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ABOUT COVER

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The primary aim of *World Journal of Cardiology* (*WJC*, *World J Cardiol*) is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJC mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

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FIELD OF VISION

Oliver Wendell Holmes' 1836 doctorate dissertation and his journey in medicine

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Abstract

Oliver Wendell Holmes' 1836 hand written doctorate dissertation on acute pericarditis was discovered in the archives of the Boston Medical Library 101 years after it was successfully defended. It was then printed as an unabridged monograph with an explanation of its provenance. The dissertation has received little scrutiny since then. Holmes gathered materials for the scholarly work while he was a third and fourth year student at Ecole de Medecine in Paris. His mentor, Pierre-Charles-Alexandre- Louis insisted on the meticulous gathering and recording of every patient's history and findings. Each category of data was given a weighted numerical value of diagnostic importance and the information was placed in a registry. Holmes became a disciple of Louis in gathering data by direct observation and measuring outcomes in a "statistical" fashion. Holmes dissertation on acute pericarditis describes the state of knowledge about the illness in the 1830s. When Holmes and other students who had studied in Paris returned to the United States, they helped turn American Medicine from opinion and strong personal bias toward scientific objectivity. Oliver Wendell Holmes eventually became both a professor of anatomy/physiology and a dean at Harvard Medical School. He is recognized as a leader in medicine and a popular author in America and beyond. In his late and infirmed years, Holmes questioned the wisdom of his unswerving advocacy for the scientific underpinnings of medicine. In retrospect he had overlooked the importance of also advocating that each patient be approached with comforting compassion.

Key words: Acute pericarditis; Medical statistics; Childbed fever; Harvard medical school; Pierre-Charles-Alexandre- Louis

Core tip: Oliver Wendell Holmes' 1836 Doctorate Dissertation on Acute Pericarditis has

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received little scrutiny since its publication 100 years after it was successfully defended at Harvard Medical School. The state of knowledge about pericarditis in the mid eighteen hundreds was unusually sound considering the inability to study tissue with microscopy. However treatment was a matter of opposing expert opinions and the fashion of the day in Paris was to disparage professors who disagreed. Paris was a mecca for students. Cadavers were plentiful for study. Lectures and clinics were free.

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COMMENTARY ON HOT TOPICS

Medical education and medical practice is constantly changing. Medical schools intermittently modify their curricula to engage their students and have them achieve excellence rather than mere competence. It is said that if one does not have knowledge of history, one does not understand the present. Oliver Wendell Holmes early medical education and observations in Boston was at a time when doctors were guided by opinions derived from their own experiences and those of their highly respected peers. Many of the most respected had studied in London, Scotland or Paris. While a student in Paris, Holmes learned to value his own observations, to record his observations, to give variable weight to symptoms, physical findings and the revelations of autopsy pathology to arrive at a diagnosis. His mentor, Louis, meticulously collected and analyzed such data in an early attempt at a crude scientific method. When Holmes and other American Medical students returned from Paris and gained positions of authority, they instigated and accelerated reforms in medical education and the treatment of patients.

Oliver Wendell Holmes' 1836 Doctorate Dissertation and His Journey in Medicine is about an early attempt to separate fact from fiction, truth from opinion, statistics from mere numbers that ultimately evolved into the scientific method we rely upon today.

AN OVERVIEW OF HOLMES' DOCTORATE DISSERTATION

Oliver Wendell Holmes' 1836 doctorate dissertation at Harvard Medical School has received relatively little scrutiny since it was successfully defended before a board of examiners. At that time, the very last requirement towards a doctor of Medicine degree was a dissertation on a medical subject[1]. The next step was to establish a practice. "In the state of Massachusetts, the Harvard degree alone entitled the student to practice in the state; graduates of other institutions were examined by the state medical society[2]".

Holmes' handwritten, hurriedly completed manuscript lay hidden in the archives of the Boston Medical Library for 101 years. In 1937 it was discovered, preserved, and transformed into an unabridged printed monograph with a brief explanation of its provenance[1].

