Multi-Drug Resistant Organisms (MDROs)

Rabee Adwan MD.

Infectious Diseases Consultant.

Head of ID Unit and IPAC Committee- Al-Makassed Hospital- AlQuds

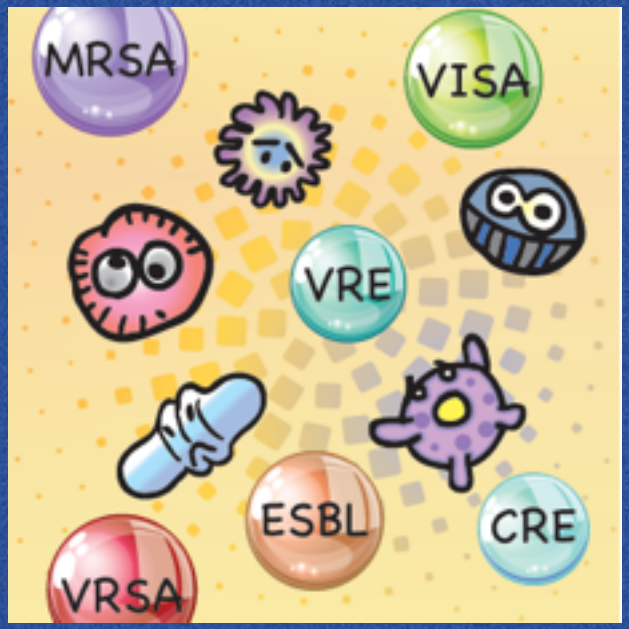
Head of IPAC Istishari Arab Hospital-RamAllah

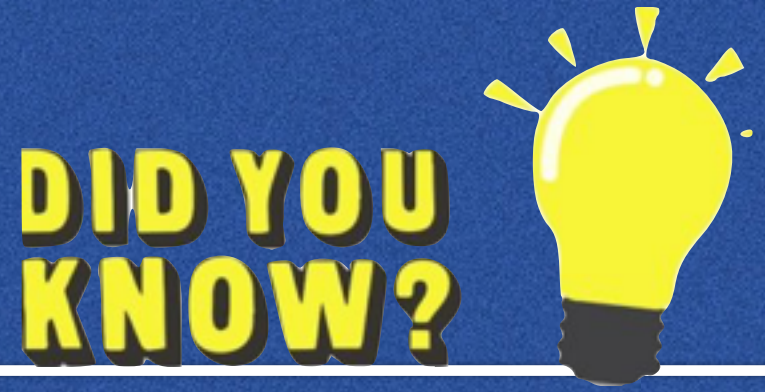
Objectives:

- Define Multidrug Resistant Organisms (MDRO)
- Identify the Risk factors
- Name The MDROs
- General Preventive Strategies

MDRO:-

- A microorganism that has developed resistance to several antimicrobial agents and that is of special clinical or epidemiological significance.

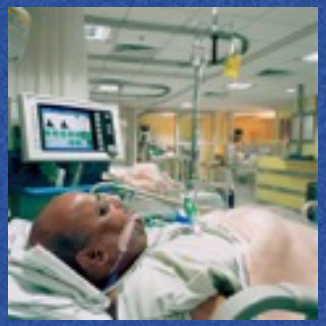




Some Facts

Why Concern over MDROs?

- Cause serious, difficult-to-treat infections that can result in substantial:



  - Morbidity,
  - Mortality,
  - Increased lengths of stay and
  - Excess cost

- Frequently preventable –
  - Usually acquired via transmission by:
    - caregiver-to-patient, environment-to-patient, or patient-to-patient

Example

- Patient with MRSA infection is estimated to cost $14,841, with an incremental cost due to the MRSA of $8,997.
- In comparison, the incremental cost to prevent a case of MRSA has been shown to be approximately $20.
- Even in settings where MRSA has become endemic, control measures have been found to be cost-effective.

