Journal of Community Hospital Internal Medicine Perspectives

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BRIEF HISTORICAL PERSPECTIVE

The price they paid

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Background: Several individuals integral to the development of evidence-based medicine endured hardship for their efforts and beliefs.

Case presentation: We present the history of three individuals who were integral to the formation of evidence-based medicine. All three individuals suffered as a result of resistance to change from colleagues as well as from within the profession.

Conclusion: Individual and professional collegiality in the face of change should be maintained. The efforts of our predecessors are honored and provide us with inspiration.

Keywords: *evidence-based medicine*; *medical history*

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Received: 27 October 2014; Revised: 5 December 2014; Accepted: 8 December 2014; Published: 3 February 2015

The rich fabric of medical history is replete with images and echoes of individuals dedicated to patient care who suffered personal and professional tribulations as a result. These giants of medicine were clinicians as we are, and they possessed the same human desires and frailties which we bear. We discuss here three pioneers of evidence-based medicine whose initiative and perseverance provide us a legacy of empathy, advocacy and empiricism. The lives of Ignaz Philipp Semmelweis, Florence Nightingale and Ernest Amory Codman were separated by oceans and time, but were joined by their contributions to the nascent growth of evidence-based medicine and quality measures.

We see glimmers of empiric medicine practiced by physicians in antiquity, but a formal, professionally accepted process of testing and comparing outcomes is a modern phenomenon. Statistics and outcomes were not the manner of practice in 1844 when Ignaz Philipp Semmelweis received his Doctor of Medicine degree from the University of Vienna and began the practice of obstetrics. Historically, obstetrics was at times not considered a part of medical practice. Midwives and home birth were standard, and the "advancement" of lying-in hospitals created a perfect environment for the spread of puerperal fever (1). The young Dr. Semmelweis observed that the maternal mortality rate from puerperal fever between two clinics was dramatically different (2). This initial observation was followed by a second observation that the fatal illness his colleague suffered after sustaining a wound during an autopsy was similar to this disease. Semmelweis cleverly deduced that the "cadaveric poison" from the autopsy ward, which was visited by the students before visiting the high mortality clinic, was etiologic in puerperal fever. This led to a protocol and testing, showing a dramatic decrease in mortality employing hand washing. Although convinced of the efficacy of his treatment, and although statistical proof was present, no cause and effect could be explained. Disease causing unseen agents were postulated by clinicians such as Susruta thousands of years ago, but although Leeuwenhoek visualized microscopic organisms in the late 1600s, the works of Pasteur, Lister and Koch were yet to be known, understood and applied. This medical discovery was followed by personal and professional tragedy. Statistical proof was trumped by professional pride. The implication that the deaths were iatrogenic from "dirty hands" was met with resistance and antagonism. This dedicated clinician was vilified, denied a clinical appointment, became personally affronted by the situation and did not live to see the fruition of his work (3). This outstanding physician ended his life in an asylum, where at age 47 he died after reportedly being physically beaten by guards. The "Semmelweis Reflex" describes the tendency to reject new information or thought which rejects established beliefs. We have seen this in modern times, as when Dr. Dean Ornish was labeled a California "nut" for suggesting that diet might impact coronary disease. We saw it again when there was disbelief that an infection might cause peptic ulcer disease. Dr. Barry Marshall and Dr. Robin Warren shared in the 2005 Nobel Prize, but only when Dr. Marshall developed symptoms after inoculating himself by drinking an extract from a patient infected with H. pylori. His pre-ingestion H. pylori

Citation: Journal of Community Hospital Internal Medicine Perspectives 2015, **5**: 26436 - http://dx.doi.org/10.3402/jchimp.v5.26436

negative EGD was followed by both the onset of symptoms and H. pylori positivity on post-ingestion EGD, with subsequent symptom resolution by taking metronidazole.

