

# Outpatient Parenteral Antimicrobial Therapy

## Lyon experience

(Products [agents & devices] – types, routes, transport,  
storage, administration)

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**HCL**  
HOSPICES CIVILS  
DE LYON



# Outpatient Parenteral Antimicrobial Therapy

## OPAT

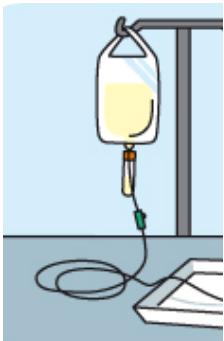
- Relevant for patients with BJI
  - **Empirical treatment** at home pending the results
  - **Targeted** therapy in patients with few/no oral options
- Limitation:
  - Max. number of nurse visits at home per day: **2**

WHY  
OPAT'ing?



# Outpatient Parenteral Antimicrobial Therapy

## CLASSICAL IV PERFUSION



- 30 min perfusion
- Every 12 or 24 hours
- Use only drugs that have a long half life
- Ex: ceftriaxone

## OPAT

### ELASTOMERIC PUMP



- Continuous infusion
- Flow rate not perfectly accurate
  - Viscosity, Temperature
- Use only drugs that are stable after dilution
- Ex: piperacilline/tazobactam

Need for a vascular access  
Mid-line or PICC-line



Patient exposed  
to catheter complications

## HOW OPAT'ing?



### ELECTRONIC INFUSION DEVICE

- Preparation
- For sequential administrations
- Every 24h
- High infusion rate accuracy
- Use only drugs that are stable after dilution
- Ex: **fosfomycin (4 hours-infusion each 8 hours; in combination)**

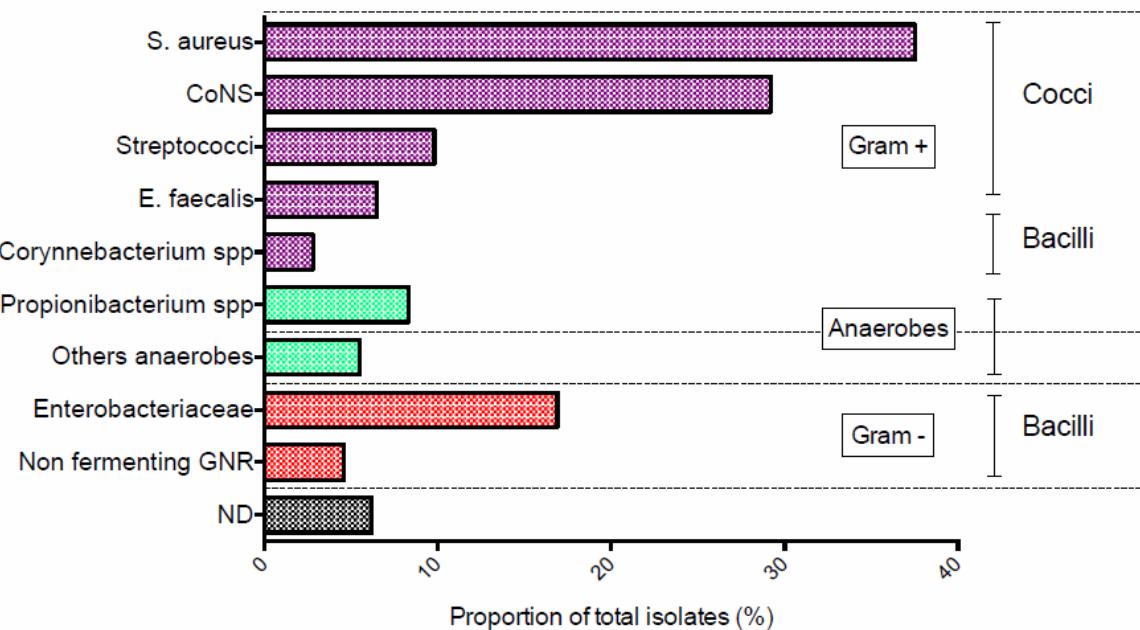
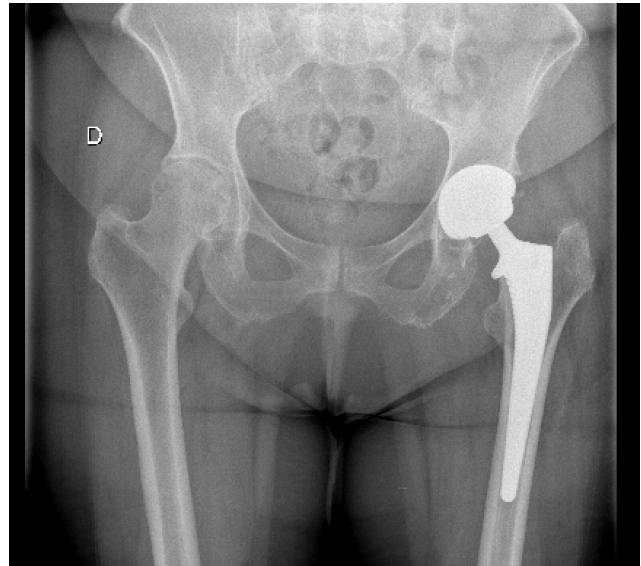
# Clinical case #1

64-year-old woman

71 kg, normal creatinine clearance

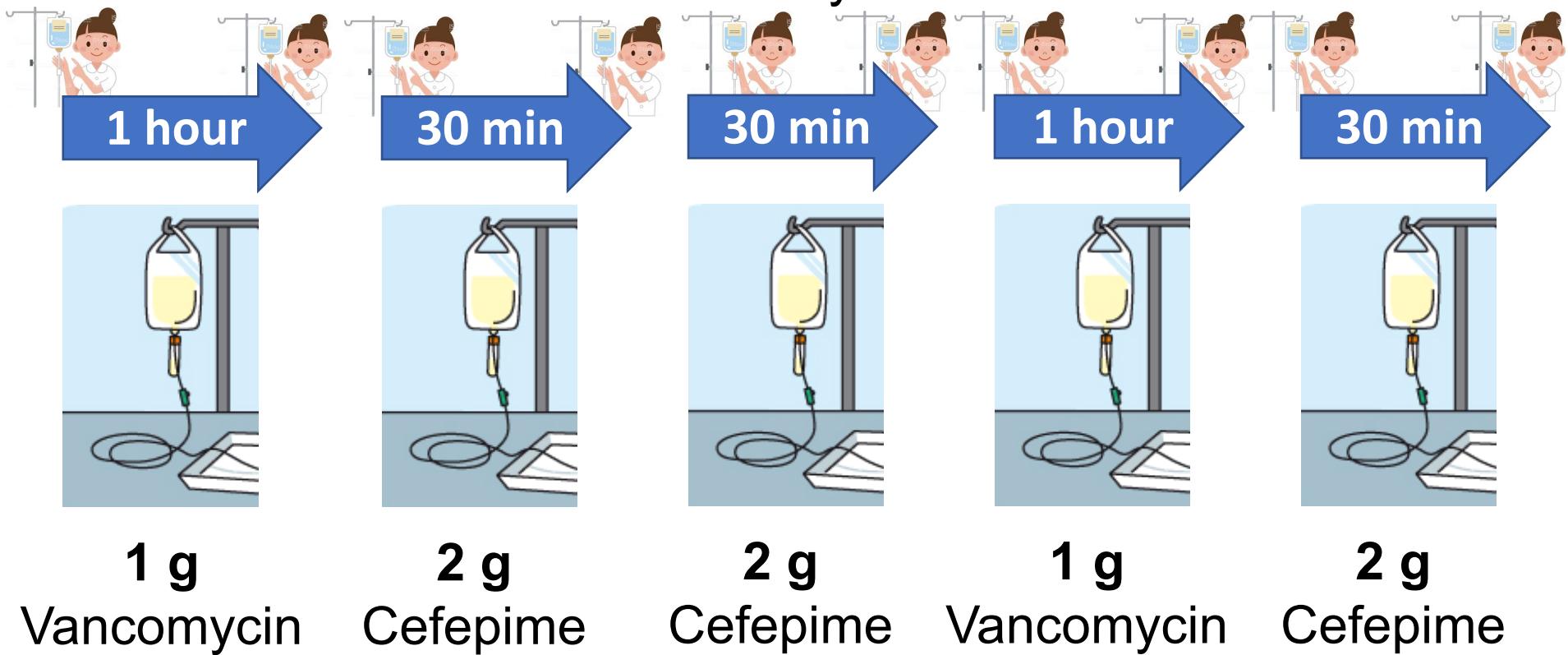
Acute PJI

Treated with ‘DAIR’



