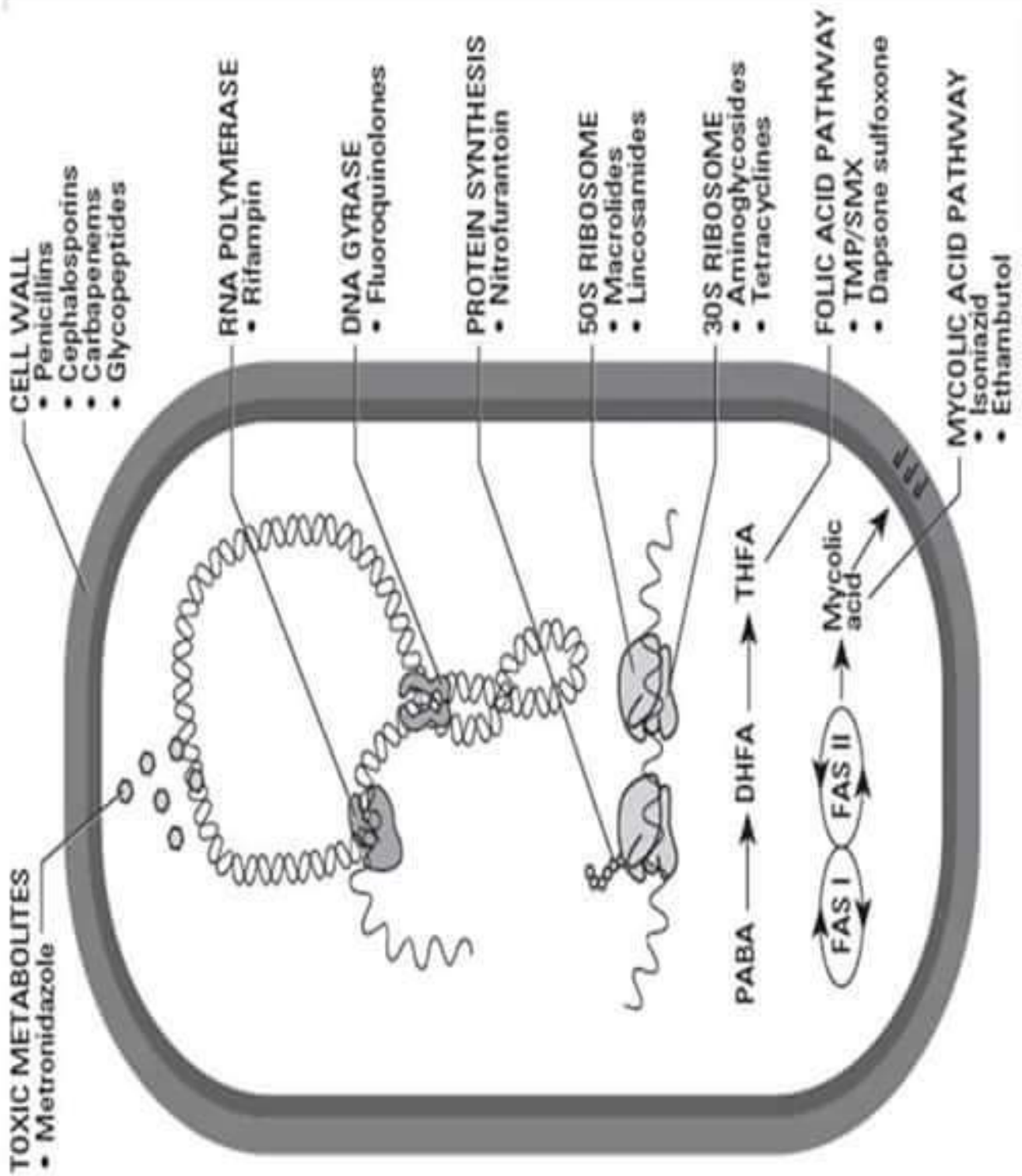




. Mechanism of action of antibiotics



Bactericidal Antibiotics	Bacteriostatic Antibiotics
"Very Finely Proficient At CCell Murder"	"ECSTaTiC"
Vancomycin	Erythromycin (and other macrolides)
Fluoroquinolones	Clindamycin
Penicillin	Sulfamethoxazole
Aminoglycosides	Trimethoprim
Cephalosporins	Tetracyclines
Carbapenems	Chloramphenicol
Metronidazole	

