OUTPATIENT ANTIBIOTIC THERAPY (OPAT)

Bugs, Drugs and...
OPAT Data (RJH & CDH)

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Director, Antimicrobial Stewardship
Vancouver Island Health Authority
OBJECTIVES

- Review the IV antibiotics commonly used in OPAT (focus on cellulitis)
- Review OPAT data from RJH (2006)
- Review some recent OPAT data from CDH (2012)
- You learn something new useful
Out-Patient Antibiotic Therapy (OPAT) and Home IV are really the same thing

1. True
2. False
Why do we give IV antibiotics when we have oral antibiotics that have nearly 100% bioavailability

1. Oral antibiotics never work as well as IV antibiotics in any infection
2. IV antibiotics often have increased blood levels and usually help to treat infections more rapidly
3. Oral antibiotics are unreliable in severe infections where patients are really sick
4. IV antibiotics provide more patients confidence even though oral antibiotics may work
Cellulitis Yes or No
The clinical presentation of cellulitis is similar to other conditions, and diagnostic errors are common.

Study #1: Levell et al (2011)
N=635 pts diagnosed with cellulitis
Confirmed cellulitis = 425 (67%)

Study #2: David et al (2011)
N=145 pts diagnosed with cellulitis
Confirmed cellulitis = 104 (72%)

Research indicates that about half of cases of misdiagnosed cellulitis are venous eczema; a smaller percentage are lymphoedema and lipodermatosclerosis (Quartey-Papafio, 1999; Cox, 2002; Levell et al, 2011).
FIG. 3. Severe irritant contact dermatitis with focal areas of vesiculation.
**Table 1.** Differential diagnosis for cellulitis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Distinctive clinical features</th>
</tr>
</thead>
</table>
| Stasis dermatitis       | Bilateral involvement  
|                         | Prominence over medial malleoli  
|                         | Post-inflammatory  
|                         | hyperpigmentation changes  
|                         | Response to leg elevation, compression, and topical steroid use  |
| Contact dermatitis      | Presence of pruritis  
|                         | Nonorganic or geometric distribution of skin reaction  
|                         | Report of exposure to an irritating agent  |
| Thrombophlebitis and DVT| Presence of risk factors for DVT  
|                         | (active cancer, history of immobilization, positive family history)  
|                         | Elevated D-dimer test  
|                         | Positive compression ultrasound test  |
| Panniculitis            | Lesions at multiple sites  
|                         | Recurrence of lesions  
|                         | History of previous episodes  |
| Erythema migrans       | Targetoid lesion with central clearing (in some cases)  
|                         | Occurrence in the spring or summer  
|                         | History of a tick bite (in some cases)  
|                         | Recent travel to endemic areas (Northeast, Upper Midwest, and Northwest United States, and parts of Canada, Europe, and Asia)  |
| Cellulitis              | Erythema, pain, warmth, and edema  
|                         | Unilateral (in most cases)  
|                         | Smooth and ill-defined borders  
<p>|                         | History of predisposing factors (skin trauma, tinea pedis or onychomycosis, lymphatic or vascular compromise, immunosuppression or neutropenia)  |</p>
<table>
<thead>
<tr>
<th>Primary Infections</th>
<th>Secondary Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erysipelas</td>
<td>Diabetic foot infections</td>
</tr>
<tr>
<td>Impetigo</td>
<td>Pressure sores</td>
</tr>
<tr>
<td>Lymphangitis</td>
<td>Bite wounds</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Animal</td>
</tr>
<tr>
<td>Necrotizing fasciitis</td>
<td>Human</td>
</tr>
<tr>
<td>Type I</td>
<td>Burn wounds</td>
</tr>
</tbody>
</table>

**Primary Infections**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erysipelas</td>
<td>Group A streptococci</td>
</tr>
<tr>
<td>Impetigo</td>
<td><em>Staphylococcus aureus</em>, group A streptococci</td>
</tr>
<tr>
<td>Lymphangitis</td>
<td>Group A streptococci; occasionally <em>S. aureus</em></td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Group A streptococci, <em>S. aureus</em>; occasionally other gram positive cocci, gram-negative bacilli, and/or anaerobes</td>
</tr>
<tr>
<td>Necrotizing fasciitis Type I</td>
<td>Anaerobes (<em>Bacteroides</em> spp., <em>Peptostreptococcus</em> spp.) and facultative bacteria (<em>streptococci, Enterobacteriaceae</em>)</td>
</tr>
<tr>
<td>Necrotizing fasciitis Type II</td>
<td>Group A streptococci</td>
</tr>
</tbody>
</table>

**Secondary Infections**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic foot infections</td>
<td><em>S. aureus</em>, streptococci, <em>Enterobacteriaceae</em>, <em>Bacteroides</em> spp., <em>Peptostreptococcus</em> spp., <em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>Pressure sores</td>
<td><em>S. aureus</em>, streptococci, <em>Enterobacteriaceae</em>, <em>Bacteroides</em> spp., <em>Peptostreptococcus</em> spp., <em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>Burn wounds</td>
<td><em>Pseudomonas aeruginosa, Enterobacteriaceae, S. aureus</em>, streptococci</td>
</tr>
</tbody>
</table>

[http://infectionnet.org/notes/microbiology/]
For uncomplicated cellulitis in an OPAT setting, which of the following IV antibiotics would you choose?

