**Gompf’s**

**Antibiotics**

**Redux**

**A Pocket Tool for the Medical Student, or Resident on the**

**Infectious Diseases Clinical Rotation**

**or**

**Just about anyone who could use a pocket antibiotic tool**

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**ANTIBIOTIC PEARLS**

1. Penicillins generally cover Gram +s, anaerobes, certain Gram –s depending on the antibiotic.

2. Cephalosporins generally cover Gram +s (EXCEPT Enterococcus!), Gram –s, & *oral* anaerobes--those *above* the diaphragm. ONLY ceftazidime/cefepime/ceftolozane cover Pseudomonas..

3. Aztreonam, a monobactam, covers ONLY Gram –s, incl. Pseudomonas. Reserve for beta lactam-allergic patients.

4. Aminoglycosides generally cover Gram +s (except tobramycin) & Gram –s, NO anaerobes, some Mycobacteria. Increasing resistance. Best in combination with beta lactams unless uncomplicated cystitis/pyelonephritis, but most use is declining due to nephrotoxicity & dual beta lactam options.

5. Quinolones cover Gram –s best (except moxifloxacin/delafloxacin, which are “respiratory quinolones” most active against Gram +s & anaerobes), some Mycobacteria.

6. Trimethoprim/sulfamethoxazole (TMP/SMX) generally covers MSSA/MRSA, Nocardia, Listeria, Pneumocystis, most Gram –s except Pseudomonas. Probably *OK* for Streptococcus pyogenes/agalactiae cellulitis as well.

7. Clindamycin generally covers Gram +s, incl anaerobes except Clostridia, like anaerobic/microaerophilic Strep/Peptostrep, Actinomyces (better for infections above the diaphragm).

8. Metronidazole covers *gut* anaerobes like Bacteroides, Prevotella, Clostridia; +/-Peptostrep (infections *below* the diaphragm).

9. Carbapenems in general are very broad & among our “last line” beta lactams. Use sparingly. Ertapenem covers most organisms except Pseudomonas. Imipenem, meropenem, & doripenem include Pseudomonas. Resistance in one carbapenem doesn’t predict resistance in others.

10. A word about Enterococcus! Enterococcus in well-defined polymicrobial infections (cholecystitis, GI perforation, decubitus infections) tends to be somewhat of an opportunist & clears once source control is achieved, even if it spills into blood). Isolated Enterococcus faecalis/faecium bacteremia or hematogenous infection (septic arthritis, vertebral osteomyelitis, endocarditis, “community-acquired" bacteremia without an immediately source) should raise as much concern as Staphylococcus aureus. In that setting, even if reported as very ampicillin/penicillin-susceptible, and ampicillin is considered “drug of choice”, know that these organisms have *lower*-affinity penicillin-binding proteins than other Gram + cocci, and “tolerance” may also occur with intermittent dosing of ampicillin/penicillin, which should be considered bacterioSTATIC. Synergistic combination therapy is preferred for these infections, such as amp + gentamicin. Amp + ceftriaxone/ceftaroline is increasingly preferred due to nephrotoxicity with gent & gent resistance. The combination of these beta lactams binds more PBPs that ampicillin alone & lowers the ampicillin MIC. In addition, know that vancomycin is bactericidal for most GPCs *except Enterococcus* (bacterioSTATIC).

Shameless plug:

Visit [www.gompfsidpearls.net](http://www.gompfsidpearls.net) for more regularly updated ID clinical tools & links I find useful in practice. :}

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**Do’s & DON’Ts**

1. ***Don’t use an antibiotic if you don’t need to.***
* If a bacterial infection is not high in the differential and the patient is not clinically toxic, forgo antibiotics. They are poor antipyretics.
1. ***Persistent fevers require work-up, not more antibiotics.***

If you are treating with broad antibiotics and fevers persist, ***stop them***; they aren’t helping.

* + Look for undrained foci of infection/pus à drain it.
	+ Look for non-infectious cause à treat it.
	+ True FUO in a rapidly deteriorating patient may warrant empiric anti-TB therapy à Call ID.
1. ***DO use an oral antibiotic when you can; use one narrow antibiotic when you can; stop antibiotics when you can.***
* Antibiotics are not cheap; switch to PO when reasonable.
* Two antibiotics don’t always prevent resistance better than one, and neither do broad spectrum drugs. More drugs = more resistance.
	+ But NEVER give Rifampin alone! Rapid high-level resistance occurs.
	+ TB/Atypical mycobacteria: *NEVER* use 1 drug in *active* TB
* DON’T treat viral infections (or noninfectious syndromes) with antibiotics beyond the point at which you have ruled out bacterial infection.
1. ***Don’t combine 2 of the same class of antibiotics (e.g. 2 beta lactams, 2 quinolones) unless you have* data *or your friendly neighborhood ID specialist (or PharmD) to back it up. They may unpredictably antagonize, synergize, or double the adverse effects.*** E.g. Clindamycin-rifampin combo dramatically reduces clindamycin serum concentration***.*** [<https://doi.org/10.1016/j.jinf.2015.03.013>; <http://dx.doi.org/10.1684/ejd.2013.2213>]
2. ***Always monitor for antibiotic adverse effects.***
* Antibiotics are a double-edged sword. Respect them.
* Watch for hypersensitivity/bone marrow suppression/interstitial nephritis/hepatotoxicity/drug fever with beta lactams, acute tubular necrosis/irreversible ototoxicity with aminoglycosides, & Clostridium difficile with almost all of them.
* Watch for yeast overgrowth/Candidemia with prolonged/multiple antibiotic therapy.
* C. diff. is easy to miss in 2 situations:
	+ Colostomies – stumps/small bowel can be infected with C.diff.!
	+ Spinal cord injured patients – unexplained abdominal distension & leukocytosis are a clue
* RIFAMPIN (& possibly others) REDUCES EFFECTIVENESS OF ORALCONTRACEPTIVES! Tell female patients to *add barrier contraception until the next new pill pack* after finishing antibiotics.

**Antifungal coverage in general:**

**fluconazole** = Cryptococcus, Coccidioides, dermatophytes, Candida EXCEPT Candida krusei/auris/some glabrata and all molds; high CSF/urine levels

**itraconazole** = Candida, Histoplasma, Crypto, Cocci, Aspergillus, Sporothrix, Paracocci, Talaromyces

**voriconazole** = Candida, Histo, Crypto, Aspergillus (except a few rare species, Fusarium, NOT initially for Mucor/Rhizopus, but OK as step-down after ampho B/source control; good CSF/poor urine levels

**posaconazole** = same as vori, + Mucor/Rhizopus; variable CSF levels

**isavuconazonium 372mg (= isavuconazole 200mg)** = same as posa, some Mucor, INFERIOR to caspofungin for *candidemia; few drug interactions; poor CSF/urine levels*

**enchinocandins (caspofungin/micafungin/anidulafungin/rezafungin)** = Candida incl C. auris, Aspergillus, SOME Cryptococcus, NOT Fusarium/Mucor/Rhizopus/Trichosporon, NOT Histo/Blasto/Coccidioides; poor levels in CSF/urine/vitreous humor. Poor urine penetration, but does penetrate renal parenchyma, so may be effective in pyelonephritis, maybe cystitis. May allow you to avoid ampho B in the case of fluconazole resistant Candida.

