IV to oral switch in children: what is the evidence?

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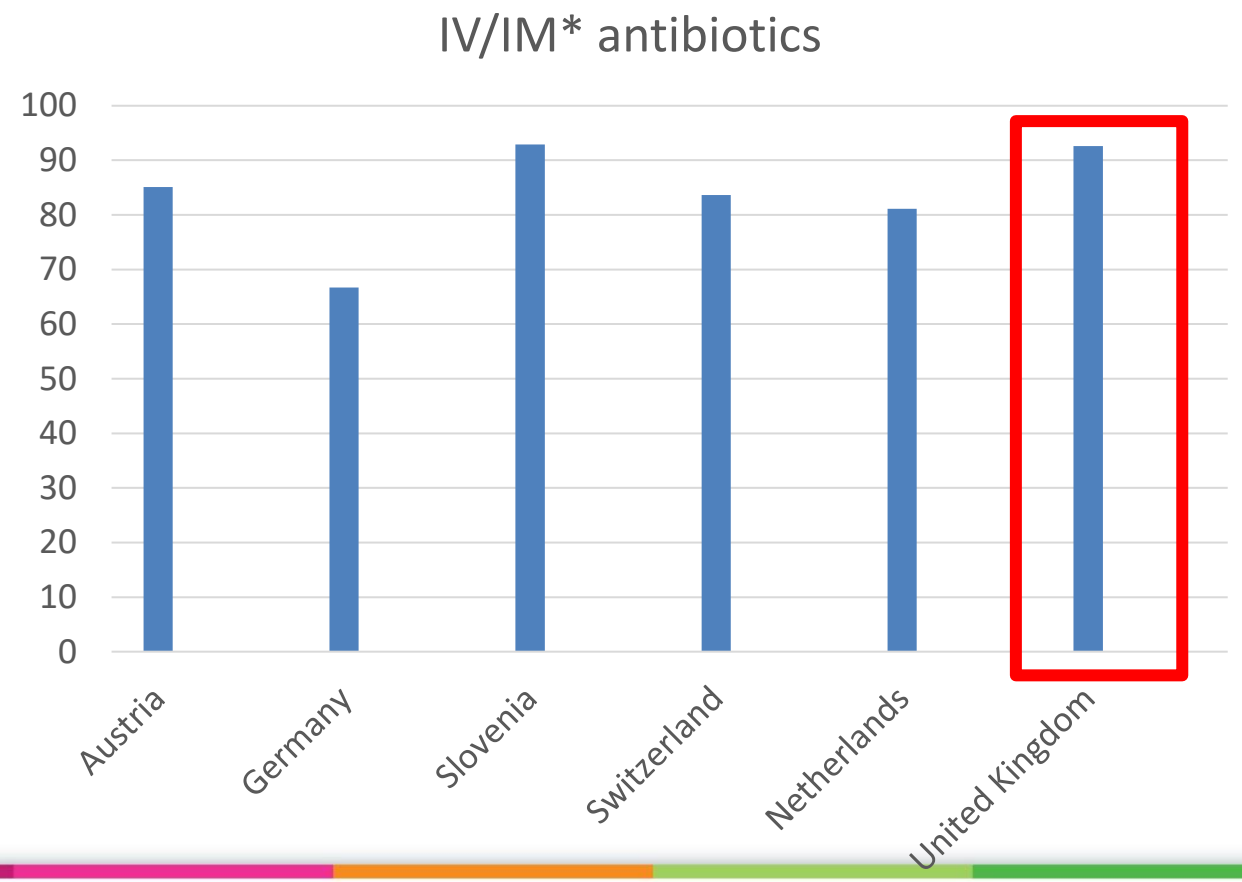
Contents

- The size of the problem: antibiotic use in children
- Why choose oral antibiotics instead of IVAbs
- How do antibiotics work – PK / PD
- The evidence supporting early IVOS (or exclusive oral therapy) in specific infection phenotypes

We use a lot of IV antibiotics in children (2016-19 data)

