Antibiotics Antibacterial Spectrum — A Primer for the Cardiac Surgeon

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Practically speaking, in deciding which antibiotics are best suited for a particular patient, one needs to recollect the antibiotic spectrum of various antibiotics.

1. If the antibiotic covers gram positive organisms, is it effective against MRSA or only MSSA? Does it cover Enterococcus?
2. If it covers gram negative bacilli, is it effective against *Pseudomonas aeruginosa*? Does it work against ESBL-, AmpC-, and Metallo-beta-lactamase-producing organisms?
3. Does it cover anaerobes — in particular *B. fragilis* (the predominant gut anaerobe)?
4. In specific cases one may also need to know whether the antibiotic covers atypical organisms (*Mycoplasma* spp., *Chlamydia* spp., *Legionella* spp.) or any other specific organism (e.g. *Mycobacterium tuberculosis*, *Treponema pallidum* (syphilis), *Neisseria* spp., *Pasteurella* spp.)

With this in mind, let us look at the various groups of antibiotics.

Penicillins

Penicillins cover gram positive organisms (but not MRSA) and, as a class, demonstrate progressively increasing Gram-negative coverage with each subsequent subclass. None of the Penicillins have coverage for atypical organisms.

Penicillins are broadly divided into 4 classes:

1. Natural penicillins
2. Anti-staphylococcal penicillins
3. Aminopenicillins
4. Anti-pseudomonal penicillins

Natural Penicillins

Pen G (PO, IM, IV)

These have good *Streptococcus* coverage. Notably, Pen G is first line for many Streptococcal infections (*S. pyogenes*, *S. pneumoniae*). *Staphylococcus* spp. are resistant to these penicillins because of the production of lactamases (>90% clinical isolates).[1]

These penicillins are effective against some Enterococci (namely *E. faecalis*) and also active against many oral anaerobes. Also of note, penicillin has activity against gram negative organisms, notably *Treponema pallidum* (syphilis), *Neisseria* spp., *Pasteurella* spp.[2,3]

Anti-staphylococcal Penicillins

Nafcillin (IV), Dicloxacillin (PO), Oxacillin (PO)

Staphylococcus spp. are classified clinically based on methicillin susceptibility: methicillin-resistant (MRSA, MRSE) or methicillin-sensitive (MSSA). Approximately 40–47% of healthcare-associated *S. aureus* isolates are MRSA; a significant proportion of *S. epidermidis* isolates are also methicillin-resistant (MRSE).[3,4]

Anti-staphylococcal penicillins are highly effective against MSSA, CoNS (MRSE-negative strains), and *Streptococcus* spp., but are ineffective against MRSA, MRSE, *Enterococcus* spp., or Gram-negative bacteria.

Aminopenicillins

Ampicillin and Amoxicillin

This group of Penicillins was developed to provide additional gram-negative coverage (*E. coli*, *Proteus* spp., *H. influenzae*). They however do not cover *Klebsiella* spp., *Pseudomonas* spp. or anaerobes. Their Gram positive spectrum is similar to that of the natural penicillins, covering *Streptococcus* and *Enterococcus* spp.

Beta-lactamase inhibitor combinations (amoxicillin-clavulanate, ampicillin-sulbactam) extend the spectrum to include MSSA, CoNS, and *Enterococcus* spp. These combinations are first line for *Enterococcus faecalis* infections but have variable activity against *E. faecium*. These antibiotics are also effective against a wider range of gram negative bacteria (*E. coli*, *Proteus* spp., *H. influenzae*, and *Klebsiella* spp.) but not *Pseudomonas*. Additionally, these combinations are effective against gut anaerobes. ESBL-producing Gram-negative infections may respond; however, AmpC producers remain resistant and typically require carbapenem therapy.

Pneumonic (gut Gram-negative bacteria — PEcK): P. aeruginosa, E. coli, Klebsiella spp.

