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This article discusses the current needs and trends in wound care with particular reference to future trends in diagnostics and provides examples of some emerging techniques.

Across the globe the increasing prevalence of diabetes and cardiovascular disease, and the rise in the number of elderly people in the populations of developed countries are driving growth in wound care treatments, and increasing the burden of problems in wound management.

The exact global incidence and costs of wound care, plus the additional costs incurred when wounds become infected, are difficult to determine exactly due to differences in wound care within and between countries and differences in how wound care costs are categorised within health services.

Studies in different regions indicate that wound care is a significant cost to healthcare providers, however. As an example, we can consider some reports in the literature related to the UK, illustrating the scale of the problem in a developed country of some 60 million people. Posnett and Franks (2007) reviewed the literature from the UK wound care community and estimated the incidence and costs of common chronic wounds for the year 2005/2006. The incidence and costs are summarised in Table 1.

Overall, the total estimated cost of chronic wound care in the UK for the year 2005/2006 was £2.3 billion to £3.1 billion, and this is likely to increase as the UK population increases. This trend will be mirrored in other countries and thus it is clear that governments will find that wound care is a significant part of their healthcare costs. In addition to chronic wound care costs, there are costs associated with other acute wound types, for example burns and post surgical care.

The other area of interest globally in wound care is that of wound infection. This again is largely studied on a regional or per hospital basis by centres for infection control or other interested bodies. It is clear from the media and literature that Hospital Acquired Infections (HAIs) are problematic in most healthcare systems, and the public have an increased awareness and concern about this.

One route for HAIs to enter the body is via a wound, either through surgical site infection or by cross infection during wound treatment by hospital staff. A significant proportion of HAIs are wound related. Again, looking at the UK as an example, a survey in Scotland in 2005/2006 indicated that the prevalence of all types of HAIs among patients was 9.50% for acute hospitals and 7.32% for non-acute hospitals (Reilly et al., 2008).

Of these HAIs 15.8% and 3.0% were surgical site infections in acute and non-acute hospitals respectively, and 11.0% and 26.8% of all HAIs were soft tissue or skin infections. A similar survey of HAIs for England, Wales, Northern Ireland and the Republic of Ireland in 2006 indicates that the prevalence of HAIs among patients was between 5.43% and 8.19% (Smyth et al., 2008). From a wound care perspective the percentage of these HAIs that were surgical site infections was between 0.5% and 11.7%, and the remainder were soft tissue or skin infections of between 11.0% and 26.8% of all HAIs.

Thus there are two areas of concern for healthcare providers: firstly how to best manage wound care in a large and growing population of patients with a range of chronic and acute conditions; and secondly, how to reduce infection and manage infected wounds.

The availability of better diagnostics for wounds would provide the possibility of earlier intervention, better dressing selection and improved wound care protocols for patients.

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The availability of better diagnostics for wounds would provide the possibility of earlier intervention, better dressing selection and improved wound care protocols for patients. This in turn would reduce costs and staff time due to better use of dressings, possibly fewer dressing changes and more treatments being tailored to the individual patient’s needs.

To understand what types of diagnostics can improve wound care it is useful to consider the current best practise in wound healing and in diagnosis of infection.

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Table 1. Estimated incidence and costs of chronic wounds in the UK in 2005/2006

<table>
<thead>
<tr>
<th>Wound Type</th>
<th>Incidence</th>
<th>Cost per patient</th>
<th>Total annual cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous leg ulcer</td>
<td>108,600</td>
<td>£1,549 - £1,822</td>
<td>£168 million - 196 million</td>
</tr>
<tr>
<td>Pressure ulcer</td>
<td>370,000 - 465,000</td>
<td>£4,300 - £6,400</td>
<td>£1.76 billion - 2.64 billion</td>
</tr>
<tr>
<td>Diabetic ulcer</td>
<td>63,700</td>
<td>£4,710</td>
<td>£300 million</td>
</tr>
<tr>
<td>Total cost</td>
<td></td>
<td></td>
<td>£2.3 billion - 3.1 billion</td>
</tr>
</tbody>
</table>
Best practise - clinical guidelines

Acute wounds normally heal through four phases: haemostasis, inflammation, proliferation and remodelling. These phases occur within a specific time frame dependent on the severity of the wound. Chin et al (2005), and Johnstone et al (2007) provide a more detailed account of these phases.

Clinical intervention can help the healing process, depending on the type of wound. There are three clinical methods by which wounds are healed: in primary intention the wound edges are held together by sutures, staples or glue; with secondary intention the wound is left open to allow the formation of granulation tissue and epithelialisation; and tertiary intention is a combination in which the wound is left open for several days to remove contamination before bringing the edges together.

In effective healing of a wound several parameters are important. The wound bed is an important aspect in wound healing since this is the physical and biochemical base that the wound has to heal from. In optimal treatment any underlying diseases must be treated, an adequate blood supply to the wound should be ensured, and the wound history and characteristics should be assessed and monitored (Schultz et al, 2005).