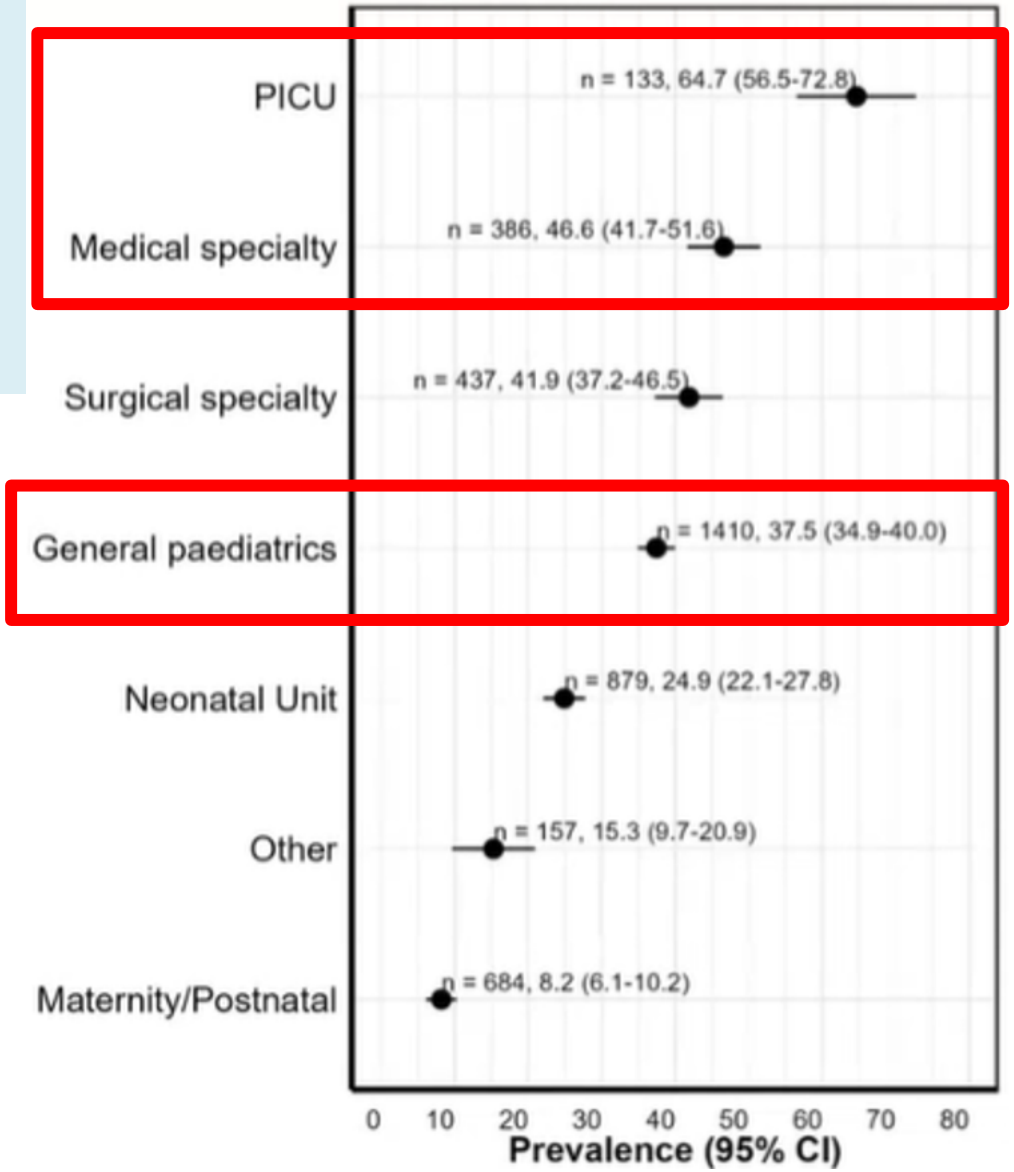
A total of 1318 of 1549 episodes (85.1%) with a bacterial phenotype received empiric systemic antibiotics (in the first 2 days of admission). NOTE: recruited children who had blood tests performed



Kolberg, L et al (2024). Raising AWaRe-ness of Antimicrobial Stewardship Challenges in Pediatric Emergency Care: Results from the PERFORM Study Assessing Consistency and Appropriateness of Antibiotic Prescribing Across Europe. *Clinical infectious diseases*, *78*(3), 526–534.

