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ALPHONSE RAYMOND DOCHEZ

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*A Biographical Memoir by*  
MICHAEL HEIDELBERGER, YALE KNEELAND, JR. AND  
KATHERINE MILLS PRICE

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*Biographical Memoir*

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# ALPHONSE RAYMOND DOCHEZ

*April 21, 1882–June 30, 1964*

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**T**HERE ARE, among scientists, some who prefer to work mainly with their hands, gathering, recording, and disseminating new facts. At the other extreme are the thinkers, who listen, read voraciously, and synthesize the handiwork of the first group into theories that show the way to further progress. Alphonse Raymond Dochez began his scientific career as a simple worker in the laboratory, but matured rapidly into the rare combination of the gatherer of facts and the thinker. In addition, he possessed the gift of articulate expression, and as he loved to talk, he radiated inspiration and ideas to an admiring and ever-expanding circle of colleagues.

Dochez was born in San Francisco, of Belgian descent, on April 21, 1882. His parents were Louis and Josephine Dietrich Dochez. Little is known of his early childhood except that his mother and her several small children went to Indianapolis where Alphonse received his pre-college education. Eventually they settled at his mother's parents' farm in Harford County, Maryland. Here young Dochez fished in the streams emptying into upper Chesapeake Bay, hunted, and wandered in the hills. The while his mother instilled in her son a strict conformity to the rituals of the Catholic church as well as a broad tolerance

and an undeviating kindliness. For his formal education he commuted daily to Baltimore on the Baltimore and Ohio Railroad, which passed near his home. After acquisition of a B.A. degree at Johns Hopkins in 1903, he was still undecided as to a career but began the study of medicine at the insistence of an eccentric and visionary uncle who soon after departed for Venezuela and was never again heard from. At this period the family operated a small cannery on the farm, putting up corn and other products.

Dochez received his M.D. degree in 1907. While he apparently enjoyed his undergraduate medical education, it is uncertain when his bent as an investigator began to develop. It is said that at about Christmas-time of his first year in medical school he was informed that in all likelihood he would fail anatomy. Shocked by this information, he expressed incredulity. The professor replied that he had never seen him in the laboratory on Saturdays for the entire autumn term. "But," interjected Dochez, "I always go shooting on Saturday." The conversation must have had some effect, for he did pass anatomy, but his career as a hunter was curtailed if not terminated.

Immediately after graduation he entered the laboratory of pathology at Johns Hopkins, where he spent a year studying the effects of an iodine-free diet upon animals. Hearing by chance that the newly organized Rockefeller Institute for Medical Research might have an opening, Dochez went to New York for an interview with Dr. Simon Flexner, the director, since no young aspiring unknown could be appointed without Dr. Flexner's personal approval. Dochez evidently passed muster, for he was given a fellowship in pathology at the Rockefeller Institute with Dr. Eugene Opie, who, at this writing, was again at work there in spite of his great age. Dochez referred to his year or two with Opie as "only too short." The results of his studies with Opie were included in four papers on the activation of trypsin and other enzymes. Many years

later Dochez looked back with great interest on this pioneering work with proteolytic enzymes in the liver and regretted that the findings did not seem to have been much heeded.

In 1910 the hospital of the Rockefeller Institute was opened under the directorship of Dr. Rufus Cole. Dochez was offered an assistant residency, and also the position of bacteriologist to the hospital. He remembered years later with some amusement having asked Hideyo Noguchi, who was also at the Institute, if one could possibly become a bacteriologist in three weeks. Whether Noguchi replied affirmatively is not recorded, but in any event Dochez became a bacteriologist and remained a microbiologist to the end of his life. His appointment at the hospital of the Rockefeller Institute was also a clinical one, and he remained as assistant resident and resident for five years, during which he was a major participant in the famous studies which were instituted there on lobar and bronchial pneumonia. Broadly speaking, Dochez's contributions may be summarized as follows: he established a biological classification of pneumococci into specific types. He and Oswald T. Avery discovered the soluble specific substance which confers type-specificity upon the pneumococci and yields precipitates with the homologous antiserum, showed that the substance was of capsular origin, and demonstrated its frequent presence in the blood and urine of patients during the acute stage of pneumonia. Dochez loved to tell how he and Avery reasoned that, since the soluble substance occurred in the blood of patients gravely ill with pneumonia, being soluble and diffusible, it should also pass through the kidneys and appear in the urine. They accordingly sent for a sample of the urine of a patient with a severe Type II pneumonia and set it up against some Type II antipneumococcal serum. No precipitation occurred, so they sat around glumly looking at the clear liquid in the test tube, wondering how and why their reasoning could have been wrong. Finally, one of them walked over to

the vase of urine and looked at the label: it was from another patient! Needless to say, the test was positive when the proper specimen was obtained.

