Development of wound therapy from the Dark Ages to the present1

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Introduction
While the history of wounds and their management in the ancient world has been treated to a fascinating and scholarly account by Majno (1975), modern developments in the field do not appear to have merited similar treatment. Wound management has been influenced by advances made in a number of scientific fields including biology, chemistry, bacteriology, pharmacology and, not least, those made in surgery itself. Many are already difficult to date accurately and many pioneers remain relatively unknown— even in such well-researched areas as the introduction of antisepsis.

The demonstration that the antiseptic treatment of wounds could prevent wound infection and septicaemia was preceded about 40 years earlier by the introduction of a number of effective topical antimicrobials. Numerous compounds have been introduced in the last 150 years and a number of them are reintroductions of substances used by ancient or primitive peoples. During the past century there has been a huge amount of research into wounds, wound healing and wound therapy, which began towards the end of the nineteenth century with the identification of the cellular components of the wound and continued with the investigation of inflammation. Since the Second World War, the influence of nutrition and blood supply has been clarified while the importance of good surgical technique and careful selection of surgical materials has also been studied. In the past decade there has been renewed interest in the chemistry of inflammation, stimulated by the discovery of the prostaglandins. Parallel with these advances there have been numerous additions to the number of preparations available for treating wounds. The aim of this paper is to put these advances into perspective.

Toward the Renaissance
The works of Celsus and Dioscorides in the first century AD, together with Galen's writings about a century later, indicate that the art of surgery had attained a degree of sophistication by the time they were compiled. The practice of copying manuscripts by successive generations of scribes led to the embodiment of errors that enshrined misconceptions in the texts. Thus slavish adherence to the texts— especially those of Galen— and the rigidity of thought that dominated the Middle Ages led to a conservatism and limitation in surgical techniques such that by the sixth century standards had declined. This decline continued through the Middle Ages in Europe, while standards were better maintained in the Middle East by Jewish and Arab surgeons.

The Jews, the Arabs and the early Christian Church had all held surgery in low regard. The sick were considered unclean and no educated person would consider touching a patient. Thus surgery became a profession practised by itinerant barbers, cutters and others, while physicians came from better-educated backgrounds. Lack of systematized surgical teaching caused a number of important observations on wound treatment to be overlooked and forgotten. The use of the ligature to tie off bleeding vessels disappeared and debridement and

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secondary suture of wounds were no longer attempted. Greater reliance came to be placed on the application of remedies to the wounds, together with purges and diets. Foul mixtures came to be recommended with the aim of promoting the formation of suppuration in the wound. The concept of *pus bonum et laudabile* was to dominate wound treatment until microorganisms were shown to be responsible for wound infection.

There were few advances in wound treatment between the fifth and fifteenth centuries. Cautery, which came into wide usage in Islamic surgery, was quickly adopted in Europe when Moorish and Christian surgery came into contact with each other in Spain in the twelfth century. Although a few more enlightened surgeons tried to teach more rational methods of wound treatment, wounds were almost universally probed, packed and smeared with irritant ointments to guarantee suppuration. By the twelfth century the secular universities had begun to assume responsibility for the care of the sick—previously the exclusive province of the Church. Many of the more renowned practitioners were still clerics.

The introduction of gunpowder into European warfare during the fourteenth century led to the appearance of what was considered to be a new type of wound that was thought to be more dangerous than the traditional war wound. Gunshot wounds were considered to be contaminated with powder that was thought to be particularly poisonous. Who first propagated this idea is not known for certain, but one of its chief protagonists was Giovanni de Vigo (1460–1520) and it was he who introduced the treatment of gunshot wounds with boiling oil. Argument about the correct treatment of these injuries was to rage for almost a century until the notion of gunpowder as a special poison was dispelled by Leonardo Botello (1530–?) in 1560.

