Topic 3: Reducing the development, emergence and spread of antibacterial resistance

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Outline

- Review the progressive nature of bacterial resistance

- Molecular epidemiology of resistant pathogens
  - MRSA
  - *Carbapenem-resistant Enterobacteriaceae* (CRE)
  - *Carbapenem-resistant A. baumannii* (CRAB)

- How to reduce resistance development and spread
  - Antimicrobial stewardship
  - Rapid molecular detection and Infection control
  - Multilayered and multilevel Education
In the population of bacterial, resistance cells must compete with its susceptible counterparts. In the presence of antibiotics, the resistant bacteria will proliferate to dominate the bacterial population. The resistant bacteria may be maintained in the environment.

Minimizing resistant clones is one key way to stop emerging resistance.
Ecology of antibiotics and resistance


The two antibiotic reservoirs are intimately connected, which leads to the cycling of antibiotics and resistant bacteria between the *in vivo* and *ex vivo* environments.
Ecology of antibiotics and resistance

- Antibiotics exert selective pressure on bacteria in humans, animals and plants.

- This imposes a widespread selective pressure on bacteria, leading to the selection of resistant strains, which are also capable of transmitting between different environments, thereby creating the potential for the global movement of antibiotic resistance genes and determinants.
SARS clone distribution and evolution in mainland China

Respiratory tract infections: 58.2%;
Bloodstream infections: 44.8%;

Evolutionary mechanisms of MRSA

- ST239-MRSA-III-spa t037 clone was replaced by the emerging ST239-MRSA-III-spa t030 clone

- Thirteen critical gene clusters were identified to be contributors to the evolution of host specificity and antibiotic resistance in Chinese S. aureus

Changing trends in antimicrobial susceptibility of *A. baumannii* in 13 teaching hospitals in China (CMSS)
OXA-23-producing ST92 is the most predominant clone among CRAB in China from 1999 to 2011.
Antimicrobial susceptibility trends of *K.pneumoniae* in 13 teaching hospitals in China (CMSS)

KPC-2 and NDM-1 producing Enterobacteriaceae has continued to spread in China

Reducing resistant bacteria dissemination

How to test?
Finding easy and rapid routine screening method

How to carry out antibiotics stewardship

Reducing antibiotic abuse

Clinical Laboratory

Control and monitor nosocomial infection

Searching New drugs/existing drugs

Reducing resistance: Multidisciplinary efforts

Health Ministry
1. Regulate antibiotics stewardship
2. Resistance surveillance
Target groups of education about prudent antibiotic use

- Combines education of children, campaigns for the adult public, and antibiotic stewardship programs for medical professionals

Strategy 1: From the point of view of clinical use of antibiotics

Antibiotic stewardship strategies for prevention and treatment of infections due to CRE

- Nationwide Antimicrobial stewardship has been conducted in China since 2013 by MOH
- Overall decrease in antimicrobial use
  - reduce inappropriate use of antibiotics
  - education of physicians and patients
  - patient demands are the major reason to prescribe probably unnecessary antimicrobial agents
- Duration of therapy
- Optimal dosing
- Combination therapy*

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Strategy 2: From the point of view of prevention: 2“R” and 2“P”

- **Reduce reservoirs of resistant bacteria** and execute infection-control measures to prevent transmission of resistant bacteria

- **Resistance surveillance** not only nosocomial infection but also environmental surveillance

- **Policy making and supervision system**
  Standard antibiotic use include healthcare and animal husbandry

- **Public knowledge popularization about antibiotics real-name system, etc** (community infection)

Correlation between carbapenem consumption and antimicrobial resistance in *A. baumannii* in a Chinese Hospital

The consumption of IPM, MEM, and total carbapenem is significantly correlated with CRAB.

Total carbapenem consumption is significantly correlated with MEM resistance in *A. baumannii*.

Overall decrease in antibiotic use

• The role of formulary interventions in controlling CRE is not well studied

• Therefore, rather than targeting a specific class or limiting specific agents, overall reduction in antibiotic use is recommended as a focus for ASPs

• A patient’s cumulative antibiotic exposure history is likely to be more important than any one specific exposure when determining the likelihood of developing a CRE infection

• We need to perform the basic research study on the effect of various antibiotics regimens on the selection of resistance.
Intervention of horizontal transmission of CRE

Control the \textit{A. baumannii} outbreak
Early detection of antimicrobial-resistance pathogens using new methods

◆ Phenotypic Screening method (Carba NP, SUPERCARBA)
◆ DNA microarrays
◆ Multiplex real-time PCR array
◆ MALDI-TOF MS
◆ Xpert MDRO Assay/ Xpert Carba-R test

Microfluidics Chips based on multiplex PCR chip

✓ Sine-shaped infusing channels
✓ Simultaneous 63 target DNA
✓ Identify 8 bacteria, 13 resistance genes
✓ 4 hours

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Summary

- Resistance rate of key pathogens is increasing in China
  - Clone and plasmid mediated nosocomial dissemination
- Control measures need multiaspect efforts
  - Education: the public, medical professionals
  - Antimicrobial stewardship
  - Strict Infection Controls measures
    - Rapid diagnosis and tracking of MDRO
Thanks for your attention!