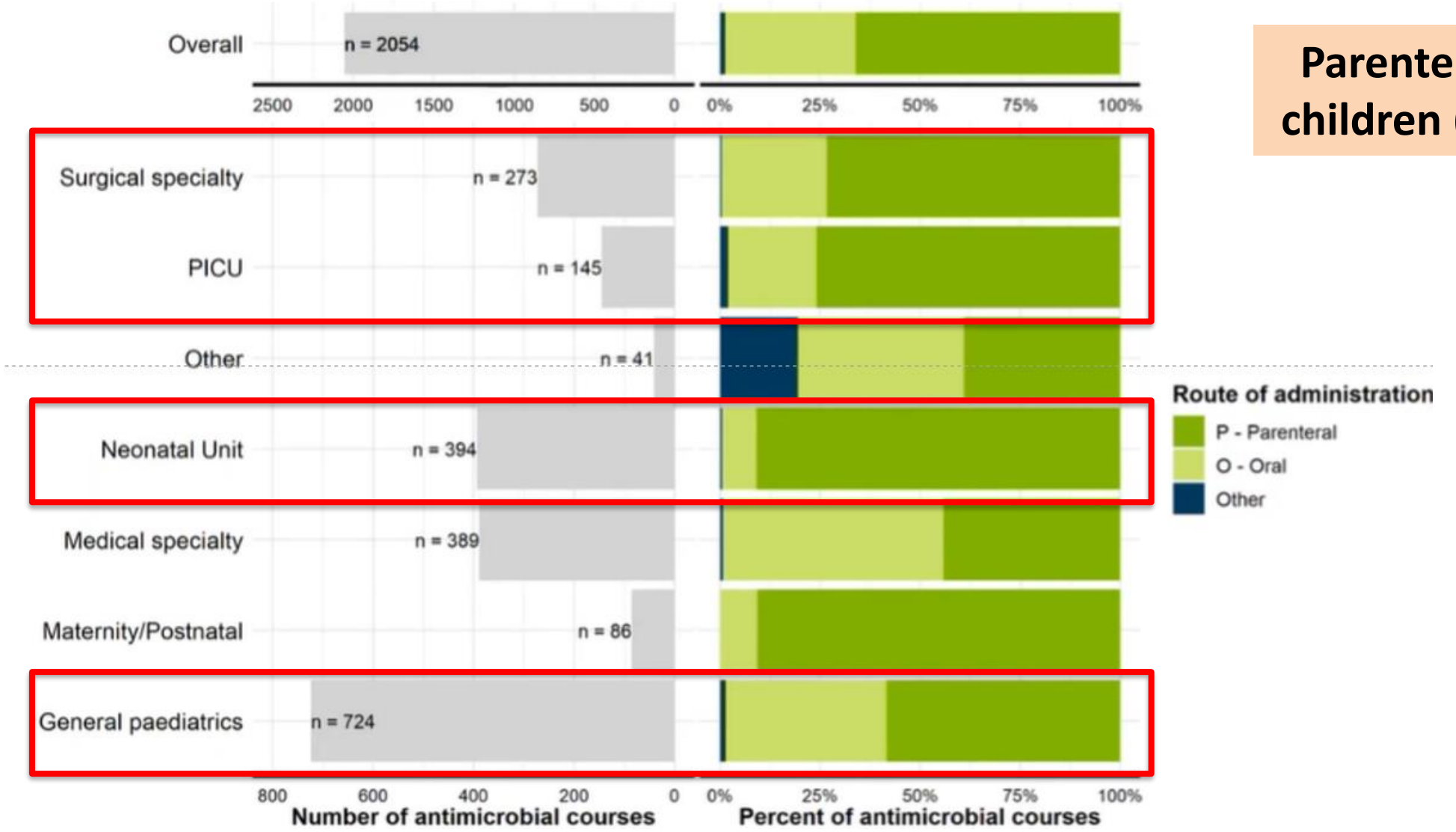
UK HSA point prevalence survey (2023 data)

