



August 2007 Vol 5 No 4

## Diabetic foot ulcers - a comprehensive review

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abstract

As the incidence of diabetes mellitus is increasing globally, complications related to this endocrine disorder are also mounting. Because of the large number of patients, foot ulcers developing in the feet of diabetics have become a public health problem. The predisposing factors include abnormal plantar pressure points, foot deformities, and minor trauma. Vulnerable feet usually already have vascular insufficiency and peripheral neuropathy. The complex nature of these ulcers deserves special care. The most useful prognostic feature for healing remains the ulcer depth, ulcers heal poorly if they clearly involve underlying tendons, ligament or joints and, particularly, when gangrenous tissue is seen. Local treatment of the ulcer consists of repeated debridement and dressing. No 'miraculous' outcome is expected, even with innovative agents like skin cover synthetics, growth factors and stem cells. Simple surgery like split skin grafting or minor toe amputations may be necessary. Sophisticated surgery like flap coverages are indicated for younger patients. The merits of an intact lower limb with an abnormal foot have to be weighed against amputation and prosthesis in the overall planning of limb salvage or sacrifice. If limb salvage is the decision, additional means like oxygen therapy, and other alternative medicines, might have benefits. The off-loading of footwear should always be a major consideration as a prevention of ulcer formation.

*Keywords: diabetes, foot ulcer, amputation*  
*Surgeon, 1 August 2007 219-31*

### INTRODUCTION

#### The clinical problem

The incidence of diabetes mellitus is increasing globally.<sup>1</sup> Patients with diabetes have a 12 - 25% lifetime risk of developing a foot ulcer.<sup>2,3</sup> Foot ulcers have become a major and increasing public health problem; the morbidities, impairment of the quality of life of patients, and the implied costs for management have attracted the attention of health policy providers.<sup>4,5</sup>

In spite of their rising importance, the management provided for foot ulcers is often inadequate, resulting in delayed healing and, eventually, the possibility of amputation.<sup>6,7</sup>

This article provides a comprehensive review of the current state of the problem, assessing epidemiology, pathophysiology, treatment modalities and prevention of diabetic foot ulcers.

#### Epidemiology

Since diabetic foot ulcers occur mostly among elderly people, there might still be doubts about whether the presence of diabetes mellitus really enhances the risk of ulcer formation. A study was undertaken in the USA in 2004 through the 2002 National Hospital Discharge Survey, looking at 275,000 in-patient records from 500 hospitals, since 1996. This indicated that elderly diabetics had twice the risk of developing a foot ulcer, three times the risk of developing a foot abscess and four

times the risk of developing osteomyelitis.<sup>8,9</sup> The same group of people requiring either local amputations or higher amputations, were also patients suffering from diabetes.<sup>10-14</sup>

Since different regions of the world tend to have populations with differing body builds, habits and lifestyles and different types of footwear - all of which could affect the development of ulcerations - one may expect to find differences in the prevalence of diabetic foot ulcers. Such differences are likely to be found in Asia or Africa and America, for example. Developing countries will experience the greatest rise in the prevalence of Type 2 diabetes in the next twenty years. The people living in these countries, therefore, could expect greater risks of ulceration.<sup>15-18</sup>

At present, the habit of not using tight footwear in South Asia is a special blessing to the people there, as they have a lower risk of ulcer formation. The North-West Diabetes Foot Care Study, completed in Manchester, UK, focused on Type 2 diabetics among migrant populations of South Asia and African-Caribbean populations, compared with data from Europeans living in the UK, and revealed a three to four times higher incidence of ulceration in the latter. Therefore, South Asians with diabetes, living in the UK, were facing a third of the risk of foot ulceration, compared with Europeans. The lower risk was attributed to the lower rates of foot deformities, insulin usage, peripheral vascular disease and neuropathy.

