**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**

**By**

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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, few or NO anaerobes. ONLY ceftazidime/cefepime cover Pseudomonas. They do not cover SPACEK/SPICE**\*** Gram negatives reliably; ceftriaxone/cefepime may be fine in less serious infections.

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.

5. Quinolones cover Gram –s best (except moxifloxacin, best for respiratory Gram +s & anaerobes), some Mycobacteria.

6. Sulfas generally cover some Gram +s/MRSA, Nocardia, Listeria, Pneumocystis, most Gram –s except Pseudomonas.

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

8. Metronidazole generally covers Gram— anaerobes like Bacteroides, Prevotella, Clostridia; +/-Peptostrep (better for infections below the diaphragm).

9. Carbapenems are Big Gun Beta Lactams & Expensive. Use sparingly. Ertapenem covers most organisms except Pseudomonas. Imipenem, meropenem, & doripenem include Pseudomonas. Resistance in one carbapenem doesn’t predict resistance in others.

10. Keys to Antibiotics for Resistant Gram +s: Vancomycin, teichoplanin (Europe) cover all but vancomycin-resistant Gram +s; daptomycin, linezolid, quinupristin-dalfopristin are VERY EXPENSIVE ($100+ a day) & generally reserved for vancomycin-resistant Gram +s. Vancomycin is bacteriCIDAL, except bacterioSTATIC in Enterococcus. Daptomycin & quin-dalfo are CIDAL. Linezolid & tigecycline are bacterioSTATIC, NOT the right choice for bacteremia unless no other options are possible, and best not as monotherapy. Tigecycline is associated with higher mortality than comparators for FDA-approved indications in after-market review of pooled clinical trials.

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.***
2. If a bacterial infection is not high in the differential and the patient is not clinically toxic, forgo antibiotics. They are poor antipyretics.
3. ***Persistent fevers require work-up, not more antibiotics.***
4. If you are treating with broad antibiotics and fevers persist, stop them; they aren’t helping anyway.
   * Look for undrained foci of infection/pus 🡪 drain it.
   * Look for non-infectious cause 🡪 treat it.
   * True FUO in a rapidly deteriorating patient may warrant empiric anti-TB therapy 🡪 Call ID.
5. ***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 usually prevent resistance better than one, and neither do broad spectrum drugs. More drugs = more resistance opportunities. Yet multi-drug synergy *is* desirable in:
   * Pseudomonas sepsis/SIRS: May consider antipseudomonal PCN + 1 dose 5mg/kg IV aminoglycoside.
   * Rifampin + vancomycin/tetracyclines/TMP-SMX/etc for some S. aureus infections – NEVER rifampin alone 🡪RAPID resistance
   * TB/Atypical mycobacteria: *NEVER* use 1 drug in *active* TB
   * Cryptococcosis: 5-flucytosine + amphoB
   * Molds, Fusarium: voriconazole + an echinocandin (caspofungin has most data) or lipid-based amphotericin OR lipid-based amphotericin + caspofungin/echinocandin
   * DON’t treat viral infections (or noninfectious syndromes) with antibiotics beyond the point at which you have ruled out bacterial infection.
   * NEVER give Rifampin alone! Rapid high-level resistance occurs. Use in combinations.
6. ***Always monitor for antibiotic adverse effects.***
7. Antibiotics are a double-edged sword. Respect them.
8. 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.
9. Watch for yeast overgrowth/Candidemia with prolonged/multiple antibiotic therapy.
10. 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
11. RIFAMPIN 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, Candida EXCEPT Candida krusei/glabrata

Itraconazole = Candida, Histoplasma, Crypto, Aspergillus

Voriconazole = Candida, Histo, Crypto, Aspergillus, Fusarium, NOT Mucor/Rhizopus

Posaconazole /isuvaconazole = same as vori, + Mucor/Rhizopus

Caspofungin/Micafungin/Anidulafungin (enchinocandins) = Candida, Aspergillus, NOT Fusarium/Mucor/Rhizopus, SOME Crypto

Amphotericin = all, +/- Fusarium, NOT Candida lusitaniae/guillermondi, NOT

Scedosporium (Pseudallescheria)

**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; NOT other azoles/enchinocandins

DON’T USE Ampho + itra/keto = ANTAGONISTIC.