**amphotericin B** = all, +/- Fusarium, NOT Candida lusitaniae (variable)/guillermondi/auris, NOT

Scedosporium (Pseudallescheria), Lomentospora (Scedosporium); Aspergillus terreus

**flucytosine (5-flourocystosine)** - increases penetration of above drugs, rapid resistance alone; good CSF/eye/urine levels

**terbinafine** =Trichophyton/tinea infections, Scedosporium chromoblastomycosis

**ibrexafungerp** = recurrent vulvovaginal candidiasis. *Contraindicated in pregnancy!* Contraception required thru 4 days after last dose; check beta HCG before each monthly dose during 6 month course.

**oteseconazole** = recurrent vulvovaginal candidiasis. *Contraindicated in reproductive age persons with a uterus!*

**Fusarium:** Vori 6mg/kg IV Q24H or 300mg PO x 1 d, then 4mg/kg/d IV or 200mg PO BID + Ampho B 1.2 mg/kg/d or ABLC 5mg/kg/d

**Mucor:** Ampho B 1.5mg/kg/d or liposomal ampho B or ABLC 5mg/kg/d + posaconazole/isuvaconazole (active metabolite of isuvaconazonium); NOT other azoles/enchinocandins

**BacteriCIDAL vs. BacterioSTATIC**

A consideration in choosing treatments for serious infection like severe sepsis, bacteremia, meningitis, pneumonia, endocarditis, neutropenic fever. A “cidal” drug kills quickly; a “static” drug slows or stops replication and/or toxic production. Whether it matters is somewhat controversial.

***Beta lactams are CIDAL and penetrate tissues and inflamed meninges well.*** They are preferable in serious infection, including bacteremia, endovascular infection, CNS infection, and streptococcal cellulitis. Their microbial action is *time-dependent*, meaning that they are most effective the longer the concentration of drug in the affected site remains above the MIC of the bacteria. Thus, they can be dosed by *continuous or extended infusion*, which may also facilitate home & hemodialysis dosing. (UpToDate has a helpful chart; most drug databases like ePocrates, etc, don’t offer alternative dosing recommendations.) Ceftazidime, cefepime, and ertapenem are stable enough to be given 3 times a week after hemodialysis. Ampicillin is stable at least 24 hrs for extended and continuous infusion.

**Extended Spectrum Beta Lactamase (ESBL)-Producing Gram Negative Bacilli:** It’s complicated & evolving as fast as these organisms!

**SPICE/SPACE/KEC** are mnemonics for bacteria that *may* either have *intrinsic* (chromosome-based, aka “constitutive”) and/or *inducible* beta lactamases (chromosome- OR mobile genetic element/plasmid-mediated beta lactamases). **These organisms may demonstrate variable resistance to commonly prescribed beta lactams and may require carbapenem\* treatment**. In addition, *inducible* beta lactamases in KEC organisms may become reversibly de-repressed (or “switched on”) upon 1- 7 days’ exposure to a beta lactam and result in treatment failure. **Cefepime is a weak AmpC inducer** and stands up to hydrolysis by AmpC β-lactamase, so is generally a good choice if the organism is susceptible.



**TL/DR:** If suspecting severe sepsis, use ceftolozane-taz, ceftaz-avibactam, meropenem, or piperacillin-taz if MIC <16mg/L\*\*; otherwise, can deescalate to cefepime if MIC ≤ 1 mg/L if stabilized, off pressors, etc. Some beta lactams are weak inducers of

**KEC(Y) –** Grouped by Family Enterobacteriaceae with **moderate-high risk of *inducible*, chromosomal beta-lactamase (AmpC, Group C, cephalosporinase)—KNOW that these may trick you by testing S to ceftriaxone/ceftazidime🡪 treatment with cephalosporins may *induce* R**. Inducible beta lactamases may become reversibly de-repressed (or “switched on”) upon 1- 7 days’ exposure to a beta lactam and result in treatment failure.

[Aside: Klebsiella pneumoniae & some E.coli often acquire a non-inducible, plasmid-based Group A beta lactamase (TEM) with a narrow spectrum against ampicillin & 1st-gen cephalosporins. Just be aware that this pattern comes up often in susceptibility testing & does not confirm or rule out an inducible ESBL.]

**K**lebsiella aerogenes (formerly Enterobacter)

**E**nterobacter cloacae

**C**itrobacter freundii

**Y**ersinia enterocolitica

(Note: There’s also a mnemonic, HECK-Yes, in which H is Hafnia alvei. It’s very uncommon clinically.)

**SPACE/SPICE** – **Treat based on susceptibility report and severity.** [These species’ ampC mutations are***usually not inducible***, so **these DO test R to ceftriaxone/cefta**zidime, so *this mnemonic has fallen out of favor*.] **Consider:** Severity of infection (bacteremia, meningitis), high inoculum/source control (UTI/pyelonephritis vs endocarditis), presence of biofilm (infected device), & MICs to cefepime (≤ 1 mg/L) & pip-tazobactam (≤ 16 mg/L)\*\* can help guide whether to use cefepime, pip-taz, or a carbapenem. Quinolones (bactericidal), trimethoprim-sulfamethoxazole (TMP-SMX), tetracyclines, and aminoglycosides are options if susceptible.

Presence of **chromosomal (“constitutive”, “intrinsic”)** or **mobile genetic element-**acquired (**plasmid**-mediated) beta lactamases.

**S**erratia/**S**almonella/**S**higella

**P**roteus (non-P. mirabilis/”**I**ndole +”)/**P**rovidencia

**P**seudomonas

**A**cinetobacter baumanii complex

**C**itrobacter species

**E**nterobacter complex

(**Y**ersinia enterocolitica – not enough data)

E. coli and Klebsiella are the most common ESBL producers, so many labs screen those isolates if MIC for ceftazidime is >/= 2 mg/L. Remember that **Klebsiella** almost all have a constitutive chromosome-based beta lactamase (usually SHV-1) & test R to ampicillin/ticarcillin.

\*Note that carbapenems and the monobactam, aztreonam *are* beta lactams, as they *all* have a beta lactam ring. This may be confusing initially when you read about beta-lactam resistance and recommendations to use a beta lactam “versus” carbapenem; many articles gloss over this.

