



Basic Concepts of Antibiotics

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Disclaimer

This presentation reflects my own views and should not be construed to represent FDA's views or policies.



Outline

- Classification of antibiotics- selected antibiotics
- Complications of antibiotics
- Antibiotic resistance- mechanisms, threats
- Prevention efforts and action plan



History FDA

Ancient times

- In Greece and Serbia, mouldy bread was traditionally used to treat wounds and infections.
- Sumerian doctors gave patients beer soup mixed with turtle shells and snake skins.
- Babylonian healed the eyes using a mixture of frog bile and sour milk.

Modern times

- 1928 England Sir Alexander Fleming discovered the antibiotic substance penicillin from the fungus *Penicillium notatum*
- 1932 Germany Gerhard Domagk discovered Sulfonamidochrysoidine (Prontosil)
- 1940's and 50's streptomycin, chloramphenicol, tetracycline, erythromycin discovered
- Selman Waksman used the term "antibiotics" (1942)

Antibiotics FDA

Bacterial spectrum

- Broad**
Active against both Gram-positive and Gram-negative organisms e.g tetracyclines, 3rd and 4th generation cephalosporins, fluoroquinolones
- Narrow**
Limited activity, useful against particular species of organisms e.g glycopeptides, aminoglycosides, imidazoles

Route of administration

- Intravenous/ Intramuscular
- Oral

Type of activity

- Bactericidal**
Kill target organisms, e.g cephalosprins, penicillins, quinolones, aminoglycosides
- Bacteriostatic**
Inhibit or delay bacterial growth and replication, e.g tetracyclines, macrolides

Classification FDA

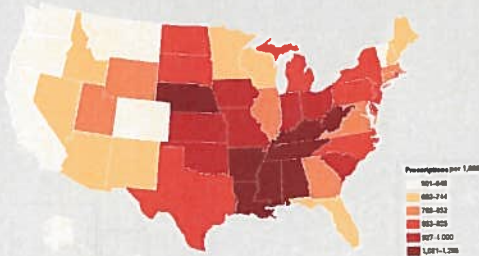
Prophylactic Use



- Surgery (i.e, cardiac, orthopedic, GI tract surgery)
- Bacterial endocarditis
- Neutropenia
- Young women with recurrent urinary tract Severe rheumatic carditis.

Community Antibiotic Prescriptions per 1,000 Population by State — 2014

At least 30% of antibiotics prescribed in doctors' offices, emergency departments and hospital clinics are unnecessary *



- 266.1 million courses of antibiotics were dispensed to outpatients (2014)
- Azithromycin and amoxicillin are among the most commonly prescribed



Complications of Antibiotics




- Adverse drug reactions
 - Direct Toxicities
 - Superinfections
 - *Clostridium difficile* colitis
 - Drug interactions
- Antibiotic resistance



Misuse and Resistance FDA

- Antibiotics used for viral infections
- Broad spectrum antibiotics when not indicated
- Inadequate antibiotic dosing
- Failure to complete the antibiotic course
- Failure to cover all the pathogens
- Omission of surgical drainage



Google images

Antibiotic Resistance FDA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:


At least **2,049,442** illnesses, **23,000** deaths

*Bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least **250,000** illnesses, **14,000** deaths

How Antibiotic Resistance Happens



1. Lots of germs. A few are drug resistant.
2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.
3. The drug-resistant bacteria are now allowed to grow and take over.
4. Some bacteria give their drug-resistance to other bacteria, causing more problems.

Penicillins FDA

- Ampicillin
- Active against *Bordetella pertussis*, *E. coli*, *Salmonella*, *Shigella*
- Some uses: Group A streptococcal pharyngitis, otitis media, respiratory tract and urinary tract infections
- Adverse reactions: rash, diarrhea, etc.

Cephalosporins FDA

Cephalosporins				
1 st Gen	2 nd Gen	3 rd Gen	4 th Gen	5 th Gen
Cephalexin Cefazolin	Cefotetan Cefuroxime	Ceftriaxone Ceftazidime	Cefepime	Ceftaroline

Google images

Cephalosporins FDA

Uses

Cefazolin: Respiratory tract infections (*S. pneumoniae*, *S. aureus*, *S. pyogenes*)

Urinary tract infections (*E. coli*, *P. mirabilis*)

Skin and skin structure infections (*S. aureus*, *S. pyogenes*)

Cefotetan: active against *Bacteroides*, prophylaxis and therapy of infections in the abdominal and pelvic cavities

Cephalosporins



Ceftriaxone: Acute bacterial otitis media, urinary tract infections, uncomplicated gonorrhea

Ceftazidime: antipseudomonal activity

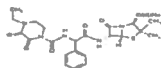
Cefepime: Also with antipseudomonal activity, pneumonia, urinary tract infections, intraabdominal infections

Ceftaroline: like ceftriaxone but with improved gram-positive activity, Community acquired pneumonia, skin infections

