Biofilm-Therapie bei TEP-Infektionen: PRO

Andrej Trampuz
Charité – Universitätsmedizin Berlin
Septic surgery unit
Improved survival in breast cancer

- 10-year survival increased from 55% to 95%
- Interdisciplinary work: oncologists, gynecologists, plastic surgeons, radiologists, pathologists
  - Early diagnosis by routine screening
  - Improved combination treatment (surgery, hormonal, chemotherapy)
- Less mutilation & less toxicity
- Today still common, but curable disease

Parallels for PJI?
Implants: improve function or replace missing anatomic structure
## Risk of implant-associated infection

<table>
<thead>
<tr>
<th>Device</th>
<th>No. inserted in the US per year</th>
<th>Rate of infection, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fracture fixation devices</td>
<td>2,000,000</td>
<td>5–10</td>
</tr>
<tr>
<td>Dental implants</td>
<td>1,000,000</td>
<td>5–10</td>
</tr>
<tr>
<td>Joint prostheses</td>
<td>600,000</td>
<td>1–3</td>
</tr>
<tr>
<td>Vascular grafts</td>
<td>450,000</td>
<td>1–5</td>
</tr>
<tr>
<td>Cardiac pacemakers</td>
<td>300,000</td>
<td>1–7</td>
</tr>
<tr>
<td>Mammary implants</td>
<td>130,000</td>
<td>1–2</td>
</tr>
<tr>
<td>Mechanical heart valves</td>
<td>85,000</td>
<td>1–3</td>
</tr>
<tr>
<td>Penile implants</td>
<td>15,000</td>
<td>1–3</td>
</tr>
<tr>
<td>Heart assist devices</td>
<td>700</td>
<td>25–50</td>
</tr>
</tbody>
</table>

Darouiche RO. *Clin Infect Dis* 2001;33:1567–1572
Goal

- Functional implant
  - Highly efficient concept (90% cure)
  - Least invasive (retention, whenever possible)

- Eradication of infection
  - Combination of surgery + antibiotics (bundle)
  - Not antibiotic suppression (whenever possible)

- Scientific evidence
  - In vitro
  - Animal models
  - Clinical studies

What do we know?
Biofilms: life on surfaces

- Most bacteria in nature live in biofilms
- One of the most resistant forms of life

Hot, acidic pools in Yellowstone National Park

Glaciers in Antarctica
Biofilm: characteristics

- Adherent to surface (min-h)
- Embedded in matrix (70%)
- Slowly replicating (stationary-growth)
- 78-y-o female
- Primary hip prosthesis 09/2013 (cemented)
- Since implantation pain, walking distance now 20 m
- CRP normal, no loosening on x-ray
Which antibiotic?

Aspiration 4 months after implantation

**Mikroskopische Untersuchungen**

<table>
<thead>
<tr>
<th>Grampräparat</th>
<th>Leukozyten</th>
<th>Mikroorganismen</th>
<th>mässig</th>
<th>nicht messbar</th>
</tr>
</thead>
</table>

**Kulturelle Ergebnisse**

1. *Staphylococcus epidermidis*

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Sensibel</th>
<th>Intermediär</th>
<th>Resistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin + Clavulansäure</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefalotin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxon</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamycin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cotrimoxazol</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetrazyklin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxacillin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusidinsäure</td>
<td>R</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*S = sensibel, I = intermediär, R = resistent, PV = positiv*

validiert durch: Irene Grohsellus
Delayed (low-grade) infection

- CRP normal, no prosthesis loosening
- Repeated joint aspiration 04/2014: *Staphylococcus epidermidis* (same susceptibility)
- Synovial fluid: WBC 59,000/µl, 90% PMN

- Prosthesis exchange: 1- or 2-stage exchange (short interval)
- Which antibiotic? Sugar pills or wonder drugs?
The key to success...

