Identification and Management of Wound Infection

St. Luke’s Hospital
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Emilio Galea
International Medical Diretor
URGO Medical
Identification
The Wound Infection Continuum

Contamination

- the presence of non-proliferating microbes within a wound at a level that does not evoke a host response

Wound healing is not impeded or delayed

Colonisation

- Bacteria or other microbes move deeper into the wound tissue and proliferate at a rate that invokes a response in the host

Spreading infection

- Systematic infection

- Wound infection from a wound affects the body as a whole

- Wound healing is impeded

Local infection

- Increasing microbial virulence and/or numbers

- Intervention required

- Systemic and topical antimicrobials

- Topical antimicrobial

- No antimicrobials indicated

- Vigilance required

BIOFILM

Risk of Infection

• The risk of wound infection is increased by:
  o any factor that debilitates the patient, impairs immune resistance or reduces tissue perfusion, e.g.:
    • comorbidities
      o diabetes mellitus, immunocompromised status, hypoxia/poor tissue perfusion due to anaemia or arterial/cardiac/respiratory disease, renal impairment, malignancy, rheumatoid arthritis, obesity, malnutrition
    • medication
      o corticosteroids, cytotoxic agents, immunosuppressants
    • psychosocial factors
      o hospitalisation/institutionalization, poor personal hygiene
  • unhealthy lifestyle choices

  *certain wound characteristics or poor standards of wound care related hygiene*
Criteria of wound infection

- **Traditional criteria**
  - Abscess
  - Cellulitis
  - Discharge (serous exudate with inflammation; seropurulent; haemopurulent; pus)

- **Suggested additional criteria**
  - Delayed healing (compared with normal rate for site/condition)
  - Discoloration
  - Friable granulation tissue that bleeds easily
  - Unexpected pain/tenderness
  - Pocketing at base of wound
  - Bridging of the epithelium or soft tissue
  - Abnormal smell
  - Wound breakdown

### SIGNS AND SYMPTOMS

#### ACUTE WOUNDS

**eg surgical or traumatic wounds, or burns**

<table>
<thead>
<tr>
<th>Localised infection</th>
<th>Spreading infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] Classical signs and symptoms:</td>
<td>As for localised infection PLUS:</td>
</tr>
<tr>
<td>- new or increasing pain</td>
<td>[ ] Further extension of erythema</td>
</tr>
<tr>
<td>- erythema</td>
<td>[ ] Lymphangitis (Box 5, see page 10)</td>
</tr>
<tr>
<td>- local warmth</td>
<td>[ ] Crepitus in soft tissues (Box 5, see page 10)</td>
</tr>
<tr>
<td>- swelling</td>
<td>[ ] Wound breakdown/dehiscence</td>
</tr>
<tr>
<td>- purulent discharge</td>
<td></td>
</tr>
<tr>
<td>[ ] Pyrexia – in surgical wounds, typically five to seven days post-surgery</td>
<td></td>
</tr>
<tr>
<td>[ ] Delayed (or stalled) healing (Box 5, see page 10)</td>
<td></td>
</tr>
<tr>
<td>[ ] Abscess</td>
<td></td>
</tr>
<tr>
<td>[ ] Malodour</td>
<td></td>
</tr>
</tbody>
</table>

#### Notes

- Burns – also skin graft rejection; pain is not always a feature of infection in full thickness burns
- Deep wounds – induration (Box 5, see page 10), extension of the wound, unexplained increased white cell count or signs of sepsis may be signs of deep wound (ie subfascial) infection
- Immunocompromised patients – signs and symptoms may be modified and less obvious

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# SIGNS AND SYMPTOMS

## CHRONIC WOUNDS

e.g. diabetic foot ulcers, venous leg ulcers, arterial leg/foot ulcers or pressure ulcers