Antipseudomonal Penicillin

Piperacillin and Tazobactam (IV)

This is the broadest spectrum penicillin and has broad coverage against Gram positives (but not MRSA), enteric Gram negatives, *Pseudomonas aeruginosa*, and gut anaerobes. The principal advantage over ampicillin-sulbactam is the addition of *Pseudomonas* coverage.

Cephalosporins

Cephalosporins are classified into 5 generations. Quite like the penicillins, first-generation agents provide the strongest Gram-positive coverage; subsequent generations provide progressively enhanced Gram-negative coverage (with the exception of the fifth generation, which has MRSA activity also). Cephalosporins however have no *Enterococcus* or atypical bacterial coverage (except as noted in later generations).[5]

1st Generation

Cefazolin (IV) and Cephalexin (PO)

They have excellent gram positive coverage and can be used against MSSA, CoNS and *Streptococcus* spp. There is very limited Gram-negative coverage. Cefazolin is the cephalosporin of choice for surgical prophylaxis.[6]

2nd Generation

Cefuroxime (PO, IV), Cefaclor (PO), Cefofetan (IV), Cefoxitin (IV)

Cefuroxime is widely used as surgical prophylaxis in cardiothoracic surgery and therefore it is important to note its antibacterial spectrum. In addition to the first generation Gram positive cover, this generation of cephalosporins also covers Gram negative organisms (*H. influenzae*, *Klebsiella* spp., *E. coli*). However, the coverage for *Enterococcus* spp. and *Pseudomonas aeruginosa* is missing.

Even though the cephamycins (cefoxitin, cefofetan) are effective against anaerobes including *Bacteroides*, cefuroxime or cefaclor are not.[5]

3rd Generation

Ceftriaxone (IV), Cefotaxime (IV), Cefdinir (PO), Cefpodoxime (PO), Ceftazidime (IV), Cefaperazone (IV)

This generation has lesser Gram positive cover (only strep, no staph) but has expanded cover against Gram negative organisms like *Enterobacteriaceae*, *H. influenzae*. Only Ceftazidime and cefaperazone, from this group, is effective against *Pseudomonas aeruginosa*.[5]

4th Generation

Cefepime (IV)

In addition to the cover provided by the 3rd generation, cefepime has additional activity against *Pseudomonas aeruginosa* and AmpC producing organisms.[5] (AmpC are beta lactamase enzymes produced by some gram negative bacteria that confer resistance to aminopenicillin–beta lactamase inhibitor combinations and 3rd generation cephalosporins.)

Advanced Generations (Fifth Generation and Novel Beta-Lactam Combinations)

These agents provide additional coverage for multidrug-resistant organisms (MDROs):

- **Ceftaroline**: Activity against MRSA.[7] FDA-approved in October 2010 for acute bacterial skin and skin structure infections and community-acquired pneumonia caused by susceptible isolates, including MRSA.
- **Ceftolozane-tazobactam**: Activity against *Pseudomonas aeruginosa*, ESBL, and AmpC.[8]

- **Cefiderocol (IV)**: A novel siderophore cephalosporin uniquely stable against all classes of beta-lactamases including MBLs, making it one of the few agents active against pan-drug-resistant Gram-negative organisms including NDM-producing CRE, carbapenem-resistant *Pseudomonas*, and *Acinetobacter baumannii*. FDA-approved for Gram-negative infections with limited treatment options and hospital-acquired pneumonia.[9]
- **Ceftazidime-avibactam**: Effective against ESBL, AmpC, and some carbapenemase (KPC, Oxa-48) producing organisms.[10]

Carbapenems[1,11]

Meropenem / Imipenem / Doripenem

They are the broadest antibiotic class providing coverage against Gram-positive cocci (except MRSA and *Enterococcus*), Gram-negative bacilli (*Enterobacteriaceae* and *P. aeruginosa*) including ESBL- and AmpC-producing strains. Some agents also cover anaerobic and atypical organisms. When combined with novel beta-lactamase inhibitors (e.g., imipenem-cilastatin-relebactam), activity is extended to include additional carbapenem-resistant Gram-negative organisms.

