Evidence-Based Surgical Wound Management

Treatment of Surgical Wound Infections

No conflicts of interest
Fred Y. Aoki, MD

Objective

- Review clinical surgical wound infection
- Review the available treatment modalities with emphasis on the evidence base for their use

Infection – History Revisited

Dr. Louis Pasteur
1822-1895
Father of the Germ Theory of Disease
1862: Ingenious experiments established that putrefaction is in fact due to microbial fermentation

Prevalent hypothesis had been that putrefaction was due to spontaneous generation of microorganisms from exposure of organic materials to air (“evil humours”)

Antibiotic Era

1935+: Clinical use of sulfonamide ushered in the modern antibiotic era.
The importance of antibiotics in modern medicine is beyond question
They have made possible highly technical, complex, modern surgery that would be otherwise impossible due to infection

Sir Joseph Lister
1828-1912
Father of Modern Antisepsis
1865: Applied Pasteur’s advances in microbiology to promote the idea of sterile surgery (“antisepsis”) by washing surgical instruments in dilute carbolic acid (phenol) and treating wounds with it
Despite the value of antiseptic surgical techniques to prevent surgical wound infection and antibiotics for treating infected wound, the value of prophylactic antibiotic to further reduce surgical wound infection was resisted by many.

Acceptance of Preoperative Antibiotic to Prevent Surgical Wound Infection Hinged on Two Advances

- Demonstration that the most meticulous antiseptic methods could not prevent wound contamination and occasional infections
- Antibiotic timing preoperatively was critical for prophylaxis

Importance of the Timing of Antibiotic Administration and the Prevention of Surgical Wound Infection

Types of Surgical Wound Infection
National Healthcare Safety Network (NHSN) Definitions

- Superficial - Involves only skin and soft tissue
- Deep - Involves deep soft tissue (fascia & muscle layers)
Organ/space – Involves any part of the body opened by incision, apart from skin/fascia and muscle layer.

Incidence of Surgical Wound Infection
- Occur in 2% of all surgeries done

<table>
<thead>
<tr>
<th>Surgical Class</th>
<th>Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Clean</td>
<td>3%</td>
</tr>
<tr>
<td>II Clean-contaminated</td>
<td>5-15%</td>
</tr>
<tr>
<td>III Contaminated</td>
<td>15-40%</td>
</tr>
<tr>
<td>IV Dirty-infected</td>
<td>40-50%</td>
</tr>
</tbody>
</table>

Impact of Surgical Site Infection (SSI) in the United States
- 250,000 to 1 million SSI annually (2%)
- SSI account for 34% of all nosocomial infections
- $21,000 (2012 USD) mean cost per SSI case
- Extra length of stay (LOS) 11 days
- If MRSA, cost ↑ 105% and LOS by 50%

Microbial Etiology of SSI

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>33%</td>
</tr>
<tr>
<td>MSSA</td>
<td>17%</td>
</tr>
<tr>
<td>MRSA</td>
<td>15%</td>
</tr>
<tr>
<td>Coagulase Negative Staphylococci</td>
<td>13%</td>
</tr>
<tr>
<td>Enterococcus sp.</td>
<td>10%</td>
</tr>
<tr>
<td>E. coli</td>
<td>8%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>30%</td>
</tr>
<tr>
<td>Other</td>
<td>100%</td>
</tr>
</tbody>
</table>

Treating Infected Surgical Wounds

I. Debridement
II. Antimicrobial compounds
III. Newer treatments
- Topical growth factor
- Topical enzyme
- Engineered living skin substitutes
- Topical foams & occlusive bandages
- Intermittent negative pressure devices
- Hyperbaric oxygen

I. Debridement: Removing foreign material and debridement of devitalized tissue in treatment of surgical wound infection is important.

Investigation of S. aureus infection in the skin of human volunteers definitively established the role of foreign material in potentiating wound infection.

