Wound healing: Historical Aspects

Fig. 1. A cave drawing in Spain dating back some 20-30,000 years. This is one of the first recordings of wounds from the Stone Age.

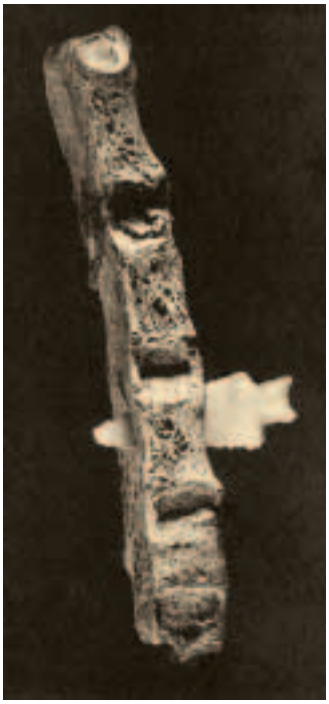

Fig. 2. a human sternum that is pierced by an arrowhead

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The earliest recording of a 'wound healing man' is in a cave drawing in Spain dating back some 20-30,000 years (Figure 1). This is one of the first recordings of wounds from the Stone Age. There is also fossilized evidence of wounds from the same period and a human sternum that is pierced by an arrowhead (Figure 2). From the earliest recorded history it is clear that the Assyrians knew about healing, not just from an observational point of view but also in terms of practical management. From them we have a description of surgical management: Figure 3 shows the cuneiform script for surgeon, which includes a hand. This represents the first concept of 'barber-surgeons': using hands and undertaking surgical operations. The barber's pole is of course related to surgery: white for the bandages and red for the blood.

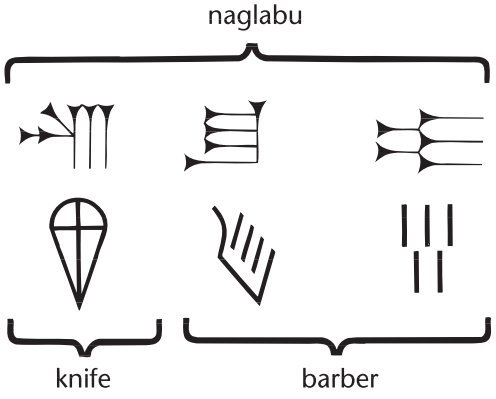

Fig. 3: Assyrian cuneiform script for 'surgeon'. Note the hand symbol.

The Egyptians also had experience in wound healing and several treatises on healing have been recorded. Figure 4 shows part of The Edwin Smith Surgical Papyrus in which the 'awy' and the 'ydr' are mentioned: the awy being a type of suture, a piece of thread, maybe on a thorn; and the ydr a type of steristrip, where strips of linen were laid across a wound to hold it together. The tools obviously worked in practice, and it is clear that the Egyptians understood the concept of primary wound healing.

The Egyptians also used antiseptics. They used the copper pigment malachite as both an eye adornment and an antiseptic. The Egyptians also knew of the value of sugar and honey. A mould can

Fig. 4. Egyptian text which contains the hieroglyphs for 'awy' (thread) and 'ydr' (strip) from the Edwin Smith papyrus.

grow on sugar but no organism grows in a concentrated solution. A honey or sugary salve can improve healing and reduce surface contamination, possibly as a topical nutrient, possibly just because it is hyperosmolar. Antiseptics used in open wounds are probably not always necessary and some antiseptics are actually quite toxic.

Soon after the Egyptians came the Indian knowledge professed by Sushruta Samhita. This document contains methods of skin suture and the details of techniques to incise an abscess. For practice, a bag of warm butter was used to simulate the feel of the knife going in and the pus coming out.

The Sushruta scripts also include a description of how insects have been applied in the healing of wounds. The earliest type of clip was based on the mandibles of certain ants. It describes how wounds in connection with the bowels caused so much juice that they were difficult to close. The mandibles from a certain 'soldier ant' were used to close these types of wounds. This technique is also found in Asia, Africa and South America. The mandibles from the *Eciton burchell* are particularly large (Figure 5). Its mandibles would close on the wound and the body would then be pinched off (Figure 6). Contemporary clips work according to the same principles but the 'ant-method' is still practised by some South American tribes.