\*\*[MERINO Trial 2018](https://jamanetwork.com/journals/jama/fullarticle/2702145) suggested higher 30-day all-cause mortality with pip-taz vs meropenem, but [other trials](https://www.idstewardship.com/piperacillintazobactam-versus-carbapenems-esbl-infections/) and [post-hoc analysis of MERINO](https://www.infectiousdiseaseadvisor.com/home/topics/sepsis/piptazo-avoided-due-to-high-oxa-esbl-ceftriaxone-resistant-bloodstream-infection/) have suggested MIC > 16mg/L to pip-taz is responsible for the difference. If MIC is low, piperacillin-tazo may be acceptable as “carbapenem-sparing” in infections with source control (e.g. pyelonephritis without obstruction). See also [Impact of the MIC of Piperacillin-Tazobactam on the Outcome of Patients with Bacteremia Due to Extended-Spectrum-Lactamase Producing Escherichia coli](https://doi.org/10.1128/AAC.00135-13), 2013; [Association Between Minimum Inhibitory Concentration, Beta-lactamase Genes and Mortality for Patients Treated With Piperacillin/Tazobactam or Meropenem From the MERINO Study](https://academic.oup.com/cid/article/73/11/e3842/5940735) 10/27/2020; [IDSA Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0](https://www.idsociety.org/practice-guideline/amr-guidance-2.0/), 3/31/2022. )

**Carbapenem (CP) Resistant Gram Negative Bacilli:**

(Carbapenem attached to the beta lactam ring is what preserves activity against ESBL.) Affects mainly **Klebsiella pneumoniae, Pseudomonas aeruginosa and Acinetobacter baumannii (CRAB)**. May possess intrinsic vs mobile genetic element carbapenemase-encoding genes that inactivate enzymes, induce efflux pumps or limit porin channels. Carbapenems are not necessarily interchangeable.

**Antibiotics for Resistant Gram + Cocci**

* Vancomycin, teichoplanin (Europe) cover all but vancomycin-resistant Gram +s.
* Vancomycin is bacterioSTATIC against Enterococcus.
* Dalbavancin, oritavancin, televancin - same mechanism as vancomycin & susceptibility generally correlates with vancomycin susceptibility; they add VRE, VISA/VRSA coverage.
* Daptomycin is bacteriCIDAL for both MRSA and Enterococcus & penetrates biofilm.
* Linezolid & tigecycline are bacterioSTATIC, NOT a choice for bacteremia unless no other options are possible, and not as monotherapy, unless you can cite legitimate supportive data.
* Tigecycline is difficult to tolerate due to 20% nausea/vomiting & associated with higher mortality than comparators for FDA-approved indications in after-market review of pooled clinical trials.
* All but vancomycin are EXPENSIVE & generally reserved for vancomycin-resistant Gram +s.

**Pseudomonas, Acinetobacter, Stenotrophomonas vs other GNR**

* These organisms are **obligate aerobes:**
* **Pearl:** If a GNR in blood culture shows *anaerobic* growth, no need to cover for Pseudomonas!
* Acinetobacter spp. are often intrinsically resistant to multiple antibiotics including **ertapenem** and may be variably susceptible to meropenem or imipenem (*susceptibility to one carbapenem does not predict susceptibility to another!*)
* Stenotrophomonas are intrinsically resistant to *carbapenems*; generally most susceptible to quinolones, sulfas, and tetracyclines.
* These species are not of the family Enterobacteriaceae & often affect patients whose microbiome has been altered by extensive antibiotic/healthcare exposure.

**Which antibiotics are bacterioSTATIC?**

“In sepsis, restore **V**olume with a **L**iter of **ST**AT **NM**L(normal) **S**aline.”

**V**ancomycin in Enterococcus – cidal for all other GPCs

**L**inezolid/**L**efamulin

**S**ulfas/trimethoprim (*especially static against Stenotrophomonas*)

**T**etracyclines/**T**igecycline

**N**itrofurantoin (cidal in cystitis if concentration > 2x MIC)

**“MLS** antibioticgroup” – clindamycin, macrolides (Note: Streptogramins are bactericidal)

Everything else is bactericidal.

*Note bene:* Clindamycin & linezolid are best studied as *adjuncts* for Staph or Strep toxic shock, severe streptococcal cellulitis or suspected necrotizing infection; *halt protein synthesis*—stops production of toxins that mediate severe inflammation, necrosis, and toxic shock. Many Staphylococcus aureus strains carry *inducible* clindamycin resistance genes, so I suggest having susceptibilities available before relying on clindamycin alone for this pathogen (if your lab doesn’t report inducible clindamycin resistance, check for erythromycin resistance--- *erm* mutation! ---as a clue). Other drugs whose mechanism of action is disruption of protein synthesis: doxycycline/minocycline/tigecycline.

**What does the MIC mean & how do we use it?**

The MIC is the lowest concentration of an antimicrobial agent that completely prevents visible growth of the test strain of an organism in culture. Each antibiotic will have a different MIC for each organism. The MIC value of an antibiotic must be compared with clinical outcomes for the disease caused by a given organism; in some cases, this is further drilled down to differentiate between clinical scenarios (e.g., meningitis vs UTI), and the pharmacokinetics of individual antimicrobials. This overview yields “*clinical* *breakpoints*” that define whether the strain is susceptible (S), susceptible dose dependent (SDD) or resistant (R) to the antibiotic. Clinical breakpoints are internationally reviewed & and adjusted yearly according to expert consensus, epidemiology, and clinical literature by EUCAST (European Committee on Antimicrobial Susceptibility Testing), the American CLSI (Clinical and Laboratory Standards Institute), and further updated by the FDA (Food and Drug Administration). Fortunately, your friendly hospital Micro lab and their automated systems do a LOT of the interpretation work for you. If Micro says it’s susceptible, it usually is—just beware of SPICE/CEK (G). And vancomycin “MIC creep” with S. aureus bacteremia—as MIC “creeps” above 1, so does treatment failure. Etc, etc.

**Pharmacokinetics & Pharmacodynamics (PK/PD)**

Important determinants of antibiotic dosing for maximal effect include time-dependent vs concentration-dependent activity, volume of distribution/Vd (obesity, serum albumin), and route of elimination (renal, hepatic [cytochrome P450 enzymes], GI).

**Time-Dependent** antibiotics depend on duration of time that free antibiotic levels remain in tissue above MIC, no post-antibiotic effect. Doses must be given at regular intervals to maintain activity. Low albumin levels may lower free antibiotic levels by allowing increased free antibiotic to be cleared before it gets into tissues (highly protein-bound antibiotics may need higher doses, esp with less susceptible organisms).

* All beta lactams, monobactam, carbapenems

**Concentration-dependent** antibiotics act by achieving a high initial concentration & have a persistent “post-antibiotic effect”—i.e. bacterial growth is inhibited or “stunned” for a long time even after concentrations are no longer above MIC. Allows for extended dose intervals. Low albumin levels may lower free antibiotic levels by allowing increased free antibiotic to be cleared before it gets into tissues. At higher doses, highly protein-bound antibiotics may maintain adequate serum concentration if enough free antibiotic is available; again, may need higher dose).

* Aminoglycosides
* Daptomycin
* Metronidazole
* Quinolones (mostly)

**Combination of Time above MIC + Post-antibiotic Effect**

* MLS group – macrolides, clindamycin, tetracyclines
* Linezolid
* Vancomycin – dosing is optimized by achieving certain concentration for certain period of time, or “area under the curve” (AUC) -based dosing



**Protein binding of antibiotics & potential impact on “in vivo” MIC**

Antimicrobials must be able to cross from plasma into tissues to work, and antimicrobials are variably protein-bound (mostly to albumin). Hypoalbuminemia reduces protein-bound concentration of drug, which is measurable as reduced total plasma concentration (bound + free drug). Strictly on pharmacokinetic principles, total free drug concentration does not change (and may increase free drug available to diffuse into tissues). Thus, therapeutic drug monitoring (TDM) data may not reflect reduced tissue availability.