1. Cefazolin
2. Clindamycin
3. Ceftriaxone
4. Vancomycin
5. Any of the above
Antimicrobial Stewardship

The best agent?

- Good activity (kill)
- Narrow spectrum
- Safety

Tie breaker .... Least costly
Vancomycin is more effective than cefazolin for staphylococcus aureus however we want to keep it in reserve because of toxicity and cost

1. True
2. False
Ceftriaxone is more effective than cefazolin for cellulitis ...and it’s better because it only needs to be given once daily

1. True
2. False
Once-Daily Intravenous Cefazolin Plus Oral Probenecid Is Equivalent to Once-Daily Intravenous Ceftriaxone Plus Oral Placebo for the Treatment of Moderate-to-Severe Cellulitis in Adults

M. Lindsay Grayson,1,2,4 Malcolm McDonald,5 Kimberley Gibson,2 Eugene Athan,5 Wendy J. Munckhof,6 Phillip Paull,3 and Fran Chambers3

1Infectious Diseases and Clinical Epidemiology Department and 2Hospital-in-the-Home Unit, Monash Medical Centre, 3Clinical Biochemistry Department, St. Vincent’s Hospital, and 4Department of Epidemiology & Preventive Medicine, Monash University, Melbourne, 5Hospital-in-the-Home Unit and Infectious Diseases Department, Geelong Hospital, Geelong, and 6Infection Management Service, Princess Alexandria and District Health Service, Ipswich Hospital, Brisbane, Australia

1440 • CID 2002:34 (1 June) • Grayson et al.
Uncomplicated Cellulitis Therapy Choices - OPAT

- Cefazolin 2gm IV + probenecid 1 gm po daily

- Clindamycin 600mg IV daily with clindamycin 450- 600mg po taken at 8 and 16 hr post IV

- Ceftriaxone 1gm IV daily

http://infectionnet.org/therapy-recommendations/cellulitis-therapy/
If you started IV antibiotic therapy in this patient with cellulitis.

When would it be OK to switch to oral therapy

1. Clear clinical improvement
   - Erythema is less intense
   - Less pain/swelling/warmth
   - Temp normalizing

2. Patient has received 2-3 days of IV therapy

Total therapy usually 7 days for uncomplicated cellulitis. Patients who are slower to respond may need longer course
Patient reports an allergy to penicillin

Reaction?

When?

Drug involved?
CUTANEOUS REACTIONS

NON-URTICARIAL

94%

Morbilliform/ Maculopapular

Pink macules with slightly raised papules

Bullous /Exfoliative

• Erythema multiforme- Minor
• Major (Stevens-Johnson)
• TEN
• Fixed Drug Eruptions

URTICARIAL (Hives)

5%

• Primary lesion a wheal
• Itchy
• Duration 1 – 24h

Boston Collaborative Drug Surveillance Program JAMA 1986;256:3358-3363

15,438 patients  Cutaneous reactions – 347 (2.2%)
PROBENECID

- Competitive inhibitor of secretion of weak organic acids (e.g. penicillins, cephs, NSAID)
- Increases antibiotic concentrations, extends elimination half-life and prolongs duration of action
- Ineffective when renal function impaired (GFR less than 50ml/min)
- May cause GI upset – take with food
- Can precipitate acute gout attack

Drug Interaction
- NSAIDs
- Methotrexate
**Clindamycin** (600mg po TID)

- Oral bioavailability 90%

**Patient Instructions:**
- Report any severe diarrhea up to several weeks following completion of therapy
- Don’t take any antidiarrheals prior to physician assessment

**Trimethoprim/Sulfamethoxazole** (1-2 DS po BID)

- Oral bioavailability greater than 90%

**Patient Instructions:**
- Drinks lots of fluid to decrease risk of urolithiasis
- Can cause photosensitivity use sunscreen

**Doxycycline** (100mg po BID)

- Oral bioavailability greater than 90%
- Avoid in pregnancy (children less than 8 yrs)

