Multidrug-Resistant Organisms – Threats and Prevention Strategies

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Presenter

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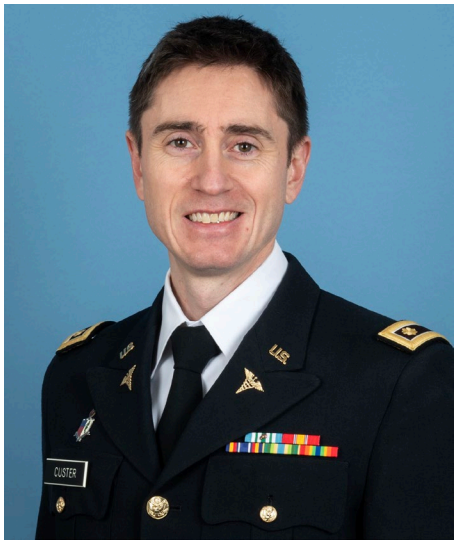

Army Maj. Benjamin Custer is an Infectious Diseases attending at Walter Reed National Military Medical Center (WRNMMC), an Assistant Professor of Medicine at the Uniformed Services University of the Health Sciences (USUHS), and currently serves as the Clinical Chair of the Infection Prevention and Control Committee (IPC) and co-chair of the Sepsis Committee at WRNMMC.

In his IPC role, he has enjoyed the dynamic challenges related to mpox, avian influenza, *C. difficile*, *Candida auris* and other MDROs, and most recently, measles. His research activities are primarily in the field of HIV, and he has the privilege of teaching medical staff and trainees on a variety of infectious diseases topics, while constantly learning from his colleagues.

He grew up enjoying the mountains in Colorado Springs, CO, where he completed his bachelor's in biochemistry at Colorado College in 2006. During his undergraduate time, he spent over a year in Taiwan, and after graduating, he spent more than five years in China. During that time, he taught himself Mandarin (with the patience and help of many native speakers) while working as a high school probability, statistics, and calculus teacher, and later as the conference coordinator for an international health conference.

In keeping with his original life plan, he finally applied to medical school in 2012 and matriculated as a Second Lieutenant in the Army at USUHS in 2013. Always interested in infectious diseases, he completed an Internal Medicine residency at WRNMMC and continued with an Infectious Diseases fellowship, culminating with a Master of Public Health and Tropical Medicine at USUHS, from which he graduated in June 2023.

Disclosures

- MAJ Benjamin Custer has no relevant financial or non-financial relationships to disclose relating to the content of this activity.
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Learning Objectives

At the end of this presentation, participants will be able to:

1. Define multidrug-resistant (MDR) bacteria and its growing threat to healthcare.
2. Explain the mechanisms by which bacteria develop resistance to antibiotics.
3. Identify common MDR pathogens and associated healthcare-associated infections (HAIs).
4. Discuss the factors contributing to the emergence of MDR bacteria.
5. Describe strategies for preventing the spread of MDR bacteria in healthcare settings, including Infection Prevention and Control (IPC) and antibiotic/diagnostic stewardship efforts.
6. Evaluate how the Multidrug-Resistant Organism Repository and Surveillance Network's (MRSN's) analysis and tools can collaborate with local Infection Prevention and Controls (IPCs) for MDR control.

Evolution of Antimicrobial Resistance (AMR)

1 min 54 sec

https://www.youtube.com/watch?v=pIVk4NVIUh8

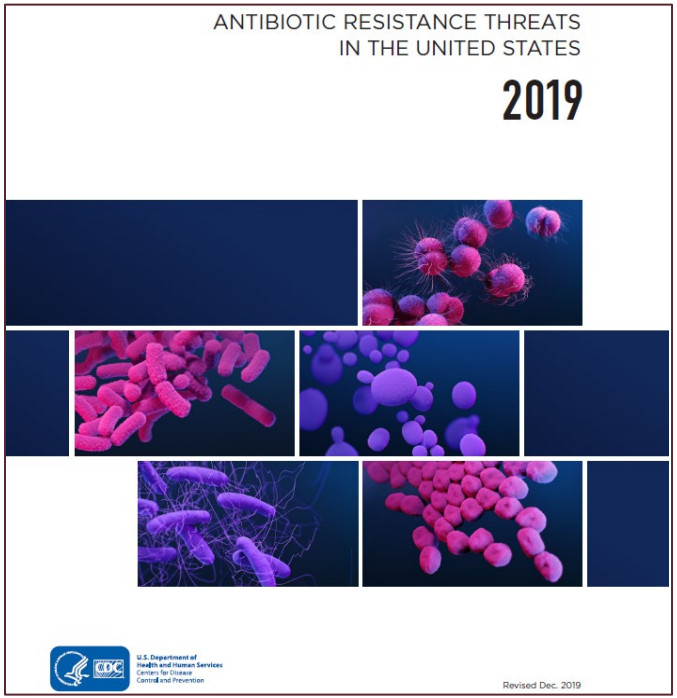
Alexander Fleming- Penicillin 1928

- In 1945, as the antibiotic was entering commercial use:
  - The “public will demand” the new miracle drug and thus would begin “an era … of abuses.”

(https://time.graphics/pt/event/755380, n.d.)

Penicillin Saves a Life

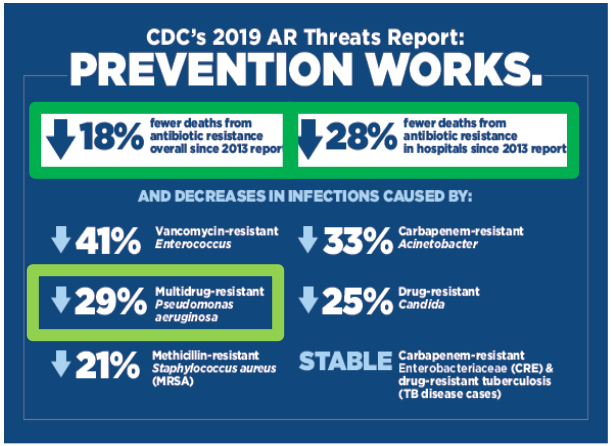
- In March 1942, Mrs. Anne Miller of New Haven, Connecticut, was near death from invasive Streptococcus following a miscarriage. Desperate to save her, doctors administered an experimental drug: penicillin, which Alexander Fleming discovered 14 years earlier.
- At the time, it had saved four of six patients who had taken it in England, but it had never been tried in the United States. Miller received her first dose at 3:30 p.m. on a Saturday. The next morning her temperature, which had hovered between 103 and 106.5 degrees, dropped to normal for the first time in four weeks.
- By Monday her appetite returned, and she had eaten four full meals. She lived to be 90 years old.
- Unlike the bacteria that threatened Mrs. Miller, bacteria today may be resistant to many or all of the antibiotics designed to kill them.



(CDC, 2019)

Six of the 18 Most Alarming Antibiotic Resistant Threats

The Threat of Antibiotic Resistance in the US



You!

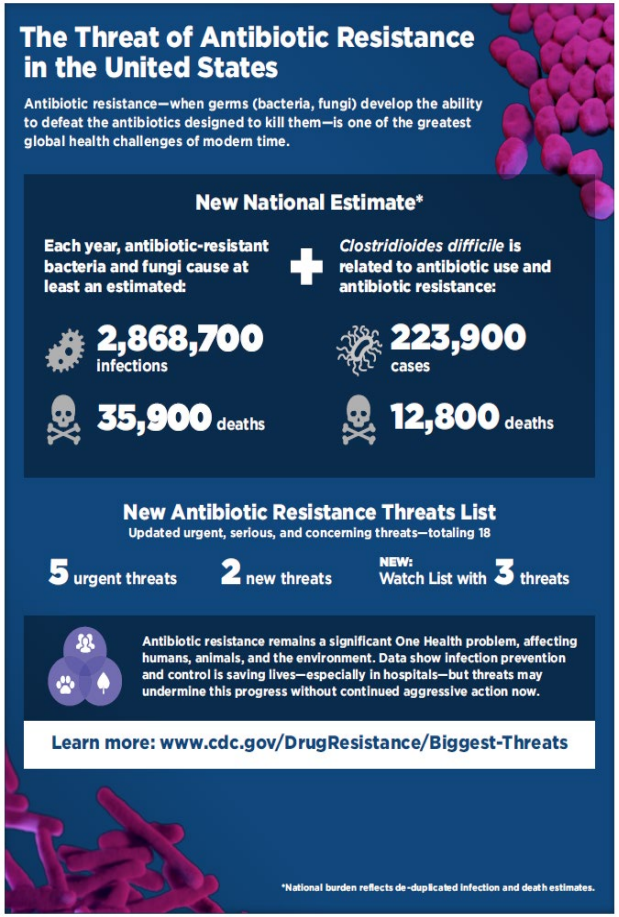
CDC strategies that work in healthcare:

- Preventing device- and procedure-related infections, such as from urinary catheters or central lines
- Stopping the spread of resistant germs within and between healthcare facilities
- Containing emerging threats through early detection and aggressive response
- Tracking and improving appropriate antibiotic use
- Infection prevention and control in non-hospital settings, such as long-term care facilities

CDC strategies that work in communities:

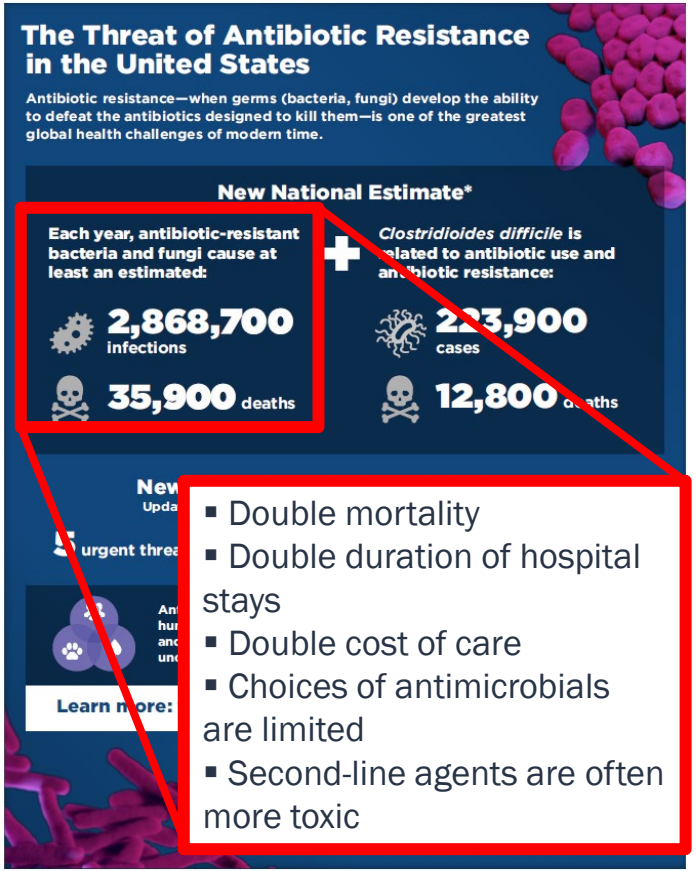
- Widespread use of vaccines to prevent infections and spread
- Routine tuberculosis and gonorrhea screening for at-risk groups and prompt treatment
- Using safer sex practices (e.g., condoms)
- Safe food handling and preparation
- Improving antibiotic use everywhere

(AR) antibiotic resistance



(CDC, 2019)

New National Estimate



- Double mortality
- Double duration of hospital stays
- Double cost of care
- Choices of antimicrobials are limited
- Second-line agents are often more toxic

(CDC, 2019)

COVID-19 Impacts

18 Antimicrobial-Resistant Bacteria and Fungi

Threat Estimates

The following table summarizes the latest national death and infection estimates for 18 antimicrobial-resistant bacteria and fungi. The pathogens are listed in three categories—urgent, serious, and concerning—based on level of concern to human health identified in 2019.

Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
Carbapenem-resistant *Acinetobacter*	8,500 cases 700 deaths	6,300 cases 500 deaths	6,000 cases 500 deaths	Stable*	7,500 cases 700 deaths **Overall: 35% Increase*** **Hospital-onset: 78% Increase***
Antifungal-resistant *Candida auris*	171 clinical cases†	329 clinical cases	466 clinical cases	▲ Increase	754 cases **Overall: 60% Increase**
Carbapenem-resistant Enterobacterales	13,100 cases 1,100 deaths	10,300 cases 900 deaths	11,900 cases 1,000 deaths	▼ Decrease*	12,700 cases 1,100 deaths Overall: Stable* **Hospital-onset: 35% Increase***
ESBL-producing Enterobacterales	197,400 cases 9,100 deaths	174,100 cases 8,100 deaths	194,400 cases 9,000 deaths	▲ Increase*	197,500 cases 9,300 deaths **Overall: 10% Increase*** **Hospital-onset: 32% Increase***
Multidrug-resistant *Pseudomonas aeruginosa*	32,600 cases 2,700 deaths	29,500 cases 2,500 deaths	28,200 cases 2,400 deaths	▼ Decrease*	28,800 cases 2,500 deaths Overall: Stable* **Hospital-onset: 32% Increase***

(https://www.cdc.gov/drugresistance/, n.d.)

Polling Question #1

Based on your personal experience, which MDROs are most frequently encountered or most problematic? Check all that apply.

a. MRSA
b. VRE
c. ESBL Enterobacterales
d. Carbapenem-resistant organisms
e. Multidrug-resistant Pseudomonas aeruginosa
f. Carbapenem-resistant Acinetobacter baumannii (CRAB)
g. Candida auris
h. Clostridioides difficile

MDR Organisms

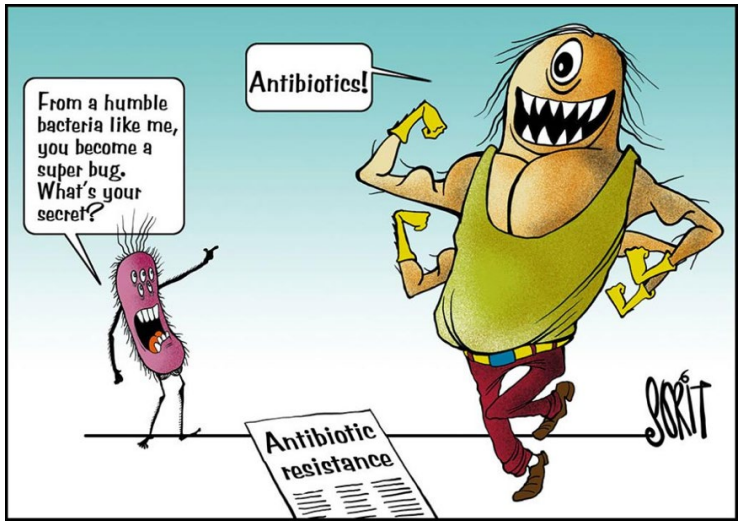
- **ESKAPE+** bacteria
  - *Enterococcus faecium (vancomycin-resistant)*
  - *Staphylococcus aureus (methicillin-resistant)*
  - *Klebsiella pneumoniae*
  - *Acinetobacter spp*
  - *Pseudomonas aeruginosa*
  - *Enterobacter spp*, *Escherichia coli*
- *Candida* spp

→ **“MDR” definition:** Non-susceptible to ≥1 drug from ≥3 classes

→ **“MDR” definition:** Non-susceptible to ≥1 drug from ≥2 classes

(Arendrup, et.al. 2017)

Germs Fight Back: Resistance Mechanisms



(https://www.biologyonline.com/dictionary/pathogen, n.d.)
(https://loonylabs.org/2014/10/04/antibiotic-resistance/, n.d.)

Germs Fight Back: Resistance Mechanisms (1 of 6)

Natural Resistance

Always occurring in the bacteria

- **Intrinsic resistance:** Always expressed in the species
- **Induced resistance:** Genes naturally present in the bacteria but only expressed to resistance levels after exposure to an antibiotic

Acquired resistance

Genes/Genetic material that confers resistance can be transferred laterally

Examples of bacteria with intrinsic resistance

Organism	Intrinsic resistance
Bacteroides (anaerobes)	aminoglycosides, many β-lactams, quinolones
All gram positives	aztreonam
Enterococci	aminoglycosides, cephalosporins, lincosamides
Listeria monocytogenes	cephalosporins
All gram negatives	glycopeptides
Escherichia coli	macrolides
Klebsiella spp.	ampicillin
Serratia marcescens	macrolides
Pseudomonas aeruginosa	sulfonamides, ampicillin, 1st and 2nd generation cephalosporins, chloramphenicol, tetracycline
Stenotrophomonas maltophilia	aminoglycosides, β-lactams, carbapenems, quinolones
Acinetobacter spp.	ampicillin, glycopeptides

(Reygaert, 2018)

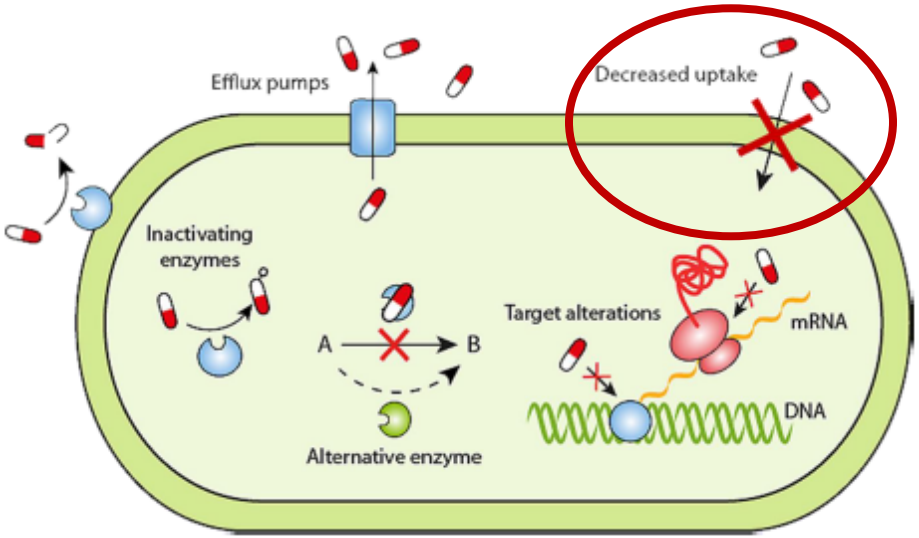
Polling Question #2

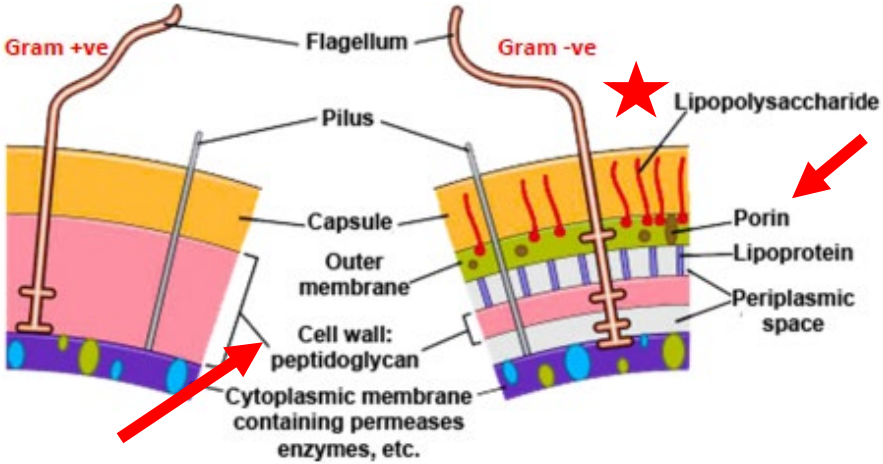
Microbes have multiple ways of resisting the effects of antimicrobials. Understanding these mechanisms helps to inform the selection of antimicrobials to overcome specific resistance mechanisms.

Name as many types/mechanisms of resistance as you can think of.

Germs Fight Back: Resistance Mechanisms (Cont. 2 of 6)

1) Decreased Uptake

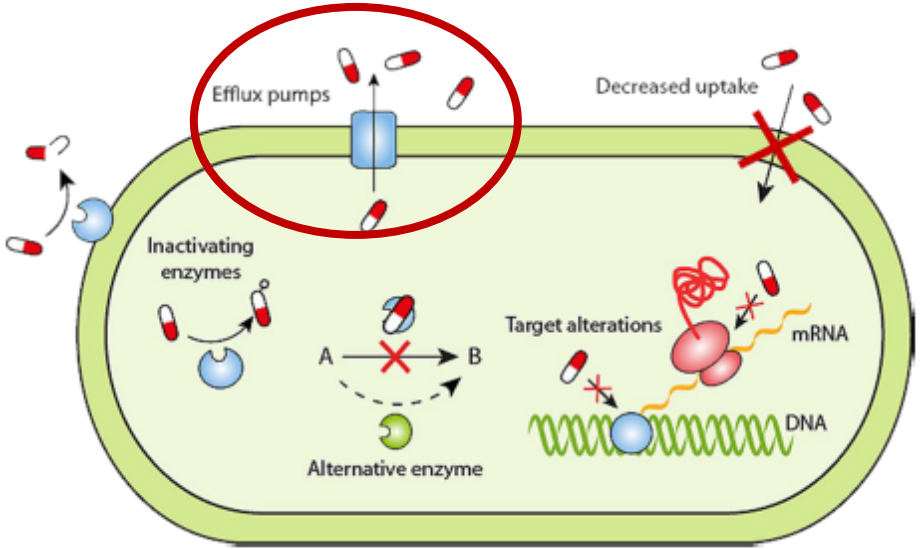


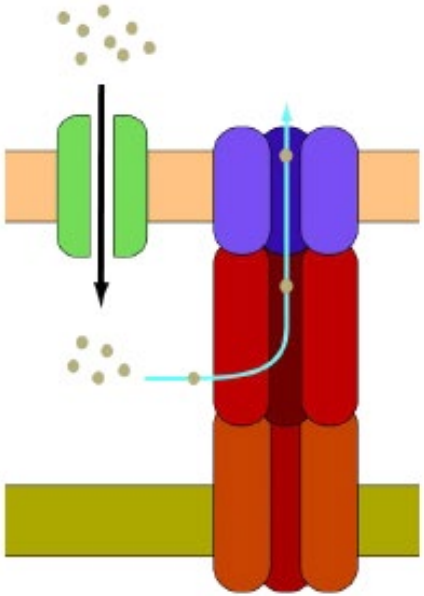


(Scott, 2017)

Germs Fight Back: Resistance Mechanisms (cont. 3 of 6)