An epidemiological study undertaken in Tanzania on diabetic foot ulcers suggested that a rising trend in peripheral vascular disease and neuropathy, related to increasing urbanisation, was increasing the risk of foot ulceration.<sup>19</sup> In another study undertaken in Cameroon in 2005, in the National Centre for Diabetes and Hypertension, the prevalence of foot ulcers was shown to be 11% for out-patients and 25.6% for in-patients. These data correlated well with reports from affluent countries.<sup>20</sup>

### **PATHOGENESIS OF DIABETIC FOOT ULCERS**

In the diabetic patient, the foot is the crossroad for many pathological processes, in which almost all components of the lower extremity are involved; from skin, subcutaneous tissue, muscles, bones and joints, to blood vessels and nerves. An understanding of these processes is necessary for the development and application of management and preventative strategies.<sup>21</sup>

The development pathway towards ulceration is multifactorial. A critical triad of neuropathy, minor foot trauma and foot deformity is responsible for over 50% of diabetic foot ulcers. In addition, other risk factors like uneven plantar pressures, joint rigidities, and impaired wound healing ability are all contributing factors. Clinically, the predisposing risk factors leading to non-healing ulcers are those outlined in Table 1.

Apart from the obvious clinical predisposing risk factors, recent studies have revealed that very complex mechanisms are involved at the tissue-molecular level, which prevent normal healing processes.<sup>23</sup> Many chemo-cytokines are involved, including matrix metalloproteinases, serine proteinases, integrins, chemokines, replicative cell senescence, growth factors and adult stem cells.<sup>24-28</sup>

Diabetic patients with tissue injury initially display impairment in the immune system response with reduced chemotactic effects to recruit inflammatory cells into the damaged tissues, thus, slowing down healing and increasing the risk of bacterial infection.<sup>27-29</sup> Following this initial period, when the inflammatory response is eventually established, the process switches to an exacerbation of inflammation and proteolysis.<sup>25</sup> The result of prolonged exposure to hyperglycaemia also generates glycation of proteins and disturbances of cell responses, thus, further hindering the process of fibrosis and tissue repair.<sup>30-35</sup>

Recent molecular studies on chronic diabetic ulcers indicated that more specific processes may be involved. For example, it has been found that leucocytes are prevented from ready entry and accumulation in the ulcers, which, therefore, fail to achieve normal healing.<sup>36,37,38</sup>

Other studies on the specific properties of fibroblasts from patients with chronic diabetic ulcers showed that these cells were different from those taken from patients without chronic ulcers in that the high molecular weight hyaluronic acid in the pericellular matrix was much more concentrated. The unique property of the fibroblasts might predispose these patients to chronic ulcer formation.<sup>39-</sup>

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### **TYPES OF ULCERS**

Clinicians have tried to classify diabetic foot ulcers into different categories and grades. Attempts have not been successful because classifications fail to help with clinical judgement and management planning. There is the University of Texas system which grades ulcers by depth and then stages them by the presence of infection and ischaemia, excluding degrees of neuropathy.<sup>45</sup>

The International Working Group on the diabetic foot proposes the PEDCS classification grades for the ulcers on the basis of perfusion, extent, depth, infection and sensation.<sup>46</sup>

This looks good but is too complicated. The size, area, depth (SAD) classification attempts to simplify the categories. Alternatively the six grade Wagner-Meggitt classification looks at the depth of ulcers and the existence of tissue gangrene.<sup>47,48</sup> Of these classifications the most practical system to help with the prediction of healing and the possibility of amputation is probably the simpler: the Wagner-Meggitt classification.<sup>49-51</sup> For Grade 2 through 6, the overall chance of local or major amputation is estimated to be around 60%.

## **INFECTION AND ULCERS**

Infection is usually the consequence rather than the cause of diabetic foot ulcers. Infected chronic ulcers may be classified as mild to moderate or severe, when osteomyelitis is involved.<sup>52-54</sup>

Appropriate tissue and bone cultures are useful to guide the use of antibiotic therapy. Gram-positive organisms account for the majority of infections, while the prevalence of methicillin resistant staphylococcus aureus has become prevalent in recent years.<sup>54-58</sup>

In the deep categories of chronic ulcers, the prevalent organism of infection is still staphylococcus. Comparing superficial swabs and bone biopsy cultures in the identification of organisms, the latter is much more reliable.<sup>59-63</sup>

Although gram-positive organisms are overwhelming in chronic diabetic ulcers, the polymicrobial nature of bacterial growth should not be ignored in the management planning, especially in developing countries.<sup>64</sup>

