

# Diagnosing wound infection: the use of C-reactive protein

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## Abstract

**Background:** The diagnosis of wound infection is often restricted to the use of clinical signs and symptoms which are not always reliable. **Aims:** To determine if systemic C-reactive protein (CRP) measurements could be used as a diagnostic marker for wounds whose healing is delayed by the effects of wound bed bioburden. **Methods:** A comparative descriptive design with a survey method was used. Patients with wounds healing by secondary intention with a duration of 4 weeks or more were placed into wound infection continuum groups based on clinical features. Wound features for each patient were listed to enable analysis of CRP results within and between groups. CRP was also analysed for all patients as a single group against individual wound features. **Results:** CRP levels were found to be significantly higher for patients in the spreading infection group, but no differences in levels were found to distinguish the other groups. Higher CRP levels were found to be statistically significant when several clinical features were present in wounds irrespective of study grouping, these were necrotic tissue, wet wounds, malodour, recent wound extension and redness of >2cm on surrounding skin. **Conclusions:** This study cannot support CRP as a diagnostic marker for determining between wounds in different groups in the infection continuum known as colonisation, critical colonisation and local infection and cannot be used alone to indicate the need for antimicrobial treatment in these groups. **Conflict of interest:** None

## KEY WORDS

C-reactive protein  
Wound infection continuum  
Secondary intention  
Critical colonisation  
Local infection

Many wounds healing by secondary intention become static causing extended periods of discomfort and inconvenience for the patient, and an increase to healthcare costs and workload. There are many reasons for this delay and the effect of wound bioburden is a common one (Browne et al, 2001) although its exact role is uncertain (Howell-Jones et al, 2005; Penhallow, 2005). The suggested range of the prevalence of chronic wound infection lies between 0.14% and 6% (Verdu Soriano et al, 2004) and

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antibiotic use for patients with chronic wounds is higher than for other patients matched for age and sex. This raises costs and contributes to the development and selection of multi-resistant micro-organisms (Howell-Jones et al, 2005).

Diagnosis of infection in wounds healing by secondary intention is primarily undertaken through the interpretation of clinical signs and symptoms. Gardner et al (2001a) developed a checklist tool from these based on an earlier list (Cutting and Harding, 1994). Known as the Clinical Signs and Symptoms Checklist, it identifies 12 signs and symptoms of infection which are:

- ▶▶ Pain
- ▶▶ Erythema
- ▶▶ Oedema
- ▶▶ Heat
- ▶▶ Purulent exudate
- ▶▶ Serous exudate with concurrent inflammation
- ▶▶ Delayed healing
- ▶▶ Discolouration of granulation tissue
- ▶▶ Friable granulation tissue
- ▶▶ Pocketing at the base
- ▶▶ Foul odour
- ▶▶ Wound breakdown.

When Cutting (1998) compared surgical nurses' clinical diagnoses of infection and his own judgements based on a similar list (Cutting and Harding, 1994) he found a poor agreement between the author and the nurses for both infected and not infected wounds (47.5%), indicating that clinical signs and symptoms alone are not sufficient to reliably identify infection.

Qualitative microbiology provides secondary corroboration. However, the link between positive wound swabs and clinical cases of infection has been shown to vary in wounds with different aetiologies. Schmidt et al (2000) found that only 22% of venous leg ulcers (VLU) with positive swabs went on to develop infection in contrast with 70% of diabetic and arterial ulcers. McGuckin et al (2003) considered that microbiological culturing of wounds was insufficiently rigorous as a scientific method, requiring further research to improve its validity as a predictor of wound infection.

Biopsy is considered the gold standard microbiological method for

research but is not often carried out in clinical practice due to exacting processing requirements and concerns over harm to the patient and so swabbing is more usual. Quantitative thresholds as indicators of infection have been used for many years (Cooper, 2002a), although the value for this method for open wounds has been questioned (Bowler, 2003). Wound surfaces and tissues have heterogeneous bacterial distribution, which presents a problem for testing accuracy (Woolfrey et al, 1981; Steer et al, 1996; Ribinik et al, 1997). Problems with swabbing consistency between professionals may lead to unreliable results (Cooper, 2002a). In one study, Starr and MacLoed (2003) found varying techniques in wound swabbing in a small group of nurses from the same ward. As there is no UK consensus on swabbing method in clinical practice including the value of pre-cleaning the wound bed (Cooper, 2002b), it is likely that results of swabbing will lack consistency.

