

Lower limb complications

The drugs don't (always) work: antibiotics and foot infections



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The issue of antibiotics causes more angst and debate than any other area of diabetic foot-care practice. Debridement, off-loading and vascular reconstruction are always regarded as essential tools in healing ulceration, and, simplistically, what discussion there is should be limited to which method is best. It is, however, not unusual for the need for antibiotic therapy to be debated, let alone which of the myriad single and combination regimens should be used. Dinh et al (2008; summarised adjacent) describe their analysis of the various diagnostic tools for determining whether an ulcer is complicated by osteomyelitis. A diagnosis of osteomyelitis is a defining point in antibiotic care and usually results in prolonged courses, even for those who use short bursts of therapy for normal ulcers. They conclude that clinical examination is the most effective way to diagnose osteomyelitis with magnetic resonance imaging (MRI) scanning coming second. Plain radiographs were low on their list for detecting bone infection. However, when clinical suspicion is high, and MRI scans expensive and hard to obtain, I still support my examination with serial radiographs, which are more effective than a single film.

Choosing an antibiotic regimen is harder than ever, with microbiologists blaming us for using a cocktail of drugs that promote *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals, even though most of my patients are treated exclusively as out-patients. When Vardakas et al (2008; summarised below) reviewed 18 randomised controlled trials of antibiotic therapy in diabetic foot infections (and I for one was surprised to see that they had found that many), different regimens had similar outcomes. The only outstanding choice was carbapenems such as meropenem, but this is limited to intravenous use. The main factor in treatment failure was the presence of MRSA. In Edinburgh, if a patient needs hospital admission for worsening infection, we assume MRSA and treat accordingly.

On a separate, but related note, if single drug therapy for painful neuropathy fails then combination therapy with gabapentin and oxycodone in combination is worth trying (Hanna et al, 2008; summarised on page 199). Rather than maximise the dose of one drug and risk side-effects, good doses of both in combination are now proven to work better than gabapentin alone and are worth considering. Further advice on this area was recently published in this journal and our sister publication *Diabetes & Primary Care*.

DIABETES RESEARCH AND CLINICAL PRACTICE

MRSA associated with antibiotic failure during foot ulcer treatment

Readability	✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 Treatment failure is a main concern in the management of diabetes-related foot ulcers. This study aimed to identify the factors associated with treatment failure, across a wide range of antibiotics,

including penicillins, carbapenems, and cephalosporins.

2 Details from 18 randomised, controlled trials of antibiotics used for diabetic foot infections were included in this analysis; overall, treatment failure was observed in 22.7% of those studied.

3 Treatment with carbapenem antibiotics was associated with fewer treatment failures; patients infected by MRSA (methicillin-resistant *S. aureus*), either alone or as part of a polymicrobial infection, however, were at increased risk of antibiotic treatment failure ($P=0.02$).

Vardakas KZ, Horianopoulou M, Falagas ME (2008) Factors associated with treatment failure in patients with diabetic foot infections: An analysis of data from randomized controlled trials. *Diabetes Research and Clinical Practice* **80**: 344–51

CLINICAL INFECTIOUS DISEASES

MRI most effective imaging method for diagnosis of osteomyelitis

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 Several different diagnostic methods are used to identify osteomyelitis in diabetes-related foot ulcers; this meta-analysis compared the sensitivity and specificity for each diagnostic method, in order to identify the most effective tool.

2 A literature search was carried out using the search period 1966 to 27 February 2007, and was limited to English papers only.

3 Inclusion criteria were: studies that assessed the accuracy of diagnostic modalities in those with diabetes and a foot ulcer; and studies that used microbiologic culture of bone specimens or histopathological examination as a test for diagnosis of osteomyelitis.

4 The sensitivities and specificities of diagnosis by magnetic resonance imaging (MRI) were found to be 0.90 and 0.79; for testing for exposed bone or probe-to-bone they were 0.60 and 0.91; and for diagnosis using radiography 0.54 and 0.68, respectively.

5 The diagnostic odds ratios were as follows: clinical examination, 49.45; radiography, 2.84; MRI, 24.36; bone scan, 2.10; leukocyte scan, 10.07. A higher score indicates better discrimination for a diagnosis of osteomyelitis compared with a person without osteomyelitis.

6 Consequently, diagnosis by clinical examination is the most effective method overall, and the most accurate imaging method to diagnose osteomyelitis is MRI scan.

Dinh MT, Abad CL, Safdar N (2008) Diagnostic accuracy of the physical examination and imaging tests for osteomyelitis underlying diabetic foot ulcers: meta-analysis. *Clinical Infectious Diseases* **47**: 519–27

EUROPEAN JOURNAL OF PAIN

Oxycodone and gabapentin combination effective for painful neuropathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The management of painful diabetic neuropathy is challenging; diagnosis is difficult, and the standard drugs used for therapy are only 50% effective.

