THE SCIENTIFIC WORLD OF JAMES W. McLAUGHLIN, M.D.

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Introduction

The James W. McLaughlin Fellowship Fund for the Investigation of Infection and Immunity, which currently supports various pre- and postdoctoral research projects, seminars, and visiting professorships here on the UTMB campus, was established by Andrew Cyrus McLaughlin (1875-1952). In 1951, Mr. McLaughlin visited the campus where his father James Wharton (1840-1909) had taught principles and practice of medicine nearly half a century earlier. Andrew Cyrus died in January 1952, leaving the bulk of a one-million-dollar estate to UTMB. The will read:

> I bequeath all other property of which I die possessed to the School of Medicine, University of Texas, to establish and maintain fellowships to be known as the James W. McLaughlin Fellowships for the Investigation of Infection and Immunity.[1]

Andrew McLaughlin, resident of California at the time of his death, was a petroleum geologist and had been involved in the development of the Rangeley Oil Field in northwestern Colorado. His handwritten will was contested for more than a year, and finally the Supreme Courts of Colorado and California upheld it. The Medical Branch awarded the first James W. McLaughlin Fellowship during the academic year 1954-55.

Andrew McLaughlin had only an indirect connection with the medical school to which he bequeathed a major portion of his estate. We know that he graduated with a B.S. degree in geology from The University of Texas at Austin in 1896, the year before his father was appointed professor of medicine in the Medical Department at Galveston. During his father's tenure in Galveston (1897-1905), the young Andrew likely received some exposure to the activities and aspirations of the medical faculty and students, and undoubtedly these early impressions were important. His most likely reason for wanting to establish a research fund in immunity and infectious disease, however, appears to have been the insight he had into his father's long-standing interest in this field. For two decades, from 1888 to his death in 1909, James McLaughlin wrote and lectured on infection and immunity. He followed closely developments in microbiology and attempted to account for the mechanisms of immunological response in terms of physico-chemical principles. Reading James McLaughlin's papers on infection and immunity provides one with a delightful glimpse of late-nineteenth-century science.

In a previous essay, I touched upon the highlights of James McLaughlin's life.[2] Briefly, he was born and received his early education in Ohio. After the Civil War, he moved to Texas, and spent most of his medical career as a general practitioner in Austin. The only academic appointment he held was in Galveston. After eight years of service in the Medical Department of the University of Texas, he resigned his chair and returned to private practice in Austin. James McLaughlin published about thirty papers and one book on infectious diseases and immunology. Most of his papers were of a clinical nature, and covered descriptions of symptoms, case histories, and methods of therapy. He wrote extensively on contemporary work relating to infection and immunity, and reiterated his own theory of immunity. As far as I know, only two papers, both on dengue fever, dealt with the results of experimental research carried out by McLaughlin.

Historical Background

In the 1880s most scientists recognized the pervasive nature of microorganisms and their involvement in a multitude of life processes. The microscopic investigations carried out within the previous decades had shown that minute organisms were the cause not only of fermentation and decomposition of organic matter but also of many infections. Medical scientists also understood something about the role of the body's natural defense mechanism in guarding against various bacteria. In McLaughlin's words:

> Observation and experience teach that we are surrounded by countless numbers of bacteria; that the food we eat, the water we drink and the air we breathe are more or less contaminated by microbes, and if it were not for the fact that many of these are harmless, and that we have natural immunity from others that are virulent, man would soon cease to exist.[3]

It was therefore important to gain a clear understanding of the body's immunological response to invading bacteria. Given his early interest in the field, McLaughlin was perhaps among the first to realize that the control of infectious diseases would greatly depend on the elucidation of the principles of immunology.

It is within the general framework of Louis Pasteur's investigations that we must review the early work in immunology. In the late 1850s, Pasteur showed that the process of fermentation was not basically chemical in nature but involved the activity of microorganisms. The yeast used in the manufacture of alcohol from grain and beet sugar consisted of living "ferments." In the next decade, Pasteur proved that each microorganism is derived from a pre-existing organism, and suggested that diseases, like various types of fermentation, may be caused by specific germs. The work carried out by Pasteur and his collaborators in the late 1870s and the 1880s on anthrax, fowl cholera, swine erysipelas, and rabies marked the establishment of immunology. These early investigations demonstrated that attenuated forms of microbes could be employed in immunizing animals and indicated the possibility of extending similar treatments to other diseases. Pasteur's work stimulated scientists to turn their attention to a new area, and to study susceptibility to disease, natural immunity as differentiated from acquired immunity.

