Is the rheumatoid ulcer a medical myth?

Rheumatoid arthritis is a chronic disease that is often associated with an increased prevalence of wounds and delayed healing. Use of the terminology 'rheumatoid ulcer' may fuel a myth that serves to blur our understanding of the problem. This article examines the prevalence and aetiology of lower limb ulceration in people with rheumatoid arthritis and questions whether attributing wounds to the underlying chronic disease contributes to our lack of knowledge and understanding in this area.

Jill Firth

KEY WORDS
Rheumatoid arthritis
Rheumatoid ulcer
Leg ulcer
Foot ulcer

The adjective 'rheumatoid' is applied to indicate that something is characteristic of, or affected by rheumatoid arthritis (RA) (US National Library of Medicine, 2006). RA is the most common form of inflammatory arthritis and affects about 387,000 adults in the UK (Arthritis Research Campaign, 2002).

RA is characterised by inflammation of the synovial membrane of the joints, and typically causes a symmetrical arthritis. Although any synovial joint may be affected, the small joints of the hands and feet are most commonly involved, particularly in early disease. The course of disease varies from one individual to another in terms of severity and progression, ranging from a self-limiting arthritis to a chronic disease featuring remissions and acute periods of disease activity. While RA primarily affects the joints, it is a systemic disease which gives rise to fatigue, malaise and early morning stiffness and often features anaemia of chronic disease. This relates to the underlying inflammatory process and is associated with impaired iron utilization and reduced erythropoietin levels. Many organs can be affected, including the heart, lungs and spleen as well as the ophthalmic and neurological systems (Wollheim, 1998). Skin manifestations include nodules and vasculitis, but the prevalence of lower limb ulceration in RA cannot be attributed to these factors alone.

While RA primarily affects the joints, it is a systematic disease which gives rise to fatigue, malaise and early morning stiffness, and often features anaemia of chronic disease.

Lower limb ulceration is often poorly defined and it is often unclear whether this terminology includes the feet and toes. It has been noted that in the older literature a leg ulcer was defined as an ulcer of the lower limb located in between the knee and the foot (Nelzen, 1997). Over time this has evolved into a variety of broader definitions, including an open sore or wound below the knee that does not heal for six weeks (Graham et al, 2003). In many studies, however, researchers do not make it clear whether ulcers on the foot were included in their investigation and almost as many fail to provide a definition of an ulcer (Graham et al, 2003). In this article the term lower limb ulceration is used, unless it is made clear that the foot was excluded (in which case the term leg ulceration will be used) or the research was solely on foot ulceration.

The prevalence and aetiology of lower limb ulceration in patients with RA

Lower limb ulceration in patients with RA is believed to be common but in actual fact surprisingly little is known about the prevalence and aetiology of chronic wounds in this client group. The studies of prevalence which have addressed this issue specifically in RA are relatively small scale, and investigation often focuses on relatively small samples of patients in secondary care.

The findings from an early case-note review of 324 inpatients with RA (Wilkinson and Kirk, 1965) indicated the validated prevalence of lower limb ulceration to be more than 8%, but these findings are hard to interpret because data was collected from the case notes of patients admitted during a six-year period, and those patients

Jill Firth is a Rheumatology Nurse Specialist at Bradford Teaching Hospitals NHS Trust. She is currently taking a full-time PhD at the University of Leeds after being awarded a Smith & Nephew foundation doctoral studentship

with ulcers that could be attributed to pressure or venous stagnation were excluded. Sampling RA patients who required inpatient treatment selects those with more severe disease and is likely to be responsible for the fact that 10 of the 27 cases were presumed to be vascular lesions suggestive of arteritis, and four were attributed to the effects of corticosteroids on skin integrity which renders skin liable to injury from minimal trauma. Twelve cases of ulceration had no obvious cause recorded.

In a later postal survey of 250 RA patients taken from a diagnostic register, while 9% reported a validated history of lower limb ulceration, with only pressure ulcers being excluded, only two patients had any evidence of vasculitis. Interestingly, this was more than twice the frequency of lower limb ulceration reported in a matched control group with degenerative arthritis (Thurtle and Cawley, 1983).

