Treatment of Cardiac Device Infections

Peter Ammann
40 yrs old patient

- Pocket infection after pacemaker change. Staph. aureus growing in blood cultures. Pacemaker dependent. Echo: no vegetations on valves or leads
  - A) local surgical revision and AB treatment
  - B) complete extraction of system and transvenous reimplantation after negative blood cultures
  - C) complete extraction of system and epicardial system
88 yrs old patient

- Pocket infection after pacemaker change. Staph. aureus growing in blood cultures. Pacemaker dependent. Echo: no vegetations on valves or leads
  - A) local surgical revision and AB treatment
  - B) complete extraction of system and transvenous re-implantation after negative blood cultures
  - C) complete extraction of system and epicardial system
Complete device and lead removal is recommended for all patients with definite CIED infection, as evidenced by valvular and/or lead endocarditis or sepsis.

Class 1 Level of Evidence: A

ESC, AHA, ACC Guidelines 2010
Number of end organ failures per 1000 recipients of CIED by year of implantation

Voigt PACE 2010
4.7% risk of death and 146,000 USD cost per device infection

Greenspon et al J Am Coll Cardiol 2011
Risk factors for CIED infections

- Early reintervention \( \text{OR}=15.04 \)
- Long term steroid use \( \text{OR}=13.9 \)
- Fever within 24h before impl. \( \text{OR}=5.8 \)
- Renal dysfunktion \((\text{GFR}<60\text{ml/min/m2})\) \( \text{OR}=4.8 \)
- Preprocedural pacing \( \text{OR}=2.4 \)
- device changes (ERI) \( \text{OR}=2.4 \)
- Diabetes, Anticoagulation

### Table 2: Reported infection rates for CRT-P and CRT-D devices since 2000

<table>
<thead>
<tr>
<th>References</th>
<th>Device (n)</th>
<th>Follow-up (months)</th>
<th>Infection rate (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alonso et al.¹²</td>
<td>CRT-P 102</td>
<td>15 ± 13</td>
<td>3.0</td>
<td>All infections within 3 months from implant.</td>
</tr>
<tr>
<td>Daoud et al.¹³</td>
<td>CRT-D 66</td>
<td>11 ± 9</td>
<td>3.0</td>
<td>Thoracotomy CRT devices not included. Both infections detected within 30 days of implant.</td>
</tr>
<tr>
<td>Knight et al.³</td>
<td>CRT-D 443</td>
<td>30 ± 13</td>
<td>1</td>
<td>Infections detected 329 ± 180 days following implant.</td>
</tr>
<tr>
<td>Kautzner et al.¹⁴</td>
<td>CRT-P 92</td>
<td></td>
<td>2.2</td>
<td>Duration of follow-up not stated.</td>
</tr>
<tr>
<td>Leon et al.⁸</td>
<td>Both CRT-P and CRT-D 1903</td>
<td>6</td>
<td>1.1</td>
<td>Includes ppm upgrades.</td>
</tr>
<tr>
<td>Romeyer-Bouchard et al.⁴</td>
<td>CRT-P 123</td>
<td>31 ± 19</td>
<td>1.6</td>
<td>All infections presented within 12 months from implant.</td>
</tr>
<tr>
<td></td>
<td>CRT-D 116</td>
<td></td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Mittal et al.¹¹</td>
<td>PPM 1740</td>
<td>6</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ICD 667</td>
<td></td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CRT-P 48</td>
<td></td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CRT-D 426</td>
<td></td>
<td>4.2</td>
<td></td>
</tr>
</tbody>
</table>

Includes only those studies which reported device-specific infection rates.
70 yrs old man after CRT-D pocket change 5 yrs after implantation
Treatment of cardiac device infections

53 yrs old man after ICD implantation
### Table 2
Clinical Presentation of Patients With CDI (n = 189)