Antimicrobial Resistance: a Growing Problem

- Approximately 2 million people experienced a hospital-acquired infection-MDROs
- 90,000 of these infections-Death
- 1 death every six minutes
- The WHO has identified antimicrobial resistance as 1 of the 3 greatest threats to human health.

Dellit TH. Clin Infect Dis 2007 Jan 15;44(2):159

Patients at Risk for MDROs

- Immunocompromised
- Elderly patients
- Higher severity of illness
- Chronic conditions - hemodialysis
- Poor compliance with Infection Prevention practices

- Extended hospital stay
- Intensive Care Unit stay
- Prior antibiotic use
- Transfers from other acute/ chronic care facilities

Associations between antimicrobial use and the emergence of MDROs?

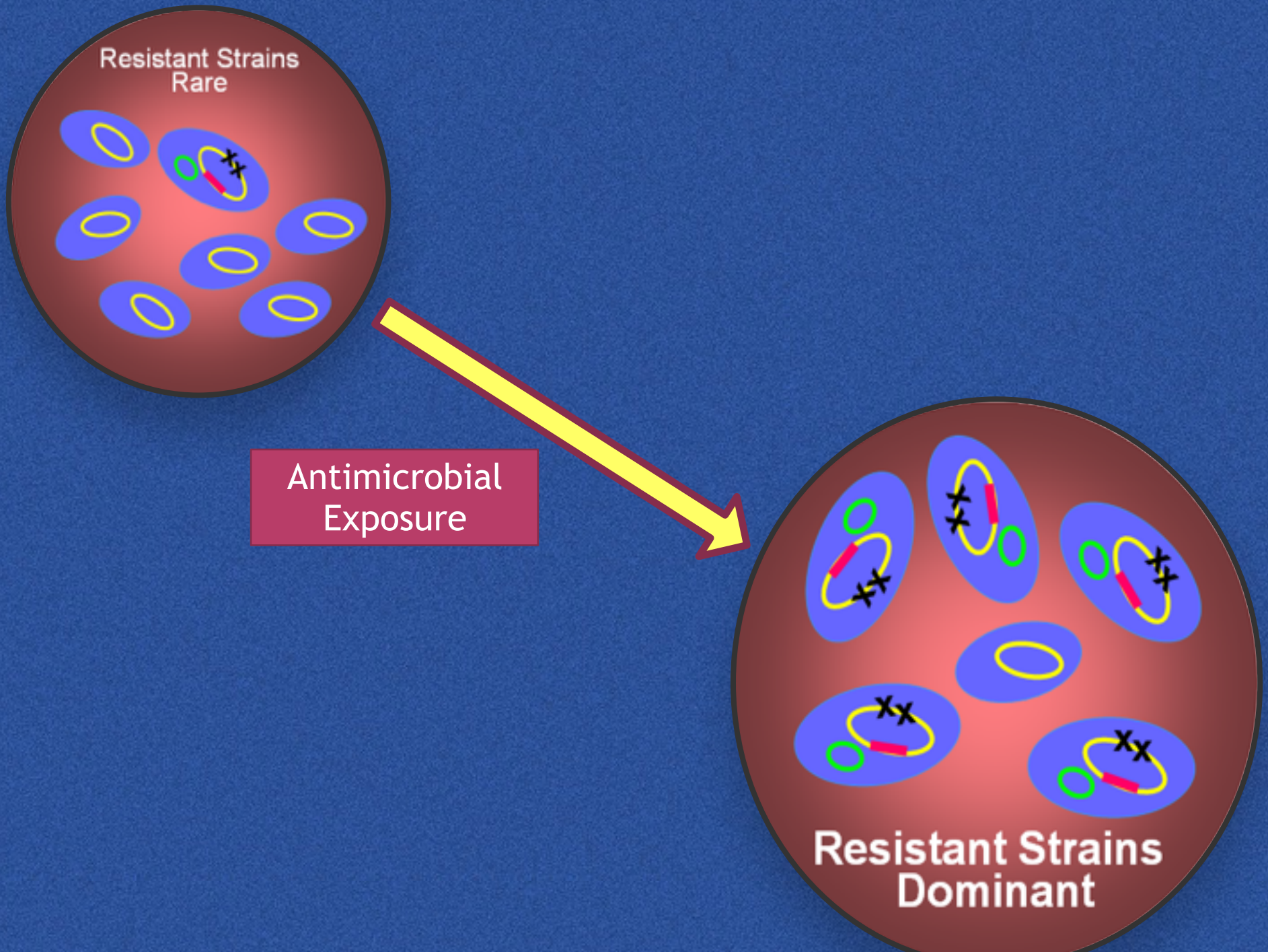
1. Changes in antimicrobial use are paralleled by changes in the prevalence of resistance.

