus. Nigg and Landsteiner had found that *Rickettsia prowazeki* could be cultivated for many generations *in vitro* "in media similar to those described by Maitland, Rivers and others for the cultivation of certain viruses. In all probability such cultures can be maintained indefinitely." The Zinsser-Fitzpatrick-Wei medium is essentially the Maitland medium sterilized by filtration and solidified by the addition of isotonic agar jelly. The minced tissue for supplying cells for the growth of rickettsiae was then spread upon the surface. This medium, for a brief period, was undoubtedly the best means of securing the abundance of rickettsiae necessary for vaccine production.[4] Dr. Zinsser was enthusiastic over the results of laboratory tests of the method and its possibilities for mass protection against typhus. It is not known what the results were of vaccine prepared from such tissue cultures which was tested in China, Mexico and South America, nor do we yet know the full potentialities of the technic. Although Zia, a pupil of Dr. Zinsser's and working in his laboratory, had earlier shown that rickettsiae could be propagated in the chorio-allantoic membrane of the chick embryo, it was not until 1939 that this technic as modified by Cox became generally employed for the cultivation of these organisms. The typhus vaccines in use in the United States today are prepared by methods worked out in the National Institute of Health following the discovery by Topping and Shear that an important "soluble antigen" hitherto discarded, is an essential component for immunization.

In 1940 Zinsser, Plotz and Enders recommended a combination of the agar tissue culture procedure and yolk sac cultures,

[4] According to recent findings of Dr. Harry Plotz, it still affords the best method for obtaining large quantities of the rickettsia of Rocky Mountain spotted fever, surpassing the productivity of the embryonated egg.

the latter used as the source of inoculum sufficient to inoculate large areas of the agar medium spread with minced normal chick embryo tissue.

Out of Zinsser's laboratory came the useful staining methods of Castaneda and Machiavello for rickettsiae in smears and tissue cultures. A very important study of the perplexing Weil-Felix reaction (the agglutination of certain strains of bacillus proteins by the serum of typhus patients) was made by Castaneda and Zia who showed that the rickettsia of murine typhus and *B. proteus* X possessed in common an antigenic soluble factor, a "residue antigen." Undoubtedly, Zinsser gave counsel in the progress of this research.[5]

Dr. Zinsser's Writings on Education

Dr. Zinsser was rated highly as a speaker on academic occasions. Usually the theme of his addresses was education, general or medical. He also wrote a small number of essays on education for "School and Society" and other publications connected with secondary schools and universities. His intimate knowledge of three American universities, his familiarity with European universities and his personal educational experiences qualified him beyond his reputation as an educator. Nearly always in his addresses and essays on education, he took occasion to champion some one thing to be remedied or an attainable goal in education. He believed that the fate of democracy depends upon our educational system. "Education has the bear of democracy by the tail and there is no letting go." Thus we find him stressing the importance of securing, through recognition and appropriate compensation, the ablest of teachers for our high schools and preparatory schools, or making a plea for greater security in tenure of office, and for better salaries for university officers below top rank—for those men "who are ready to devote their lives to teaching, thought and investigation without ambition of riches, but with the same desires for freedom from

[5] Olitsky's 1941 Sigma Xi lecture at the University of Cincinnati—"Hans Zinsser and his studies on Typhus Fever" should be read by anyone interested in a more complete account of Zinsser's typhus work.

anxiety and for commensurate community position which are possessed by normal persons in other walks of life."

He discussed university administration with great frankness and on the whole stood for a democratic faculty rule. Of the administration of an educational institution he said: "For the guidance of an institution the success of which depends upon the imponderable value of spirit and intellect is not the mechanical driving of a machine made of iron and steel. It is more like the riding of a thoroughbred, an organism with a nervous system and a temperament. Anyone with strong legs can stay on but the riding is in the lightness of the hand and the feeling of being one with the horse. We must find our way back, or part way back, to the older conception of academic leadership, avoiding the estrangement between faculty and management which these days of reorganization have threatened to establish." The date of this quotation is 1931. Dr. Zinsser did not neglect repeatedly to point out potentialities for good and for evil in the acceptance of Foundation funds. His views on medical education concerning the correlation in teaching of the fundamental medical sciences and clinical subjects were largely the result of study and teaching in France and impressed most of his colleagues as sound and desirable to put into operation. He found opportunities to strike hard at conditions and practices of which he disapproved in scientific medical fields, among which was the "practice of patenting discoveries which directly or indirectly bear upon prevention and treatment of disease."