2 This randomised, double-blind, placebo-controlled trial investigated the effects of standard gabapentin therapy with the addition of oxycodone for neuropathic pain relief.

3 A total of 338 patients diagnosed with moderate-to-severe neuropathy related to diabetes participated in this trial; all patients had already reached their maximum tolerated dose of gabapentin, and oxycodone or placebo was added to their existing treatment regimen.

4 After 12 weeks, the gabapentin plus oxycodone combination treatment caused a significant reduction in pain scores by 33%, and this treatment regimen was overall more effective than placebo ($P=0.007$).

5 Pain relief was significantly reduced by the combined treatment regimen ($P=0.003$), and patients in this group also used less escape medication and had fewer incidents of disturbed sleep ($P=0.03$ and $P<0.05$, respectively).

6 Discontinuation of treatment was also significantly different between groups, 14% in the gabapentin and oxycodone group, versus 54% of those receiving placebo.

7 This is the first evidence supporting the combined use of gabapentin and oxycodone for diabetes-related neuropathic pain.

Hanna M, O'Brien C, Wilson MC (2008) Prolonged-release oxycodone enhances the effects of existing gabapentin therapy in painful diabetic neuropathy patients. *European Journal of Pain* **12**: 804–13

DIABETES CARE

Kidney disease associated with foot ulcers and amputation

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 This study investigated the association between the prevalence of diabetic foot ulcers (DFU) or lower-extremity amputation (LEA), and chronic kidney disease (CKD).

2 The authors performed a retrospective cohort study, including data from 90 617 patients with diabetes who received care in a UK general practice between 2002 and 2006.

3 A total of 378 patients underwent an LEA and 2619 reported a DFU during the study period; in total, 26% of the patient population was diagnosed with CKD: an estimated glomerular filtration rate (eGFR) <60 ml/min per 1.73m^2 .

4 The hazard ratio for developing DFUs in patients with an eGFR between 30 and 60 ml/min per 1.73m^2 was 1.85, and for patients with an eGFR <30 ml/min per 1.73m^2 the hazard ratio was 3.92; the hazard ratios for undergoing an LEA were 2.08 and 7.71 for each group, respectively. The reference group was those with an eGFR ≥ 60 ml/min per 1.73m^2

5 Degree of CKD is a strong indicator of risk for DFU or LEA.

Margolis D, Hofstad O, Feldman HI (2008) Association between renal failure and foot ulcer or lower-extremity amputation in patients with diabetes. *Diabetes Care* **31**: 1331–6

THE BRITISH JOURNAL OF GENERAL PRACTICE

Incorrect patient views on foot ulcer prevention

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Although people with type 2 diabetes are advised to take preventative measures to minimise the risk of foot ulcers, the effect of such advice on patients is not known.

2 This study aimed to investigate patients' knowledge and beliefs of diabetic foot complications. It included

data obtained from structured one-to-one interviews with people with type 2 diabetes and no foot ulcers, on the nature of lower limb complications and preventative care.

3 Most interviewees were not sure what a foot ulcer is and many incorrectly associated the increased incidence of lower-limb amputation with poor blood circulation in the feet, rather than foot ulceration.

4 Improvements in patient education are warranted, as most participants in this study were also unaware of the most effective preventative techniques.

Gale L, Vedhara K, Searle A et al (2008) Patients' perspectives on foot complications in type 2 diabetes: a qualitative study. *The British Journal of General Practice* **58**: 555–63

DIABETES CARE

Dose-related improvement with pregabalin for neuropathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 This study analysed data from seven trials in order to determine the efficacy of treatment with pregabalin for painful diabetic neuropathy across treatment doses 150mg, 300mg and

600mg per day, administered three times daily versus twice-daily.

2 Compared with placebo, treatment with pregabalin at all studied doses administered three times daily was significantly more effective at reducing pain and related sleep interference in patients with diabetic neuropathy ($P\leq 0.007$); the only effective dose administered twice daily was 600 mg/day.

3 Thus, treatment with pregabalin significantly improves pain in neuropathy in a dose-dependent manner.

Freeman R, Durso-DeCruz E, Emir B (2008) Efficacy, safety, and tolerability of pregabalin treatment for painful diabetic peripheral neuropathy. *Diabetes Care* **31**: 1448–54

“After 12 weeks, the gabapentin plus oxycodone combination treatment caused a significant reduction in pain scores by 33%, and this treatment regimen was overall more effective than placebo ($P=0.007$).”