# INpatient Parenteral Antimicrobial Therapy

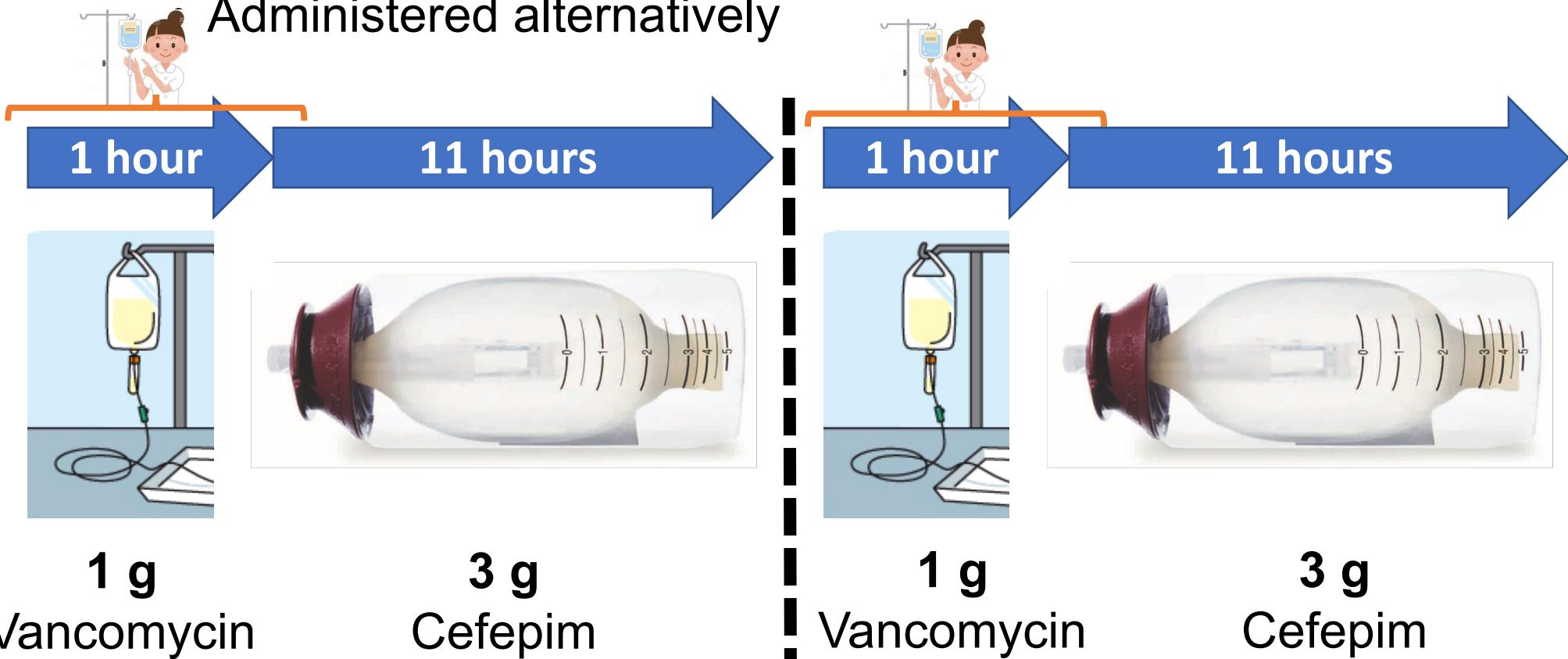
- Empirical IV antibiotherapy
  - Combination of Vancomycin (2g/d) + Cefepime (6g/d)
  - Administered alternatively



# Outpatient Parenteral Antimicrobial Therapy

- Empirical IV antibiotherapy
  - Combination of Vancomycin (2g/d) + Cefepime (6g/d)

Administered alternatively



# Antibiotics in elastomeric infusors

- **Beta-lactams**

- Rapidly metabolized by the host (short half-life)
- Requiring usually several injections per day and usable as continuous infusion
- Ex: **amoxicillin, piperacillin/tazobactam, cefepime**

# Antibiotics in elastomeric infusors

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- **Stability of the drug into the infusor is influenced**

- Dilution volume (concentration)
- Type of solvant (NaCl 0.9% or G5%)
- Temperature (body temperature)

Recommendation/Recommandations

Preparing and administering injectable antibiotics:  
How to avoid playing God<sup>◊</sup>