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The wound bed should then be managed by debridement, exudate management and controlling bacterial growth. An important framework for the preparation of the wound bed, based on systematic management of non-healing wounds, was developed by the International Wound Bed Advisory Board (Schultz et al, 2005). This framework was given an acronym TIME and these terms were further developed by the European Wound Management Association (EWMA, 2004). The TIME framework is listed in Table 2.

Thus in recent years the market in wound care has centred upon ‘advanced moisture control dressings’ and additionally, dressings with slow release antimicrobials such as silver dressings. A wide range of dressings is now available to the wound care clinician and these include dressings based on foam, alginates, silver and hydrocolloids. A report by Krasner et al, 2010, contains helpful descriptions of modern dressings and summarises the key issues in dressing selection.

**Infected wounds**

Once a wound is present it will become contaminated either by microbes from the host’s body, from airborne dust or water droplets, or from contact with clothes, equipment and carers. The level of bacteria in a wound advances from contamination to colonisation and then infection, in which the bacteria overwhelm the immune system and this can lead to systemic infection, septicaemia, bacteraemia, and death.

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**Table 2. The TIME framework for wound bed preparation**

<table>
<thead>
<tr>
<th>TIME elements</th>
<th>Pathophysiology</th>
<th>Suggested treatment</th>
<th>Clinical result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue management</td>
<td>Defective matrix and debris inhibit healing</td>
<td>Debridement</td>
<td>Viable wound base</td>
</tr>
<tr>
<td>Inflammation and infection control</td>
<td>High bacterial counts/prolonged inflammation</td>
<td>Topical or systemic: Antimicrobials, Protease inhibitors</td>
<td>Bacterial balance and reduced inflammation</td>
</tr>
<tr>
<td>Moisture balance</td>
<td>Desiccation or maceration</td>
<td>Moisture balancing dressings: Negative pressure, Remove fluid</td>
<td>Correct moisture balance</td>
</tr>
<tr>
<td>Epithelial (edge) advancement</td>
<td>Epithelial cells not migrating, Wound cells not responsive</td>
<td>Reasses cause, Corrective therapies</td>
<td>Advancing epidermal margin</td>
</tr>
</tbody>
</table>

Traditionally, it was thought that exuding wounds should be kept as dry as possible to prevent bacterial infection, which was common practice up until and including the late 1950s. This involved applying highly absorbent materials, removing as much exudate as possible from the wound. This approach was first challenged by research conducted by Winter (1962) and others thereafter who demonstrated in both pigs and humans that wounds that were kept moist healed more rapidly than those that were left uncovered, or treated with traditional highly absorbent dressings.

Under the traditional arid conditions the wound dehydrates resulting in the formation of a scab, or eschar, consisting of dried serous exudate and a layer of devitalised dermis. This scab provides an effective barrier to migrating epidermal cells, which forces the cells deeper under the scab. This effectively increases the healing time and may cause the loss of healthy tissue.

Another aspect of dressing choice and wound monitoring is that the dressing could adhere or become bound to the wound surface as the wound dries. In this situation considerable damage would be inflicted upon the delicate healing tissue when the dressing is removed.

It is possible to prevent the formation of a scab by application of an occlusive dressing. This means that the wound under the dressing is moist, allowing the rapid movement of epithelial cells across the surface of the dermis through the wound exudate at the surface of the wound. Although it is desirable that the wound should remain hydrated, excessive pooling of liquid under the wound dressing should also be avoided. This can cause further damage to the wound as it can result in maceration, which leads to the breakdown of skin barrier function and causes additional pain (Cutting and White, 2002) to the patient. In addition, excessive liquid can result in ‘strike through’ of fluid to the outer surface of the wound dressing. This provides a pathway for bacteria to pass through the dressing into the wound, reducing the protective barrier function of the wound dressing.

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AMH / April 2013 38
The European Wound Management Association position paper on wound infection (EWMA, 2005) identifies the three stages of infection in a wound as shown in Table 3.

**Table 3. EWMA infection stages**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contamination</td>
<td>All wounds may acquire microorganisms. If suitable nutritive and physical conditions are not available for each microbial species, or they are not able to successfully evade host defences, they will not multiply or persist; their presence is therefore only transient and wound healing is not delayed.</td>
</tr>
<tr>
<td>Colonisation</td>
<td>Microbial species successfully grow and divide, but do not cause damage to the host or initiate wound infection.</td>
</tr>
<tr>
<td>Infection</td>
<td>Microbial growth, multiplication and invasion into host tissue leads to cellular injury and overt host immunological reactions. Wound healing is interrupted. Local factors can increase the risk of infection.</td>
</tr>
</tbody>
</table>

**Diagnostics**

It is only relatively recently that the field has started to develop notable scientific interest in the more complex aspects of wound diagnostics beyond swabbing for bacterial infection. Given the complexity of wounds and the variation in healing between individuals, there is a need for more diagnostic parameters of relevance to be measured and considered in the healing of complex wounds.

Currently there is a real lack of analytical tools available to assess the real time status of wounds and at present clinicians still rely largely on skilled observations to evaluate the healing stage of a wound.