Much of our understanding of the association between RA and an increased prevalence of lower limb ulceration is drawn from studies that examine the underlying pathology of affected patients. It has been suggested that RA is the third most common cause of leg ulceration, following chronic venous insufficiency and arterial disease (Ertl, 1991). This conclusion was drawn from prevalence studies undertaken in the 1980s. In a survey of healthcare professionals in two health board areas of Scotland, 1,477 patients with chronic lower limb ulceration were identified, equalling a point prevalence of 1.48/1,000 total population (Callam et al, 1985; 1987). Six hundred of the patients were seen by the researchers who found that 76% of patients had evidence of venous disease, 22% of arterial insufficiency and 9% had RA (Callam et al, 1987). In the other study cited, 32% of patients with leg ulceration reported a history of some form of arthritis, but this study was based upon a small random sample of 100 patients and excluded isolated ulceration of the foot and toes (Cornwall et al, 1986).

Similarly, a history of arthritis was reported by 43% of patients attending a leg ulcer clinic, but this is not surprising when you consider that the sample was taken from a clinic initially established for patients who were over 60 years of age (Schofield et al, 2003). This was a retrospective study with a small sample of 42 new patient records. In fact, only two patients had a diagnosis of RA, and, while this was cited as the principal cause of ulceration, these did not account for the cases of vasculitis cited. The authors noted worsening of oedema during the active phase of RA. Venous ulceration is often accompanied by oedema and associated with immobility and reduced ankle movement (McRorie et al, 1994).

In a study carried out in Ireland, healthcare professionals reported the prevalence of lower limb ulceration in a two-month period as 0.12%, rising to 1.03% in patients over 70 years of age. A staggering 17.9% of all affected patients had RA (63/352), although it is interesting to note that the researchers found both primary rheumatoid and diabetic causes to be rare (O'Brien et al, 2000). Aetiology was determined through a follow-up stage in which patients with an ulcer underwent clinical assessment by a researcher. A rheumatoid cause was only suspected when venous and arterial indices were normal but clinical examination indicated vasculitis. This occurred in only one patient, while venous disease accounted for 81% and arterial disease for 16.3% of all ulcer cases.

Further afield, researchers in Australia conducted a population-based study in which they recruited 259 patients with chronic lower limb ulceration through referral from healthcare professionals and by self-referral (Baker et al, 1991). In a sub-group analysis, they examined aetiological factors in 138 patients with abnormal venous refilling time. In 64% of cases no additional aetiological factors were found, but of the remaining patients, 22% had arterial ischaemia, 12% had RA and 10% had diabetes mellitus. The complex nature of the investigation was recognised by the authors who highlighted that there are no analytical grounds for determining which abnormality is the dominant influence on wound healing.

Also in Australia, a study examined healing determinants in a community-based sample of older people with leg ulcers (Johnson, 1995). The author focused on leg ulcers of venous and venous-arterial origin and found that 10% of the affected sample (n=165) had RA diagnosed by a physician, although this may be an underestimate as oral steroid use was among the exclusion criteria.

The findings of these studies demonstrate an association between lower limb ulceration and RA. This was confirmed by the work of Nelzen, whose case-control study of medical history in lower limb ulceration patients demonstrated a significant difference between cases and controls (Nelzen, 1997) — 59% of ulcer patients reported a history of some form of arthritis compared with 31% of controls ($p<0.0001$), although it was acknowledged that patients tended to overestimate disease in relation to arthritis.

Foot ulceration in RA

Even less is known about the prevalence of isolated foot ulceration in RA, although a number of authors assert that skin ulceration occurs commonly in inflammatory rheumatic disease and that the foot is a common site for such lesions (Spiegel and Spiegel, 1982; Cawley, 1987; Vogelgesang et al, 1999). Despite the attention paid to this problem in the descriptive literature, the evidence consists of case reports and audit data. Williams and Bowden (2004) found that more than half the rheumatology patients attending clinic, 74 of whom had RA, were assessed as having poor tissue viability, based upon data collection which included the presence or history of ulceration but did not report on prevalence (Williams and Bowden, 2004).

A three-year retrospective audit of a rheumatology foot ulcer clinic found that of 149 new patients, 73% had RA, 6.4% of whom had a diagnosis of vasculitis and 1.8% peripheral vascular disease. Many patients had recurrent ulceration, not always at the same site and the authors concluded that

the importance of foot ulceration in rheumatology may be underestimated (Davys et al, 2006). This gap in knowledge is currently being addressed by the author's doctoral studies by examining the prevalence and aetiology of foot ulceration in RA.

Defining the rheumatoid ulcer

The Cochrane Collaborative Wounds Group (2006) has defined a rheumatoid ulcer as an 'area of skin loss resulting from rheumatic disease' (Cochrane Wounds Group, 2006). As a definition this is imprecise and if it is used healthcare professionals may classify ulcers wrongly and overlook more complex underlying aetiological factors and reasons for delayed wound healing.

