Epidemiology of Antibiotic Resistant Infections in SD

One Health Meeting

March 1, 2019

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Outline

- Renewed focus on antibiotic resistance
- Strategies to prevent and control
- Surveillance in the US and SD
WHO Threats to Global Health 2019

• Antimicrobial resistance

• Antibiotics, antivirals, and antimalarials are some of modern medicine’s greatest successes

• Resistance to tuberculosis drugs
  • 10 million ill
  • 1.6 million die

• In 2017, 600,000 cases resistant to rifampicin, most effective first-line drug (82% were multi-drug resistant)
CDC Focus

- April 2013
- Purpose to increase awareness of threat antibiotic resistance poses and encourage action

- >2 million individuals ill annually with 23,000 deaths*
- $20 billion in excess direct healthcare costs
- $15 billion in lost productivity

- Update anticipated in late 2019

* Re-estimated annual deaths increased 7-fold to 153,113
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 Neisseria gonorrhoeae (cephalosporin resistance)*

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.

*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 pneumonia, 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*
Four core actions to fight drug resistant infections

- Preventing infections, preventing the spread of resistance
- Track resistant bacteria
- Improve antibiotic prescribing/stewardship
- Develop new antibiotics and diagnostic tests
Examples of How Antibiotic Resistance Spreads

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

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.
5 Gaps in Knowledge to Address

- Limited capacity to detect and respond
- No systemic international surveillance
- Antibiotic use in healthcare and agriculture not systematically collected
- Programs to improve antibiotic prescribing not widely used
- Limited availability of advanced molecular diagnostics for identification
Gap: Limited capacity to detect and respond

Solution:

**CDC’s Antibiotic Resistance (AR) Solutions Initiative**

Investing to Defend the United States against Antibiotic Resistance

CDC distributes funding to all 50 states to increase capacity for rapid detection and response to outbreaks and emerging resistance related to healthcare-associated infections, and foodborne bacteria.

[www.cdc.gov/ARinvestments](http://www.cdc.gov/ARinvestments)

South Dakota: $432,756
$338,978 for Rapid Detection and Response
$93,778 for Food Safety
**Gap:** No systemic international surveillance

**Solution:**

- **8 bacteria**
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Acinetobacter* spp.
  - *Staphylococcus aureus*
  - *Streptococcus pneumoniae*
  - *Salmonella* spp.
  - *Shigella* spp.
  - *Neisseria gonorrhoeae*

- **4 specimen types**
  - blood
  - urine
  - stool
  - genital swabs
**Gap:** Antibiotic use in healthcare and agriculture not systematically collected

**Solution:**

**Flow of AU Data: From Bedside to NHSN**

- **eMAR/BCMA & ADT**
  - Pharmacists & Physicians compare and target education/interventions
  - Risk adjusted comparisons for specific locations, groupings of antimicrobials

- **Vendor/Homegrown System**
  - Monthly summary
  - Location specific & FacWideIN
    - 89 antimicrobials
    - Days present & admissions
  - Local access of data: NHSN web interface – analysis, visualization and data sharing

- **Clinical Document Architecture (CDA)**
  - Report in standard format

- **NHSN**
  - NHSN Servers
Gap: Antibiotic use in healthcare and agriculture not systematically collected

Solution:

Guidance for Industry

The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals

Submit comments on this guidance at any time. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments on the guidance at http://www.regulations.gov. All written comments should be identified with the Docket No. FDA-2010-D-0094.

For further information regarding this document, contact William T. Flynn, Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9084. E-mail: william.flynn@fda.hhs.gov.

Additional copies of this guidance document may be requested from the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at either http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm or http://www.regulations.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
April 13, 2012

Guidance for Industry

New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
December 2013
**Gap:** Programs to improve antibiotic prescribing not widely used

**Solution:**
Percentage of Hospitals Meeting all 7 Core Elements of Hospital Antibiotic Stewardship Programs* by State, 2016

Nationally, 64.2% of hospitals have met all 7 Core Elements (3,057 of 4,764); the national goal is 100% of hospitals by 2020.