<table>
<thead>
<tr>
<th>Presenting Signs/Symptoms</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Fever (&gt;38°C)</td>
<td>82 (43)</td>
</tr>
<tr>
<td>Chills</td>
<td>73 (39)</td>
</tr>
<tr>
<td>Malaise</td>
<td>79 (42)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>32 (17)</td>
</tr>
<tr>
<td>Nausea</td>
<td>16 (8)</td>
</tr>
<tr>
<td>Sweating</td>
<td>34 (18)</td>
</tr>
<tr>
<td>Hypotension (systolic blood pressure &lt;90 mm Hg)</td>
<td>18 (10)</td>
</tr>
<tr>
<td>Murmur on examination</td>
<td>66 (35)</td>
</tr>
<tr>
<td>Symptomatic heart failure</td>
<td>52 (28)</td>
</tr>
<tr>
<td><strong>Local findings at generator site</strong></td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>128 (68)</td>
</tr>
<tr>
<td>Pain</td>
<td>93 (49)</td>
</tr>
<tr>
<td>Swelling</td>
<td>127 (67)</td>
</tr>
<tr>
<td>Warmth</td>
<td>71 (38)</td>
</tr>
<tr>
<td>Tenderness</td>
<td>86 (46)</td>
</tr>
<tr>
<td>Drainage</td>
<td>95 (50)</td>
</tr>
<tr>
<td>Purulent drainage</td>
<td>65 (34)</td>
</tr>
<tr>
<td>Skin ulceration</td>
<td>59 (31)</td>
</tr>
<tr>
<td>Generator/lead erosion</td>
<td>48 (25)</td>
</tr>
<tr>
<td>Intraoperative purulence at generator pocket</td>
<td>151 (80)</td>
</tr>
<tr>
<td><strong>Laboratory abnormalities</strong></td>
<td></td>
</tr>
<tr>
<td>Leukocytosis (WBC &gt;10 \times 10^9/l), n = 188</td>
<td>82 (43)</td>
</tr>
<tr>
<td>Anemia (HCT &lt;38% in men and &lt;35% in women), n = 188</td>
<td>94 (50)</td>
</tr>
<tr>
<td>High erythrocyte sedimentation rate (ESR &gt;22 mm/h in men and &gt;29 mm/h in women), n = 76</td>
<td>47 (25)</td>
</tr>
<tr>
<td>Positive blood culture (n = 188)</td>
<td>76 (40)</td>
</tr>
</tbody>
</table>

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**Figure 1**
Microbiology of PPM/ICD Infections (n = 189)

ICD = implantable cardioverter-defibrillator; PPM = permanent pacemaker.

Sohail et al JACC 07
What do you think is mortality rate 2 years after device extraction?

- A < 5%
- B 5-10%
- C 10-20%
- D 20-30%
Long term mortality after transvenous lead removal

Survival probability at 2 yrs 84.3%
How to reduce infections????????????
### Treatment of Cardiac Device Infections

#### Operating Room versus EP Laboratory?

Data from 667 ICD Implantations

<table>
<thead>
<tr>
<th>Gender</th>
<th>Onset of Infection</th>
<th>Implantation Location</th>
<th>ICD System</th>
<th>Pulse Generator Level</th>
<th>Post-operative</th>
<th>Clinic</th>
<th>Microbial Aetiology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 M</td>
<td>Early</td>
<td>OR</td>
<td>1 lead</td>
<td>Submuscular</td>
<td>Yes, pocket-haematoma</td>
<td>Pocket Infection</td>
<td>CNS + Propionibacter spp</td>
<td>AB + total explanation</td>
</tr>
<tr>
<td>2 M</td>
<td>Late</td>
<td>OR</td>
<td>1 lead</td>
<td>Submuscular</td>
<td>No</td>
<td>Pocket Infection</td>
<td>Staphylococcus aureus + Escherichia coli</td>
<td>AB + total explanation</td>
</tr>
<tr>
<td>3 M</td>
<td>Late</td>
<td>OR</td>
<td>1 lead</td>
<td>Submuscular</td>
<td>No</td>
<td>ICD-related endocarditis</td>
<td>Staphylococcus aureus</td>
<td>1. AB 2. AB + total explanation</td>
</tr>
<tr>
<td>4 F</td>
<td>Late</td>
<td>CCL</td>
<td>2 leads</td>
<td>Subcutaneous</td>
<td>No</td>
<td>Pocket Infection</td>
<td>Candida albicans + CNS</td>
<td>AB + total explanation</td>
</tr>
<tr>
<td>5 M</td>
<td>Early</td>
<td>CCL</td>
<td>1 lead</td>
<td>Subcutaneous</td>
<td>No</td>
<td>Pocket Infection</td>
<td>Staphylococcus aureus + CNS</td>
<td>AB + total explanation</td>
</tr>
<tr>
<td>6 M</td>
<td>Late</td>
<td>CCL</td>
<td>1 lead</td>
<td>Subfascial</td>
<td>Yes, pocket-haematoma</td>
<td>Pocket Infection</td>
<td>-</td>
<td>AB + total explanation</td>
</tr>
<tr>
<td>7 M</td>
<td>Late</td>
<td>CCL</td>
<td>1 lead</td>
<td>Subfascial</td>
<td>No</td>
<td>Pocket Infection</td>
<td>Serratia marcescens</td>
<td>AB + total explanation</td>
</tr>
</tbody>
</table>