There is controversy about the role of albumin and need for alteration in antimicrobial selection and dosing in the literature (Gandia et al. [Hypoalbuminemia and Pharmacokinetics: When the Misunderstanding of a Fundamental Concept Leads to Repeated Errors over Decades. Antibiotics 2023, 12(515)](https://doi.org/10.3390/antibiotics12030515)). TDM studies measuring tissue concentrations may yield the most clinically meaningful data. The list of drugs and protein-binding below is added for scholarly interest (Ulldemolins et al. [The Effects of Hypoalbuminaemia on Optimizing Antibacterial Dosing in Critically Ill Patients. Clin Pharmacokinet 2011, 50(2)](https://doi.org/10.2165/11539220-000000000-00000)). Your mileage may vary.

**Inoculum Effect & impact on “in vivo” MIC**

Inoculum effect (IE) is the phenomenon where infections fail to clear in the setting of high bacterial burden (abscesses, endocarditis, lack of source control) despite treatment with an antibiotic with low in vitro MIC. Mechanisms are not fully understood. Inoculum effect (IE) was first recognized in cefazolin when MSSA infections, especially “deep” infections like endocarditis, failed to clear despite low MIC in vitro. We now know that IE may occur with other antibiotics (mostly beta lactams). Roughly:

HIGHER IE ---------------------------------------------------------------------------🡪 LOWER IE

vancomycin > ampicillin >>> amp-sulbactam > ceftriaxone > ceftaroline

cefazolin piperacillin pip-tazobactam cefepime daptomycin

dalbavancin amoxicillin amox-clavulanate ceftazidime ertapenem

 ceftolozane meropenem ceftaz-avibactam

**Synergistic IV Antibiotic Combinations against Specific Pathogens**

**Rule #1 – Don’t wing it!** Synergy is not that common.Some combos may be antagonistic, so combine with care (i.e. Use only combos supported by good literature).

Cell wall active agents + cell wall active agents

* serious GPC/GNR infections
	+ Beta lactams + aminoglycosides
		- AG disrupts cell wall (superoxides) 🡪 increases beta lactam cell wall penetration
		- AG also disrupts cell wall protein production
* serious Enterococcus faecalis/faecium infections
	+ Ampicillin + cephalosporins/ertapenem
		- amp binds PBP 1,4,5 + ceph/erta binds PBP 2,3 = lower amp MIC
		- beta lactam also enhances cationic peptide activity against cell wall
		- now preferred to avoid nephrotoxicity of amp + gentamicin combo
* MSSA/MRSA persistent bacteremia/endocarditis salvage
	+ daptomycin + cephalosporins (esp ceftaroline)/ertapenem
		- daptomycin has + surface charge, as does cell wall
		- beta lactams reduce + cell surface charge = improved binding
	+ cefazolin/ceftaroline + ertapenem (meropenem can be safely used with ceftaro if SA & GNR infection!)
		- binds more PBPs
		- ceph also enhances cationic peptide activity against cell wall
* KPC carbapenemase-producing GNR (blaKPC mutation)
	+ ertapenem + meropenem
	+ erta acts as (“suicide antibiotic” preferential affinity for carbapenemase—erta resistance is often alerts Micro to test for KPC)
* Carbapenem-R Acinetobacter (CRAB)
	+ Meropenem + sulbactam (as ampicillin-sulbactam—high dose 6-9g/d for most effective sulbactam dose) or sulbactam-durlobactam)
	+ Polymixin B or colistin + carbapenem, tigecycline, or amp-sulbactam – more to come!
* Invasive Aspergillosis, when avoiding nephrotoxicity
	+ Echinocandin + azole antifungal – in hematologic malignancy, combination may reduce mortality vs azole alone [Ann Intern Med. 2015;162:81-89. doi:10.7326/M13-2508]

**Drugs that penetrate the prostate:**

* quinolones
* trimethoprim-sulfamethoxazole
* doxycycline
* fosfomycin
* azithromycin
* beta lactams

**THE CLASSES (not an exhaustive list)**

**Penicillins** – beta lactams are CIDAL, good tissue penetration

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **Cerebral Spinal Fluid (CSF)** |
| **Natural Penicillins (PCN)**$IVpenicillin G (benzylpenicillin)POpenicillin VK CIDAL -targets PCN binding proteins (PBPs)🡪cell wall disruption | Group A Strep (no resistance)Strep viridansNeisseriaCapnocytophagiaActinomycesFusobacteriumClostridia perfringens/tetaniPasteurellaTreponema/LeptospirosisNOT MSSA (resistant) | Skin/soft tissue (SST) Oral/dental infections | HypersensitivityStevens JohnsonInterstitial nephritisSeizures (if high level)Bone marrow suppress-ionC.difficile | YES if inflamed |
| **Penicillinase-resistant PCN** $IV methicillin nafcillinoxacillinPOdicloxacillin CIDAL -targets PCN binding proteins (PBPs)🡪cell wall disruption-enhances cationic (cathelicidin) host peptide activity (PMNs)-resists PCNase (narrow spectrum beta lactamase) | MSSAMS S.epidermidis/other coagulase-negative StaphylococciS. lugdunensisStrep pyogenes (grp A)Strep agalactiae (grp B)Strep grp C,F,GStrep anginosus grpStrep pneumoniae (if susceptible) | SSTIBacteremiaEndovascular infections | FeverHypersensitivityStevens JohnsonInterstitial nephritisSeizures (if high level)Bone marrow suppress-ionHepatotoxicityC.difficile |
| **AminoPCN** $$ IVampicillinamp/sulbactamPOamoxicillin ampicillinamox/clavulanateCIDAL-targets PCN binding proteins (PBP 1, 4, 5)🡪cell wall disruption-enhances cationic (cathelicidin) host peptide activity (PMNs) | Add to the above:Enterococci (PBP 5 can assume PBP1-3 roles)ListeriaMSSAMost PneumococcusProteusHemophilus influ. (beta lactamase negative)Salmonella/ShigellaAnaerobes*Klebsiella are intrinsically resistant to amp/amox* (clavulanate/sulbactam don’t add much activity)Note: High-dose amp-sulbactam may used as a source of *sulbactam* in treating MDR Acinetobacter | Otitis mediaSinusitisSSTMeningitis in elderly | Above |
| **CarboxyPCN**$$IVticarcillin/clav (Europe)piperacillinpiperacillin/tazobactam CIDAL | Adds to the above:PseudomonasEnterobacteriaceae\*Stenotrophomonas (ticar)Gut anaerobesMSSAPip & Pip/tazo more potent for GNRs & more resistant to AmpC/ESBLs (See “SPICE” above)\**Klebsiella is intrinsically R to ticarcillin*  | Adds to above:Gut/surgical infectionsNosocomial pneumoniaProstateOsteomyelitis | Above |

**Cephalosporins** – Think of progressive broadening of spectrum from Gram + to Gram - with each generation. Beta lactams are CIDAL. [☺= can be dosed 3 times weekly in dialysis patients]

