Public Health Efficacy of Antibiotic Use and Resistance
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October 23, 2018
To protect and improve the health and environment of all Kansans

Antimicrobial Use in Humans

• Over half of hospitalized patients receive an antibiotic for at least one day during stay

• Most common types of infections treated with antibiotics by hospital clinicians
  • Lung infections, 22%
  • Urinary tract infections, 14%
  • Infections caused by drug-resistant Staphylococcus (e.g. MRSA), 17%

Antibiotic Prescribing

- Antibiotic prescriptions in U.S.
  - 835 per 1,000 population (2015)
- Antibiotic prescriptions in KS
  - 992 per 1,000 population (2015)
- At least 30% of antibiotics prescriptions unnecessary
  - Outpatient and hospital settings
- 2006 to 2012, 40% increase use of carbapenems

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Antibiotics in Nursing Homes

- Up to 70% of nursing home residents receive antibiotic treatment in a year
  - $38-$137 million spent on antibiotics

- Up to 75% of antibiotics are prescribed incorrectly
  - Used for prevention of urinary and respiratory tract infections
  - Often residents are given antibiotics when patients are colonized with bacteria

At least 80 million antibiotic prescriptions each year are unnecessary.
Antimicrobial Resistance

- Minimum estimates related to antimicrobial resistance:
  - Over 2,000,000 illnesses each year
  - 23,000 deaths

- Other effects of overuse
  - Adverse drug events
  - *Clostridioides difficile* infection
    - 15,000 deaths in one year
  - Costly treatment
  - Depletion of effectiveness of available antimicrobials

Resistance in organisms is on the rise

Causes of resistance:
- Innate
- Shared
- Antimicrobial use (selection pressure)

Can infect anyone
Mechanisms of Antimicrobial Resistance

1. Impermeability (modified cell wall protein)
2. Modification (modified drug target)
3. Pumping out (increasing active efflux of the drugs)
4. Inactivation (add an phosphate group on the antibiotic, which will reduce its ability to bind to the bacterial ribosomes)
BACTERIA CONSTANTLY CHANGE AND DEVELOP NEW WAYS TO RESIST ANTIBIOTICS

Bacteria can become resistant because of antibiotic use

- We have lots of germs in and on our bodies, some are resistant
- Antibiotics kill the weak germs, but resistant germs remain
- Drug-resistant germs can take over

Bacteria can copy and share resistance, then combine it with other resistance, to avoid our best defenses

Sharing Resistance Materials

COPY

Already tough-to-treat germs, like “nightmare bacteria” CRE, can combine these defense strategies and become completely untreatable

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Antimicrobial Resistance

Some resistance come from the food we eat

- Animals get antibiotics, drug-resistant organisms thrive
- Poorly-handled or undercooked meat
- Contaminated water used for crops

400,000 people sickened with resistant *Campylobacter* or *Salmonella* every year

Salmonellosis Outbreak (Preliminary)

- Church-sponsored election day Indian taco luncheon

- First illness reported to public health three days later

- Public health officials at KS and the local health department initiated outbreak investigation
  - Online survey, media releases, testing leftover food, accessed food prep practices
Salmonellosis Outbreak (Preliminary)

- Tomatoes isolated with same strain of *Salmonella* Newport as ill individuals
- Environmental assessment conducted by Missouri and identified poor sanitation practices
- *Salmonella* not isolated from any environmental samples taken (delayed response)
- Non-potable water used for cleaning tomatoes before being sold
- Unable to identify a source of contamination
Salmonellosis Outbreak (Preliminary)

- 64 individuals reported gastrointestinal illness after consuming Indian tacos
  - *Salmonella* Newport
  - 11 lab-confirmed cases

- Median age: 62
- Hospitalizations: 12
- No deaths
Carbapenem-Resistant Enterobacteriaceae (CRE)

- Enterobacteriaceae are gut bacteria that can spread to other parts of the body causing infection

- These bacteria develop resistance to one or more carbapenem antibiotics
  - Ertapenem, imipenem, meropenem, and doripenem

- Carbapenems are often last resort antibiotic for difficult to treat infections
• Bacteria produce a carbapenemase enzyme that hydrolyze (destroy) antibiotics

• Five different enzymes have been discovered
  • *Klebsiella pneumoniae* carbapenemase (KPC) most common in the United States

• Genes encoded on mobile elements that can spread to other gram-negative bacteria
Carbapenemase-Producing CRE in KS