Ertapenem — It is a first line agent for ESBL *E. coli* in moderate to severe infections in adults and children ≥3 months, with complicated intra-abdominal infections; complicated skin and skin structure infections including diabetic foot infections without osteomyelitis; community-acquired pneumonia; complicated urinary tract infections including pyelonephritis; and acute pelvic infections. It has the benefit of once daily dosing.

Monobactams[1]

Aztreonam

It is the only clinically available monobactam. It has a narrow spectrum limited to aerobic Gram-negative bacilli, including *Pseudomonas aeruginosa*, with no Gram-positive, anaerobic, or atypical organism coverage. It is particularly useful in patients with severe beta-lactam allergy (with the caveat of cross-reactivity with ceftazidime due to an identical R1 side chain).[12] Its primary clinical role is as an alternative agent for serious Gram-negative infections in penicillin- or cephalosporin-intolerant patients. Should be avoided in patients with documented allergy to ceftazidime due to cross-reactivity (shared identical side chains).

Monobactam and Beta-lactamase Inhibitor

Aztreonam-avibactam

Aztreonam-avibactam is a fixed-dose monobactam/beta-lactamase inhibitor combination that addresses a critical therapeutic gap. With synergistic mechanism of action — aztreonam is intrinsically stable against Metallo-beta-lactamases (MBLs), but MBL-producing organisms frequently co-produce other beta-lactamases (ESBLs, AmpC, KPC) that degrade aztreonam — avibactam blocks these, restoring aztreonam's activity. Making the combination effective against MBL-producing carbapenem-resistant *Enterobacterales* (CRE).[13]

Fluoroquinolones

This class provides good gram negative bacilli cover and atypical organism cover. One needs to be aware of the side effects of this group of antibiotics which include QTc prolongation, increased risk of aortic aneurysms and dissections, tendon rupture, encephalopathy, *Clostridium difficile* infection.

Ciprofloxacin

Ciprofloxacin provides good gram negative bacilli cover including *Pseudomonas aeruginosa* and is also effective against atypical organisms. Increasing resistance among *E. coli* and *P. aeruginosa* is an emerging concern.

Levofloxacin

It provides improved gram positive coverage compared to ciprofloxacin — notably, MSSA, CoNS, and *Streptococcus* spp. — and also covers *Enterococcus* spp. In addition, it is highly effective against a broad range of gram negative organisms i.e. *Enterobacteriaceae*, *H. influenzae*, and *Pseudomonas aeruginosa*. Covers atypical organisms and some oral anaerobes (e.g., *Peptostreptococcus*). The drug is commonly used in urinary and respiratory infections. Oral levofloxacin is often not well tolerated and causes loss of appetite and nausea. IV administration requires slow infusion over 30–60 minutes at a concentration of 5 mg/mL, necessitating a significant infusion volume in fluid-restricted patients.

Moxifloxacin

Moxifloxacin has Gram-positive coverage similar to levofloxacin — MSSA, CoNS, *Streptococcus* and *Enterococcus* spp. — but with limited Gram-negative activity, no anti-pseudomonal cover, and is ineffective for urinary tract infections due to inadequate urinary excretion. It has the broadest anaerobic coverage of the fluoroquinolone class, making it particularly useful in aspiration pneumonia and intra-abdominal infections. Its potent bactericidal and sterilising activity against *Mycobacterium tuberculosis*, excellent tissue penetration into lung parenchyma and macrophages, and convenient once-daily oral dosing make it a valuable agent in both drug-sensitive and multidrug-resistant TB — where it is classified as a WHO Group A agent, prioritised in virtually all MDR-TB regimens.[14] Given this critical role in TB, indiscriminate use for routine infections risks selecting for fluoroquinolone-resistant *M. tuberculosis*, and judicious prescribing is therefore strongly recommended.

Aminoglycosides

Amikacin (IV, IM), Gentamicin (IV), Plazomicin (IV), Tobramycin (IV)

Used to treat infections caused by Gram-negative bacilli and *P. aeruginosa*. Gentamicin is the only aminoglycoside with significant Gram-positive activity and is used synergistically (with cell-wall–active agents such as ampicillin or vancomycin) to treat enterococcal endocarditis.[1] Aminoglycosides have no anaerobic or atypical coverage. All aminoglycosides can cause oto- and nephrotoxicity. Plazomicin is a newer aminoglycoside with activity against some ESBL-producing organisms.