Dochez, Avery, and their co-workers demonstrated the importance of type-specific antibodies in the mechanism of recovery from pneumococcal pneumonia. This led directly to the production of type-specific antipneumococcal horse serum, and they demonstrated the efficacy of this serum in the treatment of Type I pneumonia. Type-specific antisera, especially those later raised in rabbits, and, more particularly, the purified globulin of the rabbit antisera, remained the only effective therapy of pneumococcal pneumonia until the introduction of the sulfa-drugs and penicillin. Dochez's studies of the pneumococcus lasted for about nine years, and this body of work fully warrants the application of that somewhat overworked word "classical."

Dochez continued his clinical studies of respiratory diseases as a major in the Medical Corps in World War I and made many trips in efforts to control outbreaks. In 1919 he returned to the Johns Hopkins Medical School as Associate Professor of Medicine. It was here that he began his studies of the streptococcus and its relationship to scarlet fever which he continued after he joined the staff of the College of Physicians and Surgeons of Columbia University in 1921 as Professor of Medicine. At the time Dochez started his studies of scarlet fever, the streptococcal etiology of that disease had not been established and, in many quarters, was regarded with skepticism. Dochez showed that there was a direct relationship between streptococcal pharyngitis and scarlet fever, and that most of the strains of streptococci isolated from patients with scarlet fever belonged to a single, specific type.

Dr. Franklin M. Hanger, Jr., later also Professor of Medicine at the College of Physicians and Surgeons of Columbia University, writes of this work: "I remember well when

Dochez injected melted agar under the skin of a young pig and inoculated it with his Pr 1 strain of streptococcus. A few days later, at about eleven o'clock at night, he called me excitedly on the phone to come up to his laboratory. There was his little pig, as rosy as a boiled lobster! The logical next step was to immunize a horse by the same procedure, and this Doh, as he was familiarly called, started in the stables of the Rockefeller Institute." The antiserum, injected intradermally, blanching the rash of scarlet fever, and given parenterally, had a striking therapeutic effect. An epidemic of scarlet fever in New Haven provided the first large-scale opportunity to test the serum, and its beneficial effects were enthusiastically reported by a number of observers.

Unfortunately, Dochez's studies of streptococcal infections were terminated by a legal decision handed down in favor of George F. and Gladys H. Dick of Evanston, Illinois. They had obtained British patent 243675, dated November 28, 1924, and U.S. patent 1,547,369, dated July 28, 1925, making broad claims as to the isolation of streptococci specific to scarlet fever, the preparation of a scarlatinal toxin, the injection of animals to obtain an antitoxin, and the antitoxin itself. Dochez had earlier taken out British patent 232181, dated April 14, 1924, but his U.S. patent 1,585,090, dated May 18, 1926, and assigned to the Presbyterian Hospital of New York, was issued after that of the Dicks. This apparently served as the basis for the decision of infringement of their patent, even though Dochez's ingenious method of production of the antitoxin in animals was not specifically mentioned in the Dicks' patent.

At the enforced conclusion of his studies of scarlet fever, Dochez shifted to the last of the three major fields of his endeavor. This was the common cold, or perhaps, more literally, common upper respiratory infection. His studies here were pursued in an orderly and systematic fashion. Dochez and his

younger collaborators Gerald S. Shibley, Alvin F. Coburn, Franklin M. Hanger, Jr., Yale Kneeland, Jr., and Theodore Badger first studied the bacterial flora of the upper respiratory tract and convinced themselves that these were not of primary etiological significance. Similar studies failed to incriminate the gram-negative filter-passing anaerobes. Then, using first chimpanzees and later *homo sapiens* as experimental animals, Dochez showed that typical colds could be produced by exposure of the subjects to bacteria-free filtrates, thus indicating a viral etiology. Attempts at cultivation of these filtrable agents showed promise, but the techniques of viral cultivation of the period were not adequate for the indefinite propagation of such infectious agents.

At the end of the 1930s Dochez found himself more and more involved in administrative work. In 1940 he was appointed chairman of the Department of Bacteriology at the College of Physicians and Surgeons, a post which he held for nine years, although he escaped as often as possible to return nearly every day for afternoon tea in his old haunts in the Department of Medicine. Here one was always privileged to drop in for half-an-hour's stimulating discussion with "Doh" of a "hot" problem or one that merited attention. Dochez retired in 1949, with the title of John E. Borne Professor of Medical and Surgical Research Emeritus, and continued his active interest in biological problems until nearly the moment of death. One of the last of his intellectual achievements was a profound and perceptive study of the problems of carcinogenesis, and he would discourse remarkably energetically upon these with visitors to his room in the Harkness Pavilion of the Presbyterian Hospital in New York. There he died on June 30, 1964, at the age of eighty-two. He had suffered progressive physical incapacitation for several years and had lived perforce a very secluded life.