<table>
<thead>
<tr>
<th>Localised infection</th>
<th>Spreading infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>• New, increased or altered pain*</td>
<td>• As for localised infection PLUS:</td>
</tr>
<tr>
<td>• Delayed (or stalled) healing* (Box 5, see page 10)</td>
<td>• Wound breakdown*</td>
</tr>
<tr>
<td>• Periwound oedema</td>
<td>• Erythema extending from wound edge</td>
</tr>
<tr>
<td>• Bleeding or friable (easily damaged) granulation tissue</td>
<td>• Crepitus, warmth, induration or discoloration spreading into periwound area</td>
</tr>
<tr>
<td>• Distinctive malodour or change in odour</td>
<td>• Lymphangitis (Box 5, see page 10)</td>
</tr>
<tr>
<td>• Wound bed discoloration</td>
<td>• Malaise or other non-specific deterioration in patient's general condition</td>
</tr>
<tr>
<td>• Increased or altered/purulent exudate</td>
<td></td>
</tr>
<tr>
<td>• Induration (Box 5, see page 10)</td>
<td></td>
</tr>
<tr>
<td>• Pocketing (Figure 2)</td>
<td></td>
</tr>
<tr>
<td>• Bridging (Figure 3)</td>
<td></td>
</tr>
</tbody>
</table>

**Notes**

- In patients who are immunocompromised and/or who have motor or sensory neuropathies, symptoms may be modified and less obvious. For example, in a diabetic patient with an infected foot ulcer and peripheral neuropathy, pain may not be a prominent feature.
- Arterial ulcers – previously dry ulcers may become wet when infected
- Clinicians should also be aware that in the diabetic foot, inflammation is not necessarily indicative of infection. For example, inflammation may be associated with Charcot's arthropathy

*Individually highly indicative of infection. Infection is also highly likely in the presence of two or more of the other signs listed.
Common bacteria in wounds

**Aerobic**
- *Staph. Aureus*
- *Staph. epidermis*
- MRSA
- *Enterococcus faecalis*
- *Streptococcus pyogenes*
- *Pseudomonas aeruginosa*
- *Enterobacter*
- *Escheria coli*
- *Klebsiella spp*
- *Proteus spp*

**Anaerobic**
- *Bacteriodes spp*
- *Prevotella spp*
- *Peptostreptococcus spp*
- *Clostridia*

- Aerobics are able to use oxygen
- Anaerobic bacteria can sustain itself without the presence of oxygen
- Aerobic bacteria can detoxify oxygen
- Anaerobic bacteria cannot sufficiently break down food molecules as much as aerobic bacteria
Danish scientist Hans Christian Gram devised a method to differentiate two types of bacteria based on the structural differences in their cell walls.

- **Gram−positive** bacteria retain the crystal violet dye because of a thick layer of peptidoglycan.
- **Gram−negative** bacteria do not retain the violet dye and are colored red or pink.

**Gram-negative** bacteria are more resistant to antibiotics because their outer membrane comprises a complex lipopolysaccharide (LPS) whose lipid portion acts as an endotoxin. They also develop resistance sooner.
(Chronic Wound) Slough

- Moist devitalized host tissue
- The color will vary from cream, yellow and tan depending on hydration
- It can firmly attached or loose
- May be slimy, gelatinous, stringy, clumpy or fibrinous consistency
- May be liquefying necrosis
- Recent suggestion of biofilm related slough

Contains:

- fibrin (fibrous, non-globular protein)
- deoxyribonucleo-protein (a nucleoprotein that yields DNA on hydrolysis)
- leucocytes (white blood cells)
- bacteria
- proteinaceous material (protein)
- serous exudate and pus (dead white blood cells (as neutrophils)
- tissue debris
- pathogenic microorganisms (as bacteria)