Macrolides

Azithromycin (PO, IV), Erythromycin (PO, IV), and Clarithromycin (PO)

Macrolides are effective against Gram-positive organisms (MSSA and *Streptococcus* spp.) and considered first line of management for atypical bacteria (*Chlamydia* spp. and *Mycoplasma* spp.). They have variable Gram negative activity. Azithromycin and clarithromycin have some activity against *H. influenzae* but macrolides are ineffective against enteric Gram-negative bacteria and *Pseudomonas* spp. They do not cover anaerobic organisms. Key risk includes QTc prolongation.[1]

Anti-MRSA Antibiotics

Antibiotics with activity against MRSA can be considered as a separate group. For nosocomial infections (HA-MRSA), IV agents should be used. The most commonly used drugs are vancomycin, teicoplanin, linezolid and daptomycin.

Vancomycin

Vancomycin covers the entire group of Gram-positive cocci (staphylococci, streptococci, and enterococci) and is the drug of choice for MRSA.[15] Resistance to vancomycin is increasing among enterococci (vancomycin-resistant *Enterococcus*, VRE), particularly *E. faecium*, and instances of vancomycin resistance in *Staphylococcus aureus* and CoNS have also been reported. It has no gram negative activity and provides no coverage for atypical organisms. Provides some Gram positive anaerobic cover (*C. difficile*, *peptostreptococcus*) but no Gram negative anaerobic coverage.

Primary side effects include vancomycin infusion reaction (VIR) and nephrotoxicity.[11] (VIR is not a true allergy and can be mitigated by slowing the infusion rate and pre-treatment with antihistamines.)

Teicoplanin

Like vancomycin, its action is restricted to gram positive infections. It shows greater potency than vancomycin in the treatment of anaerobic Gram positive infections. It does not cover Gram negative bacteria and has no Gram negative anaerobic cover.

Linezolid (IV/PO)

Provides solely Gram-positive coverage and is the first line agent for VRE.[12] Many institutions use linezolid as 1st line therapy for MRSA pneumonia. Primary side effects are myelosuppression with prolonged use and risk of serotonin syndrome when used with other serotonergic agents.[1,17]

Tedizolid (IV/PO)

Tedizolid phosphate is a newer antibiotic that is given in an inactive form and then converted inside the body into its active form, tedizolid. It belongs to the same class as Linezolid, but has been modified to improve its effectiveness. Due to changes in its chemical structure, it is more potent and can work against some bacteria that are resistant to linezolid. It is also active against certain bacteria carrying the cfr gene, which is known to cause antibiotic resistance. However, its effectiveness may be reduced if the bacteria have specific ribosomal

mutations. Overall, tedizolid offers a stronger and more effective option for treating some resistant infections.

Daptomycin (IV)

Daptomycin provides only Gram-positive coverage specifically against multidrug resistant strains such as MRSA, VRE and penicillin resistant streptococci, and is also effective against anaerobic Gram positive infections. It cannot however be used for MRSA pneumonia as it is deactivated by surfactant in the lungs. It is a preferred alternative to vancomycin for MRSA bacteraemia and right-sided endocarditis. Not recommended for urinary tract infections despite its Gram-positive activity. Primary side effect is rhabdomyolysis.[1,18]

Clindamycin (PO, IV)

It has good Gram-positive coverage (*Staphylococcus*, *Streptococcus*, *Clostridium* spp.), but no aerobic Gram-negative activity. It provides broad Gram positive and Gram negative anaerobic coverage; however, because of emerging resistance in *Bacteroides fragilis* it is not recommended for abdominal infections. Clindamycin has been advocated for community acquired MRSA pneumonias (inducible resistance must be excluded by D-test). Major drug adverse effect includes *C. difficile* infections.[1]