5FC increases penetration of above drugs.

**BacteriCIDAL vs. BacterioSTATIC**

A consideration in choosing treatments for serious infection like sepsis or bacteremia of meningitis, pneumonia, endocarditis, osteomyelitis, neutropenic fever. A “cidal” drug kills quickly; a “static” drug slows or stops replication and/or toxic production.

***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 infusion. (Google Johns Hopkins Continuous Antibiotic Infusion for their helpful guide; most drug databases don’t offer alternative dosing recommendations.) Some are also stable enough to be given 3 times a week after hemodialysis.

**SPICE/SPACEK are mnemonics for bacteria that are often beta lactam resistant or prone to developing it:**

**SPACEK**

**S**erratia

**P**seudomonas/indole + Proteus

**A**cinetobacter

**C**itrobacter

**E**nterobacter/**E**.coli

**K**lebsiella

**SPICE**

**S**erratia

**P**seudomonas

**I**ndole + Proteus

**C**itrobacter

**E**nterobacter/E.coli

These organisms may all demonstrate resistance to commonly prescribed beta lactams and may require carbapenem\* treatment. The SPACE organisms may produce inducible chromosome-based broad-spectrum beta lactamases as part of the Enterobacteriacae group, and resistance/failure may be induced during beta lactam treatment, even though they initially test susceptible. E. coli and Klebsiella are the most common extended spectrum beta lactamase (ESBL) producers, so many labs screen those isolates if MIC for ceftazidime is >/= 2 microG/mL. Just remember that most Enterobacter should be suspect for ESBLs, & may require carbapenem treatment. Remember that **Klebsiella** also has a constitutive (or inherent) chromosome-based beta lactamase that confers resistance to ampicillin/ticarcillin, so these drugs are never a good choice for this bacterium. Preferred treatment in serious infection is a carbapenem.

\*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 (carbapenem); many references gloss over this, and clinically we often use carbapenems as if they’re a completely different animal.

**Which antibiotics are bacteriostatic?**

In sepsis, restore **V**olume with a **L**iter of **ST**AT **NML** (normal)saline.

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

**L**inezolid

**S**ulfas/trimethoprim

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

(at)

**N**itrofurantoin

**“ML**S antibioticgroup” – clindamycin, macrolides (the streptogramins are bactericidal)

Everything else is bactericidal & probably better for sepsis and serious infections!

*Note bene:* Clindamycin is used as an adjunct for Staph or Strep toxic shock, severe streptococcal cellulitis or suspected necrotizing infection; it halts protein synthesis—i.e 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. You can also use linezolid, doxycycline/minocycline/tigecycline for toxin-inhibition in severe Staph infection.

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

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

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| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **Cerebral Spinal Fluid (CSF)** |
| **penicillin G**  $  CIDAL | Group A Strep (no resistance)  Strep viridans  Neisseria  Capnocytophagia  Actinomyces  Fusobacterium  Clostridia perfringens/tetani  Pasteurella  Treponema/  Leptospirosis  NOT Staph aureus (resistant) | Skin/soft tissue (SST) or  mouth infections | Hypersens-itivity  Stevens Johnson  Interstitial nephritis  Seizures (if high level)  Bone marrow suppress-ion  C.difficile | YES if inflamed |
| **AminoPCN**  $$  amoxicillin\*  ampicillin\*  amox/clavu  amp/sulbact  CIDAL | Add to the above:  Listeria  MSSA  Most Pneumococcus  Proteus  Hemophilus influ. (beta lactamase negative)  Salmonella/Shigella  Anaerobes  *\* Klebsiella are intrinsically resistant to amp/amox* (clavulanate/sulbactam don’t add much activity) | Otitis media  Sinusitis  SST  Meningitis in elderly | Above |
| **CarboxyPCN**  $$  ticarcillin/  clavulanate  piperacillin  piperacillin/tazobactam  CIDAL | Adds to the above:  Pseudomonas  Enterobacters  Stenotrophomonas (ticar)  Gut anaerobes  MSSA  Pip & Pip/tazo more potent for GNRs | Adds to above:  Gut/  surgical infections  Nosocomial pneumonia  Prostate  Osteomyel-itis | Above |