By the end of the 1880s, a new branch of science called immunology began to emerge along two lines.[4] On the one hand, scientists became engaged in work of a practical nature, using Pasteur's method of inoculation with attenuated bacteria or viruses. On the other hand, investigators occupied themselves with speculations on the nature of immunity. Two schools of thought arose regarding immunity. The supporters of the humoral theory, individuals such as J. Fodor and G.H.F. Nuttall, explained immunity in terms of substances in the bloodstream that were inimical to the growth of infective agents. Another view, put forward and championed by E. Metchnikoff, attributed the immunological mechanism to the activity of cells (phagocytes) that engulfed the invading pathogens. The controversy among the adherents of the humoral and cellular theories of immunity continued through the 1890s and beyond.[5]

McLaughlin's Experimental Work

James McLaughlin became interested in immunological studies during the initial stages of development of this new branch of medicine. He published his first research paper in 1886, reporting the results of his investigations on dengue. In 1885, the year Louis Pasteur first tested his rabies vaccination on man, an epidemic of dengue hit Texas, severely affecting the populations of Galveston and Austin. McLaughlin suspected, given the contagious nature of the disease, "that microorganisms are the source of its infection, and these microorganisms find in the blood a suitable environment for their growth and multiplication."[6] His research on dengue consisted of the microscopic examination of blood samples drawn from patients during different stages of the disease. He employed various chemicals and staining agents, and described at length his methods of sterilizing the test tubes and other instruments used in experiments. Believing that he had isolated the "bacteria" responsible for dengue fever,[7] he published his results in a prominent medical journal. At the same time, however, McLaughlin was aware of the shortcomings of his research work. First, he had not fully tested Koch's postulates with regard to the dengue microorganism. Secondly, his original hopes of finding a method of therapy and prophylaxis, as he himself admitted, were unrealistic. Such extensive projects required special laboratories and investigators who could spend full time in research. A physician like himself "engaged in active practice," he said, "has but little time, whatever his inclination may be, to indulge in experimental work."[8] He urged that the state or federal government sponsor medical research aimed at preventing disease by inoculation.

The work on dengue fever constituted the only experimental research James McLaughlin undertook. Although he published a second paper on dengue in 1895, it did not include new experiments, but rather a discussion, with illustrations, of what he had seen in the blood of dengue patients.[9] The rest of his publications on immunological topics remained at a theoretical level. In a paper published in 1888, McLaughlin put forward his views on causation of disease, and pointed out the similarities between the processes of fermentation and infection.[10] Since the fermentation theory of disease was a commonly expressed view at the time, that portion of his work did not contain anything original. However, he went one step further and attempted to explain immunological response in terms of molecular physics.[11] Then followed a series of nine papers published in **The Texas Sanitarian** in 1891-92,[12] which later formed the basis of his monograph **Fermentation, Infection and Immunity** (1892).

McLaughlin on Infection and Immunity

McLaughlin referred to his theory of immunity as "the physical theory," and insisted that all biological phenomena should be explained by considering physicochemical principles that govern the physical world.

> . . . I became convinced that chemical and physical action occurring within animal and vegetable structures offers no exception to this law of nature, and, that a solution of the problem involved in the causation of fermentation, infection and immunization could not be arrived at except by investigating these subjects from a physical standpoint.[13]

Taking a mechanistic approach, McLaughlin tried to argue that scientific explanations given in terms of "vitalistic forces" hindered medical progress. "We desire to state our belief," he said, "that the chief difficulties which stand in the way of a correct knowledge of immunity, are the obscure vitalistic conceptions which are entertained regarding the physical forces of the body."[14] At the molecular level, atoms of living matter did not behave any differently from those of inanimate matter. Only one set of principles, the laws of particulate matter in motion, which had been revealed through the investigations of physicists like Lord Kelvin and James Clerk Maxwell, applied to the "living and non-living alike." McLaughlin further entertained a belief in the existence of ether as "a continuous universal medium" that transmitted atomic and molecular motions in the form of ether waves.[15] Thus it is not surprising to find that his theory of infection and immunity necessitated explanations given in terms of wave motions of pathogenic organisms and "albumin molecules" of the host.[16]

