

OPAT: Mythbusters EM Grand Rounds 2019

Based on some small 4x RCT + Cochrane review 2010:
PO appears to be non-inferior to IV treatment for non-purulent SSTI.

Why Oral antibiotics might have failed?

1. Is the antibiotic getting where it needs to be?
2. Is the patient Under dosed (think obese BMI>30)
3. Do we have the right source/ antibiotic? (ie. Clindamycin =high resistance to strep)
4. Non-compliant patient
5. Timeline (minimum 48h)
6. Is there an infection? (think: cellulitis mimics!)
7. Is it a complicated infection?
→ poor blood supply, adequate source control?, foreign bodies?

Treatment failure timeline:
- no validated defn'

minimum 48h - 96h likely acceptable, as per expert opinion.

EP Role in OPAT:

1. Decide if indication for OPAT
2. Appropriate selection of antimicrobial
3. Duration of therapy
4. Subsequent medical evaluations

Bioavailability:

The percentage of the medication that enters the circulation

IV for patients with:

1. Poor perfusion (critically ill)
2. GI malabsorption
3. Obesity (BMI>30)

SSTI

Cefazolin + Cephalexin combined → **has NO evidence**

Cefazolin + Probenecid → B-hemolytic strep + MSSA coverage (dec. risk of C.diff + narrower spectrum of activity compared to Ceftriaxone) **ONLY STUDIED IN UNCOMPLICATED SSTI, no evidence for its use in Complicated or Polymicrobial SSTI (ie. DFI, chronic wounds, animal/human bites, trauma, OM septic arthritis, deep infections.)**

Obese patients: high risk of po failure (due to: underdosing, poor volume of distribution) if high BMI>30, consider **IV Ceftriaxone 3g daily, or 2g BID**

Predictors associated with oral Abx failure (Yadav 2019)

Dx of cellulitis past year
Erosion/ulcer, chronic
RR>20
MRSA hx

DFI

Complicated and polymicrobial → low threshold to refer to ID
Preferred Management:

1. Start with **Ceftriaxone 2g daily + Metronidazole 500mg po BID +/- Vancomycin (if MRSA)**
2. Baseline XR for all (IDSA guidelines + local expert preference)
3. Would cultures → only if wound appropriately debrided, and a true deep wound swab, otherwise useless!
4. Ensure appropriate footwear, and improvement of pressure points

Ertapenem only if:

- prior hx of ESBL
- recent travel hx
- recent antibiotic exposure
- positive cultures

PTA/periodontal abscess

IV Clinda = second line agent, PO Clinda has 90% bioavailability

Clinda Safety Risk: Meta-analysis show that there is a high risk of CDI + pseudomembranous colitis with Clinda use compared to PCN.

PTA/ Periodontal infections = polymicrobial, mixed anaerobic>aerobic bacteria

Preferred Management:

1. Source control is key!
2. **Ceftriaxone 2g IV + Metronidazole 500mg po TID**
3. **Amox/Clav 875mg BID**
4. **Penicillin V 300-600mg po QID + Metronidazole 500mg po BID**

IV Clindamycin

ONLY if:

- True penicillin allergy + patient unable to swallow

When to Consult ID

- Complicated things
→ History of multidrug resistance, Multiple drug allergies, DFI
- Asplenic patients (+fever)
- Bites or weird exposures (low threshold)
- Bone infections (OM)
- Vancomycin patients (low threshold)
- >4 days of IV Abx treatment with little/no improvement
- Ultimately a judgement call! Consider early > later

OPAT R/A NOTE suggestions to include:

- Regular Impressions
- Patient co-morbidities
- Investigations: ordered/seen
- If referrals made (ID etc.)
- Plan:
→ original EP plan, reason for IVT, changes in mgmt (plan and why), expected clinical course, suspected pathogen.

(these notes should only be used as a guide, and should not replace appropriate clinical judgment)

Local Hospital and Community Antibiograms, as well as Bioavailability Chart of Common Antimicrobials used.