**Cephalosporins** – Think of progressive broadening of spectrum from Gram + to Gram - with each generation. Beta lactams are CIDAL.

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **CSF** |
| **1st Generation**  $$  cefalothin  cefazolin  CIDAL | GPC, E. coli, Proteus, Klebsiella  NOT Enterococci | SSTI  Uncomplicated/Non-diabetic Osteomyelitis  PreOP prophylaxis | Hypersens-itivity  Bone marrow suppression Diarrhea  C.difficile | POOR |
| **2nd Generation**  $$  cefuroxime (IV/PO)  cefaclor (PO)  Cefamycins:  cefoxitin (IV)  cefotetan (IV) | GPC  Pneumococc-us  Neisseria  Some GNR except Pseudomonas  Cefamycins add anaerobes  NOT Enterococci | Community acquired pneumonia (CAP)  meningitis  OM/sinusitis  Gonorrhea | Hypersens-itivity  RASH/Stevens Johnson w/ cefaclor  High INR/PT w/ cefoxitin/  cefotetan  Bone marrow suppression  C.difficile | YES if inflamed |
| **3rd Generation**  $$  ceftriaxone (QD dosing)  cefotaxime  ceftazidime  CIDAL | Above, plus Pseudomonas for ceftazidime | Meningitis  CAP  Most community-acquired infections  Gonorrhea  Pyelonephritis | Above |
| **4th Generation**  $$  cefepime  CIDAL | Above, plus Pseudomonas  Resists beta lactamases/ESBLs  Less freq dosing than ceftazidime  NOT Enterococci | Above, plus neutropenic fever | Above |
| **Anti-MRSA**  $$$  ceftaroline  CIDAL | Similar to 3rd generation, plus MRSA, VISA/VRSAVRE faecalis (NOT E. faecium), pneumococc-us, beta-lactamase + H.flu/  Moraxella | Complicated SSTI, CAP (NOT MRSA-insufficient data) | Above |
| **Advanced-generation**  ceftolazane-tazobactam  ceftazidime-avibactam  CIDAL | NOT Enterococci or Staphylococci  ceftolaz-taz covers GNRs incl Pseudomonas, ESBLs, NOT carbapenems  caz-avi covers KPC+ carbapenemase (1st line agent)  caz-avi covers GNRs incl Pseudomonas, adds coverage for ceftaz-R, ESBLs, some ampC-R, some carbapenemases (NOT metallobetalactamase) | Complicated UTI/pyelo  Complicated intraabdominal infection  caz-avi adds HAP | Above  Nausea, diarrhea, headache, fever, renal insufficiency (ceftolazane-t) | ceftazidime – YES if inflamed (NOT avibactam)  ceftoazane – UNKNOWN |

**Monobactam**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **CSF** |
| aztreonam  $$  CIDAL | GNRs only | GNR infections  NOT a replacement for all aminoglyco-side uses (no synergy for GPC, NO Enterococcal coverage) | Low | YES if inflamed  [Modal J et al. AAC. 1986;29:281-3.] |