Fermentation and infection, McLaughlin repeatedly emphasized, were similar processes. This idea had been first suggested by Robert Boyle in the seventeenth century, and a number of physicians had since maintained the same view.[17] It was not until after Pasteur's early investigations on fermentation, however, that Boyle's original idea could be defended on scientific grounds. The fermentation theory of disease was revived in the 1870s and discussed widely in the literature.[18] McLaughlin's views may be summarized as follows:

Both fermentation and infection were caused by "living ferments" or microorganisms. The yeast cells served the same function in the production of alcohol as the pathogenic bacteria in the causation of disease. These organisms multiplied alike during the process of fermentation and of infection, and they produced "only their own kind." Just as the nature of fermentation varied with the specific ferment involved, a specific bacterium resulted in a specific disease. Again, both ferments and pathogenic bacteria could be destroyed by heat, antiseptics, and other methods, or could be attenuated by artificial techniques and environmental causes.[19]

The process of fermentation was self-limiting in the sense that when the production of alcohol reached a certain level the reaction stopped. Similarly, pathogenic bacteria gave rise to certain end products (toxins), which inhibited further bacterial activity (and the patient recovered). "The resulting products of the process," wrote McLaughlin, "whether they be infectious or fermentative, are antibodies which tend to inhibit or to arrest the process of which they are the products." That is, the sugar in fermentation or the albumin molecules of the body in pathogenesis were broken down by microorganisms, and the end products eventually interfered with the process.[20]

In terms of this model of pathogenesis based on fermentation, McLaughlin explained immunity to a specific disease by the absence of "susceptible" albumin molecules. Certain species of animals or certain individuals would remain immune to a given pathogenetic agent as long as "body juices do not contain susceptible albuminoids."[21] While admitting that factors such as fear and other emotional disturbances, fatigue, and drugs could decrease the natural resistance of the body to disease, McLaughlin did not explain how these factors could affect the chemical constitution of the body.

Concluding Remarks

However speculative it may seem to us now, the above discussion defines the scientific context within which James McLaughlin considered the problems of infection and immunity. His writings on the topic coincided with some of the early developments in immunology. McLaughlin was a contemporary of Robert Koch, Louis Pasteur, Emil von Behring, Paul Ehrlich, Elie Metchnikoff, and Richard Pfeiffer, individuals whose work helped to establish immunology on a scientific basis. His theory of immunity incorporated many elements of then current research and was in line with the scientific speculations of the period. Although McLaughlin continued to defend the fermentation theory of disease with certain modifications for nearly two decades, he was aware of the changing nature of immunology and its implications for medicine. In a lecture he gave at the Texas Academy of Science in 1909, he expressed perhaps his last thoughts on the issue:

> It seems, therefore, in the present state of knowledge, that the nature and action of pathogenic agents, the origin and nature of specific antibodies, and the character of immunizing changes that toxins produce in the tissues of the body in the process of its infection and immunization are not sufficiently definite to afford a sound basis on which to construct a rational and lucid theory of pathogenesis and immunization; and yet no subject, surely no medical subject, has received within the present decade greater consideration or more scientific investigation by persons equipped for the work.[22]

A physician for nearly half a century, McLaughlin dealt with infectious disease on a daily basis and knew well the devastation caused by disease. His long-time interest in the contemporary developments in microbiology and immunology was indeed an expression of his faith in science as a tool to alleviate human misery. If McLaughlin himself did not have the opportunity to conduct medical research, he understood its importance, and believed that a physician "can greatly prolong human life and decrease human suffering by promulgating his knowledge of the medical sciences."[23]

The James W. McLaughlin Fund, which presently suppports an active research program in infectious disease and immunology on the UTMB campus, was established by A.C. McLaughlin in memory of his father. James McLaughlin's professional aspirations and concern for medical research undoubtedly had direct bearing on the establishment of the Fund. Some of us, while trying to keep up with the fast pace of contemporary living, may be inclined to disregard the past as irrelevant. Upon investigation, however, we may find that the aspirations of past figures have molded our own activities and ambitions.