It has been proposed that a continuum of gradually-increasing bioburden exists in open wounds ranging from healing wounds with simple colonisation and without host response to overt infection (Dow et al, 1999). Names for the staged points on this infection continuum have been suggested (Kingsley, 2001; Kingsley et al, 2005) and are colonisation, critical colonisation, local infection, and spreading infection. The term critical colonisation, first introduced by Davis (1997), has been the subject of debate (Cooper, 2005; Jorgensen et al, 2005; White and Cutting, 2006) but is used by many wound care experts to identify when topical antimicrobial therapy is required to optimise wound healing (Jorgensen et al, 2005). However, clinical diagnosis, being dependent on the skills of the clinician, leaves scope for either over-treatment with antimicrobials when it is not truly warranted or under-treatment when managing the bioburden would assist wound healing.

If a simple and reproducible diagnostic test was available to indicate

**Table 1**

**Characteristics of wounds in each of the wound infection continuum group**

**Colonised**

A wound that is considered to be progressing normally. There will be no necrotic tissue, and limited slough which is thin and mobile in depth and character. There will be some firm granulation tissue which is normally a salmon red-pink colour and moist, and there may be pink/purple epithelial tissue (Sibbald et al, 2000).

**Critically colonised**

A wound that is considered to be indolent (ie not healing and not deteriorating) despite seemingly appropriate therapy. The wound is wet and there is likely to be thick slough (at >50% cover of base) but no new (within two weeks of referral to tissue viability) necrotic tissue (there may be residual necrosis from original wounding event), there may be odour but not cellulitis. The wound may bleed easily at slightest touch and if previously granulating the tissue may be an unhealthy dark colour. Alternatively the wound base may be clean, free of active granulation and pale in colour or pale and oedematous.

**Locally infected**

A wound that has some cellulitis as a flare on the adjacent skin or encircling the wound no greater than 2cm (Dow et al, 1999) from the wound edge. There may be slough (>50% of base) and necrotic tissue (appeared suddenly in a previously healing wound and this may be in the absence of cellulitis (Kingsley, 2001), the wound base if previously granulating may be an unhealthy deep red colour that bleeds at the slightest touch, the wound is wet or wetter than it was recently, and there may be odour. Some wounds may not exhibit cellulitis but show recent wound extension. Others may show cellulitis <2cm from the edge but show extension.

**Spreading infection**

There is cellulitis surrounding the wound that is greater than 2cm from the edge. The wound may be wetter than normal, tissue may be friable and bleed easily, the wound may have extended or new satellite skin breaks have appeared in addition to the cellulitis. Odour may be offensive, there may be pyrexia, lymphangitis or lymphadenitis or bacteraemia.

when the use of antimicrobial therapy would be necessary for wounds that were not healing due to the effects of wound bed bioburden then early treatment might improve outcomes and lower costs. Measuring C-reactive protein (CRP) levels is a potential test that has been used successfully in other areas to improve diagnosis over standard bacteriology and clinical impression (Gulich et al, 1999), such as identifying sepsis in major trauma (Stahl et al, 1985), and detecting wound infection following trauma and orthopaedic surgery (Gupta et al, 2002). If it could be established that CRP levels distinguish between the different wound infection continuum states then prompt initiation of treatment of the abnormal states, particularly critically colonised wounds with delayed healing and absence

of classic signs of infection, could be undertaken with confidence. Equally if high CRP levels were found to associate with particular wound features or certain micro-organisms then this could form the basis for further research into the prediction of infection.

**CRP testing — a possible solution**

CRP is a member of the acute phase family of proteins, released from hepatocytes whose levels rise significantly in response to monocyte-origin mediators such as interleukin-1 (IL-1) and 6 (IL-6), because of infection, tissue injury (Houshian et al, 2000) and inflammatory or neoplastic diseases (D'Amore, 2005). CRP is a highly conserved protein and no deficiency has been noted in any human population studied