2. Antimicrobial resistance is more prevalent in HAI, compared with those from community-acquired infections.

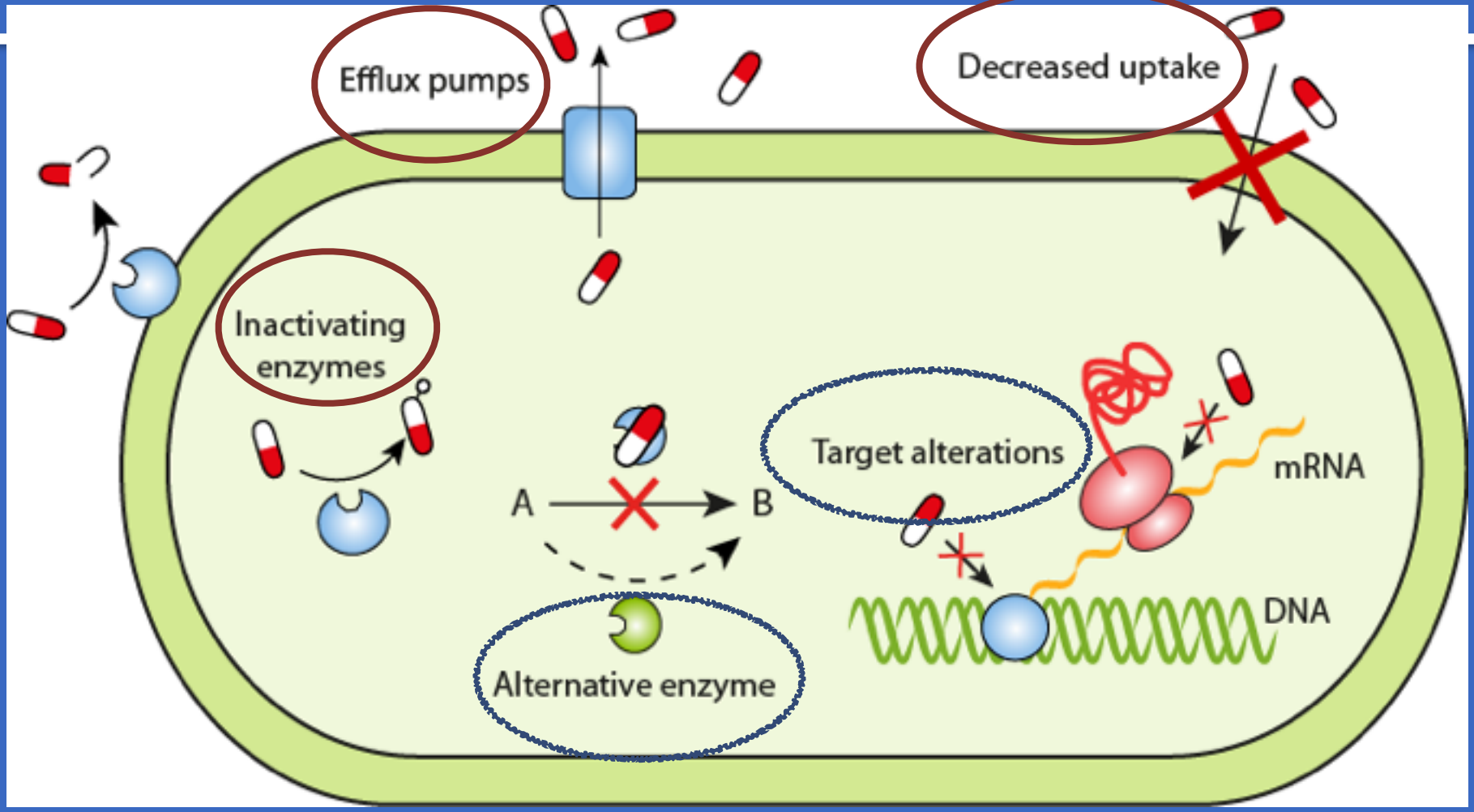
3. Patients with HAI caused by MDRO are more likely to have received prior antimicrobials.