Empiric Antimicrobial Therapy

- Choose antibiotic(s) to cover for most likely and lethal organisms for the type of infection
- Prior to obtaining laboratory results (usually reserved for serious infections)
- Adjust antibiotic(s) based on C&S
 - if causative organism identified, use antibiotic to which organism is sensitive
 - if causative organism not identified, re-evaluate need for ongoing antimicrobial therapy (and continue with empiric antibiotic(s) if indicated)



Reasons for Combination Therapy

- Polymicrobial infection
- Empiric therapy pending culture results
- Synergy for difficult to treat pathogens (e.g. *Enterococcus* spp. causing endocarditis)
- To prevent emergence of resistance

Classification

- Cell Wall Inhibitors
- Glycopeptides
- Protein Synthesis Inhibitors
- Topoisomerase Inhibitors
- Anti-metabolites
- Anti-mycobacterials
- Sulfones

Cell Wall Inhibitors

• Include :

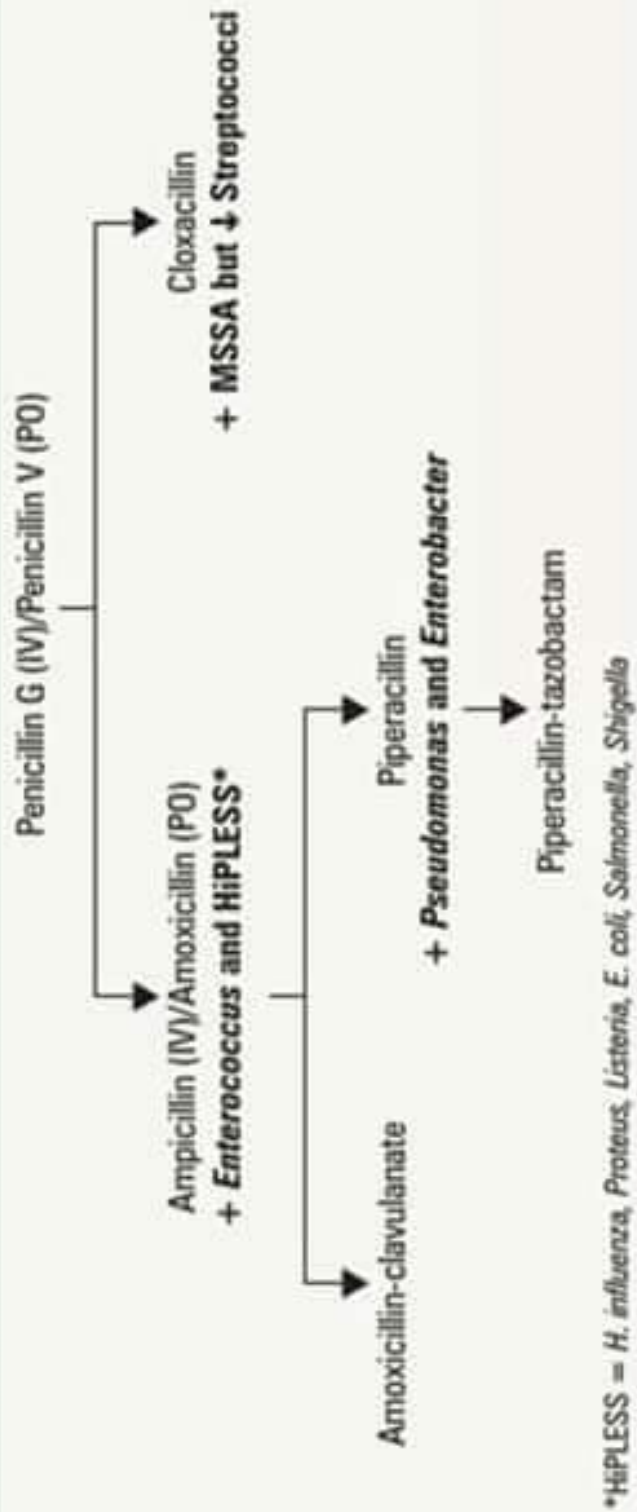
-penicillins

-cephalosporins

-carbapenems

-glycopeptides

Penicillins



Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Penicillins					
Benzyl penicillin - penicillin G IV/IM - penicillin V PO	GP <i>except</i> <i>Staphylococcus</i> , <i>Enterococcus</i> Oral anaerobes	Bactericidal: β -lactam inhibits cell wall synthesis by binding penicillin binding protein (PBP) preventing cross-linking of peptidoglycan	Immediate allergy (IgE): anaphylaxis, urticaria Late-onset allergy (IgG): urticaria, rash, serum sickness Interstitial nephritis Dose related toxicity: seizures Diarrhea	Mild to moderately severe infections caused by susceptible organisms including actinomycosis, streptococcal pharyngitis, streptococcal skin and soft tissue infections, pneumococcal pneumonia, syphilis	Hypersensitivity to penicillin
Aminopenicillin - ampicillin IV - amoxicillin PO (Amoxil®)	Same as penicillin AND <i>Enterococcus</i> <i>Listeria</i>	See above	See above	Bacterial meningitis and endocarditis (IV ampicillin), acute otitis media (AOM), streptococcal pharyngitis, sinusitis, acute exacerbations of COPD, part of multidrug therapy for <i>H. pylori</i> treatment, Lyme disease, pneumococcal pneumonia; UTI (amoxicillin and ampicillin) for most enterococci and susceptible gram-negative pathogens	Hypersensitivity to penicillin or β -lactam antibiotics
Isoxazolyl penicillin - cloxacillin - methicillin - nafcillin - oxacillin	Methicillin-sensitive <i>Staphylococcus aureus</i> ; streptococci	See above	See above	Bacterial infections caused by staphylococci and streptococci including skin soft-tissue infections	Hypersensitivity to cloxacillin or any penicillin
