Wound Infection - Challenges and Opportunities in Diagnosis and Treatment

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Modern medicine provides new opportunities for bacteria

- New entry portals
- Catheters/surgery
- Survival of the unfit
- Immuno-suppression
- Cancer $R_x$ / transplants
- Vulnerable clustered in hospital
Diagnosis of Infection

Definition

Infection occurs when the presence of multiplying bacteria in body tissues results in spreading cellular injury

White RT et al. (2006).
Wound Infection

- Cost to heal a chronic ulcer $40000

  Joint Commission on Accreditation of Health Care Organisations 2006

- Cost of Single Infection
  - HAI $13973
  - MRSA $ 20891
  - SSI $ 15646
  - Chronic wound $11809
  - Burns $102518

  Am J Inf. Control 2002
The challenges

• Determining risk factors
• Discriminating colonisation from infection
• Gold standard for diagnosing wound infection
• Evidence based therapeutic interventions
• Antimicrobial Stewardship
Risk factors for wound infection

**Systemic**
- Diabetes mellitus
- Vascular disease
- Immune disorders
- Malnutrition
- Oedema
- Pharmacotherapy
- Alcoholism
- Prior Surgery

**Local**
- Mechanism of injury
- Foreign body
- Reduced tissue perfusion
- Degree contamination
- Duration of wound
- Size and depth of wound
- Presence necrotic tissue
Bacterial Burden considerations in chronic wounds

Which of these wounds are infected?
Infected?
Infected?
Infected?
Diagnosis of Infection

Local Infection
- Abnormal granulation tissue
- Bleeding
- Pain *
- Odour
- Bridging
- Delayed healing *

Cutting + Harding 1994
Gardner et al 2001
Optimal Technique for sampling using a swab:

Can you be confident this is always done?

- Clean wound **without** disinfectants
  - removal of slough by cleansing
  - removal of anti-microbial substances
- Wipe with dry gauze
- Wait 1-2 minutes for interstitial fluid to collect in the base of the wound
- **Take specimen**
How accurate are clinicians at identifying location of bacteria?
HOW CONFIDENT AND HOW ACCURATE?

18 Clinicians 90 images
62% Wound Experts
79% of images not maximum site of bacteria
Confidence Score of 6.9 (1-10)
Clinical Usefulness Score of 8.2 (1-10)

Naik FIS 2017
Diagnosis of Infection – Gold Standard

Tissue biopsy
95 patients’ surgical wounds
If closure delayed until
<10^5 bacteria / gm tissue
96% success^4

What is the value of microbiological diagnostics?

The sole reporting of genus and species is only a limited information and not always the answer to the question clinician wants to know.

It is important that you know what you need to know in order to make a clinical decision!

**Most important question:** Will a certain result change clinical management of a patient.

**Treat your patients, Never treat a microbiological report**
Colonisation or Infection

Bacterial Products

Bacterial Burden

Clinical Infection

Virulence

Host Response

Williams CID 2004
Cytokine Levels in DFU & Microbial Diagnosis

Cytokine concentration (pg/ml)

- IL-2
- IL-4
- IL-5
- IL-10
- IL-12 p40
- IL-12 p70
- IL-13
- IFN-γ
- TGFβ1
- TNFα2

Non-infected < 10^6 CFU/ml
Infected =/> 10^6 CFU/ml

p-values:
- p = 0.002
- p = 0.033
- p = 0.008
- p = 0.038
- p = 0.027
- p = 0.006
- p = 0.017
- p = 0.010
- p = 0.006
- p = 0.040

Clark et al 2014 WRR
Maintaining a high level of clinical suspicion

- Wound infection is a common complication
- At least 5% of patients develop infection after a surgical procedure
- Around 50% of chronic wounds may be infected
- Around 60% of chronic wounds contain biofilm
- Diagnosis is primarily based on clinical assessment of signs and symptoms
Wound Healing in Clinical Practice

- Improve
- Fluctuate
- Static
- Deteriorate
Chronic Wounds: Advanced Wound Dressings and Anti-microbial dressings

• Dressings provide optimal environment for healing
• They work by physical or chemical means typically by controlling moisture levels
• Few RCT’s
• Many low quality
• Effects are uncertain
• Use cheapest dressing
• Consider frequency of dressing change
• Silver should not be used unless clinical signs or symptoms of infection are present

NICE guidance 2016
Evidence for therapeutic interventions in infection

- Topical antiseptic agents 7-10
- Antimicrobial therapy 11-12
- Systemic antibiotics 13
- Surgical debridement 14-15
- Topical negative pressure 16
- Granulocyte-colony stimulating factor 17


12. NICE. Chronic wounds: advanced wound dressings and antimicrobial dressings. Available at: https://www.nice.org.uk/advice/esmpb2/chapter/Evidence-review, NICE Advice ESMPB2, March 2016.


The reality of Diabetic foot disease
Guidelines for diagnosis and management of diabetic foot infections

Based on a Systematic Review of the Effectiveness of Interventions in the Management of Infection in the Diabetic Foot’ and ‘Expert Opinion on the Management of Infections in the Diabetic Foot’.

Diagnosis

• Every diabetic patient with a foot wound should be assessed for the presence of infection.