- 4000 children
- 40% <1 month of age
- >50% tertiary hospitals



Antimicrobial use

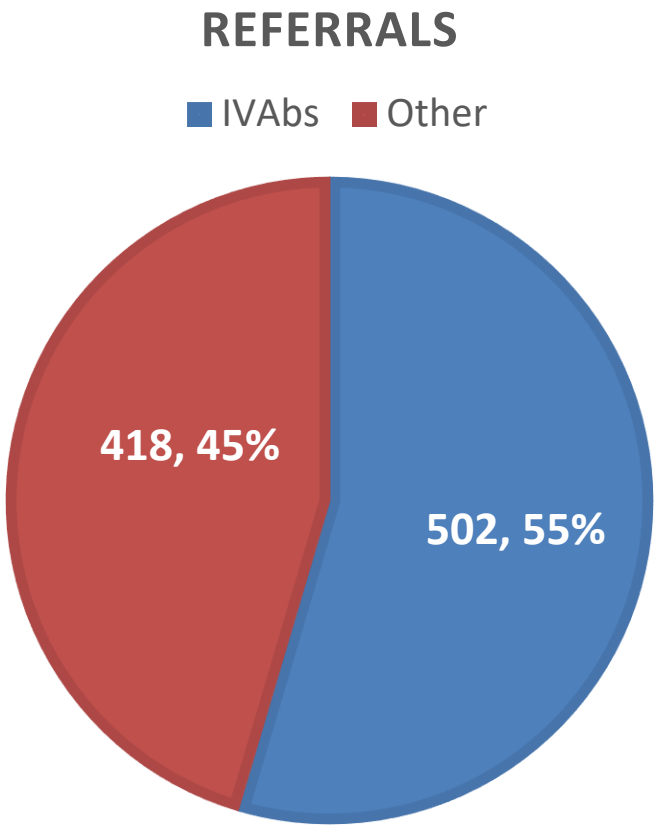
30% of general paediatric use for respiratory tract infections

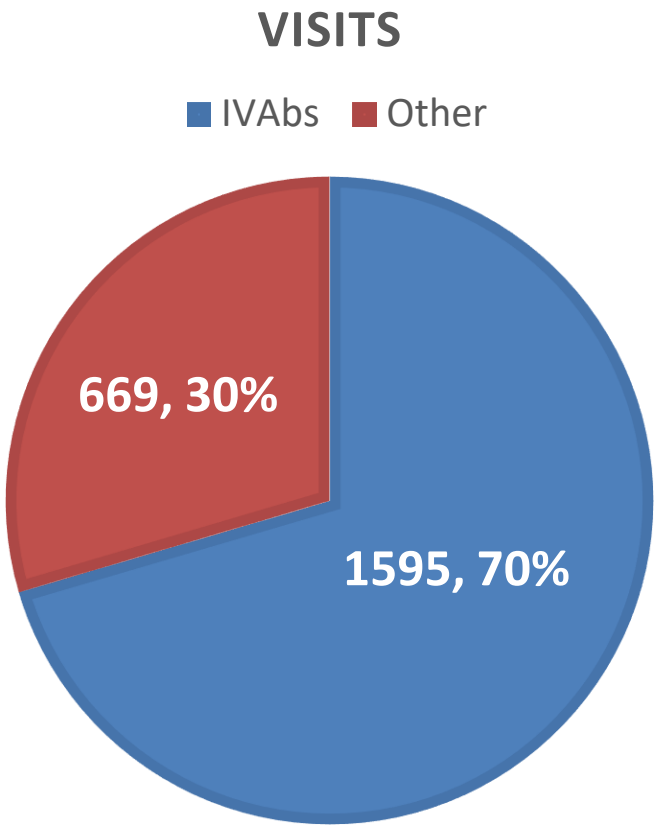


Parenteral use 66% in children (57% in adults)

UK HSA PPS (AMS and HCAI 2023)