*Longuet et al.  
Médecine et maladies  
infectieuses 2016*

# Stability of antibiotics into infusor is influenced by the final concentration

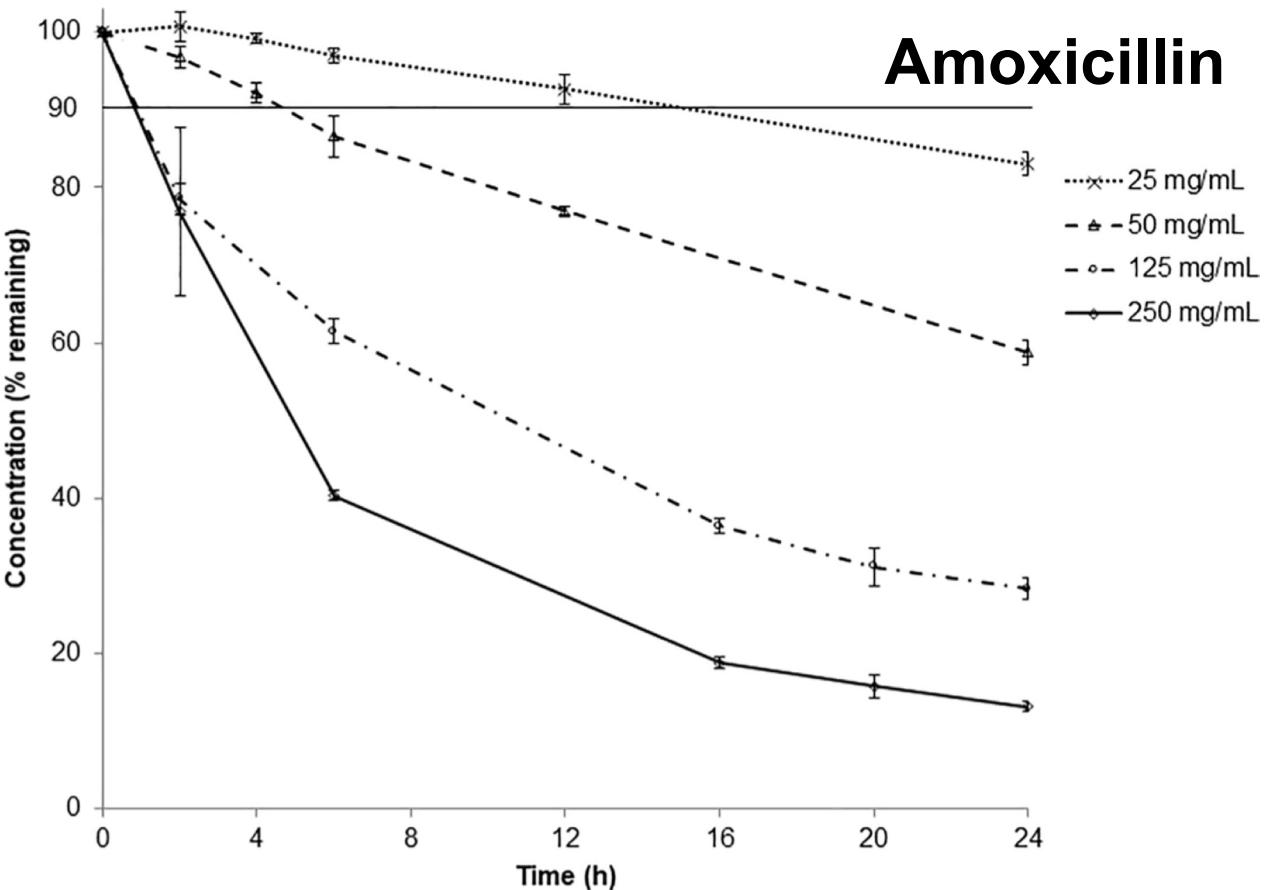


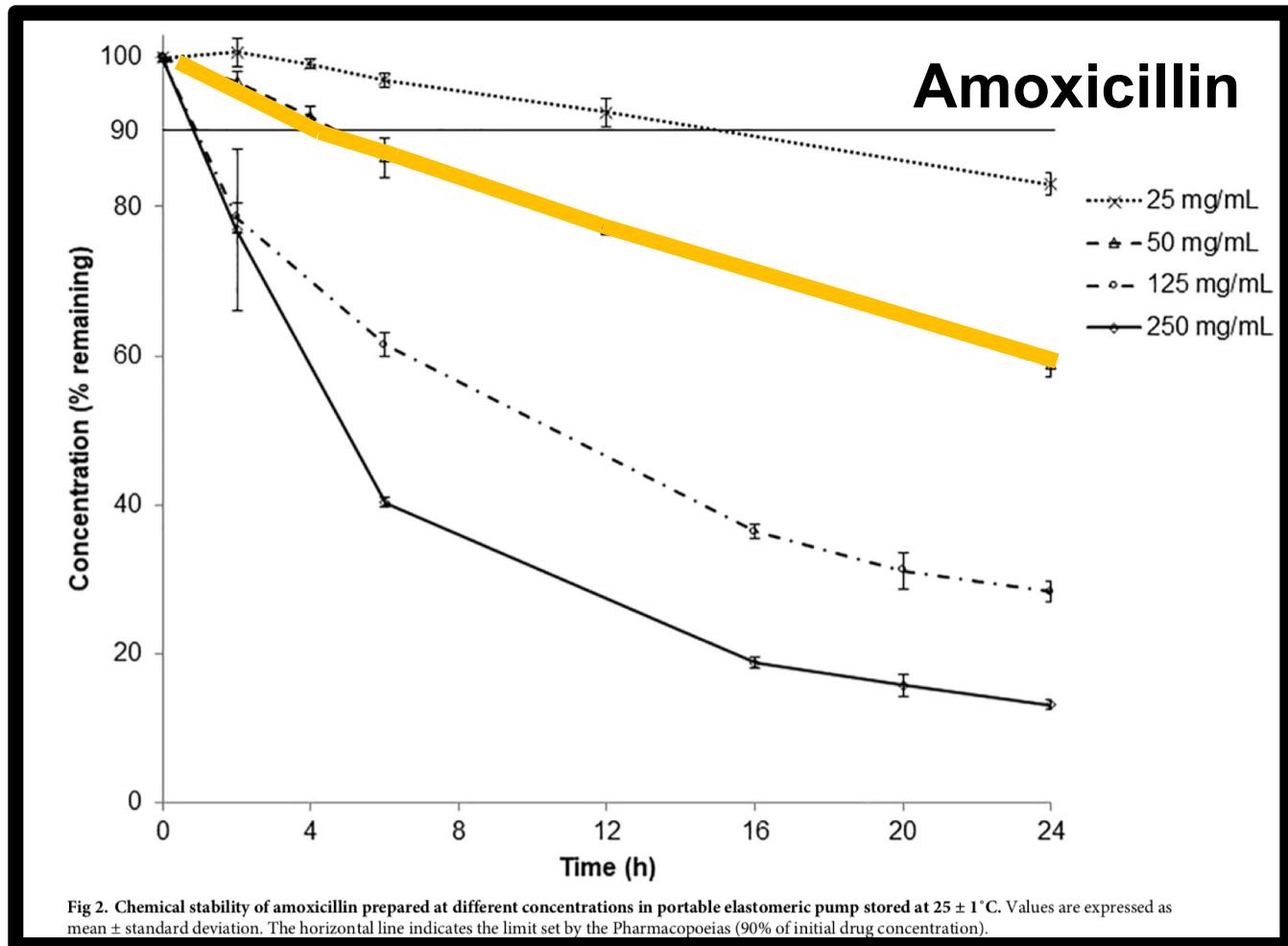
Fig 2. Chemical stability of amoxicillin prepared at different concentrations in portable elastomeric pump stored at  $25 \pm 1^\circ\text{C}$ . Values are expressed as mean  $\pm$  standard deviation. The horizontal line indicates the limit set by the Pharmacopoeias (90% of initial drug concentration).