- Earliest detected case in 2014
- CRE reportable disease in KS as of May 2018
- CRE isolates are submitted to KS for carbapenemase testing.
- Carbapenemase identified in KS
  - KPC, $n=19$
  - NDM, $n=6$
  - IMP, $n=2$
  - KPC/OXA-48, $n=1$
Carbapenemase-Producing CRE in KS

- International healthcare exposure a risk factor for CRE colonization and infection
- Case-patient had *Klebsiella pneumoniae* isolated from blood.
- Tested positive for KPC and OXA-48-like genes
- Resistant to all antibiotics tested for at hospital
- CDC susceptibility for 27 antibiotics determined non-susceptible to all by 2 antibiotics
<table>
<thead>
<tr>
<th>ANTIMICROBIC</th>
<th>MIC (μg/mL)</th>
<th>Interp.</th>
<th>ANTIMICROBIC</th>
<th>MIC (μg/mL)</th>
<th>Interp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>&gt;64</td>
<td>R</td>
<td>Chloramphenicol</td>
<td>&gt;16</td>
<td>R</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>&gt;32</td>
<td>R</td>
<td>Ciprofloxacin</td>
<td>&gt;8</td>
<td>R</td>
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<tr>
<td>Aztreonam</td>
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<td>R</td>
<td><strong>Colistin</strong></td>
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<td>Cefazolin</td>
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<td>R</td>
<td>Doripenem</td>
<td>8</td>
<td>R</td>
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<tr>
<td>Cefepime</td>
<td>&gt;32</td>
<td>R</td>
<td>Ertapenem</td>
<td>&gt;8</td>
<td>R</td>
</tr>
<tr>
<td>Cefotaxime</td>
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<td>R</td>
<td>Gentamicin</td>
<td>&gt;16</td>
<td>R</td>
</tr>
<tr>
<td>Cefotaxime-clavulanic acid**</td>
<td>&gt;32</td>
<td></td>
<td>Imipenem</td>
<td>8</td>
<td>R</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>&gt;16</td>
<td>R</td>
<td>Levofloxacin</td>
<td>&gt;8</td>
<td>R</td>
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<tr>
<td>Ceftazidime</td>
<td>&gt;128</td>
<td>R</td>
<td>Meropenem</td>
<td>8</td>
<td>R</td>
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<tr>
<td><strong>Ceftazidime-avibactam</strong></td>
<td>1/4</td>
<td>S</td>
<td>Piperacillin-tazobactam</td>
<td>&gt;128/4</td>
<td>R</td>
</tr>
<tr>
<td>Ceftazidime-clavulanic acid**</td>
<td>&gt;64</td>
<td></td>
<td>Tetracycline</td>
<td>32</td>
<td>R</td>
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<tr>
<td>Ceftolozane-tazobactam</td>
<td>&gt;16/4</td>
<td>R</td>
<td>Tigecycline</td>
<td>4</td>
<td>I</td>
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<tr>
<td>Ceftriaxone</td>
<td>&gt;32</td>
<td>R</td>
<td>Tobramycin</td>
<td>&gt;16</td>
<td>R</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Trimethoprim-sulfamethoxazole</td>
<td>&gt;8/152</td>
<td>R</td>
</tr>
</tbody>
</table>

**Drug combination tested for detection of ESBL production. This drug combination is not available for therapeutic use.**
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Responding to AMR Threats

Prevention Strategies

• Preventing infections
  • Immunizations, handwashing, safe food preparation, healthcare-associated infection prevention efforts

• Antimicrobial Stewardship
  • “Systematic effort to improve antibiotic use to improve patient outcomes in order to help patients and combat antibiotic resistance” – CDC, 2017

Containment Strategies

• Detection and Tracking
  • Causes of infection, risk-factors
  • Reporting resistant organisms to public health

• Public Health Response
  • High-risk contact screening
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Healthcare-Associated Infections & Antimicrobial Resistance Program

• KDHE established HAI 2009, added antimicrobial resistance in 2016
• Coordinate statewide prevention, surveillance, and resistance containment efforts
• Foster key relationships between the healthcare provider community and state agencies
• Provide consultative services
• Provide education and resources
• Outbreak investigations
Wide-range of stakeholders represented
• Nurses, pharmacists, veterinarians, medical doctors, infection preventionists, and epidemiologists

Guides HAI/AR activities in the state of KS
• Education and resources to all types of providers and the general public

Coordinating state-wide efforts across organizations and stakeholders
• Antibiotics Awareness Week Proclamation
• Antibiotic Stewardship Activities
Antibiotic Stewardship