Materials, methods and personalities known to Holmes while he was a third and fourth year medical student in Paris are included in his dissertation. Holmes selects observations about "acute pericarditis written by authoritative physicians of the French School" and elsewhere. He describes cases of acute pericarditis from his personal experience at the teaching hospitals in Paris, some autopsied cases by faculty anatomist Gabriel Andral and likely other cases from the registry of his Parisian mentor, Pierre-Charles-Alexandre-Louis, who, for practical reasons of brevity, was simply called and answered to "Louis".

The theme of Acute Pericarditis is "…to present the most recent and best established recent ideas upon its history and treatment as they are expounded in the most approved authorities or as they result from a certain number of cases subjected to analysis[1]". Holmes was aware that Louis had published a memoir on pericarditis in 1826, but seldom refers to it. Holmes' contemporaneous-fellow-American student in Paris, James Jackson Jr, in a letter to his father dated January 6, 1832, summarized Louis' four important conclusions about pericarditis. "It is a common disease. Like

pleurisy, it is often latent, being attended neither with pain, nor any of that assemblage of horrid symptoms by which it is generally described. It can be diagnosed by percussion and not divined, as Laennec has said of it. It is by no means so fatal as has been generally supposed[3]".

One might ask—why did Holmes pursue his clinical medical education in Paris and how did that experience influence his journey in medicine?

EARLY LIFE OF OLIVER WENDELL HOLMES

Oliver Wendell Holmes was raised in Cambridge, Massachusetts. His father, Abiel, was a Calvinist and a minister. Holmes' mother, Sarah Wendell, had roots that extended to Scotland. His parents instilled a system of life-long values. They were hard work, discipline and living within one's financial means.

UNDERGRADUATE AND GRADUATE EDUCATION IN THE UNITED STATES

Holmes attended Phillips Academy preparatory school. He then graduated from Harvard College in 1829. Thereafter he briefly attended Harvard Law School. After becoming disenchanted, Holmes changed career goals from the law to medicine. He enrolled in a private proprietary medical school that shared some facilities and faculty with the Massachusetts Medical College of Harvard. There are several sources that specify that Holmes attended a private proprietary medical school rather than Harvard Medical School. The most authoritative is Oliver Wendell Holmes, who in his Farewell Address to the Medical School of Harvard University said, "The Private Medical School that I had joined was one established by Dr James Jackson, Dr Walter Channing, Dr John Ware, Dr Winslow Lewis and Dr George W Otis[4]". Not all of these doctors were on the faculty of the Massachusetts Medical College of Harvard. In addition, three medical historians agree that Holmes was enrolled at a private proprietary medical school. James F Ballard, the director of the Boston Medical Library wrote in the introduction to dissertation on acute pericarditis that Holmes … took two courses at a private medical school in Boston[1]. John T Morse Junior, a relative and biographer of Oliver Wendell Holmes, cites a quotation among Holmes' reminiscences in Life and Letters of Oliver Wendell Holmes Volume I, "The head of the private school at which I studied was Dr James Jackson, a very wise and good man, … Dr Jackson never talked of curing a patient other than in its true etymological sense of taking care of him[5]". Elinor M Tilton, a historian and biographer wrote on several occasions that Doctor Oliver Wendell Holmes attended a private medical school[6].

Early on, Holmes developed an admiration for his mentor, Dr. James Jackson Sr who was on the faculty of both schools. The curricula included two annual courses of lectures for three or four consecutive months each winter to be supplemented by an apprenticeship with a clinician or clinicians for an inclusive time span of approximately three years.

CLINICAL MEDICAL INSTRUCTION IN PARIS, FRANCE

Holmes spent two and a half years in Boston and the remainder of his formal medical studies during 1833 through 1835 at Ecole de Medecine in Paris, considered to be a Mecca of medical expertise and innovative teaching. Holmes sailed for Europe on March 30, 1833 and returned to United States soil on December 14, 1835. Students and fully certified doctors studied in Paris to achieve advanced knowledge, to enhance their skills, to better serve their patients and to gain greater standing within their profession.

Unlike America, Paris had full-time faculty, abundant free lectures, free clinics to all foreign students and 4000 unclaimed corpses each year for dissection[7]. In a letter dated November 14, 1833, Holmes marveled that Ecole de Medecine's enormous anatomy lab could accommodate enough corpses to be dissected by 600 students in a single session[5].

