Gangrene Therapy and Antisepsis Before Lister: The Civil War Contributions of Middleton Goldsmith of Louisville

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It is commonly accepted that Louis Pasteur is the father of microbiology and Joseph Lister is the father of antisepsis. Middleton Goldsmith, a surgeon in the Union Army during the American Civil War, meticulously studied hospital gangrene and developed a revolutionary treatment regimen. The cumulative Civil War hospital gangrene mortality was 45 per cent. Goldsmith’s method, which he applied to over 330 cases, yielded a mortality under 3 per cent. His innovative work predated Pasteur and Lister, making his success truly remarkable and worthy of historical and surgical note.

The American Civil War was the bloodiest conflict that occurred on American soil. More soldiers died during those 4 years than in all other United States conflicts up to the Vietnam War, combined. By the time Robert E. Lee surrendered at Appomattox Courthouse in April 1865, nearly 700,000 combined Union and Confederate soldiers had perished. Only one-third actually died as a direct result of battlefield trauma; the remaining two-thirds succumbed to disease. Although not recognized at that time, microbes represented the primary culprit. Frenchman Louis Pasteur did not publish his groundbreaking work on microbes until well after the end of the war whereas Joseph Lister published his sentinel paper linking microbes to surgical infection as well as his proposed preventive measures and treatment techniques in 1867.

Oliver Wendell Holmes, Sr., a physician and former dean of Harvard Medical School, was known (and ridiculed) for advocating hand washing to prevent the spread of puerperal fever during childbirth beginning in the early 1840s. By the outset of the Civil War, he had retired from practice to focus on his writing, poetry, and social and medical activism. He stated in an 1861 speech, “I firmly believe that if the entire materia medica, as now used, could be sunk to the bottom of the sea, it would be all the better for mankind, and all the worse for the fishes.” However, some physicians were making great progress in the research and treatment of the infectious diseases so entwined with Civil War morbidity.

Hospital Gangrene

For surgeons, formidable foes when treating wounded patients were the infectious problems of wounds sustained during battle. Of the myriad of wound problems, soldiers feared hospital gangrene above all others. Although it affected thousands of soldiers throughout the 4-year conflict, it accounted for only one quarter of 1 per cent of all fatalities in combatants. This was in contradistinction to the popular myths on the contribution of gangrene to overall combat mortality.

At the outset of the War, wound infections and their consequences were not new problems in surgery and military medicine. The concept of “laudable pus” dated back to Hippocrates. In the 16th century the French military surgeon Ambrose Paré regarded the appearance of a cream-colored discharge 2 to 3 days after a traumatic injury as a welcomed sign of healing. In fact, surgeons early in the Civil War continued to attribute the rapid decline of a patient’s health after the appearance of this pus to factors unrelated to the wound itself, such as fatigue, loss of morale, and poor constitution. Surgeons considered hospital gangrene the most threatening of all wound problems.

A characteristic foul-smelling odor often accompanied patients with hospital gangrene on the wards. Based on their gangrene experience during the Crimean War a decade earlier, British surgeons recommended that patients should have at least 1600 cubic feet to themselves. Union surgeon W. W. Keen lamented that during a hospital gangrene outbreak he encountered in Philadelphia, the “available air” per patient was approximately 175 cubic feet, less than a six-foot cube, nearly 10 times less than the British recommendation.
Unfortunately, actions taken to improve airflow occasionally backfired. Julian Chisholm, a Union surgeon, referred to a particular outbreak of hospital gangrene where an attempt to improve ventilation prompted surgeons to cut multiple holes in the ceiling of the affected ward. They hoped this would increase airflow between it and the ward above it, which had windows. Within a day and a half, a number of patients on the upper ward who had traumatic wounds developed hospital gangrene as well.

Another epidemic reported from a Nashville hospital strengthened the correlation of human excrement and hospital gangrene. Ward Number One sat adjacent to a garbage and excrement-filled alleyway that had windows opening to it. Additionally, this same ward had several openings to the cellar, which communicated directly with the city sewer. Ironically, surgeons placed those patients with the “lowest vitality” closest to these windows to give them the greatest airflow. Though well intentioned, these patients also started to acquire hospital gangrene.

Some care-providers began to realize, even before major outbreaks began, that hospital gangrene could also spread via direct inoculation by surgeons, nurses, and hospital stewards. In his 1861 treatise, Dr. Frank Hamilton recommended immediate isolation of affected patients. Additionally, he not only recommended thorough cleaning of the wards, but also that “each patient should have his own sponge and in no case should the dressings be allowed to be used twice... it is better to make it a rule to burn them as soon as they are removed.” In 1861, Ignaz Semmelweiss of Austria published his classic paper arguing that washing hands in a chlorinated soda solution drastically understaffed. Therefore, the dissemination of new findings and treatments, in the Confederacy in particular, remained disjuncted and often affected change regionally at best. Additionally, even if treatment advances, such as those promoted by Semmelweiss, were accepted, instituting these concepts was simply not feasible, especially in wartime. Hospitals were over-crowded, supplies were scarce on both sides, and hospitals of all sizes were drastically understaffed.