β lactam- β lactamase inhibitors



- Binds to the β lactamase and protects antibiotic from destruction
- Extends spectrum of activity



Examples:

- Ampicillin- sulbactam- include most strains of *S. aureus* and beta-lactamase producing *H. influenzae*, some *Enterobacteriaceae*, and anaerobes (sinusitis, otitis media etc)

β lactam- β lactamase inhibitors



- Piperacillin-tazobactam- include beta-lactamase producing *S. aureus*, *H. influenzae*, *Neisseria gonorrhoeae*, some *Enterobacteriaceae*, and anaerobes
- Ceftolozane/tazobactam- most extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*, intrabdominal and urinary tract infections
- Ceftazidime/avibactam- includes *Pseudomonas*, *Enterobacteriaceae* including those that produce AmpC beta-lactamase, (ESBL), intrabdominal and urinary tract infections

Carbapenems

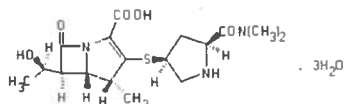


Broad spectrum- gram positives and gram negatives, anaerobes

Examples: Imipenem, meropenem, doripenem

Uses: Sepsis, pneumonia, intraabdominal infections, urinary tract infections

Adverse reactions: Gastrointestinal effects, hypersensitivity, suprainfections, etc



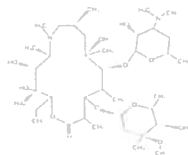
Macrolides



Examples: azithromycin, clarithromycin

Uses: Legionnaire's disease, whooping cough, Diphtheria, Chlamydial infections, Walking pneumonia (mycoplasma) Fidaxomicin- *C. difficile* colitis

Adverse Reactions: Gastrointestinal effects, drug interactions etc



Fluroquinolones

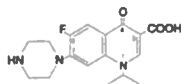


Examples: ciprofloxacin, moxifloxacin, levofloxacin, delafloxacin

Uses :infections of respiratory tract, GI tract, bones, joints, skin and soft tissues.

Ciprofloxacin-typhoid fever, plague, anthrax

Adverse Reactions:
nausea, vomiting, diarrhea, achilles tendon rupture, disabling side effects involving tendons, muscles, joints, nerves, CNS.



Aminoglycosides



Spectrum: aerobic gram-negative bacilli, inactive against most gram-positive bacteria and anaerobes

Examples: Gentamicin, Tobramycin, Amikacin.

Adverse Reactions: Ototoxicity, Nephrotoxicity

Uses: Sepsis, urinary tract infection, skin, bone, soft tissue infections, peritonitis
Covers agents of tularemia, plague
Streptomycin- Tuberculosis

Glycopeptides



Examples: Vancomycin, Dalbavancin, Oritavancin

Uses: Pneumonia, sepsis, bone and joint infections
Oral vancomycin- *C. difficile* colitis
Dalbavancin, oritavancin- Skin and soft tissue infections

Activity against Methicillin resistant *S. aureus* (MRSA).
Adverse reactions:
Vancomycin- Ototoxicity
Dalbavancin- rash, elevated liver function tests

Tetracyclines



-Broad spectrum antibiotics
-Uses: Rocky mountain spotty fever, typhus fever, Q fever, infections caused by *chlamydia trachomatis*, brucellosis, cholera, pneumonia caused by *Mycoplasma pneumoniae*, Lyme disease, gastric infections with *Helicobacter Pylori*, acne

-Adverse Reactions:
Gastrointestinal - nausea, vomiting, diarrhea)
Effects on bones and teeth (teeth discoloration in children under 5 years old)
Photosensitivity
Liver toxicity
Kidney toxicity

Trimethoprim-sulfamethoxazole

-Uses: urinary tract infections, otitis media, bronchitis, shigellosis, traveller's diarrhea, *Pneumocystis Carinii* pneumonia.

-Active against MRSA, broad spectrum

-Adverse reactions: nausea, vomiting, rash. Rarely-hypersensitivity reactions, blood dyscrasias, renal damage

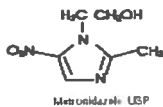
Metronidazole

-Nitroimidazole

-Active against obligate anaerobes

-Uses: It is used in CNS infections, intraabdominal infections, bones, joints, skin, soft tissues, *C difficile* colitis and genitourinary tract (Trichomoniasis, bacterial vaginosis). It is used in combination against *Helicobacter Pylori*.

