One small step for diabetic podopathy

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Abbreviations

CRP C-reactive protein
IDSA Infectious Diseases Society of America
IWGDF International Working Group on the Diabetic
Foot

The paper by Jeandrot and colleagues in this issue of *Diabetologia* sets out to provide evidence in the one subspecialty area of diabetes in which evidence is most lacking: disease of the foot. This field is of enormous importance in terms of both cost and suffering, and yet remains grossly neglected. There are three main reasons for this. The first is that no one likes feet, especially those with chronic ulcers, or which are smelly and necrotic. The second is that the response to treatment is poor and often unrewarding, while management tends to be delegated to nurses and podiatrists. The third is that the field is extremely complex, and the overlapping influences of neuropathy, peripheral arterial disease and infection make trial design difficult. The consequence of this neglect is a low general level of knowledge about foot care, and an extremely limited evidence base for treatment strategies.

Many patients are managed badly. The response of the medical profession to this, predictably, is one of denial, thus compounding the neglect rather than setting out to rectify it. There was, for example, not a single oral session on feet at the recent meeting of the European Association for the Study of Diabetes. It is time for professional attitudes towards foot disease in diabetes to come of age, and for the problem to attract attention commensurate with the suffering it causes.

It is against this background that Jeandrot et al. [1] provide further evidence to underpin the use of antibiotics, by examining the response of inflammatory markers to different clinical grades of infection in the foot. These grades of infection have been proposed by the Infectious Diseases Society of America (IDSA) and by the International Working Group on the Diabetic Foot (IWGDF) [2, 3]. The grades were originally based on expert opinion derived from clinical experience, although Lavery et al. [4] have recently provided supporting evidence by demonstrating differences in the incidence of amputation between those with infections of differing grades in 267 newly presenting ulcers in the USA. If valid, these clinical grades could be used to categorise infectious events, and could potentially be linked to management guidelines. They could provide a basis for comparisons of treatment outcomes in different centres, and could prove useful in prospective research. The grades themselves are straightforward in that they simply rank clinical episodes by severity, but the study by Jeandrot et al. [1] shows that this ranking is reflected by differences in levels of inflammatory markers, including C-reactive protein (CRP), procalcitonin, and total white cell and neutrophil counts. Very high levels of response are no surprise in those with systemic symptoms and signs, of course, but the real interest of this study lies in the distinction it makes between those with no clinical signs

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Fig. 1 Signs of mild infection (IDSA–IWGDF classification) complicating a pre-existing ulcer: less than 2 cm of surrounding inflammation, limited to skin and subcutaneous tissues

and those with mild or moderate infection. Thus, compared with non-ulcerated controls, the concentration/count of any individual marker did not differ in those with clinically non-infected ulcers, whereas the response of every single inflammatory marker (other than total white cell count) was greater in those with mild or limited disease (Fig. 1). These observations confirm the reliability of a clinical diagnosis in mild or limited infection, and emphasise the need for appropriate antimicrobial treatment in such cases. They also suggest that the absence of clinical signs can normally be relied upon to exclude infection, and hence to identify those people in whom antimicrobial therapy is not only unnecessary but actually contraindicated, for prescribing should be limited to those in whom there is a clear clinical need.

Jeandrot et al. also compared the ability of different markers to discriminate between those with and without evidence of mild infection, and found that CRP and procalcitonin performed best. They suggest a formula for combining these two variables to improve discrimination still further, but I suspect that in practice the non-availability of procalcitonin assays, not to mention the need for a calculator, will mean that most clinicians will rely on just one measurement in combination with the now validated clinical signs of mild infection.

These interesting results prompt further questions. Although the authors did not specifically address more severe disease, they found no difference in the inflammatory responses to mild and to moderate infection, the concentrations/counts of all measures (except, possibly, CRP) being very similar. This suggests that the difference between mild and moderate grades in the IDSA–IWGDF system is not

necessarily based on the severity of the infection itself, but on the overall condition of the infected lesion—its depth, for instance, or the association with peripheral arterial disease.

The other question that follows from this work is the extent to which inflammatory markers, such as CRP, or the suggested CRP/procalcitonin formula, can be used to determine when soft tissue infection has been eradicated. If anything, this is an even greater question in clinical practice and one of the principal difficulties in designing clinical trials of antimicrobials, for which there is no specific marker of effectiveness. In clinical practice, it can be almost impossible to determine when spreading infection has been eliminated, especially when there is persisting surface contamination (as is common in ischaemic ulcers). It can be equally difficult to determine when infection has been eradicated from bone because the clinical signs of inflammation sometimes persist beyond the point at which clinical infection has been arrested. This may occur because the preceding infection has triggered persistent vasodilatation in those with abnormal vasomotor regulation as a result of associated neuropathy. The absence of a yardstick for successful treatment encourages clinicians (including this one) to continue antibiotic treatment for longer than is necessary, and this promotes the spread of resistant organisms. Now that Jeandrot and colleagues have highlighted the usefulness of inflammatory markers as a guide to the presence of infection, it would be feasible to explore their usefulness in determining when infection has been eliminated. Patients with infection could be randomised to have treatment discontinued either on the basis of changes in the chosen inflammatory marker or on the basis of clinical signs and/or usual practice. If the use of inflammatory markers results in shorter courses of treatment with no increase in relapse, it would have an immediate and major effect on clinical care. It would be a giant leap forward—not just in managing infection, but also for the emerging science of podopathy.

Duality of interest The author declares that there is no duality of interest associated with this manuscript.

References

1. Jeandrot A, Richard JL, Combescure C et al (2007) Serum procalcitonin and C-reactive protein concentrations to distinguish mildly infected from non-infected diabetic foot ulcers: a pilot study. *Diabetologia* DOI [10.1007/s00125-007-0840-8](https://doi.org/10.1007/s00125-007-0840-8)
2. Lipsky BA, Berendt AR, Deery HG et al (2004) Diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 39:885–910
3. Lipsky BA (2004) A report from the international consensus on diagnosing and treating the infected diabetic foot. *Diabetes Metab Res Rev* 20:S68–S77
4. Lavery LA, Armstrong DG, Murdoch DP, Peters EJJ, Lipsky BA (2007) Validation of the Infectious Diseases Society of America's diabetic foot infection classification system. *Clin Infect Dis* 44:562–565