**Carbapenems (Reserved for Multidrug Resistant Organisms – MDRO)**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY** | **CSF** |
| imipenem/  cilastin  meropenem  meropenem-vaboractam  $$$ | Gram +s EXCEPT MRSA  Gram –s EXCEPT Stenotrophomonas/Burkholderia  ESBL+& ”SPICE” GNR  Anaerobes (incl Cutibacteirum)  Listeria  Pneumococcus  Nocardia asteroides (NOT brasiliensis)  Legionella  Mycobacterium avium  +/- Enterococcus  mero-vaboractam adds *carbapenemase+ Klebsiella pneumonia (KPC)*, class A carbap-R Enterobacteraciae (NOT metallobetalactamase/OXA carbap-R, NOT carbap-R Pseudomonas/Acinetobacter) | Resistant GNR infections  Serious gut infections  Necrotizing pancreatitis | IV/IM  Hypersensit-ivity  (~10% cross-allergy with beta lactams)  Seizures (if renal insufficiency or high levels used) with imipenem  Candida overgrowth/  infections  C.difficile  Encephalo-pathy | YES |
| doripenem  $$$  CIDAL | Above, possibly lower MICs to Pseudomonas & Acinetobacter | Above | Above |
| ertapenem  $$$  CIDAL | Above, without Pseudomonas coverage | Postpartum uterine infections  Postsurgical Abdominal infections (not Pseudomo-nas) | Above |

**Aminoglycosides**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/**  **MISC** | **CSF** |
| gentamicin  streptomycin  spectinomycin  tobramycin  amikacin  liposomal amikacin  $-$$$  CIDAL | Gent: GPCs & GNRs incl Pseudomonas  Tobra/Amik: GNRs incl Pseudomonas  Amik: Mtb, NTM  Strepto  -Yersinia  -MDR Mtb  Gent/Strept  -Tularemia  Spectino  -Gonorrhea | Synergy with beta lactams for GPC/Pseud-omonas infections  Usually not used alone except for UTIs | IV/Aerosol  Acute tubular necrosis (reversible)  Ototoxicity/  Vestibular toxicity (irreversible)  When possible:  -stop after 3-5 d  -use once-daily dosing  -avoid in elderly  Liposomal amik – hypersensitivity pneumonitis, hemoptysis, bronchospasm, exacerbation of lung disease  Neuromuscular blockade (may exacerbate myasthenia gravis & paralytic agents) | NO-UNKNOWN |
| fosfomycin  $$  CIDAL | Enterococcus  GNRs | Simple cystitis in women  Off-label q3days for complicated or MDR GNRs, VRE if susceptible | PO only  Above, significant diarrhea |
| plazomicin  $$  CIDAL | GNRs incl MDR/KPC/metalobetalact/CRE GNRs,variable Pseudomonas (use only if known susceptible), NOT Steno, Acinetobacter | Complicated UTI/pyelo | IV only  Above  Limited data |

**Sulfonamides/Sulfas**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| trimethoprim-sulfamethoxazole  co-trimoxazole  $  STATIC for Staph | Staph. aureus (incl MRSA)  Legionella  Stenotroph-omonas  Listeria  Pneumo-cystis  Nocardia  Burkhold-eria cepacia  Yersinia  Francisella tularensis  Some common coliforms | UTI  MRSA SSTI  Specific agents at left | IV/PO  RASH/Stevens Johnson  Elevated creatinine or K+(competes with Cr for tubular secretion, blocks K+ excretion)  Kernicterus in neonates  C.difficile  Sun sensitivity | YES |