**Patient Instructions:**
- Take with food to decrease gastric irritation and potential esophageal irritation
- Caution photosensitivity
A few words about MRSA

http://infectionnet.org/therapy-recommendations/community-acquired-mrsa/

<table>
<thead>
<tr>
<th>Table 1 Differences between HA-MRSA and CA-MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Presence of risk factors</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Type of SCCmec gene</td>
</tr>
<tr>
<td>Panton-Valentin leukocidin</td>
</tr>
<tr>
<td>Resistance to &gt;3 antibiotics</td>
</tr>
<tr>
<td>Invasive infections</td>
</tr>
<tr>
<td>SSTI</td>
</tr>
<tr>
<td>Associated clinical syndromes</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Skin and soft tissue infections (furuncles, skin abscesses, cellulitis, folliculitis, impetigo, fasciitis, pyomyositis, wound infections), postinfluenza necrotizing pneumonia</td>
</tr>
<tr>
<td>Typical antimicrobial susceptibilities</td>
</tr>
<tr>
<td>Vancomycin</td>
</tr>
<tr>
<td>Linezolid</td>
</tr>
<tr>
<td>Rifampin</td>
</tr>
<tr>
<td>TMP/SMX</td>
</tr>
<tr>
<td>Tetracycline</td>
</tr>
<tr>
<td>Clindamycin</td>
</tr>
<tr>
<td>Macrolides</td>
</tr>
<tr>
<td>Gentamicin</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
</tr>
</tbody>
</table>

S = susceptible; R = resistant; V = variable; TMP/SMX = trimethoprim/sulfamethoxazole
OPAT EVALUATION

Preliminary data

Dr. Richard Bachand
Manager, Clinical Programs
Department of Pharmacy
Data is being collected by the OPAT team using a detailed data collection form...and entered an access database
EVALUATION

Dates: 05-Sept-06 to 24-Nov-06 (11.5 weeks)

Number of Patient Encounters: 112

Percent of OPAT Visit by Individual Patients

Only one or two repeats
Distribution of OPAT Patients by Visit Duration

Visit Duration (Hr) | Number of Patients
--- | ---
0.5 | 4
1 | 13
1.5 | 19
2 | 10
2.5 | 23
3 | 15
3.5 | 9
4 | 4
5 | 2
6 | 1

Total count 100
OPAT Age Distribution by Gender

Number of Patients

AGE

Female

Male

4 14 5 3 4 2 1

3 3 5 8 3 1 1

10-20 20-30 30-40 40-50 50-60 60-70 70-80 80-90 90-100
## MRSA STATUS

<table>
<thead>
<tr>
<th>MRSA</th>
<th>CountOfMRSA</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>16</td>
<td>14.3%</td>
</tr>
<tr>
<td>Unknown</td>
<td>72</td>
<td>64.3%</td>
</tr>
<tr>
<td>Yes</td>
<td>24</td>
<td>21.4%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>112</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

![OPAT MRSA Distribution Diagram](image-url)
## DISTRIBUTION by Infectious Disease Diagnosis

<table>
<thead>
<tr>
<th>Infectious Diagnosis</th>
<th>Count Of Infectious Diagnosis</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated Cellulitis</td>
<td>48</td>
<td>42.9%</td>
</tr>
<tr>
<td>Complicated Cellulitis</td>
<td>42</td>
<td>37.5%</td>
</tr>
<tr>
<td>Diabetic Foot</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>Bone &amp; Joint</td>
<td>3</td>
<td>2.7%</td>
</tr>
<tr>
<td>Odontogenic</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>UTI</td>
<td>2</td>
<td>1.8%</td>
</tr>
<tr>
<td>Respiratory Tract</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>6.3%</td>
</tr>
<tr>
<td>N/A</td>
<td>7</td>
<td>6.3%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>112</strong></td>
<td><strong>100.0%</strong></td>
</tr>
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</table>
OPAT OUTCOME
First Clinic Visit

1: 4.5 patients switched to oral therapy on the first visit
Percentage of Antimicrobial Regimen Use
OPAT

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Cefazolin</th>
<th>Ceftriaxone</th>
<th>Clindamycin</th>
<th>Vancomycin</th>
<th>Ertapenem</th>
<th>Fluconazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td>57.5%</td>
<td>17.5%</td>
<td>2.5%</td>
<td>18.8%</td>
<td>2.5%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>
OPAT – CDH
Aug 1 - 27, 2012

Patients = 53
CDH- OPAT Patients  
(Aug 1-27, 2012)

Age Distribution by Gender

Female

[Bar chart showing age distribution for females with median age of 33 years]

Male

[Bar chart showing age distribution for males with median age of 51 years]
CDH- OPAT Patients
(Aug 1-27, 2012)

Total Patients = 53
CDH- OPAT Patients
(Aug 1- 27, 2012)

SSTI

- Ceftriaxone 39% (15 patients)
- Cefazolin 55% (21 patients)
- Clinda 5%
- Clinda + Vanco 3%

N = 38
CDH- OPAT Patients
(Aug 1- 27, 2012)

UTI

N = 9
CDH- OPAT Patients
(Aug 1- 27, 2012)

**Duration of IV therapy**
- Mean: 4 days (Range 1 – 13)
- Median: 3 days

**Number of OPAT patients/day**
- Mean: 7.8 patients (Range 3 – 11)
- Median: 8 patients
CLINDAMYCIN
600 mg in 100 mL 5% Dextrose in Water

Refrigrerato
LOT: 0912061   EXP: 07NOV12
VHA (58) Pharmacy