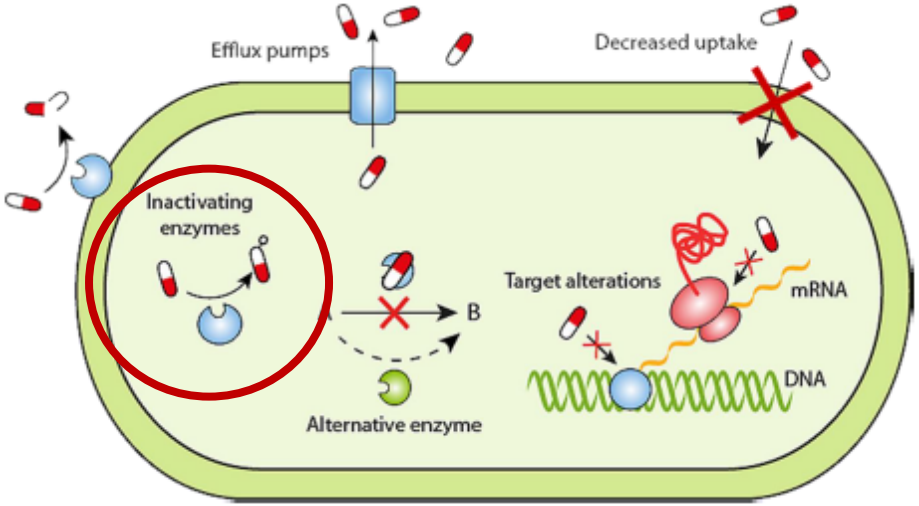
1) Decreased Uptake
2) **Efflux Pumps**



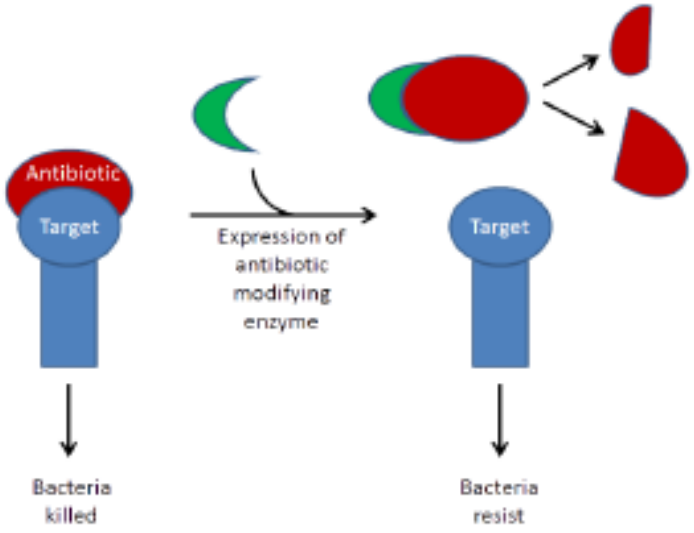


(Scott, 2017)

Germs Fight Back: Resistance Mechanisms (cont. 4 of 6)

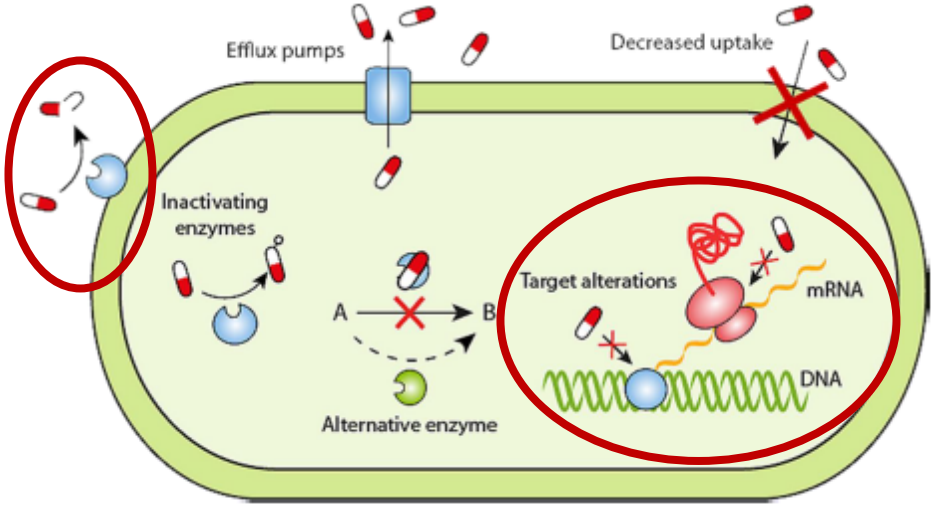


1) Decreased Uptake
2) Efflux Pumps
3) **Enzyme Inactivation**

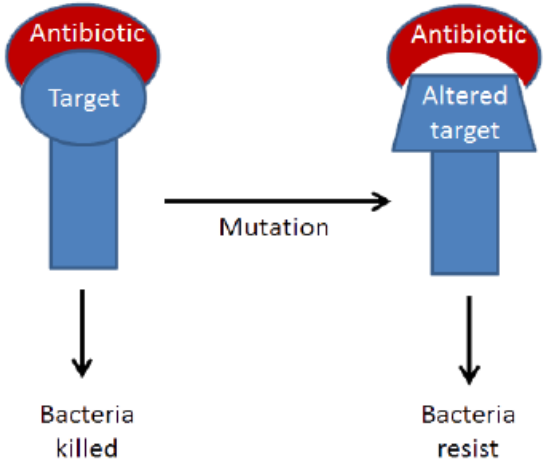


(Scott, 2017)

Germs Fight Back: Resistance Mechanisms (cont. 5 of 6)

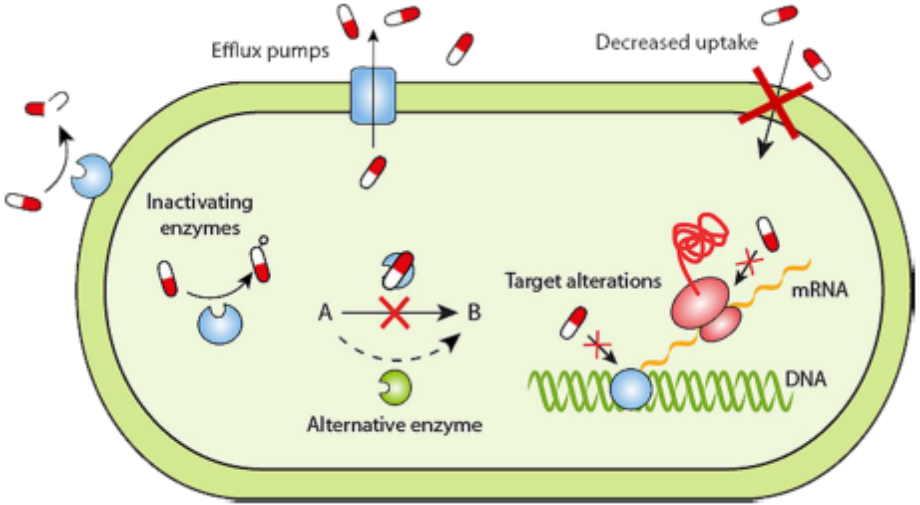


1) Decreased Uptake
2) Efflux Pumps
3) Enzyme Inactivation
4) **Mutation**

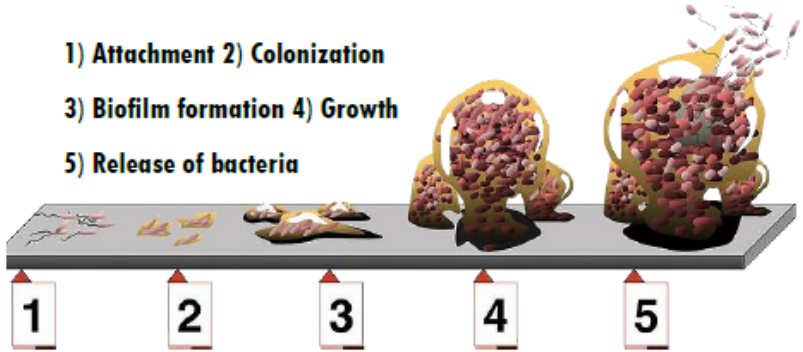


(Scott, 2017)

Germs Fight Back: Resistance Mechanisms (cont. 6 of 6)



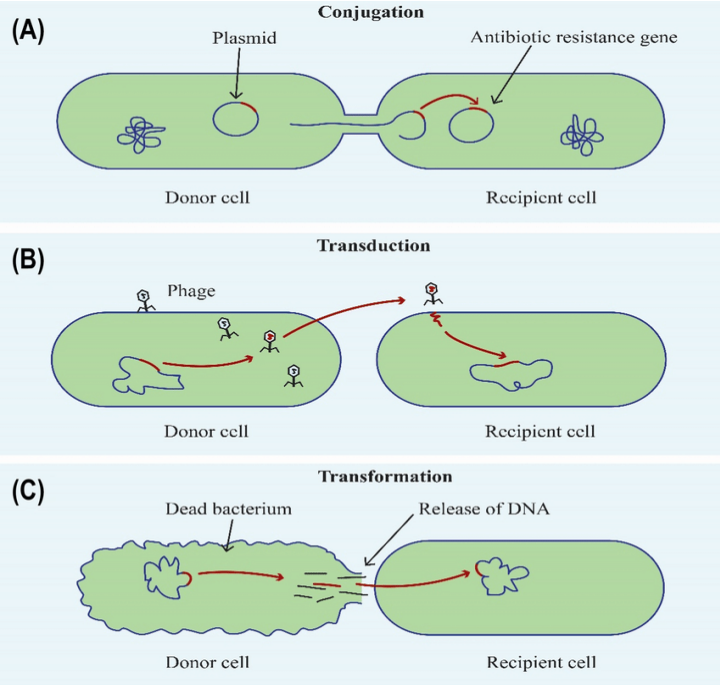
1) Decreased Uptake
2) Efflux Pumps
3) Enzyme Inactivation
4) Mutation
5) Biofilms = "Persistence" not "Resistance"



(Scott, 2017)

Passing Resistance Mechanisms

Imagine plasmids as tiny USB drives that bacteria can use to share important information (like AMR genes) with other bacteria by plugging themselves in



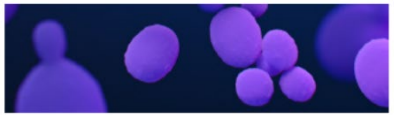
(Scott, 2017)
(Mutuku, 2022)

Urgent and Serious Threats

Urgent Threats

These germs are public health threats that require urgent and aggressive action:

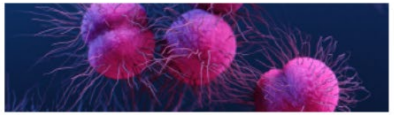
CARBAPENEM-RESISTANT
ACINETOBACTER



CANDIDA AURIS

CLOSTRIDIOIDES DIFFICILE

CARBAPENEM-RESISTANT
ENTEROBACTERIACEAE



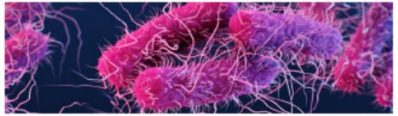
DRUG-RESISTANT
NEISSERIA GONORRHOEAE

Serious Threats

These germs are public health threats that require prompt and sustained action:

DRUG-RESISTANT
CAMPYLOBACTER

DRUG-RESISTANT
CANDIDA



ESBL-PRODUCING
ENTEROBACTERIACEAE

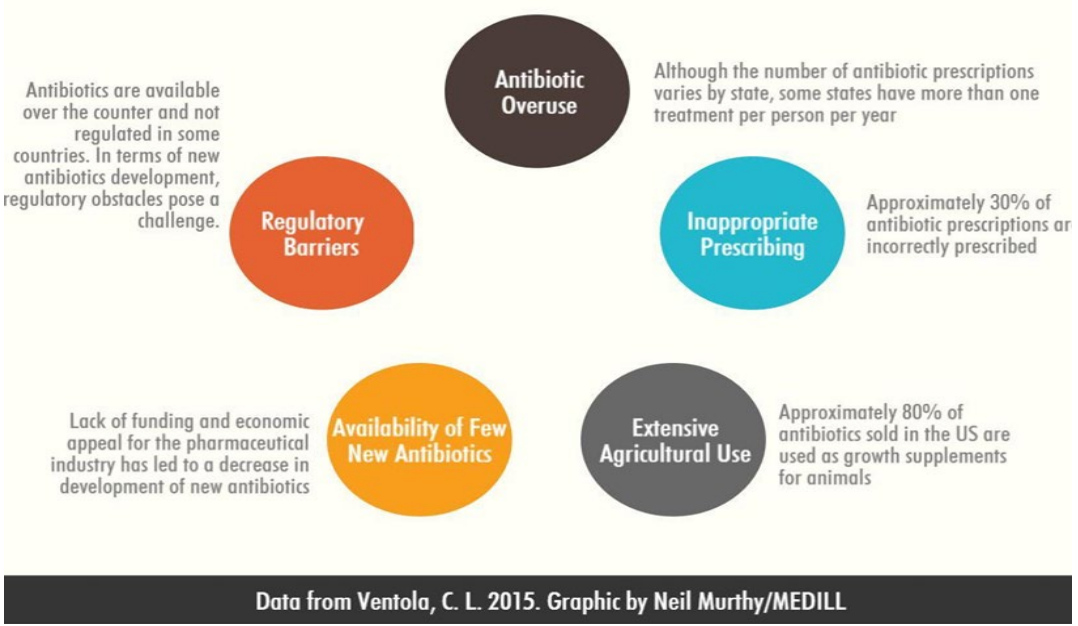
VANCOMYCIN-RESISTANT
ENTEROCOCCI

MULTIDRUG-RESISTANT
PSEUDOMONAS AERUGINOSA

(CDC, 2019)

Drivers of Resistance

- Causes of “the global resistome”:
  - Excessive use of antibiotics in animals (food, pets, aquatic) and humans
  - Antibiotics sold over-the-counter
  - Increased international travel
  - Poor sanitation/hygiene
  - Release of non-metabolized antibiotics or their residues into the environment through manure/feces
- It has been estimated that there are over 20,000 potential resistance genes present



Drivers of Resistance, continued

Antibiotics sold over-the-counter
Poor antibiotic stewardship

Poor infection control / sanitation / hygiene

Weak AMR surveillance systems

(https://www.linkedin.com/posts/dr-cary-adams-4a942737_international-dialogue-on-sustainable-financing-activity-7206259512947658752-Y8L0, 2024)
https://healthcare-in-europe.com/en/news/who-updates-list-of-essential-medicines-diagnostics.html, 2019)

International Travel Contributes to Antimicrobial Resistance Dissemination

- 1,847 travelers were MDR organism (MDRO)-negative before travel and had available samples after return
- 633 (34.3%) acquired ESBL (+) (Enterobacterales) during international travel
- Highest number of acquisitions in those who travelled to southern Asia: 136 of 181 (**75.1%**, 95% CI 68.4–80.9)

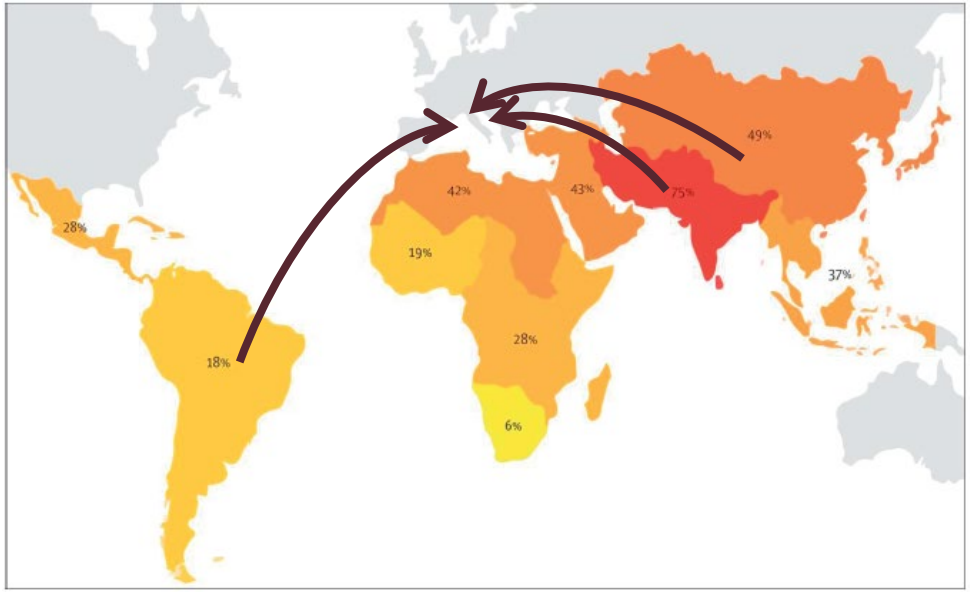
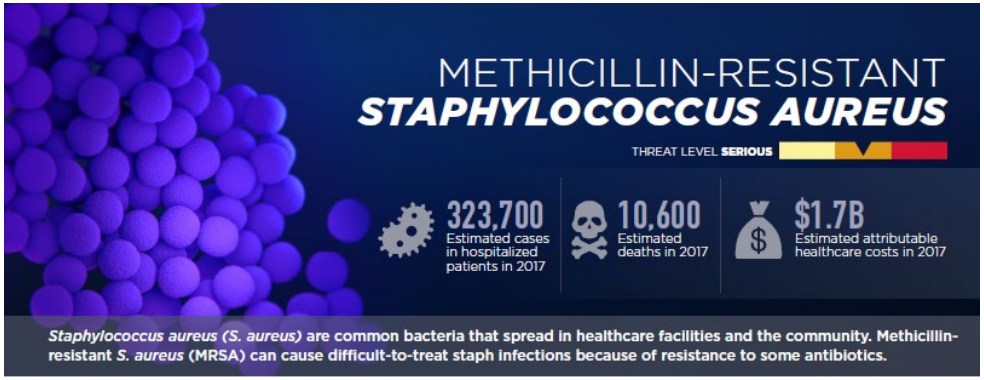


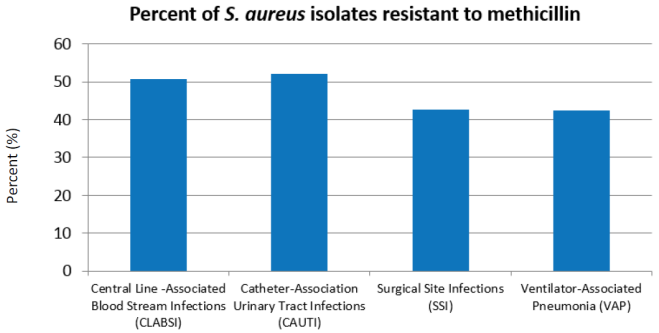
Figure 1. Percentages of travellers that acquired β-lactamase-producing Enterobacteriaceae per subregion, according to the United Nations geoscheme

(Arcilla, et.al. 2017)

Methicillin-Resistant Staphylococcus Aureus (MRSA)

- MRSA is one of the most important causes of hospital infections worldwide
- High-level resistance to methicillin is caused by the mecA gene, which encodes an alternative penicillin-binding protein (PBP 2a)
- Mortality among those with MRSA bacteremia ranges between 15-50%
- MRSA is the leading cause of healthcare-associated infections in neonatal intensive care units (NICUs)

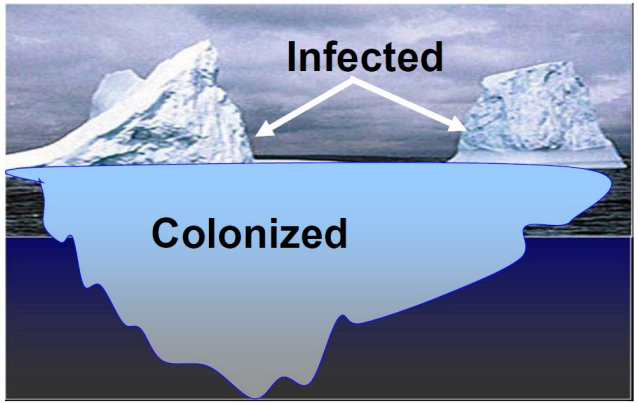


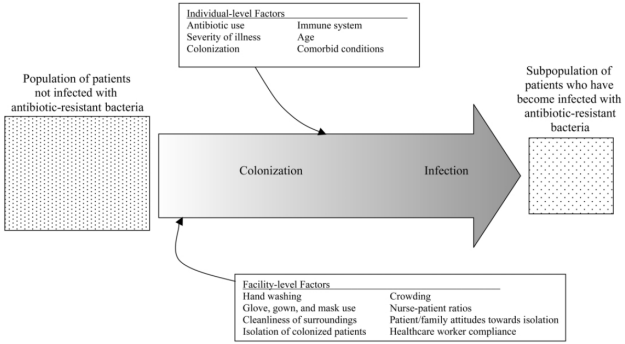


(Wiener, et al. 2016)

The Problem of Colonization

- Studies show that about 33% of the population are colonized with S. aureus
- Between 1 to 1.8% of the general population is colonized with MRSA
- MRSA rates among healthcare workers is 5-7%
- A national cohort study conducted in the United States indicated that MRSA colonization among community adults aged 40–85 is associated with a significantly increased mortality risk (hazard ratio, 1.75; 95% CI 1.12–2.73)





Factors that influence acquisition of nosocomial antibiotic-resistant bacterial infections (Hasanpour, et al. 2023)

Routes of MRSA Transmission

- Most commonly transmitted to patients via contaminated hands of health care personnel
- Hospitalized patients may also acquire MRSA from contaminated environmental surfaces
- Community-associated MRSA is commonly transmitted by direct contact with a colonized or infected individual

MRSA INFECTIONS CAN BE PREVENTED

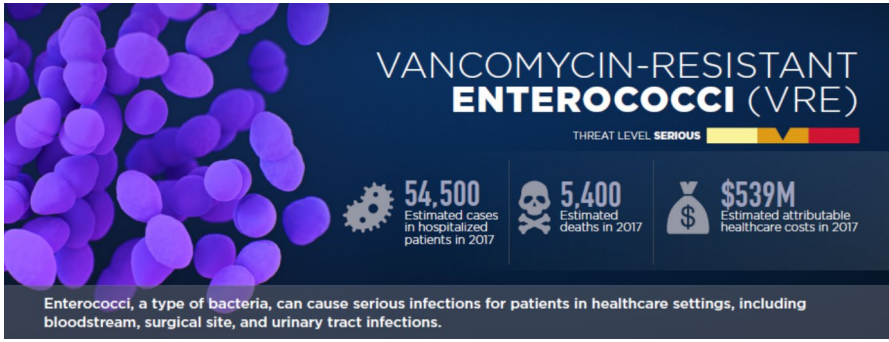
MRSA infections are preventable and many lives have been saved through effective infection control interventions. Veterans Affairs (VA) medical centers reduced rates of MRSA by 55% between 2005 and 2017. This success was driven by the implementation of CDC-recommended interventions at 153 VA hospitals across the country. The VA took steps to prevent the spread of MRSA and device- and procedure-associated infections. This included screening all patients for MRSA on admission, tracking MRSA infections, using Contact Precautions (such as gloves and gowns) for people with MRSA, and increasing the emphasis on hand hygiene.