Lectures were by luminaries who encouraged students to accompany them on daily early morning ward rounds. At the bedside, these master-clinicians taught the subtle uses of Renee Laennec's recently invented monaural stethoscope to detect markers of

inner-body illness. Technical modifications and nuances of its use were evolving when Oliver Wendell Holmes was in Paris.

Holmes believed that the worst doctor on the staff of Ecole de Medecine surpassed the best doctor in America, with the exception of his American mentor, James Jackson Sr In a letter home dated August 18, 1833, Holmes wrote that American Medicine is "…where stupidity is tolerated, where mediocrity is applauded and where excellence is deified[5]".

During his exhilarating Paris experience, Holmes quickly became fluent in spoken and written French and bonded with two students from Harvard Medical School who also chose to expand their knowledge at the Mecca. Each had a lineage of medical aristocracy in Boston. Their fathers were founders of the Massachusetts General Hospital. Holmes' comrades were James Jackson Jr, the son of his Boston mentor and Jonathan Mason Warren, the son of John Collins Warren who was the second Professor of Anatomy and Surgery at Harvard Medical School. Mason's grandfather, John Warren, was its first Professor of surgery and founder of the school.

At Ecole de Medecine, Holmes became a disciple of Louis who had developed what might be termed an observation-based numerical method of documenting the symptoms and physical findings of each patient's illness. After a disease caused the death of its host, a post-mortem autopsy was performed and the clinical-pathological data became part of the record. The sum of each patient's findings was organized and placed into a registry. Illness became unified rather than segmented and could be subjected to statistical analytics based on Louis' numerical system. Holmes spent hours at the bedside documenting the symptoms and physical findings of each assigned patient. If death occurred, he personally performed the autopsy and recorded the findings.

Louis specialized in diseases of the chest. He was an expert among experts in the nuances of percussion that was rediscovered by Jean Nicholas Courvisant (1771-1821), an academic French physician who perfected the art of percussion. Louis was also an expert in auscultation of the heart and lungs, especially the treasure of new auscultatory knowledge gained with Renee Laennec's stethoscope.

THE 1836 DOCTORATE DISSERTATION

In Acute Pericarditis, Holmes approaches the topic as he was taught by Louis. The presentation is divided into symptoms, physical findings and patho-physiologic findings. Following the academic custom when he was in Paris, Holmes attacks those who falsely claim priority for having described a pericardial symptom or sign that was first noted by another. The dissertation reflects the status of unenlightened medicine in the 1830s. Yet, it is surprisingly accurate in some areas and not-so-surprisingly inaccurate in other areas —such as treatment.

In Oliver Wendell Holmes' 1836 doctorate dissertation, he describes familiar symptoms and signs that result from pericardial inflammation and an excessive volume of pericardial fluid.

The familiar symptoms are shortness of breath, cough, oppression, anxiety, anguish, precordial chest pain—at times made better or worse during altered bodily position, syncope, chills and perspiration. The familiar signs are fever, rapid heart rate, an enlarged area of precordial dullness, a palpable precordial thrill, distant heart sounds, a "leathery" rub and a pulse that might be irregular or variable in amplitude.

Without the benefit of measurements, Holmes correctly reasoned that cardiac tamponade results from excessive pericardial fluid under pressure that inhibits the ventricles from filling[1].

Autopsied hearts were grossly described. Holmes did not have the benefit of precision tools found in a modern pathology laboratory. The monocular compound microscope was just emerging as a potential diagnostic aid and Holmes wisely procured one in Paris to use upon his return to Boston. The usual pale transparent pericardium of normal hearts, when inflamed from pericarditis, appeared red, possibly thickened and over time calcified. Pericardial fluid was quantified and the color described as clear, turbid, hemorrhagic, yellow, brown, green or thickened with pus. Holmes separates "clear-serous" from "turbid" fluid and comments that the sequelae of the transformed turbid "plastic lymph" might result in fibrous bands that connect the parietal and visceral pericardial layers or actually seal the layers together[1].