-Adverse reactions: Nausea, vomiting



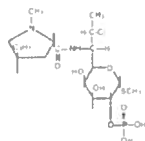
Clindamycin

- Lincosamide

- Active against gram positive cocci, most community acquired MRSA, anaerobes

- Uses: Skin and skin structure infections due to *Streptococci*, *Staphylococcus*, anaerobes, pelvic, intraabdominal infections, *Streptococcus pneumoniae* empyema, lung abscess

-Adverse reactions:
GI effects
C. Difficile colitis



Urgent Threats
Clostridium difficile
 Carbapenem-resistant Enterobacteriaceae (CRE)
 Drug-resistant *Neisseria gonorrhoeae*

Serious Threats
 Multidrug-resistant *Acinetobacter*
 Drug-resistant *Campylobacter*
 Fluconazole-resistant *Candida* (a fungus)
 Extended spectrum β -lactamase producing Enterobacteriaceae (ESBLs)
 Vancomycin-resistant *Enterococcus* (VRE)
 Multidrug-resistant *Pseudomonas aeruginosa*
 Drug-resistant Non-typhoidal *Salmonella*
 Drug-resistant *Salmonella* Typhi
 Drug-resistant *Shigella*
 Methicillin-resistant *Staphylococcus aureus* (MRSA)
 Drug-resistant *Streptococcus pneumoniae*
 Drug-resistant tuberculosis

Concerning Threats
 Vancomycin-resistant *Staphylococcus aureus* (VRSA)
 Erythromycin-resistant Group A *Streptococcus*
 Clindamycin-resistant Group B *Streptococcus*

Antibiotic threat Report, 2013



WHO priority pathogens list for R&D of new antibiotics

Priority 1: CRITICAL
Acinetobacter baumannii, carbapenem-resistant
Pseudomonas aeruginosa, carbapenem-resistant
 Enterobacteriaceae, carbapenem-resistant, ESBL-producing

Priority 2: HIGH
Enterococcus faecium, vancomycin-resistant
Staphylococcus aureus, methicillin-resistant, vancomycin-intermediate and resistant
Helicobacter pylori, clarithromycin-resistant
Campylobacter spp., fluoroquinolone-resistant
Salmonellae, fluoroquinolone-resistant
Neisseria gonorrhoeae, cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM
Streptococcus pneumoniae, penicillin-non-susceptible
Haemophilus influenzae, ampicillin-resistant
Shigella spp., fluoroquinolone-resistant



Prevention efforts

- Promote healthy habits: clean hands, uptodate vaccines, prevent foodborne and water borne illness, prevent STDs
- Proper use of antibiotics
- Antibiotic resistance education programs
- Travel health- uptodate vaccines



HEALTHCARE ASSOCIATED INFECTIONS WHAT PATIENTS CAN DO

BE INFORMED BE EMPOWERED BE PREPARED **6 WAYS TO BE A SAFE PATIENT**

- 1. SPEAK UP**
Talk to your doctor about all questions or concerns you have. Ask about what they are doing to prevent you from getting an infection.
If you have a catheter, ask each day if it is necessary.
Ask your doctor how he or she prevents surgical site infections. Also ask how you can prepare for surgery to reduce your infection risk.
- 2. KEEP HANDS CLEAN**
Be sure your hands always stay clean before touching your hands.
- 3. GET SMART ABOUT ANTIBIOTICS**
Ask if you will be able to make some of the right choices to prescribing.
- 4. KNOW THE SIGNS AND SYMPTOMS OF INFECTION**
Some signs of infection, such as MRSA, appear as redness, pain, or drainage at an IV catheter site or surgery site. Often these symptoms come with a fever. Tell your doctor if you have these symptoms.
- 5. WATCH OUT FOR DEADLY PNEUMONIA**
Tell your doctor if you have 3 or more different symptoms in 24 hours, especially if you have been taking an antibiotic.
- 6. PROTECT YOURSELF**
Get vaccinated against the most common infections to avoid complications.

CDC

Education

- Take antibiotics exactly as the doctor prescribes. Do not skip doses. Complete the prescribed course of treatment, even when you start feeling better.
- Only take antibiotics prescribed for you. Do not share or use leftover antibiotics.
- Do not save antibiotics for the next illness. Discard any leftover medication once the prescribed course of treatment is completed.
- Do not ask for antibiotics when your doctor thinks you do not need them.

Antibiotic threat report, 2013

Core actions

Preventing infections, preventing spread

Surveillance systems- to track resistance patterns

- Active Bacterial Core surveillance (ABCs): Tracking infections caused by *N. meningitidis*, *S. pneumoniae*, Groups A and B *Streptococcus*, and MRSA
- Gonococcal Isolate Surveillance Project (GISP),
- National Tuberculosis Surveillance System (NTSS),
- Healthcare-Associated Infections-Community Interface (HAIC)

National Antimicrobial Resistance Monitoring Program

Core actions



- Antimicrobial stewardship- proper use of antibiotics**
- Ensure all orders have dose, duration, and indications
 - Get cultures before starting antibiotics
 - Reassessing antibiotics after 48-72 hours

Research and Development of new antibiotics and diagnostic tests



Conclusions



- While antibiotics have a therapeutic benefit, they also produce life-threatening drug resistant organisms
- Proper use of antibiotics from both the healthcare provider and patient is essential
- Educate yourself about the side effect of antibiotics
- Antibiotics will not cure viral illness