Chronic ulcers are frequently co-existing with fungal infections of the foot and it has been said that bacterial infection could be predisposed by fungal infection. A study of 13,271 patients with diabetes has shown that 78.4% have fungal infection of the feet. Among these infections, 70.8% are of Tinea pedis type. The investigators, therefore, consider fungal infection a risk factor for foot ulcers.<sup>65</sup> Other studies try to delineate the different types of tinea, i.e. different Candida species, but have not succeeded in identifying species of higher risk.<sup>66</sup> As the link between infection and foot ulcers is so strong in diabetics, the question of whether these patients are immunologically compromised arises. Limited studies have shown that secondary immunodeficiency in both cellular and humoral immune parameters, in patients with chronic bacterial foot infection, is not unexpected.<sup>67</sup>

## **NEUROPATHY AND ULCERS**

Peripheral neuropathy and sensory loss in the diabetic foot is always considered to be the most prominent risk factor in the development of ulcers.<sup>68</sup> The sensory disturbances on the other hand, are further jeopardised by abnormal pressure points under and around the foot and ankle, as well as deformities at different levels of the foot resulting from ageing and arthritis.<sup>69,70</sup> The same pathology is responsible for the slow healing, non-healing and recurrence of foot ulcers.<sup>71</sup>

Assessing the state of neuropathy, therefore, is of vital importance with particular reference to prognosis of healing and prevention of recurrence. While it is vital to point out that treating diabetic ulcers without a proper clinical assessment on the state of sensation is totally unacceptable, the practical means of obtaining objective data for proper clinical judgement needs to be discussed. The two most commonly performed tests are the Semmes-Weinstein monofilament test and the biothesiometer test.<sup>72-74</sup>

Sensation testing of the intact skin using the Semmes-Weinstein monofilament is performed by pressing the monofilament onto the site being tested until it bends. The failure to detect the touch indicates that neuropathy is severe and protective sensation is absent. The standard sites to be tested include the plantar surface of the great toe, the metatarsal heads, the heel and any other site under the threat of pressure because of deformities.

More sensation testing is achieved using a biothesiometer, which measures the vibration threshold felt by the patient. The head of the instrument is held perpendicularly to the plantar aspect of the at-risk point, while vibration is gradually increased until detected by the patient. These two simple measuring methods have been validated for reliability by various workers who confirm that highly acceptable intercessional correlations and limited repeatability errors are achieved.<sup>75,76,77</sup>

A podiatry study undertaken in Australia showed that the neuropathy group of diabetics have an annual occurrence of ulceration of 4% for those with an abnormal biothesiometer reading, but who still feel the monofilament, 10% for those who cannot feel the monofilament, and 26% for those

with previous ulceration or amputations.<sup>78</sup> The same group of investigators have estimated that, with reasonable podiatric care, only one ulcer develops in 367 diabetic subjects without peripheral neuropathy. However, the number increases to 1 in 45 for those with neuropathy, 1 in 18 for those who cannot feel the monofilament and one in seven for those who have already experienced ulceration or toe amputation.

There is one other aspect of neuropathy occurring among diabetic patients which is often overlooked. Proprioceptive involvement leading to Charcot arthropathy of the foot and ankle joints often co-exists with chronic foot ulcers.<sup>79-81</sup> It should be realised that many major amputations are done because of uncontrolled neuropathic arthropathy; early awareness with the provision of effective bracing might succeed in limb preservation.<sup>82</sup> A study of 115 patients and 127 limbs with neuroarthropathy has shown a 2.7% annual rate of [168]amputation, 23% requiring bracing but 49% developing recurrent ulceration.<sup>83</sup>

With neglected cases, when Charcot arthropathy has been present for a long time, it might be difficult to differentiate it from pyogenic arthritis or osteomyelitis.<sup>84,85</sup> While Charcot joint most commonly affects the tarso-metatarsal and tarsal joint and is painless, osteomyelitis is almost exclusively adjacent to skin ulcers and occurs most frequently around the metatarso-phalangeal joints and the calcaneum.<sup>86</sup>

