Multidisciplinary Antibiotic Stewardship Programme in the Department of Medicine & Geriatrics

Dr. Chan Kai Ming
Associate Consultant
Clinical Pathology
Tuen Mun Hospital
Per 100,000 population per year

Alexander Fleming & Penicillium notatum
“One can think of the middle of the twentieth century as the end of one of the most important social revolutions in history, the virtual elimination of the infectious disease as a significant factor in social life”

Sir MacFarlane Burnett
(nearly 40 years ago)
Table 1: Estimated Cases of Hospital-Acquired Infections Caused by Selected Resistant Bacteria in the United States in 2002

<table>
<thead>
<tr>
<th>Antibiotic-Resistant Bacteria</th>
<th>Estimated Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin/S. aureus</td>
<td>102,000</td>
</tr>
<tr>
<td>Methicillin/CNS</td>
<td>130,000</td>
</tr>
<tr>
<td>Vancomycin/enterococci</td>
<td>26,000</td>
</tr>
<tr>
<td>Ceftazidime/P. aeruginosa</td>
<td>12,000</td>
</tr>
<tr>
<td>Ampicillin/E. coli</td>
<td>65,000</td>
</tr>
<tr>
<td>Imipenem/P. aeruginosa</td>
<td>16,000</td>
</tr>
<tr>
<td>Ceftazidime/K. pneumoniae</td>
<td>11,000</td>
</tr>
</tbody>
</table>

**Source:** Centers for Disease Control and Prevention, Division of Healthcare Quality Promotion

These preliminary estimates were extrapolated by CDC staff from data collected from hospitals that participate in the National Nosocomial Infections Surveillance System. NNIS hospitals are disproportionately large, urban, and affiliated with medical schools and are more likely to have more seriously ill patients. As such, these estimates should be interpreted cautiously. CNS=Coagulase-negative staphylococci
## Table 2: History of Antibiotic Discovery and Approval

<table>
<thead>
<tr>
<th>Year Introduced</th>
<th>Class of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>1935</td>
<td>Sulfonamides</td>
</tr>
<tr>
<td>1941</td>
<td>Penicillins</td>
</tr>
<tr>
<td>1945</td>
<td>Cephalosporins</td>
</tr>
<tr>
<td>1944</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>1949</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>1950</td>
<td>Tetracyclines</td>
</tr>
<tr>
<td>1952</td>
<td>Macrolides/Lincosamides/Streptogramins</td>
</tr>
<tr>
<td>1956</td>
<td>Glycopeptides</td>
</tr>
<tr>
<td>1957</td>
<td>Rifamycins</td>
</tr>
<tr>
<td>1959</td>
<td>Nitroimidazoles</td>
</tr>
<tr>
<td>1962</td>
<td>Quinolones</td>
</tr>
<tr>
<td>1968</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>2000</td>
<td>Oxazolidinones</td>
</tr>
<tr>
<td>2003</td>
<td>Lipopeptides</td>
</tr>
</tbody>
</table>

**Source:** Food and Drug Administration (modified)

Chart 1: Resistant Strains Spread Rapidly

Source: Centers for Disease Control and Prevention

This chart shows the increase in rates of resistance for three bacteria that are of concern to public health officials: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and fluoroquinolone-resistant *Pseudomonas aeruginosa* (FQR). These data were collected from hospital intensive care units that participate in the National Nosocomial Infections Surveillance System, a component of the CDC.
### Table 3: Percent of Drug Resistance in Hospital-Acquired Infections in 2002

<table>
<thead>
<tr>
<th>Drug/Pathogen</th>
<th>Resistance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin/S. aureus</td>
<td>57.1</td>
</tr>
<tr>
<td>Vancomycin/enterococci</td>
<td>27.5</td>
</tr>
<tr>
<td>Quinolone/P. aeruginosa</td>
<td>32.8</td>
</tr>
<tr>
<td>Methicillin/CNS</td>
<td>89.1</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;-gen. Ceph./E. coli</td>
<td>6.3</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;-gen. Ceph./K. pneumoniae</td>
<td>14.0</td>
</tr>
<tr>
<td>Imipenem/P. aeruginosa</td>
<td>22.3</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;-gen. Ceph./P. aeruginosa</td>
<td>30.2</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;-gen. Ceph./Enterobacter spp.</td>
<td>32.2</td>
</tr>
<tr>
<td>Penicillin/S. pneumoniae</td>
<td>11.3</td>
</tr>
</tbody>
</table>

**Source:** CDC National Nosocomial Infections Surveillance System, August 2003 for all, except penicillin resistant *Streptococcus pneumoniae*, which is the Active Bacterial Core Surveillance of the Emerging Infections Network.