• Appropriate use of antimicrobials to:
  • Optimize outcomes for patients
  • Reduce resistance
  • Reduce other adverse effects

• Patient and staff education

• Not the “antibiotic police”

• Not saying “don’t use antibiotics”
HAI/AR Program Stewardship Activities

• Critical Access Hospitals (less than 25 beds)
  • Developed Stewardship Program Toolkit
  • Provide HAI support and resources
  • National Healthcare Safety Network AUR Module

• Long-term Care Facilities (Nursing Homes)
  • Infection Control and Prevention training
  • Asymptomatic UTI Toolkit

• Pharmacies
  • Posters and materials for patient education
• Specific to unique aspects of CAHs

• Invited to CDC to help develop national toolkit
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Chills, Cough and/or Cold – Oh My!

Antibiotics only treat bacterial infections. Viral illnesses cannot be treated with antibiotics. When an antibiotic is not prescribed, ask your pharmacist or primary healthcare provider for tips on how to relieve symptoms to make you feel better.

<table>
<thead>
<tr>
<th>Illness</th>
<th>Usual Cause</th>
<th>Antibiotic Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold/Ruuny nose</td>
<td>Virus, Bacteria</td>
<td>No</td>
</tr>
<tr>
<td>Bronchitis/Chest cold in otherwise healthy children and adults</td>
<td>Virus, Bacteria</td>
<td>No</td>
</tr>
<tr>
<td>Whooping Cough</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Stomach Flu</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Strep Throat</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Fluid in Middle Ear (otitis media with effusion)</td>
<td>Yes</td>
<td>Maybe</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>Maybe</td>
<td>Maybe</td>
</tr>
<tr>
<td>Respiratory Flu</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Sinus Infection</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**Antibiotics are not Always the Answer Your Pharmacist can help you select the right cough and cold medication for you or may direct you to your primary care provider.**

**CRE Fact Sheet**

**What are CRE?**

CRE, which stands for Carbapenem-resistant Enterobacteriaceae, is a family of germs that are difficult to treat because they have high levels of resistance to antibiotics and are resistant to carbapenem antibiotics. CRE is an important emerging threat to public health.

Common Enterobacteriaceae include Klebsiella pneumoniae, Escherichia coli, and Enterobacter species. These germs are found in normal human intestinal flora. Sometimes these bacteria can spread outside the gut and cause serious infections, such as urinary tract infections, wound infections, and pneumonia. Enterobacteriaceae can cause infections in all types of healthcare and community settings.

**What are carbapenem antibiotics?**

Carbapenems are a group of antibiotics that are usually reserved to treat serious infections, particularly when those infections are caused by germs that are highly resistant to other antibiotics. Sometimes carbapenems are the only antibiotics that can treat these germs. Germs that become resistant to carbapenem antibiotics are called CRE.

**How do CRE become resistant to carbapenem antibiotics?**

Some Enterobacteriaceae can no longer be treated with carbapenems because they have developed resistance to these antibiotics and are referred to as CRE. Resistance makes the antibiotics ineffective in killing the resistant germs. Resistance to carbapenems can be due to a few different mechanisms. One of the more common ways by which Enterobacteriaceae become resistant to carbapenems is due to production of antimicrobial carbapenemases (enzymes). CRE can develop in small numbers in patients predated by CRE that were first identified in the 1980s. CRE have been linked with carbapenem antibiotics making them ineffective. Other CRE have developed in ICUs, caused by CRE that are resistant to carbapenems and lead to the development of CRE, but they are uncommon in the United States.

**How are CRE spread?**

To get a CRE infection, a person must be exposed to CRE germs. CRE germs are usually spread person to person through contact with infected or colonized (asymptomatic) people, particularly with wounds or stom. CRE can cause infections when they enter the body, often through medical devices like ventilators, intravenous catheters, urinary catheters, or wounds caused by injury or surgery.

**Who is most likely to get an infection with CRE?**

Healthy people usually don’t get CRE infections. CRE primarily affect patients in healthcare settings like hospitals and long-term care facilities. Such facilities are especially at risk if they have compromised immune systems or patients whose care requires devices like ventilators or other medical devices like urinary (bladder) catheters, or intravenous (IV) catheters. Use of certain types of antibiotics might also make it more likely for patients to get CRE.

**Can CRE be treated?**

Many people with CRE will have the germs in or on their body without showing any signs or symptoms. These people are not to be colonized with CRE, and they do not need antibiotics for CRE. In CRE, anti-organisms are the only antibiotics that will fight against it, but some options are often available. In some, some infections might be able to be treated with other therapies. Others might have germs that are resistant to all antibiotics are very rare but have been reported.