β -lactam/ β -lactamase Inhibitor combinations - amoxicillin clavulanate (Clavulin®, Augmentin®) - piperacillin/tazobactam (Tazocin®)	Same as penicillin AND <i>Staphylococcus</i> <i>H. influenzae</i> <i>Enterococcus</i> Anaerobes (oral and gut)	β -lactamases produced by certain bacteria inactivate β -lactams Lactamase inhibitors prevent this process, preserving antibacterial effect of β -lactams	See above	Various β -lactamase producing bacteria, Clavulin® sensitive bacteria including RTI, sinusitis, AOM, skin and soft tissue infections, UTI, and severe intra-abdominal and pelvic infections	Hypersensitivity to penicillin or cephalosporin History of Clavulin®-associated jaundice or hepatic dysfunction

Cephalosporins (IV/PO)

- **1st generation:** cephalixin/cefazolin (mostly GP, some GN)
- **2nd generation:** cefuroxime/cefuroxime (some GP and some GN, *anaerobes)
- **3rd generation:** cefixime/cefotaxime, ceftriaxone (good Streptococcal coverage, mostly GN) and ceftazidime (no GP, mostly GN, Pseudomonas)
- **4th generation:** --/cefepime (most GP, most GN, Pseudomonas)

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Cephalosporins					
P0	GP	GN			
1st cephalexin (Keflex [®])	Good with the exception of <i>Enterococcus</i> and MRSA	<i>E. coli</i> , <i>Klebsiella</i> , <i>Proteus</i> , <i>H. influenzae</i> (not all isolates)	10% penicillin allergy cross-reactivity Nephrotoxicity	Skin and soft tissue infections, prevention of surgical site infections (cefazolin); infections caused by susceptible organisms (esp. <i>Staph.</i> and <i>Strep.</i> infections)	Hypersensitivity to cephalosporins or other β -lactam antibiotic
2nd cefuroxime (Zinacof [®]) cefotaxime (Cefin [®]) cefprozil (Cefzil [®])	Weaker activity than 1 st	More coverage than 1 st (*includes anaerobes)	See above	Upper and lower respiratory tract infections (there have been failures in bacteremia pneumococcal pneumonia; soft tissue)	See above
3rd ceftriaxone (Rocephin [®]) cefotaxime (Claforan [®]) ceftriaxime (Fortax [®])	<i>S. aureus</i> + streptococcal coverage (cefotaxime and ceftriaxime) especially <i>S. pneumoniae</i>	Broad coverage (*includes <i>Pseudomonas</i> for ceftazidime only)	~1% penicillin allergy cross-reactivity	Community-acquired pneumonia (cefotaxime, ceftriaxone), gonorrhea (use ceftriaxone), community-acquired bacterial meningitis (ceftriaxone, cefotaxime); abdominal and pelvic infections (cefotaxime or ceftriaxone in combination with metronidazole). Once-daily administration makes ceftriaxone convenient for outpatient IV therapy	Severe hypersensitivity (Type I) to other β -lactam antibiotics
4th cefepime (Maxipime [®])	Broad spectrum	Broad coverage including <i>Pseudomonas</i>	See above	Empiric therapy for febrile neutropenia	See above

