Antimicrobial Resistance and Stewardship

Why?

Antibiotic resistance is among the greatest public health threats today, leading to an estimated 2 million infections and 23,000 deaths per year in the United States.

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

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

*bacteria and fungus included in this report
Antibiotic vs. Antimicrobial

- An antibiotic is a type of drug that kills or stops the growth of bacteria.
- An antimicrobial is a type of drug that kills or stops the growth of microbes, such as bacteria, viruses, fungi, and parasites.
Antibiotic Resistance

Antibiotic resistance is the ability of bacteria to resist the effects of an antibiotic – that is, the bacteria are not killed, and their growth is not stopped. Resistant bacteria survive exposure to the antibiotic and continue to multiply in the body, potentially causing more harm and spreading to other animals or people.

-CDC

History of Antibiotics

- 1940: penicillin-R Staphylococcus
- 1962: methicillin-R Staphylococcus
- 1988: vancomycin-R Enterococcus
- 1996: levofloxacin-R pneumococcus
- 2011: ceftaroline-R Staphylococcus

- 1943: penicillin
- 1960: methicillin
- 1985: imipenem & ceftazidime
- 1996: levofloxacin
- 2010: ceftaroline

https://www.cdc.gov/drugresistance/about.html
Examples of Disease-Causing Microbes

1. Strep throat
   - Bacteria
   - Group A Streptococcus

2. Food poisoning
   - Bacteria
   - Salmonella

3. Common cold
   - Virus
   - Rhinovirus

4. Flu
   - Virus
   - Influenza virus

5. Athlete’s foot
   - Fungi
   - Trichophyton

6. Malaria
   - Parasite
   - Plasmodium

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.

https://www.cdc.gov/getsmart/week/promotional-materials/graphics.html
Examples of How Antibiotic Resistance Spreads

1. Animals get antibiotics and develop resistant bacteria in their guts.
2. Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.
3. Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.
4. Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.
5. Resistant genes spread directly to other patients or indirectly on unclean hands of healthcare providers.
6. Patients go home.
7. Resistant bacteria spread to other patients from surfaces within the healthcare facility.
8. George gets antibiotics and develops resistant bacteria in his gut.
9. George stays at home and in the general community, spreads resistant bacteria.
10. George gets care at a hospital, nursing home, or other inpatient care facility.

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

Risk of CRE Infections

1. Local Short-Stay Hospital
   - Jan has a stroke and is in the hospital. She is stable but needs long-term critical care at another facility.

2. Long-Term Acute Care Hospital
   - Other patients in the facility have CRE. A nurse doesn’t wash his hands, and CRE is spread to Jan. She develops a fever and is put on antibiotics without proper testing.

3. Local Short-Stay Hospital
   - Jan becomes unstable and goes back to the hospital, but her new doctors don’t know she has CRE. A doctor doesn’t wash her hands after treating Jan. CRE is spread to other patients.

How CRE Take Over

1. Lots of germs, 3 or 2 are CRE
2. Antibiotics kill off good germs
3. CRE grow
4. CRE share genetic defenses to make other bacteria resistant

SOURCE: CDC, 2013
Biggest Threats

**HAZARD LEVEL URGENT**

These are high-consequence antibiotic resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

Clostridium difficile (C. difficile), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant Methicillin-resistant Staphylococcus aureus (MRSA)

**HAZARD LEVEL SERIOUS**

These are significant antibiotic resistant threats for varying reasons (e.g., low or declining domestic incidence or reasonable availability of therapeutic agents), they are not considered urgent, but these threats will worsen and may become urgent without ongoing public health monitoring and prevention activities.

Multi-drug-resistant Acinetobacter, Drug-resistant Campylobacter, Plasmid-mediated NST-Enterococcus, Vancomycin-resistant Enterococcus (VRE), Multi-drug-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 (MDR and XDR)

**HAZARD LEVEL CONCERNING**

These are bacteria for which the threat of antibiotic resistance is low, and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause severe illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.