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

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| **Macrolides**  erythromycin  clarithromycin  azithromycin  $$  STATIC | Pneumo-coccus  MSStaph. aureus (not MRSA)  Legionella  Listeria  Neisseria meningitis  Hemophilus  Moraxella  Mycoplasma  Chlamydia  Actinomyces  Atypical mycobacteria | LRTI/  bronchitis  Sinusitis  Dental/  oral infections  Atypical mycobac-teria  (incl MAC prophy in HIV) | IV/PO  Nausea/  vomiting  Abdominal cramps/  diarrhea (Lowest with Azithro)  C.difficile  Ototoxicity with chronic use  Rare association with cardiovascular mortality with QTc prolongation, low Mg++/K+.  Interactions:  Ery/Clari induce P450!  Neuromuscular blockade with Ery (may exacerbate myasthenia gravis & paralytic agents) | POOR |
| **Lincosamides**  clindamycin  $$  STATIC | CIDAL for Group A streptococc-us, MSStaph. aureus (MRSA, but  watch for inducible *erm* resistance. Clue is resistance to erythromycin)  Pneumo-coccus  Inhibits toxic proteins in severe Strep A & S. aureus/  necrotizing fasciitis.  Oral anaerobes: Gram + such as Peptostrepto-coccus, Fusobacter-ium, Prevotella, Actinomyces, & Clostridial spp other than Clostridium difficile  Gram – 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 infections  Lung abscess/  aspiration pneumonia (tip: no teeth = no oral anaerobes)  Bacterial vaginosis  Babesiosis  Toxoplasma in HIV | IV/PO  C.difficile!! (>30% develop it on a week of clinda)  Watch for hepatitis/obstructive jaundice  Neuromus-cular blockade (may exacerbate myasthenia gravis & paralytic agents) | POOR except for Toxo-plasmosis in HIV |

**Nitrofuran**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CNS** |
| nitrofurantoin  $  CIDAL | Gram –s 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 | UTI/Cystitis  ONLY reaches therapeutic level in URINE | PO only  Nausea/  vomiting  C.difficile | NONE |

**Quinolones (Resistance is rising due to overuse)**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| **“Gram negative”**  **Quinolones**  ciprofloxacin  levofloxacin  norfloxacin  $-$$  CIDAL | Gram –s including Pseudomo-nas  Levo covers pneumococcus well  “Atypical” pneumonia: Mycoplasma, Chlamydia, Moraxella  Some mycobacteria/TB | UTI/GU infection  Intraabdomi-nal infections  Endometritis  Hospital-associated lung infections  Levo best for acute sinusitis/  CAP  Norflox: UTI only | IV/PO (Norflox PO)  *IV=PO (bioequivalent)*  Dizziness/CNS  Diarrhea  Hypo-/hyperglycemia  Sun sensitivity  May exacerbate myasthenia gravis & paralytic agents (inhibits GABA receptors)  May prolong QTc (watch for palpitations/syncope)  Rare spontaneous tendon rupture (watch for pain at tendon sites)  C.difficile | YES, HIGH DOSE |
| **“Gram positive or Respiratory” Quinolone**  moxifloxacin  $$  CIDAL | Pneumococcus, Streptococci, Staphylococcus (NOT MRSA)  Legionella  Gut anaerobes  Atypical mycobac/TB | CAP/community-associated respiratory infections  Acute sinusitis  Intraabdom-inal infections  SSTI | IV/PO  *IV=PO (bioequivalent)*  Above | UNKNOWN |
| **“Gram positive or SSTI” Quinolone**  delafloxacin  $$  CIDAL | Streptococci, Staphylococcus (NOT MRSA)  Legionella  Gut anaerobes  Atypical mycobac/TB | SSTI | IV/PO  *IV=PO (bioequivalent)*  Above | UNKNOWN |

**Nitroimidazole**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| metronidazole  $$  CIDAL | Gram – anaerobes incl. Bacteroides fragilis and all Clostridia  Entamoeba coli | *“Infections below the diaphragm”*  Intraabdominal abscess, peritonitis, diverticulitis, etc  Endometritis/  Bacterial vaginosis  Clostridium difficile colitis  Amebic liver abscess/  dysentery  NOT to be given alone for lung abscess/ENT infections | IV/PO  Disulfiram-like reaction (vomiting) if ethanol consumed within 3 days of therapy  Aseptic meningitis/  neuropathies, rare | YES |