**240 mL  
10 mL/h**

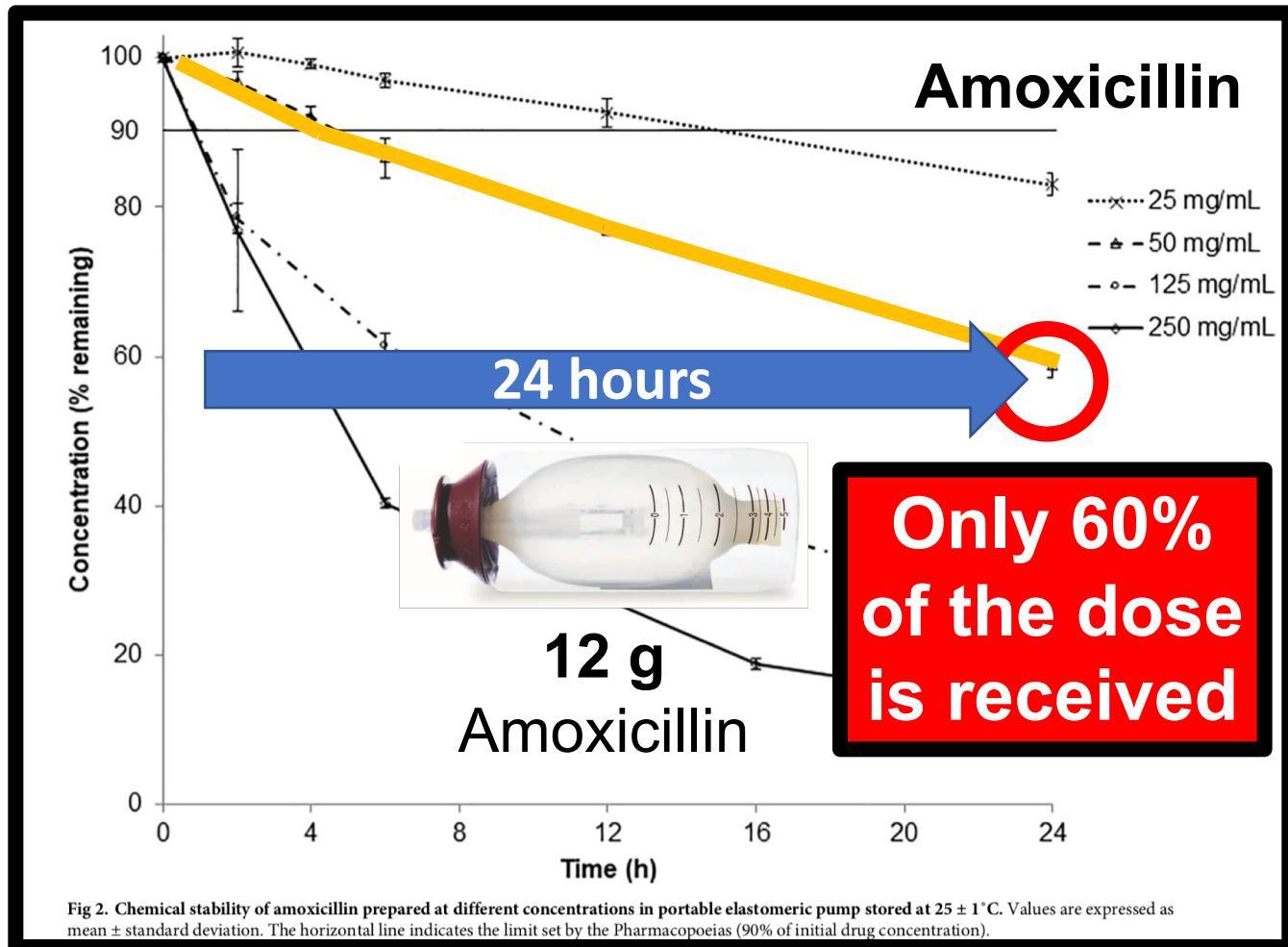
**Goal:  
12 g amoxicillin  
per day**

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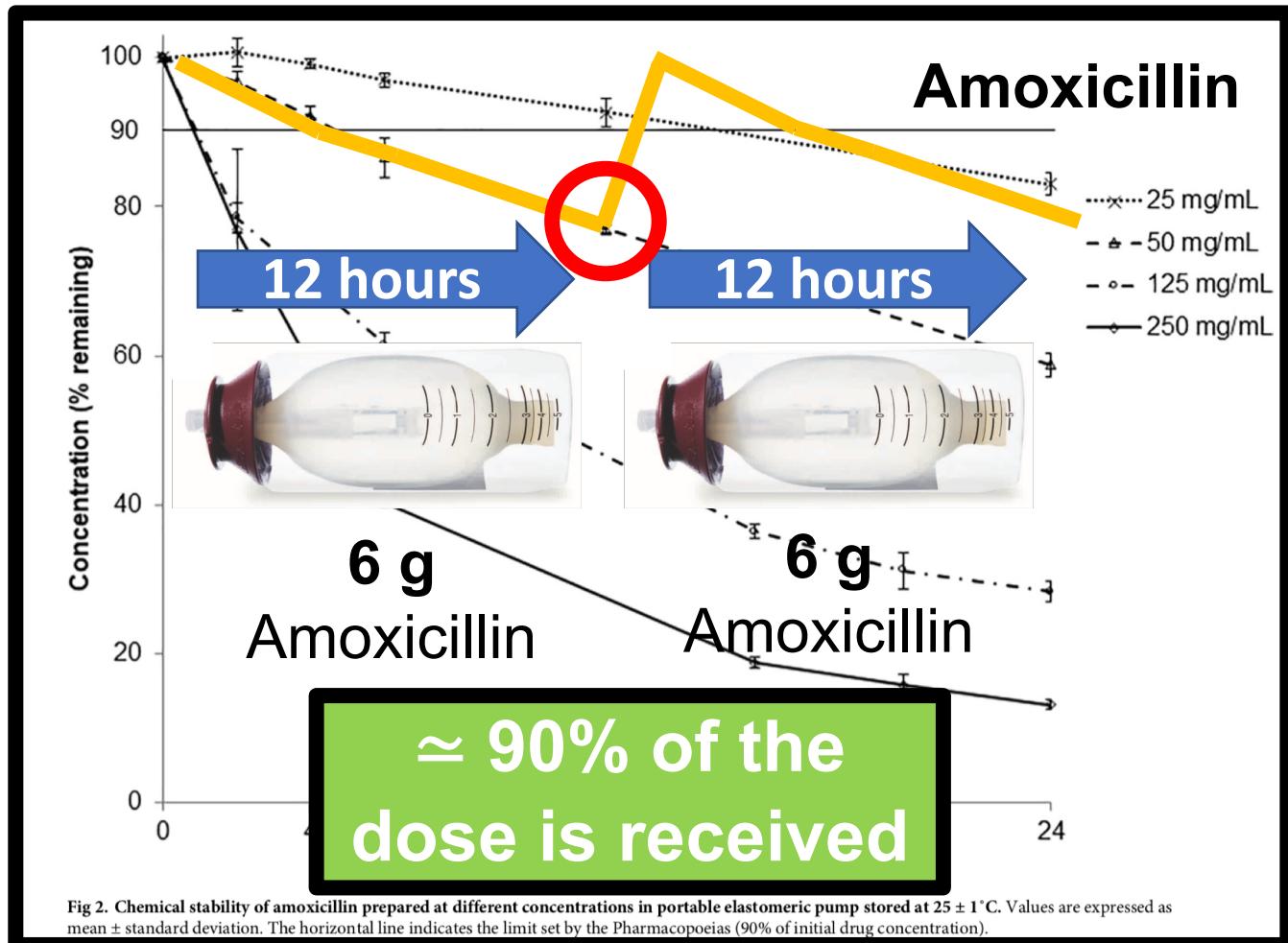
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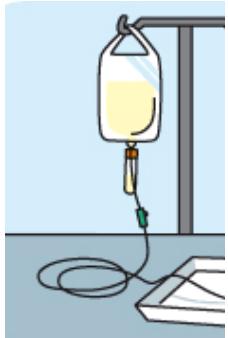


**Goal:**  
12 g amoxicillin  
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# Outpatient Parenteral Antimicrobial Therapy

**CLASSICAL IV  
PERFUSION**

**OPAT**



**WHICH  
ALTERNATIVE  
TO OPAT?**

# Outpatient SubCutaneous Antimicrobial Therapy

**OSCAT**



**SUBCUTANEOUS  
INFUSION**

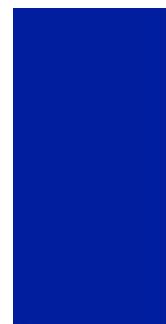
**HOW and WHY  
OSCAT'ing'?**

# 2018 IDSA Clinical Practice Guideline for the Management of Outpatient Parenteral Antimicrobial Therapy<sup>a</sup>

Anne H. Norris,<sup>1</sup> Nabin K. Shrestha,<sup>2</sup> Genève M. Allison,<sup>3</sup> Sara C. Keller,<sup>4</sup> Kavita P. Bhavan,<sup>5</sup> John J. Zurlo,<sup>6</sup> Adam L. Hersh,<sup>7</sup> Lisa A. Gorski,<sup>8</sup> John A. Bosso,<sup>9</sup> Mobeen H. Rathore,<sup>10</sup> Antonio Arrieta,<sup>11</sup> Russell M. Petrak,<sup>12</sup> Akshay Shah,<sup>13</sup> Richard B. Brown,<sup>14</sup> Shandra L. Knight,<sup>15</sup> and Craig A. Umscheid<sup>16</sup>

Subcutaneous antimicrobials have been used in other countries for some time [39–41] but their use in the United States is still investigational.