### **ISCHAEMIA AND ULCERS**

The vascular state of the diabetic foot with ulcers is affected by the general circulatory state, together with the peripheral vascular condition of the diabetic patient. The local manifestations of cutaneous microangiopathy could be considered the result of the general circulatory state, which obviously affects skin perfusion.<sup>87</sup>

It is important to recognise that diabetic patients with co-existing neuropathy and ischaemia may remain asymptomatic. The clinician, therefore, should check the peripheral pulses carefully, including a femoral, popliteal, posterior tibial, peroneal and dorsalis pedis. The presence of a femoral artery or popliteal artery bruit strongly indicates the presence of treatable peripheral vascular disease. The absence of a bruit, which is more common, indicates generalised vascular occlusion.<sup>88</sup> The Doppler device is a helpful tool at this stage. If there is no clinical indication of vascular compromise, no further investigations are usually required. In contrast, those with suggestions of peripheral vascular disease should be investigated with standard angiographic studies. Those suffering from dry gangrene, rest pain, and/or deep ulceration with absent peripheral pulses require further vascular work-up.

Since not all patients are suitable for vascular reconstruction, (e.g. in late presentations, generalised atherosclerosis, elderly age, co-existing morbidities etc.), other tests like transcutaneous oxygen saturation may help to identify those patients who may have better chances of wound healing.<sup>89</sup> Likewise, if the blood pressure of the unaffected great toe is >30mmHg, it stands a much better chance of ulcer healing.

## **TREATMENT**

### **General management**

Foot ulceration is a complication caused by diabetic disease and is invariably infected. The diabetic state, therefore, needs to be well controlled and infection should be effectively treated. The control of diabetes in chronic ulcer situations is usually standard and does not pose special difficulties. However, before the infection is put under control, hyperglycaemia tends to fluctuate. There is always the question of whether the stability of the blood sugar level would affect ulcer healing.

A large-scale study was planned in Nottingham in 2003 to look at the effect of close glycaemic control on the healing of diabetic foot ulcers. The design was a prospective, parallel group randomised trial with two arms. One continuing with the hypoglycaemic measures being used, the other with an intensive monitoring for a tighter control of blood sugar. All attending diabetic patients with chronic ulcers of more than four weeks duration were invited to join the study. The intention was to randomise a total of 50 patients over six months and compare ulcer healing. Unfortunately, this study was not completed because of failure to get support from ulcer patients.<sup>90</sup> It therefore remains uncertain whether blood sugar levels affect chronic ulcer healing.

### **Infection control**

The predominant pathogens causing diabetic foot infections are gram-positive cocci, however

other pathogens are involved so infection should be considered polymicrobial.<sup>64,91-93</sup> The choice of antibiotic, therefore, is broad-spectrum based while bearing in mind that methicillin-resistant strains are frequently encountered.<sup>94-97</sup> Newer antibiotics and their combinations, such as vancomycin and daptomycin, may be considered.<sup>98</sup>

Appropriate wound swab cultures or bone biopsy cultures should be required for proper management of infection. There are a few randomised controlled trials setting guidelines for the infection control of diabetic chronic ulcers.<sup>56,91</sup> When the culture from an ulcer yields no bacterial growth, it is more logical to withhold antibiotics. For mild, soft tissue infection, oral antibiotics are good enough. Moderate to severe infections require parenteral, combination therapy. The use of topical antibiotics is usually not recommended.

The prevention of infection is not achieved through the use of medications but could be achieved with patient education; foot hygiene, proper protection of pressure points and early local care of shallow ulcers.<sup>99</sup>

### **Ulcer care**

Although a multitude of factors affect the healing of chronic diabetic foot ulcers, and local care of the ulcer does not guarantee its healing, proper local management is still crucial. Daily or more frequent cleaning and dressing are essential requirements. Regular daily bathing in saline or dilute antiseptic solution offers a better chance of cleaning the ulcers, compared with dressing alone.<sup>100</sup>

New dressing methods and new dressing materials are now available to help remove the exudate and to promote a more rapid shrinkage of the ulcers. The use of vacuum-assisted closure or dressing, which is popular in other surgical areas, has started to be used in the foot and ankle areas. Repeated minor surgical debridement followed by vacuum dressing has been shown to be useful in the promotion of ulcer healing.<sup>101</sup>