The most interesting theme, which recurs in varying lengths in his addresses, is that of the place of science in liberal education. Dr. Zinsser expressed his strong conviction that instruction in science should take front rank with instruction in the "humanities" or rather, that there should be no distinction for he said: "Indeed, if one could revert to the conception of the 'humanities' held by the early humanists, a modern definition of this term would include the non-specialistic and non-vocational parts of both the sciences and the liberal arts." Dr. Zinsser's conception of an educated man was one who could "properly appraise the civilization of our time." Only by reading a fair number of

his publications on educational subjects and essays for lay readers can an appraisal be made of the range and penetration of his thinking and of his activities which entitle him to rank as a "humanist."

Dr. Zinsser as Author and Poet

In the world of letters Zinsser is distinguished for his two books written for lay readers, "Rats, Lice and History" and "As I Remember Him. The Biography of R. S." Both have received great commendation from literary critics and established him in the public's mind as a writer of ability and charm who could compel sustained interest through the blending of entertainment and instruction. No one who has read these books carefully can have doubts concerning the intellectual breadth and the cosmopolitan qualities of the author's thoughts. In both books he reveals in fragmentary fashion his social, political and religious philosophies and exhibits his keen sense of humor and his mastery of ridicule and satire—always deservedly administered—as can be done only by a well stocked mind, intent upon service.

For many years Zinsser had signed his poems with the initials "R.S." for the purpose of concealing his authorship of verse from his professional brethren. His choice of these initials has been the subject of a number of speculations. Dr. John Enders, his colleague and close friend for many years, has disclosed that Dr. Zinsser told him that they stood for the initials of Rudolf Schmidt, the author of a book in German entitled "Pain, Its Causation and Diagnostic Significance in Internal Disease" which he translated into English in 1908.

"As I Remember Him" is actually an intimate and frank autobiography. Written in the third person it is more analytical and critical of its subject than any other biographer observing the rule "De mortuis nil nisi bonum" would dare or indeed care to be, because intimate knowledge of Dr. Zinsser's personality, whether revealed by actual contact or by study of his writings, cannot fail to inspire affection and respect for him. In this book Dr. Zinsser the philosopher is articulate; in it he belies to considerable degree the agnosticism he professed.

After Dr. Zinsser's death a volume of his poems was published (Alfred A. Knopf, New York, 1942) entitled "Spring, Summer and Autumn." This volume should be consulted by anyone interested in Dr. Zinsser's life. The level of merit of his verses has been highly appraised by qualified critics. His last sonnet, written shortly before his death, is in all ways his best and unquestionably will live for all time because of its beauty and popular appeal.

Hans Zinsser, the Man

In "As I Remember Him," Dr. Zinsser has revealed with little reserve his emotional and intellectual make-up. To all his revealed characteristics there should be added magnanimity in judgment of others, compassion, a great sense of justice, a rigid code of honor and great capacity for friendship.

He had great physical vigor and kept himself lean and muscular, fit for strenuous exercise and long hours in the laboratory. That he was able to accomplish so much in diverse fields was because he commanded, jealously and firmly, the disposal of his time. He served on an astonishingly large number of committees and boards. He was a Trustee of the Massachusetts General Hospital. He was on the editorial boards of five scientific and medical journals. He was a member of more than a dozen fraternities, clubs and honorary societies, and of 36 scientific societies, including the Association of American Physicians, American Philosophical Society, National Academy of Sciences, American Academy of Arts and Sciences, National Academy of Tropical Medicine, American Association for the Advancement of Science, New York Pathological Society (President, 1915), American Association of Immunologists (President, 1919) and Society of American Bacteriologists (President, 1926).