Western Europe was ravaged by almost continual wars from the twelfth to the seventeenth centuries and the armies required surgeons to care for the wounded. Field hospitals were not introduced until the sixteenth century; prior to that the injured were cared for by the soldier's comrades-in-arms and, if the wounded man could be moved from the battlefield, by women camp followers. Serious injuries requiring surgical intervention—usually amputation—were treated by army cutters employed by the army commander; he would be accompanied throughout a campaign by his own physicians and surgeons who were responsible only for his care. The post of army surgeon was not an attractive one and usually the bounty offered by a successful campaign was the only incentive to join up. Thus often army surgeons were young and inexperienced barber-surgeons or field cutters. However, in the fifteenth century a new class of skilled army surgeons developed — the wound surgeons, *wundarznei* — who had learned their trade on the battlefield.

Three German wound surgeons were to achieve some renown by writing books on wounds and their treatment. The first of these was the poorly-educated Heinrich von Pfölspeundt (dates unknown) who wrote his ‘Buch der Bündth-Erztnei’ in 1460. While dealing predominantly with the care of arrow wounds, he does make passing mention of the necessity of removing gunpowder from gunshot wounds. Von Pfölspeundt used dressings of oil of turpentine to make his wounds suppurate—probably with a high degree of success! About a generation later, Hieronymus Brunschwig (c. 1450–1533) wrote his ‘Cirurgia, ein handbuch der Wundarznei’ (1497) which was mainly concerned with the treatment of gunshot wounds and recommended the use of ‘Narcotic’ dressings. The third of the German wound surgeons was also the most erudite: Hans von Gersdorff (dates unknown), in his beautifully illustrated ‘Feldtbuch der Wundarznei’ (1517), advocated the removal of gunpowder from contaminated injuries and suggested using warm oil on such wounds to cause suppuration and sloughing of the contaminated tissues. This idea was taken up by de Vigo who improved the chances of causing sloughing of the tissues round the wound by advocating the use of boiling oil—which soon became accepted treatment.

In 1536 the inexperienced barber-surgeon Ambroise Paré (1510–1590) joined his first military campaign as a field cutter and spent two years in Italy. He published his experiences in 1545 in his ‘La Méthode de Traicter les playes Faictes par Harquebutes et Aultres Bastons de Feu’ in which he tells the, now famous, story of how he was forced to dress the wounds of a large number of soldiers with egg-yolk, rose oil and turpentine after his boiling oil ran out.
following a particularly bloody battle. When he examined the wounds the following morning, he found those treated with boiling oil to have fared much worse than the others who were generally more comfortable, while the former were febrile and in great pain. He resolved never again to use such cruel treatment (Paré 1840).

Though Paré is usually considered a Renaissance surgeon he was basically conservative and held to Galenic teaching, and was not above using alchemical remedies. While in Italy on the campaign of 1536–1538 he went to considerable pains to insinuate himself into the confidence of a famous Italian surgeon in order to obtain the recipe for his much-praised wound salve; Paré succeeded, and used the salve for many years. It was made by boiling newly pupped young whelps in oil of lilies together with worms and Venetian turpentine. The surgeons, barbers and wound surgeons were not the only people treating wounds and even the experts were not beneath accepting advice from laymen. Paré himself was helped by a countrywoman who advised him to try raw onions rubbed in salt to prevent a burn blistering. He tried it on a severely burned boy, applying the onions to part of the burn and his usual 'refrigerating' cream to the remainder. On the next day he found the parts treated with onion to be unblistered and the rest severely blistered (Paré 1840). Other remedies may be found in literature from the same period. Thus a goatherd treated Don Quixote's wounded ear with a paste of rosemary leaves chewed and mixed with salt, and assured the Knight that it would heal his injury—which it did (Cervantes 1604).

In spite of Paré's reputation and admonition against the use of boiling oil, both it and the use of cautery were to continue for a further two hundred years. Although the Renaissance led to great advances in anatomy and physiology and scientists showed a greater readiness to critically observe disease processes and treatments, there was no significant improvement in the treatment of wounds. Few new drugs were introduced, which necessitated reliance on long-established remedies such as plant extracts, grease, honey, wine and vinegar or stronger alcoholic mixtures. Paré abandoned his whelps for pastes of honey and alum or, later, brandy and turpentine. In general, the latter part of the sixteenth century saw a more humane treatment of the wounded, with fewer packings, fewer dressing changes and a reduction in the number of irritants applied to wounds (Fähreus 1944).