Local Gangrene Therapy

Many case reports frequently described a complete gangrene treatment regimen consisting simply of whiskey, a cathartic, a “balanced” diet, and some type of topical agent applied directly to the gangrenous wound. Sharp debridement was commonplace. However, surgeons often debrided either too late in the disease process or the debridement itself worsened contamination. An abundance of case reports that described the surgical debridement of gangrenous wounds began to appear late in the war.

Because an effective topical agent remained elusive, surgeons early in the war experimented with all sorts of substances. A “poultice” was a common but nonspecific topical treatment for many traumatic wounds and many soft tissue ailments from puncture wounds to erysipelas and hospital gangrene. A poultice could be cotton cloth that held mud or clay on top of the wound, which would soothe the wound and provide moisture. Dr. Samuel Gross, former Chair of Surgery in Louisville, stated in his textbook, Military Surgery, poultices with “flaxseed and slippery elm were decidedly best.” A charcoal poultice was probably the most commonly used poultice in the treatment of hospital gangrene.

As the Civil War progressed, topical solutions became the mainstay of local therapy. Different chloride solutions were early favorites. The same chlorinated soda water recommended for hand washing also functioned as a topical agent applied directly to gangrenous tissue. Another chloride-containing compound, Labarraque’s Solution, showed signs of effectiveness. Labarraque’s Solution was the sodium hypochlorite precursor to the Dakin’s solution credited for savings thousands of lives during World War I. Though effective against hospital gangrene, Labarraque’s was approximately 10 times stronger than Dakin’s solution, making it quite overpowering, painful, and difficult to tolerate.

Topical nitric acid later became the “standard of care” for local treatment of hospital gangrene. Hargrove Hinkley, an Alabama surgeon, wrote a case series of all of his hospital gangrene patients. He claimed every one of his patients who received a regimen that contained nitric acid as a key component, survived. However, many of the patients he described actually received a combination of therapies, including large and frequent applications of nitric acid, but also concurrent doses of Labarraque’s solution, tinctures of iodine and iron, and turpentine. This made it difficult to assess the effectiveness of nitric acid alone for the simple reason that Hinkley and other surgeons tended to use many different agents on the same patient. Reports from Chisholm and others elucidated the usefulness, or lack thereof, of nitric acid. They noted that nitric acid treated hospital gangrene by simply burning the infected tissue. This removed bacteria, necrotic tissue, and plenty of healthy tissue as well.
Middleton Goldsmith, Early Life and Career

Middleton Goldsmith, a Union surgeon working primarily in the Louisville area, had an interest in hospital gangrene, as those patients filled his wards. The son of surgeon Alban Goldsmith, Middleton was born in Port Tobacco, Maryland in 1818. His uncommon first name was his mother's maiden name. His father was Professor of Surgery at Kentucky School of Medicine in Louisville in the mid 1830s. Young Middleton served as anatomy prosector and surgical assistant for his father and performed at least one above the knee amputation before the age of 18. After his father's appointment as Lecturer on Surgery at the New York College of Physicians and Surgeons in 1837, Middleton enrolled there as a student and graduated in 1840.

Goldsmith was a dynamic young man and stood over 6 feet tall. His childhood in Kentucky gave him extensive exposure to thoroughbred horses, which made him an impressive mounted equestrian in his New York militia’s frequent parades. He played the guitar and banjo, knew Greek and Latin, and was an excellent storyteller. He frequently quoted Shakespeare and his friends considered him a master of the English language. He became quite popular in the medical, religious, and social circles of mid-19th century New York City.

Before leaving New York for his first academic surgery appointment, his interest in anatomy and pathologic specimens led him to cofound the New York Pathologic Society. In 1844, he became Chair of Surgery at Castleton Medical College in Vermont. After 12 years there, including a term as President of the Vermont Medical Society, he succeeded his father as Chair of Surgery at the Kentucky School of Medicine in Louisville in 1856. Soon, he also became Dean of the Faculty for the young school. At the outbreak of the Civil War in 1861, Goldsmith promptly offered his services to the Union Army as Brigade Surgeon. He quickly ascended through the ranks and after his first year, the Surgeon General appointed Goldsmith Surgeon-in-Chief of all military hospitals in Kentucky as well as the Army of the Ohio. Among many duties, he supervised the daily operations of multiple hospitals, including Jefferson General Hospital (Fig. 1) and Marine Hospital (Fig. 2).

