What’s hot in infective endocarditis?

Partial oral endocarditis antibiotic treatment – the POET trial.

Claus Moser, MD, PhD
Department of Clinical Microbiology, Rigshospitalet.
Copenhagen University Hospital.
Denmark.

Stade de la Beaujoire, Nantes on July the 7th in 1998 last game for Denmark for the Laudrup brothers in the World Cup quarterfinal against Brasil (2-3).
Recommended treatment of infectious left-sided endocarditis

- 4 to 6 weeks in-hospital
- iv antibiotics (iv lines)
- Work-up for endocarditis
- Work-up for primary focus
- Heart valve surgery ~50% of cases
- Daily ward rounds
- Careful monitoring - “Institutionalised” 24/7/4-6
Why try to reduce in-hospital treatment?

- The long admissions are associated with increased risk of complications
- Reductions in the length of hospital stay have been associated with improved outcome in other patient groups
- Reduce costs in the health care system
Length of stay and number of admissions in Denmark

From 2007 to 2013 we had a 3,000 hospital bed reduction (20%).

In 2017/18 the average length of stay is less than 3 days.
“Oh no – I had just succeeded in closing the door.”
Options for modifying these regimens

- Reduce duration of iv antibiotic treatment
- Use *Outpatient Parenteral Antibiotic (Antimicrobial) Therapy* (OPAT) regimens
- or – to maintain recommended duration, but in stable patients swap from an initial iv regimen to an oral regimen – in the out-patient clinic
When to switch from iv in-hospital (IPAT) to out of hospital – OPAT?

Depends on *timing* of major adverse outcomes or complications in infectious endocarditis

- Death
- Heart failure
- Emboli
Impact of Valve Surgery on 6-Month Mortality in Adults With Complicated, Left-Sided Native Valve Endocarditis: A Propensity Analysis on whether valve surgery is associated with reduced mortality.

Vikram et al. JAMA 2003
Timing of fever in 123 patients with infective endocarditis in a Kaplan-Meier plot that shows cumulative frequency of defervescence.


© 2001 by the Infectious Diseases Society of America
Timing of heart failure (HF) in patients who have infective endocarditis and aortic insufficiency (AI) or mitral insufficiency (MI).


© 2001 by the Infectious Diseases Society of America
Timing and incidence of embolic events in patients with infective endocarditis. pt-days, Patient-days.


© 2001 by the Infectious Diseases Society of America
Proposed guidelines for the use of inpatient antibiotic therapy (IPAT) and outpatient parenteral antibiotic therapy (OPAT) for infective endocarditis (IE)


<table>
<thead>
<tr>
<th>Phase of treatment</th>
<th>Guidelines for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical phase (weeks 0–2)</td>
<td>Complications of IE occur most frequently during this phase, and timely diagnosis is important for achieving optimal outcome. Preferred management: IPAT for 2 weeks. Exceptions: OPAT can be considered at 1 week for patients who meet the following 3 criteria: (1) infection with viridans streptococcal IE, (2) medically stable condition without fever and with negative blood culture results, and stable electrocardiogram at time of proposed discharge; (3) no complications of IE and not in high-risk subgroup (see below).</td>
</tr>
<tr>
<td>Continuation phase (weeks 2–4 or 2–6)</td>
<td>Most patients who have not suffered complications of IE are likely to remain stable during the remainder of therapy, but side effects of parenteral antibiotic therapy may still occur. Preferred management: OPAT can be considered for the majority of patients who are medically stable (see above). Exceptions: IPAT should generally be continued for patients with any of the following characteristics: (1) complications of IE, such as congestive heart failure, conduction abnormality, mental status change, or evidence of paravalvular abscess on a transesophageal echocardiogram; (2) members of a high-risk subgroup: acute IE, aortic valve disease, prosthetic valve disease, or IE caused by Staphylococcus aureus or other virulent organisms.</td>
</tr>
<tr>
<td>Essential elements of OPAT therapy</td>
<td>Patients should be educated and fully informed about the complications of IE and indications for and method of contacting their physician or IE care team. Patients and family should be reliable, compliant, and live close to the hospital. Routine postdischarge evaluation should include biweekly office or IE care team home visits during OPAT. Same-day evaluation by a member of the IE care team should be available for patients with recurrent fever or new symptoms.</td>
</tr>
</tbody>
</table>

---

a Expert consultation on individual patients may identify other low-virulence, low-risk organisms for which a similar approach may be taken. 

b Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis, Neisseria gonorrhoeae, beta streptococci, gram-negative bacteria, and fungi.
2015 ESC Guidelines for the management of infective endocarditis
(Habib et al. Eur Heart J 2015)

<table>
<thead>
<tr>
<th>Phase of treatment</th>
<th>Guidelines for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical phase (weeks 0–2)</td>
<td>• Complications occur during this phase</td>
</tr>
<tr>
<td></td>
<td>• Preferred inpatient treatment during this phase</td>
</tr>
<tr>
<td></td>
<td>• Consider OPAT if: oral streptococci or</td>
</tr>
<tr>
<td></td>
<td>Streptococcus bovis,(^a) native valve,(^b) patient stable, no complications</td>
</tr>
<tr>
<td>Continuation phase (beyond week 2)</td>
<td>• Consider OPAT if medically stable</td>
</tr>
<tr>
<td></td>
<td>• Do not consider OPAT if: HF, concerning echocardiographic features, neurological signs, or renal impairment</td>
</tr>
<tr>
<td>Essential for OPAT</td>
<td>• Educate patient and staff</td>
</tr>
<tr>
<td></td>
<td>• Regular post-discharge evaluation (nurses 1/day, physician(^c) in charge 1 or 2/week)(^d)</td>
</tr>
<tr>
<td></td>
<td>• Prefer physician-directed programme, not home-infusion model</td>
</tr>
</tbody>
</table>

Criteria that determine suitability of outpatient parenteral antibiotic therapy for infective endocarditis (Adapted from Andrews and von Reyn. CID 2001)
Outpatient parenteral antimicrobial therapy

Ann L N Chapman consultant in infectious diseases

Short communication

Outpatient parenteral antimicrobial therapy for infective endocarditis: A cost-effective strategy

Traitement parentéral ambulatoire des endocardites infectieuses : une stratégie coût-efficace

A. Lacroix a, M. Revest a,d, S. Patrat-Delon a, F. Lemaître b,d, E. Donal c, A. Lorraine’h a, C. Arvieux a, C. Michelet a,d, P. Tattevin a,*d,e

a Service des maladies infectieuses et réanimation médicale, CHU Pontchaillou, 2, rue Le-Guilloux, 35033 Rennes cedex, France
b Département de pharmacologie clinique, CHU Pontchaillou, 35033 Rennes cedex, France
c Département de cardiologie et maladies vasculaires, CHU Pontchaillou, 35033 Rennes cedex, France

OPAT saved 15,000 euros per patient
Speculation

Does a microbial agent exposed to an antibiotic die more if the antibiotic come into the body through
• a line in the vein compared to
• entering through the mouth?
Intravenous Followed by Oral Antimicrobial Therapy for Staphylococcal Endocarditis

RICHARD H. PARKER, M.D.; and BYRON E. FOSSIECK, Jr., M.D.; Washington, D.C.

Ann Intern Med 1980

N=33, Staph aur, cardiac murmurs, 16 days iv + 26 days oral; all cured

TREATMENT OF RIGHT-SIDED STAPHYLOCOCCUS AUREUS ENDOCARDITIS IN INTRAVENOUS DRUG USERS WITH CIPROFLOXACIN AND RIFAMPICIN

R.J. Dworkin ¹, M.A. Sande, B.L. Lee, H.F. Chambers

Lancet 1989

Ciprofloxacin iv initially. N = 10, all cured
Oral Antibiotic Treatment of Right-sided Staphylococcal Endocarditis in Injection Drug Users: Prospective Randomized Comparison with Parenteral Therapy

Alan W. Heldman, MD, Tina V. Hartert, MD, Stuart C. Ray, MD, Emile G. Daoud, MD, Thomas E. Kowalski, MD, Vincent J. Pompili, MD, Stephen D. Sisson, MD, William C. Tidmore, MD, Keith A. vom Eigen, MD, Steven N. Goodman, MD, PhD, Paul S. Lietman, MD, PhD, Brent G. Petty, MD, Charles Flexner, MD, Baltimore, Maryland

RSSE:
Right-sided Staphylococcal endocarditis

Randomized to:
Po – ciprofloxacin and rifampicin,
IV oxacillin or vancomycin,
Both combined with gentamicin for 5 days.

4 weeks treatment.