\*\*\*CROSS-ALLERGY (same side chains) between aztreonam – ceftazidime – cefiderocol\*\*\*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **CSF** |
| **1st Generation**$$IV/IMcefazolin ☺POcephalexin cefadroxilCIDAL-targets PCN binding proteins (PBP 1,2)🡪cell wall disruption-enhances cationic (cathelicidin) host peptide activity (PMNs) | GPC/MSSA/streptococci, E. coli, Proteus, some Klebsiella (increasingly ampC+/ESBL)NOT Enterococci | SSTIUncomplicated/Non-diabetic osteomyelitisPreOP prophylaxis | HypersensitivityBone marrow suppression DiarrheaC.difficile |  POOR |
| **2nd Generation**$$POcefuroxime cefaclor IVcefuroximecefamycins: cefoxitin cefotetanCIDAL-targets PCN binding proteins (PBP 2, 3)🡪cell wall disruption-enhances cationic (cathelicidin) host peptide activity (PMNs) | Streptococci, uncomplicated MSSAPneumococcusNeisseriaSome GNR except Pseudomonas**Cefamycins are the only ones that reliably cover *anaerobes***NOT Enterococci | Community acquired pneumonia (CAP)meningitisOM/sinusitisGonorrhea | HypersensitivityRASH/Stevens Johnson w/ cefaclorHigh INR/PT w/ cefoxitin/cefotetanBone marrow suppressionC.difficile | YES if strongly inflamed-- ceftriaxone >90% protein bound, low BBB penetration |
| **3rd Generation**$$POcefpodoximeIVceftriaxone cefotaximeCIDAL-targets PCN binding proteins (PBP 2, 3)🡪cell wall disruption-enhances cationic (cathelicidin) host peptide activity (PMNs) | Above; covers viridans streptococci, pneumococcus, but reduced PBP binding in MSSA | MeningitisCAPMost community-acquired infectionsGonorrheaPyelonephritisBest *PO* ceph for GU is cefpodoxime (20-30% protein-bound, vs PO cefdinir, which is poorly excreted in urine & up to 70% protein-bound) | Above Ceftriaxone: *Pseudo-cholelithiasis* (biliary sludge)  |  |
| **4th Generation/Anti-pseudomonal**$$ceftazidime (IV)☺ cefepime☺CIDAL | Above, plus PseudomonasMore resistant to beta lactamases/ESBLs (See “SPICE” above) because it is not porin-dependentNOT Enterococci | Above, plus neutropenic fever | Above Cefepime: *Encephalopathy*, non-convulsive status epilepticus |  |
| **Advanced-generation/Anti-pseudomonal**$$$IVceftolozane-tazobactamceftazidime-avibactamCIDAL-targets PCN binding proteins (PBP 2, 3)🡪cell wall disruption-enhances cationic (cathelicidin) host peptide activity (PMNs) | Viridans streptococciNOT Enterococci or Staphylococciceftoloz-taz covers GNRs incl Pseudomonas, ESBLs, *some* carbapenemase-producing P. aeruginosa (CRPA), NOT KPC+ceftaz-avi covers ESBL & KPC+ carbapenemase (1st line agent)ceftaz-avi covers GNRs incl Pseudomonas, adds coverage for ceftaz-R, ESBLs, some ampC-R, *some* carbapenemases (NOT metallobetalactamase) | Complicated UTI/pyelo Complicated intraabdominal infection ceftaz-avi adds HAP | Above Nausea, diarrhea, headache, fever, renal insufficiency (ceftolaz-taz) | ceftazidime– CSF, YES if inflamed (NOT avibactam)-- 90% renal excretion, unchanged (avibactam 97%)-- <10% protein boundmetolazone-– CSF UNKNOWN-- > 95% renalexcretion, unchanged-- 30% protein bound |
| **Anti-MRSA cephalosporin**$$$IVceftarolineCIDALMOA:-Targets PCN binding proteins, esp PBP2a (MRSA) & PBP 2b, 2x, 1a (PCN-R pneumo)🡪cell wall disruption-increases host cethelicidin peptide activity (PMNs) | Similar to 3rd generation, plus MRSA, VISA/VRSA/VRE faecalis (NOT E. faecium), PCN-R pneumococcus, beta-lactamase + H.flu, Moraxella Listeria NO Pseudomonas | Complicated SSTI, CAP (NOT MRSA-insufficient data) | Above | YES if strongly inflamed |
| **Siderophore cephalosporin**IVCefiderocolSimilar side chains as cefep & ceftazCIDAL-targets PCN binding proteins PBP 3, PBP1a (PSA), PBP2 (KPC)🡪cell wall disruption-Trojan horse siderophore: Chelates Fe++, so drug is actively transported with Fe++ via siderophore channels  | Reliably covers XDR/carbapenem-R:*Metallobetalactamase* producers (MBL)Klebsiella pneumoniae (KPC+)Pseudomonas aeruginosa (CRPA)Enterobacteriaceae (CRE)Acinetobacter baumanii (CRAB)StenotrophomonasBurkholderia cepacianColistin-R GNRsNO GPC! | Complicated UTI/pyelo HAP |  | Yes if inflamed |

**Monobactam**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **CSF** |
| aztreonam$$IVCIDAL-targets PCN binding proteins (PBP 3)🡪cell wall disruption | ONLY GNRs, incl Pseudomonas Covers metallobetalactamase carbapenemases, but not ESBL (resistance usually occurs together)—combination of aztreonam + ceftaz-avibactam might be used in salvage cases ([CID 2021;72:1871](https://doi.org/10.1093/cid/ciaa586)) | GNR infections; NOT a replacement for all aminoglyco-side uses (no synergy for GPC, NO Enterococcal coverage) | Low Good alternative for beta lactam allergies EXCEPT with ceftazidime, cefiderocol | YES if inflamed [Modal J et al. AAC. 1986;29:281-3.] |

**Carbapenems (Beta lactams reserved for Multidrug Resistant Organisms – MDRO)**

[☺= can be dosed 3 times weekly in dialysis patients]

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **CSF** |
| $$$IVimipenem-cilastinmeropenemmeropenem-vaboractamimipenem-cilastin-relebactam CIDAL-targets PCN binding proteins (PBP 1,2,3,4) 🡪cell wall disruption | GPCs EXCEPT MRSAGNRs EXCEPT Stenotrophomonas/BurkholderiaESBL+ & ”SPICE” GNRsAnaerobes (incl Cutibacterium)ListeriaPneumococcusNocardia asteroides (NOT brasiliensis)LegionellaMycobacterium aviumEnterococcus (NOT E. faecium)mero-vaboractam adds *carbapenemase+ Klebsiella pneumonia (KPC)*, class A carbap-R Enterobacteraciae (NOT metallobetalactamase/OXA carbap-R, NOT carbap-R Pseudomonas/Acinetobacter)Relebactam is not active against Morganellacea group (Morganella, Proteus, Providentia) | Resistant GNR infectionsSerious gut infectionsNecrotizing pancreatitis | IV/IMHypersensitivity(~10% cross-allergy with beta lactams)Seizures with imipenem (if renal insufficiency or high levels used) Candida overgrowth/infectionsC.difficile | YES |
| $$$IVdoripenemCIDAL | Above, possibly lower MICs to Pseudomonas & Acinetobacter | Above Higher mortality than imipenem in VAP | Above |
| $$$IV/IMertapenem ☺CIDAL | Above, without Pseudomonas coverage | Postpartum uterine infectionsPostsurgical Abdominal infections (not Pseudomo-nas) | Above *Encephalopathy* |