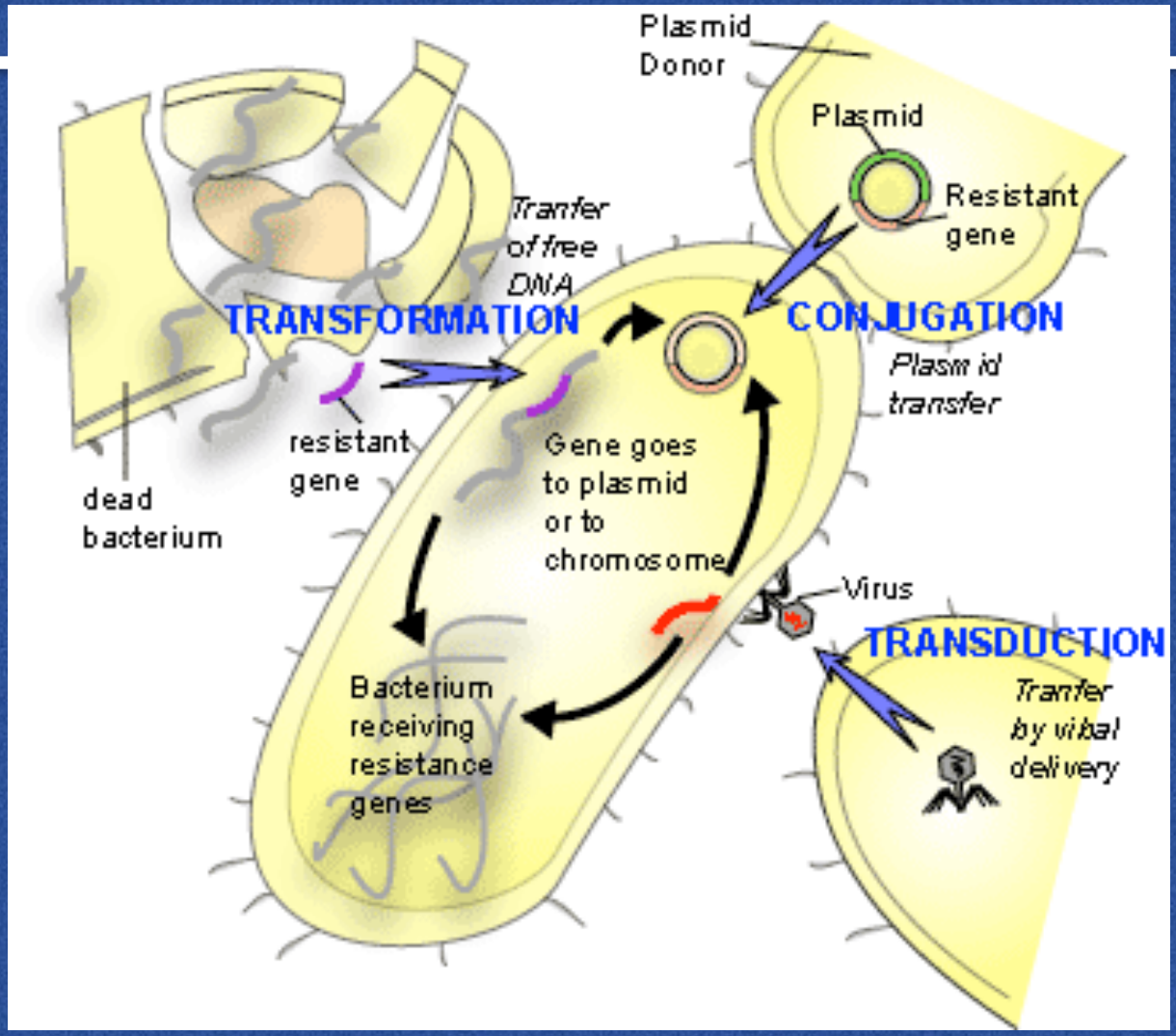
4. Areas within hospitals that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use.

