Dakin’s Solution: Past, Present, and Future

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ABSTRACT
Dakin’s solution has been used for almost a century. It is a dilute solution of sodium hypochlorite, which is commonly known as household bleach. When properly applied, it can kill pathogenic microorganisms with minimum cytotoxicity. This article reviews its history and discusses how evolving technology might pave the way for a new role for this antiseptic.

KEYWORDS: Dakin’s solution, antisepsis, wound care, medical history, negative-pressure wound therapy

INTRODUCTION
It can be easy to forget that the evolution of wound care is forged in war, human suffering, and the progress of civilization. In the 20th century, wound care became intertwined not just with history, but with development of modern science and technology. The story of Dakin’s solution illustrates not only the intersection of medicine and history, but also demonstrates how medical advances owe their genesis to the struggle and lives of individuals. Dakin’s solution has been part of the wound care armamentarium for almost a century, and the men responsible include not only the biochemist Henry Drysdale Dakin, PhD, but also Alexis Carrel, MD, an ambitious Nobel Prize winning physician whose science and politics went darkly wrong. Were it not for Dr Carrel, the solution created by Dr Dakin would be unknown to us today.

Dakin’s solution is simply a dilute mixture of sodium hypochlorite—the primary ingredient of household bleach. Sodium hypochlorite is used to whiten clothes, remove stains, and to disinfect kitchens, bathrooms, and swimming pools. Undiluted household bleach comes as a 5% solution of sodium hypochlorite, and “full-strength” Dakin’s is sold over-the-counter as 0.5%, or 1/100 of the household concentration. This is the concentration recommended by the Centers for Disease Control and Prevention (CDC) as an effective disinfectant.

In its concentrated form, sodium hypochlorite can liberate dangerous amounts of chlorine or chloramine if mixed with acids or ammonia, and anhydrous sodium hypochlorite is explosive. Ingestion can cause vomiting and corrosive injury to the gastrointestinal tract, and skin contact causes chemical burns and liquefactive necrosis. When properly diluted and applied, a buffered solution of sodium hypochlorite can kill pathogenic microorganisms with minimum cytotoxicity. This article reviews the history of Dakin’s solution and discusses how evolving wound care technology might create an expanded role for this time-honored antiseptic.

HENRY DAKIN AND ALEXIS CARREL ARRIVE IN NEW YORK CITY
Henry Drysdale Dakin, PhD, was born in London in 1880 and studied at the Lister Institute of Preventive Medicine. He was interested in biochemistry and performed studies on enzymes and amino acid metabolism when the field was in its infancy. He came to the United States in 1905 on the invitation of Christian Herter, MD, a wealthy New York City physician affiliated with Bellevue Hospital Medical College, who established a research laboratory on top floor of his home on Madison Avenue. In the Herter Laboratory, Dakin experimented with the chemistry of proteins, working alone and unknown until developments in world history conspired to make his name part of the wound care lexicon.

Alexis Carrel, MD, was born in a village near Lyon, France, in 1873. His mother was an embroiderer, which may have set the stage for his interest in suturing. He studied medicine at the University of Lyon and specialized in surgery. His perfection of techniques for anastomosis of blood vessels in 1902 at age 29 would revolutionize vascular surgery and make organ transplantation possible. He came to North America in 1904 and spent time in Montreal, Quebec, Canada, then continued on to the University of Chicago where he continued his experiments on anastomosis of blood vessels and organ transplantation.

Dr Carrel built a reputation that gained the attention of Simon Flexner, director of the Rockefeller Institute of Medical Research in New York City, New York, where Carrel began work in 1906. He experimented with surgery of the heart, blood vessels, and organ transplantation, and, in 1912, he won the Nobel Prize for physiology and medicine in recognition of his studies in vascular anastomosis. Carrel had the distinction of being the youngest Nobel laureate and the first American scientist to win the Prize.