Diagnosis  
Antibiotics  
Surgery
# Classification

<table>
<thead>
<tr>
<th>Time after implantation</th>
<th>0–3 months</th>
<th>3–24 (36) months</th>
<th>Any time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of infection</strong></td>
<td>Early postoperative</td>
<td>Delayed (low grade)</td>
<td>Late</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>Perioperative</td>
<td>Haematogenous</td>
<td></td>
</tr>
<tr>
<td><strong>Signs</strong></td>
<td>Acute: fever, effusion, warmth, dehiscence</td>
<td>Chronic: Persistent pain, loosening, fistula</td>
<td>Acute or subacute</td>
</tr>
<tr>
<td><strong>Pathogen</strong></td>
<td>S. aureus, Streptococci, Enterococci</td>
<td>Coagulase-negative staphylococci, <em>P. acnes</em></td>
<td>S. aureus, <em>E. coli</em></td>
</tr>
</tbody>
</table>
Definition

- Sinus tract (fistula)
- Visible purulence
  - Wound discharge, abscess
- Acute inflammation in tissue histology
  - ≥1 to ≥10 neutrophils/high-power field
- Leukocytes in synovial fluid
  - Knee: ≥1.7 x 10⁹/l leukocytes, ≥65% neutrophils
  - Hip: ≥4.2 x 10⁹/l leukocytes, ≥70% neutrophils
- Microbial growth
  - Synovial fluid
  - ≥3 periprosthetic tissue (for low-virulent organisms >1 positive)
  - Sonication fluid (>50 CFU/ml)

---

1 Pseudopus: metal-on-metal prostheses
2 Excluded: Early postoperative (3 months) and inflammatory joint diseases
Route of implant infection

- **Intraoperatively:** ≥100 bacteria sufficient
- **Postoperatively:** risk <48 hours

Distant urinary, skin and respiratory infections

Perioperative

Hematogenous
Antibiotics with antibiofilm activity

1. Staphylococci: Rifampin (in combination)
2. Streptococci: Penicillin G
3. Enterococci: Fosfomycin? (in combination)
4. Gram-negative bacilli: Ciprofloxacin (fosfomycin?)
5. Candida: echinocandins (caspofungin)?
Animal data:
Guinea pig foreign-body infection model

**Inoculum per cage:** $10^5$ cfu  
**Duration of infection:** 24 hours  
**Duration of treatment:** 4 days
Foreign-body infection (FBI) model

- 4 Teflon cages implanted subcutaneously in guinea pigs
- Aspiration of cage fluid (planktonic bacteria)
- Cages removed 5 days after treatment (eradication)

Efficacy in the guinea pig infection model (MRSA)

Rifampin resistance rate

Activity of fosfomycin and rifampin against MRSA in the guinea pig model

Highest cure rate with FOS+RIF (83%), which was superior to other RIF-combinations.

No *in vivo* emergence of FOS resistance was observed in mono- or combination therapy.

Activity of fosfomycin and gentamicin against *E. faecalis* biofilm

Treatment against adherent *P. acnes* in the guinea pig model

• No spontaneous cure
• Rifampin necessary for eradication of *P. acnes* biofilm

Activity of lipoglycopeptide dalbavancin against MRSA (telavancin, oritavancin)

- NaCl: 0%
- RIF (12.5): 33% (38% RIF-resistance)
- DAL (40): 0%
- DAL (60): 0%
- DAL (80): 0%
- DAL (40) + RIF (12.5): 33% (25% RIF-resistance)
- DAL (60) + RIF (12.5): 25% (8% RIF-resistance)
- DAL (80) + RIF (12.5): 36% (0% RIF-resistance)

Baldoni D & Furustrand Tafin U. IJAA 2013
Clinical evidence
ROLE OF RIFAMPIN IN IMPLANT-RELATED INFECTIONS: Randomized controlled trial: acute staph. infections

*Treatment*: Initial débridement and antibiotics:

2 weeks i.v.
(Flucloxacillin or Vancomycin) + (Rifampin or Placebo)

followed by:

3-6 months p.o.
Ciprofloxacin + (Rifampin or Placebo)

Zimmerli W et al. JAMA 1998
<table>
<thead>
<tr>
<th></th>
<th>Ciproflox-placebo (n=15)</th>
<th>Ciproflox-rifampicin (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microbiology:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- S. aureus</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>(0/26 methicillin-resistant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- S. epidermidis</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>(2/7 methicillin-resistant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial iv-treatment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Flucloxacillin</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>- Vancomycin</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>33 (15-41)</td>
<td>35 (24-46)</td>
</tr>
<tr>
<td>(median,range)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Zimmerli W et al. JAMA 1998
# Results