• The diagnosis of diabetic foot infection is based on clinical findings of inflammation, rather than solely the results of culture.

• The severity of infection should be assessed after debridement of callus and necrotic tissue on the basis of its extent and depth and the presence of any systemic inflammatory findings.

• Hospitalisation is needed for all patients with a severe infection, many patients with a moderate infection but few with mild.

**Recommendation:** classification & diagnosis

Table 1. *The classification systems for defining the presence and severity of an infection of the foot in a person with diabetes developed by the Infectious Diseases Society of America (IDSA) and the infection part of the PEDIS classification of the International Working Group on the Diabetic Foot (IWGDF) (29,30).*

<table>
<thead>
<tr>
<th>Clinical classification of infection, with definitions</th>
<th>IWGDF / IDSA classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uninfected:</strong> No systemic or local symptoms or signs of infection</td>
<td>1 (Uninfected)</td>
</tr>
<tr>
<td><strong>Infected:</strong></td>
<td></td>
</tr>
<tr>
<td>- At least 2 of the following items are present:</td>
<td>2 (Mild infection)</td>
</tr>
<tr>
<td>• Local swelling or induration</td>
<td></td>
</tr>
<tr>
<td>• Erythema &gt; 0.5 cm* around the wound</td>
<td></td>
</tr>
<tr>
<td>• Local tenderness or pain</td>
<td></td>
</tr>
<tr>
<td>• Local warmth</td>
<td></td>
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<tr>
<td>• Purulent discharge</td>
<td></td>
</tr>
<tr>
<td>- Other causes of an inflammatory response of the skin should be excluded (e.g., trauma, gout, acute Charcot neuro-osteoarthritis, fracture, thrombosis, venous stasis)</td>
<td></td>
</tr>
<tr>
<td>- Infection involving only the skin or subcutaneous tissue (without involvement of deeper tissues and without systemic manifestations as described below).</td>
<td></td>
</tr>
<tr>
<td>- Any erythema present extends &lt; 2 cm* around the wound</td>
<td></td>
</tr>
<tr>
<td>- No systemic signs or symptoms of infection (see below)</td>
<td></td>
</tr>
<tr>
<td>- Infection involving structures deeper than skin and subcutaneous tissues (e.g., bone, joint, tendon, muscle) or erythema extending &gt;2 cm* from the wound margin.</td>
<td>3 (Moderate infection)</td>
</tr>
<tr>
<td>- No systemic signs or symptoms of infection (see below)</td>
<td></td>
</tr>
<tr>
<td>- Any foot infection with the systemic inflammatory response syndrome (SIRS), as manifested by ≥2 of the following:</td>
<td>4 (Severe infection)</td>
</tr>
<tr>
<td>• Temperature &gt;38° or &lt;36° Celsius</td>
<td></td>
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<tr>
<td>• Heart rate &gt;80 beats/minute</td>
<td></td>
</tr>
<tr>
<td>• Respiratory rate &gt;20 breaths/minute or PaCO2 &lt; 4.3 kPa (32 mmHg)</td>
<td></td>
</tr>
<tr>
<td>• White blood cell count &gt;12,000 or &lt;4,000/mm3, or &gt;10% immature (band) forms</td>
<td></td>
</tr>
</tbody>
</table>

*Note: *In any direction, from the rim of the wound; The presence of clinically significant foot ischemia makes both diagnosis and treatment of infection considerably more difficult.*

IWGDF Guidance on the diagnosis and management of foot infections in persons with diabetes
Papers published up to 30 June 2014
37 RCTs
3 Cohort studies
40 in total

Of these:
15 RCTs – antibiotics for skin and soft tissue
10 RCTs – antibiotics for osteomyelitis

Others:
Surgical procedure
Topical antiseptics
NPWT
HBO

Conclusions
No clear guidance possible, rely on expert opinion

Diab Met Rev 2015
Conclusion

- Download the recommendations from http://iwgdf.org/guidelines/guidance-on-infection/
- Implement recommendations
- Develop national guidance to improve outcomes in patients with diabetes

Antibiotic Stewardship in Wounds

Factors contributing to Antimicrobial Misuse

- Diagnostic Uncertainty
- Clinical Ignorance
- Clinician Fear
- Patient Demand
Lipsky, AIM 1990

- Healing 75%
- Further treatment and healing 15%
- Failed 9%

- No recurrence 84% (15 months)

- 25% grew organisms resistant to antimicrobial prescribed but wound healed
Antibiotic Stewardship in Wounds

- Only prescribe antibiotic for wounds that are clinically infected.
- Select empirical antibiotic therapy based on available clinical and laboratory data.
- Revise and continue therapy based on clinical response and culture/sensitivity results.
- Provide antibiotic therapy for the shortest duration needed to treat infection.

Lipsky et al JAC 2016
Definition of Biofilm

A structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface\textsuperscript{6}. 
Which of these wounds has a biofilm present?
Summary

• All open wounds will be contaminated by microbes.
• Wounds can heal normally when contaminated.
• Need to ensure the contamination does not lead on to infection.
• Infection will inhibit healing.
• Infection will elicit inflammatory response, which will also inhibit healing.
• Inflammatory response may also be caused by other factors.
• Early modulation of inflammatory response in at risk or infected wounds will have positive effect on healing.
Thank You!

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