**Tetracyclines/Glycylcycline**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| **Tetracyclines**  Minocycline  Doxycycline  $  STATIC | **MRSA**/MSSA Pneumococcus, +/- GAS  E. coli  Legionella  N. meningitidis  Hemophilus  Moraxella  Mycoplasma  Chlamydia  Listeria  Brucella  Actinomyces  Rickettsia  Vibrio  Anaerobes: Fusobacterium, Cutibacterium, Peptostreptococcus, Clostridium, some Bacteroides fragilis/melanogenicus | SSTI  CAP, esp under age 40  Dog/cat bite prophy as alternative to amox/clav | IV/PO  Discoloration of permanent teeth in children  Pseudotumor cerebri, esp minocycline! (watch for headache)  Sun sensitivity  C.difficile  Inhibit lipopolysa-ccharide-induced proinflam-matory products | YES |
| **Glycylcycline**  tigecycline \*\*  $$  eravacycline\*  omadacycline  sarecycline (acne only)  STATIC | Above, plus  Staph. epidermidis  Enterococci  Corynebacterium  N. gonorrhea  ESBL + E.coli/Klebs  Stenotrophomonas  Acinetobacter  Salmonella  B. fragilis/  anaerobes  Clostridia incl. C.difficile  NOT Pseudomonas or Proteus  \*eravacycline adds ESBL, carbap-R Acinetobacter | SSTI  Intraabdom-inal infections  CAP/HAP  Severe C.difficile  Y alveolar, soft tissue, bile/gut entry  Poor bone/joint, CNS  \*\* Bacteriostatic - NOT for serious infections;  **Increased mortality** vs. comparators in after-market review of pooled clinical trials, incl in FDA-approved indications. | IV only  Above  20% tige, 6.5% erava - nausea, vomiting  Inhibit lipopolysaccharide-induced proinflammatory products  \*/\*\*  Ampicillin/  Amoxicillin CIDAL-preferred in VRE that is amp-susceptible. | UNKNOWN |

**Glycopeptides, lipoglycopeptides**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/**  **MISC** | **CSF** |
| vancomycin  $  CIDAL except *STATIC for Enterococci* | Gram + cocci except VRE/VRSA  *Most* Gram + rods (but see below)  Corynebacterium  Listeria  C.diff (only PO)  Increasing vancomycin MICs > 1 assoc with treatment failures (“MIC creep”)  **Instrinsic resistance in:**  Leuconostoc  Lactobacillus  Propionobacterium  Pediococcus  Erysipelothrix  Clostridia(non-diff.) | SSTI due to MRSA  HAP/CAP due to MRSA  Infections due to VRE | Vanc IVPO – PO not absorbed from gut  Vanc 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 hours  Leukopenia  Thrombocytopenia  Rare interstitial necrosis  Ototoxicity (abrupt, irreversible, usually elderly) | YES |
| dalbavancin  $$$ | MSSA, MRSA, Group A, B streptococci, Strep anginosus group | SSTI  1500mg IV x1 OR  1000mg IV then 500mg in 7 days | Nausea, headache, diarrhea  “Red man syndrome” with vanc (histamine release) if infused too rapidly—infuse over 1-2 hours |  |
| televancin  $$$ | MSSA, MRSA/VISA/VRSA, Group A, B streptococci, Strep anginosus group, VSEnterococcus | SSTI  HAPneumonia due to MRSA/VISA | N/V, foamy urine  QTc prolongation  Mortality > with mod/sev renal impairment compared with vanco  Possibly 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 |  |
| oritavancin  $$$  CIDAL including *Enterococci* | MSSA, MRSA, Group A, B, C streptococcus, Streptococcus anginosus group, VSEnterococcus | SSTI  1200mg IV x1, over 3 hr | Headache, N/V  “Red man syndrome” with vanc (histamine release) if infused too rapidly—infuse over 1-2 hours  Artificially 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 testing  Coadministration with warfarin may result in higher exposure of warfarin and increase risk for bleeding; monitor frequently for signs of bleeding |  |

**Cyclic Lipopeptides**

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| **DRUG** | **COVER-AGE** | **USES** | **TOXICITY/**  **MISC** | **CSF** |
| daptomycin  $$$$  CIDAL | All Gram + cocci incl. Vanc-/Amp-resistant\* Entero-coccus  MRSA/VRSA | SSTI  Bacteremia  Osteomyelitis, Joint infections  May be active in biofilms (which usually inactivate antibiotics) | IV only  Nausea/vomiting  Rhabdomyolysis & associated renal insufficiency (weekly creatinine, CPK)  Rare asthmatic pulmonary eosinophilia  NOT 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**