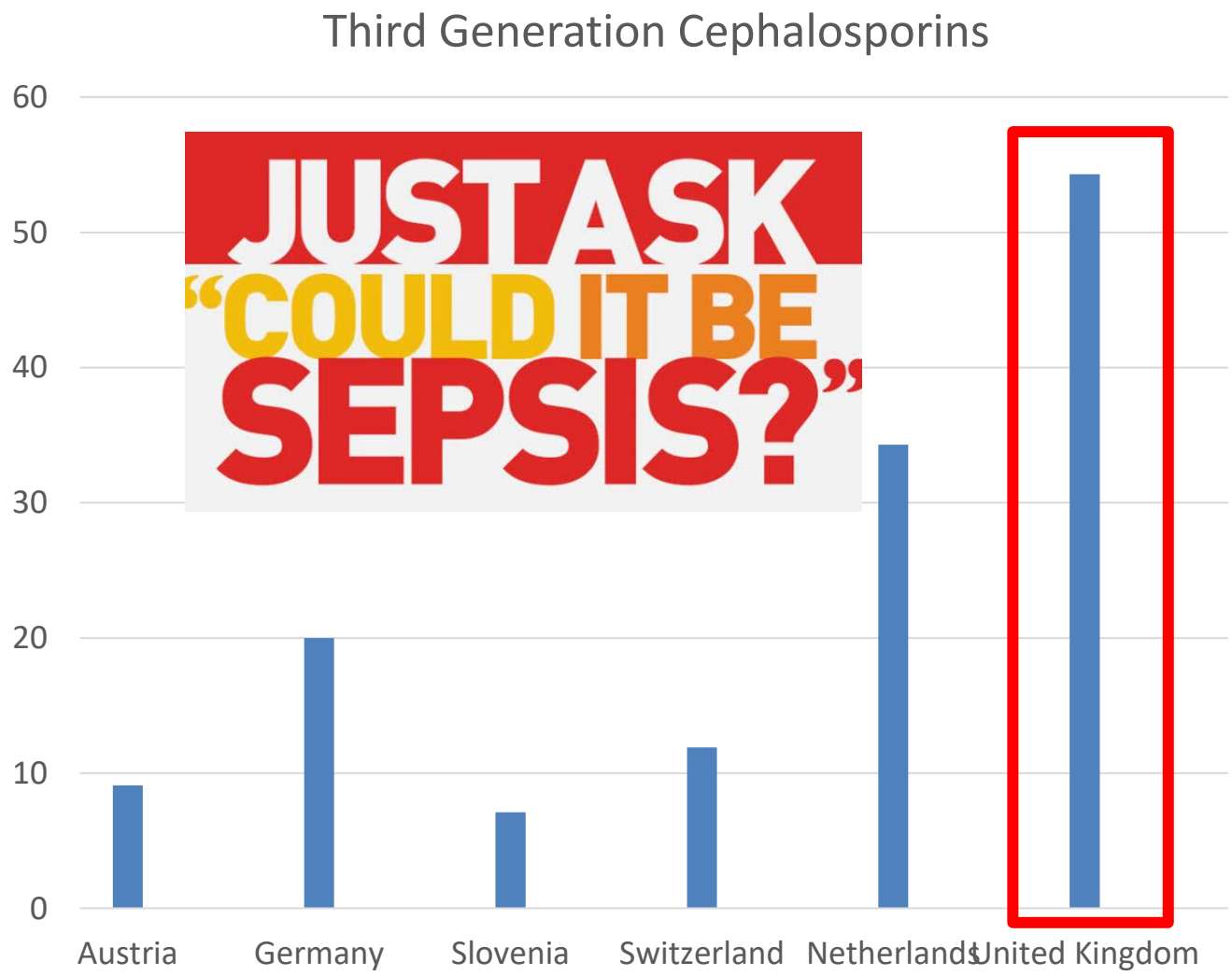
The use of IVAbs within H@H services Tower Hamlets H@H service (Jan-Oct 2024)





Thanks to Zoe Tribble

We use a lot of 3rd generation cephalosporins in the UK



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The benefits of oral antibiotics

- Economic argument:
  - Reduced length of stay / addressing bed pressures
  - Cost of IVAbs / nursing time administering IVAbs
  - Cost for families of being in hospital
- Patient satisfaction – earlier discharge and ↓cannulation
- Carbon footprint of IVAbs[1]
- Patient safety:
  - Adverse drug reactions/ need for genetic testing (aminoglycosides)
- Antimicrobial resistance (AMR)
  - In the individual: narrow versus broad spectrum Ab use