Both Drs Dakin and Carrel were in New York City at the behest of wealthy patrons who wished to advance medicine. The Herter Laboratory where Dr Dakin worked was on Madison Avenue in New York, New York. Dr Levine has disclosed he has no financial relationships related to this article. Acknowledgment: The author thanks Arlene Shaner, acting curator and reference librarian for historical collections at the New York Academy of Medicine, for providing critical assistance with the references for this article. Submitted November 10, 2012; accepted November 28, 2012.
near 68th Street, and the Rockefeller Institute was 6 blocks east on York Avenue and 66th Street. In the rarefied world of science and society, it is likely that the Nobel Prize winner and Dr Dakin knew of each other’s work.

THE COLLABORATION OF DAKIN AND CARREL IN WORLD WAR I

On June 28, 1914, Archduke Franz Ferdinand of Austria was assassinated, triggering the onset of World War I. On August 1, 1914, Germany declared war on France, and soon afterward, Dr Carrel returned to his native homeland to run a military hospital and research center funded by the Rockefeller Foundation. Dr Dakin accompanied Carrel to the war zone, where he would direct the chemical laboratory and accomplish the work that would make his name part of wound care history.

By 1915, the Western Front was marked by the deadly tactic of trench warfare. Vast areas of interwoven trenches and muddy dugouts became killing fields for hundreds of thousands of soldiers on both sides. History tells us that the greatest killer was not bullets or shrapnel, but disease and infection. Wounds in trench warfare combined tissue damage with deeply embedded debris, including mud and human waste. Clearly, improvements in medical care and asepsis would be a tool to win the war and prevent suffering, and this is where the collaboration of Drs Dakin and Carrel created innovation.

Not far from the frontlines, Dr Carrel revolutionized war surgery by pioneering techniques of debridement, cleanliness, and antiseptic methods. In the introduction to his classic work, *Treatment of Infected Wounds*, Dr Carrel wrote: “The suppression of wound infection would protect a large number of men from incapacity or death, and would bring about the rapid restoration to health of the greater number of those whose anatomic lesions are compatible with life. Such progress would result in great saving in money and men.”

Dr Carrel reviewed contemporary medical practices and observed that many surgeons did not use aseptic technique, and research studies of wounds rarely used measurement of bacteria and healing rates. In addition, there were few studies that showed quantitative changes in pathogenic bacteria when antisepic agents were used. Dr Carrel proposed using a substance that did not irritate skin, yet had sufficient bactericidal power to kill microbes present in a wound. This is where Dr Dakin’s work became an essential component of Dr Carrel’s innovations.

Dr Dakin developed the antisepic solution that became the cornerstone of Carrel’s surgical method. Dr Dakin tested more than 200 substances, measuring their action on tissues and bacteria before finally deciding on chloramines that can be converted to hypochlorite of soda. His goal was to identify a solution with minimal tissue toxicity that could sterilize a wound. Dr Dakin meticulously demonstrated his results with quantitative measurement of germicidal action.

The complexity and scope of choosing an antisepic is reflected in Dakin’s book, *A Handbook of Antiseptics*, which he coauthored with a professor of pathology at Bellevue Hospital. The authors review all known chemical antiseptics, their chemical structure, and pros and cons of each. They found that hypochlorites fit the criteria to minimize irritant qualities, while still maintaining antiseptic action. They observed that the germicidal properties of hypochlorites were short acting and concluded that the solution should be continuously instilled into wounds.

Using the solution developed by Dr Dakin, Dr Carrel developed techniques to quantify healing. These included measuring the wound surface with traced drawings and planimetry and calculating wound volume by measuring water poured into the wound. With these methods, Dr Carrel concluded that continuous instillation of Dakin’s solution both sterilized wounds and accelerated healing.