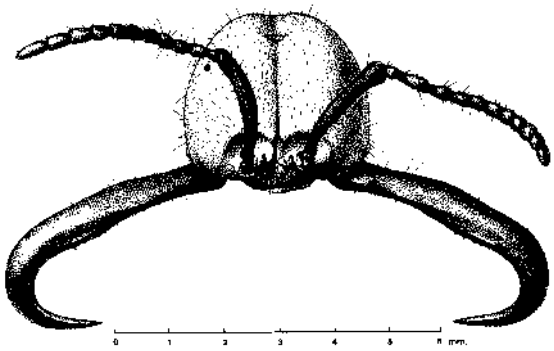

Fig. 5. The mandibles from the Eciton burchell *are particularly large.*

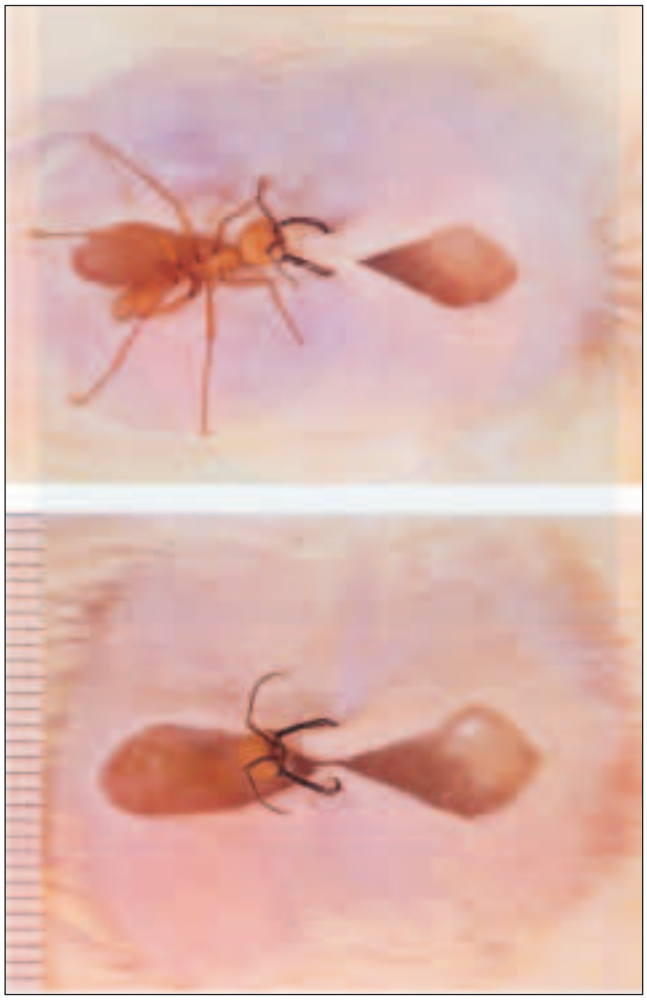

Fig. 6. The mandibles would close on the wound and the body would then be pinched off.

Fig.7. Listening to the'vayu'. It was believed that if you listened to a venous ulcer and the winds were blowing the right way, it might heal.

We also know of a Hindu practice which involved listening to the winds of the body, the 'vayu'. It was believed that if you listened to a venous ulcer and the winds were blowing the right way, it might heal (Figure 7).

The father of medicine, Hippocrates, who lived nearly 2500 years ago, wrote several accounts on wound healing and was aware of the importance of infection in relation to wound healing. He understood the concepts of primary and secondary wound healing, using antiseptics such as wine. Figure 8 shows the purpose of using wine for a different reason other than as a stimulant. In only a few hours, wine can eliminate certain types of bacteria such as cholera vibrios, E. typhi, S. Aures and, as shown, in the figure E. coli. The effect has been much disputed but cannot be due only to the alcohol in the wine. When taking the same concentration of alcohol the effect has been shown to be limited. Hippocrates pointed to the significant role of compression in the treatment of patients with leg ulcers, but even today this knowledge is not widely accepted.