There are changing perspectives in the local management of diabetic ulcers which include, apart from new dressings, skin substitutes and growth factors.<sup>102-104</sup>

In large ulcers once granulation growth becomes healthy and infection controlled, skin grafting can be considered. Waiting for spontaneous epithelialisation takes too long. Mesh graft is preferred because entrapment of exudation does not occur and the result of re-surfacing is not inferior.<sup>105</sup>

Many artificial dermagrafts are available for temporary granulation coverage. These are not genuine grafts because they basically serve as dressing material, to support ulcer shrinkage, as spontaneous epithelialisation occurs from around the ulcer edges. The dermagrafts are either manufactured from human tissue like amniotic membrane or synthetic material which is bioengineered into a thin covering sheet comprised of dermal fibroblasts.<sup>106</sup>

Most chronic foot ulcers occur among elderly diabetics. The poor circulatory state, neuropathy, and co-morbid conditions do not allow sophisticated surgery. However, when chronic ulcers occur in healthy younger patients, surgical closure with special techniques could be considered.

### **ULCER SURGERY**

Abundant data show that simple surgery consisting of extensive debridement of ulcer wounds and removal of devitalised tissues is the single most important therapeutic step leading to ulcer healing and limb salvage. Chronic ulcers are the result of prolonged biological hazards. Therefore, good outcomes are measured in weeks and months rather than days. At least six to ten weeks is the expected time for healing of these complicated lesions.<sup>107</sup>

Split skin-grafting for weight bearing plantar defects is often a poor option because of the inadequate recipient bed and defective durability of the skin cover. Breakdown of split skin-grafted areas is common with daily ambulation and footwear pressure. Local random flaps have marginal use, because limited local mobility does not allow the skin adjacent to the chronic ulcer to be mobilised. Pedicled muscle flaps have been used as an alternative approach.<sup>108</sup> However, flap viability is still a problem. Under special circumstances, free skin flap transfer using a microvascular technique is feasible and there are many such reported cases. Enthusiasm for these procedures remains low because of the risk of arterial occlusion and the compromised fitness of diabetic patients.<sup>109</sup>

Diabetic ulcers over the heel are common. This weight-bearing area needs an epithelial cover that is durable and supports the body weight. The reverse sural flap may be a good choice. The technique and details of the procedures have been described in many reports and ulcers around the ankle and heel have been adequately resurfaced.<sup>110-113</sup> It is considered particularly useful when

chronic osteomyelitis is underlying the chronic ulcers.<sup>114,115</sup> The reverse sural flap survives well and possesses the correct thickness for heel and ankle coverage.

### **SURGERY TO FACILITATE ULCER HEALING**

Chronic diabetic foot ulcers combined with functional problems add further risks to the formation of more ulcers. Such situations can arise when the Achilles tendon becomes tight as a result of prolonged disuse of the ankle. The plantar-flexed ankle imposes more pressure on the metatarsal heads which may be responsible for pressure ulcer development. The tight Achilles tendon can be lengthened, so as to release metatarsal head pressure. After the lengthening, there is an initial weakening of the plantar flexion pull, which returns to normal in approximately eight months time.<sup>116</sup>

At the same time as releasing of the metatarsal head pressure, the metatarsal head can be removed, via the plantar ulcer or via separate incisions.<sup>117,118</sup> Under special circumstances, metatarsal head resection can be combined with Achilles tendon release. Other tendon balancing procedures can also be added when functional problems are observed. Peroneus longus tendon lengthening is another commonly performed adjuvant measure in cavus foot deformity related to plantar ulceration.<sup>119,120</sup> The diabetic patient with chronic ulceration of the foot often has co-existing deformities which might need to be corrected to prevent ulcer recurrence or new ulcer development. Orthopaedic procedures are then required as the deformities commonly occur in the toes. Correction of Keller's arthroplasty and metatarso-phalangeal joint fusion are two common procedures to correct deformity of the great toe.<sup>121-122</sup>