M = male, F = female, OR = operating room, CCL = cardiac catheterisation laboratory, CNS = coagulase-negative Staphylococci, AB = antibiotic(s).

Remmelts et al Neth Heart J 2009
Prevention of infection
Pre Implantation

- **Correct 3 min hand disinfection**
  - **Preoperative skin washing** with chlorhexidin gluconate 4% solution night before and morning before implantation
  - **Strict 3 min dry time** before surgical skin preparation with chlorhexidin gluconate 2% and isopropyl alcohol at time of implantation
  - Study by Koeberl et al Circulation 2011;124:A10041 in 3874 pts (2622 before and 1251 after)
  - Reduction of Infection 1% to 0.24% (HR 4.2)
Antibiotics before implantation?

Only one RCT: Cephazolin i.v. vs Placebo

- Study stopped prematurely after inclusion of 649 patients (planed 1000)
  - 91% brady-devices; 53% device change

- 13 infections: 2 vs 11 (RR 19 p=0.016)
A 19-Year Study on Pacemaker-Related Infections: A Claim for Using Postoperative Antibiotics

JANEK M. SENARATNE, B.Med.Sc., M.D., ANUSHKA JAYASURIYA, B.Sc., MARLEEN IRWIN, SAJAD GULAMHUSEIN, M.D., and MANOHARA P.J. SENARATNE, M.B.B.S., Ph.D.

From the Division of Cardiac Sciences, Grey Nuns Hospital, Edmonton, Alberta, Canada

4 day oral cephalexin or clindamycin
Under investigation: antibacterial envelope (TYRX)

biocompatible mesh coated with minocycline/rifampicin that elute within 7-10 days
Citadel/Centurion Study Results: Use of Antibacterial Envelope is Associated with Low 12-month CIED Infection Rates

Charles A. Henrikson, MD, M. Rizwan Sohail, MD, Grant R. Simons, MD, Daniel J. Lerner, MD, Steve Sisk, MSc Pharm
Citadel (replacement ICD procedures)

**Purpose:** Prospectively define the rates of CIED infection and mechanical complication in the 12 months following non-\textit{de novo} single or dual chamber ICD implantation with the TYRX\textsuperscript{TM} Antibacterial Envelope

**Design:** 2,300 patient cohort enrolled at 55 U.S. sites, compared to published controls (12-month control infection rate of 2.2\%\textsuperscript{1})

**Visits:** Enrollment, wound check, 3, 6, and 12 months

**Endpoints:** CIED Infection and mechanical complication

\textsuperscript{1}Gould \textit{et al.} \textit{Heart Rhythm} 2008;5(12):1675-1681

ClinicalTrials.gov NCT01043861
Centurion (replacement CRT procedures)

**Purpose:** Prospectively define the rates of CIED infection and mechanical complication in the 12 months following non-de novo CRT implantation with the TYRX™ Antibacterial Envelope

**Design:** 2,000 patient prospective cohort compared to 2,000 patient site- and case-matched retrospective control cohort enrolled at 55 U.S. sites