In terms of parameters that are of interest in the healing wound these divide between biomarkers and physical parameters. Among the biomarkers there is interest in measuring a range of parameters in wound exudate and tissue, including bacterial load and species, enzyme activity (particularly metalloproteases), growth factors, hormones and cytokines. The physical parameters of interest include wound moisture, temperature and pH.

**Current situation in wound diagnostics**

Analytical measurements such as wound pH, accurate wound sizing and moisture balance would enable an objective measurement of healing to provide the clinician with the most efficient and effective techniques to heal the wound.

For infected wounds, products that will enhance clinical decision making and intervention need to be able to quickly distinguish bacteria early enough in the colonisation phase, and indicate that bacteria is not only growing, but is reaching ‘critical colonisation’ and getting ready to fully infect the host.

Thus products need to be able to quantify bacterial load, be portable and require minimal sample volumes. Of the products currently available that use advanced technology to speed up and improve accuracy of bacterial tests, the leaders are those using molecular diagnostic techniques.

The suppliers in this field range from multinationals to emerging SMEs with new molecular detection techniques. They are in competition to some extent with the lateral flow assay companies, but lateral flow assays have less sensitivity if they are rapid, point of care tests.

There is also a growing interest in wound dressings that can detect infection and react to it, including dressings that change colour in the presence of bacteria. There are as yet no medically approved dressings on the market for direct detection of bacteria in the dressing so it remains to be seen if these technologies will be developed fully for the commercial sector.

Although rapid diagnostics of wound markers and status is an emerging field in wound management there are some new tools already available, and some are given below as examples. There are a significant number of additional device technologies coming into the field and the range of such devices for wound diagnostics is discussed in detail by Dargaville et al., 2013, in their recent review of sensors for wound diagnostics.

In terms of the metalloprotease enzymes a colour change test has now been developed that is commercially available (Serena et al., 2011). For this test the clinician samples wound exudate onto a membrane system at the time of dressing changes. Elevated protease levels may indicate the need for intervention with specialised dressings.

In our laboratory, in the Department of Biomedical Engineering at the University of Strathclyde, we have a programme to develop a range of real time diagnostic sensors for wound management, including sensors that can be incorporated into any wound dressing. For example, the hydration status of a wound or wound dressing can be measured by reading a low voltage, low current electrical signal which detects the presence of moisture.

We have developed a small, disposable sensor based on this principle that can be placed inside any wound dressing. The sensor detects dry, wet and optimal wetness states on healing wounds without the need to disturb the dressing, using a hand held meter that is connected to the dressing as required (McColl et al 2007).

This saves staff time and costs on unnecessary dressing changes, reduces pain and trauma for patients, and limits opportunities for infection of the wound. The system is CE marked and already in use in the UK, Saudi Arabia and Qatar.

The system’s hand held meter reports five moisture levels measured by the sensor on a five drop scale. These are:

1. Wet
2. Wet to moist
3. Moist
4. Moist to dry
5. Dry

**Further research**

Clearly in a diagnostics platform other parameters would be of interest for wound care. Bacterial sensing and pH sensing are both being pursued in our research work.

In a new collaborative project with Hammad Medical Corporation, funded by the Qatar National Research Fund, we are researching a disposable pH sensor for wound exudate monitoring.

The pH of the wound environment can help or hinder wound healing. There is a demand from the clinical community to have immediate pH information about patients’ wounds during wound dressing changes, but to date no usable sensor has
come to market. Wound pH is considered important as an indicator for health of the tissue environment, inflammatory status and presence of bacteria, but it has not been possible to extensively study patient populations to confirm this due to the difficulty of using traditional pH measurement systems in the wound environment.

In addition, if a real time bacterial sensor can be developed for use within a dressing then early warning of an infection will allow a clinical care giver to intervene in a timely manner with drug and dressing therapies that can prevent the infection from taking hold in the wound.

We have conducted several in vitro bacterial growth studies to test the hypothesis that we can monitor the growth of bacteria in situ through electrical impedance signatures. The ultimate objective of this research is to develop a system that consists of a sensor that can be placed on the wound surface underneath the dressing. Ideally measurements would then be performed with a handheld device to return an immediate analysis of the bacterial environment. Early indications from our studies in bacterial broths are encouraging (Farrow et al, 2012) and the work continues.

Conclusions

In summary, the field of wound treatment is facing a growing burden of patients, but wound diagnostics is advancing and we can expect to see more diagnostic tools and parameters becoming available to the clinical community. This is a multidisciplinary field requiring interactions between clinicians, engineers and life scientists and therefore complex, but worthwhile as it will bring benefits to clinicians, patients and healthcare providers.

References

While space constraints prevent a full list of references in our printed edition, these will be available on our website at: www.amhmagazine.com

Author

Professor Patricia Connolly has worked across Europe in the medical industry and academia, researching and developing medical devices. She is based in the Department of Biomedical Engineering at the University of Strathclyde and is currently Director of Strathclyde Institute of Medical Devices and CEO of Ohmedics Ltd. Her research has mainly been in bioelectronics and medical diagnostics, and in recent years her translational research has been directed towards advancing medical instrumentation and diagnostics, particularly minimally invasive monitoring systems for wound care and transdermal diagnostics.

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