11-2020

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AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

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William A. Hinton, M.D. (Image used with permission of the artist, Stephen Coit. All rights reserved.)

The Waterhouse Room is where faculty council meets, where we host events to send off retiring members of our community, convene to mourn people we have lost, or to celebrate when members of the faculty are appointed to an endowed chair, as a few examples. I think it is fair to say that it is the school's principal "grand space." The portraits (both paintings and photographs) displayed on its walls are a selection of past deans, pioneers, and other notable figures from the school's history.

The Waterhouse Room is the main convening space in our Harvard Medical School administration building, and it is emblazoned with the oil portraits of our founders and past deans (not all, but the most recent). Oliver Wendell Holmes, Sr., the father of the great jurist is there, as are photo portraits of four illustrious female faculty members. There had previously been a photo portrait of Hinton but we sourced a glorious oil portrait that served as a major upgrade, and we celebrated the unveiling with a fantastic tribute ceremony. It stands as a great honorific to a remarkable physician, scientist, and pioneer.

As a brilliant scientist and educator, Dr. Hinton belongs there. But this first large-scale oil painting of an African American in the Waterhouse Room also represents

Citation Munson E. 2020. Biographical Feature: William A. Hinton, M.D. J Clin Microbiol 58:e01933-20. https://doi.org/10.1128/JCM.01933-20.

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Accepted manuscript posted online 5 August 2020
Published 21 October 2020

an expression of Harvard's reckoning with its own history, and of the centrality of diversity and inclusion to its own mission today. From my standpoint as a faculty member, this is what Harvard Medical School aspires to be.

The preceding passages are from M. William Lensch, Ph.D., George Q. Daley, M.D., Ph.D., and Scott Podolsky, M.D., who hold the titles of Strategic Advisor, Dean of the Faculty of Medicine, and Professor of Global Health and Social Medicine, respectively, at Harvard Medical School in Boston, Massachusetts. (Dr. Podolsky also serves as Director of the Center for the History of Medicine for the Harvard Countway Library.) These were provided in response to an inquiry regarding the significance of the portrait gallery located in the Waterhouse Room within Gordon Hall of Harvard Medical School. This brief monograph will attempt to shed significance on the career of William A. Hinton, M.D., the first African American to be honored by commission of an oil portrait (illustrated at the beginning of this feature) in the Waterhouse Room.

William Augustus Hinton was born in Chicago, IL, in December of 1883. Both of his parents were freed slaves, with his father becoming a farmer and a railroad porter and his mother also becoming a farmer. Following graduation from high school in Kansas City at the age of 16, Hinton undertook undergraduate studies at the University of Kansas from 1900 to 1902 before completing his baccalaureate degree at Harvard College in 1905. Prior to his matriculation at Harvard Medical School in 1909, Hinton furthered his studies of physiology and bacteriology at the University of Chicago, taught embryology at Meharry Medical College in Nashville, TN, and taught other science coursework at Oklahoma Colored Agricultural and Normal University (now Langston University) in Langston, OK, and at Walden University, also in Nashville. He received the Hayden Scholarship (noncompetitive award for African American students with an estimated value of $250) during his early tenure at Harvard Medical School; Hinton was also awarded the competitive Wigglesworth Scholarship (estimated value, $200) toward the end of his medical studies. He further supplemented his income during medical school by working in the laboratories of clinical hematologist Richard Clarke Cabot (a social work pioneer and cofounder of the Case Records of the Massachusetts General Hospital) and the neuropathologist and neuropsychiatrist Elmer E. Southard (founder of the Wassermann Laboratory within Harvard Medical School in 1909).

Dr. Hinton was unable to obtain a surgical residency or internship opportunities upon his graduation from Harvard Medical School with honors in 1912 because of his race. He instead took a position teaching serologic techniques at the Wassermann Laboratory and became familiar with serologic methods for laboratory diagnosis of syphilis, as well as their potential limitations. Dr. Hinton also was a voluntary assistant in the Massachusetts General Hospital Department of Pathology (chaired by influential pathologist and second cofounder of the Case Records of the Massachusetts General Hospital James Homer Wright) from 1912 to 1915, performing autopsies on all deceased individuals suspected of having syphilis. He also worked on *in vivo* cultivation methods for *Treponema pallidum* subsp. *pallidum* using the rabbit host. In 1915, Dr. Hinton was selected as Director of the Laboratory Department at the Boston Dispensary (a predecessor to Tufts Medical Center). In that same year, the financial support of the Wassermann Laboratory was transferred from Harvard Medical School to the Massachusetts Department of Health. This transaction likely coincided with 1915 Massachusetts legislation to make syphilis serologic testing free of charge. Dr. Hinton was appointed Chief of the Wassermann Laboratory and Associate Director of the State Biologic Laboratories (located off campus in the Jamaica Plain neighborhood of Boston). He served in those administrative capacities until his retirement in 1953.