- Significance of exudate
- Amount, color and consistency needs to be noted

<table>
<thead>
<tr>
<th>Description</th>
<th>Pigment</th>
<th>Possible Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear/ light pink</td>
<td><img src="image" alt="Image" /></td>
<td>Serosanguineous drainage, typically normal wound exudate.</td>
</tr>
<tr>
<td>Clear/ amber</td>
<td><img src="image" alt="Image" /></td>
<td>Serous drainage, often considered ‘normal’, but may be associated with infection by fibrinolyis-producing bacteria. Usually clear and thin serous fluid with granulation tissue visible in the wound bed.</td>
</tr>
<tr>
<td>Cloudy/ creamy</td>
<td><img src="image" alt="Image" /></td>
<td>Fibrinous exudate, indicating the presence of fibrin strands as a response to inflammation. Purulent drainage, indicating infection containing white blood cells and bacteria.</td>
</tr>
<tr>
<td>Pink/ red</td>
<td><img src="image" alt="Image" /></td>
<td>Sanguineous drainage or haemorrhagic exudate, usually occurring in the presence of red blood cells and indicating capillary damage</td>
</tr>
<tr>
<td>Dark red</td>
<td><img src="image" alt="Image" /></td>
<td>Haemopurulent drainage usually contains neutrophils, dead or dying bacteria and inflammatory cells. Usually indicative of an infection.</td>
</tr>
<tr>
<td>Green/ grey</td>
<td><img src="image" alt="Image" /></td>
<td>Another type of purulent drainage, a common indication of infection when present. Can also appear thick and grey.</td>
</tr>
<tr>
<td>Yellow/ brown</td>
<td><img src="image" alt="Image" /></td>
<td>Occurs due to the presence of wound slough or material from an enteric fistula.</td>
</tr>
</tbody>
</table>
Biorburden

• The presence of $>10^5$ colony-forming units (CFUs) per gram of tissue (as demonstrated by biopsy) is generally accepted as a guideline for diagnosing a clinically infected wound

• Additional factors influence whether a wound will actually heal, including:
  o Presence of $>4$ different bacterial species (highly polymicrobial status of the wound)
  o Presence of highly virulent species of bacteria (e.g. β haemolytic streptococci)
  o Ability of the patient to mount an effective inflammatory response (immune suppressed or immune compromised patients)

Identifying Bacteria in the Wound

10 point Method
- Cleanse bed
- Zig Zag and rotate 360°
- Avoid debris and frank pus

Tissue Biopsy:
- Gold Standard for quantifying bacteria
- High cost
- Limited accessibility

Identifying Bacteria in the Wound

• Preliminary analyses of 78 study wounds
  - Levine’s best of 3 swab techniques in terms of 4 validity parameters: sensitivity, specificity, positive predictive value, accuracy

Procedure:
- Clean
- Pre-moisten if wound dry
- Prepare the client/patient for momentary discomfort
- Rotate the swab tip in a 1 cm square area of clean granulation tissue x 5 seconds, using gentle pressure to release tissue exudate

NB:
Don’t swab pus, exudate, eschar, necrotic tissue
Results will only show what is on the surface, not what is actually in the live (viable) tissue

! Do not refrigerate wound swabs – send to lab before 4 hours maximum!
## When to Swab

<table>
<thead>
<tr>
<th>When to Swab</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial presence of symptoms of infection</td>
<td>To determine resistance to empirically commend antibiotics; to assess microbes</td>
</tr>
<tr>
<td>Wound not progressing after 2 weeks of appropriate treatment</td>
<td>To determine if another causative microbe is active or if an antibiotic resistance has occurred</td>
</tr>
</tbody>
</table>

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Beware of interpreting a microbiology report in isolation – consider the report in the context of the patient and the wound and, if appropriate, consult a microbiologist or infectious disease specialist.

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APPLICATION TO PRACTICE

• Assessment of wounds for infection incorporates a full evaluation of the patient and should consider how immune status, comorbidities, wound aetiology/status and other factors will affect the risk, severity and likely signs of infection

• The classical signs of infection are not always present, particularly in patients with chronic wounds or diabetes mellitus

• The diagnosis of wound infection is based mainly on clinical judgement – appropriate investigations (eg microbiology of wound samples) can support and guide management
## Superficial Infection: NERDS