Febrile iv drug-users
n=573

oral
n=287

Randomization

parenteral
n=286

Not RSSE
n=247

RSSE
n=40

RSSE
n=45

Not RSSE
n=241

28 days therapy

completed treatment & follow-up
n=19

cured
18

failed
1

cured
22

failed
3

completed treatment & follow-up
n=25

Did not complete treatment
n=21

Did not complete treatment
n=20
Oral antibiotics for infectious endocarditis; Experience in our institution

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Microbial pathogen</th>
<th>Valve(s)/material involved</th>
<th>Peroral medication</th>
<th>Treatment duration (Parental/peroral)</th>
<th>Surgery</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>43</td>
<td>β-haemolytic streptocci group g</td>
<td>Prosthetic biological mitral valve</td>
<td>Fucidin and rimactan</td>
<td>13 days/28 days</td>
<td>No</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>75</td>
<td>Staphylococcus epidermidis</td>
<td>Aortic and mitral valve</td>
<td>Linezolid and moxifloxacin</td>
<td>17 days/30 days</td>
<td>Yes prosthetic biological mitral and aortic valve</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>62</td>
<td>Staphylococcus aureus</td>
<td>Mitral valve</td>
<td>Fucidin and linezolid</td>
<td>17 days/24 days</td>
<td>No</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>56</td>
<td>Staphylococcus aureus</td>
<td>Prosthetic biological mitral valve</td>
<td>Fucidin and rimactan</td>
<td>29 days/15 days</td>
<td>No</td>
<td>Success</td>
</tr>
<tr>
<td>Female</td>
<td>74</td>
<td>Streptococcus anginosus</td>
<td>Mitral valve</td>
<td>Linezolid and moxifloxacin</td>
<td>15 days /17 days</td>
<td>No</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>54</td>
<td>Staphylococcus aureus</td>
<td>Aortic valve</td>
<td>Rimactan and linezolid</td>
<td>29 days/15 days</td>
<td>Yes prosthetic biological aortic valve</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>78</td>
<td>Enterococcus faecalis</td>
<td>Prosthetic biological mitral valve</td>
<td>Linezolid</td>
<td>20 days/10 days</td>
<td>No</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>67</td>
<td>Coagulase negative staphylococcus</td>
<td>Pacemaker electrode</td>
<td>Rimactan and linezolid</td>
<td>36 days/16 days</td>
<td>Yes, removal of infected electrode</td>
<td>Success</td>
</tr>
<tr>
<td>Female</td>
<td>65</td>
<td>β-haemolytic streptocci group g</td>
<td>Aortic valve</td>
<td>Rimactan and linezolid</td>
<td>24 days/6 days</td>
<td>Yes, prosthetic biocloclial aortic valve</td>
<td>Success</td>
</tr>
<tr>
<td>Female</td>
<td>44</td>
<td>Staphylococcus lugdunensis</td>
<td>Pacemaker electrode</td>
<td>Penicillin and linezolid</td>
<td>35 days/14 days</td>
<td>Yes, removal of infected electrode</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>67</td>
<td>Salmonella</td>
<td>Aortic valve</td>
<td>Ciprofloxacin</td>
<td>42 days/21 days</td>
<td>Yes, prosthetic biocloclial aortic valve</td>
<td>Success</td>
</tr>
<tr>
<td>Male</td>
<td>74</td>
<td>Coagulase-negative staphylococcus</td>
<td>Aortic and mitral valve</td>
<td>Penicillin</td>
<td>40 days/5 days</td>
<td>Yes, prosthetic biocloclial aortic and mitral valve</td>
<td>Success</td>
</tr>
</tbody>
</table>


Georges-Pompidou European Hospital

Local protocols:

≥7 days iv
General condition resolution of fever
Reduction CRP
Negative blood cultures
Normalization of leucocytosis
Normalization of serum creatinine
Disappearance or reduction of imaging abnormalities

If all fulfilled -> definitive oral antibiotics
The oral regimens

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Antibiotic regimen</th>
</tr>
</thead>
</table>
| Streptococci  | • Amoxicillin \(n = 84; 92\%\)  
                \(n = 91\)  
                • Amoxicillin—clindamycin \(n = 4; 4\%\)  
                • Amoxicillin—rifampin \(n = 3; 3\%\)  
| Staphylococci | • Clindamycin—(rifampin or fluoroquinolone) \(n = 15; 28\%\)  
                \(n = 54\)  
                • Fluoroquinolone—rifampin \(n = 13; 24\%\)  
                • Amoxicillin—(rifampin or fluoroquinolone or clindamycin) \(n = 9; 17\%\)  
                • Fluoroquinolone \(n = 4; 7\%\)  
                • Amoxicillin \(n = 4; 7\%\)  
                • Clindamycin \(n = 4; 7\%\)  
                • Rifampin—(Bactrim or doxycycline) \(n = 2; 4\%\)  
                • Linezolid \(n = 2; 4\%\)  
                • Rifampin \(n = 1; 2\%\)  
| Enterococci  | • Amoxicillin \(n = 21; 91\%\)  
                \(n = 23\)  
                • Amoxicillin—rifampin \(n = 2; 9\%\)  