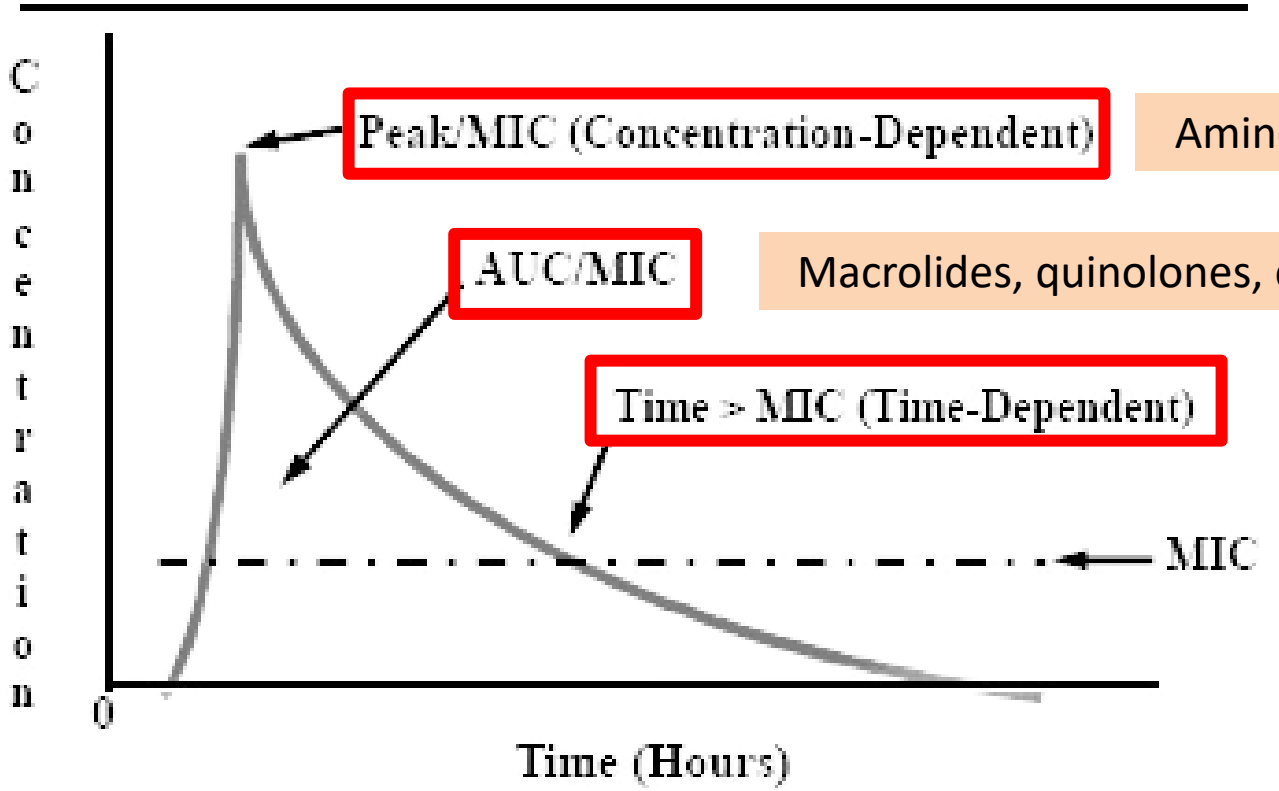
1. Eii MN, Walpole S, Aldridge C. Sustainable practice: Prescribing oral over intravenous medications. BMJ. 2023 Nov 6;383

IN THEORY, HOW DO ANTIBIOTICS WORK?

Antibiotics interact with the body – absorption, distribution, metabolism, and excretion of drugs (= **pharmacokinetics**)

Antibiotics interact with the bacteria (= **pharmacodynamics**)

