Super Bugs Need Super Heroes!
Colistin Resistance Super Hero Training Academy

Rita Owsiak MS, MT(ASCP), CIC
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Academy Courses

• Super Hero 101: Know the Enemy
  Study the history of colistin, its journey to the dark side and why plasmid-mediated resistance is a mighty foe.

• Super Hero 202: Prepare your Defense
  Fill your infection control and prevention arsenal with the tools and guidelines to keep this wicked villain at bay.

• Super Hero 303: Call for Reinforcements
  Know ‘who you gonna call’ should colistin resistance come to a Maine town near you.

• Super Hero 404: Winning the Battle
  Join the Maine Justice League – Antimicrobial Stewardship!
Your Mission...Should you choose to accept it...

• Explain why plasmid-mediated resistance is both a healthcare facility and public ‘enemy number one’

• Conduct an inventory of your facility’s Infection Control and Prevention Super Hero weapons arsenal for supplies needed to prevent the transmission of plasmid-mediated resistant organisms

• Identify other Super Heroes to call/alert when a colistin resistant organism is identified

• Defend the people of Maine from plasmid-mediated resistant super bugs by working to operationalize antibiotic stewardship programs

Super Hero 101
Know the Enemy
Colistin Resistance in the News

“The superbug that doctors have been dreading just reached the U.S.”

- 05/2016: Pennsylvania
  - Urine culture, E. coli, no travel outside USA

- 11/2015: Plasmid mediated resistance first identified in E. coli, carried on the mcr-1 gene (China).

We are looking back and finding more...

- 05/2015: New York – saved GI sample found to carry mcr-1 gene

- Update: Total of 4 known/suspected isolates in USA under investigation
  - all in North East USA (3 E. coli, 1 Klebsiella)

Colistin use in Humans

- **1949:** First isolated in Japan from a flask of fermenting *Bacillus polymyxa var. colistinus*

- **1959:** Available for clinical use as antibiotic Polymyxin
  - Effective against Gram-negative bacilli

- **1970:** Stopped using colistin in humans due to toxicity (kidney and neurological damage, occasionally irreversible)

- **TODAY:** Used as a “last-resort” antibiotic for treatment of *Pseudomonas aeruginosa* cystic fibrosis patients; multi-drug resistant *Acinetobacter* sp.; intestinal infections; and *E. coli*, *Klebsiella* sp. and CRE infections
  - Resistance to polymyxins is generally less than 10%
Colistin use in Agriculture

- Used to treat and prevent *E. coli* diarrhea in piglets
- Used to treat and prevent *E. coli* and *Salmonella* sp. infections in veal calves and poultry
- USA: approved by FDA for use in animals, but not widely used
- UK: 5th most widely used antibiotic on farms
- UK: Colistin is one of only 4 antibiotics that can be added to drinking water of egg-laying hens - no requirements to observe withdrawal period before sale of eggs.
- China: 21% of *E.coli* samples in pigs resistant to colistin
- China: 15% of *E.coli* samples from meat resistant to colistin

As of January 2016:

As of July, 2016 in USA: ⚫ human/patient (2), ⚫ farm animal [pigs (2)]
Antibiotic Resistance

Intrinsic Resistance

- Inherited resistance

- Natural resistance from an attribute that protects the organism
  - For example:
    - *E. coli* is intrinsically resistant to vancomycin because the vancomycin molecule is too large to pass through the porin channels in its cell wall.
    - Gram positive bacteria have no porin channels and are thus intrinsically resistant to vancomycin.

- Infection Control concern = None
Acquired Resistance

- Non-inherited resistance
- A result of a change in genetic composition of a microorganism so that an antimicrobial agent that was once effective against the organism is no longer effective.
  - Acquires resistance through **internal** genetic change due to exposure to antibiotics
    - Resistance happens over several generations
    - Example: VISA
  - Acquires already resistant DNA from an **external** source
    - Immediate transfer of resistance genetics [Plasmid Mediated Resistance]
    - Example: VRSA [VRE shared genetics with MRSA]

- **Infection Control concern:**
  - Internal genetic change = Yes
    - Future generations carry genetic change and person to person transmission is possible through direct or indirect contact.
  - Plasmid Mediated Resistance = YES!
    - Public health threat too!
    - Immediate sharing of resistant DNA
    - Creates new resistant strains

Plasmid Mediated Resistance

- Plasmids move bacterial genes from one bacterial cell to another, this is known as horizontal gene transfer.

- Three types of plasmid-encoded antibiotic resistance
  - **Conjugative:** most common
    - Cell-to-cell DNA transfer
    - Gram negatives
  - **Transduction:** less common
    - DNA enclosed in a bacteriophage is transferred to another bacterium of the same species
    - Gram positives
  - **Transformation:** least clinical problem
    - Free DNA is picked up from environment from a cell belonging to a closely related or same strain
SH101: FINAL EXAM

• Why is plasmid-mediated resistance both a healthcare facility and public ‘enemy number one’?