**Aminoglycosides**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/****MISC** | **CSF** |
| $-$$$IVgentamicinstreptomycinspectinomycintobramycin amikacinNebulizedtobramycinliposomal amikacinCIDAL-disrupts cell wall (superoxides) 🡪 increases beta lactam cell wall penetration -disrupts cell wall protein production | Gent: VSE/VRE/variable Staph, GNRs incl PseudomonasTobra/Amik: GNRs incl PseudomonasAmik: TB, non-TB MycobacteriaStrepto -Yersinia -MDR Mtb Gent/Strepto-Tularemia Spectino-Gonorrhea NO coverage for:Acinetobacter/StenotrophomonasAnaerobes Pneumococcus | Synergy with beta lactams for GPC/Pseud-omonas infections Usually not used alone except for UTIs | IV/Aerosol Acute tubular necrosis (reversible) Cochlear toxicity (genetic predisposition) Vestibular toxicity (irreversible)When possible:-stop after 3-5 d-use once-daily dosing-avoid in elderly Liposomal amik – hypersensitivity pneumonitis, hemoptysis, bronchospasm, exacerbation of lung disease Neuromuscular blockade (may exacerbate myasthenia gravis & paralytic agents) | NO or UNKNOWN (use intrathecal) |
| $$PO only, in U.S.fosfomycin CIDAL | EnterococcusStaph. aureusGNRs | Simple cystitis in womenOff-label q3days for complicated or MDR GNRs, VRE if susceptible*Prostatitis* | PO onlyAbove, significant diarrhea |
| $$ IV plazomicin CIDAL | GNRs incl MDR/KPC/metalobetalact/CRE GNRs,variable Pseudomonas (use only if known susceptible), NOT Steno, Acinetobacter | Complicated UTI/pyelonephritis | IV onlyAboveLimited data |

**Sulfonamides/Sulfas (*INTRACELLULAR* ACTIVITY)**

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| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| $IV/POtrimethoprim-sulfamethoxazole (co-trimoxazole)-synergistic combo-sequentially inhibit folic acid pathway🡪protein synthesis inhibitionSTATIC -each drug aloneCIDAL?-GNRs in urine-variable depending on organism; may not be cidal for Staph | Staph. aureus (incl MRSA)*(NOT Enterococcus, Pseudomonas, Acinetobacter)**Legionella**Stenotrophomonas**Listeria**Pneumocystis**Nocardia* Burkholderia cepaciaMoraxellaYersiniaFrancisella tularensis*Toxoplasma*Atypical mycobacteria (*M. marinum*)Some common coliforms | Cystitis/pyelonephritis*Prostatitis*MRSA SSTISpecific agents at left*Dosing depends on what you’re treating* | IV/PORASH/Stevens Johnson NauseaFever Bone marrow suppressionHemolysis (if G6PD deficient) Hepatotoxicity*Elevated creatinine despite normal GFR* (competes with Cr for tubular secretion*Hyperkalemia* (blocks Na+ channels & thus K+ excretion)Kernicterus in neonatesC.difficileSun sensitivity | YES |

**Pleuromutilins (*INTRACELLULAR* ACTIVITY)**

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| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| $$$IV/POLefamulin\*\*STATIC -Protein synthesis inhibitor – multiple binding sites to ribosome, higher resistance barrier | S. pneumoniae MSSA, ?MRSAHemophilus influenzae Mycoplasma pneumoniae Chlamydia pneumoniae Legionella pneumophila | CAP/community-acquired pneumonia \*\* Bacteriostatic – be aware of this when empirically treating serious infections. | Nausea, hepatotoxicity, CNSHypokalemiaProlonged QTcTeratogenicityC. difficile | UNKNOWN70% fecal excretion |

**Macrolides/Lincosamides (Macrolide-Lincosamide-Streptrogramin B class, or MSL—all bind 50s ribosome subunit & share resistance genes)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| **Macrolides**$$IV/POErythromycinPOclarithromycinazithromycinSTATIC-protein synthesis inhibitor, binds 50s ribosomal subunit | Pneumococcus IF local resistance is <25%MSStaph. aureus (not MRSA)LegionellaListeriaHemophilusMoraxellaMycoplasma *Pertussis*Neisseria meningitisChlamydia/Hemophylus ducreyiCampylobacterHelicobacter pylori Salmonella/Shigella*Bartonella* Borrelia burgdorpheri (*Lyme* disease*Babesia* microtiActinomycesAtypical mycobacteria | LRTI/bronchitisSinusitisDental/oral infections*Prostatitis*Atypical mycobacteria(incl MAC prophy in HIV) | IV/PONausea/vomitingAbdominal cramps/diarrhea (Lowest with Azithro)C.difficileOtotoxicity with chronic useRare association with cardiovascular mortality with QTc prolongation, low Mg++/K+. Interactions: Ery/Clari induce P450!Neuromuscular blockade with Ery (may exacerbate myasthenia gravis & paralytic agents) | Adequate – better for Mycoplasma, Legionella, Chlamydia |
| **Lincosamides**$$IV/POclindamycinSTATIC-protein synthesis inhibitor, binds 50s ribosomal subunit | CIDAL for Group A streptococcus, MSStaph. aureus (MRSA, but watch for inducible *erm* resistance. Clue is resistance to erythromycin)PneumococcusInhibits toxic proteins in severe Strep A & S. aureus/necrotizing fasciitis.Oral anaerobes: Gram + such as Peptostrepto-coccus, Fusobacterium, Prevotella, Actinomyces, & Clostridial spp other than Clostridium difficileGram – such as Bacteroides (may not cover in up to 25% of cases or strains with MIC >/= 8 mcg/mL)Babesiosis | Severe SSTI, necrotizing fasciitis, MRSA*“Infections above the diaphragm”*Head and neck/dental infectionsLung abscess/aspiration pneumonia (*tip: no teeth = no anaerobes*)Bacterial vaginosisBabesiosisToxoplasma in HIV |  IV/POC.difficile!! (>30% develop it on a week of clinda)DysgeusiaRash, fever, eosinophiliaErythema multiformeReversible neutropenia/thrombocytopeniaWatch for hepatitis/obstructive jaundice, severe liver injuryNeuromuscular blockade (may exacerbate myasthenia gravis & paralytic agents) | POOR except for Toxoplasmosis in HIV |

**Nitrofuran**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CNS** |
| $ POnitrofurantoinCIDAL in urine-multiple targets including protein synthesis | GNRs EXCEPT Pseudomonas, Proteus, and Enterococcus incl susceptible VRE Multiple sites of action, inhibits synthesis of DNA, RNA, proteins, cell wall – higher resistance barrier than most antibiotics | CystitisSusceptible ESBL GNRsONLY reaches therapeutic level in URINE | PO onlyNausea/vomitingC.difficilePulmonary – acute, chronic, reversibleHepatotoxicityNeuropathy if prolonged use | NONE |