The rheumatic diseases have diverse clinical presentations and underlying pathophysiology that may predispose to ulceration in different ways. For example, Raynaud's phenomenon is a common feature of the connective diseases and vasculitis and occurs more frequently than in RA, so the nature of wounds in these disparate groups cannot be considered collectively. Concentrating solely on RA, the clinical picture is no less complex. In the same way that patients with diabetes experience neuropathic or ischaemic foot ulcers, RA patients may experience venous insufficiency or vasculitic ulcers.

The aetiology of ulceration in RA has not been studied with any rigour and the majority of the studies that exist rely on retrospective data capture. Lower limb ulceration in RA is often attributed to vasculitis, although there is little evidence for this as few studies have critically evaluated the role of individual risk factors in ulceration (Hafner and Trueb, 1999; McRorie et al, 1994). Those which have, albeit in studies with small sample sizes, conclude that the aetiology of the ulcers was multifactorial, with venous and arterial insufficiency, trauma or pressure to be factors commonly involved (McRorie et al, 1998; Pun et al, 1990; Thurtle and Cawley, 1983). In a small study of 20 RA patients with non-healing leg ulceration sampled from general practice, 10 had multifactorial aetiology and 15 had signs of venous insufficiency. Eleven had histopathological evidence of vasculitis, but this was the only aetiological factor detected in just one of these cases (Oien et al, 2001).

In a clinical review, McRorie et al (1994) highlighted possible aetiological factors that include known risk factors for lower limb ulceration, such as venous insufficiency, peripheral arterial disease, peripheral neuropathy and cutaneous vasculitis and foot deformity, in addition to *pyoderma gangrenosum* and skin fragility in this client group. These factors were examined in a recent review by the author (Firth, 2005) along with other factors that affect tissue viability in people with RA, such as being less able to care for themselves, nutrition, medication, ill-fitting footwear and raised plantar pressures.

There is an assumption of shared meaning regarding the terminology used in wound care that may be serving to obscure rather than enlighten our understanding. At the moment our understanding of the nature of the 'rheumatoic ulcer' is limited.

It has also been postulated that, in the absence of vascular disease, arthritis of the knee and ankle may lead to ulceration by affecting blood and lymphatic flow (Schofield et al, 2003). Loss of movement at the ankle joint impairs the venous muscle pump leading to an increase in mean venous pressure in the lower leg and prolonged elevation of pressure may, in turn, directly damage the veins leading to venous reflux (Gaylarde et al, 1990).

Discussion

The difficulty of gaining a clear understanding of the aetiology of wounds is not necessarily confined to the rheumatic diseases, which are complex and often poorly understood. In a point prevalence survey of leg and foot ulceration in an acute trust, 1.8% of patients had open ulceration (Dealey, 1999). Of the 17 patients this represented, the aetiology of the ulceration was reported to be mixed and only one case was attributed to RA. However, several nurses expressed concern that they were uncertain of the aetiology of the ulceration and co-existent pathology was not recorded or validated from the case notes. Furthermore, the majority of healthcare interventions for patients with RA take place in an outpatient setting, so this client group may well have been underrepresented in the acute trust. Indeed, a large burden of care falls to community-based nurses and podiatrists as 83% of all leg ulcer patients have been found to be managed entirely in the community (Callam et al, 1985).

The problems are twofold. First, the evidence base regarding ulceration in RA is growing, but there needs to be further work to elucidate the risk factors for ulceration that occur in patients with RA and contribute to the increased prevalence of wounds in this group. Nurses and podiatrists have made little contribution to work in this field, despite being at the forefront of wound care. Second, there is an assumption of shared meaning regarding the terminology used in wound care that may be serving to obscure rather than enlighten our understanding. At the moment our understanding of the nature of the 'rheumatoid ulcer' is limited.

Wilkinson and Kirk (1965) suggested that a failure to appreciate the relationship of lower limb ulceration to RA may result in unsatisfactory therapy. The complexity of the relationship should not, however, be underestimated. The aetiology of such wounds appears to be multifactorial and there are no criteria for determining which abnormality is the major influence in wound healing (Baker et al, 1991). However, the accurate assessment of ulcer aetiology not only influences management, but also outcomes and healing rates (Salaman and Harding, 1995). Lower limb ulceration in people with RA requires objective, individual assessment both to plan the appropriate intervention to promote healing, and