The observations, record keeping and statistical analysis of Semmelweis are mirrored by Florence Nightingale, considered by many to be the mother of modern nursing. Nightingale is famous for a long list of accomplishments, including being instrumental in the formation of the first School of Nursing. Her service in the Crimean War was marked by personal illness and professional tribulation. As Dr. Philip Mackowiak details in *Post Mortem* (4), Ms. Nightingale likely contracted Brucellosis from poor food quality, which together with a host of other medical conditions remained with her for the rest of her life. Her inability to stem the tide of death in the English soldier population was not through lack of effort. She worked with medical statisticians to develop and report statistical tables regarding variables present in the onset and progression of disease in English soldiers. Rehmeyer in *Science News* (5) reports this relentless patient advocate was afraid Queen Victoria's "eyes would glaze over" reading the statistical reports. It is argued that for various reasons, some beyond her control, this nurse was unable on her own to reverse the terrible death toll of troops in the Crimean War. In some estimates the mortality rate approached 20%, primarily due to non-combat disease such as dysentery. Being ahead of her time utilizing individuals from the relatively new field of medical statistics, she presented her data using statistical tables. While many criticisms of Ms. Nightingale may be true, it does appear clear that her efforts prompted changes in sanitation and infectious control processes within the English military. They were also one of the earliest uses of medical statistics with an effort at evidence-based medicine directed to the highest level of government and decision-making. Despite these efforts, Florence Nightingale felt a personal responsibility for many of the deaths. She did receive, and continues to receive, criticism regarding her actions (6). Some of the military at the time criticized her in much the same way as Ignaz Semmelweis was vilified by the establishment of his day. The discussion in both cases was personal and harsh, focusing on individuals and events rather than upon statistics and outcomes. For these two individuals who felt a personal responsibility for the welfare of patients, it was an emotionally and professionally difficult passage. Florence Nightingale passed the remainder of her life as an unhappy recluse, with some regrets and some remorse.

As we move into the early 1900s, we turn our attention to the incredible, and sobering, life of Ernest Amory Codman. After graduating *cum laude* from Harvard College and subsequently Harvard Medical School, Dr. Codman interned at Massachusetts General Hospital and subsequently joined the Harvard faculty. His accomplishments were extensive and as detailed in *The Trilogy of Medicine* include (7):

- formation of an early anesthesia record called "The Ether Record" with colleague Harvey Cushing
- development of the first cancer registry in the US called "Registry of Bone Sarcoma"
- the first official "skiagrapher" to Boston Children's Hospital (skia Greek for "shadow"), a skiagrapher being the precursor to the modern radiologist
- the first atlas of normal x-rays
- pioneering surgery to the shoulder
- pioneering surgery for duodenal ulcer
- still relevant shoulder rehabilitation exercises called "Codman's exercises"
- the first Mortality and Morbidity conference
- the first two cases of rotator cuff repair published in English (8).

Although all are notable accomplishments, we speak of this clinician not because of these, but because in the early part of the twentieth century he was interested in "end results" (9). In addition to co-founding the American College of Surgeons in 1910, he chaired the Committee for Hospital Standardization, forerunner of the Joint Commission. The initial recommendations of this organization were that hospital staff should be graduates of a medical school, medical records should be kept for all cases, a hospital should have a laboratory and radiology, end results of cases should be reviewed, and M and M conferences should be held. As MGH refused to follow these recommendations, as most hospitals did not, Dr. Codman resigned his staff privileges and started his own hospital, the Codman Hospital. Staff members of the new hospital were required to publish their own end results. He kept a card file of his patients with notations such as "error due to lack of judgment" and "errors due to lack of technical skill." His professional relationships deteriorated. He was vilified by some of the medical, political and hospital communities. After enlisting in the military in WWI he returned to Boston. The Codman Hospital closed, he had no hospital affiliation, few referrals, little money, and no resolution to the medical quality issues in which he believed so strongly. He spent the end of his life in an isolated cabin and did not even have enough money to purchase a headstone. He was buried in an unmarked grave. It was thought that his inability to have children and the melanoma he developed may have been related to the radiation exposure he suffered doing x-rays. This incredibly accomplished clinician's obituary only mentioned "contributions made to bone sarcoma and shoulder surgery". He was quoted as saying "Honors, except those I have thrust upon myself, are conspicuously absent ... but I am able to enjoy the hypothesis that I may receive some more from a more receptive generation." Dr. Codman not only had a vision, but a vision that that vision will one day be seen. The presence of the ACS, JCAHO, peer review, quality initiatives, accreditation requirements, and

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evidence-based medicine were all in part engendered by the life of this physician, who has been honored by presentation of the annual Joint Commission's "Ernest Amory Codman Award" (10).

The three individuals from medical history discussed in this article were idealistic, humane, and pioneered the concepts of statistical analysis and evidence-based medicine. They may have been stubborn, willful, opinionated, maybe even irascible, but their concerns were totally patient centered. They teach us and demonstrate to us by example the best actions and traditions of the medical profession. Their life celebration cautions us as a profession to guard against intellectual stagnation and pomposity, which can interfere with the healing art and impair collegiality. These individuals, whose lives ended in violence, sorrow and tragedy, are toasted with a glass full of inspiration from those of us who follow in their footsteps.

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