

# New Antimicrobials in ED and Antibiotics stewardship

Samar Assem Badreddine, MD  
Consultant Infectious diseases  
Chief of medical and clinical division  
Dr Soliman Fakeeh Hospital

# “ New” and “stewardship”

- May not go well together : “New “ is inviting, “stewardship” is deterring
- *WHO global strategy for containment of anti-microbial resistance*
  - *Eliminate financial incentives that promote the misuse of antibiotics.*
  - *Monitor advertising : Develop ethical standards concerning advertising of antibiotics*
  - *Limit general access to new drugs*

# Pandemic of resistance

- The world is facing a pandemic of micro-organisms resistant to available antimicrobials
- Resistant micro-organisms are no more limited to hospitals/ ICU setting.
- Search for new drugs is now a must to effectively treat infections.

# Microbes seem to be winning the resistance battle.....

- Stories of many bacteria:
  - Staph aureus: from Penicillins to oxazolidinone
  - Strep Pneumonia: from penicillin to glycopeptides
  - E Coli: from ampicillin to ESBL and then Colistin
  - Pseudomonas: from cipro to Colistin
  - Acinetobacter: from ampicillin sulbactam to Colistin
  - Mycobacterium TB: MDR and then XDR
- Resistant to all
- Story of an antibiotic : tygecycline

# Resistance development and use of antimicrobials

- Link between Antibiotics use ( we are not talking abuse here) and resistance development is Well established
  - Patients with resistant strains are more likely to have received prior antibiotics than control groups
  - Areas within the hospital having the highest Prevalence of antibiotics use also have the highest prevalence of antibiotics resistant bacteria
  - Cross sectional prevalence study in five different communities in Iceland showed a strong association between use of penicillins and carriage of PCN resistant pneumococci in children . [BMJ,313,387-91](#)
  - The results from 11 European countries show a linear relationship between use of B-lactam & macrolides and the proportion on Penicillin resistant pneumococci. [EID ;8\(3\),March 2002](#)

# Contribution of ED physicians to the problem

- The use of third generation cephalosporin has been shown repeatedly to lead to increase in infections with **ESBL** producing enterobacteriaceae.
  - **Clin Infect Dis 2001;32:1162-71.**
  - **Ann Intern Med 1993;119:353-8.**
  - **JAMA 1998;280:1233-7**

# What happens on the cellular/ molecular level?

- Darwin's Natural selection is at its best/ fastest expression.
- Antibiotics allow the expression of already existent resistance genes by selecting them.
- Antibiotics provide a positive selective pressure that creates an environmental landscape allowing bacteria with resistant genes to proliferate.

# Of note

- A single dose can induce resistance: the case for ED rationalization of antimicrobials use
- Antimicrobials are the only class of drugs that have a societal impact.
- “*TB anywhere is TB everywhere*”: antibiotic resistant bacteria anywhere, is antibiotic resistant bacteria everywhere. e.g. NDM1-enterobacteriaceae, XDR-TB



# What can we do?

Reducing/ rationalizing antibiotics use restored sensitivity

- In hospital settings
  - 500 beds hospital: A new antibiotic guideline restricted the use of cephalosporin led to 80% reduction in hospital wide cephalosporin use in 1996 compared to 1995. ([JAMA,1998;280\(14\):1233-37](#))
    - Resulted in 44% reduction in the incidence of cephalosporin resistant klebsiella
- On Country Levels
  - In 1991 , policies in Finland restricted use of macrolides. Consumption of macrolide decreased from 2.4 DDD/1000 inhabitant /day in1991 to 1.38 in 1996. ([NEJM 1997;337:441-6](#))
    - Resistance to erythromycin decreased from 16.5% in 1992 to 8.6% in 1996.

# Hence the concept of antimicrobial stewardship

There are 2 core strategies that provide the foundation for stewardship programs.

