HOW TO MANAGE ORTHOPAEDIC IMPLANT INFECTIONS?

Real-life clinical case discussion

Marjan Wouthuyzen-Bakker
Internist-infectiologist
University Medical Center Groningen, the Netherlands
58 year old man
Hemophilia A with recurrent haemarthros
Chronic hepatitis C, SVR after treatment (2017)

Surgical history:
• 1997 Total knee prosthesis right
• 2002 Total elbow prosthesis left
• 2015 Revision total elbow prosthesis left

June 2018
Few days later…
Effusion and pain of elbow and knee
Fever
Not septic
WHAT WOULD YOU DO?

A) Immediate debridement of both prostheses (DAIR)

B) Immediate removal of both prostheses

C) Do a synovial puncture first, wait for culture results and then decide on the best surgical procedure
POSTPONING DAIR DECREASES SUCCESS RATE

Success rate decreases by 7.5% for knee PJI for each additional day of postponing DAIR.

Fig. 1. Predicted probabilities of successful implant retention with 95% confidence limits. The probability of successful implant retention is negatively correlated with duration of symptoms.

Triantafyllopoulos et al. J Arthroplasty 2015
QUESTION 3: Does identification of the pathogen prior to performing debridement, antibiotics and implant retention (DAIR) help guide the surgeon's decision making? If so, should you wait, in a clinically stable patient, until the pathogen has been identified?

RECOMMENDATION: The identification of the responsible microorganism before DAIR is desirable. However, it should not prevent timely surgical intervention if delay in surgery is believed to promote further establishment of biofilm formation and compromise the outcome of surgical intervention.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 94%, Disagree: 4%, Abstain: 2% (Super Majority, Strong Consensus)
WHAT WOULD YOU DO?

A) Immediate debridement of both prostheses (DAIR)

B) Immediate removal of both prostheses

C) Do a synovial puncture first, wait for culture results and then decide on the best surgical procedure
Next day,
4 out of 4 bloodcultures positive for S. aureus

Cefuroxime switched to flucloxacillin 12gram/24h
WOULD YOU STILL ADVISE DAIR WHEN THE MOBILE COMPONENTS CANNOT BE EXCHANGED?

A) Yes
B) No
C) I don’t know
LOWER SUCCESS RATE WHEN COMPONENTS ARE NOT EXCHANGED

Implant retention, with exchange of mobile components (n=176)

Implant retention, without exchange of mobile components (n=147)

logrank test  $p = 0.03$, HR 0.7 (CI 95% 0.52-0.99)

Wouthuyzen-Bakker et al. *J Infect* 2018
<table>
<thead>
<tr>
<th>Variables</th>
<th>OR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-reactive protein &gt; 150 mg/L</td>
<td>2.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>2.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>5.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Fracture as Indication for the prosthesis</td>
<td>5.4</td>
<td>0.01</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Exchange of modular components</td>
<td>0.35</td>
<td>0.002</td>
</tr>
<tr>
<td>Age &gt; 80 years</td>
<td>2.6</td>
<td>0.02</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>3.52</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Wouthuyzen-Bakker et al. *J Infect* 2018
PRE-OPERATIVE RISK SCORE FOR DAIR FAILURE ACCORDING TO CRIME80 SCORE

Cases with late acute *S. aureus* PJI

<table>
<thead>
<tr>
<th>Score</th>
<th>Failure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43%</td>
</tr>
<tr>
<td>2</td>
<td>42%</td>
</tr>
<tr>
<td>3</td>
<td>45%</td>
</tr>
<tr>
<td>4</td>
<td>77%</td>
</tr>
<tr>
<td>5</td>
<td>100%</td>
</tr>
</tbody>
</table>

Factors:
- **C** COPD
- **R** CRP > 150 mg/L
- **I** Rheumatoid arthritis
- **M** Indication prosthesis: fracture
- **E** Exchange of mobile components
- **80** Age > 80 years

Wouthuyzen-Bakker et al. *J Infect* 2018
CASE

DAIR elbow and knee protheses
Mobile component exchange not possible for both

2 days post-operative:
  - persistent high fever
  - septic
  - leakage of pus out of the elbow
WHAT WOULD YOU DO NOW?

A) Perform a lavage of the elbow
B) Perform a second DAIR
C) Start a broader antibiotic regimen
D) Remove the prosthesis
SUCCESS RATE

IMPLANT REMOVAL VERSUS IMPLANT RETENTION

S. aureus

% survival

follow-up (months)

Implant removal (n=46)
Implant retention with exchange mobile components (n=68)
Implant retention without exchange mobile components (n=64)

Wouthuyzen-Bakker et al. unpublished data
WHAT WOULD YOU DO NOW?

A) Perform a lavage of the elbow
B) Perform a second DAIR
C) Start a broader antibiotic regimen
D) Remove the prosthesis
REMOVAL ELBOW PROSTHESIS

Intraoperative cultures positive for *S. aureus*
CASE

- 2 days after removal of the elbow prosthesis, persistent arthritis knee prosthesis

→ Second DAIR

- Endocarditis ruled out with TEE

- Intra-operative cultures positive for *S. aureus*
WHEN DURING THE TREATMENT COURSE
WOULD YOU ADD RIFAMPIN?