<table>
<thead>
<tr>
<th></th>
<th>CIP + placebo</th>
<th>CIP + RIF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cure (ITT)</strong></td>
<td>9/15 (60%)</td>
<td>16/18 (89%)</td>
</tr>
<tr>
<td><strong>Cure (as treated)</strong></td>
<td>7/12 (58%)</td>
<td>12/12 (100%)*</td>
</tr>
<tr>
<td><strong>Drop-out</strong></td>
<td>3/15</td>
<td>6/18</td>
</tr>
<tr>
<td><strong>Follow-up (months)</strong></td>
<td>33 (15-41)</td>
<td>35 (24-46)</td>
</tr>
</tbody>
</table>

*p=0.019 (Fisher’s exact test)

Zimmerli W et al. JAMA 1998
CURRENT CONCEPTS

Prosthetic-Joint Infections

Werner Zimmerli, M.D., Andrej Trampuz, M.D., and Peter E. Ochsner, M.D.
<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Antimicrobial Agent</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em> or coagulase-negative staphylococci</td>
<td>Nafcillin or floxacillin† <em>plus</em></td>
<td>2 g every 6 hr</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>Rifampin for 2 wk, <em>followed by</em> Rifampin <em>plus</em></td>
<td>450 mg every 12 hr</td>
<td>PO or IV</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin <em>or</em></td>
<td>450 mg every 12 hr</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin</td>
<td>750 mg every 12 hr to 500 mg every 12 hr</td>
<td>PO</td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>Vancomycin <em>plus</em></td>
<td>1 g every 12 hr</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>Rifampin for 2 wk, <em>followed by</em> Rifampin <em>plus</em></td>
<td>450 mg every 12 hr</td>
<td>PO or IV</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin‡ <em>or</em></td>
<td>450 mg every 12 hr</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin‡ <em>or</em></td>
<td>750 mg every 24 hr to 500 mg every 12 hr</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Teicoplanin‡ <em>or</em></td>
<td>400 mg every 24 hr</td>
<td>IV or IM</td>
</tr>
<tr>
<td></td>
<td>Fusidic acid‡ <em>or</em></td>
<td>500 mg every 8 hr</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim—sulfamethoxazole <em>or</em></td>
<td>1 DS tablet every 8 hr</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Minocycline</td>
<td>100 mg every 12 hr</td>
<td>PO</td>
</tr>
<tr>
<td>Streptococcus species (except <em>Streptococcus agalactiae</em>)</td>
<td>Penicillin G <em>or</em></td>
<td>5 million U every 6 hr</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone for 4 wk, <em>followed by</em> Amoxicillin</td>
<td>2 g every 24 hr</td>
<td>IV</td>
</tr>
<tr>
<td>Enterococcus species (penicillin-susceptible) and <em>Streptococcus agalactiae</em></td>
<td>Penicillin G <em>or</em></td>
<td>5 million U every 6 hr</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>Ampicillin or amoxicillin <em>plus</em></td>
<td>2 g every 4–6 hr</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>Aminoglycoside¶ for 2–4 wk, <em>followed by</em></td>
<td>750–1000 mg every 8 hr</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Surgical and antibiotic treatment concepts

Debridement and retention

One stage

Two stage (short interval)

Two stage (long interval)

Onset of infection

2–4 weeks i.v.

8–10 weeks p.o.

Debridement

Explantation and implantation

Explantation and implantation

Explantation

Implantation

Implantation

(2 weeks)

“Biofilm treatment” (with rifampin)

“Osteomyelitis treatment” (no rifampin)


Borens O et al. Rev Med Suisse 2009
Controversies in management of PJI between North America and Europe

**North America**
- Standard: 2-stage exchange with long interval (6–8 weeks)
- No rifampin – dogma that infection is not possible to eradicate without implant removal
- Retention: life-long suppression of infection

**Europe**
- 4 surgical approaches according to situation (algorithm)
- Early and aggressive revision to make salvage of the implant possible
- Highest success with lowest invasiveness
Low cure of debridement & retention

  - 60% cure rate at 2 years\(^1\)
  - 32% cure rate at 2 years\(^2\)
- Chiu FY, Chen CM. *Clin Orthop Relat Res* 2007;461:130–135
  - 30% cure rate, minimum 3-years follow up\(^3\)