When diabetic neuropathy results in Charcot joints, surgical intervention often becomes necessary. Surgery may involve joint fusion at the site of the arthropathy or in the most unstable late cases, amputation. Charcot arthropathy commonly occurs at the tarsal joints, which become unstable and initiate various deformities of the foot. Debridement and fusion should be the aim but fusion of the neuropathic joint is usually difficult. In late cases, therefore, amputation at the neurophic site becomes a secondary option.<sup>123-127</sup>

### **SUPPORTIVE TREATMENT**

Abnormal pressure points undoubtedly predispose the diabetic foot to ulceration. Protecting the pressure points, therefore, becomes vital for the prevention of ulcer formation. Applying total contact casting as the means of treating early uncomplicated ulcers further supports the need for protecting the pressure points. For the healing of purely neuropathic ulcers, simple pressure relieving casting is effective.<sup>128-130</sup> However, most diabetic ulcers are complicated by peripheral arterial disease and infection. Therefore, pressure relieving devices are important mostly after treatment interventions and ulcer healing.<sup>131,132</sup> A number of these devices are commonly used. They include the simple insole shoe, a special shoe, pneumatic walking brace and bivalved total contact cast. In a study comparing the effectiveness of the four modalities, it has been found that forefoot pressure is uniformly reduced with all devices but peak pressure is reduced by the special shoe and bivalved cast.<sup>133</sup> The logic of increasing the underfoot contact area to decrease plantar foot pressure, therefore, is very sound and should be endorsed as an essential component for the treatment of diabetic foot ulcers.<sup>134</sup> Commercially available devices are used for convenience and general effectiveness. Since deformities are unpredictable in diabetic feet, the total contact cast and its derivatives remain the most efficient off-pressure applications.<sup>135</sup>

### **ADJUVANT TREATMENT**

For all difficult healing problems, the treatment provided is never limited to conventional modalities. Instead, controversial treatment modalities, frontier research-based attempts and even old traditional alternatives, are used. For chronic diabetic foot ulcers, we will review reports on oxygen therapy, molecular research items already put to trial practice and herbal treatment in alternative medicine.

#### **Oxygen therapy**

Oxygen therapy, for the majority of people, is also known as hyperbaric oxygen treatment.<sup>136,137</sup> While hyperbaric oxygen therapy is still practiced in some hospitals, topical oxygen is also used for ulcer treatment. With topical oxygen, an airtight chamber is created, using a polyethylene bag which is sealed around the limb by either a constriction device or careful taping, and a high flow of ten litres per minute of oxygen is passed through the chamber over the ulcer. The pressure around

the limb is kept just above atmospheric pressure. Topical oxygen will diffuse into the ulcer area to enhance healing. The mechanism of action, whereby topical oxygen might be helpful to tissue healing, has not been defined. There are claims of observed decreased collagen production and fibroblast inhibition as a result of high oxygen contact.<sup>138</sup>

Hyperbaric oxygen treatment is a more conventional form of therapy for chronic ulcers and diabetic gangrene. Some reports on reasonable sized series give a 70% success rate. The failures are related to poor circulation, as is revealed by low transcutaneous oxygen tensions of below 29mmHg.<sup>139</sup> The relatively high rate of failure, in spite of hyperbaric treatment, casts doubts on the true value of this form of therapy.<sup>140,141</sup>

### **Molecular biology and chronic ulcer treatment**

As the pathophysiology of wound healing is being understood at the molecular level, an increasing number of growth factors and cytokines are documented and their possible mode of action understood, the next natural development is the application of this knowledge to promote healing of chronic ulcers.

Animal studies have shown that fibroblast growth factors, used either as solitary impregnated gelatin microspheres or laid on artificial dermis, accelerates fibroblast proliferation and capillary formation.<sup>142,143</sup>

Many clinical trials of various growth factors (e.g. granulocyte colony stimulating factors, and fibroblast growth factor have demonstrated the clinical value of their topical use).<sup>144,145</sup>

Innovative attempts to save ischaemic feet with ulcers by the application of stem cells have also been carried out.<sup>146</sup> Stem cells are implanted into the skeletal muscle proximal to the chronic ulcer in an attempt to initiate angiogenesis.<sup>147</sup>

In spite of scattered clinical reports, one must realise that growth factors, and stem cell therapy remain, as yet, experimental. If the ischaemic state is really so bad that even the marginal nutritional needs for all tissues is not satisfied, the outcome is still tissue necrosis and gangrene irrespective of any form of topical or regional treatment.