| RCH site 2018 ANTIBIOGRAM Hospital-wide (% Susceptible ^a) | GRAM POSITIVE | | | | | | | | | | | |
|---|--------------------------------------|-----------------------|----------------------|--|---|---|----------------------------|---------------------------------------|---|-------------------------------------|-------------------------------------|---|
| | Coagulase Negative Staphylococcus | Enterococcus faecalis | Enterococcus faecium | Staphylococcus aureus (MSSA + MRSA) | MRSA (Methicillin Resistant Staph. aureus) | MSSA (Methicillin Susceptible Staph. aureus) | Staphylococcus lugdunensis | Streptococcus agalactiae (Group B) | Streptococcus anginosus group ^b | Streptococcus pneumoniae | Streptococcus pyogenes (Group A) | Viridans group Streptococcus ^{1a} |
| Number of Isolates | 121 | 278 | 117 | 952 | 285 | 667 | 87 | 133 | 170 | 50 | 85 | 190 |
| Penicillins | | | | | | | | | | | | |
| Cloxacillin | 37 | R | R | 70 | R | 100 | 93 | | | N | N | |
| Penicillin (IV) | N | | | N | R | N | | 100 | 100 | 91 [†] 100 [†] | 100 | 81 |
| Penicillin (Oral) | | | | | | | | | | 91 | | |
| Ampicillin/Amoxicillin | N | 100 | 4 | N | R | N | | 100 | 100 | 100 | 100 | 83 |
| Amoxicillin-Clavulanate | | | | | R | | | | | | | |
| Piperacillin-Tazobactam | | | | | R | | | | | | | |
| Cephalosporins | | | | | | | | | | | | |
| Cephalexin - 1st gen | 37 | R | R | 70 | R | 100 | 93 | | | N | 100 | |
| Cefazolin - 1st gen | 37 | R | R | 70 | R | 100 | 93 | | | N | 100 | |
| Cefuroxime - 2nd gen | | R | R | | | | | | | 100 | | |
| Cefixime - 3rd gen | | R | R | | R | | | | | N | | |
| Cefotaxime / Ceftriaxone - 3rd gen | | R | R | | R | | | 100 | 100 | 100 | 100 | 98 |
| Ceftazidime - 3rd gen | | R | R | | R | | | | | N | N | |
| Miscellaneous | | | | | | | | | | | | |
| Erythromycin ^f | 41 | | | 63 | 26 | 79 | 90 | 66 | | 76 | 73 | |
| Clindamycin | 59 | R | R | 76 | 61 | 82 | 89 | 67 | 59 | 88 | 74 | |
| Tetracycline ^h | 88 | 20 ^d | 33 ^d | 92 | 85 | 95 | | | | 76 | | |
| Linezolid - restricted | 100 | 93 | 100 | 100 | 100 | 100 | 100 | | | | | |
| Metronidazole | | R | R | R | R | R | | | | R | R | |
| Nitrofurantoin-simple cystitis only ^d | 99 | 99 | 15 | 99 | 98 | 100 | | | | R | N | |
| TMP-SMX or Cotrimoxazole | 71 | R | R | 94 | 91 | 95 | 99 | | | 76 | | |
| Vancomycin | 100 | 98 | 33 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

Table 1. Pharmacokinetic parameters for oral antibiotics used as therapy for adults.

| Group, agent | Absorption (%) | Usual dosage | Peak serum level (mg/L)* |
|-------------------------------|------------------------------|---------------|--------------------------|
| Penicillins | | | |
| Amoxicillin | 74–92 | 500 mg q8h | 3.5–5.0 |
| Amoxicillin/clavulanate | 60 | 500 mg q8h | 3.7–4.8 |
| Ampicillin | 30–55 | 500 mg q6h | 6 |
| Dicloxacillin | 35–76 | 500 mg q8h | 10–18 |
| Penicillin | 60–73 | 500 mg q6h | 4.9–6.3 |
| Cephalosporins | | | |
| Cephalexin | 90–100 | 500 mg q6h | 15–18 |
| Cephadrine | 90–95 | 500 mg q6h | 15–18 |
| Cefaclor | >52–95 | 500 mg q6h | 13–15 |
| Cefprozil | 71–95 | 500 mg q12h | 8.2–10.4 |
| Cefuroxime axetil | 30–52 | 500 mg q12h | 7 |
| Cefixime | 30–50 | 400 mg q24h | 3.7–4.8 |
| Cefpodoxime | 29–53 | 400 mg q12h | 3.9–4.5 |
| Loracarbef | 90 | 400 mg q12h | 14 |
| Macrolides | | | |
| Azithromycin | 37 | 500 mg q24h | 0.04–0.4 |
| Clarithromycin | 55 | 500 mg q12h | 0.6–1.3 |
| Erythromycin | Depends on salt of drug used | 500 mg q6h | 0.3–3.8 |
| Tetracyclines | | | |
| Doxycycline | >90 with food | 200 mg q12h | 2.5 |
| Tetracycline | >90 with food | 500 mg q12h | 3.5 |
| Quinolones | | | |
| Ciprofloxacin | 65–85 | 500 mg q12h | 2.5 |
| Ofloxacin | 98 | 400 mg q12h | 5.5 |
| Lomefloxacin | 90–98 | 400 mg q24h | 3–4.7 |
| Other | | | |
| Chloramphenicol | 75–90 (drug base) | 500 mg q6h | 10–13 |
| Clindamycin | 90 | 300 mg q6h | 3.6 |
| Metronidazole | 80 | 500 mg q8h | 11.5 |
| Trimethoprim-sulfamethoxazole | 70–90 | 160 mg/800 mg | 1–2/40–60 |