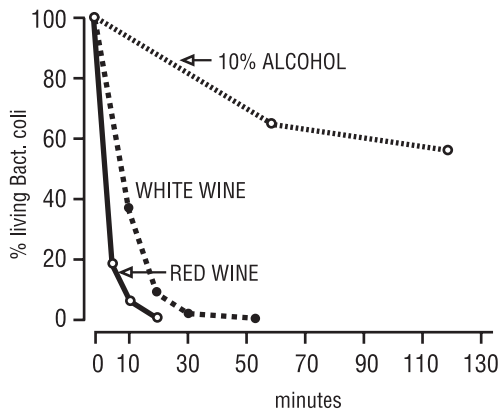

Fig. 8. The purpose of using wine for a different reason other than as a stimulant.

For centuries only limited information existed on wound healing. During the 15th century the anatomy was described in greater detail by the surgeon Andreas Vesalius. As a result surgical expertise became more acknowledged, although it was still carried out by barber surgeons. In England the Company of Barber Surgeons was constituted which laid the grounds for a surgical specialty. As the well-known wound-man shows, wound healing around this time was primarily associated with barber surgeons and acute traumatic wounds (Figure 9).

From the early history of wound healing it is apparent that Celsus in De Medicina, recognized the cardinal signs of inflammation. John Hunter, considered one of the fathers of surgery, recognized that we would not be able to operate without inflammation. Actually it was thought that the pus had to be present in order for the wound to heal. ▶

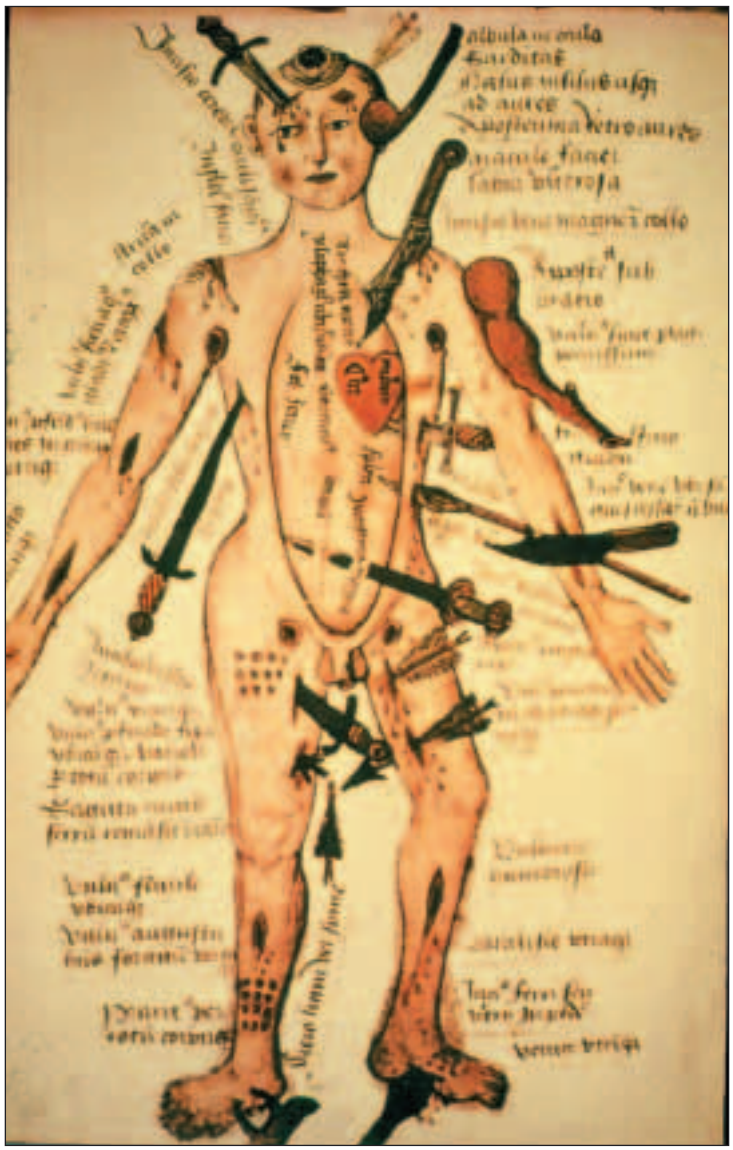

Fig. 9. In the 15th century wound healing was primarily associated with barber surgeons and acute traumatic wounds.

Fig. 10. The first patient treated with penicillin was police constable Alexander, who had already lost one eye with staphylococcal cellulitis.