This table provides a snapshot of selected drug-resistant pathogens associated with hospital infections in intensive care unit patients during 2002. CNS=Coagulase-negative staphylococci; 3rd Ceph=resistance to 3rd generation cephalosporins (either ceftriaxone, cefotaxime, or ceftazidime); Quinolone= resistance to either ciprofloxacin or ofloxacin.
A 46-year-old Maryland man received a transplant and was sent to the intensive care unit. His blood cultures grew *Acinetobacter* that was resistant to all antibiotics except colistin, a drug rarely used because it is very toxic. He died.

April 2004.
香港發現首宗社區抗藥惡菌死亡病例

資料來源：中央社
張貼時間：01/06 11:33

（中央社記者邁克爾米勒香港六日電）濫用抗生素的惡果逐漸在香港社區浮現。根據官方消息，香港首次發現健康市民感染社區性抗藥性金黃葡萄球菌，引發腦膜炎後迅速死亡的罕見病例。此事已引起衛生當局及專家高度關注。根據香港官方網站發布的消息，衛生署轄下的衛生防護中心發言人昨晚表示，不幸染病死亡的三十七歲女子原本健康良好，擔任文職工作，一年內也未曾入院。

抗藥惡菌襲公立醫院
4月6日 星期二 03:00

【東方日報專訊】抗藥性細菌肆虐公立醫院的情況愈來愈嚴重，其中復康醫院靈實醫院近日便出現病人集體感染抗藥性細菌。其中一個約四十人的病房，四分三病人感染抗藥性金黃葡萄球菌個案。混典型的抗藥性細菌呈廣譜霉抗藥反應，另有一名年長者感染幾乎無藥可醫的抗藥性綠膿桿菌，此病菌可透過病人咳嗽時傳播。

抗藥惡菌恐擴散全港
(明報)
11月17日 星期五 05:05AM【明報專訊】可致命的超級惡菌「社區性抗藥性金黃葡萄球菌（CA-MRSA）」恐已廣佈全港，衛生署繼上月接獲最少3宗有關呈報後，本月首2周再接獲4宗分怖於元朗、葵涌、將軍澳及大嶼山的個案，2男2女患者同屬22至40歲年輕一族，全部均是長出膿瘡需往醫院放膿，始發現身染惡菌。衛生署正積極研究將CA-MRSA列作法定傳染病，以及實施所須的具體措施。
Only about five new antibiotics are in the drug pipeline, out of more than 506 agents in development.

Table 4: New Antibacterial Agents Approved Since 1998

<table>
<thead>
<tr>
<th>Antibacterial</th>
<th>Year</th>
<th>Novel</th>
</tr>
</thead>
<tbody>
<tr>
<td>rifapentine</td>
<td>1998</td>
<td>No</td>
</tr>
<tr>
<td>quinupristin/dalfopristin</td>
<td>1999</td>
<td>No</td>
</tr>
<tr>
<td>moxifloxacin</td>
<td>1999</td>
<td>No</td>
</tr>
<tr>
<td>gatifloxacin</td>
<td>1999</td>
<td>No</td>
</tr>
<tr>
<td>linezolid</td>
<td>2000</td>
<td>Yes</td>
</tr>
<tr>
<td>ceftoloxime pivali</td>
<td>2001</td>
<td>No</td>
</tr>
<tr>
<td>ertapenem</td>
<td>2001</td>
<td>No</td>
</tr>
<tr>
<td>gemifloxacin</td>
<td>2003</td>
<td>No</td>
</tr>
<tr>
<td>daptomycin</td>
<td>2003</td>
<td>Yes</td>
</tr>
<tr>
<td>telithromycin</td>
<td>2004</td>
<td>No</td>
</tr>
</tbody>
</table>

