The Rationale for Local Antibiotic Use in Surgery to Prevent Post-Operative Infection
Myth or Science?

Argument in Favour of Myth

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The views expressed are of a professional but personal nature & are not necessarily those of the RCSI & Beaumont Hospital, Dublin.

I have recently received research funding from Pfizer & Astellas. I have also provided professional advice or education for Pfizer.
Outline Argument

1. Measures to reduce surgical site infection (SSI) & involving antibiotics
2. Lack of & or poor quality of evidence for topical or local antibiotics
3. Unintended consequences
4. Conclusions
Measures to Reduce SSI & Involving Antibiotics
NICE - SSI Prevention & Treatment, 2017

Pre-operative
e.g. antibiotic prophylaxis

Intra-operative
Do not use wound irrigation to reduce the risk of SSI
Do not use intra-cavity lavage to reduce the risk of SSI
Do not use intra-operative skin re-disinfection or topical cefotaxime in abdominal surgery to reduce the risk of SSI

Post-operative
Do not use topical antimicrobial agents for surgical wounds that are healing by primary intention to reduce the risk of SSI
WHO Recommendations 2016

“... antibiotic incisional wound irrigation before closure should not be done”

Conditional Recommendation

Low quality of evidence

Gentamicin collagen sponges (GCS)
- Colorectal surgery, SSI higher with GCS
- Cardio-thoracic, mixed evidence
- GCS not approved by FDA in USA

Infect Control Hosp Epid 2014; 35: 566-588
Timing of Prophylactic Antibiotics & Risk of SSI

- Elective surgery in Salt Lake City
- ~3,000 patients, 55% of total eligible
- 100%, for 24h & 80% for ≥ 48h

Timing of Prophylaxis & Risk of SSI

- Age, gender, surgeon & postsurgical procedures were not significant

A Review of 28 Studies of Antibiotic Prophylaxis & Quality Indicators

Indication, timing, choice & duration

Compliance – 9-80%, but up to 100% after interventions overall
19-91%, with indication
30-95%, for timing

Interventions – education, MDT, computer-based ordering, etc.

Epidemiol Prev 2015; 39: Suppl 1, 27-32
Lack of & or Poor Quality of Evidence for Topical or Local Antibiotics
Intra-Wound Antibiotics (IWA), Infection & Spinal Fusion Surgery

- 9,823 patients in 20 Washington State Hospitals, 55% receiving IWA
- 111 (1.1%) with SSI; 0.8% (IWA)* vs 1.5% (no IWA)
- After adjustment, no difference

*Surg Infect 2016; 17: 177-186
Local Gentamicin to Wound for Abdominoperineal Resection

- 582 articles from search (1988-2012) but only 8 suitable
  - 4 RCTS
  - 3 consecutive studies
  - 1 cohort (no controls)
- Sponges (3), beads (4), injection (1)
- Substantial heterogeneity in studies
- Evidence does not support perineal application of gentamicin

*World J Surg* 2015; 39: 2786-2794
GCS, Sternal SSI after Cardiac Surgery

Phase 3, single blind, RCT of 1502 patients at high risk (DM or BMI > 30)

JAMA 2010; 304: 755-762
## GCS & Sternal SSI after Cardiac Surgery

<table>
<thead>
<tr>
<th>Per Protocol Analysis</th>
<th>GCS (727)</th>
<th>Control (749)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any SSI</td>
<td>8.4%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Surgically treated SSI</td>
<td>3.2%</td>
<td>4.9%</td>
</tr>
<tr>
<td>Superficial SSI</td>
<td>6.6%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Deep SSI</td>
<td>1.8%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Re- hospitalisation for SSI</td>
<td>3.0%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Post-operative length of stay</td>
<td>6.0 d</td>
<td>6.0 d</td>
</tr>
</tbody>
</table>

*JAMA 2010; 304: 755-762*
GCS & Colorectal Surgery

- 2 sponges (260 gentamicin) to patients in 39 US sites
- From 674 enrolled, 602 randomised (GCS 300, control 302)
- Adjusted SSI of 29% in GCS group & 21% in control (p=0.03)
- GCS patients more likely to visit ED or surgeon’s office (19.7% v 11%, p = 0.004)
- 15 gentamicin resistant isolates, 13 in GCS group

GCS & Colorectal Surgery

- Initial effect but not sustained due to a lack of sustained antibiotic levels

Figure 2. Kaplan–Meier Estimates of the Number of Days from Surgery to Surgical-Site Infection (SSI) within the 60-Day Postoperative Period, According to Study Group.

- Collagen sponge may be a mechanical barrier to rapid & effective closure of wound

Unintended Consequences
Impact of Topical Vancomycin in Spinal Surgery

• Retrospective review of 981 patients receiving 1-2 gr vancomycin, 2011-13
• 6.7% SSI – 5.2% had + ve cultures; 44/51 (86%) Gram + ve, & 31 (61%) Gram negative

Historical controls had Gram-vees in 21% (p=0.0001)

• Use of topical vancomycin for prophylaxis shifts causes to Gram negative

Spine 2014: 39: 530-555
Impact of Topical Antibiotics on Flora

- Animal studies on rats & impact of antibiotics on flora, i.e. cephazolin, kanamycin, metronidazole & combinations
- Saline lavage does not alter anaerobic flora
- Antibiotics had transitory impact on flora, re-colonisation at 4h

* = significant p < 0.05

World J Surg 1990; 14: 176-183
Antibiotics & Intra-Abdominal Adhesions

<table>
<thead>
<tr>
<th>Group 1</th>
<th>16 rats + saline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>8 rats + cefazolin</td>
</tr>
<tr>
<td>Group 3</td>
<td>8 rats + tetracycline</td>
</tr>
</tbody>
</table>

More adhesions after 2/52 in groups 2 & 3 compared to group 1
Mesothelial thickening & extensive collagen deposition, especially in Group 3

GCS, Sternal SSI after Cardiac Surgery
Impact of Gentamicin

- Levels taken 2h before & 2,4,8,12 & 24h after closure of wound
- No difference in adverse events

JAMA 2010; 304: 755-762
Vancomycin Levels & Sternotomy Wounds

• 500 mg vancomycin power or dissolved in saline
• Levels taken 30 min – 720 min
• Mean concentration in urine was 24.4 at day 1

*Eur J Cardio-Thoracic Surg 2003; 23:765-770*
Safety Quality of Antibiotic Preparation

**Site of Preparation of Antibiotic Solutions**

<table>
<thead>
<tr>
<th>Preparation Site</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR prior to use during procedure</td>
<td>30</td>
</tr>
<tr>
<td>In compounding pharmacy then sent to OR</td>
<td>25</td>
</tr>
<tr>
<td>In satellite pharmacy for the OR</td>
<td>10</td>
</tr>
<tr>
<td>In satellite pharmacy for Labor and Delivery</td>
<td>5</td>
</tr>
<tr>
<td>I do not know</td>
<td>40</td>
</tr>
</tbody>
</table>

n = 106

*Am J Infect Control 2017; 45: 1259-1266*
1. Almost all of the studies showing a benefit for topical antibiotics are flawed.

2. RCTs suggest no impact & or even possibly increased SSI.

3. Risks include increased resistance, altered flora & adhesions.

4. Focus on SSI bundles including timing, choice & duration of surgical antibiotic prophylaxis as in recommendations.
Thank you