Antimicrobial Stewardship Guidelines • CID 2007:44 (15 January)

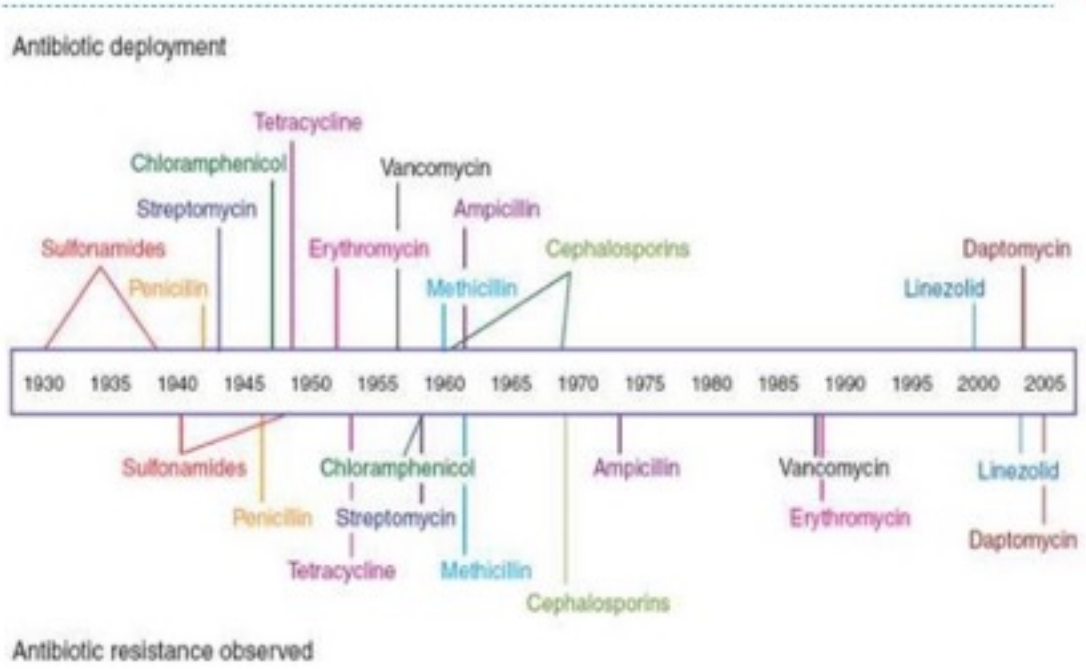

Resistant Strains
Rare
Antimicrobial
Exposure
Resistant Strains
Dominant

Mechanism of Resistance




Plasmid
Donor
Plasmid
Resistant
gene
Tranfer
of free
DNA
TRANSFORMATION
CONJUGATION
Plasmid
transfer
resistant
gene
dead
bacterium
Gene goes
to plasmid
or to
chromosome
Virus
TRANSDUCTION
Tranfer
by viral
delivery
Bacterium
receiving
resistance
genes

Timeline of Antibiotic Resistance

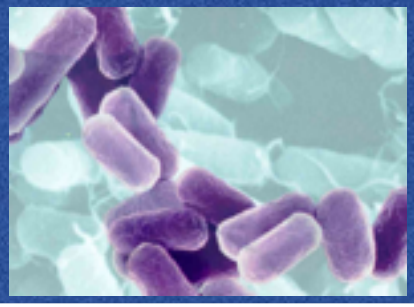


Antibiotic	Year of deployment	Onset of resistance
Chloramphenicol	1947	1959
Tetracycline	1948	1953
Erthromycin	1952	1988
Vancomycin	1956	1988
Methicillin	1960	1961
Ampicillin	1961	1973
Cephalosporins	1960s	late 1960s

Table 1. Dates of antibiotic deployment for clinical use and the subsequent evolution of resistance [5]

How Are Antibiotic-Resistant Organisms Spread?