### **Alternative medicinal treatment**

If a wound has received a wide range of treatments yet has failed to heal, alternative treatment is an option. Different modalities are frequently tried, from the old traditional herbal treatment (topical or systemic) to more innovative ultrasonic therapy.<sup>148,149</sup> Many reports are available in Chinese language medical journals, describing the effectiveness of herbal combinations in ulcer healing. However, these reports are not validated by proper clinical trials.

In Hong Kong, a comprehensive investigation has just been completed on a popular herbal formula. In the laboratory, the formula is studied by its effects on fibroblast culture, and wound healing through granulation formation and angiogenesis, and so far the outcome has been very positive.<sup>149</sup> A randomised placebo controlled trial was conducted on 80 patients with non-healing diabetic ulcers occurring in legs which had been listed for major amputation, using the same herbal formula. 85% of the legs were salvaged and the herbal treatment group revealed better granulation, more rapid healing, better surface oxygen tension and microcirculation.<sup>150</sup>

### **AMPUTATION**

Amputation of the toe(s) with non-healing ulcers or gangrene can sometimes be the only solution towards limb salvage. Amputation sacrificing the whole leg is a life-saving procedure for large, unhealed ulcers which are usually accompanied by other complications of neuropathy and ischaemia. Patients on the whole would prefer to retain the limb and the attending medical team should be supportive of limb salvage, if feasible.<sup>151,152</sup>

In a large cohort study undertaken in 2004, of 24,616 individuals with diabetic neuropathic foot ulcers treated within a multicentre wound care network in the past ten years, 6.7% had amputations of which 46.3% were minor, e.g. limited to a toe. Over a ten-year period, 60% of those who previously received minor amputations needed further amputations.<sup>153</sup> In this study, there were no gender or age difference, and the need for amputation was unrelated to the number or duration of ulceration. In hospital settings, the incidence of amputations, whether minor or major, tends to be higher because of the need for hospital admission when the ulcer reaches a more advanced state.<sup>154</sup> The statistics from one general hospital in Hong Kong (Kwong Wah Hospital), for example, indicates that in a ten-year period from 1995 to 2005, 154 of the 851 patients admitted with diabetic foot ulcers underwent major lower limb amputation (18.1%).

Amputation has been used as a marker of the quality of foot care in diabetes because care centres

document the incidence and use it as an indicator for progress assessment. While different care centres would have their own cohort of clients, cross centre comparison using amputation rate is obviously unfair. However, for an intra-departmental assessment, it could be a simple and useful indicator.<sup>155</sup>

### **QUALITY OF LIFE**

Major amputations are done when the ulcerated foot either threatens patient survival or when reasonable function can no longer be expected. However, an inappropriately conservative approach could conceivably enhance suffering by condemning a person to months of incapacity before they die with a non-healed ulcer. The consideration of the quality of life in patients with non-healed ulcers or different levels of amputation is, therefore, of importance. With non-healing ulcers, diabetic patients run a high risk of depression. In joint research between medical departments and the biobehavioural department on 494 patients with diabetic neuropathy, it was found that the incidence of depression was not directly related to the severity of neuropathy but rather with the perceptions of unpredictable outcome, lack of treatment control, restrictions in activities of daily living and changes in social perceptions (quality of life).<sup>156</sup>

Other studies have indicated that health-related quality of life indices do suffer in patients with chronic foot ulcers, mainly due to disruption of leisure activities and constraints secondary to treatment.<sup>157</sup> The indices show marked improvement after ulcer healing.<sup>158</sup>

### **CONCLUSION**

Despite much efforts towards the treatment of diabetic foot ulcers, the incidence of lower extremity amputation rate remains about the same. Amputation is a costly outcome and should be prevented as far as possible. Ulcers should be prevented and if they have already occurred, should be treated early.<sup>159</sup> There is little doubt that they'll require special care, since these ulcers heal differently from other ulcers, because of the unique predisposing causes including peripheral neuropathy, vascular insufficiency and hyperglycaemia which invites infection, and the lack of an orderly and predictable healing process. Assessment still relies mainly on clinical judgement. Risk factors should be detected on the first encounter; the vascular state should be carefully assessed through pulse studies and surface circulation, and the neuropathic state tested by performing the 10gm Semmes-Weinstein monofilament test. The depth of the chronic ulcer is more important prognostically than other criteria such as size, number and duration.