(Ahlers and Schonheyder, 1990; Du Clos and Mold, 2002). Changes in CRP levels can occur within 24–48 hours in response to the presence or removal of the stimulation (Pepys, 1981), such as a bacterial infection. CRP elevates rapidly in response to relevant stimulus and is considered to have a stable decay rate (Okamura et al, 1990). Larsson et al (1992) found that the post-surgery CRP response was not affected by use of prophylactic antibiotics or anti-inflammatory drugs indicating that it reacts to a relevant stimulus in the body and is not altered by circulating medications. It is, therefore, reasonable to presume that CRP levels, elevated because of infection, will fall in response to effective antimicrobial therapy. CRP is a non-specific marker of inflammation and its potential as a diagnostic indicator for wound infection may be restricted depending on the presence of other inflammatory pathologies in individual patients. However, vascular vessel damage associated with venous disease was found not to raise CRP above routine clinical levels (Blomgren et al, 2001) and Goodfield (1988) found that venous eczema was also unable to raise CRP levels.

There is currently no single predictor of wound infection that is considered perfect (Browne et al, 2001). This study aims to investigate the possibility of using CRP levels to categorise infection levels.

**Method**

A comparative descriptive design using a survey method was used to search for a link between CRP level and open wounds categorised into the four states of the wound infection continuum (colonisation, critical colonisation, local infection and spreading infection) (Table 1). Ethical approval was received from the North and East Devon Local Research Ethics Committee. Sixty-four patients with wounds of more than four-weeks duration were recruited purposively from a single UK tissue viability nursing service. Exclusion criteria, based on work by Goodfield (1988), were stipulated to prevent inclusion of

**Table 2**

Essential and corroborating criteria used to allocate wounds into study groups

Allocation group	Essential criteria (must exhibit at least one)	Corroborating criteria (may exhibit 0–all)
Colonised (C)	<ol style="list-style-type: none"> <li>1. Progressing normally</li> <li>2. No necrotic material</li> <li>3. Some granulation</li> </ol>	<ol style="list-style-type: none"> <li>1. Granulation tissue normally red/pink and moist</li> <li>2. There may be pink/purple epithelium</li> </ol>
Critically colonised (CC)	<ol style="list-style-type: none"> <li>1. Is indolent</li> <li>2. Is wet</li> <li>3. No new necrosis</li> <li>4. No cellulitis</li> </ol>	<ol style="list-style-type: none"> <li>1. Likely to be thick slough (&gt;50% cover of base)</li> <li>2. Possible odour</li> <li>3. May be friable</li> <li>4. May have unhealthy dark granulation</li> <li>5. Granulation may be absent</li> <li>6. Base may be pale or pale and oedematous</li> </ol>
Locally infected (LI)	<ol style="list-style-type: none"> <li>1. Cellulitis — as flare or encircling wound — no greater than 2cm</li> <li>2. If no cellulitis wound has extended recently</li> <li>3. If no cellulitis sudden appearance necrotic tissue</li> <li>4. Is wet or wetter than it has been</li> </ol>	<ol style="list-style-type: none"> <li>1. May have thick slough (&gt;50% cover of base)</li> <li>2. May have odour</li> <li>3. May be friable</li> <li>4. May have unhealthy dark granulation</li> <li>5. Granulation may be absent</li> <li>6. The base may be pale or pale and oedematous</li> </ol>
Spreading infection (SI)	<ol style="list-style-type: none"> <li>1. Cellulitis &gt;2cm surrounding the wound</li> </ol>	<ol style="list-style-type: none"> <li>1. May have offensive odour</li> <li>2. May be friable</li> <li>3. May be wetter than normal</li> <li>4. May have wound extension</li> <li>5. May have new satellite lesions</li> <li>6. May have pyrexia, lymphangitis, lymphadenitis or bacteraemia</li> </ol>

patients who might have had reasons other than wound infection for a CRP rise, fall or suppression that would reduce the validity of the results. Exclusions were acute trauma wounds (<4 weeks), surgery or a myocardial infarction within the preceding seven days, an unresolved infection elsewhere in the body, and patients with active inflammatory conditions such as rheumatoid arthritis, inflammatory bowel disease, vasculitis, pyoderma gangrenosum or Buerger’s disease. Patients with diabetes and foot ulceration were excluded because the associated neurological damage and microvascular changes can lead to masking of the usual visual cues or experienced symptoms for infection, notably through absence of pain and inability to vasodilate in response to infection (Edmonds and Foster, 2004;

Falanga, 2005). Patients were also excluded if they had conditions or were taking medications that might suppress the normal inflammatory responses, such as systemic steroids, cancer chemotherapy, and antimicrobials taken or applied for greater than 48 hours, as they are either direct or indirect inflammation suppressants.