**Visits:** Enrollment, wound check, 3, 6, and 12 months

**Endpoints:** CIED Infection and mechanical complication
## Patient Characteristics

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>ICD-Prospective (n=459)</th>
<th>CRT-Prospective (n=670)</th>
<th>All TYRX™ (n=1,129)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>155 (33.8)</td>
<td>264 (39.4)</td>
<td>419 (37.1)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>255 (55.6)</td>
<td>628 (93.7)</td>
<td>883 (78.2)</td>
</tr>
<tr>
<td><strong>NYHA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>48 (10.5)</td>
<td>44 (6.6)</td>
<td>92 (8.1)</td>
</tr>
<tr>
<td>II</td>
<td>120 (26.1)</td>
<td>171 (25.5)</td>
<td>291 (25.8)</td>
</tr>
<tr>
<td>III</td>
<td>73 (15.9)</td>
<td>370 (55.2)</td>
<td>443 (39.2)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (0.7)</td>
<td>23 (3.4)</td>
<td>26 (2.3)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>72 (15.7)</td>
<td>144 (21.5)</td>
<td>216 (19.1)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>77 (16.8)</td>
<td>115 (17.2)</td>
<td>192 (17.0)</td>
</tr>
<tr>
<td>Fever &lt; 24h prior to implantation</td>
<td>2 (0.4)</td>
<td>4 (0.6)</td>
<td>6 (0.5)</td>
</tr>
</tbody>
</table>
Results: Major CIED Infection

CID Infections - TYRX™ Vs. Non-TYRX™ Published Control

<table>
<thead>
<tr>
<th></th>
<th>TYRX 5/1,129</th>
<th>Comparator 10/451</th>
</tr>
</thead>
<tbody>
<tr>
<td>TYRX</td>
<td>0.44%</td>
<td></td>
</tr>
<tr>
<td>Non-TYRX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p = 0.023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.2% (Gould et al.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Use of TYRX Envelope associated with 80% fewer infections**

Results: Mechanical Complications

Hematoma Rates - TYRX™ vs. Non-TYRX™ Published Results

<table>
<thead>
<tr>
<th></th>
<th>TYRX 18/1129</th>
<th>Gould 12/533</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematoma Rate</td>
<td>1.6%</td>
<td>2.3%*</td>
</tr>
<tr>
<td>P = 0.1738</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Percent displayed was the 3 month rate. It is greater than the 12 month rate, so the 3 month rate was used for comparison.

No significant difference in hematoma rate was observed with the use of the TYRX Envelope

presented at HRS 2015 Boston
Special Article

Randomized Cluster Crossover Trials for Reliable, Efficient, Comparative Effectiveness Testing: Design of the Prevention of Arrhythmia Device Infection Trial (PADIT)

Stuart J. Connolly, MD, François Philippon, MD, Yves Longtin, MD, Amparo Casanova, PhD, David H. Birnie, MD, Derek V. Exner, MD, Paul Dorian, MD, Ratika Prakash, MD, Marco Alings, MD, and Andrew D. Krahn, MD

*Population Health Research Institute, Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada
†Quebec Heart Institute, Laval Hospital, Quebec City, Quebec, Canada
‡University of Ottawa Heart Institute, Ottawa, Ontario, Canada
§Libra Cardiosurgical Institute of Alberta, University of Calgary, Calgary, Alberta, Canada
¶University of Toronto, Toronto, Ontario, Canada
‖Dalhousie University, Halifax, Nova Scotia, Canada
*Working Group on Cardiosurgical Research: The Netherlands, Utrecht, The Netherlands
*bUniversity of British Columbia, Vancouver, British Columbia, Canada

Arms

Experimental: Conventional
Preoperative Antibiotics: Cefazolin preoperative, vancomycin in penicillin allergic patients.

Experimental: Incremental
Preoperative antibiotics (Cefazolin and Vancomycin) Bacitracin pocket wash and 2 days of oral Cefalexin post operative.
Future will go leadless and subcutaneous
Recurrence after complete extraction: 7/354 = 1.9%

Recurrence without complete extraction: 10/23 = 43%

Mortality: 6.3%
  - with extraction: 5%
  - without extraction: 17%

Infection recurrence

Death with infectious process
Treatment of cardiac device infections

Treatment: extraction

Prospective study
425 patients/381 extractions
FU 55 ± 31 months

1. Transoesophageal echocardiography

Vegetation Size

- <20 mm: Percutaneous extraction
- >20 mm: Surgical extraction

Surgical procedure refused or judged too risky

Antimicrobial treatment
Treatment of cardiac device infections

Percutaneous vs surgical extraction

• Percutaneous extraction:
  • 337 patients.

• Surgical extraction
  • 44 patients (16%)
    • second intention after failure of percutaneous extraction in 10 patients.