Vancomycin-resistant Staphylococcus aureus (VRSA), Erythromycin-resistant Streptococcus Group A, Clindamycin-resistant Streptococcus Group B

U.S. Map: Clinical cases of *Candida auris* reported by state, United States, as of February 28, 2018

Number of *C. auris* clinical cases:
- 0
- 1
- 2-10
- 11-50
- 51-100
- 101 or more
### Examples of Resistance Mechanisms (or Strategies)

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<th>Mechanism</th>
<th>Description</th>
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| **Restrict access of the antibiotic**         | By limiting the number or changing the size of the openings in the cell wall, resistant bacteria can keep antibiotic drugs from entering the cell altogether.  
  *Example*: Gram-negative bacteria have an outer layer that protects them from their environment. These bacteria can use this membrane to selectively keep antibiotic drugs from entering. |
| **Get rid of the antibiotic**                 | Resistant bacteria can use pumps in their cell walls to remove antibiotic drugs that enter the cell.  
  *Example*: Some Pseudomonas aeruginosa bacteria can produce pumps to get rid of several different important antibiotic drugs, including fluoroquinolones, beta-lactams, chloramphenicol, and trimethoprim. |
| **Destroy the antibiotic**                    | Some resistant bacteria use enzymes to break down the antibiotic drug and make it ineffective.  
  *Example*: Klebsiella pneumoniae bacteria produce enzymes called carbapenemases, which break down carbapenem drugs and most other beta-lactam drugs. |
| **Change the antibiotic**                     | Other resistant bacteria use enzymes to alter the antibiotic drug so that it loses its effectiveness.  
  *Example*: Staphylococcus aureus bacteria add compounds to aminoglycoside drugs to change its function. |
| **Bypass the effects of the antibiotic**      | Some antibiotic drugs are designed to disrupt important processes critical to a bacteria’s survival, like the process of making nutrients. If successful, the antibiotic drug will keep the bacterium from performing all the steps needed in the process. Some resistant bacteria, however, have developed different and new processes to get around these drug disruptions. The new process may be slower but they can still bypass the effects of the drug.  
  *Example*: Some Staphylococcus aureus bacteria can bypass the drug effects of trimethoprim. |
| **Change the targets for the antibiotic**     | Many antibiotic drugs are designed to single out and destroy specific parts (or targets) of a bacterium. Resistant bacteria can change the look of their targets so that the antibiotic does not recognize and destroy them, allowing the bacteria to survive.  
  *Example*: E. coli bacteria with the mcr-1 gene can add a compound to the outside of the cell wall so that the drug colistin cannot latch onto it. |
Consequences of Antibiotic Resistance

- Resistant infections may cause severe illness resulting in:
  - Increased recovery time
  - Increased medical expenses
  - Increased mortality

- Physicians have to recommend second-or third-choice drugs for treatment when the bacteria that cause infections are resistant to the drug of choice and this drug doesn’t work. But the alternative drugs might be less effective, more toxic, and more expensive. Preserving the effectiveness of antibiotics is vital to protecting human and animal health.

So what can we do about it?
Antibiotic Resistance (AR) Solutions Initiative

Improve antibiotic use through antibiotic stewardship, sepsis recognition, and prevention.

- Set national goals to improve antibiotic use.
  - Cut inappropriate prescribing practices by 50% in doctors' offices and 20% in hospitals.
- Implement effective stewardship programs using CDC’s Core Elements and recommendations in doctors' offices, hospitals, and nursing homes, integrated with sepsis early recognition programs.
- Support collaboration to develop and evaluate stewardship activities.

- Provide data about antibiotic use and trends to better understand prescribing practices. For example:
  - Expand and use CDC's National Healthcare Safety Network (NHSN) data to guide improvement of antibiotic use in hospitals.
  - Better understand differences in prescribing patterns in doctors' offices by states and develop strategies for improvement.
- Expand State HAI/AR Prevention Programs to help implement best practices around improving antibiotic prescribing.
- Support early recognition of sepsis. Heighten public awareness to prevent sepsis and its complications, and to improve antibiotic use.
Core Actions to Combat Resistance

1. Preventing Infections, Preventing the Spread of Resistance
   Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2. Tracking
   CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

3. Improving Antibiotic Prescribing/Stewardship
   Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4. Developing New Drugs and Diagnostic Tests
   Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.
Antibiotic Stewardship

Antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration.

