Single Stage Cementless Revision

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Prosthetic Joint Infection

Challenges:

✓ Recurrences
✓ Defects
✓ RE-Revision
✓ Rehabilitation
✓ Costs
Biofilm on bone and implants

Microbial Biofilms: Sticking Together for Success

Waiting to grow
Bacteria can shrink to a spore-like state to wait in water, soil—even rock or tissue—until conditions are right for active growth.

Meeting the challenge
While antimicrobials damage outer cell layers, the biofilm community can survive.

Finding a niche
Chemical gradients create micro-environments for different microbial species or levels of activity.

Changing their spots
Active bacteria will attach to virtually any surface. Within minutes, changes in gene expression transform “swimmers” to “stickers.”

Getting breakfast in bed
Nutrients diffuse into the matrix as they flow by.

Building houses of slime
Attached bacteria multiply and encase their colonies with a slimy matrix.

Senting the right signals
Close proximity of cells facilitates the exchange of molecular signals that regulate behavior.

Persisters
“Persisters”

Dispersers
“Wall formers”

Dividing the labor?
Genetic regulation may allow a degree of differentiation among cells of a single species to serve the community as a whole.

Peg Dirckx, Center for Biofilm Engineering
Biofilm multicellularity results in better bacterial defenses

Nutrient depletion can create zones of altered activity.

Inner layers of biofilm cells have more time to initiate stress response.

Effective deployment.

"Persisters" may be present in higher numbers.

© 2003, Center for Biofilm Engineering at MSU–Bozeman
Run for the surface

Biofilm is mature after 3 weeks!
Debridement + Conventional Antibiosis

- Removes predominant amount of bacterial load
- May eliminate planktonic bacteria
- May disrupt biofilms

- May not remove microscopical biofilm remnants
  - sessile phenotypes in glycocalix require up to 1000x AB concentration

Minimum Biofilm Eradicating Concentration (MBEC)
5 Basic requirements for eliminating biofilm associated infection

1. LOCALIZE
   Localize habitats of microbes as exactly as possible.

2. REDUCE
   Drastically reduce their number and their means of livelihood by removing all identified avital material as radically as possible;

3. DISRUPT
   Disturb the community live of eventual remaining biofilm colonies by mechanically disrupting their established structures as thoroughly as possible;

4. FILL
   Avoid re-establishment of colonization grounds by filling dead space with inaccessible material as completely as possible;

5. ELIMINATE
   Eliminate sessile bacteria inside remaining fragments using antimicrobial substances in concentrations as high and as consistent as possible.
Sensitivity sessile - planktonic
MBEC versus MIC

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>Penicillin G</th>
<th>Cloxacillin</th>
<th>Streptomycin</th>
<th>Ceftiofur</th>
<th>Tetracycline</th>
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<tbody>
<tr>
<td>Arcanobacterium pyogenes</td>
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<td>&lt; 2</td>
<td>&lt; 2</td>
<td>4</td>
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<tr>
<td>Staphylococcus aureus</td>
<td>MBEC</td>
<td>&gt; 1024</td>
<td>&gt; 1024</td>
<td>256</td>
<td>&gt; 1024</td>
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<tr>
<td>Staphylococcus aureus</td>
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<td>&lt; 2</td>
<td>512</td>
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<tr>
<td>Staphylococcus aureus</td>
<td>MBEC</td>
<td>&gt; 1024</td>
<td>512</td>
<td>&gt; 1024</td>
<td>256</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>MBEC</td>
<td>&gt; 1024</td>
<td>64</td>
<td>128</td>
<td>256</td>
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<tr>
<td>Streptococcus agalactiae</td>
<td>MIC</td>
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<td>&lt; 2</td>
<td>&lt; 2</td>
<td>&lt; 2</td>
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<tr>
<td>Streptococcus agalactiae</td>
<td>MBEC</td>
<td>&gt; 1024</td>
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<td>&lt; 2</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Streptococcus suis</td>
<td>MBEC</td>
<td>&gt; 1024</td>
<td>128</td>
<td>&gt; 1024</td>
<td>1024</td>
</tr>
<tr>
<td>Corynebacterium renale</td>
<td>MIC</td>
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<td>&lt; 2</td>
<td>&lt; 2</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Corynebacterium pseudotuberculosis</td>
<td>MBEC</td>
<td>&gt; 1024</td>
<td>&gt; 1024</td>
<td>128</td>
<td>&gt; 1024</td>
</tr>
</tbody>
</table>

MIC — minimum inhibitory concentration; MBEC — minimum biofilm eradication concentration

Reaching MBEC: Locally applied antibiotic

- Vanco / Tobra:
  - Poor resorption / tissue penetration

- Local levels high
- Systemic levels low
Vanco susceptibility of staphylococcal biofilm

Local concentration > 500 µg/ml during days

Established Procedure: Multiple Stage

- Removal
- Debridement
- („Spacer“)
- 6 weeks (i.v.) antibiotics
- Reimplantation
- Antibiotics postop.
- Disablement for months
Established Procedure: Single Stage with AB-cement

- Removal
- Debridement
- Reimplantation with cement, AB-loaded

- Requires preop cultures
- Less popular

- Massive problems in case of failure
Why multiple stages?