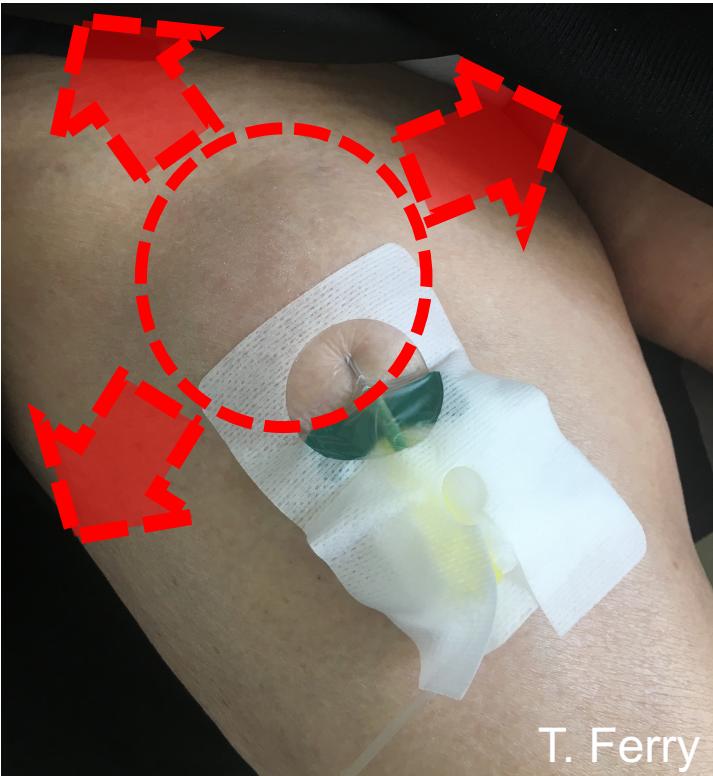
39. Forestier E, Gros S, Peynaud D, et al. Ertapenem administered intravenously or subcutaneously for urinary tract infections caused by ESBL producing enterobacteriaceae. *Med Mal Infect* 2012; 42:440–3.
40. Gauthier D, Schambach S, Crouzet J, Sirvain S, Fraisse T. Subcutaneous and intravenous ceftriaxone administration in patients more than 75 years of age. *Med Mal Infect* 2014; 44:275–80.
41. Peeters O, Ferry T, Ader F, et al.; Lyon BJI Study Group. Teicoplanin-based antimicrobial therapy in *Staphylococcus aureus* bone and joint infection: tolerance, efficacy and experience with subcutaneous administration. *BMC Infect Dis* 2016; 16:622.



# Clinical case #2

85-year-old woman

Acute PJI resistant *K. pneumoniae*  
‘DAIR’ and SC ertapenem



Ertapenem  
1g

50 mL  
NaCl 9%

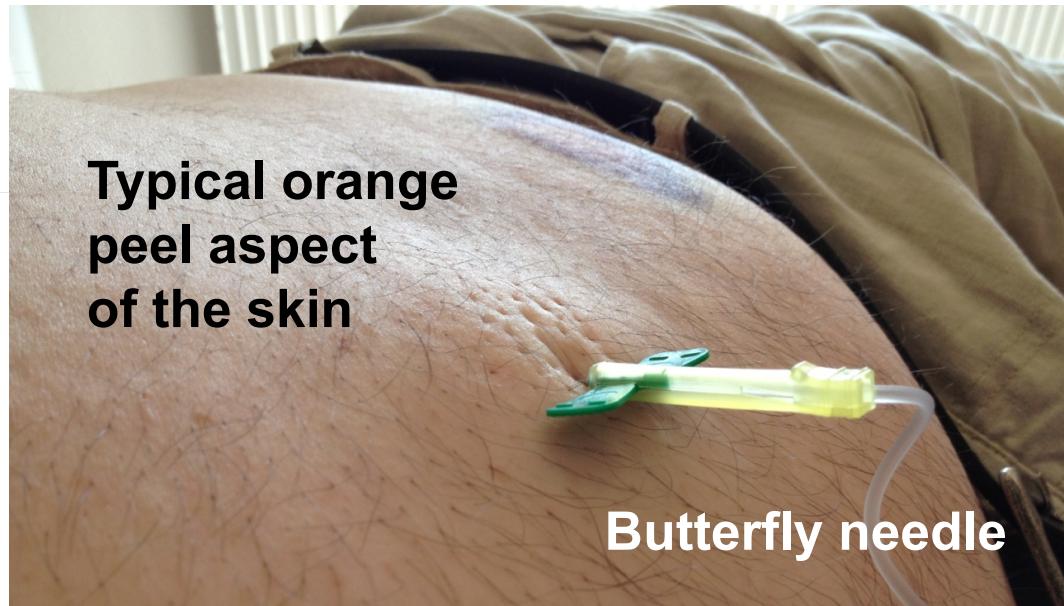
30 min  
gravity  
infusion



# Post-traumatic chronic boil caused by *Butyricimonas* despite multiple doses of ertapenem administered to a 30-year-old obese man

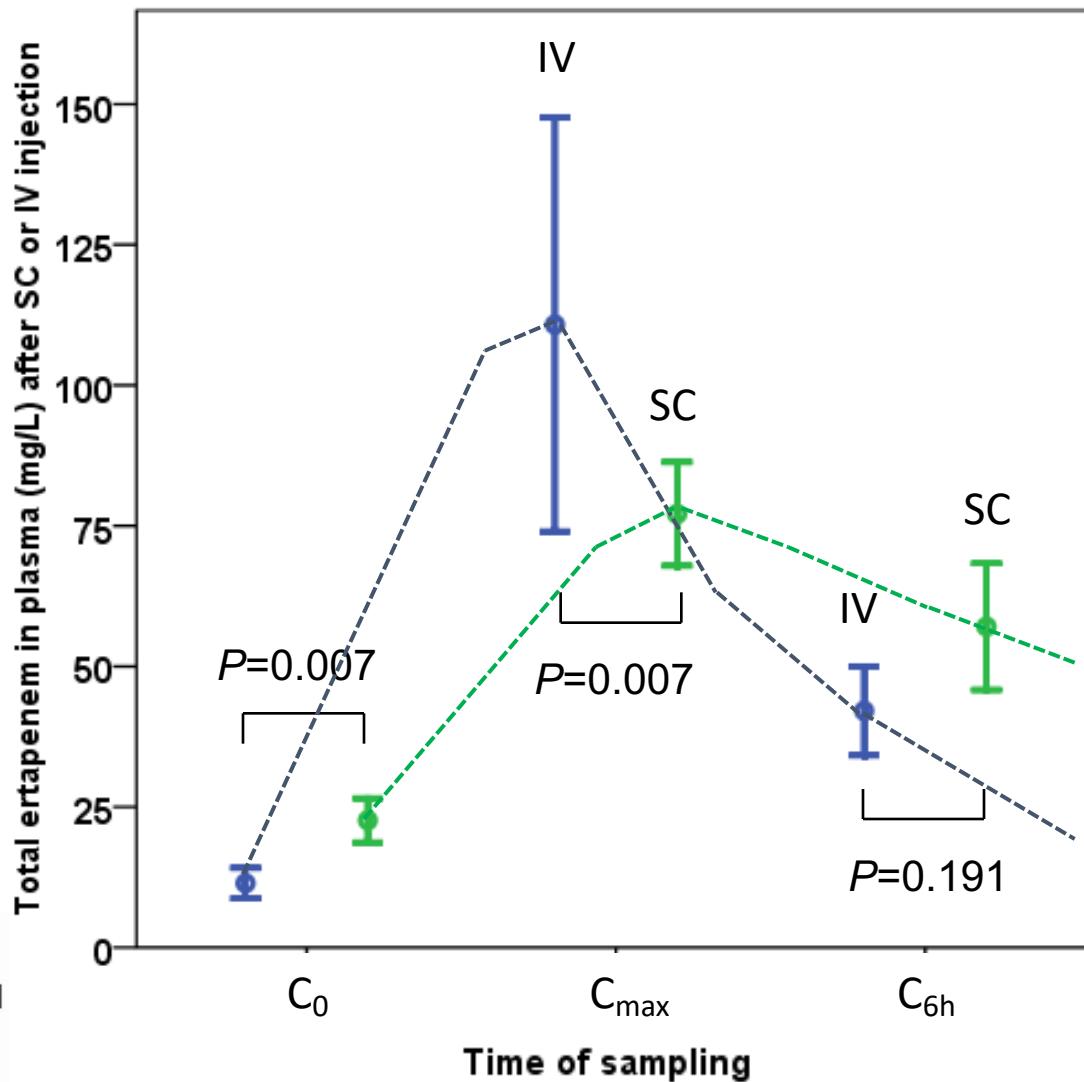
T Ferry,<sup>1,2,3</sup> F Laurent,<sup>1,2,3</sup> P Ragois,<sup>4</sup> C...  
Study Group