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| **DRUG** | **COVER-AGE** | **USES** | **TOXICITY/**  **MISC** | **CSF** |
| quinupristin-  dalfopristin  $$$$  CIDAL | 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**

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| **DRUG** | **COVER-AGE** | **USES** | **TOXICITY/**  **MISC** | **CSF** |
| linezolid  $$$$  STATIC except CIDAL for streptococci | All Gram + cocci incl. \*\*  Vanc-/Amp-resistant\* Enterococcus  MRSA/VRSA  TB/Atypical mycobacteria  Binds 23S rRNA-blocks formation of 50s/70s ribosomal initiation complex | SSTI  MRSA HAP/CAP due to MRSA  Osteomyelitis/  Joint infections (very Y bone penetration)  \*\*NOT for bacteremia without a well-defined and removal or draining focus, NOT for endovascular infections | *IV=PO (bioequivalent)*  Nausea/  vomiting/  diarrhea  Headache  Thrombocytopenia/  Neutropenia after 7 days  Peripheral/  Optic neuropathies with extended use  Lactic acidosis (nausea, fatigue)  **Serotonin syndrome:**  Avoid high tyramine food/drink  (> 100mg tyramine per meal). E.g. aged cheeses, dried/processed meats, ethanol, sauerkraut, soy sauce, or yeast extract/supplements, ferments  \*/\*\*Ampicillin/Amoxicillin (CIDAL) preferred in VRE that is amp-susceptible.  \*\*Associated **with treatment failure in bacteremia**, incl line & endovascular infections. | GOOD  Myrianthefs et al. Serum and CSF concentrations of linezolid  in neurosurgery patients. AAC 2016. 50(12): 3971-6. |
| tedizolid  $$$$  STATIC | All Gram + cocci incl. \*\*  VRE, Amp-resistant\* Enterococcus,  MRSA/VRSA  Binds 50s ribosomal subunit | SSTI | *IV=PO (bioequivalent)*  6 days tedizolid Qdaily = 10 days linezolid BID = higher lipid solubility/higher tissue levels  Nausea/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)**

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| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| colistin  polymixin B  colistimethate  $$$  CIDAL | Gram - including Pseudomonas, Acinetobacter  membrane disruption, binds lipopolysacch-aride (LPS)/  Gram - endotoxin | Intraabdominal infections  UTI/GU infections  Pneumonia/  Hospital-associated respiratory infections  Potent anti-LPS binding/  neutralizing activity | IV/Aerosol  30% Nephrotoxi-city!  Peripheral/  Optic neuropathies  Neuromusc-ular blockade (may exacerbate myasthenia gravis & paralytic agents) | YES |

**Rifamycins**

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| --- | --- | --- | --- | --- |
| **DRUG** | **COVERAGE** | **USES** | **TOXICITY/MISC** | **CSF** |
| rifampin  $-$$  Only rifampin is discussed here, in context of use outside of mycobac-terial infections  CIDAL | Very broad, incl Gram +/ Gram - , mycobacteria; use is *condition*-specific  RAPID 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 carriage  Combination treatment in serious S. aureus, Streptococcal infections  Combination treatment of Legionella, Anthrax, Brucella, Bartonella, Anaplasma, Ehrlichia  Combination treatment of tuberculous and non-tuberculous Mycobacteria | IV/PO  Red urine, sweat, tears, saliva – hold soft contact use  Nausea,  abd pain  Hepatotoxi-city (avoid ethanol & hepatotoxins), hyper-bilirubinemia  Type I & Flu-like hypersensi-tivity  Autoimmune reactions  Many drug interactions – always check an updated reference | YES |

**References:**

<http://webedition.sanfordguide.com/>

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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