**Quinolones (Resistance is rising due to overuse; single-step mutation🡪 resistance may arise *while on therapy*;** ***INTRACELLULAR* ACTIVITY; high concentration in bone, prostate, CSF)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| **“Gram negative”****Quinolones**$-$$IV/POciprofloxacinlevofloxacinPOnorfloxacinCIDAL-targets DNA gyrase and topoisomerase IV-inhibits DNA synthesis | GNRs including PseudomonasLevo covers pneumococcus & Stenotrophomonas well “Atypical” pneumonia: Mycoplasma, Chlamydia, MoraxellaSome mycobacteria/TB | Cystitis/pyelonephritis*Prostatitis*Intraabdominal infectionsEndometritisHospital-associated lung infections Levo best for acute sinusitis/CAPNorflox: UTI only | IV/PO *IV=PO (bioequivalent)*Dizziness/CNSDiarrheaHypo-/hyperglycemiaSun sensitivityMay exacerbate myasthenia gravis & paralytic agents (inhibits GABA receptors)May prolong QTc (watch for palpitations/syncope; avoid if QTc > 500msec, cardiomyopathy)Rare spontaneous tendon rupture (watch for pain at tendon sites)\*Aortic dissection association\*C.difficile | YES, HIGH DOSE |
| **“Gram positive or Respiratory” Quinolone**$$POmoxifloxacinCIDAL-targets DNA gyrase and topoisomerase IV-inhibits DNA synthesis | Pneumococcus, Streptococci, Staphylococcus (NOT MRSA)Legionella Gut anaerobesAtypical mycobac/TB | CAP/community-associated respiratory infectionsAcute sinusitisIntraabdom-inal infectionsSSTI | IV/PO *IV=PO (bioequivalent)*Above>60% *liver* excretion | UNKNOWN |
| **“Gram positive or Respiratory” Quinolone**$$IV/POdelafloxacinCIDAL-targets DNA gyrase and topoisomerase IV-inhibits DNA synthesis | Streptococci, Staphylococcus *MRSA*PseudomonasLegionellaGut anaerobesAtypical mycobac/TB | SSTI CAP/community-associated respiratory infections | IV/PO *IV=PO (bioequivalent)*Above | UNKNOWN |

**Nitroimidazole**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| $$IV/POmetronidazoleCIDAL-degrades DNA by formation of N+-linked free radical-inhibits protein synthesis | Gram – anaerobes incl. Bacteroides fragilis and all ClostridiaEntamoeba coli | *“Infections below the diaphragm”*Intraabdominal abscess, peritonitis, diverticulitis, etcEndometritis/Bacterial vaginosisClostridium difficile colitisEntamoeba liver abscess/dysenteryNOT to be given alone for lung abscess/ENT infections  | IV/PODisulfiram-like reaction (vomiting) if ethanol consumed within 3 days of therapyAseptic meningitis/neuropathies, rare | YES |

**Tetracyclines/Glycylcycline (*INTRACELLULAR* ACTIVITY)**

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| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| **Tetracyclines**$IV/POMinocyclineDoxycyclineSTATIC | **MRSA**/MSSA PneumococcusEnterococci (incl VRE. faecalis/faecium)+/- GASE. coliLegionellaN. meningitidisHemophilusMoraxellaMycoplasmaChlamydia ListeriaBrucellaActinomycesBorrelia burgdorferiRickettsiaVibrioTreponema Anaerobes: Fusobacterium, Cutibacterium, Peptostreptococcus, Clostridium, some Bacteroides fragilis/melanogenicus | Acne/rosaceaSSTICAP, esp under age 40Dog/cat bite prophy as alternative to amox/clav Tickborne diseases*Prostatitis* | IV/PODiscoloration of permanent teeth in children Esophageal ulcerHepatotoxicityPseudotumor cerebri, esp minocycline! (watch for headache)Sun sensitivityC.difficileInhibit lipopolysa-ccharide-induced proinflammatory products | YES (neuroborelliosis, syphilis) |
| **Glycylcycline**$$IVtigecycline >\*\*eravacycline\*IV/POomadacyclinesarecycline (acne only)STATIC | Above, plus Staph. epidermidisEnterococciCorynebacteriumN. gonorrheaESBL + E.coli/Klebs(NOT KPC)StenotrophomonasAcinetobacterSalmonellaB. fragilis/anaerobesClostridia incl. C.difficileNOT Pseudomonas, Burkholderia\*eravacycline adds ESBL, carbap-R Acinetobacter | SSTIIntraabdo-inal infectionsCAP/HAP*Prostatitis*Severe C.difficileY alveolar, soft tissue, bile/gut entryPoor bone/joint, CNS\*\* Bacteriostatic – be aware of this when empirically treating serious infections.> **Increased mortality** vs. comparators in after-market review of pooled clinical trials, incl in FDA-approved indications. | IV onlyAbove20% tige, 6.5% erava - nausea, vomiting Inhibit lipopolysaccharide-induced proinflammatory products\*/\*\*Ampicillin/Amoxicillin CIDAL-preferred in VRE that is amp-susceptible. | UNKNOWN |

**Glycopeptides, lipoglycopeptides**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/****MISC** | **CSF** |
| $-$$$IV/POvancomycinCIDAL, except *STATIC for Enterococci* | Gram + cocci except VRE/VRSA *Most* Gram + rods (but see below)CorynebacteriumListeriaC.diff (only PO)Increasing vancomycin MICs > 1 assoc with treatment failures (“MIC creep”)**Instrinsic resistance in:**LeuconostocLactobacillusPropionobacteriumPediococcusErysipelothrixClostridia(non-diff.) | SSTI due to MRSAHAP/CAP due to MRSAInfections due to VRE | Vanc IV$\ne $PO – PO not absorbed from gutVanc requires a **central IV line**, due to phlebitis (which may cause fevers, unnecessary antibiotics/cultures/increased lengths of stay…)“Red man syndrome” with vanc (histamine release) if infused too rapidly—infuse over 1-2 hoursLeukopeniaThrombocytopeniaRare interstitial necrosisOtotoxicity (abrupt, irreversible, usually elderly)Rarely, DRESS | YES |
| $$$IVdalbavancinCIDAL | MSSA, MRSA, Group A, B streptococci, Strep anginosus group | SSTI, osteomyelitis/prosthetic joint infection, endocarditis, bloodstream infection1500mg IV x1 OR1000mg IV then 500mg in 7 days | Nausea, headache, diarrheaHepatotoxicity“Red man syndrome” with vanc (histamine release) if infused too rapidly—infuse over 1-2 hours |  |
| $$$IVtelevancin CIDAL | MSSA, MRSA/VISA/VRSA, Group A, B streptococci, Strep anginosus group, VSEnterococcus | SSTI HAPneumonia due to MRSA/VISA | N/V, foamy urine NephrotoxicityQTc prolongationMortality > with mod/sev renal impairment compared with vancoPossibly teratogenic—avoid in pregnancy unless maternal benefit exceeds fetal risk “Red man syndrome” with vanc (histamine release) if infused too rapidly—infuse over 1-2 hours Interferes with coag tests but not coagulation |  |
| $$$IVoritavancinCIDAL including *Enterococci* | MSSA, MRSA, Group A, B, C streptococcus, Streptococcus anginosus group, VSEnterococcus | SSTI\*\*FAILED for osteomyelitis\*\*1200mg IV x1, over 3 hr | Headache, N/V“Red man syndrome” with vanc (histamine release) if infused too rapidly—infuse over 1-2 hoursHepatotoxicityArtificially prolong PT/INR for up to 12 hr (5.1); aPTT for up to 120 hours, and may prolong PT and INR for up to 12 hr and ACT for up to 24 hr—Use Factor Xa assay for coagulation testingCoadministration with warfarin may result in higher exposure of warfarin and increase risk for bleeding; monitor frequently for signs of bleeding |  |