*More information on CDC’s Core Elements of Hospital Antibiotic Stewardship Programs can be found at: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html
Source: CDC’s National Healthcare Safety Network (NHSN) Survey
**Gap:** Limited availability of advanced molecular diagnostics for identification

**Solution:**

[Map showing molecular surveillance centers across the U.S.]
Surveillance for Antibiotic-Resistant Infections

- Healthcare Associated Infections Program
  - Carbapenem resistant *Enterobacteriaceae* (CRE)
  - *Candida auris*
- National Healthcare Safety Network
  - *Clostridium difficile*
  - Methicillin-resistant *Staphylococcus aureus*
- National Antimicrobial Resistance Monitoring System
  - [https://wwwn.cdc.gov/narmsnow/](https://wwwn.cdc.gov/narmsnow/)
  - *Salmonella*
  - *Campylobacter*
  - *Shigella*
Enterobacteriaceae

- Normal human gut flora and environmental organisms
- More than 70 species
  - *Enterobacter* species
  - *Escherichia coli*
  - *Klebsiella* species
- Range of human infections: UTI, wound infections, pneumonia, bacteremia
- Important cause of healthcare-and community associated infections
- Some of the most common organisms encountered in clinical laboratories
Carbapenem Resistant *Enterobacteriaceae*

*Enterobacteriaceae* that are:

- **Resistant** to one of the following carbapenems:
  - Doripenem
  - Ertapenem
  - Meropenem
  - Imipenem

OR

- Documentation that the isolate possesses a Carbapenemase
Carbapenemases

Definition: are enzymes produced by bacteria that break down Carbapenems and make them ineffective. They are often contained on mobile genetic elements that facilitate transfer of resistance among Enterobacteriaceae and other gram-negative organisms.
Carbapenemase-producing Carbapenem Resistant Enterobacteriaceae (CP-CRE)

- CP-CRE is a subset of CRE
- Ability to spread rapidly by transfer of Carbapenemase-encoding plasmid
- Resistance mechanisms include:
  - KPC: Klebsiella pneumoniae Carbapenemase
  - NDM: New Delhi metallo-β-lactamase
  - OXA-48: oxacillinase-48
  - VIM: Verona integron-encoded metallo-β-lactamase
  - IMP: imipenemase
Surveillance for CP-CRE
KPC Detected in all 50 States

Patients with KPC-producing *Carbapenem-resistant Enterobacteriaceae* (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of December 2017, by state.
NDM Detected in 34 States (N=379)

Patients with NDM-producing *Carbapenem-resistant Enterobacteriaceae* (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of December 2017, by state.
First NDM CP-CRE Detection in 2018

- Patient had outpatient visit on April 25
- Outpatient procedure for cystoscopy on May 1
- Presented to emergency dept. on May 2
- Admitted directly to ICU
- SD Public Health Lab resulted NDM (+) E. coli on May 4
  - Urine culture (OP1)
  - Urine culture (OP2)
  - Blood culture (ED)
- SD-DOH notified on May 4
- Patient placed in contact precautions same day
- SD-DOH consulted with CDC and admitting hospital
OXA-48 Detected in 27 States (N=146)

Patients with OXA-48-Type-producing *Carbapenem-resistant Enterobacteriaceae* (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of December 2017, by state.
IMP Detected in 13 States (N=36)

Patients with IMP-producing Carbapenem-resistant Enterobacteriaceae (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of December 2017, by state

SOUTH DAKOTA DEPARTMENT OF HEALTH
VIM Detected in States (N=57)

Patients with VIM-producing *Carbapenem-resistant Enterobacteriaceae* (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of December 2017, by state.

None

Reported
MCR Gene Detected in States (N=21)

MCR-1, -2, and -3 genes cause resistance to colistin, a last-line antibiotic.