Eligible subjects were allocated to one of the four wound infection continuum study groups following comparison of clinical signs and symptoms to a pre-defined checklist based on published expert views available before the start of data collection in 2003 (Cutting 1994; Cutting and Harding 1994; Thomson and Smith 1994; Davis 1997; Davis 1998; Dow et al, 1999; Sibbald et

**Table 3**

Linkage of clinical feature to a mean raised CRP level (>8mg/L) as tested by ANOVA

Statistically significant	Not statistically significant
Necrotic tissue (p < 0.001)	Wound type (not ANOVA tested)
Wet or wetter than normal (defined by patient or by researcher as obviously wet on observation) (p=0.017)	Diabetes (p = 0.306)
Malodour (p=0.026)	Granulation (healthy and unhealthy including overgranulation and discoloured granulation) (p = 0.105)
Recent wound extension (p=0.01)	Friable/bleeding tissue (p=0.503)
Redness (>2cm from wound edge) (p=<0.0010)	New 'satellite' lesions (p=0.586)
Spreading infection group (p=<0.001)	Redness (<2cm from wound edge) (p=0.344)

**Table 4**

Further results on clinical features related to the allocated wound infection continuum study groups

Clinical feature	Result
Tissue discolouration	<ul style="list-style-type: none"> <li>» Discolouration present in 30% of CC group and 16% LI group</li> <li>» Darkly discoloured wounds had lower mean CRP (36.8mg/L) compared with non-discoloured wounds (50 mg/L)</li> </ul>
Friable tissue	<ul style="list-style-type: none"> <li>» Found most commonly in LI group (4 of 13 wounds)</li> <li>» None of the four LI group wounds with friable tissue had concomitant cellulitis</li> </ul>
Overgranulation	<ul style="list-style-type: none"> <li>» Overgranulation was only found in the CC group (4 of 20 wounds) and LI groups (2 of 13)</li> <li>» Four of the six (66.6%) overgranulated wounds bled easily compared with 3 of the 58 (5.2%) without overgranulation present</li> </ul>
Necrotic tissue	<ul style="list-style-type: none"> <li>» Five of 7 wounds which still had necrotic tissue present from the original injury were categorised as infected (LI and SI)</li> <li>» Wounds containing necrotic tissue had a higher mean CRP than those without it (p=&lt;0.001)</li> </ul>
Wet (researcher defined) or wetter than normal (patient defined) wounds	These wounds had a higher mean CRP than those wounds considered to have lower levels of exudation, irrespective of clinical group allocation (p=0.017)
Malodour	<ul style="list-style-type: none"> <li>» Malodour was part of the CC group descriptors but was actually found most commonly in the LI group (5 of 13 wounds)</li> <li>» High mean CRP and malodour were significantly linked (p=0.026)</li> </ul>
Wound extension	Recent extension of the wound had occurred in 11 of the 64 study wounds and was linked to a high mean CRP (p=0.01). Half (n=8) of the wounds with four bacterial species isolated had extended, as had 15.3% of wounds with three isolates, 17.6% with two isolates and 30% with 1 isolate, and 20% of wounds recording 'no growth'.
Indolence (delayed healing)	Mixed bacterial cultures coincided more frequently in CC wounds which were indolent by study definition. Only 1 of 10 wounds with 'no growth' were allocated to the CC group, and in contrast 7 of 17 with 2 isolates, 7 of 13 with 3 isolates and 2 of 4 with 4 isolates were allocated to the CC group

al 2000; Kingsley 2001) (Table 2). As a secondary aim of the study microbiological samples were taken to look for any potential associations between the organisms identified, the clinical groups of the wound infection continuum and wound features such as necrosis and CRP level. Following group allocation by the single researcher swabs for aerobic and anaerobic analysis were taken using a standard procedure defined as protocol 2 by Kingsley and Winfield-Davies (2003). Venous blood samples for CRP assay were collected by vacuum specimen tube (Vacuette®, Greiner Bio-One Ltd, Gloucestershire). Wound size was measured with single-use, clean, non-sterile paper metric rulers using the perpendicular method to estimate surface area after the technique used by Daltrey et al (1981).