(SHEA., 2023)

Essential practices	
1	Implement a MRSA monitoring program. (Quality of evidence: LOW)
2	Conduct a MRSA risk assessment. (Quality of evidence: LOW)
3	Promote compliance with the CDC or WHO hand hygiene recommendations. (Quality of evidence: MODERATE)
4	Use contact precautions for MRSA-colonized and MRSA-infected patients. A facility that chooses or has already chosen to modify the use of contact precautions for some or all of these patients should conduct a MRSA-specific risk assessment to evaluate the facility for transmission risks and to assess the effectiveness of other MRSA risk mitigation strategies (eg, hand hygiene, cleaning and disinfection of the environment, single occupancy patient rooms), and establish a process for ongoing monitoring, oversight, and risk assessment. (Quality of evidence: MODERATE)
5	Ensure cleaning and disinfection of equipment and the environment. (Quality of evidence: MODERATE)
6	Implement a laboratory-based alert system that notifies HCP of new MRSA-colonized or MRSA-infected patients in a timely manner. (Quality of evidence: LOW)
7	Implement an alert system that identifies readmitted or transferred MRSA-colonized or MRSA-infected patients. (Quality of evidence: LOW)
8	Provide MRSA data and outcome measures to key stakeholders, including senior leadership, physicians, nursing staff, and others. (Quality of evidence: LOW)
9	Educate healthcare personnel about MRSA. (Quality of evidence: LOW)
10	Educate patients and families about MRSA. (Quality of evidence: LOW)
11	Implement an antimicrobial stewardship program. (Quality of evidence: LOW)
Additional approaches	
Active surveillance testing (AST)	
1	Implement a MRSA AST program for select patient populations as part of a multifaceted strategy to control and prevent MRSA. (Quality of evidence: MODERATE). Note: Specific populations may have different evidence ratings.
2	Active surveillance for MRSA in conjunction with decolonization can be performed in targeted populations prior to surgery to prevent post-surgical MRSA infection. (Quality of evidence: MODERATE)
3	Active surveillance with contact precautions is inferior to universal decolonization for reduction of MRSA clinical isolates in adult ICUs. (Quality of evidence: HIGH)
4	Hospital-wide active surveillance for MRSA can be used in conjunction with contact precautions to reduce the incidence of MRSA infection. (Quality of evidence: MODERATE)
5	Active surveillance can be performed in the setting of a MRSA outbreak or evidence of ongoing transmission of MRSA within a unit as part of a multifaceted strategy to halt transmission. (Quality of evidence: MODERATE)
Screen healthcare personnel (HCP) for MRSA infection or colonization	
1	Screen HCP for MRSA infection or colonization if they are epidemiologically linked to a cluster of MRSA infections. (Quality of evidence: LOW)
MRSA decolonization therapy	
1	Use universal decolonization (daily CHG bathing plus 5 days of nasal decolonization) for all patients in adult ICUs to reduce endemic MRSA clinical cultures. (Quality of evidence: HIGH)
2	Perform preoperative nares screening with targeted use of CHG and nasal decolonization in MRSA carriers to reduce MRSA SSI, in surgical procedures involving implantation of hardware. (Quality of evidence: MODERATE)
3	Screen for MRSA and provide targeted decolonization with CHG bathing and nasal decolonization to MRSA carriers in surgical units to reduce postoperative MRSA inpatient infections. (Quality of evidence: MODERATE)
4	Provide CHG bathing plus nasal decolonization to known MRSA carriers outside the ICU with medical devices, specifically central lines, midline catheters, and lumbar drains, to reduce MRSA clinical cultures. (Quality of evidence: MODERATE)
5	Consider postdischarge decolonization of MRSA carriers to reduce postdischarge MRSA infection and readmission. (Quality of evidence: HIGH)
6	Neonatal ICUs should consider targeted or universal decolonization during times of above-average MRSA infection rates or targeted decolonization for patients at high risk of MRSA infection (eg, low birthweight, indwelling devices, or prior to high-risk surgeries). (Quality of evidence: MODERATE)
7	Burn units should consider targeted or universal decolonization during times of above average MRSA infection rates. (Quality of evidence: MODERATE)
8	Consider targeted or universal decolonization of hemodialysis patients. (Quality of evidence: MODERATE)
9	Decolonization should be strongly considered as part of a multimodal approach to control MRSA outbreaks. (Quality of evidence: MODERATE)
Universal use of gowns and gloves	
1	Use gowns and gloves when providing care to or entering the room of all adult ICU patients, regardless of MRSA colonization status. (Quality of evidence: MODERATE)
Unresolved issues	
1	Universal MRSA decolonization
2	Mupirocin and chlorhexidine resistance
3	MRSA-colonized HCP

Vancomycin-Resistant Enterococci (VRE)

- Enterococci are bacteria that normally live in the gut and environment
- Decreased susceptibility to penicillin, ampicillin, and aminoglycosides
- High-level resistance to most cephalosporins and all semi-synthetic penicillin, and clindamycin
- Risk factors for VRE infection include:
  - Stays in long-term care hospitals or intensive care units (ICUs)
  - Undergoing organ transplant or treatment for certain types of cancer
  - People with history of surgical procedures
  - Nearly all VRE infections happen in patients with healthcare exposures
- They rank 2nd in the USA, only after Staphylococci, in nosocomial infections, CLABSI, and hospital-associated endocarditis
- NHSN: 80% of *E. faecium* = VRE, 7% of *E. faecalis* = VRE



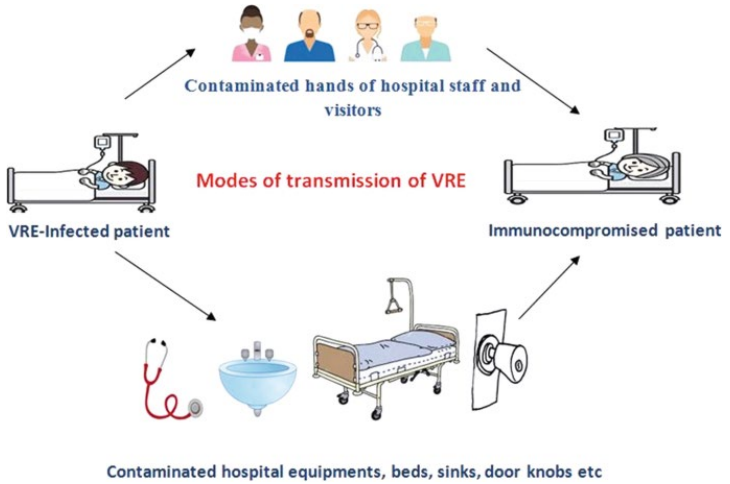
(Mina, et al. 2024)
(Davis, et al. 2020)

Routes of VRE Transmission

- VRE frequently colonize nursing facility residents
- Colonization associated with infection
  - 8% will develop an infection <30 days
- Direct transmission directly from person to person (gastrointestinal tract or skin)
- Transmission can occur indirectly from environment to person
  - VRE can survive for extended periods in the hospital environment: countertops, bedrails, telephone, stethoscope
  - 46% of healthcare workers who touched bedrails and bedside tables in the rooms of colonized patients contaminated their gloves
  - 11% rate of transmission to clean surfaces after contact with contaminated sites
  - ICU rectal thermometer-linked, burn intensive care unit electrocardiogram lead-linked outbreaks

Six Nursing Facilities in Southeastern Michigan

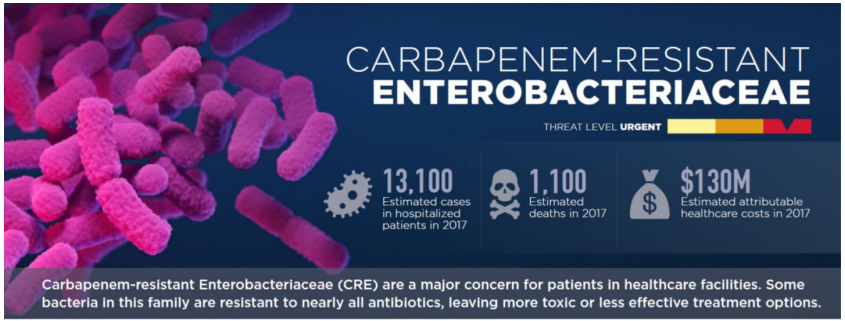
Epidemiological Measure	VR- *E. faecium*	VR- *E. faecalis*
Prevalence (n=651)	21.0%	11.7%



(Sharma et al., 2018)
(Davis et al., 2020)

Carbapenem-Resistant Enterobacteriaceae (CRE)

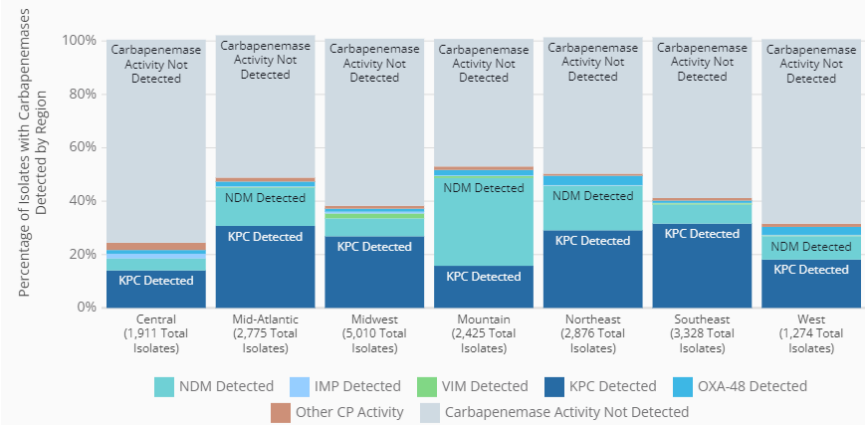
- Enterobacterales are Gram (-) bacteria and a normal part of the gut
  - Klebsiella pneumonia, Escherichia coli, Enterobacter spp.
- Carbapenem-resistant Enterobacterales (CRE) are resistant to many classes of antibiotics
- Enzymes called carbapenemases make β-lactam antibiotics ineffective
  - Klebsiella pneumoniae Carbapenemase (KPC)
  - New Delhi Metallo-beta-lactamase (NDM)
  - Verona Integron-encoded Metallo-beta-lactamase (VIM)
  - Imipenemase Metallo-beta-lactamase (IMP)
  - Oxacillinase-48-like beta-lactamase (OXA-48)
- Infections have high mortality rates (~40-50%) due to few therapeutic options available
- CRE is associated with clusters and outbreaks in healthcare settings
- Resistance can be transferred between patients and between different species of bacteria via plasmids



(Gall & Long,, 2020)

Routes of CRE Transmission

- Largely associated with nosocomial transmission
  - Ventilator-associated pneumonia, central line-associated bloodstream infection, catheter-associated urinary tract infection
- CRE are predominantly transmitted directly through person-to-person contact in healthcare settings
- Transmission can also occur indirectly through contact with environmental fomites (contaminated with stool, body fluids)
- Risk factors for infection and/or colonization:
  - Prolonged inpatient stays
  - Patients in long-term care facilities
  - Those who received medical care in CRE-endemic regions (colonization)
  - Intensive care unit (ICU)
  - Poor functional status
  - Underlying medical conditions
  - Receipt of antibiotics

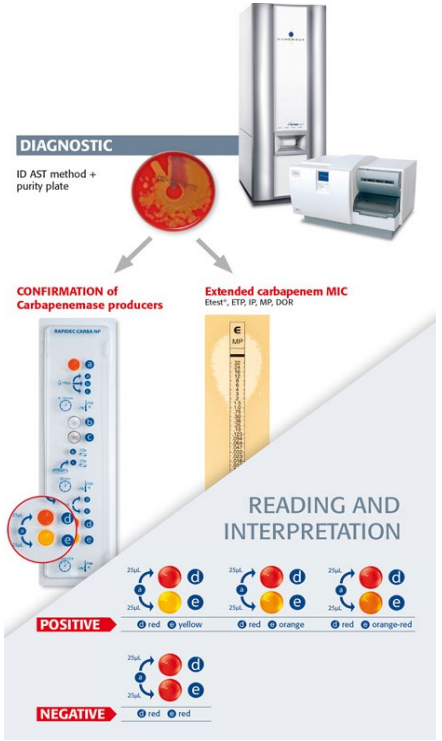


(McConville, et. al., 2017)
(Gall and Long, 2020)
(CDC, n.d.)