Nitrofuran

Nitrofurantoin

It is an oral antibiotic used exclusively for lower urinary tract infections (cystitis) — it achieves excellent urinary concentrations but negligible tissue and serum levels, making it entirely unsuitable for pyelonephritis, urosepsis, or any systemic infection. Its spectrum covers the most common uropathogens including *E. coli*, *Enterococcus* spp., and *Staphylococcus saprophyticus*, but it is inactive against *Pseudomonas aeruginosa* and *Proteus* spp. (which alkalinise urine, inactivating the drug). The effectiveness of nitrofurantoin in covering *Klebsiella pneumoniae* UTI is a topic of discussion and should be supported by antibiotic susceptibility. A major clinical advantage is its retained activity against ESBL-producing *E. coli*. It should be avoided in renal impairment (eGFR <30 mL/min) as reduced urinary excretion results in both subtherapeutic urinary levels and systemic accumulation of toxic metabolites; prolonged use carries a risk of pulmonary toxicity and peripheral neuropathy.[1,19]

Phosphonic Acid Group

Fosfomycin

It is available in two formulations with distinct clinical roles — oral fosfomycin (single 3g dose) is used exclusively for uncomplicated lower urinary tract infections, where it achieves exceptionally high bactericidal urinary concentrations and is particularly valuable for ESBL-producing *E. coli* and VRE cystitis; IV fosfomycin (though not US-FDA-approved) is used as part of combination therapy for serious multidrug-resistant infections including ESBL/carbapenemase-producing *Enterobacterales*. A major practical advantage in the Indian context is its retained activity against ESBL and carbapenem-resistant organisms, offering a carbapenem-sparing option; however, local susceptibility testing remains essential as resistance rates are variable, and it should never be used as monotherapy for anything beyond uncomplicated cystitis.[20]

Molecular Detection of Resistance:

Gram-negative Bacilli

Gene / Family	Resistance Conferred	Key Organisms	Detection Method	Clinical Relevance
blaTEM, **blaSHV**, **blaCTX-M**	ESBL — inactivates penicillins and 3rd-generation cephalosporins	E. coli, K. pneumoniae, Proteus spp.	PCR / multiplex PCR Double disc synergy test (DDST) ESBL E-test WGS	Resistance to penicillins + 3rd-gen cephalosporins; carbapenem or cephamycin required. Nitrofurantoin retains activity for UTI.
blaKPC	KPC carbapenemase — hydrolysis of carbapenems	K. pneumoniae, E. coli, Enterobacter spp.	Modified Hodge test (MHT) Carba NP test Lateral flow assay (LFA) PCR / WGS	Carbapenem-resistant; ceftazidime-avibactam active. Imipenem-relebactam also active.
blaNDM, **blaVIM**, **blaIMP**	Metallo-β-lactamases (MBLs) — hydrolyse all β-lactams except aztreonam	K. pneumoniae, E. coli, P. aeruginosa, Acinetobacter spp.	EDTA-based inhibition test Carba NP test PCR (NDM-specific) LFA / WGS	Pan-drug resistant risk; aztreonam-avibactam or cefiderocol are treatment options. Avibactam alone NOT effective.
blaOXA-48	OXA-type carbapenemases — partial carbapenem hydrolysis	K. pneumoniae	Modified carbapenem inactivation method (mCIM) PCR LFA / WGS	OXA-48 susceptible to ceftazidime-avibactam;
ampC (chromosomal & plasmid)	AmpC β-lactamase — resistance to aminopenicillins, cephamycins, 3rd-gen cephalosporins	Enterobacter spp., Citrobacter spp., Serratia spp., P. aeruginosa	AmpC disc test Modified 3D test PCR for plasmid AmpC WGS	Not inhibited by clavulanate. Cefepime (4th gen) or carbapenems required.

