Antibiotic Resistant Organisms and Emerging Pathogens

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- Define multidrug resistant organisms
- Describe the evolution of antimicrobial resistance
- Identify strategies to prevent further escalation

Did you know?

- Antibiotic Resistance is one of the world's most pressing public health threats
- Antibiotics are the most important tool to combat life-threatening bacterial infections....they come with side effects
- Antibiotic overuse increases the development of antibiotic resistant bacteria

Definition

ANTIBIOTIC RESISTANCE is the ability of bacteria or other microbes to resist the effects of an antibiotic. Antibiotic resistance occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to cure or prevent infections. The bacteria survive and continue to multiply causing more harm.

Development of Drug Resistant Bacteria



Mechanisms of Antibiotic Resistance



Antibiotic deployment



Antibiotic resistance observed

Scope of the problem

- Antibiotic resistance is associated with:
 - Increased risk of hospitalization
 - Increased length of stay
 - Increased hospital costs
 - Increased risk of transfer to the intensive care unit
 - Increased risk of death

Resistance in the United States

NATIONAL SUMMARY DATA

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, **214,000** deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.



U.S. Department of Health and Human Services Centers for Disease Control and Prevention





Source: *The Epidemic of Antibiotic-Resistant Infections*, CID 2008:46 (15 January) Clin Infect Dis. (2011) May 52 (suppl 5): S397-S428. doi: 10.1093/cid/cir153

http://www.cdc.gov/getsmart/campaign-materials/week/images/anti-dev.png

Antibiotics are misused in a variety of ways

- Given when they are not needed
- Continued when they are no longer necessary
- Given at the wrong dose
- Broad spectrum agents are used to treat very susceptible bacteria
- The wrong antibiotic is given to treat an infection

In-patient Settings

- Of the patients receiving antibiotics, half (50%) will receive unnecessary or redundant therapy resulting in overuse
- Unnecessary use of antibiotics creates risk of adverse drug events and *Clostridium difficile*, a deadly diarrheal disease that is on the rise
- Some infections in hospitals are now resistant to all available antibiotics

Antibiotic misuse adversely impacts patients – resistance

- Getting an antibiotic increases a patient's chance of becoming colonized or infected with a resistant organism
- Increasing use of antibiotics increases the prevalence of resistant bacteria in hospitals
- Antibiotic resistance increases mortality

Antibiotic misuse adversely impacts patients - *C. difficile*

- Antibiotic exposure is the single most important risk factor for the development of *Clostridium difficile* associated disease (CDAD).
- Up to 85% of patients with CDAD have antibiotic exposure in the 28 days before infection
- Epidemic strain of *C. difficile* is associated with increased risk of morbidity and mortality.

27,000 nursing home residents have antibioticresistant infections ¹

2 out of 3 nursing home residents receive at least one course of antibiotics annually²

250,000 nursing home residents have infections³

1.6 million people live in nursing homes⁴

Out-patient Settings

- Each year, tens of millions of antibiotics are prescribed unnecessarily for viral upper respiratory infections
- In states where there is more antibiotic use, there are more antibiotic-resistant pneumococcal infections
- The presence of antibiotic-resistant bacteria is greatest during the month following a patient's antibiotic use and may persist for up to 12 months.

Good News / Bad News Antibiotics prescribed for acute respiratory infections in kids younger than 15 years of age



Source: MMWR. 2011;60:1153-6

http://www.cdc.gov/getsmart/campaign-materials/week/promotional-media.html?tab=6#TabbedPanels1

Community Antibiotic Prescribing Rates by State (2013/2014)*

50% of all antibiotics prescribed in U.S. health provider offices are either unnecessary or inappropriate

*Antibiotic prescriptions per 1000 persons Prescribing data from 2014; population data from 2013

Source: IMS Health



Today's Superbug - CRE

Carbapenem-resistant Enterobacteriaceae (CRE)

Enterobacteriaceae:

- Family of germs that are difficult to treat because they have high levels of resistance to antibiotics.
- Normal part of the human gut bacteria, that can become Carbapenem-resistant.
- Causes a range of human infections: urinary tract infections, wound infections, pneumonia, bacteremia
- Important cause of healthcare- and communityassociated infections

CRE and it's resistance mechanisms

- KPC (Klebsiella pneumoniae carbapenemase)
- NDM (New Delhi Metallo-beta-lactamase).
- (KPC and NDM are enzymes that break down carbapenems and make them ineffective)
- VIM (Verona Integron-Mediated)
- (VIM and Metallo-β-lactamase have also been reported in *Pseudomonas*)

http://www.cdc.gov/HAI/organisms/cre/

Why are CRE Clinically and Epidemiologically Important?