A) Immediately after the first DAIR

B) When culture results and the antibiogram is available

C) After the wound is dry
Best biofilm drug

Induction of resistance
Factors affecting development of rifampicin resistance in biofilm-producing *Staphylococcus epidermidis*

Erik Svensson, Håkan Hanberger, Maud Nilsson and Lennart E. Nilsson

Drug concentration

- Rifampin resistant variants
- High inoculum
- Intermediate inoculum
- Low inoculum
48 PJI cases with rifampin-resistant staphylococci
(10 S. aureus, 38 CNS) matched with 48 PJI rifampin-susceptible controls

- 85.4% cases treated with rifampin
- 41.7% controls treated with rifampin
Independent significant predictors for rifampin resistance:

- Male sex OR 3.6
- ≥ 3 previous surgical revisions OR 4.7
- High initial bacterial load OR 4.9
- Inadequate rifampin therapy OR 5.4
WHEN DURING THE TREATMENT COURSE
WOULD YOU ADD RIFAMPIN?

A) Immediately after the first DAIR

B) When culture results and the antibiogram is available

C) After the wound is dry
HOW LONG WOULD YOU TREAT?

A) 6 weeks after the second DAIR of the knee
B) 3 months after the second DAIR of the knee
C) 6 months after removal of the elbow prosthesis
D) Lifelong antibiotic suppressive therapy
CAN PJI BE TREATED FOR 6 WEEKS?

Per protocol analysis

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Duration</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>95%</td>
<td>12-24 wk</td>
<td>n=20</td>
</tr>
<tr>
<td>92%</td>
<td>8 wk</td>
<td>n=24</td>
</tr>
</tbody>
</table>

Levofloxacin (750 mg once daily) plus rifampin (600mg once daily)

175 eligible patients, 63 included. (=36%)

Many of the patients excluded carried an initial poor prognosis, with higher odds of developing early failure.

**CAN PJI BE TREATED FOR 6 WEEKS?**

**Authors:** Jamie Lora-Tamayo, David Warren, Mikel Manchena-Losa, Marius Arndt, Christian Lausmann, Marius Arndt

**QUESTION 12:** What is the optimal length of antibiotic treatment following debridement, antibiotics and implant retention (DAIR) for acute periprosthetic joint infections (PJIs)?

**RECOMMENDATION:** The optimal length of antibiotic treatment following DAIR remains relatively unknown as there is considerable heterogeneity regarding the length, dose and administration of treatment. A minimum of six weeks of antibiotic therapy seems to be sufficient in most cases of PJIs managed by DAIR-provided surgical treatment.

**LEVEL OF EVIDENCE:** Moderate

**DELEGATE VOTE:** Agree: 91%, Disagree: 6%, Abstain: 1% (Super Majority, Strong Consensus)
HOW LONG WOULD YOU TREAT?

A) 6 weeks after the second DAIR of the knee

B) 3 months after the second DAIR of the knee

C) 6 months after removal of the elbow prosthesis

D) Lifelong antibiotic suppressive therapy
CRP EVOLUTION

First presentation

Haemartros knee, cultures negative

End of antibiotic treatment
CASE

• 27-09-2018: end of antibiotic treatment

• 4-10-2018: acute pain and effusion of knee, no fever, CRP 60

→ Removal of the prosthesis

Cultures: *S. aureus*, rifampin susceptible
IN CASE OF S. AUREUS BACTEREMIA, WHAT IF... THE PATIENT HAD NO CLINICAL SIGNS OF PJI?

A) I would leave the joint alone

B) I would leave the joint alone but will add rifampin

C) I would perform synovial fluid puncture for culture

D) Considering the high risk of secondary PJI, I would still perform a DAIR to be sure
4 patients developed PJI due to *S. aureus* during FU \(\rightarrow = 4\%\) (range after 174 – 670 days)

Table 4: Orthopedic Characteristics of the Joint Arthroplasties in Place at Time of SAB

<table>
<thead>
<tr>
<th></th>
<th>No PJII (n = 100)</th>
<th>Hematogenous PJII (n = 39)</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of joint arthroplasty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee</td>
<td>46 (43%)</td>
<td>25 (64.1%)</td>
<td>.12</td>
</tr>
<tr>
<td>Hip</td>
<td>48 (43%)</td>
<td>11 (28.2%)</td>
<td></td>
</tr>
<tr>
<td>Shoulder</td>
<td>5 (5%)</td>
<td>3 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Elbow</td>
<td>1 (1%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Revision surgery before SAB†</td>
<td>13 (13.3%)</td>
<td>15 (42.8%)</td>
<td>.01</td>
</tr>
<tr>
<td>Time from arthroplasty implantation to SAB, in y</td>
<td>7.9 (3.3-14.4)</td>
<td>11.3 (3.0-16.0)</td>
<td>.67</td>
</tr>
<tr>
<td>Time from last surgery to SAB, in y</td>
<td>7.3 (3.0-12.2)</td>
<td>5.7 (2.5-11.3)</td>
<td>.35</td>
</tr>
<tr>
<td>Joint symptoms and examination‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint pain</td>
<td>14 (14%)</td>
<td>38 (97.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Periarticular erythema</td>
<td>2 (2%)</td>
<td>7 (17.9%)</td>
<td>.002</td>
</tr>
<tr>
<td>Drainage</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Periarticular warmth</td>
<td>0</td>
<td>18 (46.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Swelling/effusion</td>
<td>3 (3%)</td>
<td>24 (61.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Decreased range of motion</td>
<td>1 (1%)</td>
<td>8 (20.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>None of the above</td>
<td>83 (83%)</td>
<td>1 (2.6%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

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