- Intestinal colonization is a risk factor for the development of systemic CRE infection (16.5%, higher in ICU patients)
- In endemic areas, colonization prevalence ranges from 3-7% or higher among ICU patients

Carbapenemases

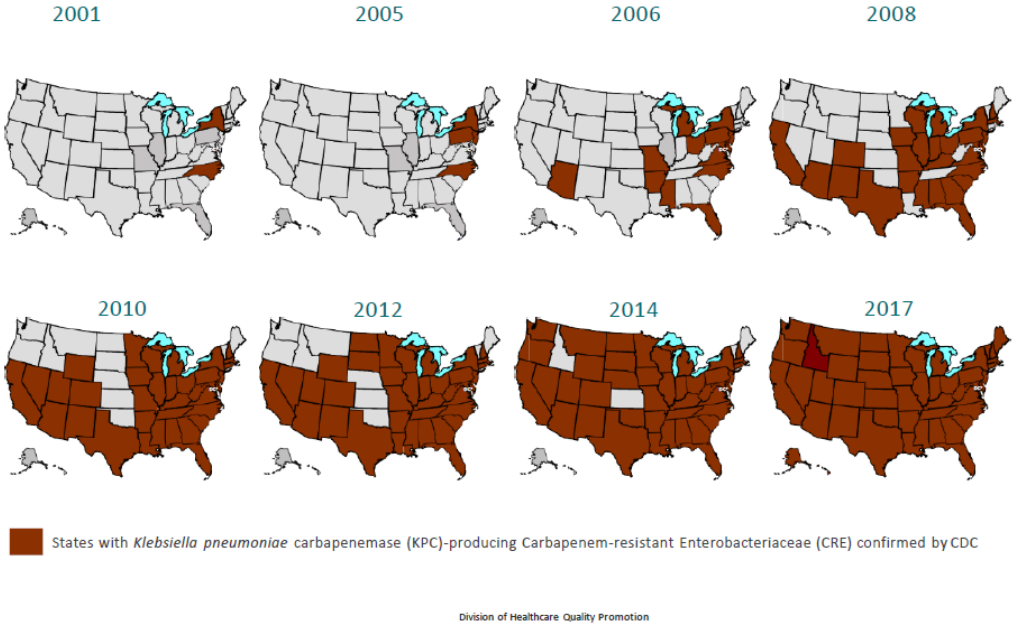
- Carbapenemases are enzymes found exclusively in Gram (-) that confer resistance to ALL β-lactams
  - Penicillins, Cephalosporins, Aztreonam, Carbapenems (imipenem, meropenem, ertapenem)
  - Molecular testing required to confirm presence/type
- Class A & D have a serine-based hydrolytic mechanism
  - Most common are KPC, oxacillin (OXA), and Guiana-Extended-Spectrum (GES) families
  - Ceftazidime-avibactam exhibits activity against them
- Class B are metallo-β-lactamases
  - Most common are NDM, VIM, IMP
  - Aztreonam is resistant to hydrolysis
- Plasmid and transposon mediated (mobile)



(https://www.biomerieux.com/nl/en/our-offer/clinical-products/rapidec-carba-np.html, n.d.)

National Spread of Klebsiella Pneumoniae Carbapenemase

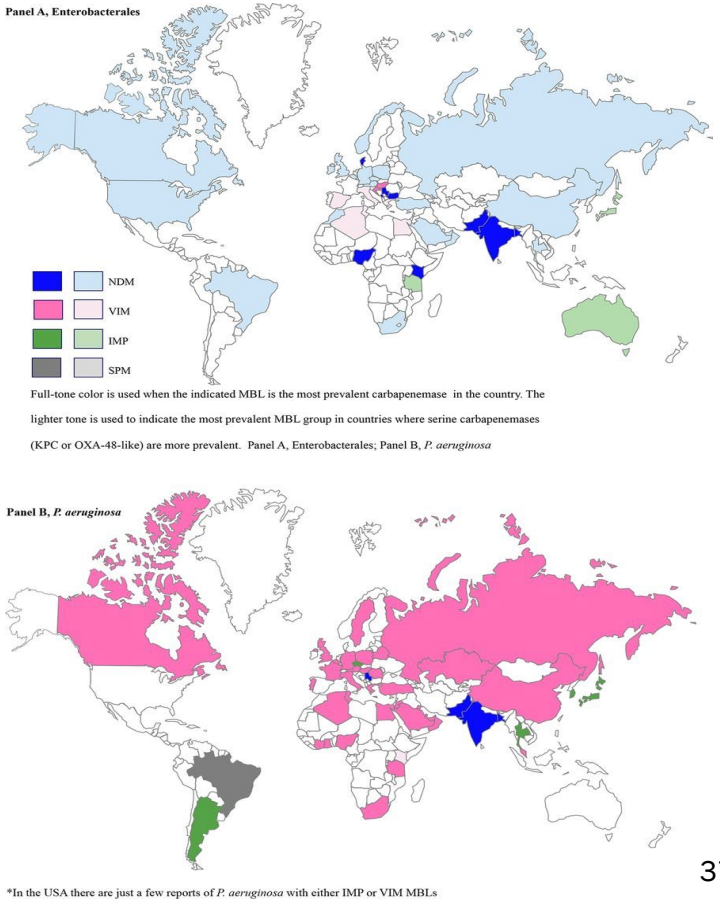
- *KPC* (+) bacteria found first in the U.S.
- Spread from two states in 2001 to 49 states, DC, and PR in 16 years
- KPC is the most commonly identified carbapenemase in the U.S.



Alex Kallen, CDC, 2018

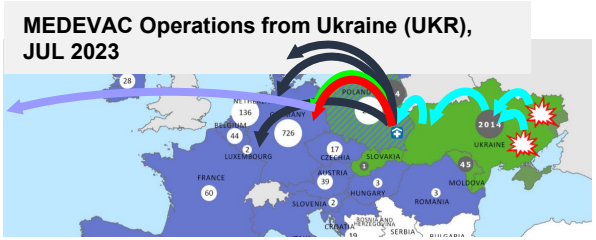
Metallo-β Lactamases (MBLs)

- MBLs hydrolyze all currently available β-lactam antibiotics except monobactams (e.g., aztreonam)
- Plasmid associated MBLs are most clinically important
  - **Imipenemase (IMP)**, discovered in the 1990's in Japan, now >85 sequence variants
  - **Verona integron-encoded metallo-β-lactamase (VIM)**, discovered in 1997 in PsA, now >69 variants
  - **New Delhi metallo-β-lactamase (NDM)**, discovered in 2008 in Klebsiella and *E. coli*, now >29 variants
- MBL producers generally resistant to multiple aminoglycosides, fluoroquinolones, and other agents
- Only available β-lactam combination available is ceftazidime-avibactam + aztreonam



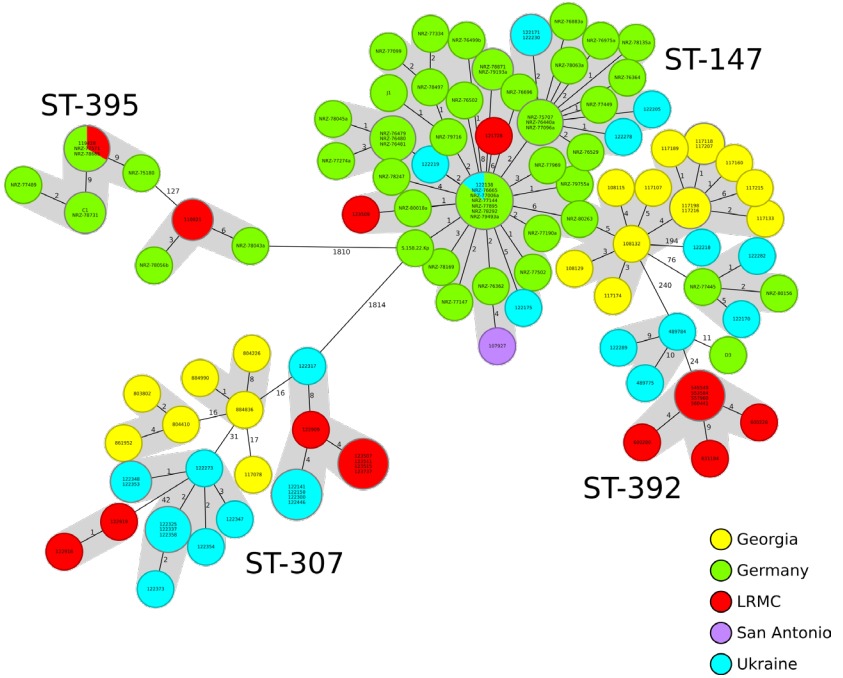
(https://www.researchgate.net/figure/Global-distribution-of-acquired-MBLs_fig2_343081192, n.d.)

Russo-Ukrainian War and MDRO Transmission Trends



https://erccportal.jrc.ec.europa.eu/ECHO-Products/Maps#/maps/4511

- Nearly genetically identical MDR K. pneumoniae detected among patients independently evacuated from UKR to German hospitals (including Landstuhl Regional Medical Center)
- These MDROs are closely related to isolates collected from Ukrainian hospitals in 2016-2017
- Isolates are generally more resistant than related bacteria from 2016-2017
  - *K. pneumoniae*, *P. aeruginosa* & *A. baumannii* evolve resistance through a combination of horizontally-acquired genes and chromosomal mutations that accelerate during treatment
  - Majority of these MDROs are resistant to ALL first-line antibiotics
- Emphasis on infection prevention & control is required to contain transmission within and outside of the military health system (MHS)

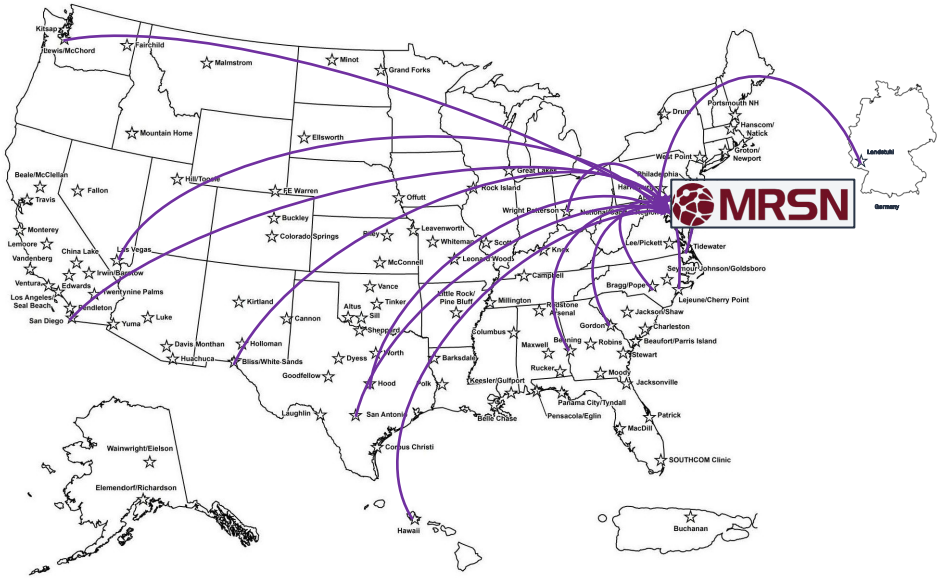


Klebsiella pneumoniae from patients throughout Europe (**including LRMC**), 2022-2023