**Cyclic Lipopeptides**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/****MISC** | **CSF** |
| $$$$IVdaptomycinCIDAL  | All Gram + cocci incl. Vanc-/Amp-resistant\* Entero-coccusMRSA/VRSA  | SSTIBacteremiaOsteomyelitis, Joint infectionsMay be active in biofilms (which usually inactivate antibiotics) | IV onlyFalse Prothrombin Time prolongationNausea/vomitingRhabdomyolysis & associated renal insufficiency (weekly creatinine, CPK)Rare asthmatic pulmonary eosinophiliaNOT for primary pneumonia because it is inactivated in alveolar fluid BUT seems effective in embolic lung infection/septic emboli due to Gram +s, since the infection is more parenchymal.\*ampicillin/amoxicillin (CIDAL) preferred in VRE that is amp-susceptible.  | UNKNOWN |

**Streptogramins**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVER-AGE** | **USES** | **TOXICITY/****MISC** | **CSF** |
| ~~quinupristin-~~~~dalfopristin~~~~$$$$~~~~CIDAL~~Discontinued by Pfizer 2022 | ~~Vanc-/Amp-resistant\* Enteroco-ccus faecium~~ ~~MSSA~~~~Group A Strep~~~~NOT Enteroco-ccus faecalis or MRSA~~ | ~~SSTI/non-MRSA~~~~Bacteremia~~~~Endocarditis due to VRE faecium~~~~Extremely limited use.~~  | ~~IV only~~~~Needs~~ **~~central IV line due to frequent pain, phlebitis, fever~~**~~>30+%~~ **~~Myalgias/~~****~~Arthralgia~~**~~s~~~~Nausea/~~~~Vomiting/~~~~Diarrhea~~ ~~\*ampicillin/~~~~amoxicillin (CIDAL) preferred in VRE that is amp-susceptible.~~  | ~~UNKNOWN~~ |

**Oxazolidinone (*INTRACELLULAR* ACTIVITY)**

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| --- | --- | --- | --- | --- |
| **DRUG** | **COVER-AGE** | **USES** | **TOXICITY/****MISC** | **CSF** |
| $$$$IV/POlinezolidSTATIC except CIDAL for streptococci | All Gram + cocci incl. \*\*vanc-/amp-resistant\* EnterococcusMRSA/VRSATB/Atypical mycobacteriaBinds 23S rRNA-blocks formation of 50s/70s ribosomal initiation complex  | SSTIMRSA HAP/CAP due to MRSAOsteomyelitis/Joint infections (good bone penetration)\*\*NOT for bacteremia without a well-defined and removal or draining focus, NOT for endovascular infections | *IV=PO (bioequivalent)*Nausea/vomiting/diarrheaTemporary tooth stainingHeadacheThrombocytopenia/Neutropenia after 7 daysPeripheral/Optic neuropathies with extended useLactic acidosis (nausea, fatigue)**Serotonin syndrome:**Avoid high tyramine food/drink, SSRIs (> 100mg tyramine per meal). E.g. aged cheeses, dried/processed meats, ethanol, sauerkraut, soy sauce, or yeast extract/supplements, ferments\*/\*\*ampicillin/amoxicillin (CIDAL) preferred in VRE that is amp-susceptible.\*\*Associated **with treatment failure in bacteremia**, incl line & endovascular infections.  | GOODMyrianthefs et al. Serum and CSF concentrations of linezolidin neurosurgery patients. AAC 2016. 50(12): 3971-6. |
| $$$$IV/POtedizolidSTATIC | All Gram + cocci incl. \*\*VRE, Amp-resistant\* Enterococcus, MRSA/VRSABinds 50s ribosomal subunit  | SSTI | *IV=PO (bioequivalent)*6 days tedizolid Qdaily = 10 days linezolid BID = higher lipid solubility/higher tissue levelsNausea/headache/diarrhea Lower thrombocytopenia than linezolid; similar neuropathic events; no longer term data**Serotonin syndrome:**Avoid high tyramine food/drink (> 100mg tyramine per meal). E.g. aged cheeses, dried/processed meats, ethanol, sauerkraut, soy sauce, or yeast extract/supplements, ferments | NO DATA – suspect similar to linezolid |

**Colistin/Polymixin B (Reserved for multi-drug resistant organisms - MDRO)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| $$$IVcolistinpolymixin BcolistimethateCIDAL | Gram - including Pseudomonas, Acinetobactermembrane disruption, binds lipopolysaccharide (LPS)/Gram - endotoxin | Intraabdominal infectionsUTI/GU infectionsPneumonia/Hospital-associated respiratory infectionsPotent anti-LPS binding/neutralizing activity | IV/Aerosol30% Nephrotoxi-city!Peripheral/Optic neuropathiesNeuromuscular blockade (may exacerbate myasthenia gravis & paralytic agents) | YES |

**Rifamycins**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| $-$$IV/POrifampinPOrifabutinOnly rifampin is discussed here, in context of use outside of mycobac-terial infections CIDAL | Very broad, incl GPC/GNR, mycobacteria; use is *condition*-specificRAPID RESISTANCE if given alone – *Use in combinations*Inhibits DNA-dependent RNA polymerase | *Only* used alone as prophylaxis against Neisseria meningitidis (2 days), Hemophilus influenza b (4 days) in contacts/nasal carriageCombination treatment in serious S. aureus, Streptococcal infectionsCombination treatment of Legionella, Anthrax, Brucella, Bartonella, Anaplasma, EhrlichiaCombination treatment of tuberculous and non-tuberculous Mycobacteria | IV/PORed urine, sweat, tears, saliva – hold soft contact useNausea, abd painHepatotoxicity (avoid ethanol & hepatotoxins), hyper-bilirubinemia Type I & Flu-like hypersensitivityAutoimmune reactionsMany drug interactions – always check an updated reference | YES |

**Triazaacenaphthylenes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| $$$POgepotidacinCIDALInhibits 2 topoisomerase II enzymes (DNA replication) | Escherichia coli, Klebsiella pneumoniae, Citrobacter freundii, Staphylococcus saprophyticus, Enterococcus faecalisNeisseria gonorrhea | Uncomplicated UTI in women | Diarrhea, nausea, abdominal painHeadache, dizzinessDysarthriaSevere C. difficile colitisQTc prolongationAcetylcholinesterase inhibition (caution in myasthenia gravis & succinylcholine neuromuscular blockers)No data in pregnancy/lactationInteracts with multiple drugs (*avoid* strong CYP3A4 inhibitors/inducers) | N/A |

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Thank YOU, dear Colleague, for your dedication to the Art and Science of Medicine.

I hope that you find this tool of help in your care of the VIP at the center of our efforts:

The Patient.

Dr. G