Carbapenems

✓ (broad coverage: GP, GN and anaerobes)

- **imipenem** (+ Pseudomonas)
- **meropenem** (+ Pseudomonas)
- **ertapenem**

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Carbapenems					
imipenem (Primaxin®)	GP except MRSA GN including <i>Pseudomonas</i> + <i>Enterobacter</i> , ESBLs, anaerobes	β -lactam inhibits PBP and prevents cross-linking of peptidoglycan	Penicillin allergy cross- reactivity Seizures	Treatment of infections caused by GNB producing extended- spectrum β -lactamases, serious infections caused by susceptible organisms	Hypersensitivity to imipenem
meropenem (Merrem®)	See above. Does not cover <i>Enterococcus</i> .	See above	See above	See above	Hypersensitivity to β -lactams
ertapenem (Invanz®)	GP except <i>Enterococcus</i> , MRSA GN including <i>Enterobacter</i> (but not <i>Pseudomonas</i>), anaerobes	See above	See above	See above. Once-daily administration makes it convenient for outpatient IV therapy	Hypersensitivity to β -lactams

Glycopeptides

✓ (all GP and *C. difficile*— the oral form)

- **vancomycin**

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Glycopeptides Vancomycin (Vancocin®)	GP including MRSA, not VRE <i>C. difficile</i> if PO	Glycopeptide sterically inhibits cell wall synthesis	Red Man Syndrome Nephrotoxicity Ototoxicity Thrombocytopenia	Severe or life-threatening GP infections, patients with β -lactam allergy May only be taken orally for severe <i>C. difficile</i> infection	Hypersensitivity to vancomycin

Macrolides

✓ [GP, Hemophilus, and atypical bacteria
(Legionella, Chlamydophila,
Mycoplasma)]

- erythromycin
- clarithromycin
- azithromycin

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Macrolides					
erythromycin (Erybid [®] , Eryc [®])	GP except <i>Enterococcus</i> GN: <i>Legionella</i> , <i>B. pertussis</i> "Atypicals": <i>Chlamydia</i> , <i>Mycoplasma</i>	Binds to 50S ribosomal subunit inhibiting protein synthesis	GI upset Acute cholestatic hepatitis Prolonged QT	Susceptible RTI, pertussis, diphtheria, <i>Legionnaires' disease</i> , skin and soft tissue infections	Hypersensitivity to erythromycin Concurrent therapy with astemizole, terfenadine
*This agent is rarely used due to GI upset					
clarithromycin (Biaxin [®])	See above	See above	See above	Susceptible RTI, skin infections, non-tuberculous mycobacterial infections, part of multidrug therapy for <i>H. pylori</i> treatment	Hypersensitivity to macrolides
azithromycin (Zithromax [®])	See above	See above	See above	Susceptible RTI, acute exacerbations of COPD, community-acquired pneumonia, skin infections, <i>Campylobacter</i> infections if treatment indicated, chlamydia	Hypersensitivity to macrolides

Lincosamides

- **clindamycin** (most GP, GN anaerobes)
- **chloramphenicol** (broad-spectrum)
- **linezolid** (for resistant GP infections)

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Lincosamides					
clindamycin (Dalacin [®])	GP <u>except</u> <i>Enterococcus</i> , most community-acquired MRSA Anaerobes	Inhibits peptide bond formation at 50S ribosome	Pseudomembranous colitis GI upset	Treatment of suspected or proven infections caused by GP, anaerobes including skin and skin structure infections, oropharyngeal infections, in combination with GN coverage for intra-abdominal and pelvic infections	Hypersensitivity to clindamycin Infants < 30 d
chloramphenicol	GP GN Anaerobes	Inhibits peptidyl transferase action of tRNA at 50S ribosome	Aplastic anemia Grey Baby Syndrome	Serious infections by susceptible organisms when suitable alternatives are not available including meningococcal disease in patients with anaphylaxis to β -lactams	Hypersensitivity to chloramphenicol
linezolid (Zyvoxam [®])	GP including VRE + MRSA	Binds 50S ribosome and prevents functional 70S initiation complex	HTN (acts as MAOI) Risks with prolonged use: myelosuppression optic neuropathy, peripheral neuropathy	Vancomycin-resistant <i>Enterococcus faecium</i> infections including intra-abdominal, skin and skin-structure, and urinary tract infections, MRSA infections as out patient therapy	Hypersensitivity to linezolid

Aminoglycosides

✓ (GN aerobic bacilli)