- The single most important mode of transmission is via transiently colonized <u>Hands of health care workers.</u>
- The unrecognized colonized patient/ resident presents a particular risk for transmission to other patients/residents.



Bad bugs, no drugs: No ESKAPE

CID 2009; 48: 1 - 12

E *nterococcus faecium* **VRE**

S *taphylococcus aureus* **MRSA**

K *lebseilla pneumoniae* **CRE**

A *cinetobacter baumanii*

P *seudomonas aeruginosa*

E *nterobacter species* **Including ESBL/ AMP-C**

Clostridium difficile & *E. coli*

1. Enterococcus (VRE)

- Causes nosocomial bacteremia, surgical wound infection, endocarditis, and urinary tract infections.

- The bacteria can survive for long periods of time inside hospitals on a variety of surfaces as well as in soil and sewage.

- Hospitalized patients with gastrointestinal carriage of VRE are the major reservoir.

2. Staphylococcus aureus (MRSA, VISA, VRSA)

- The carriage of Staphylococcus aureus is an important source.
- MRSA is common and often found in the nose or on the skin.
- Most of the time these bacteria do not cause any symptoms (Colonizer).
- The spectrum of Staphylococcus infections can range from skin abscess to life-threatening infections such as septicaemia or endocarditis.

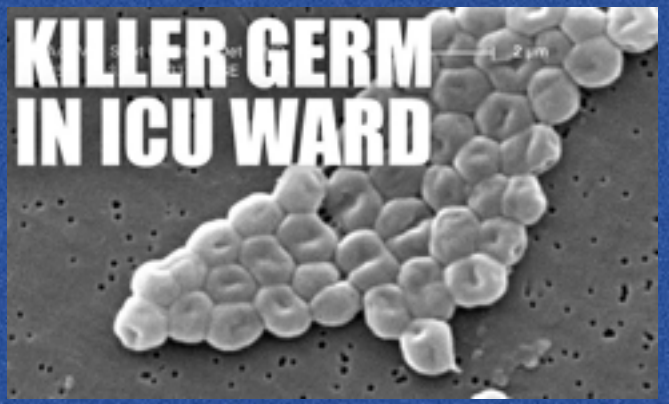
3. Klebsiella pneumoniae (CRE)

- Klebsiella bacteria can be spread through person-to-person contact or by contamination of the environment.

- Patients in healthcare settings may be exposed to Klebsiella when they are on ventilators, or have intravenous catheters or wounds.; which can be fatal.