Clinical features were recorded for each of the 64 wounds so it was possible to analyse CRP levels against wound features as a single series irrespective of the clinical group to which the patient had been allocated for the main aim of the study. The following clinical features were examined against CRP levels:

- » Wound type
- » Diabetic status
- » Wound size
- » Wound age
- » Granulation tissue
- » Discoloured tissue
- » Friable/bleeding granulation tissue
- » Overgranulation
- » Necrotic tissue
- » Sloughy tissue
- » Exudate level
- » Malodour
- » Wound extension (extension of margins and those with new 'satellite' lesions beyond the immediate margins of the pre-existing wound)
- » Cellulitis (<2cm and >2cm from the wound edge).

**Results**

The design was non-experimental and patient sub-groups were analysed descriptively using summary statistics. Statistical analysis of CRP levels against wound groups and features

was undertaken using a one-way unrelated ANOVA with the software SPSS version 11.5. The total 64 cases were allocated using clinical signs and symptoms into the four different study groups, 21 into colonised (C), 20 into critically colonised (CC), 13 into local infection (LI), and 10 into spreading infection (SI). CRP data was missing on three cases. Two were in the LI and one in the SI groups. Analysis of CRP results and their linkage to clinical features within and between groups were undertaken in 61 cases, whereas simple percentage calculations on the presence or absence of clinical features were based on the full 64 cases.

A clear difference between the SI group and the other groups emerged when the means of the CRP levels were compared (ANOVA  $p < 0.001$ ). The SI group mean was 167.88mg/L (standard deviation (SD)=122.17). All of the other groups had mean CRP values that were above normal (equal to or less than 8mg/L): C=27.33 (SD=27.87), CC=33.85 (SD=32.22), LI=29.54 (SD=32.94). However, it was not possible in this study to distinguish with statistical significance between the C, CC and LI groups using CRP as the diagnostic marker.

For wounds with an extending cellulitis (SI) a statistically significant higher mean CRP was recorded against all the other groups in the study.

Wound types in the study were mostly venous ulcers ( $n=26$ ; 40.6%), with the remainder being made up of pressure ulcers ( $n=9$ ), arterial ( $n=1$ ), mixed ( $n=8$ ) and hydrostatic leg ulcers ( $n=3$ ), trauma ( $n=4$ ), surgical wounds ( $n=7$ ), heart failure-associated leg-swelling ulcerations ( $n=2$ ), friction rub from orthotic shoe ( $n=1$ ), oedema blister ( $n=1$ ), wound over an old poliomyelitis operation site ( $n=1$ ) and a wound of unknown aetiology ( $n=1$ ).

#### Wound extension

Extension occurred in 17.18% of the wounds in this study suggesting it to

be a feature worthy of consideration. Those wounds with recent extension had a statistically significant higher mean CRP than those without.

#### Microbiology results

In this study 16 wounds contained an isolate of Streptococcus either group B ( $n=3$ ), D ( $n=8$ ) or G (5). Extension was recorded on five occasions, of which group G was the most common ( $n=3$ ), with B and D both having a single wound extension.

#### Wound duration

The relationship between CRP levels and wound age was tested and was not found to be significant ( $p=0.156$ ). The SI group had the lowest mean age (3.22 months) against a combined mean of all the other groups (C, CC and LI) (20.27 months), but this did not produce a significant result ( $p=0.232$ ).

#### Trauma

The four wounds originating from trauma at four weeks or greater from enrolment to the study all featured in the problem groups, with one in the CC and three in the SI group.

#### Discolouration

Discolouration was found in 10 wounds and was more common in CC than LI wounds. In the 20 CC wounds, six were discoloured and five of these were darkly so. These dark wounds had a higher mean CRP result than those in the CC group without this dark discolouration. However, when comparing mean CRP in all the darkly discoloured wounds across the categories with all the wounds without discolouration, the mean CRP was lower. The most common organisms found in the darkly discoloured CC cases were coliforms (4/5). Of the total seven wounds in all the study groups with dark discolouration five were VLU and one was a mixed venous/arterial ulcer.