Outbreak Detection in the Military Healthcare System

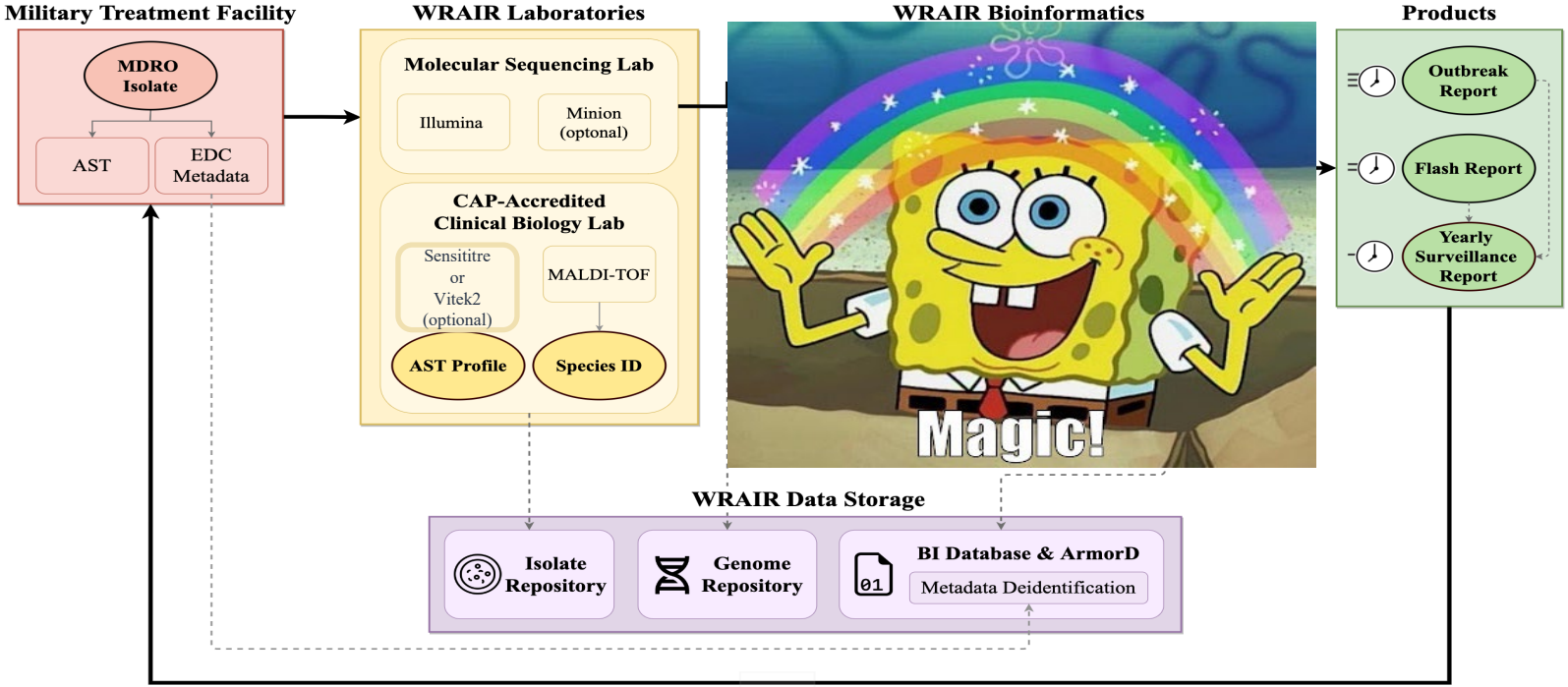
Detecting HAIs

- **MHS: world's largest network benefiting from real-time surveillance**
- Currently at 15 DoD and 1 VA hospitals
- State-of-the-art, automated, genome-based technology: ~15,000 isolates/year
- Biobank of >130K bacterial isolates
- 108 alerts of transmission events in 2023



(MRSN, n,d,)

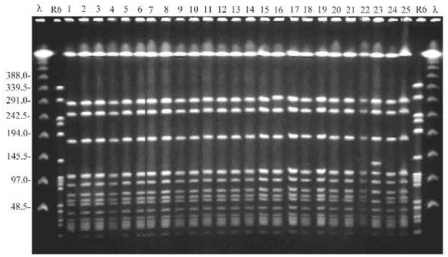
MRSN Infrastructure & Workflow



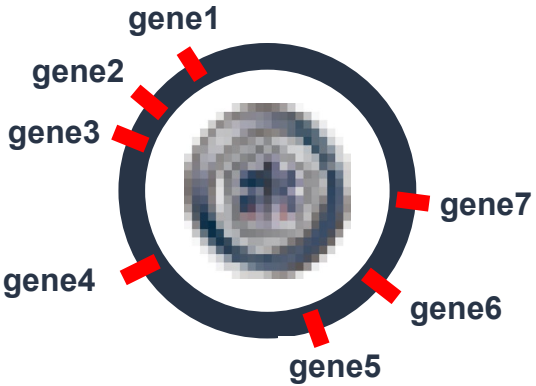
AST – Aspartate transferase
EDC – Electronic Data Capture
CAP – College of American Pathology
BI – Bioinformatics
WRAIR – Walter Reed Army Institute of Research

(https://medium.com/@kesiparker/productive-day-of-a-technical-writer-e63ec99cf008)

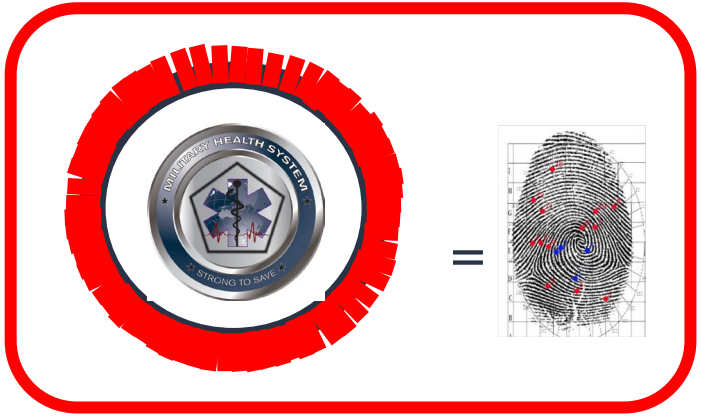
The Power of Whole Genome Sequencing



Pulse Field Gel Electrophoresis



Multilocus sequence typing (MLST) compares
7 housekeeping genes

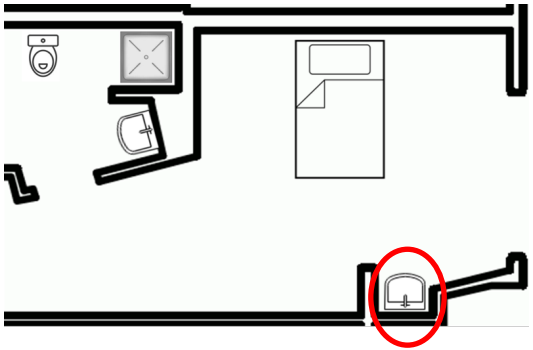


cgMLST compares
>3,000 core genes

Pulse Field Gel Electrophoresis counts “just the number of chapters” to determine relatedness,
Whole Genome Sequence compares all the words in a book

(Grkraj.org, 2025)

Sink Drains as Reservoirs of Bacterial Pathogens



(stock.adobe.com, n.d.)

Hunting for MDROs in One MHS facility

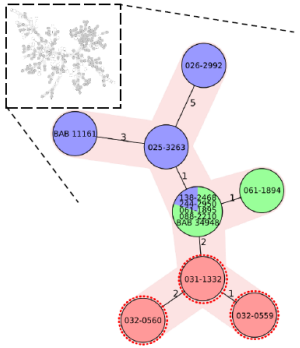
MRSN MULTIDRUG-RESISTANT ORGANISM REPOSITORY & SURVEILLANCE NETWORK

Possible Transmission Alert

WRAIR Walter Reed Army Institute of Research — Defense Health • Global Health

Report #24-007

Genome-based analysis[a] revealed that 12 *Pseudomonas aeruginosa* collected from 2 patients and various environmental sources at Army Medical Center were highly genetically related. The most recent patient isolate was collected on February 1st, 2024, and was closely related to isolates collected in throughout 2022.



Patient ID:
- Patient A
- Patient B
- Environment
- Most Recent

☐ First detection
☒ Protracted
Most Recent Isolate: 02/01/2024

95* Patients
339* Isolates
29* Wards

Notable Resistances[b]

☒ Aminoglycosides	☒ 3rd and 4th Cephalo.
☒ Carbapenems	☒ Fluoroquinolones

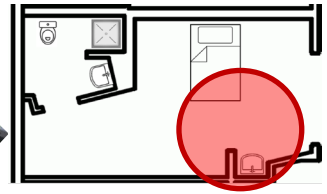
Notable Resistance genes[b]

☐ Carbapenemase ☐ ESBL ☐ Other

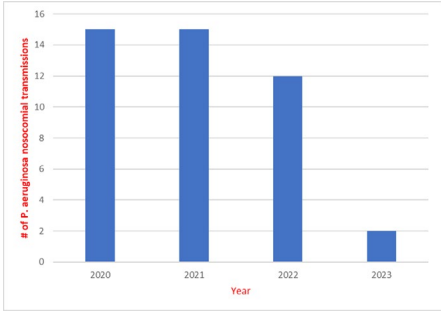
Isolates belonged to ST-621. SNP distances between patient A and the 9 isolates in this report range between 1-6 SNPs.
*This large outbreak of ST-621 *P. aeruginosa* has been the subject of extensive, past communications. The first epidemic isolate was collected on 05/19/2011. The full list of ST-621 isolates/patient is available upon request. Contamination from abiotic surfaces, sinks and/or plumbing is suspected.