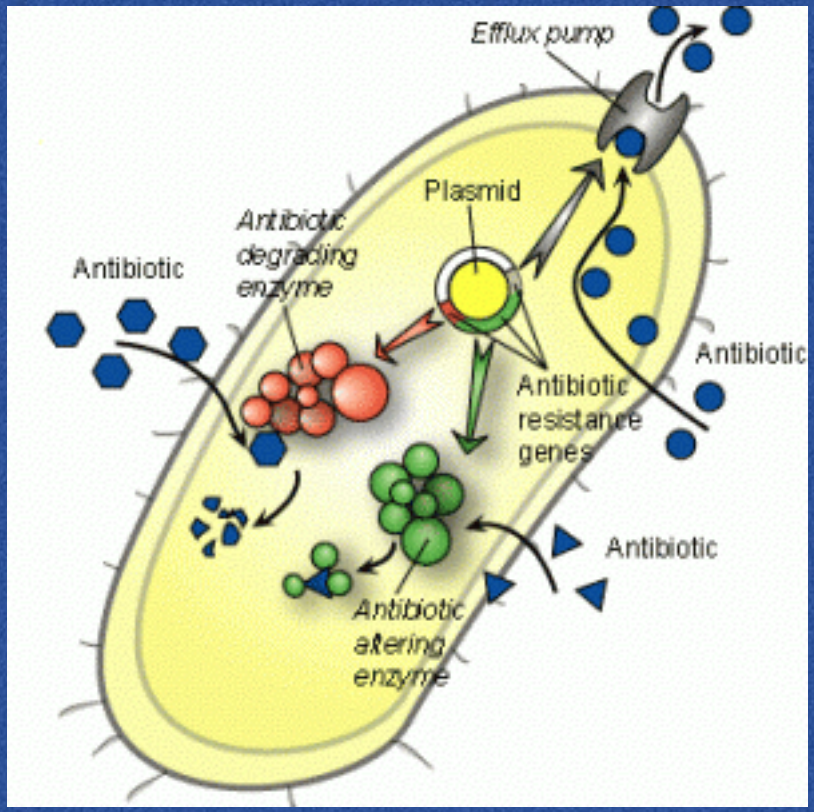
4. Acinetobacter baumannii

- Rapidly emerging pathogen in the health care system.
- Usually introduced into a hospital by a colonized patient.
- Main driver for it is the constant use of antibiotics by patients in the hospital
- Causes a wide range of infection including bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection.
- Has the ability to survive under a wide range of environmental conditions for extended periods of time.



5. Pseudomonas aeruginosa

- Serious infections of P. aeruginosa usually occur in the immuno- compromised (Opportunistic Infection).
- Infections of the blood, pneumonia, and infections following surgery can lead to severe illness and death in these people.
- The highly susceptible nosocomial patients include those on breathing machines, premature babies and patients with wounds from surgery or from burns.



6. Enterobacter species (ESBL, Amp-C, CRE)

- Enterobacter species, are important nosocomial pathogens responsible for various infections; including bacteremia, lower respiratory tract infections, skin and soft- tissue infections.

- Risk factors include hospitalization of greater than 2 weeks, invasive procedures in the past 72 hours, treatment with antibiotics in the past 30 days, and the presence of a central venous catheter.

- Specific risk factors include the recent use of broad-spectrum cephalosporins or aminoglycosides and ICU care.

ESBLs

- Plasmid mediated, transmissable, always “on”
  - Found in all Enterobacteriae (usu *E coli* or *Klebsiella*)
- Decr susceptibility to cephalosporins and aztreonam
  - usu suscept to cefoxitin, but avoid
  - Likely ok to use cefepime if MIC ≤ 2
- Best Rx option: carbapenems or pip/tazo

TESTING INDICATES THAT THIS ISOLATE PRODUCES AN EXTENDED SPECTRUM BETA LACTAMASE. THE ORGANISM IS RESISTANT TO ALL PENICILLINS, CEPHALOSPORINS, AND AZTREONAM.

CultURe UR:

ESCHERICHIA COLI
*** ESBL PRODUCER ***

Culture & Susceptibility

Antibiotic	Organism		Organism	O
	ESCHERICHIA COLI			
AMIKACIN	<=8 mcg/mL	S		
AMOXICILLIN + CLAUVULANATE	>16/8 mcg/mL	R		
AMPICILLIN	>16 mcg/mL	R		
AZTREONAM	mcg/mL	R		
CEFAZOLIN	>16 mcg/mL	R		
CEFEPIME	mcg/mL	R		
CEFOTAXIME	mcg/mL	R		
CEFOXITIN	>16 mcg/mL	R		
CEFTAZIDIME	mcg/mL	R		
CEFTRIAXONE	mcg/mL	R		
CIPROFLOXACIN	<=0.5 mcg/mL	S		
GENTAMICIN	<=2 mcg/mL	S		
IMIPENEM	<=1 mcg/mL	S		
LEVOFLOXACIN	<=1 mcg/mL	S		
NITROFURANTOIN	<=16 mcg/mL	S		
PIPERACILL +TAZOBACTAM	4/4 mcg/mL	S		
TETRACYCLINE	>8 mcg/mL	R		
TOBRAMYCIN	<=2 mcg/mL	S		
TRIMETHOPRIM + SULFAMETHOXAZOLE	<=0.5/9.5 mcg/mL	S		