-Infectious Diseases Society of America

Antimicrobial stewardship is a coordinated program that promotes the appropriate use of antimicrobials (including antibiotics), improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms.

-APIC
Antibiotic Stewardship

Antibiotic stewardship is the effort to measure antibiotic prescribing; to improve antibiotic prescribing by clinicians and use by patients so that antibiotics are only prescribed and used when needed: to minimize misdiagnoses or delayed diagnoses leading to underuse of antibiotics; and to ensure that the right drug, dose, and duration are selected when an antibiotic is needed.

-CDC

In a nutshell...

It’s about patient safety and delivering high-quality healthcare.
Call to Action

This is the time to be a good steward and protect your community from the ever advancing threat of antimicrobial resistance!
Commitment

A commitment from all health care team members to prescribe antibiotics appropriately and engage in antibiotic prescribing is crucial in improving antibiotic prescribing. Every person involved in patient care can act as an antibiotic steward.
Protecting Patients and Preventing Outbreaks

Inpatient Healthcare Providers
- Know what types of drug-resistant infections are present in your facility and patients.
- Request immediate alerts when the lab identifies drug-resistant infections in your patients.
- Alert receiving facility when you transfer a patient with a drug-resistant infection.
- Protect patients from drug-resistant infections.
- Follow relevant guidelines and precautions at every patient encounter.
- Prescribe antibiotics wisely.
- Remove temporary medical devices such as catheters and ventilators as soon as they are no longer needed.

Protecting Patients and Preventing Outbreaks

Health Care CEOs, Medical Officers, and Other Healthcare Facility Leaders
- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections and alert clinical and infection prevention staff when these bacteria are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.
ANTIBIOTIC STEWARDSHIP PROGRAMS AND ACTIVITIES CAN:

**IMPROVE PATIENT OUTCOMES**
By reducing unnecessary antibiotic prescribing, antibiotic stewardship programs and activities can improve the treatment of infections and prevent avoidable side effects, reactions, and other problems for patients.

**DECREASE C. DIFFICILE INFECTIONS**
Antibiotic stewardship programs and activities significantly reduce C. difficile infections. For example, reducing the use of high-risk antibiotics (fluoroquinolones) by 30 percent can lower C. difficile infections by 26 percent in hospitals. Reducing overall antibiotic prescribing in outpatient settings by 10 percent could lower C. difficile infections in the community by 17 percent.

**DECREASE ANTIBIOTIC RESISTANCE**
Preventing infections and improving antibiotic prescribing could save 37,000 lives from antibiotic-resistant infections over 5 years.

**DECREASE COSTS**
Antibiotic stewardship programs have consistently demonstrated annual savings of $200,000 to $400,000 in hospitals and other healthcare facilities. According to a University of Maryland study, implementation of an antibiotic stewardship program saved one hospital a total of $17 million over 8 years.

Communication Strategies

Don’t take antibiotics for granted...
Core Elements of Hospital Antibiotic Stewardship Programs

- Leadership Commitment: Dedicating necessary human, financial and information technology resources
- Accountability: Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective
- Drug Expertise: Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- Action: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours)
- Tracking: Monitoring antibiotic prescribing and resistance patterns
- Reporting: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
- Education: Educating clinicians about resistance and optimal prescribing

https://www.cdc.gov/antibiotic-use/healthcare/pdfs/core-elements.pdf
http://www.qualityforum.org/Publications/2016/05/National_Quality_Partners_Playbook__Antibiotic_Stewardship_in_Acute_Care.aspx

Resources

https://www.cdc.gov/antibiotic-use/week/
"I don’t need easy, I just need possible.”

-Emily Mellish


Etc., Etc......