Dr Dakin was not listed as coauthor of Carrel’s book, titled *The Treatment of Infected Wounds*, but Carrel borrowed extensively from Dr Dakin’s writings. A close read of Carrel’s book reveals a nearly complete word-for-word reprint of Dakin’s paper titled, “On the Use of Certain Antiseptic Substances in the Treatment of Infected Wounds.” Dr Carrel also borrowed liberally from another of the biochemist’s publications, which recounted the history and background of the antisepic’s ingredients. It must have been difficult for a biochemist to challenge...
authorship by a Nobel Prize–winning surgeon and director of a military hospital in the midst of a world war. Dr Carrel’s surgical technique for wound healing relied heavily on Dakin’s solution as an antiseptic. He preceded its application by meticulously removing shreds of clothing, projectiles, splinters, blood clots, and necrosed tissue and accomplished careful hemostasis. He warned against packing a contaminated wound as this can protect microbes against antiseptics. Dr Carrel advised practitioners to cleanse and debride the wound as soon as possible and to localize residual projectiles and foreign bodies using radiography. He devised techniques for continuous delivery of Dakin’s solution using irrigation through a network of bottles, glass cylinders and stopcocks, and rows of perforated rubber tubes surrounded by absorbent fabrics (Figures 2 and 3). Large syringes with rubber bulbs were also used. These techniques were reported by contemporary nurses as messy and labor intensive, but effective in healing wounds.12 Dr Carrel demonstrated efficacy of his techniques with clinical observations and quantitative bacterial examination. He measured outcomes, including time for wound closure, decrease in amputations, and diminution in length of treatment. He also provided a cost analysis that showed how decreased disability from use of his techniques would result in pension savings paid by the state.13 Dr Carrel made the groundbreaking claim, “…it has been possible to prevent, in the greater number of cases, infection of wounds and to abolish, almost entirely, suppuration in hospitals.”14

DAKIN AND CARREL PART WAYS BUT THEIR NAMES REMAIN LINKED

Dr Dakin settled with his wife on an estate overlooking the Hudson River 30 miles north of New York City. He married the widow of Dr Christian Herter, the patron who brought him to Manhattan and underwrote his experiments with protein chemistry. He continued his research, working alone and living a quiet life as his eponymous antiseptic was adapted by doctors worldwide. The antiseptic, however, bore not only the name of Henry Dakin, but was hyphenated with the name of Alexis Carrel. Review of the medical literature between the World Wars shows many studies referencing the Carrel-Dakin technique and Carrel-Dakin solution.15,16 In contrast with Dr Dakin, who retreated to a secluded country lifestyle, Dr Carrel not only continued his scientific
work but also expanded his association with famous and influential people. He returned to the Rockefeller Institute in 1919 and became friends with Thomas Edison and Henry Ford. He continued to pioneer new frontiers, developing techniques of tissue culture. At the Rockefeller Institute, Dr Carrel became the first to cultivate tumor tissue in vitro—a huge accomplishment in the pre-antibiotic era. In the 1930’s, he teamed up with Charles Lindbergh to create a perfusion apparatus designed to keep organs alive outside the body. Alexis Carrel also turned his mind and career toward improving the human race through eugenics—an effort that would lead him to serve the wrong side of politics and blot his reputation in history. While at the Rockefeller Foundation, he used his research facilities to breed a superior race of mice. He summarized his eugenic theories in a book entitled, Man the Unknown. Published in 1935, this best-selling book advocated creation of a human utopia under the direction of an intellectual elite—a view that echoed the politics of fascism at a time when Hitler and Mussolini were gaining power in Europe.

In blunt and chilling terms, Dr Carrel described his philosophy and plan for “...the salvation of the white races in their staggering advance toward civilization.” He proposed techniques to mold the human race into a strong and superior group using psychology, nutrition, education, and spiritual enrichment. For undesirable people of society, such as criminals and the insane, Dr Carrel suggested that they “...should be humanely and economically disposed of in small euthanastic institutions supplied with proper gases.” When his book was introduced to Germany in 1936, Carrel added praise to the Nazi regime for their “energetic measures” to promote eugenic theories.

During World War II, Dr Carrel rejoined the war effort in Europe. He took a job underwritten by the Vichy regime in occupied France, becoming head of an institute named The French Foundation for the Study of Human Problems. Its aim was to investigate the reconstruction of man in the spirit of his book, “Man the Unknown.” After the Allies reached Paris in August of 1944, Dr Carrel was arrested and accused of being a Nazi collaborator. He died shortly thereafter on November 5, 1944, at the age of 71.

