Topical antimicrobial agents in wound care

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Antimicrobial agents

- Antibacterial agents
- Antifungal agents
- Antiviral agents
- Antiparasitic agents
- Others
  - Disinfectants, antiseptics, etc
  - Phage therapy
  - Heavy metals
  - Bacteriocine treatment
  - Essential oils
Desired properties of antimicrobial agents

- Selectively toxic
- Broad spectrum
- Cidal activity
- Non-toxic to the host
- Tissue distribution
- Low protein binding
- No interference with other drugs
Bactericidal v Bacteriostatic

- **Bactericidal** - irreparable damage to a limited number of sites
  - cell wall/membrane
  - DNA
  - protein synthesis

- **Bacteriostatic** inhibits growth reversibly
Target sites in bacterial cells

- Penicillin
- Cephalosporins
- vancomycin
- quinalones
- Rifampicin
- Erythromycin
- chloramphenicol
- Tetracycline
- gentamicin
- polymixins
Acute v chronic wounds

- **Acute wounds**
  - minor trauma
    - accidental lacerations/superficial
  - major trauma
    - burns
    - Surgery
  - Single species

- **Chronic Wounds**
  - pressure sores
  - Leg ulcers
    - Non healing wounds
  - Multiple species-role of biofilm
Infection or colonisation?

- When is a wound infected?
  - Clinical signs
    - Pain, redness, swelling, increased exudate, change in exudate colour, bad wound odour, increased wound temperature
      - properties of the microbe
      - Wounds sterile immediately after trauma but inevitably become colonised
  - What infects a wound?
    - Mixed skin flora from the patient
    - endogenous pathogens (from other body sites)
    - exogenous pathogens (from other patients, staff)
Typical wound pathogens

**Gram positive**
- *Staphylococcus aureus* (MRSA...GRSA)
- *Streptococcus pyogenes*
- other streptococci
- Enterococci (VRE)

**Gram negative**
- *Pseudomonas aeruginosa*
- Gram-negative bacilli (*Acinetobacter sp*, *Klebsiella sp*, *E.coli*) - Extended spectrum beta lactamase producers (ESBL’s)

**Fungi**
- *Candida sp and Aspergillus sp*

**Anaerobes** (dependant upon site)

**Viruses**
- Herpes and CMV
Infection v Colonisation

- Immunological Status of the host
- Nutritional status of the host
- Bacterial population
- Depth and site of Infection
- Virulence factors
- Environment-Dressings
Antiseptics in wound care

- Dressings and creams/ointments
  - silver
  - iodine
  - PHMB (polyhexamethylene biguanide)
  - Honey
    - Manuka honey
<table>
<thead>
<tr>
<th>Agent</th>
<th>Mode of action</th>
<th>Activity /Microbe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silver</td>
<td>Interacts with DNA, binds to proteins and functional groups</td>
<td>Bacteria, fungi, viruses</td>
</tr>
<tr>
<td>PHMB</td>
<td>Membrane damage, cellular leakage</td>
<td>Bacteria, fungi, viruses</td>
</tr>
<tr>
<td>Iodine</td>
<td>Highly active oxidising agent</td>
<td>Bacteria, mycobacteria fungi, viruses, spores</td>
</tr>
<tr>
<td>Honey</td>
<td>Properdin, flavanoids, Enzymes, hydrogen peroxide, probiotics?</td>
<td>Bacteria, ?fungi, ?viruses</td>
</tr>
</tbody>
</table>
Silver sulphadiazine

- AgSD
  - combination of 2 antibacterial agents
  - broad spectrum
  - binds to cellular components including DNA
  - inhibits cell division
  - damages cell envelope
  - $\text{Ag}^{2+}$ causes release of $K^+$
  - binds to enzymes
Silver - anti-microbial effects

- Destroys proteins and enzymes
- Changes DNA
- Blocks "breathing" of cell
- Destroys proteins and enzymes
Silver dressings
When silver is sputtered under typical deposition conditions, the resulting film is smooth with virtually no pores, allowing limited diffusion of water and for silver release. The crystals are elongated along the film interface with crystal boundaries being thepredominant feature. Crystal sizes range from 100nm to greater than 200nm.

The structure of silver antimicrobial delivery coating is evident in this. The physical vapour deposition process creates a material, which is very porous and consist of equiaxed nanocrystals, which allow for rapid exposure to water and subsequent silver release. These crystals are generally organized as aggregates in a columnar structure. The crystals range in size from about 10nm to 22nm with an average size of 15nm and rapidly release silver as ions, radicals and clusters when exposed to water. *(13, 14)*

Demling and Burrell
Nanocrystalline silver

- Average particle size is diminished 20-120nm in size
- Larger surface area—more available silver ions
- Continual sustained release of Ag⁺ when exposed to water
- Dressings proving to be very effective
- Also inhibit matrix metalloproteases

Dunn & Edwards-Jones 2004 Burns 30, S1-9
Povidone Iodine

- Iodophor formed by reaction of iodine and a non-surfactant compound polyvinylpyrrollidone (PVP) - 1% available iodine
- Stable
- PVP allows slow release of iodine
- Cadexomer iodine-beads of dextrin and epichlorhydrin that carry iodine
Polyhexamethylene biguanide (PHMB)

Polymeric biguanide (12 units)
Mw-3000 (approx)
Polymer of many biguanide groupings separated by a hydrophobic chain - superior to the bisbiguanides because of their multivalent binding to the membrane

Not affected by efflux pumps - minimal resistance

Bisbiguanide – e.g. chlorhexidine (2 biguanide groupings separated by a hydrophobic chain)
Honey

- fructose, glucose, sucrose and maltose.
- Water molecules comprise less than 20% of the weight of honey and it contains low levels of other sugars, organic acids, proteins and minerals.
- Honey is acidic and its pH ranges from 3.2 to 4.5 (the average is 3.9)
- Properdin, flavanoids, enzymes, hydrogen peroxide,
Important features of antimicrobial agents

- Influencing usage
  - What is it?
  - What does it do?
  - Where does it go?
  - When is it used?
  - Any Problems?
  - **What is the cost?**
When should you use an antimicrobial agent?

- Prevention of infection
  - High risk patients
- Decontamination

- Is the dressing fit for purpose
- ?other properties?
  - Barrier
  - Absorbent-sequestering of bacteria and fluid
What to use?

- High levels / low levels of antimicrobial agent?
  - Toxicity
  - Cidal v static
  - Action within the dressing/ released onto the surface of the wound
  - Cream v dressing
  - Type of dressing
Could debridement help with removal of the biofilm?

- Biofilms are notorious difficult to remove from surfaces
  - Physical removal with cleaning agents
  - High pressure wash
  - Sonication

- Debridement will remove dead tissue from which the bacteria gain their nutrition and also disrupt the physical structure of the biofilm.
Removal of biofilm?

- Debridement
- Removal of slough
  - Autolytic
  - Sharp
  - Larval
  - Enzymatic
  - Mechanical
- Application of topical antimicrobial
Bacterial Balance

Recommendations for WBP

• Routine wound cleansing
• Exudate management
• No indication for cultures
• Appropriate dressings
Bacterial Balance

Recommendations for WBP

- Debridement
- Exudate Management
- Critical colonisation / Local Infection
  – consider topical antimicrobials
Bacterial Balance

Recommendations for WBP

- Debridement
- Exudate Management
- Infection – consider antibiotics if systemic signs of infection
- Topical antimicrobials (Ag⁺, slow release Iodine, PHMB, honey)