PASSED!
Select a Mask!

Super Hero 202
Prepare your Defense
Think of The Incredibles

- Identify
- Isolate
- Inform

Infection Control

- **Step 1: Identify**
  - Can your laboratory identify these cases?
    - Colistin resistance cut-off: \( \geq 4 \text{ mg/L} \)
    - Is colistin even on your antibiotic sensitivity panel?
  
  - Do you have a protocol for lab to contact IP when a “value of healthcare importance” is identified?

  - Do you (the IP) have a method to identify cases in your facility?
    - If new pathogen: Review micro reports from last 6-12 months
    - If pathogen is already in Maine: consider point-prevalence study
Infection Control

**Step 2: Isolate**  (infected or colonized) --- follow CRE guidelines!

- ACH, LTACH, NHs (w/vent units):
  - Plasmid Mediated (PM) Resistance: **Contact Precautions**
  - Acquired Resistance: **Standard or Contact Precautions**
    - Do you see mostly non-PM resistance (Standard) or some PM resistance (Contact)?
    - Is organism fairly sensitive (Standard) or fairly resistant (Contact) to other drugs?
    - How good is facility Hand Hygiene and Environmental/Equipment Cleaning/Disinfection: Pretty Darn Good (Standard) or Could be Better (Contact)?
- NHs: (for all acquired resistance)
  - Resident is vent-dependent, incontinent of stool, has draining secretions/wounds that cannot be controlled, is dependent on staff for ADLs, HH a challenge: **Contact Precautions**
  - Resident able to perform HH, has contained stool and secretions, is not dependent on staff for ADLs: **Standard Precautions**.
    - Consider use of gown/gloves for bathing, assisting with toileting, changing of briefs, changing of wound dressing, manipulating indwelling devices.

Infection Control

**Step 3: Inform**

- System to communicate history of (or current) colonization or infection MDRO

- System for inter-facility communication at time of patient/resident transfers
Infection Prevention

• Tier 1 Prevention
  – Hand Hygiene
    • Monitor compliance/feedback?
  – Environmental Cleaning
    • Who owns cleaning?
    • Properly trained?
    • Contact Time?
    • Monitor compliance/feedback?
    • Frequency?
  – Antimicrobial Stewardship
  – Limit use of Indwelling Devices
  – Education
  – Patient/Resident Placement
    • In shared rooms, consider MDRO colonization/infection status

• Tier 2 Prevention
  – Look for Cases (a.k.a. Screening)
    • Point Prevalence Study
    • Active Surveillance Cultures for high-risk patients
      – if antibiotic routinely used
      – If cases identified in area (how many?)
    • Contacts/Epi-links (e.g. roommate) to plasmid-medicated resistant case
  – Chlorhexidine Bathing for high-risk patients/residents

The Colistin Resistance Super Bug has FRIENDS!
More Tools for the Utility Belt:

• CSTE Position Statement
  – That CDC, in collaboration with SHEA, APIC, and CSTE, develop guidance, by January 2018 for clear, standardized inter-facility communication to prevent the spread of MDROs and other communicable diseases across multiple healthcare settings, including recommended actions in relevant IC guidance documents for healthcare facilities, transporters, surveyors, and accreditation processes.

  – That CDC, SHEA, APIC develop clear guidance by January 2018 on transmission-based precautions for LTC facilities that address considerations for how to balance the need to contain the spread of microorganisms while respecting resident and patient rights not to be unduly confined to their rooms, including surveyor and accreditation processes.

• CSTE Board approved at national conference
• CDC accepts/declines by end of year (typically)

SH202: FINAL EXAM

What needs to be in your facility’s Infection Control and Prevention Super Hero weapons arsenal to prevent the transmission of plasmid-mediated resistant organisms?

EXCELLENT! Pick a Weapon!
Super Hero 303
Call for Reinforcements

You have identified this Super Bug in Maine...

“Who you gonna call?”
Super Bug Busters!

We NEVER cross the streams!

Maine CDC hotline: 1-800-821-5821
Available 24/7

Notifiable Condition?

YES!

Under the following rules...

- Any case of unusual illness of infectious cause
- Any cluster/outbreak of illness with potential public health significance
Laboratory Testing at State Public Health Lab

• All isolates with an MIC to colistin of 4µg/ml or higher should be tested for confirmation AND the presence of mcr-1.
  
  – Send specimens to state public health laboratory, they will forward specimen to federal CDC.
  
  – HETL is working towards offering PCR testing for mcr-1 in the future.

• It is not necessary to test Enterobacteriaceae with intrinsic colistin resistance (e.g., Proteus, Providencia, Morganella, and Serratia species)

Microbiome Study – Coming Soon!

• Colistin Resistance
• CRE
• VRE
• MRSA
• Maybe more!
SH303: FINAL EXAM

Who you gonna call when a colistin resistance organism is identified?