One of the largest advances we owe to Ignaz Semmelweis, a Hungarian obstetrician who lived in Vienna. The obstetrician discovered that if you went from the post-mortem room to the delivery room, but washed your hands in between using chloride of lime, the maternal mortality was reduced. He did not know what the washed-off particles consisted of, only that they had a significant and appalling smell. By introducing obligatory hand washing the mortality rate fell from over 10% to 1% in two years. Sadly Semmelweis published his work too late and it did not receive the attention it deserved.

Lord Lister introduced antiseptics containing carbolic acid and realized that by using antiseptics compound fractures could heal and amputation be avoided. The idea of cleansing wounds was further developed by Alexander Fleming who was one of a group of scientists who discovered that penicillin could treat infections. The first patient treated with penicillin was police constable Alexander, who had already lost one eye with staphylococcal cellulitis (Figure 10). He responded to the treatment, but although the penicillin was recovered from his urine the supply ran out and Alexander died. The year was 1940.

Certain antiseptics can cause a negative effect on new as well as old tissue, and today antiseptics are rarely used in the treatment of open wounds. Alexander Fleming suggested in 1920 that the value of the antiseptic (antimicrobial) effect of antiseptics should be weighed against their toxicity in tissues. Although he did not perform any studies in this specific area there is good evidence that antiseptics are toxic and their value should be carefully judged.

Contemporary surgery is based on the results from these surgeons. In the early 1800s Ephraim McDowell performed the first elective abdominal operation on a large ovarian cyst. Had he failed he would have been lynched, but the patient, who sang hymns during the procedure

Fig. 11. By the 1920s major elective surgery was commonplace with general anaesthesia and the surgeons using gloves but no masks. Surgery in Baltimore.

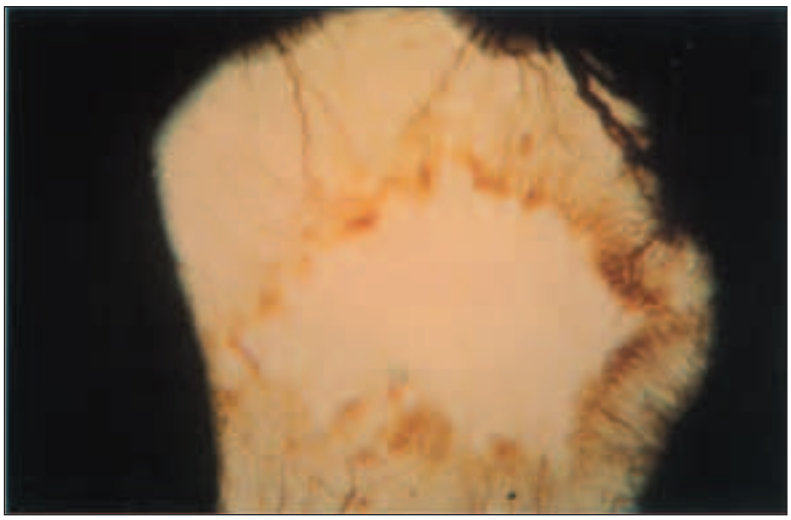

Fig. 12. The rabbit ear chamber allows direct visualization of the healing process and the formation of granulation tissue.

after taking wine, recovered uneventfully. By the 1920s major elective surgery was commonplace (Figure 11) with general anaesthesia and the surgeons using gloves but no masks. From these artisans came the aphorism of 'cut well, sew well, get well'.

Since then, research has produced many results and significant improvements have been made. Several experimental methods can be used for wound healing research, some are crude and others relatively sophisticated. We can grow fibroblasts or other cells involved in wound healing in culture and with supravital stains easily ascertain whether these cells are alive or dead.