It can be seen that Dochez's efforts resulted in major con-



tributions in three distinct and separate areas. As the late Oswald T. Avery remarked when presenting to him the Kober Medal of the Association of American Physicians, "Throughout his studies there is a unique continuity of thought centering in the dominant problem of acute respiratory diseases. The results of his work are not random products of chance observation. They are the fruits of years of wise reflection, objective thinking, and thoughtful experimentation."

His long-time co-worker, Katherine Mills, now Mrs. H. Stewart Price, writes: "I worked for Dr. Dochez as a laboratory technician for over thirty years. We on his laboratory staff felt we were working *with*, as well as for, him. He encouraged us to consider ourselves his research assistants. Our names were included in publications; indeed, on many of Dr. Dochez's papers, the order of names frequently began with that of a younger colleague or a lesser member of the team. I came in the autumn of 1924, when he was starting his research on the common cold. In the first interview he outlined the general strategy, planning to begin with an intensive study of the role of the usual respiratory pathogens and a separate consideration of the then recently described gram-negative filter-passing anaerobes. If, as Dr. Dochez thought even then, these studies showed that bacteria could not be implicated as the primary cause, he planned the study of viral agents. This was to be done by transmission experiments in carefully quarantined human beings and apes. If, and when, a viral etiology was established we would attempt to isolate and cultivate the agent, always with particular attention to finding a suitable small animal or a definitive laboratory test that would make possible large numbers of experiments. It was exciting to see the broad concept of the problem behind the technical details with which I would be concerned.

"This reasoned approach was characteristic. We were encouraged to look for new phenomena or hopeful leads, but to

keep to the main purpose and not wander down rosy by-paths. We were also urged to dig exhaustively into the archives. Dr. Dochez himself had an encyclopedic knowledge of the literature, and was scrupulously exact in citing the work of others.

"We were fortunate in the laboratory, for it was here that we saw Dr. Dochez frequently and on an informal basis. His lifetime interest in laboratory work never abated, despite the press of clinical and administrative demands. I think he enjoyed even the smell of a laboratory. It was amazing to see how he knew the smallest details of the daily routine. When he joined in the actual work his technique was a delight to watch. His instant grasp of a problem was of inestimable value. I well remember that when we ran into the agglutination of red cells by the pneumonia virus of mice we were baffled by the fact that, although the agglutination was striking in blood oozing from a cut surface of the lung, it could not be demonstrated in ground suspensions. This was during World War II and Dr. Dochez was not in the laboratory as often as usual. He came in one day, looked at a few Petri dishes with the cut lungs, said immediately that the agglutination was very definite, that something must be inhibiting it in the suspension, and to try inactivation with heat. With that he sauntered out, having solved the whole difficulty.

"We had tea in the laboratory every afternoon. While the basic group of our 'Tea Club' was small, it was extraordinary how many doctors developed a sudden thirst if they happened to catch a glimpse of 'the Boss' in his usual chair by the window. They would come in, quite casually of course, for discussions of their own work, and his interest and knowledge were always given with generous enthusiasm. Talk was generally along scientific lines, but also ranged from world affairs to the latest flurry in the stock market or the standing of the baseball teams. Dr. Dochez did not give the impression of being

an outdoorsman. He once told me that he had taken a camping trip, and thereafter it was years before he would stand in the shade of a tree! He was, however, an excellent shot in a duckblind, and his golf game was in the 70s. I believe he was one of the few golfers to have two holes-in-one to his credit. These feats delighted him almost as much as a successful experiment.

“Through all these years of spontaneous and uncensored conversation I never heard Dr. Dochez make an unkind remark about anyone or their work. He might keep silent, but he did not criticize, even with ample provocation. The loyalty and devotion of those who worked for Dr. Dochez were universal. This is all the more remarkable as he was very reserved and somewhat remote. But young and old, men and women, from porters to professors, regarded him with admiration and trust. His absolute lack of pettiness was reflected in the smooth functioning of the department. When one rather bitter feud smoldered in the lower echelons, personal animosities ran high, but both sides were agreed on at least one thing: the Boss should not be disturbed nor the work affected. He, of course, was aware of the friction—he didn’t miss much—but ignored it serenely, and eventually harmony was restored. He had a way of bringing out the best in people. We all realized we were privileged to work for a great man. His own work will stand for all time and that of many others was stimulated by him.”