Gram-positive Bacteria

Gene / Family	Resistance Conferred	Key Organisms	Detection Method	Clinical Relevance
mecA, **mecC**	Altered PBP2a — resistance to all β-lactams including methicillin (MRSA/MRSE)	S. aureus (MRSA), S. epidermidis (MRSE), CoNS	Cefoxitin disc screen (surrogate) PCR (mecA / mecC specific) Latex agglutination (PBP2a) MRSA chromogenic agar MALDI-TOF + PCR / WGS	Defines MRSA clinically. Vancomycin, teicoplanin, linezolid, daptomycin, ceftaroline used. mecC is cefoxitin screen-negative — requires PCR.
vanA, **vanB**, **vanC**	Altered peptidoglycan precursor — vancomycin resistance (VRE)	E. faecium (vanA/vanB), E. faecalis (vanB), E. gallinarum (vanC — intrinsic)	PCR (vanA / vanB most critical) VRE chromogenic agar Vancomycin MIC (E-test / broth microdilution) WGS	vanA: high-level resistance to vancomycin + teicoplanin. vanB: variable; teicoplanin may retain activity. Linezolid / daptomycin are treatment options.
erm (A/B/C), **mef** (A/E)	MLSB resistance / efflux (macrolide-lincosamide-streptogramin B)	S. aureus, S. pyogenes, S. pneumoniae, Enterococcus spp.	D-zone test (inducible erm detection) PCR Erythromycin / clindamycin disc diffusion	D-zone test critical before clindamycin use in MRSA — inducible resistance predicts treatment failure. erm confers cross-resistance to clindamycin; mef does not.

Gene / Family	Resistance Conferred	Key Organisms	Detection Method	Clinical Relevance
			WGS	
aac(6')-aph(2''), **ant(6)**	High-level aminoglycoside resistance (HLAR) in enterococci	E. faecalis, E. faecium	HLAR screening agar (gentamicin 500 µg/mL; streptomycin 2000 µg/mL) PCR / WGS	Abolishes aminoglycoside synergy with ampicillin or vancomycin in endocarditis. Critical to test before combination therapy for enterococcal endocarditis.

Abbreviations: ESBL = extended-spectrum β-lactamase; MBL = metallo-β-lactamase; CRE = carbapenem-resistant Enterobacterales; MRSA = methicillin-resistant S. aureus; VRE = vancomycin-resistant Enterococcus; CoNS = coagulase-negative staphylococci; HLAR = high-level aminoglycoside resistance; WGS = whole genome sequencing; MIC = minimum inhibitory concentration; MLSB = macrolide-lincosamide-streptogramin B; PCR-polymerase chain reaction

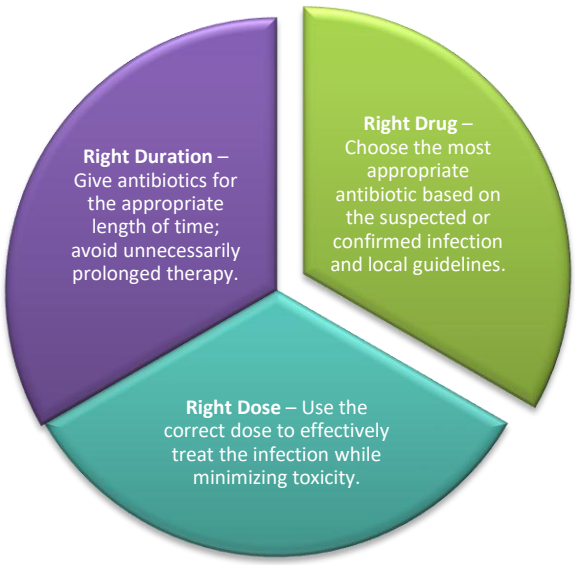
WGS is the definitive reference standard for all resistance genes listed. Phenotypic screening should be confirmed with molecular methods when clinically relevant.

Role of Surgeon in antimicrobial Stewardship:

- Surgeons should follow antimicrobial stewardship (AMS) principles for all surgical patients.
- Appropriate antibiotics should be selected based on guidelines and local sensitivity patterns.
- Antibiotics should be given at the correct dose, timing, and duration, especially for surgical prophylaxis.
- Unnecessary or prolonged antibiotic use should be avoided.
- Early review of antibiotics is recommended once culture reports are available.
- De-escalation or stopping antibiotics should be done whenever possible.
- Measures should be taken to prevent Antimicrobial Resistance.