Mzabi et al. *Clinical Microbiology and Infection* 2016
22, 607-612DOI: (10.1016/j.cmi.2016.04.003)

Georges-Pompidou European Hospital

Local protocols:
- ≥7 days iv
- General condition resolution of fever
- Reduction CRP
- Negative blood cultures
- Normalization of leucocytosis
- Normalization of serum creatinine
- Disappearance or reduction of imaging abnormalities

If all fulfilled -> definitive oral antibiotics

2 relapses
4 reinfections

9 relapses
8 reinfections

Fewer comorbidities and criteria of severity
Fewer with *S. aureus*

Commented in details in CMI 2017.
Davido et al.

Primary objective

To determine the safety and efficacy of *partial* oral antibiotic treatment of IE compared with traditional full-length parenteral antibiotic treatment
Design

- Un-blinded
- Prospective
- Randomised
- Multicenter, nationwide
Inclusion criteria 1

• Left-sided endocarditis based on the Duke criteria

• Infected with one of the following microorganisms (> ¾ of all left sided IE):
  – *Streptococcus spp*
  – *Enterococcus faecalis*
  – *Staphylococcus aureus*
  – Coagulase-negative staphylococci
Inclusion criteria II

- ≥ 10 days of appropriate parenteral antibiotic treatment overall, and at least 1 week of appropriate parenteral treatment after valve surgery
- $T < 38.0 \, ^\circ\text{C} > 2$ days
- C-reactive protein dropped to less than 25% of peak value or $< 40 \text{ mg/L}$, and white blood cell count $< 15 \times 10^9/\text{L}$ during antibiotic treatment
- No sign of abscess formation revealed by trans-oesophageal echocardiography $< 48$ h before inclusion
- At least 10 days of antibiotic treatment had to remain at randomization
Exclusion criteria

- Body mass > 40
- Concomitant infection requiring iv antibiotics
- Suspected reduced GI absorption
- Inability to give informed consent
- Reduced compliance
Primary endpoint

- Combined endpoint within 6 months after antibiotic treatment was terminated
  - All-cause mortality
  - Unplanned cardiac surgery
  - Embolic events
  - Relapse of positive blood cultures with the primary pathogen
Secondary endpoints

- Quality of life after completion of antibiotic treatment
- Costs associated with management of endocarditis
- Shift of antibiotics during treatment
- Duration of antibiotic treatment
- Complications associated with intravenous catheters
Choice of antibiotics

Patients randomised to iv treatment:
  – Treated according to guidelines from Danish Cardiac Society (DSC)

Patients randomised to oral treatment:
  – Treated according to new study guidelines
International experts' practice in the antibiotic therapy of infective endocarditis is not following the guidelines


Clinical Microbiology and Infection
Volume 23, Issue 10, Pages 736-739 (October 2017)
DOI: 10.1016/j.cmi.2017.03.007
Antibiotics - Safety

- Minimal Inhibitory Concentration (MIC) determinations for relevant antibiotics (E-test)
- Pharmacokinetic profile in all patients
  - Day 1 (oral and i.v.)
  - Day 5 (oral – i.e. at steady state after shift from initial i.v. to oral)
Criteria for treatment in out-patients clinic

- No heart failure
- No significant arrhythmia or conduction defects
- No changes in cerebral status during admission
- No clinically identified embolic events during admission
- No other significant disabilities
Follow-up of out-patients

- Reports morning temp >38 °C and other new symptoms to the ward
- Seen 2 (3) times a week
  - Clinically (+ ECG, BP, temp, SAT) (“ward round”)
  - Blood testings 3 times per week (CRP, WBC, haemoglobin, renal and hepatic parameters)
Follow-up after treatment

- 1 week (5-9 days)
- 1 month (25-35 days)
  Incl. transthoracic echocardiography
- 3 months (80-100 days)
- 6 months (170-190 days)
  Incl. transthoracic echocardiography
Statistics