REFERENCES

[1]The University of Texas Medical Branch at Galveston. **A Seventy-Five Year History by the Faculty and Staff** (Austin: University of Texas Press, 1967), p. 77.

[2]I.A. Bowman, "James Wharton McLaughlin (1840-1909)," **The Bookman** 7(5):3-8, 1980.

[3]J.W. McLaughlin, **Fermentation, Infection and Immunity** (Austin: Eugene von Boeckmann, 1892), p. 88.

[4]W. Bulloch, **The History of Bacteriology** (London: Oxford University Press, 1960), p. 255.

[5]Ibid., pp. 256-57.

[6]J.W. McLaughlin, "Researches into the Etiology of Dengue," **Jour. Amer. Med. Assoc.** 6:673, 1886.

[7]We now know that dengue is a disease of viral origin, and with the microscopes available to him McLaughlin could not have seen the dengue virus. The pathogen in question was not isolated until 1953.

[8]McLaughlin, "Researches into the Etiology of Dengue," p. 673.

[9]J.W. McLaughlin, "The Bacteriology of Dengue," **Texas Med. News** 5:11-15, 1895.

[10]J.W. McLaughlin, "The Etiology of Infectious Diseases," **Daniel's Texas Med. Jour.** 3:266-74, 1888.

[11]J.W. McLaughlin, "An Explanation of the Phenom-

ena of Immunity and Contagion, based upon the Action of Physical and Biological Laws," **Med. Rec.** (N.Y.) 38:29-38, 1890.

[12]J.W. McLaughlin, "Contagion and Immunity," **The Texas Sanitarian** 1:1-14, 73-86, 1891; 1:193-205, 243-55, 293-308, 355-72, 401-18, 445-59, 487-505, 1892.

[13]McLaughlin, **Fermentation, Infection and Immunity**, p. 4.

[14]Ibid., p. 92.

[15]Ibid., Chapter 4.

[16]J.W. McLaughlin, "The Fermentation Theory of Infection and Immunity," **Amer. Jour. Med. Sci.** 76:901, 1903. McLaughlin wrote:

> The forces involved in the fermentation theory of immunity are those operating in nature within and without the living organism. They are the forces which constitute motion in matter, and are the same when manifested in the operations of the telephone, the phonograph, or in wireless telegraphy, that they are in bringing about atomic rearrangement in albumin molecules in the production of immunity.

[17]Ibid., p. 887. McLaughlin stated:

> That the phenomena of fermentation and of infection and immunity are strictly analogous processes and that these analogies point unerringly to a common causation has been recognized for more three hundred years; yet the common cause has heretofore remained a mystery.

[18]J. Tyndall, **Fermentation and Its Bearing on the Phenomena of Disease** (London: William Collins, Sons, & Company, 1877).

H. Knapp, "Fermentation, Putrefaction, and Suppuration, with Demonstrations and Experiments," **Med. Rec.** (N.Y.) 30:701-705, 1886.

[19]McLaughlin, **Fermentation, Infection and Immunity**, pp. 25-27.

[20]McLaughlin, "The Fermentation Theory of Infection and Immunity," p. 894. Here is another sentence that sheds light on McLaughlin's conception of an antibody:

> There may be unfermented sugar and yeast cells ready to ferment it, but no fermentation will take place while the percentage of alcohol remains. The sugar is immune to the activity of the yeast cells, and alcohol is the immunizing agent, because its wave energy opposes that of the yeast and sugar; it is, therefore, an antibody.

[21]Ibid., p. 896.

[22]J.W. McLaughlin, "A Catalytic Theory of Infection and Immunity," **Med. Rec.** (N.Y.) 75:749, 1909.

[23]J.W. McLaughlin, "Address to Students, delivered at the Opening of the Session of 1899-1900," **The University Medical** (Galveston) 5(1):5, 1899.