Source: Spellberg et al., Clinical Infectious Diseases, May 1, 2004 (modified)

Chart 2: Antibacterial Agents Approved, 1983-2004

Source: Spellberg et al., Clinical Infectious Diseases, May 1, 2004 (modified)
Antibiotics work so fast and so well, they produce weak returns on investment for manufacturer.
In 2002 out of 89 new drugs, no new antibiotics were approved.
Bad Bugs! No Drugs!
Know your bugs!

- Viruses
- Bacteria
- Fungus
MISSION: IMPOSSIBLE!

Think before you act. Use the right equipment.
Multidisciplinary Antibiotic Stewardship Programme in the Department of Medicine & Geriatrics
Clinical Audit of the Use of Antibiotics in Acute Medical Wards

Dr. Chan Kai Ming
MBBS (HK), MRCP (UK), FHKAM (Medicine), FHKCP, DipID (HKU), DTM&H (Lond)
Specialist Infectious Disease
Microbiology / Infectious Disease Team
Department of Pathology / Department of Medicine & Geriatrics
Tuen Mun Hospital

2005 HA Convention Presentation
Conclusion

- Appropriate antibiotic use is associated with shorter length of stay
- Overall prescribing behaviour of clinicians did not change over the past year
- Active expertise participation in patient management is recommended for achieving appropriate antibiotic use and better outcome
Antibiotic Stewardship Program to optimize antibiotic usage in Hospital Authority

Dr. Raymond Yung
Head, Infection Control Branch, CHP cum ICASP, the Hospital Authority
8 May 2007

2007 HA Convention Presentation

Strategy to Combat Antimicrobial Resistance
Multidisciplinary Approach
MID Team

• Microbiologist
• Infectious Disease Physicians
• Pharmacist with special interest in Infectious Disease
• Infection Control Nurses
• Parent Team and ward caring nurses

Broad Spectrum Antibiotics
- Cefepime
- Ceftazidime
- Meropenem
- Sulperazon
- Tazocin
- Teicoplanin
- Tienam
- Vancomycin
- IV Ciprofloxacin
- IV Levofloxacin

SARS
Step by Step

• Phase I
  – Introduction of Antibiotic Order Form

• Phase II
  – Pilot study to examine the clinical outcome and financial impact of the implementation of multidisciplinary antibiotic stewardship programme.

• Phase III
  – Full implementation of antibiotic stewardship programme to ALL medical wards
Antibiotic Order Form (AOF)

(Tienam, Meropenem, Vancomycin, Teicoplanin ONLY)

<table>
<thead>
<tr>
<th>Affix GUM Label Here</th>
<th>MO’s Signature: ____________________________</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MO’s Name/Code: __________________________</td>
</tr>
<tr>
<td></td>
<td>____________________<strong><strong>(</strong></strong>_ )</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Ward:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialty:</td>
<td>HN:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date Started:</th>
<th>Culture Taken: Yes/No</th>
<th>Organism (if known)</th>
<th>Sensitivity (if known)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected Infection:</td>
<td>Site:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Empirical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Culture-based</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>□ Tienam/□ Meropenem</th>
<th>Dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Intended Duration</th>
</tr>
</thead>
</table>

- **Infections attributed to ESBL-producing bacteria**
- **Empirical treatment of neutropenic fever in high risk patients**
- **Documented infection with bacteria strains ONLY sensitive to Tienam/Meropenem**
- **LIFE-THREATENING infections (e.g. patients with septic shock)**
Pilot Study