The proximity of the Wassermann Laboratory to the Peter Bent Brigham Hospital (established in 1913) further facilitated a career of expertise for Dr. Hinton relative to syphilis serology. In this venue, Dr. Hinton rounded on syphilis patients and became proficient in the correlation of laboratory data with clinical presentation in both inpatient and outpatient settings. To provide some historic perspective, one of the

earliest laboratory modalities for serum diagnosis of syphilis was the complement fixation-based Wassermann test, published in 1906 (1). Because of the initial belief that syphilis detection was immunologic in nature, livers of infants who had died of prenatal syphilis were utilized as the source of antigen. The first non-complement fixation-based assay for laboratory detection of syphilis was published in 1907. Michaelis (2) reported visible precipitate upon the mixing of syphilitic serum with watery extracts of syphilitic liver. As this technique became more refined and investigators began to utilize alcohol extracts of heart muscle as the antigen, it was determined that the precipitate formed in this laboratory assay consisted mainly of lipids. Colloids coming out of suspension (as a result of interaction with syphilitic serum) to form flocs or flakes was known as a flocculation reaction.

Perhaps the first widely utilized flocculation reaction for laboratory detection of syphilis in the United States was the Kahn test, published in 1922 (3). Kahn deduced that the performance characteristics of the assay, as well as time to detection, were influenced by antigen concentration and addition of a sodium chloride solution. Kline and Young (4) subsequently published an adaptation of the three-tube Kahn test to allow the assay to be performed on a microscope slide.

In 1927, Dr. Hinton published a study (5) in which the addition of glycerol to non-complement fixation assays for syphilis enhanced the laboratory diagnosis of the disease. Dr. Hinton hypothesized that glycerol addition resulted in both the formation of larger aggregates of cholesterol (with a complete clearing of fluid) and the protection of cholesterol from degradation. Also important to the test was a combination of cholesterol and beefsteak muscle indicator (Dr. Hinton refrained from using the term "antigen" when characterizing his assays, opting for the term "indicator" because the tests were not immunologic in nature [6]). In an initial assessment, the Hinton test was reported to be positive in 113 cases of clinically diagnosed syphilis; the Wassermann test was positive in 61 of those cases. In 368 nonsyphilitic patients (over 50% of which were pregnant women), the Wassermann test returned 3 positive results, with the Hinton test returning none. Two years later, Hinton and Berk (7) reported that modification of the Kahn test protocol to include glycerol improved the performance characteristics of the Kahn test but not to the extent of those reported from the Hinton test.

Cheever and Splaine (8) compared the performance characteristics of the Wassermann test, Kahn test, Kline and Young microscope slide test, and Hinton test on a population of 1,610 consecutive patients admitted to medical, gynecology, genitourinary, dermatology, and selected other departments of a large U.S. hospital; some patients were screened for syphilis more than once during the investigation. Over one-quarter of these patients were clinically diagnosed with syphilis. Concordant results over all four tests were documented for 84% of patients. With respect to a subset of 77 patients with clinically diagnosed syphilis that yielded discordant results throughout the investigation, positive detection rates of 91%, 72%, 69%, and 57% were noted with the Hinton, Wassermann, Kline and Young, and Kahn tests, respectively. In a subset of 9 patients who consistently yielded negative Hinton test results, results derived from Kahn, Kline and Young, and Wassermann testing were reported positive in 56%, 44%, and 33% of instances, respectively. In the same study cohort, the Hinton test was reportedly 50% more sensitive than the Wassermann test in the diagnosis of what was categorized as asymptomatic syphilis, with a paucity of false-positive results (9). Root and Stuart (10) later confirmed the relatively high specificity of the Hinton test in a study of 1,078 diabetic blood specimens and determined that a proclivity for false-positive results derived from the Wassermann test and the Kahn test was independent of variations in blood glucose, cholesterol, pH, and albumin.