Including suture material with the intradermal staphylococcal inoculum reduced the inoculum needed to cause a pustule by 10,000 (from $10^6$ to $10^2$ CFU).
Hence, The Importance of Removing Devitalized Tissue in Infected Surgical Wound

II. Topical Antimicrobial Compounds

Two classes
A. Antimicrobial drugs: antibiotics – organism specific
   - Mupirocin
   - Neomycin-polymyxin B-bacitracin (Polysporin®)
   - Neomycin-polymyxin B (Neosporin®)
   - Fucidin
   - Clindamycin
   - No RCT data
B. Antiseptics

Mupirocin: Mupirocin TID or oral erythromycin or flucloxacillin for 4-10 days for surgical & other skin infections in general practice

<table>
<thead>
<tr>
<th></th>
<th>Mupirocin</th>
<th>Oral Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impetigo</td>
<td>45</td>
<td>37</td>
</tr>
<tr>
<td>Infected wound</td>
<td>40</td>
<td>38</td>
</tr>
<tr>
<td>Others</td>
<td>18</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>103</td>
<td>99</td>
</tr>
</tbody>
</table>

Mostly S. aureus and S. pyogenes on culture

Result

<table>
<thead>
<tr>
<th></th>
<th>Mupirocin</th>
<th>Erythromycin</th>
<th>Flucloxacillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured</td>
<td>86%</td>
<td>47%</td>
<td>76%</td>
</tr>
<tr>
<td>Improved</td>
<td>13%</td>
<td>20%</td>
<td>23%</td>
</tr>
<tr>
<td></td>
<td>99%</td>
<td>67%</td>
<td>99%</td>
</tr>
</tbody>
</table>

Conclusion: Topical mupirocin may be as efficacious as oral flucloxacillin for surgical skin wounds (& impetigo) mostly due to S. aureus and S. pyogenes

Experimental Model of Wound Infection

- On the forearm of healthy volunteers, 3 localized blisters were induced with topical NH₃OH₃. Blister skin was removed. Occlusive dressing was applied.
- After 24 h, each site was inoculated with a low virulence, pansensitive Staphylococcus aureus 4x10⁶ CFU. Two hours after inoculation, topical therapy was begun BID. Wounds were covered between treatment.

Topical Neomycin-Polymyxin B-bactracin Ointment, a Wound Protectant, and Antiseptics for the Treatment of Human Blister Wounds Contaminated with Staphylococcus aureus

J Fam Pract 1987; 24:601
Treatments

- Neomycin-polymyxin B-bacitracin ung (Neosporin®)
- Polymyxin B-bacitracin ung (Polysporin®)
- Benzalkonium spray
- Thimerosal
- Hydrogen peroxide 3%
- Tincture of iodine
- Camphor-phenol
- Johnson & Johnson first-aid cream
- No treatment (control)

Mean Time to Healing

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neomycin-polymyxin B-bacitracin ointment</td>
<td>9.2</td>
<td>4-16</td>
</tr>
<tr>
<td>Polymyxin B-bacitracin ointment</td>
<td>8.6</td>
<td>7-16</td>
</tr>
<tr>
<td>Wound protectant</td>
<td>9.6</td>
<td>7-16</td>
</tr>
<tr>
<td>Benzalkonium chloride-spray</td>
<td>14.7</td>
<td>7-29</td>
</tr>
<tr>
<td>Mercurochrome (Merbromin)</td>
<td>13.1</td>
<td>7-21</td>
</tr>
<tr>
<td>No treatment</td>
<td>13.3</td>
<td>7-21</td>
</tr>
</tbody>
</table>

Conclusion: Neomycin-polymyxin B-bacitracin treated wounds healed faster than all except polymyxin B-bacitracin and wound protectant wounds.

S. aureus Concentration 16-24 h After 2 Treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neomycin-polymyxin B-bacitracin ointment</td>
<td>2.7</td>
<td>0.00-4.77</td>
</tr>
<tr>
<td>Polymyxin B-bacitracin ointment</td>
<td>6.7</td>
<td>0.00-7.51</td>
</tr>
<tr>
<td>Wound protectant</td>
<td>5.0</td>
<td>3.30-6.77</td>
</tr>
<tr>
<td>Benzalkonium chloride-spray</td>
<td>5.8</td>
<td>2.20-9.11</td>
</tr>
<tr>
<td>Mercurochrome (Merbromin)</td>
<td>7.1</td>
<td>6.16-7.35</td>
</tr>
</tbody>
</table>

Conclusion: Neomycin-polymyxin B-bacitracin was more effective at eradicating S. aureus than any other treatment.