As of November 2, 2018
C. auris Clinical Cases Detected in 12 States (N=551)

As of December 31, 2018

Additional 750 colonizations identified.
CRE Epidemiology in SD
### Reportable Diseases – South Dakota

**+Category I diseases:** *Report immediately on suspicion of disease*

**Category II diseases:** *Report within 3 days*

*Send isolate or specimen to South Dakota Public Health Laboratory*

**Effective Date:**

1 January 2019

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**Anthrax** *(Bacillus anthracis)*

Anaplasmosis *(Anaplasma phagocytophilum)*

Arboviral encephalitis, meningitis and infection *(West Nile, Zika, St. Louis, Eastern equine, Western equine, Chikungunya, California, Japanese, Powassan, LaCrosse, Colorado tick fever)*

Babesiosis *(Babesia spp)*

**Botulism** *(Clostridium botulinum)*

**Brucellosis** *(Brucella spp)*

Campylobacteriosis *(Campylobacter spp)*

Carbon monoxide poisoning

Chancroid *(Haemophilus ducreyi)*

Chlamydia *(Chlamydia trachomatis)*

Cholera *(Vibrio cholerae)*

Coccidiodomycosis *(Coccidioides spp)*

**Coronavirus respiratory syndromes**, such as MERS (Middle East respiratory syndrome) and SARS (Severe acute respiratory syndrome)

Cryptosporidiosis *(Cryptosporidium spp)*

Cyclosporiasis *(Cyclospora cayetanensis)*

Dengue viral infection *(Flavivirus)*

**Diphtheria** *(Corynebacterium diphtheriae)*

Drug resistant organisms:

- Carbapenem-resistant *Enterobacteriaceae* *(CRE)*
- *Candida auris*
- Meticillin-resistant *Staphylococcus aureus* *(MRSA)*, invasive
- Vancomycin-intermediate & resistant *Staphylococcus aureus* *(VISA, VRSA)*

**E. coli, shiga toxin-producing** *(Escherichia coli)*, includes *E. coli* O157:H7, O26, O111, O103 and others

*Ehrlichiosis** *(Ehrlichia spp)*

Giardiasis *(Giardia lamblia / intestinalis)*

Gonorrhea *(Neisseria gonorrhoeae)*

*Haemophilus influenzae*, invasive disease

Hantavirus pulmonary syndrome or infection

Hemolytic uremic syndrome

Hepatitis, viral, acute A, B and C; chronic B and C; and perinatal B & C

Human immunodeficiency virus *(HIV)*

- Infection, including:
  - Stage III, Acquired Immunodeficiency Syndrome (AIDS)
  - CD4 counts in HIV infected persons
  - HIV viral loads
  - Pregnancy in HIV infected females
  - HIV gene sequencing
  - HIV antiviral resistance
  - Confirmatory results, positive or negative, following a reactive HIV screening test

**Influenza, novel strains**

- Hospitalizations
- Deaths
- Lab confirmed cases (culture, DFA, PCR)
- Weekly aggregate totals of rapid antigen positive (A and B) and total tested

**Lead**, elevated blood levels

**Legionellosis** *(Legionella spp)*

Leprosy / Hansen’s disease *(Mycobacterium leprae)*

Leptospirosis *(Leptospira)*

Listeriosis *(Listeria monocytogenes)*

**Lyme disease** *(Borrelia burgdorferi)*

Malaria *(Plasmodium spp)*

**Measles** / *Rubella* *(Paramyxovirus)*

Meningococcal disease, invasive *(Neisseria meningitidis)*

Mumps *(Paramyxovirus)*

Paratyphoid fever

**Pertussis** *(Bordetella pertussis)*

Pesticide-related illness and injury, acute

**Plague** *(Yersinia pestis)*

**Polio** *(poliovirus)*

Psittacosis *(Chlamydophila psittaci)*

Q fever *(Coxiella burnetti)*

**Rabies**, human and animal *(Rhabdovirus)*

**Rubella** and congenital rubella syndrome *(Togavirus)*

Salmonellosis *(Salmonella spp)*

Shigellosis *(Shigella spp)*

Silicosis

**Smallpox** *(Variola)*

**Spotted fever rickettsiosis** *(Rickettsia)*

**Streptococcus pneumoniae**, invasive

Syphilis *(Treponema pallidum)* including primary, secondary, latent, early latent, late latent, neurosyphilis, late non-neurological, stillbirth, and congenital

