

## 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 <sup>a</sup> )	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 <sup>b</sup>	Streptococcus pneumoniae	Streptococcus pyogenes (Group A)	Viridans group Streptococcus <sup>1a</sup>
<b>Number of Isolates</b>	121	278	117	952	285	667	87	133	170	50	85	190
<b>Penicillins</b>												
Cloxacillin	37	R	R	70	R	100	93			N	N	
Penicillin (IV)	N			N	R	N		100	100	91 <sup>†</sup> 100 <sup>†</sup>	100	81
Penicillin (Oral)										91		
Ampicillin/Amoxicillin	N	100	4	N	R	N		100	100	100	100	83
Amoxicillin-Clavulanate					R							
Piperacillin-Tazobactam					R							
<b>Cephalosporins</b>												
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	
<b>Miscellaneous</b>												
Erythromycin <sup>f</sup>	41			63	26	79	90	66		76	73	
Clindamycin	59	R	R	76	61	82	89	67	59	88	74	
Tetracycline <sup>h</sup>	88	20 <sup>d</sup>	33 <sup>d</sup>	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 <sup>d</sup>	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)*
<b>Penicillins</b>			
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
<b>Cephalosporins</b>			
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
Cefepodoxime	29–53	400 mg q12h	3.9–4.5
Loracarbef	90	400 mg q12h	14
<b>Macrolides</b>			
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
<b>Tetracyclines</b>			
Doxycycline	>90 with food	200 mg q12h	2.5
Tetracycline	>90 with food	500 mg q12h	3.5
<b>Quinolones</b>			
Ciprofloxacin	65–85	500 mg q12h	2.5
Ofloxacin	98	400 mg q12h	5.5
Lomefloxacin	90–98	400 mg q24h	3–4.7
<b>Other</b>			
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 <sup>1</sup>	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 <sup>2</sup>	157		R									R							
Pseudomonas aeruginosa	114					81								92	87	96	95	99	
Streptococcus pneumoniae <sup>3</sup>	100	>95	>95	60	>95		60	47	60	98		>70	72						

<sup>1</sup>Results of ampicillin testing can be used to predict results for amoxicillin.  
<sup>2</sup>Susceptibility 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.  
<sup>3</sup>Detailed 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 <sup>1</sup>	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 <sup>2</sup>	227	100	78	100	100	78	79	78	100		100		R	100
Group B Streptococcus <sup>2</sup>	77	100	47	100	100	47	51	47	97		100		R	100

<sup>1</sup>Isolates susceptible to tetracycline are predictably susceptible to doxycycline; however, some isolates that are resistant to tetracycline may be susceptible to doxycycline.  
<sup>2</sup>Groups 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 <sup>1</sup>	Ceftriaxone	Cephalothin / Cephalexin	Ciprofloxacin	Fosfomycin <sup>2</sup>	Gentamicin	Nitrofurantoin	Tetracycline <sup>3</sup>	TMX
Escherichia coli	36585	59	92	54	84	98	93	97	75	78
Group B Streptococcus <sup>4</sup>	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

<sup>1</sup> Results of ampicillin testing can be used to predict results for amoxicillin.  
<sup>2</sup> Fosfomycin testing was performed on a limited number of E. coli (n=2551) and E. faecalis (n=269) isolates.  
<sup>3</sup> Isolates susceptible to tetracycline are predictably susceptible to doxycycline; however, some isolates that are resistant to tetracycline may be susceptible to doxycycline.  
<sup>4</sup> 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.