1. Improper patient selection
2. Insufficient surgical debridement
3. No rifampin use for biofilms
PJIs (n = 118)

Treatment outcome in 118 PJIs (1994–2006)*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
<th>Infection-free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Debridement and retention</td>
<td>75/81</td>
<td>(93%)</td>
</tr>
<tr>
<td>One-stage exchange</td>
<td>13/14</td>
<td>(93%)</td>
</tr>
<tr>
<td>Two-stage exchange</td>
<td>15/15</td>
<td>(100%)</td>
</tr>
<tr>
<td>Prosthesis removal</td>
<td>5/5</td>
<td>(100%)</td>
</tr>
<tr>
<td>No surgery</td>
<td>2/3</td>
<td>(67%)</td>
</tr>
</tbody>
</table>

*Infections included hip (n=78), knee (n=22), ankle (n=10) and shoulder (n=8)
Hip and knee PJI (n = 68)


- Adequate treatment
- Partially adequate treatment
- Inadequate treatment

Failure-free survival

Time after PJI diagnosis, months

Elbow PJI (n = 27)

According to algorithm

Probability of relapse-free survival

Time after diagnosis of infection, years

0.0
0.2
0.4
0.6
0.8
1.0

0
1
2
3

n=15

n=12

58%

33%

100%

Achermann Y et al. Clin Microbiol Infect 2010
Hip PJI (n = 63), 1985-2001

According to algorithm

Not according to algorithm
Staphylococcal PJI

El Helou et al. EJCMID 2010
Prosthetic join infection: Outcome
(Charité Berlin)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Long interval w/o optimal AB (n =83)</th>
<th>Long interval with optimal AB (n =79)</th>
<th>Short interval with optimal AB (n = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age (years)</td>
<td>68,5 ± 7,7</td>
<td>68,6 ± 14,4</td>
<td>65,4 ± 9,6</td>
</tr>
<tr>
<td>Duration from implantation to infection (years)</td>
<td>3,2 ± 3,0</td>
<td>5,7 ± 5,1</td>
<td>4,2 ± 3,9</td>
</tr>
<tr>
<td>Interval from explantation to reimplantation</td>
<td>66,7 ± 12,8</td>
<td>66,7 ± 38</td>
<td>15,9 ± 5,8</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>25,7 ± 8,6</td>
<td>30 ± 10</td>
<td>30 ± 7</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>25,2</td>
<td>18,3</td>
<td>17,8</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>(7-68)</td>
<td>(6–29)</td>
<td>(8-19)</td>
</tr>
<tr>
<td>Aufenthalt in Geriatrie im Intervall (d)</td>
<td>204</td>
<td>210</td>
<td>0</td>
</tr>
<tr>
<td>Relapse of the infection</td>
<td>6 (32%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>No. revisionens in interval (median)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>
Long-term treatment toxicity

- **Quinolones:** tendinopathy, long QT syndrome
- **Rifampin:** hepatotoxicity, GI-intolerance, rash, polyarthralgia
- **Betalactams:** myelosuppression, interstitial nephritis
- **Cotrimoxazole:** rash → Steven Johnson, renal insufficiency, hyperkaliemia
- **Doxycycline:** phototoxicity
- **Daptomycin:** eosinophilic pneumonia, rhabdomyolysis
- **Linezolid:** myelosuppression, neuropathy
- **All:** rash, drug fever, *C. difficile* colitis (except rifampin)
Bone penetration

Median bone : serum concentration ratio

- Quinolones
- Macrolides
- Clindamycin
- Rifampicin
- Linezolid
- Glycopeptides
- Penicillins
- Carbapenems
- Cephalosporins
- Fosfomycin
- Fusidic acid
- Tetracyclines

$p < 0.05$ relative to linezolid

1 study: ratio = 0.02

Landersdorfer CB. Clin Pharmacokinet 2009
Common reasons for failure

Surgical
- No (late) surgery
- Arthroscopic instead open surgery (change of mobile parts)
- Retention attempt of loose prosthesis
- Prosthesis removal in early and hematogenous infection

Antimicrobial
- No highly-active bactericidal antibiotic (initial i.v.)
- Short duration (total 3 months)
- No rifampin for staphylococcal biofilms
- Rifampin with open wound, fistula or VAC
4 most common mistakes

