Sepsis and chronic wounds: What do you know? What should you know?

KEY WORDS
- Diabetic foot ulcer
- Leg ulcer
- Pressure ulcer
- Sepsis
- SIRS

The failure within the NHS to rapidly diagnose and treat sepsis has been highlighted by the Parliamentary Health Services Ombudsman. This article underlines why early recognition is key and that clinicians need to act promptly to prevent the progression of infections towards a potentially fatal endpoint.

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Sepsis is a life-threatening condition, usually of acute onset. Specifically, it is a systemic disease arising from infection and an over-activation of the innate immune system known by the diagnostic criteria of Systemic Inflammatory Response Syndrome (SIRS) (Daniels, 2010). It has become a major public health problem in the UK where the NHS statistics acknowledge over 37,000 deaths per annum in England alone (Richards, 2013). More recent data, as yet unconfirmed, suggest that 150,000 cases of sepsis result in approximately 44,000 deaths (Sepsis Trust, 2016). The mortality rate of approximately 30% indicates the seriousness of the condition, a factor relevant to correct and early diagnosis and appropriate interventions. In 2010, 5.1% of all UK deaths were associated with sepsis; this is, in most instances, far too high for an avoidable clinical emergency.

Many similar instances have been found, upon review, to have been avoidable insofar as early diagnostic signs and symptoms were not recognised by clinicians. The NHS has been accused of 'failing to make progress on sepsis' by the Parliamentary Health Services Ombudsman (http://www.ombudsman.org.uk/time-to-act). This statement applies across the whole gamut of clinical presentations. It is the authors' contention that it applies equally to patients suffering from chronic wounds.

Age-specific death rates show an increase from around age 10 years at 1 per 100,000 to >100 per 100,000 >70 years. ICD-10 codes show that 'circulatory' diseases account for 11.5% of sepsis-associated deaths; these will include leg ulcers. The data for pressure ulcers (PUs) are far less precise, with published literature being relatively sparse on the topic. The current prevalence of pressure ulceration in UK hospitals is 18–20%, providing some indication of the high-risk status of this patient group (Clark et al, 2004). Category III and IV PUs present a real risk of sepsis and death. Galpin et al (1976) reported PU mortality due to sepsis approaching 50%, whereas Thomas et al (1996) found that 59.5% of US patients with a PU died within 1 year of its development. With patients with category III and IV ulcers, secondary complications, most notably sepsis, occur. Although there are no data available in the UK, we can draw some parallel with the USA where >16% of all PU-related hospitalisations had sepsis. Conversely, 13.5% of all hospital stays developed sepsis (Russo et al, 2008). If translated directly into the UK health system, these percentages would not be inconsistent with the current incidence of sepsis, and may well reflect of the incidence of PU-related sepsis. There is clearly a need for widespread publication of PU incidence rates, accurate reporting on death certificates, and wider awareness of the sepsis risk in PU patients.

Early recognition of sepsis is key to appropriate interventions. This enables treatment to be administered quickly and effectively. Community nurses see a large number of patients with PUs and other chronic wounds, and are often the gatekeeper to the GP. As a consequence, the emphasis on awareness and education in sepsis recognition must be directed at this group. Nurse training on recognition of sepsis is limited, particularly on tissue viability study days and courses.

All clinicians need to act promptly if a patient with a wound shows signs of a potentially fatal infection,

e.g. signs of sepsis or extensive tissue necrosis (necrotising fasciitis or gas gangrene). The recent National Institute for Health and Care Excellence guideline (NICE, 2016) emphasises the importance of education in all settings thus: "*Ensure all healthcare staff and students involved in assessing people's clinical condition are given regular, appropriate training in identifying people who might have sepsis. This includes primary, community care and hospital staff including those working in care homes.*

Ensure all healthcare professionals involved in triage or early management are given regular appropriate training in identifying, assessing and managing sepsis. This should include:

- *Risk stratification strategies*
- *Local protocols for early treatments, including antibiotics and intravenous fluids*
- *Criteria and pathways for escalation, in line with their health care setting."*

The NHS has recently issued resource packs for managing sepsis but the crucial step is in avoidance, or at least early detection. The diagnostic features can be found in *Table 1*.

Thereafter, the UK Sepsis Trust charity has published the 'Sepsis Six' resuscitation evidence-based approach (Nutbeam, 2010). These key steps are:

- High flow oxygen
- Blood cultures
- Broad spectrum antibiotics IV
- IV fluids
- Measure Hb and lactate
- Monitor urine output.

While it is commonly accepted that the primary sources of infection that result in sepsis are the lungs, abdomen and urinary tract, there is evidence to suggest that chronic wounds (especially PUs) are also a frequent source. In any event, the broader patient population that is prone to PUs, e.g. older people, disabled people, and individuals with spinal injury, for example, are all similarly at higher risk of respiratory and urinary tract infections — as well as being in the higher age range (Munford and Suffredini, 2014).

In pathophysiological terms, sepsis is an immune-inflammatory condition in which cytokines, such as TNF-α and IL-1β, mediate a systemic response to infection (Surbatovic et al, 2013). One of the key events in the development of sepsis is the activation of immune cells by pathogenic bacteria or their products (e.g. cell wall components and toxins).

The risk factors for sepsis have been divided into two groups: a) risk factors for infection and b) risk factors for organ dysfunction (Mayr et al, 2014).