• Estimated event rate 5-10%
  – All cause mortality 2-5%
  – Unplanned surgery 1-3%
  – Risk of embolic events 1-2%
  – Risk of relapse 1-3%

• Non inferiority margin 10%
• Power 90%
• One sided confidence interval 97.5%
• N=400 (1:1 inclusion)
Study organization

• Steering committee:
  One representative per center

• Experts on antibiotics:
  One representative per region

• Safety monitoring board:
  – One cardiologist
  – One trialist
  – One specialist in infectious diseases
Oral antibiotics development - general


• Serum concentrations curves drawn
  – Lowest serum-concentration measured applied
  – Shortest T$_{1/2}$ applied

• In certain cases a theoretical serum concentration applied, based on a higher dosage.

• Single dosage kinetics.
Safety issues

• Treatment combinations (always 2 antibiotics) – purposes
  – Variations in pharmacokinetics (pharmacogenetic)
  – Reduce development of resistance
  – Potential additive/synergistic effects
  – Biofilm physiology

• Pharmacokinetic profile by HPLC on all patients (single and multiple dose kinetics) – reviewed by experts in clinical microbiology.
Pharmacokinetic variations are substantial.

(Roberts et al. CID 2014)

Antibiotic concentrationen relative to MIC in 361 critically ill patients after 50% and 100% of the dosing interval of eight different β-lactam antibiotics.

TABLE 1. Concentrations of antibiotics in sweat and blood of six healthy persons

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (g)</th>
<th>Blood</th>
<th>$C_{\text{max}}$ (μg/ml)/$T^<em>$ (h) in</em>:</th>
<th>Forearm sweat</th>
<th>MIC$_{50}$ (μg/ml) for*:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Axilla sweat</td>
<td></td>
<td></td>
<td>MSS</td>
</tr>
<tr>
<td>Benzylpenicillin</td>
<td>1.2</td>
<td>27/0.5 (9–44)</td>
<td>2.6, 2.1, 0.1$^{b}$/0.5–2</td>
<td>1.5, 0.4$^{c}$/0.5</td>
<td>0.03</td>
</tr>
<tr>
<td>Phenoxymethylpenicillin</td>
<td>1.2</td>
<td>8/1 (4.1–14)</td>
<td>0.4$^{d}$/4</td>
<td>0</td>
<td>0.06</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>1.5</td>
<td>62/1 (40–113)</td>
<td>7.8$^{e}$/0.5</td>
<td>3.1$^{f}$/3</td>
<td>1–2</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2</td>
<td>372/1 (82–480)</td>
<td>8.9/0.5 (0.7–16.2)</td>
<td>2.5/0.5 (0.9–6.0)</td>
<td>4</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>2</td>
<td>360/1 (160–920)</td>
<td>28.4/0.5 (1.1–70)</td>
<td>11/2 (1.0–23)</td>
<td>4–8</td>
</tr>
</tbody>
</table>

$^{a}$ Mean peak concentration in serum or sweat ($C_{\text{max}}$)/time after administration of drug. Ranges of $C_{\text{max}}$ are given in parentheses.

$^{b}$ Three of six persons had measurable concentrations (all are listed) (lower limit of detection, 0.1 μg/ml).

$^{c}$ Two of six persons had measurable concentrations (both are listed) (lower limit of detection 0.1 μg/ml).

$^{d}$ One of six persons had a measurable concentration (shown) (lower limit of detection, 0.1 μg/ml).

$^{e}$ One of six persons had a measurable concentration (shown) (lower limit of detection, 0.4 μg/ml).

$^{f}$ MSS and MRS, methicillin-susceptible and methicillin-resistant staphylococci, respectively (data from reference 12).

1 g oral. Serum-conc after 2 h (single dose). $T_{1/2}$ 1 h. 
MIC set at 4 mg/L for enterococci. 
MIC set at 0.125 mg/L for other bacteria.
Moxifloxacin

0.4g po. Serum-conc after 1,4h (multiple doses). $T_{1/2}$ 8h.
MIC 0.5 mg/L.
Administered once/24h.
Linezolid

0.6g po. Serum-conc after 1-2h (multiple doses). $T_{1/2}$ 5h. MIC 4 mg/L. Administered as 0.6 g/12h.
Rifampicin

0.6g po. Serum-conc after 3h (multiple doses). $T_{1/2}$ 3h. MIC 0.064 mg/L.
Administered as 0.6g/12h.
Fucidic acid