Dr. Hinton published two additional modifications of the Hinton test (11, 12) prior to having the assay endorsed by the U.S. Public Health Service in 1934. Both modifications, in part, resulted in a decreased time to a reportable result, with the third modification consolidating the assay from four tubes to a single tube. In one of these papers (11), Dr. Hinton spoke to the standardization of syphilis testing protocols: "We

wish to stress the importance of strict adherence to minutiae upon which depends the acquirement of a precise and invariable technic—a necessity for good results." Dr. Hinton foresaw success in the clinical application of his assay when these protocols were followed stringently (11).

> Many of those who have had wide experience insist upon well-trained serologists for the execution and interpretation of serum reactions for syphilis. We do not entirely agree with them. The method which we have described has been performed with excellent results by students, by young women of less than high school training, and by physicians who have had relatively little training in serology. The reliability of their results has been solely dependent upon the acquirement of sufficient *experience* to enable them first, to master their technic so that it is practically invariable from day to day, and second, to recognize significant changes.

The Hinton test performed well in additional comparative evaluations of sensitivity and specificity that were presented in the late 1920s and 1930s (13, 14). (As a side note, as decades progressed and introduction of the cardiolipin reagent [15] for syphilis flocculation reactions allowed for improved standardization, subsequent nontreponemal test comparisons could be viewed as being less necessary.) Dr. Hinton served as a Special Consultant to the Venereal Disease Division of the U.S. Public Health Service beginning in 1935. In 1936, Dr. Hinton became the first African American to author a medical textbook, *Syphilis and Its Treatment* (16). With all of this said, it is debatable whether Dr. Hinton's findings received recognition and acceptance commensurate with their importance. Marian C. Johnson-Thompson, Ph.D., Professor Emerita, University of the District of Columbia, and Adjunct Professor of Maternal and Child Health, School of Public Health, University of North Carolina, wrote, "It appears as if his work was accepted, at the time, as novel contributions. However, his overall publication record is not that great, and the reason is not clear. I also understand that his book was not well accepted in this country, but internationally it was accepted to a greater degree." Alfred DeMaria, Jr., M.D., Medical and Laboratory Consultant for the Massachusetts Department of Public Health, additionally commented, "I think his work on the Hinton test was generally highly regarded, but I wonder how the Public Health Service treated him. They used him as a consultant on treponematoses, but some correspondence in review of his work seems to be less than wholly respectful. Most of the papers following on his work (that I have seen) seem to agree with the test's enhanced performance, and these are from around the world. Even though the Hinton test was widely used and was thought by many to be an easier and more sensitive nontreponemal serology test, it is not listed among the ten tests in the history of syphilis serology in a later edition of the CDC/APHA's *A Manual of Tests for Syphilis* (1998), nor is it often mentioned in review articles."

Dr. Hinton appeared to be aware of his position within the scientific community. Dr. Johnson-Thompson, who has spent extensive time researching the life and family of Hinton, wrote, "As a black person, he was extremely insecure and adopted a real dislike for being black. He did not want the world outside of Harvard and the other places he worked to know he was black. In fact, he sequestered his immediate family from broader family members and other black people. He wanted to ensure that his work was not discounted because of his race. He was extremely inquisitive, ambitious, and sought recognition as a scientist. He did not want to be called a black scientist." Sadly, Dr. Johnson-Thompson summarized, "he was ashamed of his color."

Dr. Hinton has been described as a modest, exceedingly kind, gentle, and affable person, who was very detail oriented and deeply (but quietly) devoted to social justice. One radiant introduction of Dr. Hinton as a foremost authority on syphilis prior to a formal public presentation was rebutted by Dr. Hinton, who stated that he was "merely one who was interested in syphilis" (17). Dr. Hinton was scheduled to receive the highly coveted Spingarn Medal from the National Association for the Advancement of Colored

People in 1938. Accounts vary as to why Dr. Hinton declined this award. Some described how Dr. Hinton felt that his accomplishments were not commensurate with the honor. Others related that Dr. Hinton feared that his status and credibility as a clinical and scientific researcher (and his ability to publish his findings) would be jeopardized upon acceptance of the award. Dr. Johnson-Thompson added, "His humbleness led him to be accepting of many mistreatments fostered by a racist scientific community within the larger society."