• Procedure related death occurred in 14 patients:
  – 3 cardiac or vena cava injuries
  – 9 septic shocks
  – 2 pulmonary embolisms
  – 1 patient deceased of an associated mitral valve endocarditis, and 1 pts deceased at day 4 of ventricular tachycardia.

• A new device was implanted
  • in 244 patients (64%),
    • transvenous leads in 132 and epicardial leads in 112
Risk of septic or embolic death according to Thrombus/Vegetation size

- No vegetation: 0%
- <16 mm: 6.4%
- 16-20 mm: 8%
- >21 mm: 18%

P = 0.03
Antimicrobial treatment

If blood cultures negative, empirical antistaphylococcal therapy
Drug regimen modified according to the lead cultures results.

**Extraction procedure**

If pacing dependent:
- epicardial pacing system

If not pacing dependent:
- re-evaluation and endocardial reimplantation if required
Rochester Algorithm

Suspected PPM/ICD Infection

Blood and Generator Pocket cultures

Positive blood cultures or prior antibiotic treatment

TEE

Valve vegetation

Follow AHA guidelines for treatment of infective endocarditis

Complicated, i.e., with septic venous thrombosis, osteomyelitis, etc

Treat with 4-6 weeks of antibiotics

Lead vegetation

Uncomplicated

Treat with 2 weeks of antibiotics

Negative TEE

Other

Treat with 2-4 weeks of antibiotics

S. aureus

Treat with 2-4 weeks of antibiotics

Negative Blood cultures

Pocket Infection

Generator/lead erosion

Treat with 10-14 days of antibiotics

Treat with 7-10 days of antibiotics
Time of re-implantation: Rochester experience

- **Blood cultures (+) TEE (+)**
  - Repeat blood cultures after device removal
  - **Valve vegetation**
    - Reimplant device after 14 days of first negative blood culture
  - **Lead vegetation**
    - Reimplant if repeat blood cultures are negative for 72 hours

- **Blood culture (+) TEE (-)**
  - Repeat blood cultures after device explantation
  - Reimplant if repeat blood cultures are negative for at least 72 hours

- **Generator Pocket Infection/Generator or lead erosion**
  - Negative blood cultures for 72 hours after device removal
  - Reimplant once adequate debridement is achieved

*retrospective analysis of 189 CDI*

Sohail et al. J Am Coll Cardiol 2007
LifeVest von Zoll
AHA Scientific Statement

Update on Cardiovascular Implantable Electronic Device Infections and Their Management

A Scientific Statement From the American Heart Association

Endorsed by the Heart Rhythm Society

Larry M. Baddour, MD, FAHA, Chair; Andrew E. Epstein, MD, FAHA, FHRSA; Christopher C. Erickson, MD, FAHA; Bradley P. Knight, MD, FHRSA; Matthew E. Levison, MD; Peter B. Lockhart, DDS; Frederick A. Masoudi, MD, MSPH; Eric J. Okum, MD; Walter R. Wilson, MD; Lee B. Beerman, MD; Ann F. Bolger, MD, FAHA; N.A. Mark Estes III, MD, FAHA, FHRSA; Michael Gewitz, MD, FAHA; Jane W. Newburger, MD, MPH, FAHA; Eleanor B. Schron, PhD, RN, FAHA; Kathryn A. Taubert, PhD, FAHA; on behalf of the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Nursing; Council on Clinical Cardiology; and the Interdisciplinary Council on Quality of Care and Outcomes Research

Abstract—Despite improvements in cardiovascular implantable electronic device (CIED) design, application of timely infection control practices, and administration of antibiotic prophylaxis at the time of device placement, CIED infections continue to occur and can be life-threatening. This has prompted the study of all aspects of CIED infections. Recognizing the recent advances in our understanding of the epidemiology, risk factors, microbiology, management, and prevention of CIED infections, the American Heart Association commissioned this scientific statement to educate clinicians about CIED infections, provide explicit recommendations for the care of patients with suspected or established CIED infections, and highlight areas of needed research. (Circulation. 2010;121:458-477.)

Key Words: AHA Scientific Statements ■ infection ■ device, cardiovascular ■ implantable electronic device ■ pacemaker ■ implantable cardioverter-defibrillator ■ endocarditis