INFECTION CONTROL

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Challenges, goals and strategies for the next 10 years

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Infection continues to play a key role in the morbidity associated with the diabetic foot and as an immediate precedent to amputation. Despite its importance, there are many unanswered questions concerning the diagnosis and management of diabetic foot infections (DFIs). Perspectives on treatment have evolved over time, from an age of therapeutic nihilism, through a period of surgical absolutism, to a current debate between advocates of the need for early surgery (especially in osteomyelitis) and those who cite evidence supporting the successful treatment of many cases of DFIs with antibiotics and non-surgical therapies alone.

A search of PubMed using the term 'diabetic foot infection' reveals some 770 references published since 1998, but only 308 publications in the preceding thirty years. The first decade of *The Diabetic Foot Journal* thus represents the era when the study of DFI finally came of age, including at the level of seeking international consensus on management.

Managing diabetic foot infection

The need for guidelines for managing infection is perhaps all the greater because of the lack of high-quality evidence to dictate treatment. A recent systematic review, produced independently of the guidelines groups, concluded that there was no evidence that any one antibiotic was superior to another in the treatment of infected diabetic foot ulcers (Nelson et al, 2006), but the design and conduct of the studies necessary to resolve this issue poses considerable difficulties. This is, however, only the first of many problems, including the following.

- How can infection best be defined and diagnosed?
- Should wounds be routinely sampled for culture, what methods should be used, and how should the results be interpreted?
- In clinically uninfected ulcers, are antibiotics useful to promote healing or to prevent infection?
- For infected ulcers, for how long and by what route should antibiotics be given? Are antibiotics needed until healing occurs?
- Is it necessary to treat all the pathogens that are isolated from the wound?
- How should osteomyelitis be diagnosed? How can it be distinguished from the acute Charcot foot?
- When is surgery favoured over non-surgical treatment for osteomyelitis?
- With which antibiotics should osteomyelitis be treated and for how long?

It is only when clinicians recognise and accept that there is uncertainty in the answers to most of these questions that adequately powered, randomised studies can be devised to provide the definitive answers we so urgently need. Recent events in the UK, where hospitals have come under intense scrutiny because of outbreaks of MRSA and *Clostridium difficile* infection (Healthcare Commission, 2006; 2007), may help clinicians adjust their sense of risk and benefit with antibiotic use. Ideas of antibiotic stewardship, long the domain of the infectious diseases physician and some forward-thinking institutions, have in the UK now become a high-profile part of mainstream hospital managerial activity (Lawton et al, 2000; Dellit et al, 2007). It is especially relevant to DFIs, because widely used antibiotics, such as fluoroquinolones, significantly increase the risk of developing *C. difficile* infection and for increasing the prevalence of MRSA (Weber et al, 2003; Pepin et al, 2005). As clinicians are increasingly (and rightly) held accountable for prescribing decisions that may contribute to a higher incidence of healthcare-associated infections, we should analyse the basis of our convictions and consider changing to more frugal, narrower-spectrum and shorter-course antibiotic regimens. Such a change would pose no problem if there was trial-based evidence to demonstrate that such regimens were equally effective.

Guidelines for infection management

Current international guidelines do not yet take full account of these new pressures, however, they do attempt to define rational practices for antibiotic use. The key concepts within these guidelines are the need for systematic assessment of the individual, the limb,

the foot and the ulcer, and for a categorisation of the severity of infection. In this way those with significant systemic upset (including new onset confusion, metabolic imbalance or fever) or severe PAD can immediately be triaged as having infection which is classified 'severe' (IDSA criteria) or grade 4 (IWGDF PEDIS research classification scheme; Schaper et al, 2003). Since most people with DFIs do not mount major systemic responses, those who do are at higher risk of having accompanying bacteraemia, abscess formation, fasciitis or significant soft tissue necrosis (Armstrong et al, 1996). These individuals should be referred urgently for hospital-based management by a multidisciplinary team with immediate access to all the resources needed for optimal management.

Patients with clinically diagnosed infection but without systemic symptoms and signs are subdivided into categories of 'mild' (IDSA; IWGDF grade 2) and 'moderate' (IDSA, IWGDF grade 3) infection. Moderate infection refers to those with extensive cellulitis, abscess, and osteomyelitis, and this group also needs prompt referral for expert diabetic foot care with the necessary resources. Mild infections are superficial to the fascia, extend no more than 2 cm from the ulcer edge, and are not associated with complications.

This classification system has been validated with the dataset from the DIABETEX study (Lavery et al, 2003). Retrospectively classifying the severity of infection demonstrated that the need for hospitalisation and for limb amputation was strikingly linked to the severity score; mild infection rarely resulted in adverse outcomes and was almost exclusively managed on an outpatient basis (Lavery et al, 2007a). Thus, if served by competent diabetic foot services, many of the burgeoning numbers of people who develop DFIs can be managed successfully without producing a major drain on hospital inpatient services. Good outcomes will, however, still depend on rational treatment and prescribing behaviours. These include systematic foot assessment, appropriate debridement, effective wound dressing and pressure offloading, patient education and rational antibiotic prescribing.

Mild infections should receive therapy targeted at staphylococci and streptococci. Penicillinase-resistant penicillins are the logical and cheapest option; first generation cephalosporins are therapeutically useful but will slightly increase the risk of *C. difficile*; fluoroquinolones can be used for mild infection, but in patients with additional risks for *C. difficile* the risk–benefit ratio should be carefully considered. Current guidelines recommend a 7–14 day course of treatment, with an option to extend that for 1–2 weeks prior to re-evaluation, but these durations are under review (Lipsky et al, 2004).

Osteomyelitis

The management of osteomyelitis poses particular problems. In specialist diabetic foot clinics about 20% of those with DFIs will have clinical or radiological features suggestive of bone infection (Lavery et al, 2007b). This relatively high prevalence, in combination with high volumes and rates of re-ulceration following surgery, is driving some to consider more conservative and empiric management strategies (Jeffcoate and Lipsky, 2004). Evidence is still required, however, from controlled studies that such an approach is at least as safe and as effective as surgical treatment. In contemplating the next 10 years of management and investigation of diabetic foot infection, what advances can we envision? Consensus tools are now in place for researchers to classify various aspects of the diabetic foot and to diagnose osteomyelitis (Berendt et al, 2008). The routine use of these tools in clinical practice could also allow comparative audit of outcomes from non-standardised treatment protocols adopted by different centres. The Internet now provides us with an additional tool to make observational research enormously more powerful. Diabetic foot disease already has a precedent with the CDUK study on the acute Charcot foot in UK (Game et al, 2007). The data collection for the DOMO (Diabetic Osteomyelitis Management and Outcomes; www.domo.org.uk) study will be launched shortly, and researchers worldwide will be asked to deposit anonymised data on the demographics, treatment and outcome of cases of diabetic foot osteomyelitis.

Summary

The biblical story of the Tower of Babel is synonymous with the chaos that arises when lack of a common language impedes the sharing of information. As we look forward to a second decade of *The Diabetic Foot Journal*, we hope that the diabetic foot community will seize the opportunities now offered to use consensus definitions, consensus guidelines and Internet-based information-sharing to produce the answers we need in the management of DFIs. Since the decade to come will continue to be dominated by the threat of multi-resistant pathogens and healthcare-associated infection, as well as by huge global expansions in the number of people with diabetes, achieving the goal of evidence-based, cost-effective therapy of DFIs cannot come soon enough. ■

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