PHARMACODYNAMICS



Aminoglycosides

Macrolides, quinolones, clindamycin

B-lactams

PHARMACOKINETICS

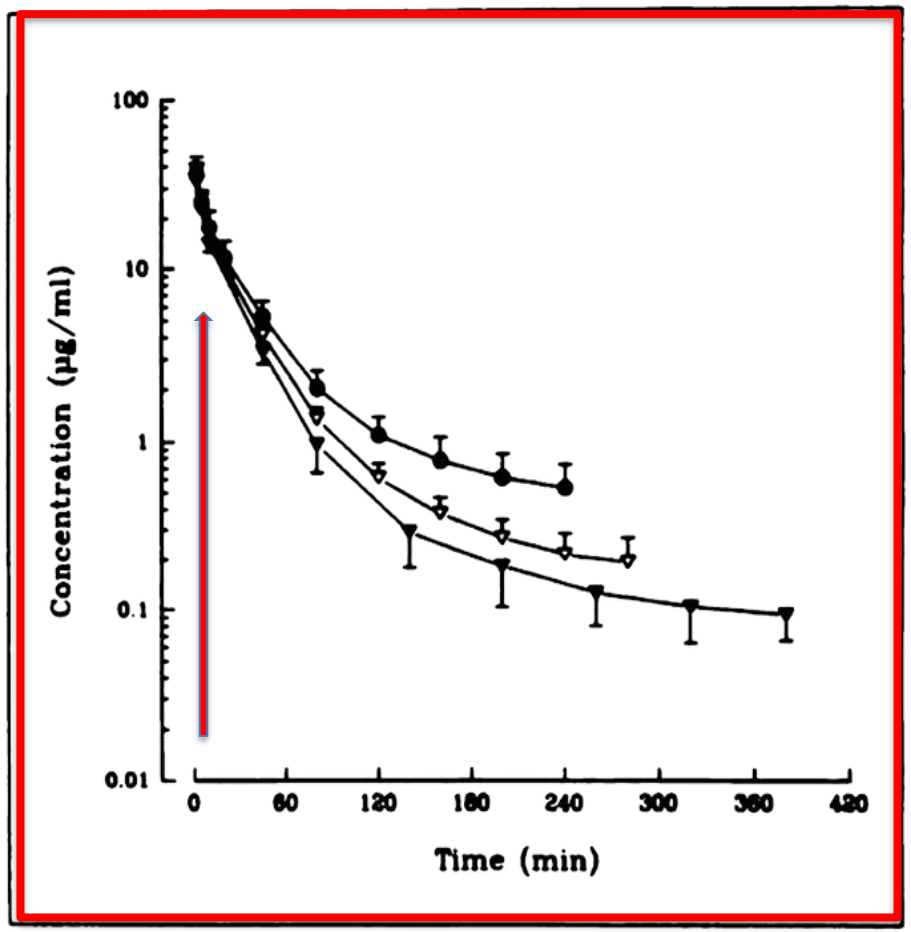


FIG. 2A *Mean plasma levels and standard deviations of cefadroxil after intravenous administration of 2.5 (●), 10 (▽), and 15 mg (▼).*

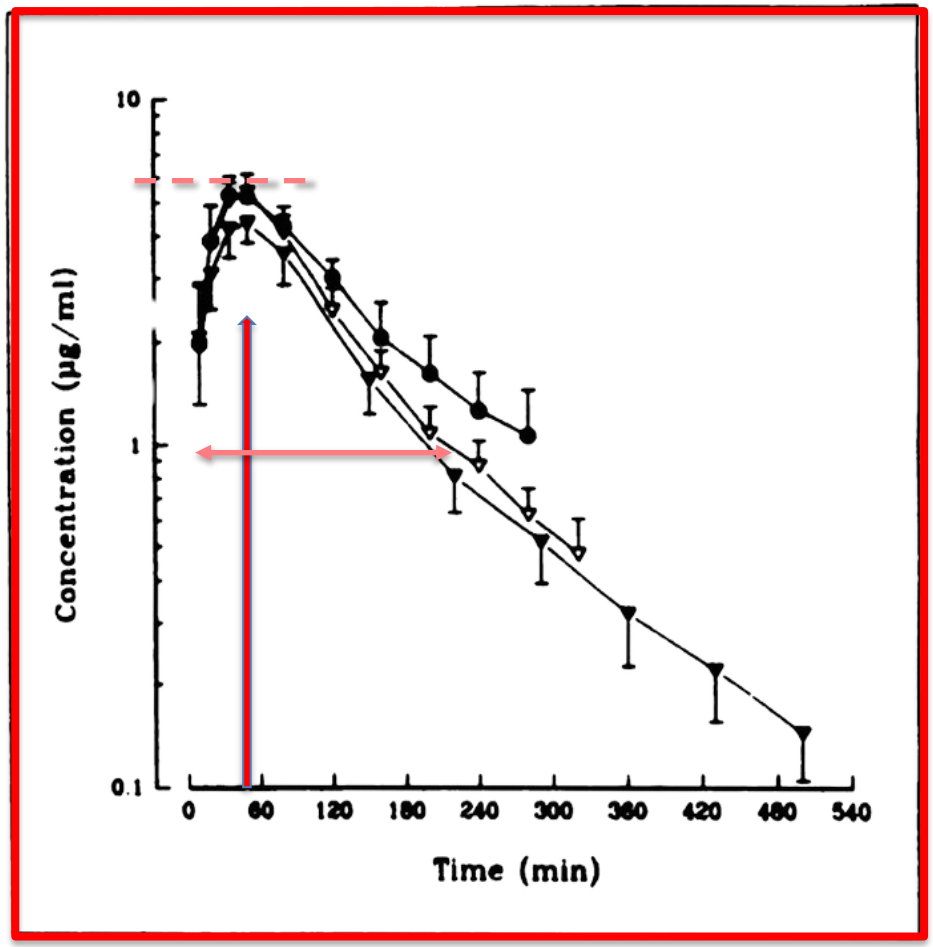


FIG. 2B *Mean plasma levels and standard deviations of cefadroxil after oral administration of 2.5 (●), 10 (▽), and 15 mg (▼).*