0.5g po. Serum-conc after 2.1h (single dose). $T_{1/2}$ 16h. At multiple doses the serum-conc is stable above 100mg/L. MIC 2 mg/L. Administered as 0.5g/8h.
Dicloxacillin

0.25g po. Serum-conc after 2h (single dose). $T_{1/2}$ 0.7h.
Theoretical 1g dose inserted in the figure.
MIC 1.5 mg/L.
Administered as 1g/6h.
Clindamycin

0.15g po. Serum-conc after 2h (single dose). $T_{1/2}$ 2.4h. Theoretical 0.6g dose inserted in the figure. MIC 0.25 mg/L. Administered as 0.6g/8h.
Regimens *Staphylococcus aureus* and CoNS.

**Penicillin sensitive**

1) Amoxicillin 1 g x 4 and fucidic acid 0.75 g x 2/rifampicin 0.6 g x 2

2) Linezolid 0.6 g x 2 and fucidic acid 0.75 g x 2/rifampicin 0.6 g x 2

**Methicillin sensitive (Penicillin resistant)**

1) Dicloxacillin 1 g x 4 and fucidic ac. 0.75 g x 2/rifampicin 0.6 g x 2

2) Linezolid 0.6 g x 2 and fucidic ac. 0.75 g x 2/rifampicin 0.6 g x 2

**Methicillin resistant**

1) Linezolid 0.6 g x 2 and fucidic acid 0.75g x 2/rifampicin 0.6 g x 2

2) Alternative regiments depending on patterns of resistance
Regimen

Enterococcus faecalis

1) Amoxicillin 1 g x 4 and (rifampicin 0.6 g x 2)/moxifloxacin 0.4 g x 1

2) Linezolid 0.6 g x 2 and (rifampicin 0.6 g x 2)/moxifloxacin 0.4 g x 1
Regimens
Non-hemolytic streptococci, hemolytic streptococci and *Streptococcus pneumoniae*

Amoxicillin sensitive
1) Amoxicillin 1 g x 4 and rifampicin 0.6 g x 2/moxifloxacin 0.4 g x 1
2) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2/moxifloxacin 0.4 g x 1

Amoxicillin resistant
1) Linezolid 0.6 g x 2 and rifampicin 0.6 g x 2
2) Moxifloxacin 0.4 g x 1 and rifampicin 0.6 g x 2/clindamycin 0.6 g x 3
Acknowledgements

Henning Bundgaard and Kasper Iversen.

Partial oral treatment of endocarditis

Financing

The Danish Heart Foundation,
The Capitals Research Foundation
Au revoir on June 26th in Russia.
General concept of inclusion

- The patient is clinically stable
- The infection is well-controlled
- The valve lesion(s) are stable
- Only certain bacteria
## Guidelines on the prevention, diagnosis, and treatment of infective endocarditis

### Table 18  Criteria which determine suitability of outpatient parenteral antibiotic therapy (OPAT) for infective endocarditis

<table>
<thead>
<tr>
<th>Phase of treatment</th>
<th>Guidelines for use</th>
</tr>
</thead>
</table>
| Critical phase (weeks 0–2)         | Complications occur during this phase.  
Preferred inpatient treatment during this phase.  
**Consider OPAT**: if oral streptococci, patient stable, no complications. |
| Continuation phase (beyond week 2) | **Consider OPAT**: if medically stable.  
**Do not consider OPAT**: if heart failure, concerning echocardiographic features, neurological signs, or renal impairment |
| Essential for OPAT                 | Educate patient and staff.  
Regular post discharge evaluation (nurses 1/day, physician in charge 1–2/week).  
Prefer physician-directed program, not home-infusion model. |

Adapted from Andrews and von Reyn.\(^{159}\)
Reasons for in-hospital treatment in infectious endocarditis 1

- To treat optimally to reduce the high mortality rate – 9-40%
  - Cardiac complications
    - Worsening valve lesions
    - Abscess formation
    - Heart failure
    - Conduction defects (AV-block) and arrhythmia
    - Pericarditis – myocarditis
  - Assessing need for - and timing of surgery
Reasons for in-hospital treatment in infectious endocarditis 2

• To treat other (associated) infections
• To treat co-morbidities; dialysis, strokes, COPD, DM
• To reduce and treat complications
  – Treatment failure
  – Emboli – neurological complications
  – Acute renal failure
  – Splenic abscess
  – Drug fever and other treatment related complications