- Fear of re-contamination
- Do multiple stages decrease the risk?
Meta-analysis, BMC 2012

✓ One stage:
  – 11 studies
  – 1,225 patients
  – reinfection **8.6%** (95% CI = 4.5 to 13.9)

✓ Two stage
  – 28 studies
  – 1,188 patients
  – reinfection **10.2%** (95% CI = 7.7 to 12.9)

Spacers? PMMA?

✓ Unstable

✓ Complications >50%
  - Dislocation
  - Breakage
  - Arrosion of bone

Elution of gentamicin from PMMA

✔ surface dependent
  – (beads > cement > spacer)

✔ Maximum within 24h

✔ After 72h below MIC

New Antibiotic Carrier

- Markedly higher concentrations
- Sustained release over weeks
Cancellous Bone

✓ Large surface
✓ Storage capability
✓ Solid structure
✓ Slow resorption

IDEAL CARRIER
Supercritical Carbon dioxide

✓ „Gas“:
  – Maximum penetration

✓ „Liquid“:
  – Maximum solvent

✓ Validated Virus Inactivation

Maximum values:
- Temperature: 50°C
- Pressure: 260 bar
Allograft, highly purified

- No lipids (inflammation)
- No cells (antigenicity)
- No connective tissue

- Matrix unaffected
  - Collagen
  - Minerals
  - Huge storage capability
**Antibiotics**

- **Vancomycin**
  - gram positive pathogens
  - agent of choice for MRSA

- **Tobramycin**
  - gram negative pathogens
  - agent of choice for pseudomonas

- **Both**
  - bactericidal
  - least cytotoxic effect
  - poor tissue penetration
Antibiotic impregnated bone matrix

- 400mg Tobramycin / 10cc (Gram -)
- 1000mg Vancomycin / 10cc (Gram +)

- Protects implant
- Decontaminates site
- Potential incorporation
# AB loaded cement versus AB loaded bone graft

<table>
<thead>
<tr>
<th>AB Carrier</th>
<th>Purified Bone</th>
<th>PMMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Storage capacity / 10cc</td>
<td>1g</td>
<td>0.1g</td>
</tr>
<tr>
<td>Availability</td>
<td>&gt;90%</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Release 1.day</td>
<td>10,000 - 20,000mg/l</td>
<td>40 - 400mg/l</td>
</tr>
<tr>
<td>Release 6.day</td>
<td>60 - 130mg/l</td>
<td>Traces</td>
</tr>
<tr>
<td>Release 100.day</td>
<td>0</td>
<td>Traces</td>
</tr>
</tbody>
</table>
Clinical Relevance:

- Antibiotic impregnated bone grafts are inaccessible for microbials
- Ideal filler for contaminated osseous defects

Reconstruction of Defects

- Prolonged release of antibiotics in high concentration
- Protection of implants, decontamination of surrounding tissue, including SCV + biofilm remnants
- One stage procedure possible without cement
1 Operation - 3 steps

1. Removal
   - Debridement
   - Rough preparation
   - Jet lavage
   - Closure (adaptive)

2. Remove draping + instruments
   - Clean OR
   - Scrub
   - New gowns, gloves
   - draping, instruments

3. Grafting
   - Corrective preparation
   - Implantation
   - Drainage
   - Closure (anatomical)
Uncemented implant as „potentially permanent spacer“

- Easy to remove – like a spacer
- Stability – like an implant

**Advantages:**
- Majority of cases will cancel 2nd stage
- Immediate weight bearing
- Less complications
- Potential of improved long term results
Implants, hip

UNCEMENTED

✓ Hemispherical Cup

✓ Rectangular Stem
Easy re-removal
The routine case

Pre-op

postop

2 years
O.V., female, 64yrs,

S. Aureus
Enterococci
CNS, Meth.res.
Impaction Grafting
Impaction grafting
postop 2yrs
L.V., male, 43yrs

✓ Polytrauma
✓ 5 revisions
✓ 2 x S.epidermidis
  - 1 MRSE
  - 1 MSSE
Preop: lateral defect
Postop
One stage procedures

✔ Follow up >2a

- 88 Hips / 6 Re-Infections
- 68 Knees / 5 Re-Infections
- 52 Osteosyntheses / 3 Re-Infections

Total:
208 One Stage Revisions / 14 Re-Infections

93% Infection free – with 1 OP!
In-patient hospital stay (cumulative) n=208

✔ < 1 week 15
✔ < 2 weeks 139 (=70%)
✔ < 3 weeks 17 (flaps)
✔ > 3 weeks 37 (complications, re-revisions)

Re-Revisions always easier than 1.surgery!
One stage is enough!

✓ One for All
  – One stage protocol for all implant related infections
    – (except life threatening septicaemia)

✓ All for One
  – All efforts should be undertaken to solve the issue with One single surgery
Uncemented one stage revision + AB impregnated graft grant ...

- Short treatment, resulting in
  - Improved functional results
  - Reduced systemic antibiotics
  - Reduced costs

- Better control of infection by addressing the BIOFILM issue

- Better long term results

- Improved conditions in case of failure
Thank you!
and
Welcome to Oxford 2016

35th Annual Meeting of the European Bone and Joint Infection Society
1-3 September 2016, Oxford, UK