There is a section in which Holmes discusses pathological processes associated with acute pericarditis. Germ theory and microbial diseases were not yet known. Undifferentiated "Rheumatism" (that likely included unrecognized acute rheumatic

fever) and diseases of the lungs and pleura were believed to be culpable. Phthisis and consumption (terms for tuberculosis) were endemic. James Jackson Jr wrote that phthisis was the disease that filled Louis' wards. "Over a period of s few months, a student might take part in the examination of as many as fifty cases of tuberculosis[8]". By direct extension from the lungs, tuberculosis rarely causes acute pericarditis, but often results in subacute pericarditis, or late constrictive pericarditis.

Treatment of acute pericarditis was an exercise in unproven opinion. The duration of the disease was three days to three months with a death rate of 15%[1]. Both antisepsis and asepsis were beyond the horizon. It is no wonder that Louis was a therapeutic minimalist and of the opinion that a patient had a better chance of improving with nature's curative powers than with intuitive manipulations to harmonize the body's fluid humors described by Galen as blood, phlegm, black and yellow bile. Standard treatment of the day included purges, emetics, blistering, bloodletting, application of leaches and nostrums. There were a limited number of herbal medications in the Pharmacopeia. Digitalis was often prescribed.

Holmes' Acute Pericarditis Dissertation in 1836 cites a slim therapeutic ray of hope for a better future. Pericardiocentesis is mentioned once without further elaboration.

In his dissertation, Holmes cites a Dr. Fordyce, who, (in contrast to Jean Babtiste Bouillaud's vigorous bloodletting treatment of pericarditis or rheumatism), avoided the practice of bloodletting for 15 years while managing several hundred patients with only 2 or 3 losses. Fordyce concluded that bloodletting hastened death[1]. Yet, at the time, Holmes' contemporaries paid no heed. Many years later, during his retirement Farewell Address, Holmes mentioned that Louis had published an essay titled "Bleeding in Some Inflammatory Diseases" in which using his meticulous observational numerical method, demonstrated to his own satisfaction, that bloodletting failed to improve acute disease such as pneumonia[4]. In 1996, Sylvan Weinberg cited specific data from Louis' experiment in an editorial titled The Quest for Medical Certainty[9].

After returning to Boston, Holmes embraced Louis' numerical-observation-based approach. He believed that a treatment should be abandoned if it was not proven to be beneficial. As he later wrote, "I firmly believe that if the whole materia medica, as now used, could be sank to the bottom of the sea, it would be all the better for mankind, and all the worse for the fishes[10]". Holmes crusaded to eliminate child bed fever. In 1843. He accused doctors who caused puerperal fever and maternal death of criminal behavior because they ignored observational evidence that they were transmitting deadly agents from their clothes and hands to their patients[11].

Acute Pericarditis presents a panoramic view of the illness. Holmes' dissertation is based on his experience in Paris. He cites knowledgeable contributors to the field. Except for Louis, it was common for an esteemed lecturer to skewer a colleague for an inaccurate statement or belief. With distain, Holmes disparages Laennec's successor, M. Bouillaud on several counts. He expropriates Laennec's leather creaking pericardial rub sign to M Collin[1]. Bouillaud "makes an unnecessary parade of what he considers his discovery[1]. He promotes the useless practice of bloodletting and he lectures "…with an egotism and censoriousness of others which imply a profound conviction of truth…[1]", he also undervalues the significance of flatness of precordial percussion[1].

HOLMES' JOURNEY AS A MEDICAL DOCTOR

After Holmes received his doctor of medicine degree from Harvard Medical School and simultaneously qualifying to practice medicine in Massachusetts, it could be said that his journey in medicine was outstanding. He eventually became the Parkman Professor of Anatomy and Physiology and a Dean of Harvard Medical School[12]. He is recognized as a leader in medicine and a popular author in America and beyond. "American Medicals" brought Louis' methods from Paris to Boston and to other medical centers in the United States[13]. It became the Coda for diagnosis and ultimately, with modifications, for research[14]. As medicine was evolving, Holmes was a committed proponent of its scientific underpinnings. Yet in his late and infirmed years, Holmes questioned the wisdom of his unwavering advocacy for Louis' analytical numeric method[10]. In an essay titled Scholastic and Bedside Teaching, he had overlooked the benefits of James Jackson Sr's artful, comforting and compassionate approach to each patient[15].

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