Goldsmith's Bromine Breakthrough

In Louisville, Goldsmith found himself surrounded by many grief-stricken hospital gangrene patients. He quickly focused his unusually high level of energy and intellectual curiosity on the hospital gangrene problem.

Fig. 1. Jefferson General Hospital during the Civil War, located in Port Fulton, Indiana, which is now a part of Jeffersonville, Indiana. Over 20 separate wards housed about 50 patients each. Middleton Goldsmith was in command of the hospital during the Civil War.

Fig. 2. Marine Hospital, Louisville Kentucky, shown in an 1860s postcard (left) and during renovation in 2005 (right). It was part of the Louisville hospital network where both Union soldiers and Confederate prisoners were treated by Goldsmith for hospital gangrene. Marine Hospital, located in the Portland neighborhood, has been on the National Register of Historic Places since 2005.
He thoroughly documented his investigations in his report to the Surgeon General titled *A Report on Hospital Gangrene, Erysipelas and Pyaemia*. Initially, he reviewed many of the documented outbreaks from early in the war. He theorized that “these three afflictions...are in some way connected (and) the search was instituted, for...the discovery of an agent possessed of the power of arresting putrefaction and of destroying the products in whatever form of those products might present themselves, solid, fluid, or gaseous.” Despite his hypothesis that something linked these disorders, a lack of knowledge of the identity of the “putrefactive agent” made his task difficult. As a surgeon, he pushed forward with incomplete information.

Goldsmith started by reviewing the agents presently in use. He rapidly concluded that the corrosive acids, including nitric acid, were quite effective in arresting the progress of gangrene, but also involved destruction of living tissue, making safe administration impossible. Additionally, other surgeons provided no evidence or data to support nitric acid’s effectiveness or safety. Aside from the acids, he noted that other topical remedies, like poultices, did not lead to arrest of gangrene. He later noted that constitutional signs never preceded local disease and therefore “constitutional remedies” like whiskey and coffee had no influence on the disease process.

For a reason that he does not describe, Goldsmith turned his attention to the halogens and halogen-like compounds. Some hospitals used bromine as an aersolized deodorant. Goldsmith noticed that hospital gangrene patients in wards with bromine deodorants seemed to recover more often than those in other wards. He recommended the placement of volatile bromine in all patient wards. The fact that bromine was a readily available fluid at room temperatures, and did not irritate the respiratory system, further interested Goldsmith. Other surgeons also noticed that bromine could help arrest troublesome bleeding during debridement. In Goldsmith’s opinion, the other halogens possessed unfavorable characteristics. Fluorine could not be effectively isolated due to its extreme reactivity. Chlorine could only be pure in gas form and Goldsmith concluded that chlorine solutions were “feeble.” He also agreed that Labarraque’s hypochlorite-containing solution overpowered both patients and surgeons. Iodine was too dilute in fluid form.

Goldsmith identified bromine as his agent of choice, and developed a method of application. Wound preparation involved surgical debridement of all sloughing and gangrenous tissue with forceps and scissors. Depending on the patient’s pain level, surgeons used chloroform as an anesthetic. After drying the debrided wound, he worked from deep to superficial, and injected the bromine solution with a hypodermic needle deep into muscular layers. Then he injected subcutaneously and finally applied it topically to the exposed surfaces. He felt no necessity for a second application unless the characteristic hospital gangrene odor returned. This decision reflected his view that the presence of this foul odor was by far the best indicator of the persistence of gangrene and he considered it pathognomonic. After the arrest of gangrene, care reverted to standard wound dressings.

Goldsmith requested that another Union surgeon, G.R. Weeks, visit the general hospitals of Louisville and generate an independent report regarding his novel treatment of hospital gangrene over a 6-month period. Weeks’ reported findings were remarkable. Of Weeks’ 115 observed cases, 104 patients received a bromine-based treatment. There were a total of seven deaths. Four of these were in the 11-patient cohort treated with topical agents other than bromine, such as nitric acid, charcoal, or chlorinated soda. Three deaths occurred in the bromine group. Weeks reported these deaths resulted from pyaemia and cellulitis after the gangrene improved. Proper interpretation or not, Weeks felt that allowed him to report Goldsmith’s regimen was 100 per cent effective in preventing death in hospital gangrene patients. Weeks noted that in other case series involving other treatment regimens, mortality seemed to average around 25 per cent.

Weeks also analyzed time elapsed from initiation of therapy to clinical improvement. Among the seven who recovered without bromine therapy, it took an average of nearly 15 days to convalesce. All of the 80 soldiers in the “dilute bromine” group who recovered did so after an average of 9 days. All of the 24 soldiers who received “pure bromine” survived; and it took an average of only 2 days! Goldsmith included Weeks’ report in his final published report to add validity to his own data.