ESBL Rx options

- Carbapenems
- Tigecycline-- limited clinical data, not for UTI, concern for bacteremia
- ß-lactam/ß-Lactamase Inhibitor Combinations
  - Variable inhibitory activity
  - Tazobactam>>sulbactam & clavulanate
  - Pip/tazo—ok for UTI (high urinary concentrations)
  - Cephalosporins—not recommended (? Cefepime)
- Fosfomycin—uncomplicated UTI only

ESBL Rx options (cont)

- AG, FQ, Bactrim:
  - Avoid—high risk of developing resistance
- Colistin:
  - No CLSI breakpoints, consider E-test
- Fosfomycin
  - Inhibits bacterial cell wall synthesis
  - ’cidal vs GP and GN
  - Uncomplicated UTI

CRE

Carbapenem-Resistant Enterobacteriaceae

- Enterobacteriaceae
  - GNR, GI tract
  - CA- and HCA-infections
  - 70 genera, but mostly *E coli*, *Klebsiella*, *Enterobacter sp*
  - Uncommon in US before 2000
  - Complex, multiple resistant mechanisms
    - Carbapenemases (KPC, NDM—India/Pakistan)
  - Mortality rates 40-50%

Risk factors for CRE

- Exposure to health care and antimicrobials
  - Carbapenems, cephalosporins, FQ, vanco
- Recent organ or stem-cell transplants
- Mechanical ventilation
- Longer LOS

CRE Rx Options

- Tigecycline
  - Limited clinical experience
  - Avoid in UTI and primary BSI
- Colistin
  - Emerging resistance
- Fosfomycin
  - Looks great in vitro

WHO publishes list of bacteria for which new antibiotics are urgently needed

Feb 27 2017

- **Priority 1: CRITICAL**
  1. *Acinetobacter baumannii*, carbapenem-resistant
  2. *Pseudomonas aeruginosa*, carbapenem-resistant
  3. *Enterobacteriaceae*, CRE, ESBL-producing
- **Priority 2: HIGH**
  1. *Enterococcus faecium*, VRE
  2. *Staphylococcus aureus*
  3. *Helicobacter pylori*, clarithromycin-resistant
  4. *Campylobacter* spp., fluoroquinolone-resistant
  5. *Salmonellae*, fluoroquinolone-resistant
  6. *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant
- **Priority 3: MEDIUM**
  1. *Streptococcus pneumoniae*, penicillin-non-susceptible
  2. *Haemophilus influenzae*, ampicillin-resistant
  3. *Shigella* spp., fluoroquinolone-resistant

Prevention Strategies for MDROs

- Hand Hygiene
- Isolation Precautions: Gown and Gloves, Every Person Every Time
- Equipment/ Environmental cleaning
- Surveillance screening
- Identification of MDRO patient and isolation when re-admitted (flagging medical record)
- Education Staff, Patients and Visitors

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

CDC
Centers for Disease Control and Prevention

In Summary – Prevention of MDROs

- **Hand Hygiene, Hand Hygiene, Hand Hygiene**
- Isolation Precautions
  - Standard Precautions for all patients
  - Contact Precautions for patients identified as having an MDRO
- Environmental Measures
- Judicious use of Antimicrobial agents

1. **Which of the following organisms are considered a MDRO?**

a. MRSA **b. *Acinetobacter* sp.** **C. C diff.** **d. all the above.**

2.acquiring a MDRO; Extended healthcare length of stay and prior antibiotic use are risk factors for:- True or False.

3. What isolation precaution is used for the MDRO C. diff?

a. Contact b. Droplet c. Airborne d. Contact Enteric

4.strategies to prevent the spread of MDROs and HAIs?

Hand hygiene, equipment cleaning, alert notification and education.

True or False