Generate Antibiotics Patient List

Intervention Wards

Gather Patient Data

Case Assessment and Recommendations

Follow up

Control Wards

No Assessment and Intervention

April 2005
## Pilot Study

<table>
<thead>
<tr>
<th></th>
<th><strong>Intervention Group</strong></th>
<th><strong>Control Group</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>41.99/1000 Patients</td>
<td>37.44/1000 Patients</td>
</tr>
<tr>
<td><strong>Length of Stay</strong></td>
<td>3.18 days</td>
<td>3.34 days</td>
</tr>
<tr>
<td><strong>Wards Involved</strong></td>
<td>2 male acute medical wards, 2 female acute medical wards</td>
<td>1 male acute medical ward, 1 female acute medical ward</td>
</tr>
<tr>
<td><strong>AOF</strong></td>
<td>Strict control</td>
<td>Loose control</td>
</tr>
<tr>
<td><strong>Level of feedbacks</strong></td>
<td>Assess the appropriateness of use of 12 targeted abx: - (Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone, IV Ciprofloxacin &amp; Levofloxacin, Meropenem, Sulperazon, Tazocin, Teicoplanin, Tienam, Vancomycin)</td>
<td>Clinicians were given full autonomy on the use of all antibiotics.</td>
</tr>
</tbody>
</table>

**P = 0.591**

April 2005
Pilot Study

- Rate of Suboptimal Antibiotic Use = 29%
- Compliance Rate to Intervention = 85%

April 2005

![Bar chart showing reduction in Defined Daily Doses (DDD) / 1000 Beddays from 146 to 121, with a 18% reduction indicated.]
Pilot Study - Total Antibacterial Expenditure / Bedday

Mar-05
HK$66.5
HK$67.4

Apr-05
HK$70.8
HK$60.1
↓ 15%

Intervention Wards (A5, C10, D9, D10)
Control Wards (A10, C9)

April 2005
Full Implementation

Generate Patient List

Gather Patient Data

Case Assessment and Recommendations

Follow up

Nov 05 - Now
Full Implementation

- Rate of Suboptimal Antibiotic Use = 17%
- Compliance Rate to Intervention = 85%
Mortality Rate (per 1000)
DDD of Broad Spectrum Antibiotics/ 1000 Beddays (2001- Mar 2008)

Pilot Study

Antibiotic Order Form

Full Implementation

↓ 36%
Intangible Benefits

• Contain antibiotics resistance
• Improve quality of patient care
• Promote optimal antibiotic use
Tangible Benefits

• Reduce Consumption of Targeted Antibiotics
• Reduction of Total Antibacterial Expenditure

Cumulative Savings over 3 years & 4 months

$ = ~HK$7.8 millions
合理使用抗生素
病人安全照顧到
Thank You Very Much
Antibiotic Stewardship Programme

Please FAX the COMPLETED ANTIBIOTIC ORDER FORM & MAR to pharmacy for continuing supply of targeted antibiotics

Dear Case MO c/o nurse i/c of ______ ward

Date:__________________

According to the policy set by Antibiotic Stewardship Program, without the receipt of a completed Antibiotic Order Form, only ONE day supply is made for the patient

(Name:__________________; HN:_________________) because

☐ the Order Form is Missing
☐ Other reason: ________________________________

☐ Cefepime  ☐ Ceftazidime  ☐ IV Ciprofloxacin  ☐ IV Levofloxacin  ☐ Meropenem
☐ Sulperazon  ☐ Tazocin  ☐ Teicoplanin  ☐ Tienam  ☐ Vancomycin

Dr. TL Que
Consultant Microbiologist, Chairman of Antibiotic Stewardship Team
Savings Calculations

* First Year Reduction of Total Antibacterial Expenditure
  = \[\frac{\text{Total Antibacterial Expenditure (Nov 04-Oct 05)}}{\text{Total Bedday (Nov 04–Oct 05)}} - \frac{\text{Total Antibacterial Expenditure (Nov 03-Oct 04)}}{\text{Total Bedday (Nov 03–Oct 04)}}\] \times \text{Total Bedday (Nov 04-Oct 05)}

# Second Year Reduction of Total Antibacterial Expenditure
  = \[\frac{\text{Total Antibacterial Expenditure (Nov 05-Oct 06)}}{\text{Total Bedday (Nov 05–Oct 06)}} - \frac{\text{Total Antibacterial Expenditure (Nov 03-Oct 04)}}{\text{Total Bedday (Nov 03–Oct 04)}}\] \times \text{Total Bedday (Nov 05-Oct 06)}