- gentamicin
- tobramycin
- amikacin

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Aminoglycosides gentamicin tobramycin amikacin (Amikin®)	GN (includes Pseudomonas)	Binds 30S subunit of ribosome inhibiting protein synthesis	Nephrotoxicity (reversible) Vestibular and ototoxicity (irreversible). Vestibular toxicity is the most important aminoglycoside toxicity	GN infections when alternatives do not exist, UTIs, used in low doses for synergy with β -lactams or with vancomycin for the treatment of serious enterococcal infections	Pre-existing hearing loss and renal dysfunction

Tetracyclines

✓ (GP, syphilis,
Chlamydophila, Rickettsia,
Mycoplasma)

• doxycycline / tetracycline

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Tetracyclines					
tetracycline (Apo-Tetra®, Nu-Tetra T®)	GP	Binds 30S subunit of ribosome inhibiting protein synthesis	GI upset Hepatotoxicity Fanconi's syndrome Photosensitivity Teratogenic Yellow teeth and stunted bone growth in children	Rickettsial infections, Chlamydia, acne (tetracycline, minocycline), PID (step-down), malaria prophylaxis (doxycycline)	Severe renal or hepatic dysfunction Pregnancy or lactation Children under 8 yr
minocycline (Minocin®)	Anaerobes *Atypicals*				
doxycycline (Doxycin®)	Chlamydia, Mycoplasma, Rickettsia, Borrelia burgdorferi Treponema				
	Malaria prophylaxis (doxycycline)				

Topoisomerase Inhibitors

- Flouroquinolones
- Rifampin
- Metronidazole

Fluoroquinolones

✓ (GN – *although resistance becoming a huge problem*)

- **ciprofloxacin** (+ *Pseudomonas*)
- **norfloxacin** (for UTI only)
- **respiratory fluoroquinolones** (some GP, GN, "atypicals", *Legionella*, *Mycoplasma*, *Chlamydophila*)
- **levofloxacin**
- **moxifloxacin** (+ *anaerobes*)

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Fluoroquinolones (FQs)					
ciprofloxacin (Cipro®) norfloxacin (Apo-Norflo®) ofloxacin (Floxin®) Respiratory FQs: levofloxacin (Levaquin®) moxifloxacin (Avelox®)	Poor GP activity GN (includes <i>Pseudomonas</i>) Atypicals Moxifloxacin also covers many anaerobes	Inhibits DNA gyrase	H/A, dizziness Allergy Seizures Prolonged QT Dysglycemia (levofloxacin, moxifloxacin)	Upper and lower RTI (not ciprofloxacin unless susceptible organism isolated), UTI, prostatitis (not moxifloxacin), bone and joint infections for susceptible organisms, skin and soft tissue infections (levofloxacin, moxifloxacin), infectious diarrhea, meningococcal prophylaxis, intra-abdominal infections (moxifloxacin, ciprofloxacin in combination with metronidazole or clindamycin), febrile neutropenia prophylaxis (ciprofloxacin, levofloxacin) or ciprofloxacin in combination with amoxicillin/clavulanate low management of "low-risk" febrile neutropenia	

Rifampin

✓ (GP mostly, H. Inf., N. meningitidis and mycobacteria)

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Rifampin	GP cocci N. meningitidis H. influenza Mycobacteria	Inhibits RNA polymerase	Hepatic dysfunction, P450 enzyme induction Orange tears/saliva/ urine	Part of multidrug treatment for active TB, alone for treatment of latent TB, part of multidrug treatment of other mycobacterial infections, endocarditis involving prosthetic valve or other prosthetic device infections in combination with other antibiotic agents, prophylaxis for those exposed to people with N. meningitidis or Hib meningitis	Jaundice Not to be used as monotherapy (except for prophylaxis)



Rifampin

- Good adjunct for treating prosthetic device infection (bacterial biofilm)
- Always used in combination with other antibiotics to reduce emergence of resistance

Metronidazole

✓ (anaerobes incl. *C. difficile*;
Trichomonas, *Entamoeba*)

Class and Drugs	Coverage	Mechanism of Action	Adverse Effects	Indications	Contraindications
Metronidazole (Flagyl®)	Anaerobes Protozoa	Forms toxic metabolites in bacterial cell which damage microbial DNA	Disulfiram-type reaction with EtOH Seizures Peripheral neuropathy	Protozoal infections (trichomoniasis, amebiasis, giardiasis), bacterial vaginosis, anaerobic bacterial infections	