<table>
<thead>
<tr>
<th><strong>NERDS</strong></th>
<th><strong>Non-Healing</strong></th>
<th>Wounds that are not 20% to 40% smaller in 4 weeks according to patient history or existing documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NERDS</strong></td>
<td><strong>Exudate</strong></td>
<td>Increase in wound exudate can be indicative of bacterial pro-inflammatory damage and leads to periwound maceration. More than 50% of the dressing stained with exudate.</td>
</tr>
<tr>
<td><strong>NERDS</strong></td>
<td><strong>Red friable tissue</strong></td>
<td>Wound bed tissue is bright red with exuberant granulation tissue. Tissue bleeds easily with gentle manipulation.</td>
</tr>
<tr>
<td><strong>NERDS</strong></td>
<td><strong>Debris</strong></td>
<td>Presence of discolored granulation tissue, slough, and necrotic/nonviable tissue.</td>
</tr>
<tr>
<td><strong>NERDS</strong></td>
<td><strong>Smell</strong></td>
<td>Unpleasant or sweet, sickening odor.</td>
</tr>
</tbody>
</table>

# Deep Infection: STONEES

<table>
<thead>
<tr>
<th>STONEES</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size Increased</td>
<td>Size as measured by the longest length and the widest width at right angles to the longest length. Depth measured with a probe straight in.</td>
</tr>
<tr>
<td>Temperature</td>
<td>Increased periwound margin temperature by more than 3°F difference between two mirror-image sites.</td>
</tr>
<tr>
<td>Os</td>
<td>Wounds that have exposed bone or that probed to bone at the time of examination have risk of osteomyelitis. (DFUs have biggest risk—57 to 89% Positive Predictive Value)</td>
</tr>
<tr>
<td>New</td>
<td>New areas of breakdown and satellite lesions</td>
</tr>
<tr>
<td>Exudate Erythema</td>
<td>Reddened skin in periwound area. Presence of swelling in periwound area. Increased amount of drainage.</td>
</tr>
<tr>
<td>Smell</td>
<td>Increase in unpleasant or sweet, sickening odor</td>
</tr>
</tbody>
</table>

An emerging problem - What are Biofilms?

Biofilm is an assemblage of microbial cells that is irreversibly associated (i.e. cannot be removed by gentle rinsing) with a surface and enclosed in matrix of primarily polysaccharide material.

Biofilms form when bacteria adhere to surfaces in aqueous environments and begin to excrete a slimy, glue-like substance that can anchor them to all kinds of material.
The Biofilm Cycle
Bacterial biofilm is a major barrier to wound healing.

- Bacteria protected from topical agents
- Low oxygen in biofilm niches
- Impaired migration and proliferation of keratinocytes
- Bacteria protected from systemic antibiotics
- Host defenses unable to clear infection
E-QUIZ

• How long does a bio-film take to develop initial extracellular polymeric substance (EPS):
  a) 12 hours  
  b) 24 hours  
  c) 2 days  
  d) 4 days

Answer in the net slide
How quickly do biofilms form?

- **Within minutes**
  - Planktonic bacteria attach within minutes

- **2–4 hours**
  - Form strongly attached micro-colonies

- **6–12 hours**
  - Develop initial extracellular polymeric substance (EPS) and become increasingly tolerant

- **2–4 days**
  - Evolve into fully mature biofilm colonies that are extremely resistant to biocides and shed planktonic bacteria
  - Rapidly recover from mechanical disruption and reform mature biofilm within 24 hours

Outline of the “step-down/step-up” approach to biofilm-based wound care
• (Adapted from Schultz et al)
Management
## Antiseptic agents

<table>
<thead>
<tr>
<th>Antiseptic</th>
<th>Formulation/notes</th>
</tr>
</thead>
</table>
| **Silver**                  | • Silver sulfadiazine: cream, impregnated dressings  
|                             | • Ionic silver: impregnated dressings  
|                             | • Nanocrystalline silver                                                                               |
| **Iodine**                  | • Povidone iodine: solution, cream, ointment, sprays, impregnated dressings  
|                             | • Cadexomer iodine: ointment, paste, powder, impregnated dressings                                     |
| **Chlorhexidine**           | Solution, powder, impregnated dressings.  
|                             | *Chlorhexidine may be used as an alternative for patients allergic to iodine*                          |
| **Polyhexamethylene-biguanide (PHMB)** | Solution, impregnated dressings  |
| **Honey**                   | Amorphous honey or impregnated dressings                                                               |
| **Acetic acid**             | Solution                                                                                               |
| **Potassium permanganate**  | Solution, tablet for dissolution                                                                       |
The silver component of dressings may appear:

- **as a coating**
  - on one or both external surfaces of the dressing (elemental or nanocrystalline silver)

> Silver on the surface of the dressing may come into contact with the wound where it exerts the antimicrobial action

- **within the structure of the dressing**
  - either as a coating on dressing materials (elemental or compound silver)
  - within the spaces of the dressing materials (elemental or compound silver)
  - compound that forms part of the dressing structure (e.g. silver alginate)

> Silver within the dressing structure acts on bacteria absorbed into the dressing with wound exudate, but is likely also to diffuse to some extent into the wound

- **as a combination of these**

Although attempts have been made to quantify the availability of silver from silver dressings, such measurements are currently of very limited value in predicting clinical efficacy
Chemistry and antimicrobial properties of silver

• In metallic (elemental) form, silver is unreactive and cannot kill bacteria
  o To become bactericidal, silver atoms (denoted as Ag or Ag0) must lose an electron and become positively charged silver ions (Ag+)
  o Elemental silver ionises in air, but ionises more readily when exposed to an aqueous environment such as wound exudate

• Compound silver refers to the presentation of silver in the active, ionic form e.g. silver nitrate or SSD

  *Irrespective of the presentation of silver in dressings, silver confers its antimicrobial effect by releasing silver cations (positively charged ion)*

  *Dressings with silver compounds usually contain lower levels of silver than elemental silver dressings and are likely to release silver over a shorter time frame in the wound*
Mechanism of Action of Silver

- Silver has a **broad spectrum** of activity
  - aerobic and anaerobic
  - Gram-positive and Gram-negative
- Silver ions interact with membrane proteins and additionally **block the respiratory chain**
- After penetration into the cell Ag+ interacts with both **DNA and proteins** and finally induces production of reactive oxygen species

Bacterial Target Sites of Silver Cations (Ag+):
Other antimicrobials - Honey

• Not all honeys are equivalent
  • In Manuka honey, methylglyoxal and leptosin have been shown to contribute to its antibacterial activity
  • Several honeys generate hydrogen peroxide on dilution however, Manuka honey does not produce detectable levels and is known as a non-peroxide honey

• Topical acidification of wounds (pH of around 3.2-4.5) promotes healing by increasing the release of oxygen from hemoglobin

• Osmosis due to high sugar level draws water out of bacterial cells

• Immunostimulatory and anti-inflammatory action

• Can be utilized as an autolytic debrider

PHMB (polyhexanide)

- Polyhexamethylene biguanide hydrochloride (PHMB)
  - disruption of the bacterial cell wall
  - binds bacterial DNA, alter its transcription, and cause lethal DNA damage

The mechanism of action of PHMB on the microbial cell membrane. There is a progressive interaction of positively-charged PHMB with the negatively-charged microbial cell membrane, leading to membrane dissolution and microbe death.

Iodine

- Povidone iodine (PVP-I):
  - a chemical complex of polyvinylpyrrolidone (also known as povidone and PVP) and elemental iodine
- Cadexomer iodine:
  - an iodine and polysaccharide complex

Chlorhexidine

- Chlorhexidine Acetate BP is a disinfectant which is effective against a wide range of vegetative gram-positive and gram-negative bacteria
- Availability of chlorhexidine in dressings:
  - cotton leno-weave fabric, impregnated with Soft Paraffin BP, containing 0.5% w/w Chlorhexidine Acetate BP

“Chlorhexidine shows some toxicity to regenerating epithelial cells such as keratinocytes and fibroblasts”

“BEST PRACTICE RECOMMENDATIONS - There is insufficient evidence on the safety of and effectiveness of chlorhexidine in reducing bio-burden and promoting wound healing in concentrations designed for wound care to make a recommendation on its use as a wound care product.”