- Cause infections associated with high mortality rates
- Treatment options are limited
- Potential for spread into the community
- In most areas in the United States this organism appears to be infrequently identified

Clinical and Epidemiologic Importance of CRE

- Resistance is highly transmissible
 - Between organisms plasmids
 - Between

patients





CRE in Kentucky

- Voluntary Reporting of CRE since Feb 2013
 - KPC producer common
 - NDM producer has not been identified
 - Associated with foreign healthcare, first identified in New Delhi, India
 - VIM producer
 - Rare KY identified 5th case in U.S.
 - Associated with foreign healthcare and medical tourism
 - KY- Largest domestic outbreak of VIM in US, included neonates and adult population

Patients with KPC-producing Carbapenem-resistant Enterobacteriaceae (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of February 2016, by state



http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

Patients with NDM-producing Carbapenem-resistant Enterobacteriaceae (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of April 2016, by state



http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

Patients with VIM-producing Carbapenem-resistant Enterobacteriaceae (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of April 2016, by state



http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

Notes from the Field: Verona Integron-Encoded Metallo-Beta-Lactamase-Producing Carbapenem-Resistant Enterobacteriaceae in a Neonatal and Adult Intensive Care Unit – Kentucky, 2015

Weekly/ February 26, 2016 / 65(7);190



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During August 4-September 1, 2015, eight cases of Verona integron-encoded metallo-beta-lactamase (VIM)-producing Carbapenem-resistant Enterobacteriaceae (CRE) colonization were identified in six patients, using weekly active surveillance perirectal cultures in a Kentucky tertiary care hospital. No cases of clinical infection or complications attributable to colonization were reported. Four of the eight isolates were identified as *Enterobacter cloacae*, other organisms included *Raoultella* species (one), *Escherichia coli* (one), and *Klebsiella pneumoniae* (two). Six isolates were reported in a neonatal intensive care unit (ICU), and two isolates in an adult trauma and surgical ICU. Patient ages at isolate culture date ranged from 21 days to 68 years. Fifty percent of the patients were male. Previously, only one VIM-producing CRE-colonized patient (an adult, in 2013) had been reported by the same hospital. The six cases are the largest occurrence of VIM-producing CRE colonization reported in the United States and the only recognized cluster of VIM-producing CRE colonization in the United States reported to include a neonatal population. Despite environmental sampling over the same period, surveying patients for exposure to health care outside the United States, surveying health care providers for risk factors, and surveillance culturing of health care provider nares and axillae, a source of VIM-producing CRE has not been identified for this cluster. Prevention measures throughout the ICUs have been enhanced in response to this cluster, as detailed in CDC's 2015 CRE toolkit update (*1*).

CRE are defined as any Enterobacteriaceae species resistant to any carbapenem or possessing a documented carbapenemase (2). Outbreaks of VIM-producing CRE have been described previously, including outbreaks in pediatric and neonatal populations in Spain (3) and Hungary (4). However, both of these outbreaks involved a single CRE species (*E. cloacae*). The first VIM to be identified in the United States was in an adult patient with *K. pneumoniae* in 2006 (5).

Clinical infections with CRE have been reported, with mortality rates of up to 50% (*d*). Enterobacteriaceae species are a common cause of infection in both health care-associated and communityassociated infections, and the potential exists for carbapenem-resistant strains to add to this burden of infections. VIM-producing CRE are a substantial threat to public health, with more complicated patient outcomes, including higher relapse rate and a prolonged duration of antimicrobial therapy (*7*). The carbapenemases can be transferred easily from organism to organism through plasmid exchange, facilitating spread of resistance (*2*).

Risk factors for CRE acquisition in the United States primarily include exposure to health care settings and antimicrobial agents (2). Travel to countries with higher prevalence also is a risk factor



Possible Transmission of *mcr-1*–Harboring *Escherichia coli* between Companion Animals and Human

Discovery of first mcr-1 gene in E.coli bacteria found in a human in United States – resistant to Colistin – big gun antibiotic!!

On September 18, 2014, the White House announced an **Executive Order** stating that the Federal Government will work domestically and internationally to detect, prevent, and control illness and death related to antibiotic-resistant infections by implementing measures that reduce the emergence and spread of antibioticresistant bacteria and help ensure the continued availability of effective therapeutics for the treatment of bacterial infections

Improving antibiotic use is a public health imperative

- Antibiotics are the only drug where use in one patient can impact the effectiveness in another
- Antibiotics are a shared resource, (and becoming a scarce resource)



Improving antibiotic use saves money

- "Comprehensive programs have consistently demonstrated a decrease in antimicrobial use with annual savings of \$200,000 - \$900,000"
- IDSA/SHEA Guidelines for Antimicrobial Stewardship Programs

http://www.journals.uchicago.edu/doi/pdf/10.1 086/510393

Core Elements of Antibiotic Stewardship programs - Hospitals

- Leadership commitment
- Accountability
- Drug Expertise
- Action
- Tracking
- Reporting
- Education

Core Elements of Antibiotic Stewardship programs – Outpatient settings

- Refrain from treating viral syndromes with antibiotics
- Prescribe: right antibiotic, right dose, right duration
- Include microbiology cultures when placing antibiotic orders
- Take an "antibiotic timeout" when a patient's culture result comes back

Core Elements of Antibiotic Stewardship programs – Outpatient settings

- Talk to your patients about appropriate use of antibiotics
- Work with pharmacists to counsel patients on appropriate antibiotic use, resistance and adverse effects
- Consider delayed prescribing
- Utilize patient and provider resources offered by CDC and other professional organizations

Goals- Get Smart for Healthcare

- Improve patient safety through better treatment of infections.
- Reduce the emergence of antimicrobial resistant pathogens and *Clostridium difficile*.
- Heighten awareness of the challenges posed by antimicrobial resistance in healthcare and encourage better use of antimicrobials as one solution.

GET SMART: Know When Antibiotics Work



GET SMART WEEK: November 14 – 20, 2016

Thank you for your attention

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