*BMJ case report*  
2015



## Prolonged subcutaneous high dose (1 g bid) of Ertapenem as salvage therapy in patients with difficult-to-treat bone and joint infection.

Ferry T, Sénéchal A, Gagnieu MC, Boibieux A, Laurent F, Perpoint T, Tod M, Chidiac C.



17 patients

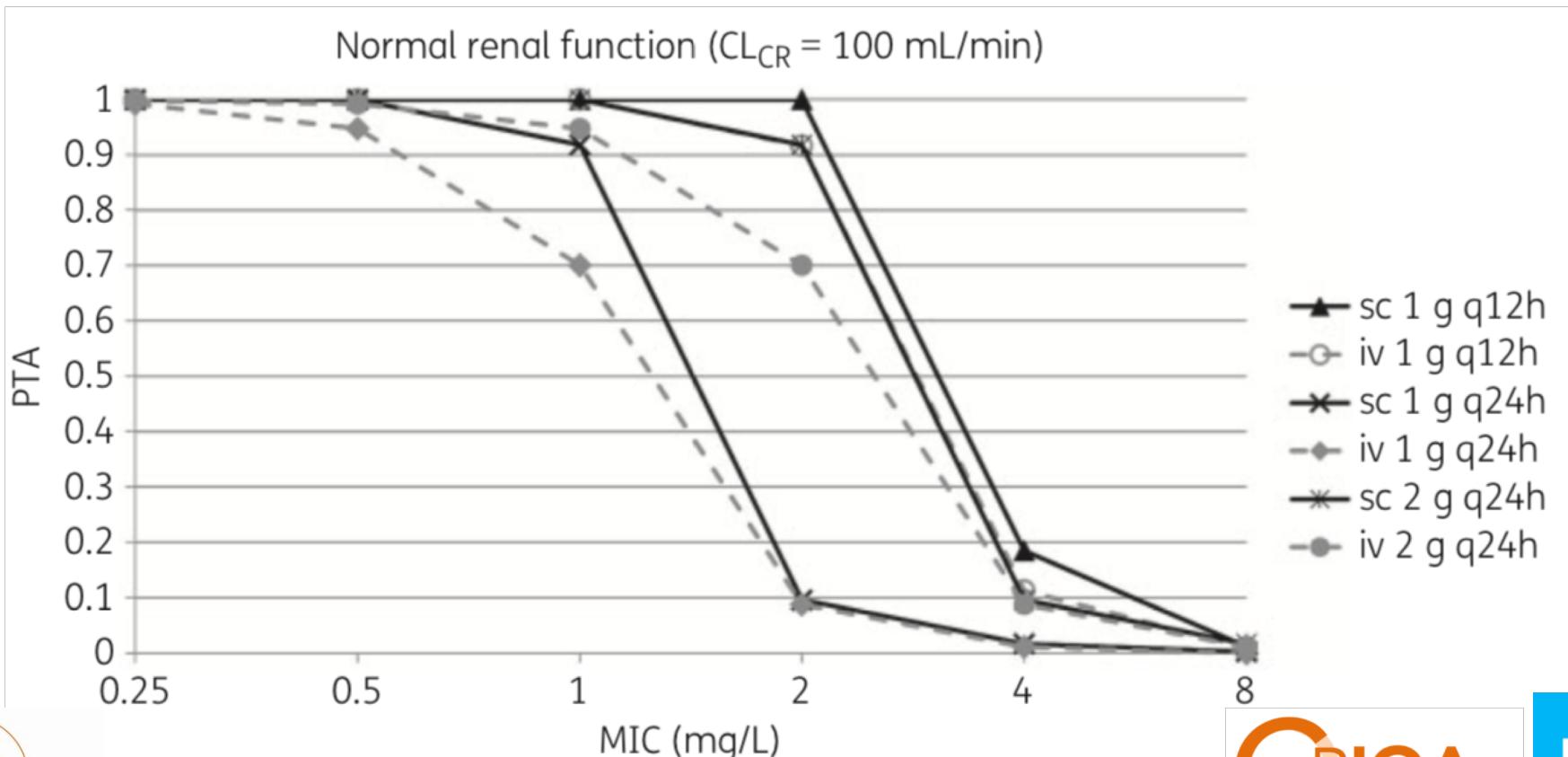
Mean duration of 3 months

>1'000 injections SC without skin necrosis

Increasing of the  $t_{1/2}$  5,9h (IQR 5,1-7,6) vs. 3,8 h with 1g IV 1x/j

# Population pharmacokinetics and probability of target attainment of ertapenem administered by subcutaneous or intravenous route in patients with bone and joint infection

Sylvain Goutelle<sup>1-3\*</sup>, Florent Valour<sup>2,4,5</sup>, Marie-Claude Gagnieu<sup>6</sup>, Frédéric Laurent<sup>2,5</sup>, Christian Chidiac<sup>2,4,5</sup> and Tristan Ferry<sup>2,4,5</sup> on behalf of the Lyon Bone and Joint Infection Study Group