Goldsmith’s report also includes a selection of colorfully detailed case reports. John H. Brinton, another high-ranking Union surgeon, traveled to Louisville to observe Goldsmith’s work and reported similar results. He referred to one soldier with hospital gangrene who initially was very ill and lethargic. One day after initiation of the prescribed bromine regimen, his only complaint was that he had not been given enough to eat for breakfast!

The final published report (Fig. 3) contains over 30 pages of case reports, an elegant 30 × 20 inch foldout table containing all of his research data, and his correspondence with other surgeons across the nation. His data collection table was striking. It contained detailed information ranging from patient’s age, military assignment, date of injury, and extent of injury, to the exact method of therapy including duration and outcome. The level of organization and detail in his impressive prospective trial during the Civil War was remarkable even when examined independently from
his results. The combination of his clinical results and his method of data collection and reporting allowed him to claim near complete eradication of hospital gangrene from his wards.7

In total, Goldsmith compiled data on 334 cases of hospital gangrene in his Louisville hospital network. His records show that 304 patients received a bromine-based therapy. Only eight bromine-treated patients died, a mortality rate of 2.6 per cent. Eight of the 13 patients in the nitric acid group died, a staggering 61.5 per cent mortality rate. Thirteen patients received “other treatments” and five succumbed, yielding 38.4 per cent mortality. Interestingly, the remaining four patients had a bromine “salvage” regimen after others failed, all survived.7

Other surgeons challenged his results. John Crowe, an assistant surgeon in Louisville, claimed that bromine was indeed efficacious against superficial cases, but deep-seated wounds did not respond. He provided no data to support this claim. Dr. W.W. Keen refuted its utility based on the pain and fumes associated with its use. Goldsmith argued that patients tolerated bromine much better than nitric acid and other topical agents. Surgeon J.E. Summers believed that Goldsmith skewed his data by considering every sloughing wound as hospital gangrene.1 This was a valid argument due to the lack of a concrete pathologic definition for the disease. However, Goldsmith, arguably the foremost authority on the topic in the country, argued that the distinctive odor was pathognomonic. A modern textbook writer contended that the now extinct entity (and thus inaccessible to modern research scrutiny) of hospital gangrene has a tendency to heal spontaneously. Goldsmith would argue that these “spontaneous recoveries” happened much more frequently after bromine application when compared with all other therapies.4

According to The Medical and Surgical History of the Civil War, the official total number of hospital
gangrene cases was 2642. Of these, 1361 soldiers recovered and 1142 died for an overall mortality of 45.6 per cent.\(^1\) The records do not specifically identify the cause of death in these cases. The remaining 139 cases officially had an “undetermined” outcome. However, Goldsmith’s bromine-based therapy overall mortality of 2.6 per cent clearly represented a monumental outcome improvement in hospital gangrene treatment.

After the war, Goldsmith’s Union ties made him quite unpopular in southern sympathizing Louisville society and he returned to Vermont. He never worked to rebuild an active private practice as he once had. Instead, he preferred to consult and assist on difficult cases, lecturing often, and volunteering as an expert witness in medico-legal cases, where he was supposedly never defeated. He also continued his extensive medical writings. To help him, Goldsmith enlisted his attractive daughters’ many suitors to reluctantly help copy and compile his medical and surgical papers for lectures and publications.

Despite the formidable fortune he had accumulated from his prewar practice, he had long since given up his aristocratic tendencies, preferring his characteristic broad-brimmed hat and woodsman-like clothes. Back in Vermont, he established and ran the Rutland Free Dispensary, which provided medicines and medical care to the poor. He fought for (and won) increased funding to improve sanitary conditions at the Vermont State Asylum. He even directly challenged the Vermont Governor to spend a night there to prove his point. Undoubtedly, Goldsmith took his greatest joy in sharing his 30 years experience with young medical professionals.\(^13\) Before his death in 1888, he donated his extensive personal library to the Academy of Medicine at New York.\(^15\)

Goldsmith’s greatest achievement, however, would have to be his contribution to surgical antisepsis and his revolutionary bromine therapy. By the conclusion of the war, surgeons applied variations of his bromine regimen throughout the country. Many surgeons even began to lament about bromine shortages.\(^1\) His meticulous approach to studying an enigmatic disease and developing a highly successful treatment is remarkable. Further, the fact that his achievement predated the work of Joseph Lister, the near eradication of hospital gangrene from his patient wards is worthy of increased historical attention and adds to the rich medical heritage of Louisville, Kentucky.

**REFERENCES**

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