Local care of the ulcer is essential. No 'miraculous' outcome can be expected, even with innovative agents like synthetics, growth factors and stem cells. However, dressings including removal of necrotic tissue and drainage of infected exudates, helps to provide better granulation formation. Control of the diabetic state and timely control of infection is also essential.

For hospital admissions, the ulcers are already deep, infection prolonged and vascular reconstruction may be too late to be beneficial (although prevention of claudication pain and avoidance of major amputation may still be achievable). One has to acknowledge that a well-performed amputation and successful rehabilitation can improve a patient's quality of life, while an abnormal foot after minor amputations is much more acceptable and useful to the elderly patient than an ulcerated foot. Salvage attempts, therefore, need to be carefully tried before ablative surgery.<sup>160</sup>

Since ulceration occurs as a result of repeated minor trauma caused by footwear pressure on the deformed foot, prevention of ulcer formation must start with the protection of the pressure points i.e. off-loading. Total contact casts and their modifications remain the most effective off-loading devices and should always be included in the consideration of foot ulcer treatment and prevention. Consideration of the social and psychological implications are also important in planning strategies for the prevention of ulcer recurrences. Since the diabetic foot ulcer has developed into a public health problem, it deserves a holistic approach including socio-economic planning.<sup>161</sup>

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TABLE 1 RISK FACTORS PREDISPOSING TO THE NON-HEALING OF DIABETIC FOOT ULCERS	
Local	Systemic
Infection/tissue necrosis/foreign bodies/smoking/ischaemia	Chronic diseases
Local cancer	Nutritional/anaemia
Venous insufficiency	Congenital healing problem e.g. epidermolysis bullosa
Pressure sore	Alcoholism/steroid/cytotoxic/therapy
Toxins/radiation/isotretinoin measures	Ageing/Cancer/Uraemia

TABLE 2. CLASSIFICATION BY ULCER DEPTH AND GANGRENE TISSUES (WAGNER-MEGGITT)	
Grade 1	Partial skin thickness
Grade 2	Full skin thickness
Grade 3	Underlying tissues (fascia, ligaments, tendons) involved
Grade 4	3+ abscess or osteomyelitis
Grade 5	4+ necrotic tissues
Grade 6	Gangrenous tissues found



Figure 3a: Diabetic foot ulceration before and after herbal treatment.



Figure 3b: Diabetic foot ulceration before and after herbal treatment.

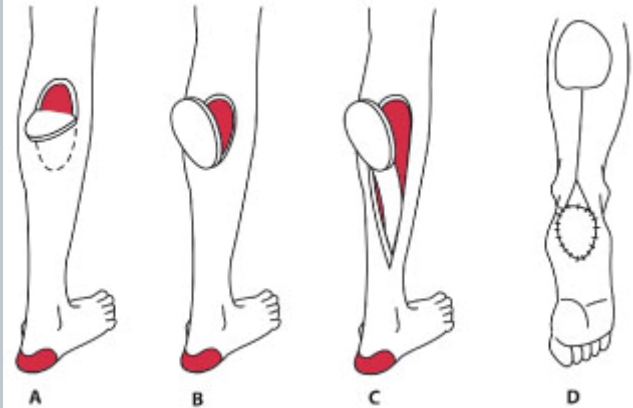


Figure 1: Illustration of the four stages of reverse sural flap reconstruction.

A. Proximal delay procedure.

B. Distal delay procedure, 1 week later.

C. The pedicle, consisting of the superficial and deep fascia, minor saphenous vein, superficial sural artery and a 3cm width of surrounding tissues, is raised 2 weeks later. The pivot point of the reverse flap is at a level 5cm above the lateral malleolus.

D. The reverse flap is tunneled through a skin bridge to be laid onto the heel defect.



Figure 2: Shaded areas of the sole represent the at-risk pressure points.