Bioavailability

Also need to consider:

1) tolerability in terms of taste and volume of liquid suspensions
2) ceiling of dosing for some oral Abs ie excessively high doses increase the chances of side effects such as nausea and diarrhoea

- **Metronidazole (100%)**
- **Linezolid (100%)**
- **Co-trimoxazole (100%)**
- **Fluconazole (100%)**
- **Rifampicin (100%)**
- **Clindamycin (95%)**
- **Ciprofloxacin (dose adj 100%)**
- **Cephalexin (90%)**
- **Amoxicillin / fluclox / co-amox (70%), azithromycin (60-90%)**

BOTTOM LINE

THE BACTERIA HAVE NO IDEA
HOW THE DRUG GOT INTO THE BODY!

A paradigm shift in infection management

- Several seminal large RCTS in adults have challenging / refuted long held beliefs about IVABs:
  - OVIVA: bone and joint infections
  - POET: infective endocarditis (left sided)

1. Li HR et al. Oral versus Intravenous Antibiotics for Bone and Joint Infection. N Engl J Med. 2019 Jan 31;380(5):425-436
2. Iverson K et al. Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis. N Engl J Med. 2019 Jan 31;380(5):415-424

Challenging Dogma in the Treatment of Childhood Infections

Oral Antibiotics and Shorter Durations

Daniel C. Tanti, MPH, BSc (Hons),† Brad Spellberg, MD,‡ and Brendan J. McMullan, BMed, PhD*†*

Tanti, D. C. et al. Challenging Dogma in the Treatment of Childhood Infections: Oral Antibiotics and Shorter Durations. *The Pediatric infectious disease journal 2024*, *43*(7)

Pyelonephritis / Gram –ve bacteraemia

- Systematic review (paeds) in infants ≤90 days of age:
  - Bacteraemic upper UTI
    - A short IV AB course of ≤7 days (after the exclusion of meningitis) versus >7 days is not associated with 30 day relapse / hospitalisation
  - Non-bacteraemic upper UTI
    - A short IV AB course of ≤3 days (after the exclusion of meningitis) versus >3 days is not associated with 30 day relapse / hospitalisation

Hikmat S at al. Short Intravenous Antibiotic Courses for Urinary Infections in Young Infants: A Systematic Review. Pediatrics. 2022 Feb 1;149(2)

Osteoarticular (OA) infections

- Danish study – multicentre
  - children aged 3 months to 17 years presenting with OA infections
  - Exclusion criteria were severe infection (ie, septic shock, the need for acute surgery, or substantial soft tissue involvement), prosthetic material
  - Randomised (1:1) to oral Abs (co-amox if ≤ 5 years, fluclox >5 years) versus IV ceftriaxone
    - Po Abs (123 children) versus IVABs (125 children)

Nielsen AB et al. Oral versus intravenous empirical antibiotics in children and adolescents with uncomplicated bone and joint infections: a nationwide, randomised, controlled, non-inferiority trial in Denmark. Lancet Child Adolesc Health. 2024 Sep;8(9):625-635.

Infective endocarditis

- The Necker experience…..

Neonatal infections (EOS and LOS)

- Dutch / Danish / Exeter experience…..

WHAT ARE THE ABSOLUTE INDICATIONS FOR USING INTRAVENOUS ANTIBIOTICS?

SEVERE SEPSIS (Phoenix)
Time to C max + impact of sepsis on GI absorption

Failure of enteral absorption or refusal

No oral option due to resistance

CNS infections – hydrophilic versus lipophilic antibiotics

Conclusions

- Robust data to support early IVOS (or exclusive use of oral Abs) in children with invasive bacterial infections
  - "very few children with invasive bacterial infections benefit from IVAbs over oral antibiotics"
    - **As long as you choose the right oral antibiotic and dose it correctly!**

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