Respiratory Tract Pathogens (Sputum)

| ORGANISM | Number of isolates tested | ANTIBIOTIC (% susceptible) | | | | | | | | | | | | | | | | | |
|---------------------------------------|---------------------------|----------------------------|-------------------------|--------------|-------------|------------|---------------|----------------|-------------|--------------|--------------|--------------|-------------------|-----|-------------|------------|-----------|-------------------------|------------|
| | | Amoxicillin - Clavulanate | Ampicillin ¹ | Azithromycin | Ceftriaxone | Cefuroxime | Ciprofloxacin | Clarithromycin | Doxycycline | Erythromycin | Levofloxacin | Tetracycline | Penicillin (oral) | TMX | Ceftazidime | Gentamicin | Meropenem | Piperacillin-Tazobactam | Tobramycin |
| Haemophilus influenzae | 213 | 98 | 67 | 100 | | 99 | | | | | 97 | R | 71 | | | | | | |
| Moraxella catarrhalis ² | 157 | | R | | | | | | | | | R | | | | | | | |
| Pseudomonas aeruginosa | 114 | | | | | 81 | | | | | | | | 92 | 87 | 96 | 95 | 99 | |
| Streptococcus pneumoniae ³ | 100 | >95 | >95 | 60 | >95 | | 60 | 47 | 60 | 98 | | >70 | 72 | | | | | | |

¹Results of ampicillin testing can be used to predict results for amoxicillin.
²Susceptibility testing for Moraxella catarrhalis is not routinely performed. Most clinical isolates of M. catarrhalis are resistant to amoxicillin but susceptible to amoxicillin-clavulanate, macrolides, trimethoprim-sulfamethoxazole, quinolones, cefuroxime, cefixime, and ceftriaxone.
³Detailed data for beta-lactam antibiotics is not available for S. pneumoniae due to differences in testing for oxacillin-susceptible and resistant strains.

Skin and Soft Tissue Pathogens

| ORGANISM | Number of isolates tested | ANTIBIOTIC (% susceptible) | | | | | | | | | | | | |
|------------------------------------|---------------------------|----------------------------|--------------|-------------|--------------------------|----------------|-------------|-------------|--------------|--------------|-----------|------------|---------------------------|-----|
| | | Ampicillin | Azithromycin | Ceftriaxone | Cephalothin / Cephalixin | Clarithromycin | Clindamycin | Cloxacillin | Erythromycin | Levofloxacin | Linezolid | Penicillin | Tetracycline ¹ | TMX |
| S. aureus (MSSA) | 8454 | | | 100 | | 84 | 100 | 79 | | | | 95 | 99 | |
| S. aureus (MRSA) | 2136 | R | | R | R | 73 | R | 26 | | 100 | R | 81 | 96 | 100 |
| Group A Streptococcus ² | 227 | 100 | 78 | 100 | 100 | 78 | 79 | 78 | 100 | | 100 | | R | 100 |
| Group B Streptococcus ² | 77 | 100 | 47 | 100 | 100 | 47 | 51 | 47 | 97 | | 100 | | R | 100 |

¹Isolates susceptible to tetracycline are predictably susceptible to doxycycline; however, some isolates that are resistant to tetracycline may be susceptible to doxycycline.
²Groups A, B, C and G streptococcal isolates are predictably susceptible to penicillin, amoxicillin and cephalosporins, therefore antimicrobial susceptibility testing is not routinely performed.

Urinary Tract Pathogens

| ORGANISM | Number of isolates tested | ANTIBIOTIC (% susceptible) | | | | | | | | |
|------------------------------------|---------------------------|----------------------------|-------------|--------------------------|---------------|-------------------------|------------|----------------|---------------------------|-----|
| | | Ampicillin ¹ | Ceftriaxone | Cephalothin / Cephalexin | Ciprofloxacin | Fosfomycin ² | Gentamicin | Nitrofurantoin | Tetracycline ³ | TMX |
| Escherichia coli | 36585 | 59 | 92 | 54 | 84 | 98 | 93 | 97 | 75 | 78 |
| Group B Streptococcus ⁴ | 6406 | | | | | | R | | | R |
| Enterococcus faecalis | 5821 | 100 | | R | 81 | 99 | | 99 | 21 | R |
| Klebsiella pneumoniae | 4295 | R | 96 | 94 | 97 | | 98 | 36 | 88 | 94 |
| Proteus mirabilis | 2231 | 79 | 97 | 92 | 89 | | 92 | R | R | 79 |

¹ Results of ampicillin testing can be used to predict results for amoxicillin.
² Fosfomycin testing was performed on a limited number of E. coli (n=2551) and E. faecalis (n=269) isolates.
³ Isolates susceptible to tetracycline are predictably susceptible to doxycycline; however, some isolates that are resistant to tetracycline may be susceptible to doxycycline.
⁴ Antimicrobial susceptibility testing is not routinely performed on urine isolates of group B Streptococcus because such infections usually respond to antibiotics commonly used to treat uncomplicated urinary tract infections, such as ampicillin, cephalosporins and nitrofurantoin. Susceptibility to fluoroquinolones is variable.