Marking time

The seventeenth and eighteenth centuries saw no further change in wound treatment despite the fact that a number of fundamental discoveries were made that would, much later, be realized to be of great importance in understanding the process of wound healing and wound treatment. The discovery of the circulation of the blood and the discovery of oxygen are two examples. Nor was the importance of James Lind's (1716–1794) discovery that lemon juice could prevent scurvy realized immediately. He suggested in 'A Treatise on the Scurvy', published in 1753, that lemon juice should be added to sailors' rations to prevent the disease; but the first trials were not made until forty-two years later, in the year after Lind's death. Naval surgeons realized that scurvy interfered with wound healing as affected sailors developed foul sores and old, healed wounds reopened, only healing again when their scurvy was adequately treated. Apparently this observation did not lead to attempts to improve the healing of other types of sore by the administration of lemon juice. Vitamin C, whose antiscorbutic effect was not demonstrated until almost two hundred years after Lind's observation, was first used to try to improve healing in 1947 in burned patients (Lund et al. 1947).

Otherwise naval surgeons, like all others at this time, were forced to rely on the same wound treatments as their predecessors. James Yonge (1646–1721), a naval surgeon who introduced the use of a muscle flap to cover amputation stumps, is quoted (Bishop 1962) as applying terra sigillata (red clay), egg white, vinegar and herbs to wounds – treatment straight from Celsus or Galen. Some interesting treatments were advocated, however. Sir Kenelm Digby (1603–1665), a colourful character who had been a privateer, became a proponent of wound treatment with the 'Sympathetic Powder' – made from moss scraped from a dead man's skull and mixed with powdered mummy's flesh – and managed to convince Francis Bacon (1561–1626) sufficiently
of its efficacy for him to include it in his scientific collection (Richardson 1925). Digby also advocated the application of gold leaf to early smallpox lesions that had been smeared with sweet almond oil; this was said to prevent scarring. Three hundred years later, in the mid 1960s, gold leaf treatment of wounds was resurrected and a number of papers appeared describing its use in chronic skin ulcers (Smith et al. 1967).

The age of antisepsis

Advances in chemistry led to the the isolation of a number of new elements in the eighteenth and nineteenth centuries. Chlorine was discovered by von Schelle (1742-1786) in 1774 and iodine by Bernard Courtois in 1811. Chlorine solutions were already in use in hospitals for cleaning purposes by the 1820s, and a number of suggestions had been made that they might also be used as a hand rinse before operations (Reddish 1957) before Semmelweis (1818-1865) published his famous report on the use of hypochlorite solution in the prevention of puerperal sepsis in 1846 (Semmelweis 1861). Oliver Wendell Holmes (1809-1894) had made a similar suggestion in 1843 (Holmes 1891) but Semmelweis provided the most convincing evidence. Reddish (1957), however, gives priority in the use of chlorine solutions in the prevention of puerperal sepsis to Robert Collins, who had used them in 1829. Chlorinated soda solution had been used on wounds at least four years earlier by Labarraque (1825), whose name is still applied to a solution of sodium hypochlorite containing not less than 4% or more than 6% sodium hypochlorite. Iodine was a commonly used disinfectant in the American Civil War (1861-1865) and was still considered the agent of choice in the First World War (Mayo-Robson 1915).

Joseph Lister (1827-1912) had not heard of Semmelweis’ work when he began his experiments to find a suitable substance with which to disinfect wounds. Carbolic acid – phenol – had been discovered in 1834 but was not used on wounds until 1860 (Lemaire 1860). In 1867 Lister – who, unlike Lemaire, appreciated the possible role of bacteria in wound infection – published his report on the treatment of compound fractures with carbolic acid, the same year that Savory suggested that it – among other substances – could be used in the treatment of pyaemia (Savory 1867). Lister’s Antiseptic System, incorporating carbolic acid, was not immediately universally accepted. While surgeons in continental Europe – particularly in Denmark and Germany – readily began using it, it took twenty years before it became widely used in Britain.