GREAT!
Choose a Super Power!

Super Hero 404
Join the Maine Justice League
Antimicrobial Stewardship!

Core Program Elements:
• Leadership Commitment
• Accountability
• Drug Expertise
• Action
• Tracking
• Reporting
• Education

Leadership Commitment...comes in many forms:

- Make a formal statement (in writing) that the facility supports efforts to improve and monitor antibiotic use. Shares with staff, patients/residents, and families.

- Includes stewardship-related duties in job description and annual performance review for medical director, clinical nurse leads and pharmacists.

- Ensures nursing staff and prescribing clinicians are aware of the facility’s expectations and are given sufficient time to contribute to stewardship activities.

- Creates a culture which promotes antibiotic stewardship (e.g. messaging, education, celebrating improvement).
Accountability

- Empower program leader(s) who will be responsible for program outcomes
  - Medical Director
  - Director of Nursing
  - Pharmacist

- Builds a support team:
  - Clinicians and Department Heads
  - Nurses
  - Infection Preventionists
  - Quality Improvement staff
  - Laboratory staff
  - Information Technology staff

Drug Expertise

- Formal training in Antimicrobial Stewardship benefits program leaders

  - Making a Difference in Infectious Disease (MAD-ID)
    - Antibiotic Stewardship course
    - [http://mad-id.org/antimicrobial-stewardship-programs/](http://mad-id.org/antimicrobial-stewardship-programs/)

  - Society for Infectious Disease Pharmacists
    - Antibiotic Stewardship Certification Program
    - [http://www.sidp.org/page-1442823](http://www.sidp.org/page-1442823)
Action

- Policies that support optimal antibiotic use
  - Document DOSE, DURATION, and INDICATION
  - Develop and implement facility specific treatment recommendations

- Interventions to improve antibiotic use
  - Antibiotic “Time-Out”
  - Prior Authorization
  - Prospective Audit and Feedback

And More Action

- Pharmacy-driven Interventions
  - Automatic changes from IV to PO antibiotic therapy
  - Dose adjustments
  - Dose optimization
  - Automatic alerts in situations where therapy might be unnecessarily duplicative
  - Time-sensitive automatic stop orders
  - Detection and prevention of antibiotic-related drug-drug interactions

- Infection and syndrome specific interventions
  - Community-acquired pneumonia – what’s the bug? Best drug? Right duration?
  - Urinary tract infections (UTIs) – does the patient/resident have symptoms?
  - Skin and soft tissue infections – what’s the bug? Best drug? Right duration?
  - Empiric coverage of MRSA infections – did the culture come back MRSA?
  - C. diff infections – stop unnecessary antibiotics on C. diff patients/residents!
  - Treatment of culture proven invasive infections - is the culture positive?
Tracking (monitoring antibiotic prescribing)

- Antibiotic use process measures
  - Track how and why antibiotics prescribed

- Antibiotic use measures
  - Track how often and how many antibiotics are prescribed
    - DOT = Days of Therapy  [NHSN Antibiotic Use (AU) Module tracks DOT]
    - DDD = Defined Daily Dose

- Outcome measures
  - Track adverse outcomes and costs from antibiotics
    - Facility onset C. diff x antibiotic usage

Reporting

- Share the TRACKING information with key stakeholders and staff!
**Education**

- Regular updates for
  - Antibiotic prescribing
  - Antibiotic resistance
  - Infectious disease management

- Many methods
  - Didactic presentations (formal or informal)
  - Posters
  - Flyers
  - Newsletters
  - Electronic communications (e.g. email)
  - Review of de-identified cases with providers
  - Web-based education resources

*Education + Interventions + Outcomes = Most Effective Method*

**AMS in Agriculture**

- Did you know?
  - Up to 70% of antibiotics sold in the USA are used in livestock and poultry
    - Primarily as prevention therapy and to grow animals fatter, faster
  - Agriculture usage has increased 23% in the last 5 years

- The Battle is On!
  - IDSA fighting to stop the use of non-judicious antibiotic use in animals, plants and marine environments – particularly drugs needed in healthcare
  - FDA, USDA, and CDC asked to develop metrics for tracking antimicrobial use in animal agriculture and companion animal practice
  - States are passing laws to prevent use of antibiotics in animal feed
  - Public Health Departments asked to work on state stewardship strategies between human and veterinary medicine and animal agriculture
SH404: FINAL EXAM

Name one element of an Antibiotic Stewardship Program that you can actively support.

ABSOLUTELY!
Make an appointment with Edna for your Super Suit!

GRADUATION!

You did it!
Now you are better prepared to join the fight against the Colistin Resistant Super Bug!
Questions?

Rita Owsiak MS, MT(ASCP), CIC
Healthcare Associated Infections Coordinator
Rita.Owsiak@maine.gov
Phone: 207-287-6028