Conclusions

- Human blister wounds contaminated with S. aureus and treated with topical neomycin-polymyxin B-bacitracin ung healed significantly faster than those treated with:
  - benzalkonium spray
  - Mercurochrome
  - and no treatment

- Tincture of iodine and camphor-phenol tended to delay healing compared to no treatment

- Only neomycin-polymyxin-bacitracin ung reduced bacterial contamination after two applications

- This human wound infection model is limited in being a mild wound infection caused by a relatively avirulent staphylococcus.
Antiseptics
Broad-spectrum non-specific microbicides
- Iodine
  - Tincture of iodine (2-7% alcohol solution)
  - Iodophors
    - Povidone-iodine (Betadine®)
    - Cadexomer iodine (Iodosorb®)
- Honey
- Silver including nanoparticles
- Copper
- Chlorhexidine
- Benzalkonium chloride

No RCT data

Topical Iodine Formulations
Povidone-iodine (Betadine®) and Cadexomer iodine (Iodosorb®) are iodophors: non-toxic, non-staining, low concentration of elemental iodine that is released into wound.

Systematic reviews of topical treatments of acute, chronic, burn wounds, pressure sores and skin grafts yielded conflicting results.

Honey As An Antimicrobial Substance
Inhibits bacterial growth due to hyperosmolarity
But release of hydrogen peroxide, flavinoids and other mechanisms may contribute


Honey:
Effects of honey on post-op wound infections following Caesarean section and abdominal hysterectomy:

50 patients
- Systemic antibiotics according to culture result
- Topical wound dressing Q 12 H
  - Crude undiluted honey vs 70% ethanol & povidone-iodine as control


Results

<table>
<thead>
<tr>
<th></th>
<th>Honey (N=26)</th>
<th>Control (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eradication of infection</td>
<td>6 ± 2 d</td>
<td>15 ± 4 d</td>
</tr>
<tr>
<td>Complete wound healing</td>
<td>11 ± 3 d</td>
<td>22 ± 7 d</td>
</tr>
<tr>
<td>Dehiscence requiring suturing</td>
<td>16%</td>
<td>50%</td>
</tr>
<tr>
<td>LOS</td>
<td>9 ± 2 d</td>
<td>20 ± 7 d</td>
</tr>
</tbody>
</table>

All P < 0.05

Conclusion: Topical application of crude honey yielded:
- Faster eradication of bacterial infection
- Accelerated wound healing
- Reduced wound dehiscence
- Reduced hospital stay and antibiotic use

III. Newer treatments

Topical growth factor

- Topical enzyme (e.g. collagenase)
- Engineered living skin substitutes
- Topical foams & occlusive bandages
- Intermittent negative pressure devices
- Hyperbaric oxygen

No RCT data

III. Topical application of growth factors: recombinant human platelet-derived growth factor (rh PDGF) in abdominal wound separation

- Infection is a risk factor for abdominal wound separation rates of 5% (Obs-Gyne) to 27% (colorectal)
- Healing after secondary closure takes 16-18 days
- Platelet-derived growth factor (PDGF) stimulates fibroblasts & accelerates healing of experimental wounds in animals

Amer / Obstet Gyne 2002; 186:701

Result of the RCT

Topical rh PDGF-gel (Regranex®) BID was compared to vehicle control in 21 patients

<table>
<thead>
<tr>
<th></th>
<th>rh PDGF gel (N=10)</th>
<th>Vehicle (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time for wound closure</td>
<td>35 ± 15 days</td>
<td>54 ± 26 days</td>
</tr>
<tr>
<td></td>
<td>P = 0.05</td>
<td></td>
</tr>
<tr>
<td>Conclusion:</td>
<td>rh PDGF may be therapeutic</td>
<td>Surgical closure may be better</td>
</tr>
</tbody>
</table>

Conclusion: rh PDGF gel (Regranex®) withdrawn 2011

Conclusion

A wide range of treatments have, and, continue to be developed.

Few modalities have been demonstrated in rigorous controlled clinical trials to be efficacious, much less superior to other treatments. Nonetheless, all treatments have proponents and seem to have a place in the management of infected surgical wounds.

The experience and practiced wisdom of the nurse and doctor may be the most important determinant of appropriate and effective treatments.

Prevention is the best treatment.