Alcoholic mixtures had been used in the treatment of wounds since wine was introduced at the time of Hippocrates. Majno (1975) reviewed the mechanisms of antisepsis of wine and found that it contains a number of polyphenols with antibacterial properties up to thirty times greater than carbolic acid (against Escherichia coli); hypochlorite solution is about 14000 times more effective (Smith et al. 1915). In 1881 Robert Koch (1843-1910) reported that dilute alcohol did not kill anthrax spores – the standard test for antiseptic effect – and therefore no further investigations of its effects were made until 1894 when Reinike showed more concentrated solutions to be antiseptic. Wirgin (1904) compared the antiseptic effects of a number of alcohols and showed that propyl alcohol was more effective than ethyl alcohol and that amyl alcohol was the most effective antiseptic. Beyer (1912) proved the efficacy of 70% (by weight) ethyl alcohol, and its availability and cheapness ensured its rapid acceptance.

Metallic antiseptics were introduced in the final decades of the nineteenth century after mercuric bichloride had passed Koch’s anthrax spore test. Bacteria rapidly develop resistance to inorganic mercurials and they fell into disfavour. Organic mercurials, such as mercuriochrome, appeared in the second decade of the twentieth century (Young et al. 1919). Silver is a more effective antiseptic, but most topical preparations are absorbable and likely to cause argyrosis. Colloidal silver preparations were used by Credé in 1897 (Reddish 1957) on wounds and he also treated skin infections with silver citrate. Katadyn silver – silver bound to ceramic powder – was introduced in 1928 and the latest silver preparation, silver sulphadiazine, in 1958; this is used widely in the treatment of pseudomonas infections in burns. The inorganic salts of a number of metals had been used on wounds since ancient times: copper, aluminium, zinc, lead and iron salts were the most common. They all have
antiseptic properties though lead is too toxic and iron relatively ineffective. Copper, too, is toxic and zinc and aluminium are now mainly used for their astringent effect – the latter being an effective antiperspirant. The local application of zinc to wounds has aroused new interest in recent years, claims having been made that it promotes healing, at least in zinc-deficient individuals (Chvapil 1974). Unna’s zinc sulphate paste is still used in the treatment of chronic leg ulcers.

The twentieth century has seen the introduction of a large number of topical preparations for wound treatment as well as research into wounds and wound healing. The mechanisms by which various types of wound arise and the factors affecting them have been clarified, and a realization has come in recent years that the topical treatment of wounds is of subordinate import. Improvement in wound care depends on good surgical technique, good nursing care and the avoidance of catabolism in the individual being treated. Metabolic abnormalities, intercurrent infections or other diseases should, as far as is possible, be treated effectively if wound infection is to be avoided and healing allowed to proceed at an optimal rate. Many topical agents have a deleterious effect on the healing process and if used should be as innocuous as possible (Forrest 1980).

The most significant advance in the treatment of infection in this century is undoubtedly the introduction of antibiotics. Sulphonamides were introduced in the mid 1930s and were applied to wounds in powder form to treat infection. Topical penicillin was first used in 1943. Corticosteroids were isolated in the late 1940s and steroid creams were soon available for the treatment of inflammatory skin conditions. They were much used to combat wound inflammation until the inhibitory effect of cortisone on wound healing was described by Sandberg in 1964. Hunt and coworkers (1969) showed that systemic vitamin A would reverse cortisone’s effects on healing.

A cornerstone of good surgical management of wounds since the First World War has been adequate debridement of contaminated or necrotic tissue from the wound. Attempts had been made since ancient times to achieve debridement by chemical rather than surgical means and many primitive peoples had used the fruit of the papaya (Carica papaya), which contains the enzyme papain, to this end. A number of other enzymatic agents – usually obtained from bacteria – were introduced between 1940 and 1960. They are used to digest collagen, fibrin or proteinaceous material on the wound surface.

Newer antiseptic agents have also appeared. Hypochlorite solution was reintroduced in 1915 as either ‘Edinburgh University Solution’, abbreviated as Eusol (Smith et al. 1915), or Dakin’s solution (Dakin 1915) – the latter being modified later by Carrel and called Carrel-Dakin’s solution. Eusol is still much used in Britain, while Carrel-Dakin’s solution is preferred in North America. Other antiseptics include quaternary ammonium compounds (introduced in 1935 as a surgical scrub and for preoperative skin disinfection); bisphenols – such as hexachlorophene (first used in 1948); dyes – such as brilliant green or methyl violet, which originate from the aniline compounds of the 1860s, while others have been used since ancient times; and newer substances such as chlorhexidine (introduced 1955).

