Bacterial Protease Activity in Chronic Wound Fluid, a Potential Indicator of Pathogenicity even in the Absence of Overt Signs of Infection

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AIM:
Pathogenic bacteria produce proteases (virulence factors) in the process of invading their host. Therefore, bacterial protease activity (BPA) may be a useful method of detecting the presence of pathogenic bacteria in wounds.

METHOD:
366 patients with chronic wounds from 6 wound care centres in the United States underwent assessment for the signs of infection using validated assessment criteria¹. The wounds were swabbed to assess bacterial protease activity levels and quantitative bacterial load.

## Background

### The Chronic Wound Infection Continuum

<table>
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<th>Stages of chronic wound infection continuum</th>
<th>Vigilance required</th>
<th>Intervention required</th>
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<tr>
<td>Not infected / Contamination</td>
<td>Colonisation</td>
<td>Local Infection / Critically Colonisation</td>
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- **Not infected / Contamination**: The presence of bacteria within a wound without host reaction.
- **Colonisation**: The presence of bacteria within the wound which do multiply or initiate host reaction.
- **Local Infection / Critically Colonisation**: Multiplication of bacteria causing a delay in healing, usually associated with an exacerbation of pain not previously reported but still with no overt host reaction.
- **Infected**: The deposition and multiplication of bacteria in tissue with an associated host reaction.

### Clinical problem:
Effectively identifying wounds that are in a ‘state of pathogenicity’ and are infected or are becoming infected and would benefit from appropriate intervention.

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Approximately 70% of wounds had more than $10^5$ colony forming units per ml.

However, only 18% of wounds exhibited signs of local infection.
In contrast to bioburden and clinical signs, about half of all wounds swabbed were positive for bacterial protease activity.

Of the BPA positive wounds, over three quarters did not have signs of local infection. We suspect that these wounds had bacteria in a pathogenic state present but had not yet progressed to overt infection.
Discussion / Conclusions

- Presence of pathogenic bacteria in a wound can cause a ‘state of pathogenicity’ that leads to local infection and impairs healing.

- Clinical examination can mis-diagnose infections in chronic wounds.
  - Some chronic wounds fail to exhibit the classic signs of infection\(^4,5\)
  - Inflammation in wounds can be misinterpreted as infection\(^6\).

- Culture techniques have limited reliability on their own, frequently leading to the over diagnosis of infection.

- Bacterial proteases are a type of virulence factor which have been implicated in a range of medical conditions, including wound infections.
  - Testing wound fluid for bacterial protease activity may be a useful method for detecting the presence of pathogenic bacteria, at a clinically significant stage in the infection continuum, even before the signs of infection are apparent.


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