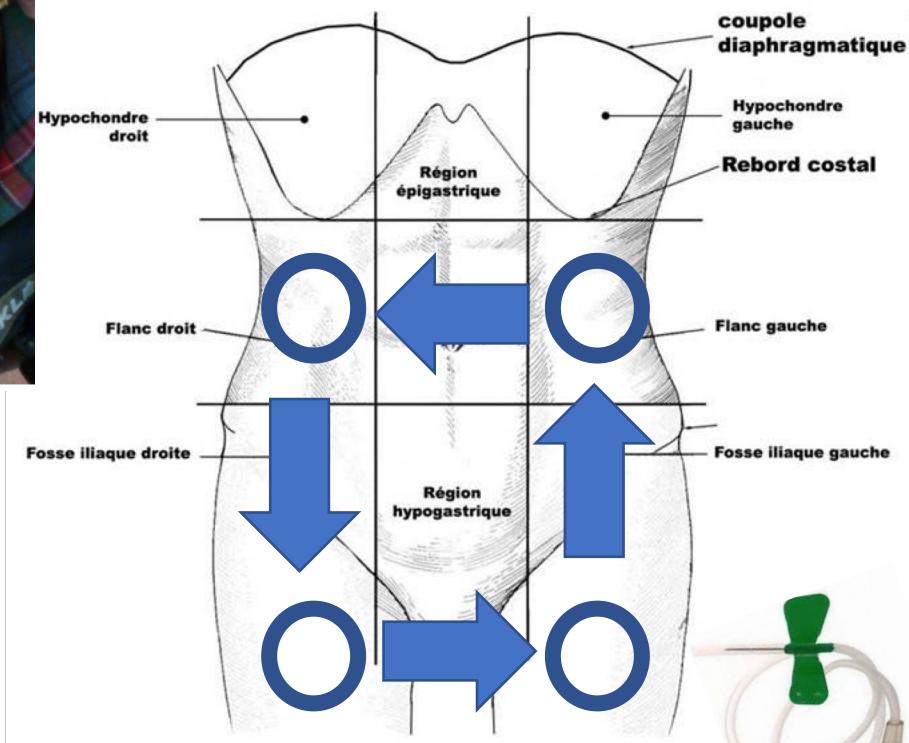


# Outpatient SubCutaneous Antimicrobial Therapy

- Experience with few drugs having a problem
  - Ceftriaxone
  - Ertapenem
  - Teicoplanin
- No direct SC infusion to avoid skin necrosis
- Dilution in 50 mL
- 30 min gravity infusion with a butterfly needle
- Caution if anticoagulant



**HOW  
OSCAT'ing'?**

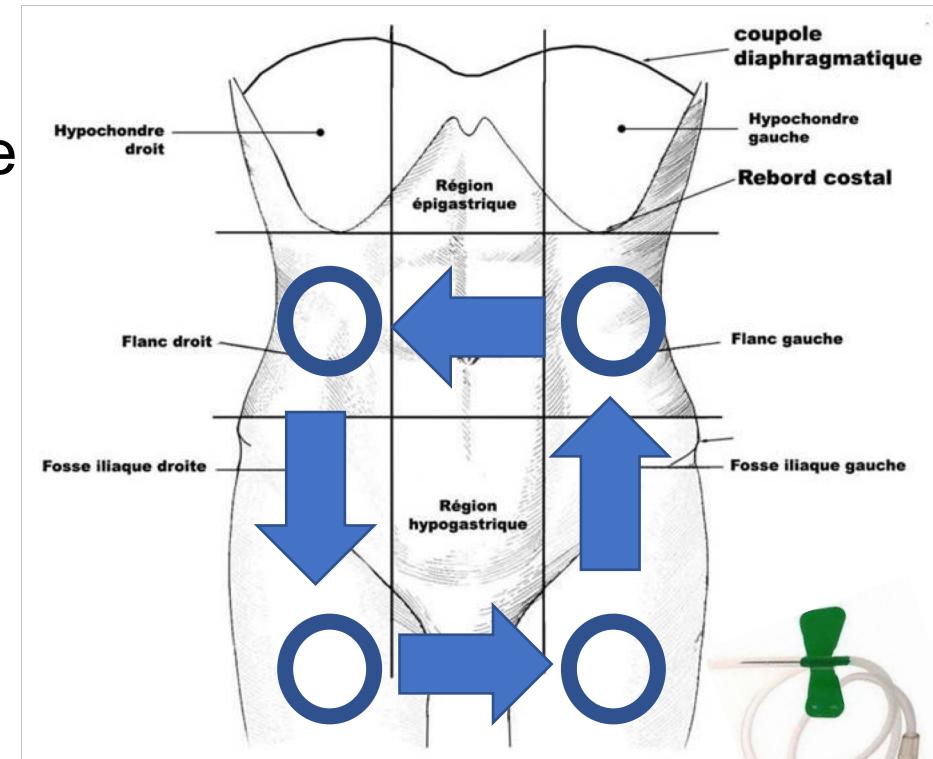


- Alternating injections into thighs and flanks

# Outpatient SubCutaneous Antimicrobial Therapy OSCAT

- Experience with few particular drugs having a prolonged half-life
  - Ceftriaxone
  - Ertapenem
  - Teicoplanin
- No direct SC infusion to avoid skin necrosis
- Dilution in 50 mL
- 30 min gravity infusion with a butterfly needle
- Caution if anticoagulant

**HOW  
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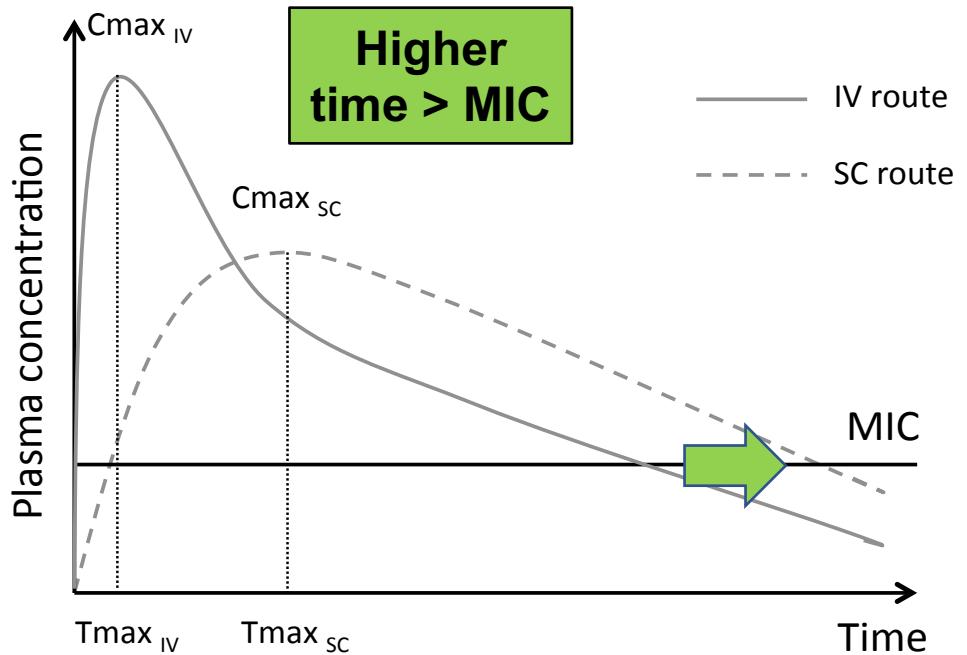
- Alternating injections into thighs and flanks

# Outpatient SubCutaneous Antimicrobial Therapy OSCAT

**WHY  
OSCAT'ing'?**

- Favorable PK/PD profile
- No need for vascular access
- No catheter complications
- 1 or 2 injection(s) per day

**BUT**  
**OFF LABEL USE**  
**Lack of investigation**



*Hernandez Ruiz et al.*  
on behalf of the GInGer group

# Clinical case #3

82-year-old obese man

Post-operative *P. aeruginosa* PJI  
(ciprofloxacin-resistant)

Treated with **iterative 'DAIRs'**,  
soft-tissue flap and intravenous  
antibiotics

**Worse evolution** with necrosis and  
finally **persistent *P. aeruginosa***



T. Ferry

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**finally persistent *P. aeruginosa***

Explantation **to cure**  
but associated with a  
**considerable loss of**  
**function**



Last DAIR +  
Necrosis resection  
+ Dermal substitute  
+ **suppressive**  
**antibiotherapy**



G COUCHE



# Subcutaneous suppressive antibiotic therapy for bone and joint infections: safety and outcome in a cohort of 10 patients

*Journal of Antimicrobial Chemotherapy*



# Subcutaneous suppressive antibiotic therapy for bone and joint infections: safety and outcome in a cohort of 10 patients