From these experimental models, new knowledge is gained on the healing process and on factors or substances that can have an impact on the healing. Alexander Fleming suggested that the toxic nature of antiseptics on the treated tissue should be examined according to the above findings/models. The viability of fibroblasts from a baby hamster kidney has been examined in cultures containing dilute antiseptics. Even at a dilution of 1:100 or 1:1000 most of the commonly used antiseptics are highly toxic. We have also looked at the level of collagen acquisition in experimental wounds, by measuring hydroxyproline (a principal amino acid in collagen). Wounds dressed once with a saline dressing, compared with a dressing containing a standard clinical-use hypochlorite antiseptic, gain hydroxyproline significantly more quickly, suggesting that there is some delay in the healing process influenced by hypochlorite. The DNA in these wounds, which is a reflection of the acute inflammatory response, is increased in the wounds treated with hypochlorite and this is histologically confirmed. The rabbit ear chamber allows direct visualization of the healing process and the formation of granulation tissue. The ear chamber allows direct measurement, for example, of pO2, lactate and glucose. We have used it for measuring the effect of antiseptics and their effects on granulation tissue. With one application of a hypochlorite, within seconds the vessels constrict with a marked exudate. The flow of blood in those capillaries can be measured using a laser Doppler velocimeter. After hypochlorite it is reduced to zero and does not recover. Within a few weeks the granulation tissue grows back into the ear chamber periphery but the ghosts of the old blood vessels remain until granulation tissue is complete (Figure 12.).

In order to understand the wound healing process, it is necessary to understand the medical patho-physiology. The ability to heal by regeneration or tissue formation is significant. Microorganisms can completely regenerate and amphibians can regrow a damaged tail. However, while humans can regenerate liver cells and grow new skin and other epithelia, we cannot replace connective tissue. Once the spinal cord is transected, for example, it remains so for ever as healing is affected by scar tissue repair. The sequence of healing and the module of acute inflammation (macrophages, fibroblasts, myofibroblasts and angiogenesis) are well known. The macrophage interrelates with all the processes of healing and clearly is the key player. ▶

Open wounds do epithelialize, but the main contribution to the closure of epithelia is the contraction effected by myofibroblasts, which produce fibrils that pull the wound together. This can be visualized on a collagen lattice and is not an electron microscopic hypothesis. Angiogenesis in the healing wound edge brings nutrients and oxygen necessary to healing. The rich vasculature of granulation tissue in a healing wound causes its red appearance. When it involutes a white scar is left, with scar protein, collagen, forming when healing is complete. It has been recognized that epithelial cells cover a defect much quicker if a scab is not allowed to form. If the wound is kept moist then contraction and epithelialization can be enhanced. A moist environment also enhances granulation tissue formation.

The best dressing of all is skin. When large venous ulcers are clean they can take a skin graft and heal. The new dressings clean up venous ulcers for example and make them ideal for grafting. However, if adequate compression is not given then a healed grafted venous ulcer will revert to square one. If microbiological swabs are taken from ulcers healing by secondary intention, many commensal, and occasionally pathogenic, organisms are commonly harvested. If the wound is not clinically infected with invasive cellulites then antibiotics are not indicated except, if beta-haemolytic streptococci or Pseudomonas are grown from the swab. Conditions with a larger probability for infections, e.g. patients with diabetic foot ulcers, will require the use of antibiotics. When acute cellulitis occurs then appropriate systemic antibiotics should be used but there is rarely a need for topical antibiotics.

Some healing wounds are difficult to manage. Should we spend 6-8 weeks using a hydrocolloid dressing to soften necrotic tissue and debride the wound? Or should we simply take the patient to theatre and remove it surgically? Several methods have been applied through time and some, e.g. larvae, have re-emerged from oblivion. Today we know a lot more, but the basic questions such as what and when have not yet been clarified.

Ischaemic ulcers can be equally difficult to treat, but new operational methods mean that patients can have their peripheral perfusion restored and there are increased possibilities of treatment. The significance of ischaemia and diabetes in the healing process, particularly that of foot ulcers, has also become clearer within the last couple of years.

Ambroise Pare, who lived in the 15th century, exclaimed that he could dress a wound, but only God could heal it. During military service Pare managed to abolish the use of boiling oil to stop bleeding and there is no doubt that this was an important contribution to medical science. We have come much further since then and modern dressings no longer rely on divine intervention for success in healing.

However there are still many unanswered questions that need to be answered before the historical part of wound treatment can be integrated into modern wound healing and treatment. What dressings should be used, how should they be applied and for how long? Are we just putting off the inevitable need for an amputation? Can we avoid pressure ulcers, which are still a major problem, by compensating for age with prophylaxis? All of us are capable of making evaluations and it is crucial that our minds remain open to new concepts and do not close in the mists of tradition. The history of wound management is rich in examples of miraculous healing methods that have been adopted as recommended treatment methods without recognising that these were all individual actions. In modern wound treatment we should not forget these examples, but it is necessary to recognise that scientific documentation must be the main principal in wound management now as well as in the future. ■

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