- Prospective audit with intervention and feedback .
- Formulary restriction and pre-authorization.
- Supplemental measures:
  - Education
  - Guidelines and clinical pathways
  - Antimicrobial cycling
  - Antimicrobial order form
  - Streamlining or de-escalation therapy
  - Parenteral to oral conversion

# Stewardship in ED

- Education , Guidelines and clinical pathways
- Radical change in Mind set:
  - Antibiotics are not antipyretics
  - Antibiotics have no role in treating the many causes of fever ( viruses, fungi, protozoan, malignancies, drug reactions, auto-immune diseases, metabolic, etc...)
- Microbiological cultures must be taken before starting antibiotics, whenever possible: Allow for De-escalation

# Stewardship: avoid broad spectrum antibiotics

- Nowadays, May not be always applicable in ED
- Broad spectrum may have to be used right away:
  - 35-45% of E.Coli are now ESBL positive in the city of Jeddah
  - Community acquired ESBL infections
  - Community acquired MRSA
- Use New antibiotics, when old ones may not provide adequate coverage

# What antibiotic to give, and when in ED

- Tonsillitis:
  - Penicillin is still the drug of choice
- Sinusitis:
  - Macrolides, 2<sup>nd</sup> gen cephalosporins and amoxicillin / clavulanate.
  - Quinolones are good, but avoid ( side effects and resistance)
- Pneumonia:
  - Doxycycline or macrolides for outpatients
  - Ceftriaxone+ macrolide for inpatients
  - Respiratory Quinolones: Gemi, Gat, Moxi,levo are all good- beware of TB resistance and of side effects.
  - Telithromycin good for resistant step pneumonia- Beware of hepatotoxicity

# Skin and soft tissue infections

- Think of Community Acquired MRSA (CA-MRSA)
- PO: Clindamycin and Bactrim are good empiric therapy if patient is stable with no co-morbidities, and if sensitivity to both in your institution is high
- Otherwise, you may need to Use new drugs:
  - Oxazolidinone: Linezolid, tedizolid
  - Newest Quinolones: Delafloxacin ( the only quinolone that covers MRSA)
  - Lipoglycopeptide. Only approved for SSTI.
    - Dalbavancin: (MRSA, VRE)
    - Oritavancin : (MRSA, VRE) Very long half life. Approved for single dose treatment  
No renal adjustments
  - Daptomycin (lipopeptide): IV therapy for MRSA bacteremia and SSTI

# Urinary tract infections

Think ESBL positive organisms

- Stable, non complicated, no fever
  - Take urine culture
  - Nitrofurantoin
  - If the above not available, start Quinolones, Bactrim,
  - Fosfomycin
- For sicker patients:
  - Meropenem
  - Ertapenem: advantage of once daily, IM
  - Doripenem : least likely to induce carbapenem resistance

# Intra-abdominal infections

- Augmentin, quinolone or Bactrim + flagyl
- pip/ tazobactam ( Tazocin)is still drug of choice
- Tygecycline: on the way to extinction



# Sexually transmitted infections

- Azithromycin PO and Ceftriaxone IM
- No more oral cephalosporin (cefixime" suprax" ) because of gonorrhoea emerging resistance
- No more quinolones because of emerging resistance
- No more doxycycline for Gonorrhoea because of emerging resistance

# CPE : ( carbapenem producing enterobacteriaceae)

- Use Colistin ( with combination??).
- If not possible, or if resistant:
  - Meropenem+Vaborbactam ( vabomere): Only approved for UTI
  - Ceftazidime+avibactam ( Avycaz) : approved for UTI and intra-abdominal infections (with flagyl)

# Newer Cephalosporins

- Ceftobiprole: advanced generation cephalosporin. Same coverage of Ceftriaxone+ MRSA ( for pneumonia but not VAP)
- Ceftriaxone + VRSA/MRSA (SSTI, CAP)
- Ceftriaxone + VRSA/MRSA (SSTI, CAP)
- Ceftolozane-tazobactam: extended coverage of gram negative including ESBL and Pseudomonas. No anaerobes, or gram positives

# How about viruses and fungi?

- Same concerns with antibiotics apply
  - Acyclovir resistant herpes, Oseltamivir resistant influenza, HIV virus resistant to ART
  - Fluconazole and Echinocandins resistant Candida
- What is new?
  - Echinocandins: anidulafungin, micafungin and caspofungin
  - Molds active agents: posaconazole and Isavuconazole
  - Many new anti HIV anti retroviral meds
  - Anti HCV therapy

# Take home messages

- Micro-organisms seem to be winning the battles with antibiotics
- There is no assurance that the development of newer antibiotics Can keep pace with the ability of bacteria to develop resistance.
- Think twice, or better million times, before prescribing an antimicrobials.
- Antibiotics are not antipyretics