During the years of World War II, and for some time thereafter, Dochez performed major services for the government. These included active membership in the Office of Scientific Research and Development and on the Board for Coordination of Malarial Studies, the Board for Control of Influenza and Other Epidemic Diseases, the Hoover Commission on the reorganization of the executive branch of the government, and a number of others. His effective work on these commissions earned him the Medal of Merit. In addition to

this and the Kober Medal, he was also the recipient of the Medal of the New York Academy of Medicine. He was a member of numerous learned societies, and served as president of the Association of American Physicians, the American Clinical and Climatological Association, and the American Association of Immunologists. He became a member of the National Academy of Sciences in 1933.

Dochez received an honorary degree from Yale University in 1926. Other honorary degrees came from New York University in 1925 and Western Reserve in 1931.

Dochez was never greatly impressed with the type of clinical investigation which consists in the acquisition of a new machine of some sort and then the recording of routine measurements. Rather he preferred to tackle a major problem from a new point of view. He always maintained that if one had a thorough and selective knowledge of the literature one could find clues. These clues one sorted in one's head until some sort of tentative hypothesis emerged and then one devised a simple experiment to test it. If this yielded what he used to speak of as an "indication," then one repeated the experiment, and if the indication was still present one devised a larger and more formal series of experiments to establish a convincing theory.

It goes without saying that such a man was constantly being consulted by his colleagues about their researches, even when these were in fields widely separated from his own. And seldom did one of them emerge from such a conference without a feeling that his thinking had been clarified and the problem better defined. If the field were related to Dochez's own, his suggestions were often miraculously helpful.

The foregoing paragraphs have indicated some of the high points of Dochez's career and have attempted some notion of his accomplishments and his *modus operandi*. But a memoir would be incomplete without further description of the man

himself, his character and personality. To begin with, he was extraordinarily handsome and endowed with a very good figure. Although he never discussed clothes, it was perfectly obvious that he liked them and had developed to a very high point the art of fastidious and elegant dressing. Seeing him on Fifth Avenue one would never in the world suspect that one was looking at a distinguished biological scientist. He was widely read and had a knowledgeable appreciation of music and the graphic arts. As an extremely attractive and eligible bachelor he was much sought after for many years in New York society. Most conspicuously, however, he was *not* a name-dropper, and the only notion of exalted social circles in which he moved came if one happened to bump into their periphery oneself. A lady once remarked to him that for a scientist he seemed to spend a good deal of time in various boxes at the opera. His rejoinder was that, while he might seem to be in a state of suspended animation, this was, in fact, the time in which he did much of his most solid and productive thinking. And it would appear that not infrequently he returned from the Metropolitan Opera, discovered Dr. Avery, with whom he shared an apartment, reading quietly in bed, and then would sit down in full evening dress and with vast animation describe to his old friend some of the illuminating thoughts on the subject of microbiology which had occurred to him during the second act of *La Traviata*, or whatever the evening's opera had been. Dochez was a devout Roman Catholic although he never discussed religion. If unable to escape from gossip, he might listen to it, but he never repeated what he heard. For him to have made an unkind or invidious remark about one of his associates or acquaintances would have been unimaginable. Occasionally, under great stress, he might show faint symptoms of annoyance, but these melted away with a laugh. If he ever lost his temper no one saw him do it. He was deeply uninterested in the more squalid aspects of life.

All those who saw anything of him in the last few years of his life were impressed by his unflagging passion for biological speculation, and it is noteworthy that two years before his death, at a time when he was already afflicted with partial motor aphasia, he composed an extraordinarily intelligent "Letter to the Editor" on the nature of the malignant cell which was published in the *Lancet*.

Those who knew Dochez well have reserved for him a special and unique place in their memories. There was no one like "Doh," nor does it seem likely to his old friends that there will ever be another comparable figure.

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## KEY TO ABBREVIATIONS

- Bull. Johns Hopkins Hosp. = Bulletin of the Johns Hopkins Hospital  
J. Am. Med. Assoc. = Journal of the American Medical Association  
J. Exp. Med. = Journal of Experimental Medicine  
Monogr. Rockefeller Inst. Med. Res. = Monographs of the Rockefeller  
Institute for Medical Research  
Proc. Soc. Exp. Biol. Med. = Proceedings of the Society for Experimental  
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Trans. Assoc. Am. Physicians = Transactions of the Association of American  
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