#### Necrotic tissue

The presence of raised CRP levels and necrotic tissue did coincide, though statistical significance may have been skewed as 5 of the 11 wounds

containing necrotic tissue were in the SI group. However, the two wounds with necrotic tissue present in the colonised group also had elevated CRP levels (16mg/L and 54mg/L) suggesting that necrotic tissue is an impetus to inflammation. Given that two (15.38%) of the total 13 LI cases had necrosis remaining from the outset of the wound, as did 3/10 (30%) SI cases, it would suggest that necrosis from the original wounding is a risk factor for infection. This finding concurs with the results from Gardner et al (2001a) and further supports the case for debridement to improve healing made by Steed et al (1996) and Williams et al (2005) by reducing likelihood of delay through the occurrence of infection. Taking all the seven wounds with residual necrosis from original injury it was found that five (71.42%) had become infected by the time of study enrolment. Therefore original residual necrosis was linked to outcome of infection, and the presence of necrosis (original or new) to higher CRP.

#### Exudate levels

Wounds with exudate levels that were considered wet or wetter than normal had a significantly higher mean CRP.

#### Odour

Ten of the 64 (15.62%) wounds in this study were malodorous, as defined subjectively by the researcher. There was a statistically significant link between malodour and a high mean CRP.

#### Discussion

The purpose of the study was to determine if different CRP levels were associated with wounds in different clinical states of the wound infection continuum. If clear differences between the levels of CRP were found to exist for each of the clinical groups of the wound infection continuum then a potential diagnostic test will have been identified for further research. In addition an aggregate view of the relationship of CRP with individual clinical features and the risk of infection were explored and several interesting findings were made.

The total number of infected cases in the study (LI and SI) defined by clinical features was 23/64 (35.93%). The sample reflected the normal clinical situation so infection appears to be common in open wounds older than four weeks referred to the tissue viability service in North Devon. If all wounds considered clinically to have bioburden problems are included (CC, LI, SI) this figure becomes 67.18% (43/64). If this pattern is repeated across the UK then it would seem paramount that tissue viability nurses have a good understanding of the management of CC and infection.

#### Wound extension

Extension might result from increased wetness macerating the wound edge or an active invasion of bacteria into wound edge tissues, although both would be expected to elicit a new or heightened inflammatory reaction and hence a rise in CRP. Extension did occur in 11 of the 64 wounds (17.18%) in this study and CRP level elevation was statistically significantly greater than for wounds without extension. New satellite lesions were less common than expansion of the circumference and CRP levels for those wounds with and without this feature did not differ significantly.

#### Microbiology results

Various studies have made links to specific organisms being the cause of healing delay, extension and larger ulcer size, for example Hansson et al (1985) point to the fungus *Candida albicans*; Schraibman (1987) identified beta haemolytic streptococci; Halbert et al (1992) reported anaerobes; Hansson et al (1995) identified *Pseudomonas aeruginosa*, and Madsen et al (1996) *P. aeruginosa*, *Staphylococcus aureus* and beta haemolytic streptococci (groups A, B, C and G).

Schraibman (1987) reported a frequency of beta haemolytic streptococci at 30% similar to the percentage in this study of 64 mixed wound types at 25% (16 wounds). Wound extension in the presence of beta haemolytic streptococci

occurred only in the infected groups demonstrating their accepted propensity to invasive infection and ability to increase wound size. The infection rate, described by clinical signs and symptoms of LI and SI in this study, for beta haemolytic streptococci was 50% (8/16). However, on none of these eight occasions were the streptococci cultured alone, being found together with anaerobes (n=2), *Proteus* (n=2), *S. epidermidis* (n=2), *S. aureus*, methicillin-resistant *S. aureus*, coliforms, and diphtheroids (all n=1). On the only occasion when a beta haemolytic streptococcus was cultured alone it was found in a wet but static CC wound, rather than in a wound displaying any of the classic signs of infection or cellulitis. Examination of the number of isolates and the presence of extension showed that wounds yielding four isolates were more likely to extend (50%). Trengove et al (1996) reported that four or more isolates caused an increased chance of failure to heal in leg ulcers so the finding that 50% of wounds with four isolates in this study were actively extending seems in keeping with their findings. The purpose of the study was not to link the microbiology of the study wounds to wound size so the results reported here are observations only.

#### Trauma

The aetiology of trauma did appear to influence the subsequent development of spreading infection after four weeks, with three of four (75%) wounds of this type presenting with this problem. While numbers in the study were too small to make any definite conclusion it would seem that trauma may be linked to greater risk of acquiring a spreading infection than for other wound types. One possibility for this is that traumatic injury may inoculate pathogens deeper into the tissues evading skin level defence mechanisms aimed at localising infection.