1. Use of oral drugs with low bioavailability: beta-lactams (penicillins, cefalosporins)
2. Use of bacteriostatic antibiotics: linezolid, clindamycin
3. Wrong interpretation of in vitro susceptibility: quinolones against staphylococci or enterococci
4. Rifampin: use in draining wounds, without implant (in prosthesis-free interval)
**Error: use of oral drugs with poor bioavailability**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral bioavailability</th>
<th>Bone penetration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin/clavulanic acid or ampicillin/sulbactam</td>
<td>15% (AUC 6x lower with PO dose)</td>
<td>7%</td>
</tr>
<tr>
<td>Cefuroxim, cefadroxil</td>
<td>10% (AUC 10x lower with PO dose)</td>
<td>12%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>70%</td>
<td>48%</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>100%</td>
<td>77%</td>
</tr>
<tr>
<td>Rifampin</td>
<td>80%</td>
<td>51%</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>85%</td>
<td>55%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>90%</td>
<td>45%</td>
</tr>
</tbody>
</table>

Sanford Guide to Antimicrobial Therapy 2013. 43rd ed.
Lorian. Antibiotics in Laboratory Medicine. 5th ed.
## Risik factors for rifampin resistance

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases (n = 48)</th>
<th>Controls (n = 48)</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated with any antibiotics</td>
<td>44 (91.7 %)</td>
<td>30 (62.5 %)</td>
<td>0.001(^f)</td>
</tr>
<tr>
<td>Treated with rifampin</td>
<td>41 (85.4 %)</td>
<td>20 (41.7 %)</td>
<td>&lt;0.001(^f)</td>
</tr>
<tr>
<td>Rifampin always adequate(^b)</td>
<td>25</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Rifampin inadequate</td>
<td>16</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Monotherapy and/or</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Empirc therapy(^c) and/or</td>
<td>6</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Other reasons(^d)</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Treatment with high bacterial load</td>
<td>34 (70.8 %)</td>
<td>13 (27.1 %)</td>
<td>&lt;0.001(^f)</td>
</tr>
<tr>
<td>&lt;2 weeks iv antimicrobial treatment</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>No surgical debridement</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>No iv and no surgical debridement</td>
<td>15</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

Debridement and retention

Two stage (short interval)

Onset of infection

2 weeks i.v. daptomycin* 10 mg/kg + rifampin p.o.

10 weeks p.o. antibiotics

Levofloxacin 2 x 500 mg
Co-trimoxazole 3 x 1 DS
Doxycycline 2 x 100 mg
Fusidic acid 3 x 500 mg + rifampin

Prosthesis

Stable

Debridement and retention

Explantation

Implantation

2 weeks i.v. daptomycin* 10 mg/kg (no rifampicin)

Loose

Two stage (short interval)

High-dose daptomycin for PJI: ongoing phase II study

*Daptomycin is not licensed for the treatment of PJI
Results (n = 72)

- Microbiology:
  - *Staphylococcus aureus* 30 cases
    (31 MRSA, 5 MSSA and 1 VISA)
  - Coagulase-negative staphylococci 33 cases
    (26 MR-CNS, 7 MS-CNS)
  - [Enterococci 9 cases (no VRE)].

- Efficacy:
  - Clinical and microbiological cure was observed in 64 patients (89%) with a median follow-up of 21.5 months. All failed cases were enterococci.
Infection-free probability: 87%
(95% confidence interval, 77-93%)
European Prosthetic Joint Infection Cohort (EPJIC)

www.pro-implant-foundation.org
March 5-6, 2015
June 1-2, 2015
September 24-25, 2015
Educational material

Infektionen des Bewegungsapparates

Grundlagen, Prophylaxe, Diagnostik und Therapie

eLearning tool (for iPad and tablets)
Essentials in diagnosing PJI
Available free for download (iTunes)
Palacademy

By the Expert Group of Swiss Societies of Orthopedic & Trauma surgeons and Infectious Diseases & Microbiology (Fall 2014)

CMSC
Centrum für Muskuloskeletale Chirurgie

JULIUS WOLFF INSTITUT
Thank you!

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Focus on implant, bone and joint-associated infections:

• Surgery: New concepts (retention, 1-stage, short interval)
• Diagnosis: Fast innovative methods
• Antibiotics: Active against biofilms