Dr. DeMaria further wrote of Hinton's remarkable work ethic. "The volume of testing in the laboratory he supervised, with a relatively small staff, was amazing. He also commuted between his home in Canton (Massachusetts), Harvard Medical School, and the Boston Dispensary in the South End, toward the end of his career driving with one leg [Dr. Hinton lost a leg following a 1941 motor vehicle accident]." When premarital syphilis serology became mandated by the state of Massachusetts in 1941, Hinton's training, expertise, and guidance increased the number of laboratories within the state that were approved to perform this testing from 10 to 117. Hinton subsequently was an early champion of quality assurance, surveying clinical laboratories, and certifying test performance. At the same time, Dr. DeMaria remarked, "He struggled to maintain his public health laboratory, making do with whatever he could get from the state and accomplishing an enormous volume of testing (syphilis serologic testing volume increased from nearly 400,000 tests in 1941 to over 700,000 in 1942). I keep thinking of the small amount of space he had, the limited staff, and all those glass test tubes that had to be cleaned for re-use in the Hinton test."

Dr. Hinton held membership in the American Medical Association, the American Society of Clinical Pathologists, and the American Association for Advancement of Science and was a fellow in the Massachusetts Medical Society. Dr. Hinton was named an honorary life member of the American Social Hygiene Association in 1948 (18). Despite being a member of the Society of American Bacteriologists (the predecessor of the American Society for Microbiology [ASM]) and having membership dues accepted by the Society (19), Dr. Hinton never attended an ASM meeting. Dr. Johnson-Thompson relayed accounts of how African American scientists in those decades experienced limited entry to meetings, could not ride on elevators at these events, and were not presented with hotel accommodation options.

Dr. Hinton additionally spent a significant portion of his career as a renowned educator. He taught Harvard School of Public Health and Harvard Medical School courses in preventive medicine and hygiene (beginning, per some accounts, in 1923) and in bacteriology and immunology (beginning, per some accounts, in 1924), respectively, under the ranks of assistant, instructor, and lecturer for nearly 30 years. One year prior to Dr. Hinton's retirement from Harvard Medical School in 1950, he was given the rank of Clinical Professor of Bacteriology and Immunology—again the first African American to attain full professor status at Harvard Medical School. Dr. Hinton's pedagogic contributions were not limited to Harvard Medical School. He taught courses at the Tufts College Schools of Medicine and Dentistry. Dr. Hinton also taught at the all-female Simmons College (now Simmons University) in Boston. He further established a laboratory technician program in 1931 at Tufts College that was open only to women; thus, Hinton was a pioneer in creating countless opportunities for women in laboratory medicine. Dr. Johnson-Thompson wrote, "A person of extreme patience, he was known for working close with laboratory aides to ensure their understanding of the laboratory research work. Additionally, he might have been one of the few to teach women in laboratory science. His concern in ensuring opportunities for women might have related to the fact that he had two daughters." One cannot help but notice a female laboratory professional in the illustration of Dr. Hinton exhibited at the beginning of this biographical feature. It is thought that the woman being depicted is Ms. Genevieve O. Stuart, who began working for Dr. Hinton as his secretary right out of high school, eventually joining him in laboratory practice (20).

In addition to his work on the serum diagnosis of syphilis, Dr. Hinton left and inspired an honorable legacy upon his death in 1959. In 1962, the estate of Dr. Hinton

bequeathed a combined cash and real estate gift of $75,000 to Harvard University to establish the Dwight D. Eisenhower scholarship fund. According to one editorial (21), the fund was named as such "in recognition of steps toward the acceptance of the principle of equal opportunity during the Eisenhower Administration." Eisenhower, in one of his postpresidency published works, wrote, "I could not recall having been given a personal distinction that had touched me more deeply." In 1974, the Massachusetts state legislature renamed the Wassermann Laboratory (syphilis testing laboratory) the Dr. William A. Hinton Laboratory. The Massachusetts State Laboratory Institute Building in Jamaica Plain, MA, was renamed the William A. Hinton, M.D., State Laboratory Institute in 2008. In 1983, African American students at Harvard Medical School and the Harvard School of Dental Medicine established the Hinton-Wright Society to encourage and support minority students in their pursuit of biomedical careers and to sponsor monthly seminars by biomedical professionals. Since 2003, the Harvard Medical School Office for Diversity Inclusion & Community Partnership has annually sponsored the Advanced Placement Biology Hinton Scholars Program as an after-school enrichment opportunity for over 100 students in Boston public schools. Benefits to students include access to career panel discussions in biomedical sciences, as well as tutoring by Harvard medical and graduate students.