Tetanus *(Clostridium tetani)*

Toxic shock syndrome *(Streptococcal and non-Streptococcal)*

Transmissible spongiform encephalopathies, such as Creutzfeldt-Jakob disease

**Trichinosis** *(Trichinella spiralis)*

**Tuberculosis, active disease** *(Mycobacterium tuberculosis)* or *(Mycobacterium bovis)*

**Tuberculosis, latent infection** (only in certain high risk persons: foreign-born <5 yrs in US, close contacts, diabetes, renal dialysis, children <5 yrs, and certain medical conditions)

**Tularemia** *(Francisella tularensis)*

Typhoid *(Salmonella typhi)*

**Vaccine Adverse Events**

Varicella / Chickenpox *(Herpesvirus)*

**Viral Hemorrhagic Fevers** (Crimean-Congo Hemorrhagic Fever virus, Ebola virus, Lassa virus, Lujo virus, Marburg virus, New World Arenaviruses – Guanarito virus, Junin virus, Machupo virus, Sabia virus)

**Vibrio** *(Vibrionaceae)*

**Yellow fever** *(Flavivirus)*

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**Outbreaks of:**

- Acute upper respiratory illness
- Diarrheal disease
- Foodborne disease
- Healthcare-associated infections
- Illnesses in child care setting
- Rash illness
- Waterborne disease

**Syndromes suggestive of bioterrorism** and other public health threats

**Unexplained illnesses or deaths** in human or animal
How to Report CRE in SD

- CRE became reportable in 2013
- *C. auris* became reportable in 2019

Report CRE via:
- **Secure website:** [http://sd.gov/diseasereport](http://sd.gov/diseasereport)
- **Telephone:** 605-773-3737 or 800-592-1861
- **Fax:** 605-773-5509
- **Mail or courier,** 615 East 4th Street
  Pierre, SD 57501
CRE Incidence by Year, South Dakota

# Cases

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<th>Year</th>
<th>Cases</th>
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<td>2009</td>
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<td>58</td>
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<tr>
<td>2017</td>
<td>64</td>
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<tr>
<td>2018*</td>
<td>52</td>
</tr>
</tbody>
</table>

* Preliminary Data
CRE Cases by Sex and Age Group, 2018

- **71% Female; 29% Male**
- **Pie Chart:**
  - 15 Female
  - 37 Male

**Age Group Distribution:**
- <1 yr: 0
- 1-4 yr: 0
- 5-14 yr: 1
- 15-24 yr: 1
- 25-39 yr: 10
- 40-64 yr: 20
- 65+ yr: 20

**Chart:**
- Bar Graph showing the distribution of cases by age group.
CRE Organism Identified, 2018

- 58% of organisms are found in urine specimens
- 35% of organisms are carbapenemase producing
Response to CRE Infections

Goals:
- Identify if transmission /dissemination occurring
- Identifying affected patients
- Ensuring appropriate control measures are promptly initiated/implemented to contain spread
- Characterize organism/mechanism to guide response action, patient management, and responses

https://www.cdc.gov/hai/containment/guidelines.html
NHSN: *Clostridium difficile*

Isolates Reported from All Participating Hospitals

- **Community Onset (CO)**
- **Hospital Onset**
- **CO, Healthcare-associated**

MRSA Surveillance

* Preliminary Data
Community Antibiotic Prescriptions per 1,000 Population by State - 2016

Each year 270.2 million antibiotic prescriptions are written in the United States; equivalent to 836 antibiotic prescriptions per 1,000 persons.
## Antiibiogram of Selected Pathogens, South Dakota 2017

### West Region

#### Gram positive organisms

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>% Susceptible</th>
<th>(n) number of isolates tested</th>
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</thead>
<tbody>
<tr>
<td>Amoxicillin/Clavulanic acid</td>
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<tr>
<td>Cefepime</td>
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</tr>
<tr>
<td>Cefotaxime</td>
<td>88(78)</td>
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</tr>
<tr>
<td>Ceftriazone</td>
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<tr>
<td>Ampicillin</td>
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</tr>
<tr>
<td>Oxacillin†</td>
<td>61(1357)</td>
<td>99(88)</td>
</tr>
<tr>
<td>Penicillin†</td>
<td>17(1357)</td>
<td>24(88)</td>
</tr>
</tbody>
</table>

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Thank You!

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https://doh.sd.gov/diseases/hai/