#### Discolouration

It has been identified that clinicians use discolouration as an aid to diagnose infection in open wounds (Cutting, 1998; Bamberg et al, 2002;

Cutting et al, 2005) even though it has been reported to have low validity for this purpose (Gardner et al, 2001b). Cutting et al (2005) found that clinicians considered dark discolouration to be a sign of infection in VLU. In this study 10 wounds had discolouration of which seven were subjectively assessed as being darkly discoloured. Five of the seven darkly discoloured wounds were from the CC group, one from the LI and one from SI groups. The mean CRP value was lower in the darkly discoloured wounds in comparison with the 51 other wounds without any discolouration but there was no statistical significance to this finding. The single case of dark discolouration in the SI group had a CRP of 12mg/L, while the other eight cases in the SI group all had normal tissue colour and all but one (CRP = 10mg/L) had much higher CRP levels (range 51–339mg/L).

#### Necrotic tissue

Seven wounds had necrotic tissue present remaining from the original injury. There were 2 (9.52%) in the C group (n=21), 2 (15.38%) in the LI group (n=13) and 3 (30%) in the SI group (n=10). Given that 5 (71.42%) of 7 wounds with necrotic tissue remaining from the original injury were classified as having either local or spreading infection, this finding is consistent with the accepted view that necrotic tissue is a risk factor for infection. A total of 11 wounds had necrotic tissue present either remaining from original injury or more recently formed, and these wounds had a higher mean CRP ( $p < 0.001$ ) than those wounds without necrotic tissue. This finding concurs with the results from Gardner et al (2001a) and further supports the case for debridement to be carried out to improve healing by reducing the likelihood of delay through the occurrence of infection (Steed et al, 1996; Williams et al, 2005).

#### Exudate levels

Wounds with more exudate than normal had a significantly higher mean CRP level. As wetness is a sign

of inflammation (Thomas, 1997) this finding concurs with expectations. Interestingly, wetter LI wounds had a distinctly higher mean CRP than their drier LI counterparts. Thus even within a single clinical group where all the wounds were diagnosed clinically as infected, increased wetness demonstrated those mounting a greater inflammatory response. This could indicate that the situation is more severe in certain cases or that host response is more dynamic in different individuals. A limitation to the use of subjectively assessed exudate levels is that wetness may be a product of poor dressing choice or infrequent dressing change rather than a physiological response to infection.

#### Odour

Odour is reasonably common with a 9% prevalence (Lindholm et al, 2005), which is greater (36%) in chronic ulcers at risk of local infection (Meaume et al, 2005) and critically colonised wounds (55%) (Jorgensen et al, 2005), showing the link between malodour and delayed healing. Antimicrobial strategies reduce odour (Kalinski et al, 2005) and restart healing (Jorgensen et al, 2005) linking odour to micro-organisms.

Lindholm et al (2005) surveyed all wounds including closed surgical wounds that would not be expected to produce malodour, so with this in mind the current study found fewer malodorous wounds than expected. Micro-organisms considered to be capable of producing odour are Gram-negative bacilli, proteus and anaerobes (Cutting and Harding, 1994; Bowler et al, 1999). Anaerobes were present in only 4/10 malodorous wounds. Fourteen wounds contained anaerobes in all of which four (28.57%) had malodour, which is consistent with the rate reported by Dow (2001), which was stated as less than 50%. Proteus species were present in eight wounds of which three (37.5%) had malodour, and 3/17 (17.64%) wounds with coliforms were odorous. The strongest coincidental isolate to odour was therefore Proteus.

The 10 malodorous wounds in this study also had exudate levels that were 'wet or wetter than normal'. Although CRP was elevated in all study groups, malodour was found in association with significantly higher CRP, suggesting that the organisms responsible for odour generation were also capable of inducing a greater inflammatory response as identified by raised CRP levels, hence the wetness, and in some cases invasion with cellulitic response. Malodour, like exudate levels, can be linked to dressing choice and the frequency of dressing changes, and this along with the subjectivity required to assess it, limits the results.