(MRSN, 2024)

The "Splash Zone"



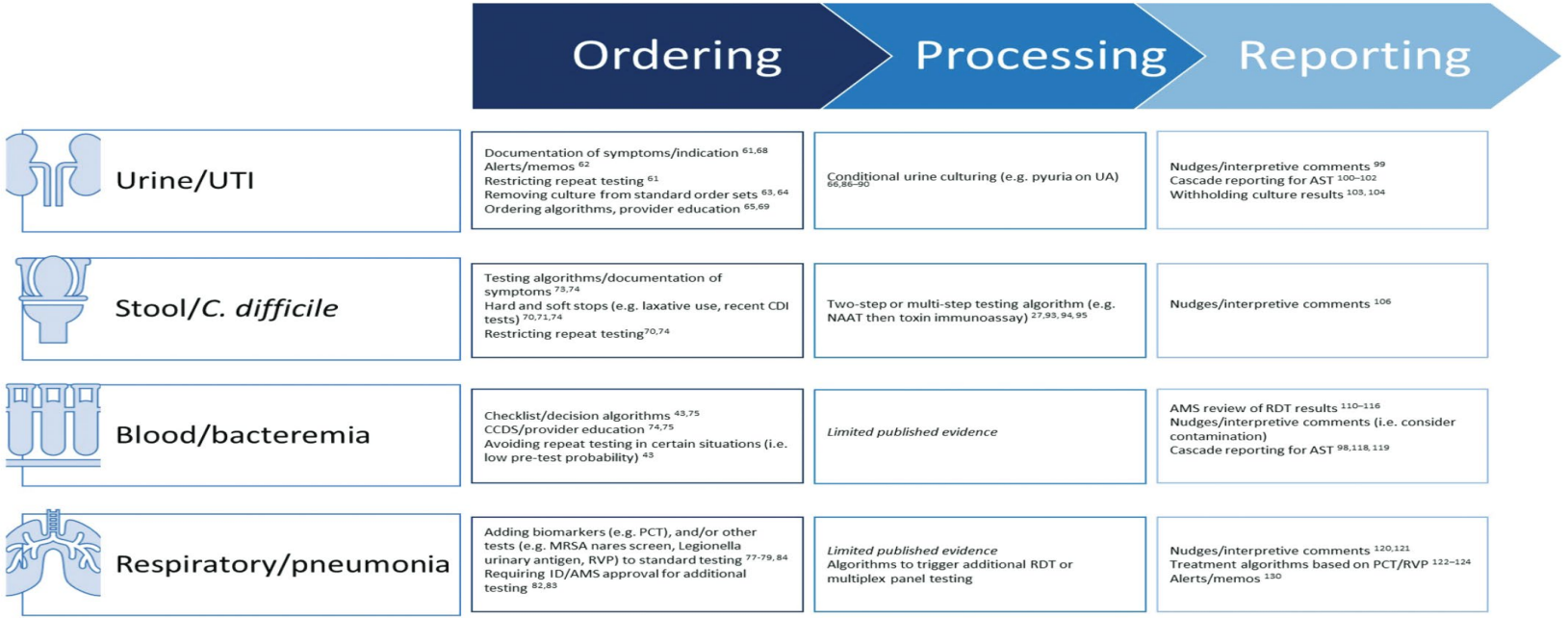
Drain Treatments with Foaming Bleach



Savings:
$1.24 - $1.72M at 1 hospital

Prevention – Diagnostic Stewardship

Figure 2. Evidence-based diagnostic stewardship examples impacting antimicrobial use.



AST, automated susceptibility testing; CCDS, computerized clinical decision support; CDI, *C. difficile* infection; ID/AMs, Infectious Diseases/Antimicrobial Stewardship; NAAT, Nucleic Acid Amplification Test; PCT, procalcitonin; RDT, rapid diagnostic testing; RVP, respiratory viral panel; UA, urinalysis; UTI, urinary tract infection

(Claeys & Johnson, 2023)

Polling Question #3

If you were to check urine cultures on young, healthy women with no signs or symptoms of UTI regularly for 6 months, what percent of them would have at least one positive urine culture? (single best answer)

a. 1-2%
b. 5-10%
c. 10-20%
d. 20-25%
e. 30-35%

Prevention – Diagnostic Stewardship, continued

- Colonization is common
  - Urine – 1.8 - 5.2% of premenopausal women
    - ✓ One study checked urine cultures of young, health American women weekly x4 and then monthly x6 and found asymptomatic bacteriuria (ASB) at least once in 22%
    - ✓ By age 80, 5 - 10% of men and 15 - 20% of women in community settings
    - ✓ 15 – 50% men and women in institutionalized settings
  - *C. difficile* – toxigenic *C. difficile* in 15% of 259 patients *without diarrhea* screened on admission
  - Lower extremity wound cultures – superficial swabs are only 49% sensitive 62% specific for infection
- The diagnostic cascade – once detected, often treated
  - A Veterans Affairs study of 2225 patients with bacteriuria found 68% with *asymptomatic* bacteriuria and *no systemic inflammatory response syndrome criteria* received antibiotics
  - In a study of 14,572 patients in Michigan, both antimicrobial stewardship and diagnostic stewardship strategies were used
    - ✓ Patients with ASB treated with antibiotics declined from 29.1% to 17.1% (aOR, 0.94 per quarter; 95% CI, 0.92-0.96)
    - ✓ Percentage of patients with a positive urine culture who had ASB declined from 34.1% to 22.5% (aOR, 0.95 per quarter; 95% CI, 0.93-0.97)
    - ✓ Percentage of patients with ASB who received antibiotics remained stable, from 82.0% to 76.3% (aOR, 0.97 per quarter; 95% CI, 0.94-1.01)

The Antimicrobial Stewardship Need

- Unnecessary antibiotics in ambulatory settings
  - 19% of all pediatric
    - ✓ 39% of pediatric pharyngitis
  - 36% of all adult
    - ✓ 44% of adult sinusitis
    - ✓ 72% of adult pharyngitis
  - 28% of all adult >64
    - ✓ 49% of adult >64 acute respiratory infections

(Hersh, King, Shapiro, Hicks & Fleming-Dutra, 2021)

	2014–2015		
Diagnosis	Estimated Annual No. of Antibiotic Prescriptions per 1000 Population[a] (95% CI)	Estimated Annual No. of Necessary Antibiotic Prescriptions per 1000 Population[c]	Percentage Unnecessary
Children aged 0–19 y			
All ARIs[d]	252 (215–290)	173	31%
Sinusitis	37 (25–49)	37	0%
Suppurative OM	85 (68–102)	85	0%
Pharyngitis	65 (48–82)	40	39%
Antibiotic-inappropriate ARIs[e]	54 (40–68)	0	100%
Pneumonia	11 (8–15)	11	0%
Other conditions[f]	157 (135–179)	157	0%
UTI	17 (10–25)	17	0%
Miscellaneous bacterial infections	17 (11–23)	17	0%
Remaining other conditions[g]	123 (104–141)	123	0%
Total[h]	409 (356–463)	330	19%
Adults aged 20–64 y			
All ARIs[d]	109 (87–131)	36	67%
Sinusitis	41 (30–53)	23	44%
Suppurative OM	6 (3–9)	5	17%
Pharyngitis	18 (11–24)	5	72%
Antibiotic-inappropriate ARIs[e]	41 (31–50)	0	100%
Pneumonia	3 (2–4)	3	0%
Other conditions[f]	272 (235–309)	207	24%
UTI	32 (25–40)	32	0%
Miscellaneous bacterial infections	12 (7–16)	12	0%
Remaining other conditions[g]	228 (197–259)	163	29%
Total[h]	381 (331–431)	243	36%
Adults aged ≥65 y			
All ARIs[d]	96 (76–115)	44	54%
Sinusitis	25 (18–33)	25	0%
Suppurative OM	…	0	…
Pharyngitis	…	…	…
Antibiotic-inappropriate ARIs[e]	52 (36–69)	0	100%
Pneumonia	9 (5–12)	9	0%
Other conditions[f]	453 (401–505)	411	9%
UTI	63 (44–83)	63	0%
Miscellaneous bacterial infections	…	0	…

Examples of Diagnostic Stewardship

- Asymptomatic bacteriuria
  - Don't culture without signs/symptoms of UTI
    - ✓ Frequency, urgency, dysuria, or suprapubic pain
- Diabetic foot wounds
  - Don't culture without signs of infection
  - Superficial wound swabs are not helpful and likely lead to antibiotic prescription regardless of whether infected or not

Clinical classification of infection, definitions	IWGDF/IDSA classification
No systemic or local symptoms or signs of infection	1/Uninfected
Infected: At least two of these items are present: • Local swelling or induration • Erythema >0.5 but <2 cm[b] around the wound • Local tenderness or pain • Local increased warmth • Purulent discharge	2/Mild
And, no other cause of an inflammatory response of the skin (e.g., trauma, gout, acute charcot neuro-arthropathy, fracture, thrombosis, or venous stasis)	

(Senneville et al. (2023)

*IWGDF - International Working Group on the Diabetic Foot
*IDSA - Infectious Diseases Society of America

Antibiotic Stewardship – Narrow, short, communicated

- Use guideline-directed empiric treatments
  - Upper respiratory infections (URIs)
    - ✓ Leverage polymerase chain reaction (PCR) panels and avoid antibiotics for viral syndromes
  - UTI first-line agents
    - ✓ Use clinical assessment to avoid treating asymptomatic bacteriuria
    - ✓ Avoid fluoroquinolone use
- Use guideline-directed durations
- Patient Communication
  - URIs
    - ✓ Antibiotics and viral illness
      - Ineffective
      - Potential side effects and resistance
    - ✓ Symptom management
    - ✓ Duration of illness
  - Non-pharmacologic interventions for lower extremity wounds and UTIs

Infection Prevention and Control

- Hand hygiene
- Personal protective equipment (PPE)
- Environmental cleaning and disinfection
- Communication of MDRO status

Polling Question #4

There isn't great data on hand hygiene compliance/utilization in outpatient settings, but based on a single study that used wireless monitoring of hand sanitizer dispensers, what do you think the compliance rate was for physicians using the dispensers at least once with each patient encounter?

a. 6%
b. 13%
c. 22%
d. 59%
e. 78%

IPC Strategies in Outpatient Setting

- Hand hygiene

Range of reported compliance estimates with WHO five moments for hand hygiene for physicians and nurses by overt observation ($N = 4$ studies)

Moment	Physician (%)	Nurse (%)
1	38.4–83.8	39.1–92.7
2	48.0–90.7	13.0–95.8
3	67.3–100	50.0–97.1
4	55.1–84.2	81.6–92.2
5	28.0–74.8	40.1–87.5

  - When – WHO's 5 Moments
  - How – alcohol (preferred)
    - ✓ Soap and water
    - ✓ Patient hand hygiene as well

(Bredin et al. 2022)

WHO Moments	CDC Indication
1	Immediately before touching a patient
2	Before performing an aseptic task (eg, placing an indwelling device or handling invasive medical devices)
3	After contact with blood, body fluids, or contaminated surfaces
4	After touching a patient
5	After touching the patient environment
	Before moving from work on a soiled body site to a clean body site on the same patient
	Immediately after glove removal
In addition, wash hands when visibly soiled, before eating, and after using the restroom.[a]	

Note. WHO, World Health Organization; CDC, US Centers for Disease Control and Prevention.
[a]Hand sanitizing with an alcohol-based hand sanitizer is preferred unless handwashing is specifically indicated, or during outbreaks of *C. difficile* or norovirus.

(Glowicz et al. 2023)

IPC Strategies in Outpatient Setting, continued

- Always use standard precautions
  - Especially appropriate PPE if expectation of possible exposure to an infectious material
  - Follow guidelines for isolation precautions (CDC)
- Environmental cleaning
  - Frequent disinfection of high-touch surfaces
  - Correct (Environmental Protection Agency (EPA)-registered and CDC-recommended) disinfectants
- Managing known MDRO colonized/infected
  - Contact precautions if warranted
  - Communicate MDRO status during transitions of care

Key Takeaways

1. The problem and impact of MDR bacteria is increasing globally and including in the U.S.
2. Bacteria are constantly developing resistance to antibiotics through various mechanisms, some of which can even be passed to other species
3. There are several key drivers of antibiotic resistance. In healthcare, antibiotic and diagnostic stewardship is critical
4. The 5 most common MDR pathogens in the U.S. are MRSA, VRE, ESBL-producing Enterobacterales, CRE, and MDR-Pseudomonas aeruginosa
5. Screening for MDROs among DoD beneficiaries at risk for acquiring/becoming colonized with MDROs in endemic regions OCONUS protects other at-risk patients
6. The MHS maintains the most advanced hospital outbreak detection network and tools available to any healthcare system in the world
7. Adherence to up-to-date infection prevention and control measures is essential to preventing the spread of MDR bacteria in the MHS

References (1 of 6)

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