*Journal of Antimicrobial Chemotherapy*

**Salvage** (exceptional) option

Elderly patients

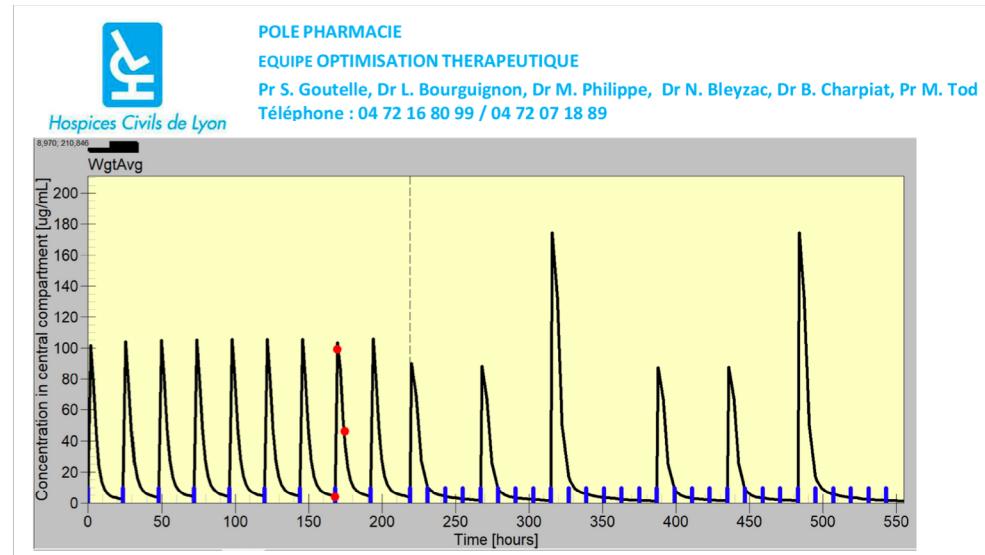
Implant-associated infections  
with MDR pathogens

Explantation is not reasonable

**Ceftazidime (n=1)**

**Ceftriaxone (n=2)**

**Ertapenem (n=7)**

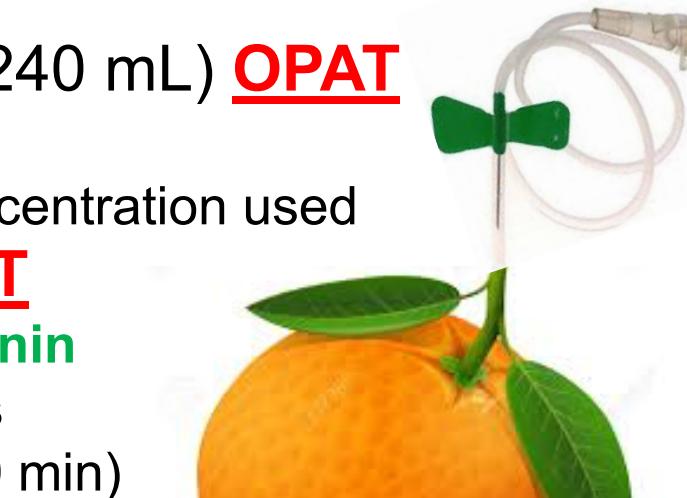
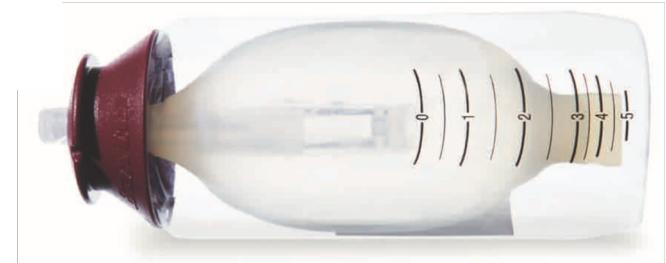


Median follow-up 14 months

*Lyon BJI Study group 2019*

# Conclusion

- **OPAT is largely used for BJI**
  - Patients infected with MDR bacteria
  - With few/no oral options
- **Lyon experience:**
  - Use of elastomeric infusors (mainly 240 mL) **OPAT**
    - Feasible with numerous antibiotics
    - Check the stability properties at the concentration used
  - Subcutaneous administration OSCAT
    - With **ceftriaxone, ertapenem, teicoplanin**
    - Elderly patients without vascular access
    - Dilution (50 mL) and gravity infusion (30 min)
- **Have to promote clinical studies to evaluate these practices**



# *Lyon BJI Study group*

**Coordinator:** Tristan Ferry

**Infectious Diseases Specialists** – Tristan Ferry, Florent Valour, Thomas Perpoint, Patrick Mialhes, Florence Ader, Sandrine Roux, Claire Triffault-Philit, Agathe Becker, Anne Conrad, Marielle Perry, Cécile Pouderoux, Marie-Elodie Langlois, Fatiha Daoud, Johanna Lippman, Evelyne Braun, Christian Chidiac

**Surgeons** – Sébastien Lustig, Elvire Servien, Cécile Batailler, Romain Gaillard, Stanislas Gunst, Julien Roger, Charles Fiquet, Michel-Henry Fessy, Anthony Viste, Quentin Ode, Gaël Gaudin, Tanguy Ledru, Adrien Van Haecke, Quentin Ode, Marcelle Mercier, Florie Alech-Tournier, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Sébastien Martres, Franck Trouillet, Yannick Herry, Cédric Barrey, Emmanuel Jouanneau, Sophie Brosset, Brice Gérenton, Ali Mojallal, Fabien Boucher, Hristo Shipkov, Philippe Céruse, Carine Fuchsmann, Arnaud Gleizal

**Anesthesiologists** – Frédéric Aubrun, Mikhail Dziadzko, Caroline Macabéo

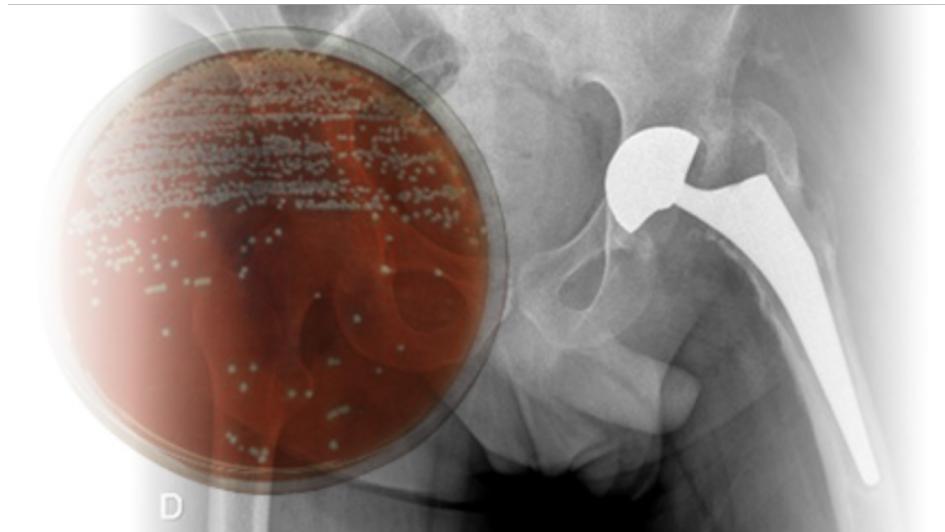
**Microbiologists** – Frederic Laurent, Céline Dupieux, Laetitia Berraud, Camille Kolenda, Jérôme Josse

**Nuclear Medicine** – Isabelle Morelec, Marc Janier, Francesco Giamarile

**PK/PD specialists** – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle

**Clinical Research Assistant and data manager** – Eugénie Mabrut

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