**What is CRE?**

Follow your healthcare provider’s instructions. If your provider prescribes you antibiotics, take them exactly as instructed and finish the full course, even if you feel better. Wash your hands with soap and water, especially after you have contact with the infected person and after using the bathroom. Follow any other hygiene advice your provider gives you.

If you are caring for someone with CRE at home. Do not need to take special precautions? CRE have primarily been a problem among people with underlying medical problems, especially those with medical devices like urinary (bladder) catheters or those with chronic wounds. Otherwise healthy people are probably at relatively low risk for problems with CRE. People providing care at home for patients with CRE should be careful about wearing their hands, especially after contact with others. Other people should be careful about not touching the infected person and about cleaning up clothing. Caregivers should also make sure to wash their hands before and after handling the patient’s medical device, such as urinary catheters. This is particularly important if the caregiver is caring for more than one person at home. In addition, gloves should be used when anticipating contact with bodily fluids or blood.

Where can I get more information about CRE? Contact your doctor or visit CDC’s website at www.cdc.gov/organigrams/cre-care-patients.html.
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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.*

Data source: IMS Health Xponent 2014.
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KDHE Stewardship Workshop

- Workshop focusing on stewardship activities in hospitals across Kansas
  - No cost for attendance
  - Reimbursement for travel expenses
  - Team-based approach

- Held in Manhattan, KS in May 2018
  - Over 175 attendees
  - Approx. 80 hospitals
Stewardship Workshop for KS Hospitals

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CDC’s 6|18 Initiative
• Addressing antibiotic overuse in outpatient settings
• Collaborative effort with managed health organizations (MHOs) and Medicaid data
• Evidenced-based practices to decrease inappropriate use
• Why do we prescribe antibiotics?
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To protect and improve the health and environment of all Kansans
Systematic approach to slow spread of targeted organisms:

- Pan-resistant organisms
- Carbapenemase-producing bacteria
- Colistin resistance (mcr-genes)
- *Candida auris*

Response tiers based on pathogen/resistance mechanism
The Containment Strategy

Systematic public health response to slow the spread of emerging AMR

DETECTION

Single case of emerging resistance

INFECTION CONTROL

Onsite assessment using standardized tools

CONTACT SCREENING

Available through ARLN

Regular infection control assessments and point prevalence surveys until transmission stops

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The Containment Strategy

- Identify individuals at high-risk of acquiring AMR organism and conduct colonization screening
- Screen individuals to identify “silent” transmission
- Enforce and enhance infection control practices
Colonization Screening: 74
Positive tests: 2 (2.7%)
U.S. average: 11%
Median age: 61
Males: 42
Females: 32

104 high-risk patients monitored in surveillance system for CRE infection
Transmission appears to have the highest risk in post–acute care facilities with higher acuity patients

- long duration of facility stay,
- less aggressive use of transmission-based precautions (concerns about resident’s quality of life),
- high staff turnover
- less expertise and training in infection control

Ongoing support required when targeted resistant organisms are identified

- infection control assessments
- Screening of contacts

CDC MMWR April 6, 2018 / 67(13);396-401
A success story in the making?

- CRE 15% decrease per year from 2006-2015
  - Risk ratio= 0.85, p<0.01
- ESBL-producing organisms decreased by 2% per year
  - Risk ratio= 0.98, p<0.001
- Increased detection and aggressive early response to emerging antibiotic resistance threats have the potential to slow further spread.

CDC MMWR April 6, 2018 / 67(13);396-401
Challenges Going Forward

• Changing the mentality of stewardship
  • Not the “antibiotic police”
  • Not saying “don’t use antibiotics”

• Competing resources within healthcare facilities

• Long-term commitment to measure success and progress

• Cooperation and targeted approach among all stakeholders
  • One Health Approach
  • Public education
Resources

Public Health’s Role in Drug Resistance (CDC)
www.cdc.gov/drugresistance/cdc_role.html

Protecting Yourself and Your Family from Drug Resistance Infections (CDC)
www.cdc.gov/drugresistance/protecting_yourself_family.html

KDHE Healthcare-Associated Infections and Antimicrobial Resistance Program
www.kdheks.gov/epi/hai.htm

CDC’s Be Antibiotics Aware: Smart Use, Best Care
www.cdc.gov/features/antibioticuse/index.html
Public Health Efficacy of Antibiotic Use

Thank you/Questions