Many honors came to Dr. Zinsser. He received honorary Doctor of Science degrees from Columbia University, 1929, Western Reserve University, 1931, Lehigh University, 1933, Yale University, 1939 and Harvard University, 1939. His decorations were: Distinguished Service Medal, U. S. A., Order of Saint Sava, Serbia, and Legion d'Honneur, France. The Sedgewick Memorial Medal of the American Public Health

Association was awarded him posthumously in October, 1940.

At the time of his death, shortly before his sixty-second birthday, Dr. Zinsser, in addition to his Professorship of Bacteriology and Immunology, held the positions of Chief of the Bacteriological Services of the Children's and Infants' Hospitals of Boston, and Consultant in Bacteriology at the Peter Bent Brigham Hospital.

He is survived by his widow, a son and a daughter. The son, Hans Zinsser, is a graduate of Harvard College, 1938, and of the College of Physicians and Surgeons, Columbia University, 1942, and saw service in Europe as a surgeon with paratroopers. In 1940 he married Anne Drinker, daughter of Professor Cecil Kent Drinker. Dr. Zinsser's daughter is the wife of Vernon Monroe, Jr. of New York City.

Although the writer enjoyed the friendship of Dr. Zinsser for many years and was honored by his confidences during the last few years of his life, and in spite of the perspective afforded by the lapse of six years since his death, he finds it impossible, because of his own limitations, to portray him adequately. He had some attributes of the animal he loved most—the thoroughbred horse—sensitive and spirited, intolerant of restraint, with barriers of reserve penetrable only by those to whom confidence and affection are given.

The aggregate of his scientific work in bacteriology and immunology is impressive and although he made no single great advance, many of his contributions are now important elements in the structure of immunology. His textbooks are outstanding because of his great knowledge and integrative ability. He was an able and much loved teacher of undergraduates. To graduate students working in his department (and they came from many countries) and to members of his department, he was more than a leader in common scientific interests. He was an awakener of new intellectual interests in other fields. I quote now from Dr. John F. Enders' memorial address—"But the extent of his general knowledge was sufficient to furnish forth

respectably two or three professor's chairs. The world of letters only recently has become aware of his broad cultivation, but for us it was an old and delightful story. For some years we all lunched together in the laboratory. As we ate, the conversation—led by him—became animated. Literature, politics, history and science—all he discussed with spontaneity and without self-consciousness. Everything was illuminated by an apt allusion drawn from the most diverse sources. . . . Here, indeed, was a liberal education to be gained pleasantly while one dined. Under such influences, the laboratory became much more than just a place to work and teach; it became a way of life."

From many sources we learn that Dr. Zinsser was deeply interested in people as persons. He was generous with his time and money in cases of need. He would go to great trouble to set matters right if he learned that he had been unjust to another person by act or thought. In his travels he sought close contacts with substantial representatives of all walks of life—fishermen, laborers, peasants, artisans, professors. Intensely patriotic and a firm believer in democracy, his culture was cosmopolitan—continental and patterned unconsciously after French standards. He felt at home in France. The way of living there suited him and temperamentally and intellectually he blended perfectly in French university circles. The late Lawrence J. Henderson is quoted as having said: "Although Hans Zinsser is almost wholly of German descent, he is the most French man whom I have ever met." Undoubtedly this was spoken in great approbation since Whitehead has said that ". . . the mentality of men like Jefferson and Franklin was French. There, indeed, was the homeland of their thoughts."

Dr. Zinsser lived a few months over two years after knowing that he had a fatal disease—leukemia. During this period he worked harder than ever and outwardly at least was composed and lived the life of a man thoroughly engrossed in his research work and keenly interested in everyday affairs and in his friends.