After the war, the name of Alexis Carrel was dropped from Henry Dakin’s antiseptic solution, but its application for infected wounds continued.

**Dakin’s Solution Today**

The human carnage of World War II stimulated a new search for agents that could fight infection. By 1943, clinical trials had demonstrated penicillin’s efficacy as an antibacterial agent, and production was scaled up to treat Allied soldiers. The antibiotic era rendered obsolete the complex and labor-intensive irrigation techniques pioneered by Dr Carrel.

In the ensuing years, many other topical antiseptic therapies were developed including bacitracin, chlorhexidine, benzalkonium chloride, iodine-containing agents, and others. Systemic antibiotics and advances in life support enabled the growth of new medical fields, such as burn science and plastic surgery. By the end of the 20th century, as changing population demographics brought an increased prevalence of pressure ulcers and diabetic wounds, other specialties became involved with wound care, including hyperbaric oxygen therapy, podiatry, and vascular surgery.

Henry Drysdale Dakin died on February 10, 1952, at the age of 72. His solution continues to be used by today’s wound care practitioners, but few are aware of its history. In addition, there is little knowledge of the requirement for continuous instillation due to short-acting bactericidal properties determined by Drs Dakin and Carrel. And, few contemporary guidelines for its use are available.

In general, topical antiseptics such as Dakin’s solution, povidone iodine, and hydrogen peroxide are frowned upon because of their adverse effects on healthy tissue. However, there is literature that suggests they can be safely used in certain highly contaminated wounds and that their use is cost-effective. Clinicians know that Dakin’s solution is inexpensive, and it is effective against a broad spectrum of aerobic and anaerobic organisms as well as fungi, including antibiotic-resistant organisms. Dakin’s solution is available commercially at full strength (0.5%), half strength (0.25%), quarter strength (0.125%), and 1/40 strength (0.0125%). The term “full strength” refers to the highest concentration tolerable to the skin, and the mixture recommended by the CDC as a household disinfectant. The product information for all 4 of these strengths is identical: once daily for lightly to moderately exudative wounds, and twice daily for heavily exudative wounds or highly contaminated wounds.

In a literature review performed by Century Pharmaceuticals, they noted no consensus for the use of topical antiseptics, and further research concluded that clinical trials are needed for the best concentrations of Dakin’s solution.

There are many unanswered questions regarding Dakin’s solution. In an era of advanced wound care when so many products are available, what is the best clinical situation for application of this mixture, and for what duration and concentration? Henry Dakin determined that because of its short half-life, the solution must be applied as a continuous irrigation, so why is it recommended only once or twice per day?

In a modern technological innovation that echoes the techniques developed by Carrel and Dakin, negative-pressure wound
therapy (NPWT) now is available with automated irrigation for wound cleansing and removal of infectious materials. Topical solutions are cyclically fed into the foam dressing via an additional set of tubes under negative pressure. Raad et al tested NPWT with Dakin’s solution irrigation on 5 patients with venous stasis ulcers with favorable results. KCI lists quarter-strength Dakin’s (0.125%) as one of the solutions compatible with their instillation technology, along with isotonic saline, silver nitrate 0.5%, sulfonamides, and others. In a pilot study of NPWT with instillation, Gabriel et al describe clearance of infection, earlier wound closure, and earlier hospital discharge—claims similar to those published by Alexis Carrel in 1917.

There is recent controversy as to whether medical eponyms should be abandoned. In the author’s opinion, eponyms honor history and remind us of our humanity. In the case of Dakin’s solution, this eponym teaches us that wound care is forged in war and the struggle for the advancement of medical science and civilization. The antiseptic solution described by Henry Drysdale Dakin has been with us for decades, and as technology seeks to evolve and push forward, this humble biochemist teaches that clinicians are not much farther along than they were almost a century ago.

REFERENCES