Very notable to the fields of clinical/medical microbiology and infectious diseases, one of Dr. Hinton's daughters, Jane Hinton, was a graduate of Simmons College in 1939 at the age of 20 and likely learned laboratory techniques from her father. Jane Hinton was also employed as a summer intern, probably as a component of her undergraduate studies, at Harvard Medical School and the Harvard School of Public Health (prior to becoming one of the first African American women to attain a doctorate in veterinary medicine). In collaboration with Dr. J. Howard Mueller at Harvard, Jane Hinton developed Mueller-Hinton agar, intended for cultivation, at the time, of *Neisseria gonorrhoeae* and *Neisseria meningitidis* (22).

Finally, in 1997, ASM established the ASM William A. Hinton Award for Advancement of a Diverse Community of Microbiologists. The charge of the award is to recognize outstanding contributions toward fostering the research training of minorities and increasing diversity in microbiology. Nominees contribute to the research training of health professional students, undergraduate students, graduate students, and postdoctoral students, as well as efforts leading to the increased participation of underrepresented minorities in microbiology. A complete listing of recipients of this award, to date, can be found with the following link: https://www.asm.org/ASM/media/Fellowships/Past-ASM-Awardees-for-Current-ASM-Awards-6-1-20_1.pdf. Gladys Alexandre, Ph.D., Professor and Head of Biochemistry & Molecular Biology at the University of Tennessee, was the recipient of this award in 2019. Dr. Alexandre wrote, "In my view, Dr. Hinton's legacy represents what scientific excellence is. Dr. Hinton was a superb bacteriologist whose research and findings advanced the well-being of people here in the United States and abroad. Without engagement of others who do not have access, as well as the mentoring and nurturing of aspiring scientists, scientific pursuits are self-serving. Dr. Hinton worked to open up the field to others, and to women in particular, and this further amplified the impact of his research accomplishments. This is the research excellence we should all aspire to." The aforementioned Dr. Marian Johnson-Thompson was a recipient of the ASM William A. Hinton Award for Advancement of a Diverse Community of Microbiologists in 2018.

While the scope of the *Journal of Clinical Microbiology* biographical feature entails primarily descriptions of contributions to the fields of clinical microbiology and public health by notable individuals, one cannot ignore the impact of insidious and overt racism on the career of William A. Hinton, M.D. (the reader is referred to an ASM Journals editorial [23] for additional discussion on related topics). Dr. Johnson-Thompson opined that, "he overcame a lot, but his personal life, impacted by racism, ended in turmoil. As such, he never overcame the obstacle of racism." One can only imagine what Dr. Hinton's research and clinical productivity would have been, as well as the subsequent magnitude of his contributions to the fields of medical

microbiology and public health, had he not been forced to deal with the obstacles inherent to racism. Instead, we can greatly benefit from the perspectives and contributions of any individual who possesses subject matter expertise and has best interests in mind (irrespective of race, ethnicity, gender, sexual preference, belief, and age) to address contemporary and future issues in clinical microbiology. We must do better in this endeavor.

ACKNOWLEDGMENTS

The author expresses humble and sincere gratitude to Marian C. Johnson-Thompson, Ph.D., and Alfred DeMaria, Jr., M.D., for their generous provisions of written correspondence for this biographical feature and critical review of the manuscript. Patrick Schloss, Ph.D., and Alexander J. McAdam, M.D., Ph.D., are additionally acknowledged for review of the manuscript. Other content within this biographical feature would not have been possible without the assistance of Gladys Alexandre, Ph.D., George Q. Daley, M.D., Ph.D., M. William Lensch, Ph.D., and Scott H. Podolsky, M.D.

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