The role of the dressing has also been examined and the requirements of the ideal dressing put forward (British Medical Journal 1979, Forrest 1979) but hitherto these do not seem to have been met. Numerous new materials have been advocated as wound coverings instead of the traditional woven gauze bandage. Skin, both autologous and xenograft, is in current use as are adherent plastic films, amniotic membranes and microspheres of carbohydrate polymer – which are reported to perform chromatography of wound exudate and remove inflammatory mediator substances from the wound (Jacobsson & Rothman 1973).

A number of easily obtained, inexpensive, naturally-occurring substances have been used in wound treatment during the last fifty years at least. Sugar, refined and unrefined, and honey are the commonest of these; the first scientific reports of their efficacy date from the 1930s (von Gozenbach & Hoffman 1936) even though honey has been used since Babylonian times (Majno 1975). How sugar acts on wounds is still debated, but honey has antibacterial properties dependent on the production of hydrogen peroxide from glucose (White et al. 1963); indeed, hydrogen peroxide has also been used on wounds though zinc peroxide and,
more recently, benzoyl peroxide are more often used. Interestingly, the use of insulin on wounds seems to predate the use of sugar. Léval (1930) described its use in non-diabetic patients, while it was apparently not used in diabetics until 1966 (Paul 1966).

Conclusion
Parallel to the development of effective antiseptics, research was undertaken into the physiology of wound healing and, in recent years, there has been a shift in the direction of this research first toward the role of surgical technique and surgical materials on wound infection and healing and, later, toward the importance of nutritional factors for the healing process. This research has led to an improvement in the general care of the patient and a realization that topical preparations play only a minor role in treatment. These agents are, however, still used in vast quantities and newer preparations still appear. Few can be convincingly demonstrated to improve wound care and many are expensive or toxic. If such agents are to be employed in wound treatment, their selection should be decided by pharmacological considerations and they should be used to treat a specific problem with as little effect as possible on the healing process.

References
Beyer A (1912) Zeitschrift für Hygiene und Infektionskrankheiten 70, 225-272
British Medical Journal (1979) ii, 689-690
Dakin H D (1915) British Medical Journal ii, 318
Forrest R D (1979) British Medical Journal ii, 1076
Forrest R D (1980) Journal of International Medical Research 8, 430-435
Jacobsson S & Rothman U (1973) IRCS (73-11) 3-11-7
Koch R (1881) Arbeiten aus dem Kaiserlichen Gesundheitsamt 1, 1-49
Labarraque A-G (1825) De l'emploi de Chlorures d'oxide de Sodium et de Chaud. Huard, Paris
Lemaire F-J (1860) Du Coaltar Saponifié Desinfectant Energetique Arretant les Fermentations de ses Applications à l'hygiène à la thérapeutique, à l'histoire Naturelle. Germer-Ballière, Paris
Léval M (1930) Wiener Klinische Wochenschrift 43, 362-365
Lister J (1867) Lancet i, 326-329
Lund C, Levenson S M, Green R W et al. (1947) Archives of Surgery 55, 557-583
Mayo-Robson A W (1915) British Medical Journal ii, 136
Paul T N (1966) Lancet ii, 574-576
Reinike E A (1894) Zentralblatt für Gynäkologie 18, 1189-1199
Richardson W G A (1925) Annals of Medical History 7, 216-219
Sandberg N (1964) Acta Chirurgica Scandinavica 127, 146
Savory W S (1867) Lancet i, 139-142
von Gosenbach W & Hoffman S (1936) Schweizerische medizinische Wochenschrift 1, 425-429
White J W, Swers M H & Schepartz A I (1963) Biochimica et Biophysica Acta 73, 57-70
Virgin G (1904) Zeitschrift für Hygiene und Infektionskrankheiten 46, 149-168
Young H H, White E C & Swartz E O (1919) Journal of the American Medical Association 73, 1483-1491