#### CRP levels as indicators of infection

Cellulitis is the expression of the inflammatory response mediated directly by the invading organisms and indirectly by the immune system attempting to eradicate those organisms and is a key sign of infection (Eron et al, 2003). In this study there was less cellulitis in the LI group than was expected by the authors. Cellulitis at <2cm from wound edge (which was one of the diagnostic features for the LI group) was not associated with a statistically significant rise in CRP, whereas wounds with recent extension of surface area did have higher mean CRP compared with wounds without that feature.

The SI group showed a statistically significant higher mean CRP against all the other cases in this study. This is clearly a group that needed treatment with systemic antibiotics as advocated by Eron et al (2003) in order to prevent potential systemic morbidity from the wound infection.

#### Conclusion

As the SI group was the only group that showed a significantly higher mean CRP, and all the other groups were indistinguishable by use of CRP, this study was unable to provide any evidence that CRP may be a useful marker for determining the clinical states of colonisation, critical colonisation and local infection. The finding that LI wounds did not having

any significant CRP elevation over the CC group, or indeed over the C group, suggests that a potential therapeutic rationale for topical antimicrobial treatment to deal with this problem based on clinical signs and symptoms could be considered. Regular CRP measurement could therefore be used to monitor whether it is necessary to move to systemic antibiotics in the event of a sudden and definite rise. This study did find that wounds older than four-weeks duration healing by secondary intention irrespective of clinical signs and symptoms of infection commonly had raised CRP, indicating an active inflammatory host response.

Mean CRP values, gathered on 61 of the 64 cases, were statistically significantly higher for a number of wound features in this study when all 64 cases were analysed as a single group. These features were redness >2cm from wound edge, necrotic tissue, malodour, wet or wetter than normal wounds, and wound extension.

#### Limitations and implications for future study

A number of significant limitations must be noted when considering the data produced in this study. Survey design is about describing only what things are like and not why they occur like that. Surveys are, therefore, useful in the development of hypotheses for deductive testing to determine cause and effect relationships. A convenience sample was used so unlike a random sample it has a greater risk of bias. The work was undertaken by a single researcher who made the allocations to the wound infection continuum study groups using an unvalidated tool. Exclusion criteria did not include patients taking non-steroidal anti-inflammatory drugs which may have had the potential to alter CRP levels and are drugs in common use among older people who were strongly represented in the sample. Clinical features, such as odour and exudate levels were assessed without recourse to a validated tool, so internal reliability was compromised. The small

numbers of patients in each of the study groups were insufficient to determine anything other than large and very obvious differences in CRP measurements.

Future studies could be directed at identifying which clinical features are indicative of the state of bioburden-influenced delayed healing without visible inflammatory host response (critical colonisation), and then validating a tool based on that information. Such a tool could then be used to identify wounds requiring antimicrobial interventions in clinical practice, or used as a base to recruit individuals into new research projects on infection in open wounds.

Finding a simple, reliable and rapid method of diagnosing wounds experiencing the detrimental effects of the bioburden they support remains an important goal. Should such a test be found it would facilitate a change in the way we approach non-healing wounds, reducing reliance on clinical diagnosis of bacterial interference in the healing process that is open to both over- and under-recognition. Early intervention with antiseptic or new novel therapies could reduce the number of wound infections that cause added discomfort for the patient, lengthen the duration to healing, require antibiotics and elevate healthcare costs. **WUK**

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## Key Points

- ▶ Wound infection in covert and overt clinical states is one of the causes of delayed healing in wounds healing by secondary intention.
- ▶ Diagnosis of wound infection is made by identification of clinical signs and symptoms, which vary from patient to patient. As clinicians differ in their recognition of signs and symptoms and the emphasis they place on individual clinical features, there can be inconsistencies in the diagnosis of infection.
- ▶ Currently there is no reliable diagnostic marker; including the use of microbiological results, that can be used to identify a wound experiencing a problem from its bioburden which has led to inconsistency in the prescription of antimicrobials.
- ▶ This study explores the use of CRP as a potential diagnostic test for the identification of wounds in need of antimicrobial interventions and for differentiation of wounds into the different states of the wound infection continuum
- ▶ Mean CRP levels from patients identified by clinical criteria as belonging to the spreading infection group were significantly higher than for patients in the other study groups.
- ▶ CRP levels could not distinguish between the groups known as colonised, critically colonised and local infected. Mean results from these three groups were raised above the normal range.

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