Thus for wound patients, age, perfusion, nutritional status, immune status, site and depth of wound, and comorbidities among other factors constitute infection risk. More than half of all severe sepsis cases occur in patients over 65 years (Mayr et al, 2010) or those with diabetes. In this context it is obvious that aged patients with PU and double incontinence are 'at risk', as are patients with large body surface area burns. These examples to the experienced wound clinician, will be widely-known risk factors. The variability in susceptibility to sepsis is attributed to 'genetic' factors (Sorensen et al, 1988). Genes for the expression of TNF, TLRs 1 and 4, and platelet activator inhibitor (PAI) -1 have been implicated (Bierne et al, 2012).

Sepsis, together with bacteraemia, is recognised as a major hazard in patients with chronic wounds (Brem et al, 2003), being reported variously in diabetic foot ulcers (Sapico et al, 1982), PUs (Jaul, 2010; Messer, 2010), leg ulcers (Ebright, 2005). Cellulitis is a common inflammatory condition which involves cutaneous tissues. It is associated with locally wounded/damaged skin with Gram-positive bacterial infection. Typical organisms implicated are group *A Streptococci* and *Staphylococci*. Its incidence is increased in diabetes and vascular insufficiency. It has been hypothesised that if chronic wound patients are 'provided with early intervention and comprehensive treatment ... they will be spared the morbidities of pain, amputation and even death' (Brem et al, 2003).

The purpose of this brief review is to raise awareness of wound-related sepsis, its risks and outcomes, as well as to draw attention to recent diagnostic and treatment guidelines with the ultimate aim of reducing morbidity and mortality. This is integral to efforts to improve the recognition and diagnosis of wound infection, and to the management of wound bioburden.

SEPSIS IN CHRONIC WOUND AETIOLOGIES: PRESSURE ULCERS

Pressure ulcers occur in all age groups, most commonly in the elderly and those with impaired

mobility. Many PU patients will have concomitant pathologies which may further complicate the clinical picture. In a survey of patients in geriatric institutions in Japan, Kanazawa (1990) found that of an incidence of pressure ulcers (PUs) of 12%, some 20% developed sepsis, i.e. approximately 2.4% of the total. The mortality of this fraction is not given, but it will be high (Galpin et al, 1976). Montgomerie (1997) has reviewed infections in spinal injury patients, including those with PU. In another study of spinal injury patients, an incidence of 13–69% infection was noted, including osteomyelitis and bacteraemia (Richardson and Meyer, 1981). Galpin et al (1976) found that, in patients with sepsis solely associated with PU, bacteraemia was documented in 76% and mortality was 48% in spite of antibiotic therapy. In PU patients, the diagnosis of osteomyelitis underlying the ulcer is difficult, complicated by the inherent difficulty in diagnosis and the complexity of the tissue pathology. In such cases, the presence of pyrexia and leucocytosis, without drainage, are indicators of joint involvement.

DIABETIC FOOT ULCERS

Diabetes has long been known to predispose the sufferer to infection, this includes local sepsis (Muller et al, 2005; Shah and Hux 2003). Indeed, such patients constitute approximately 20% of all diagnosed with sepsis (Stegenga et al, 2010). Osteomyelitis and sepsis in the diabetic foot have been described by Arenson et al (1982). As many diabetic foot ulcers are pressure ulcers, it is the influence of sepsis upon the outcome of foot ulceration that is of clinical significance (Klamer et al, 1987; Kertesz and Chow, 1992).

LEG ULCERS

The presentation of sepsis associated with leg ulceration is rare. It has been recently reported by Meagher et al (2014) in a case report which illustrates the typical presentation of a venous ulcer with active group *A Streptococcal* infection (GAS) and toxic shock. In this case the patient exhibited many of the characteristic sepsis signs including metabolic acidosis (elevated lactate, indicating the need for urgent fluid resuscitation). The others include blood cultures (although these can be negative even in severe sepsis), arterial blood gases, CRP acute phase protein level noting the rate of elevation, and white cell counts as a marker of systemic inflammation.

Table 1. The diagnostic features of the NHS resource pack.

Diagnostic criterion	Threshold
Fever	>38.3°C
Tachycardia	>90/minute
Systolic blood pressure	<90 mmHg
Procalcitonin	>0.5 ng/ml
Lymphocytopenia	<4.0 or >12 x 109/l
Neutrophil/lymphocyte ratio	>10
Thrombocytopenia	<150 x 103 uk
Lactate	> 2.0 mmol/l

CONCLUSIONS

Every clinician involved in wound management should be aware of, and recognise, sepsis and its potential for morbidity and mortality. The simple criteria of hyperthermia, acutely altered mental state, increased heart rate, plus tachypnoea should be evident to all healthcare professionals and alert them to the possibility of ongoing serious acute illness. The death rate from sepsis and its complications is far too high. To reduce this, a change in clinical practice is essential. The modern, evidence-based requirements for early and accurate diagnosis and appropriate intervention are well-documented (Koh et al, 2012; Martin, 2012; Schorr et al, 2014).

While we cannot be precise on the contribution of wounds in general to sepsis, it is quite clear that any wound has the potential to lead to an increased clinical risk. As ever, early recognition, appropriate referral and intervention are likely to reduce morbidity. WUK

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