While observing the progress of his disease and awaiting death he displayed those qualities of spirit and courage about which he wrote in 1927 in admiration and affection upon the death of

Dr. Francis W. Peabody: "Indeed the proof of a man's life—how much has been the living of a formula and how much an inward light—may often be found in the manner of his facing death. For courage is still, as it has always been, a thing of great beauty that springs, whatever its form of expression, from an inner source of moral power. We wish for ourselves and the ordinary human being, a swift and merciful death, which is most easily supported with dignity and composure. For him we would not have had it other than it came. Those who were fortunate in seeing him during those eighteen months when he and death sat face to face—who dreaded their first visits and came out glad and inspired with a new faith in the nobility and courage to which rare men can attain—these knew that the ugliness and cruelty of death were defeated."

Dr. Zinsser acquired an extraordinary number of admiring friends scattered over the world because he was a man of great charm and many talents and because his reactions in all situations were impulsively honest and understandable. To sincere persons he freely revealed his real self; to make use of artificiality in manner, pose or dress for the purpose of creating an atmosphere of importance was not in his nature. Throughout his life he carried the aura of youth and all who became cognizant of his many interests and enthusiasms, hopes and aspirations acquired great affection for him.

The writer is indebted to Mrs. Zinsser for several letters containing much information about the early years of Dr. Zinsser.

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KEY TO ABBREVIATIONS IN BIBLIOGRAPHY

Am. J. Digest. Dis. and Nutrition = American Journal of Digestive Diseases and Nutrition
Am. J. Hyg. = American Journal of Hygiene
Am. J. Pub. Health = American Journal of Public Health
Am. Med. = American Medicine
Arch. de l'Inst. Past. de Tunis = Archives de l'Institute Pasteur de Tunis
Arch. Dermat. and Syph. = Archives of Dermatology and Syphilology
Arch. Int. Med. = Archives of Internal Medicine
Arch. Path. = Archives of Pathology
Boston Med. and Surg. J. = Boston Medical and Surgical Journal
Bull. N. Y. Acad. Med. = Bulletin of the New York Academy of Medicine
C. R. de la Soc. de Biol. = Comptes Rendus des Seances de la Societe de Biologie
Harvard Alumni Bull. = Harvard Alumni Bulletin
Harvard Grad. Mag. = Harvard Graduate Magazine
Harvard Univ. Press = Harvard University Press
J. A. M. A. = Journal of the American Medical Association
J. Bact. = Journal of Bacteriology
J. Exp. Med. = Journal of Experimental Medicine
J. Immunol. = Journal of Immunology
J. Indust. Hyg. = Journal of Industrial Hygiene
J. Lab. and Clin. Med. = Journal of Laboratory and Clinical Medicine
J. Med. Res. = Journal of Medical Research
J. Preven. Med. = Journal of Preventive Medicine
J. Roy. Army Med. Corps = Journal of the Royal Army Medical Corps
Med. Rec. = Medical Record
Mem. Nat. Acad. Sci. = Memoirs, National Academy of Sciences
Mil. Surgeon = Military Surgeon
Milton Grad. Bull. = Milton Graduate Bulletin
Nat. Med. J. China = National Medical Journal of China
N. E. J. Med. = New England Journal of Medicine
N. E. Quarterly = New England Quarterly
N. Y. Med. J. = New York Medical Journal
Proc. Nat. Acad. Sci. = Proceedings of the National Academy of Sciences
Proc. N. Y. Path. Soc. = Proceedings of the New York Pathological Society
Proc. Path. Soc. Phila. = Proceedings of the Pathological Society of Philadelphia
Proc. Soc. Exp. Biol. and Med. = Proceedings of the Society for Experimental Biology and Medicine
Trans. Am. Neisserian Soc. = Transactions of the American Neisserian Society
Trans. Assoc. Am. Phys. = Transactions of the Association of American Physicians

Trans. Coll. Phys. = Transactions of the College of Physicians
Trans. Coll. Phys. Phila.=Transactions of the College of Physicians of Philadelphia
War Medicine, Paris = American Red Cross Society in France

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