- Close coordination with microbiologists and infection control teams is advised.
- Hospital antibiotic policies and protocols should be strictly followed.
- Regular audit and feedback on antibiotic use should be encouraged to improve practice.

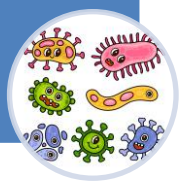
Figure1: Three Rs of Antibiotic Use



Antibiotics at a Glance

Vancomycin
Linezolid
Clindamycin
Daptomycin
Trimethoprim-Sulphamethoxazole

Gram positive with MRSA coverage

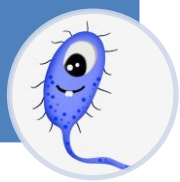


Aminopenicillins (ampicillin, amoxicillin),Ampicillin plus Gentamicin
In case of Penicillin allergy- Vancomycin
For vancomycin resistant Entercoccus- Linezolid, Daptomycin

Enterococcus spp

Penicillins (Penicillin G, Cloxacillin, Flucloaxcillin, Dicloxacillin, Amoxicilliin plus clavulanic acid, Piperacillin plus Tazobactam)
Cephalosporins (1st and 2nd generation)
Carbapenems (meropenem, imipenem)
Fluoroquinolones (levofloxacin; ciprofloxacin- poor coverage)

Antibiotics with Gram positive coverage but not MRSA



Piperacillin plus tazobactam
Some 3rd (ceftazidime/cefaperazone) and 4th generation cephalosporins (cefepime)
Carbapenems (Imipenem, meropenem, doripenem)
Fluoroquinolones (ciprofloxacin, levofloxacin)
Aminoglycosides (amikacin,tobramycin)

Antibiotics with *Enterobacteriaceae and Pseudomonas aeruginosa* coverage

Aminopenicillins (Ampicillin plus sulbactam, Ticarcillin plus clavulanate)
Cephalosporins (3rd like Cefuroxime and Ceftriaxone)

Antibiotics with Gram negative coverage (*E.coli, Klebsiella spp.*) but not *Pseudomonas aeruginosa*

Metronidazole
Broad spectrum penicillins (ampicillin plus sulbactam, amoxicillin plus clavulanate, piperacillin plus tazobactam, ticarcillin plus clavulanate)
Carbapenems (imipenem, meropenem)
Clindamycin

Antibiotics with Anaerobic coverage

Suggested Resources

a) World Health Organization. *The WHO AWaRe (Access, Watch, Reserve) antibiotic book: Web annex. Infographics*. Geneva: World Health Organization; 2022.

b) Centers for Disease Control and Prevention. *Antibiotic Prescribing and Use*. Atlanta: CDC; 2024. Available from: https://www.cdc.gov/antibiotic-use/

c) Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases Bennett JE, Dolin R, Blaser MJ, eds. Elsevier; 2020.

d) Pranita D Tamma, Emily L Heil, Julie Ann Justo, Amy J Mathers, Michael J Satlin, Robert A Bonomo, Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections, Clinical Infectious Diseases, 2024;, ciae403, https://doi.org/10.1093/cid/ciae403

e) National Centre for Disease Control; Directorate General of Health Services; Indian Council of Medical Research. *National Treatment Guidelines for Antimicrobial Use in Infectious Disease Syndromes*. Version 2.0. New Delhi: Ministry of Health and Family Welfare, Government of India; 2025.

f) Brigham C. Bratzler, Douglas W. Morgan, John E. B. Berríos-Torres, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm*. 2013;70(3):195–283.

g) Ackah JK, Neal L, Marshall NR, Panahi P, Lloyd C, Rogers LJ. Antimicrobial prophylaxis in adult cardiac surgery in the United Kingdom and Republic of Ireland. J Infect Prev. 2021 Mar;22(2):83-90. doi: 10.1177/1757177420971850. Epub 2020 Nov 24. PMID: 33859725; PMCID: PMC8014008.

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