Setting the Scene:
The Global Picture of Antibiotic Resistance

Otto Cars
Chairman
ReAct – Action on Antibiotic Resistance
Antibiotics revolutionised medicine

US, 1950’s:
The introduction of penicillin increased the chance of survival from ~25% to 85%

Pneumonia with bacteria in blood

Antibiotic resistance is now turning back the clock

Severe neonatal infections caused by multi-resistant Gram-negative bacteria

Tanzania, 2000’s:
Antibiotic resistance decreased the rate of survival from ~ 70% to 20%

Adapted from Blomberg, BMC Infect Dis 2007
Inadequate Antibiotic Treatment of Infections
A Risk Factor for Hospital Mortality Among Critically Ill Patients

Prospective study on 655 patients in intensive care with infections

- Inadequate antimicrobial therapy
  - 22.5% of patients
  - Mortality 42%

- Adequate antimicrobial therapy
  - Mortality 17.7%

From Kollef et al. Chest, 2000
- In the EU, **25 000 patients die** from selected multidrug resistant bacteria annually

- These deaths result in extra health-care costs and productivity losses of **at least EURO 1.5 billion per year**

  (ECDC/EMEA /ReAct joint technical report: The bacterial challenge: time to ReAct)

- Antibiotic-resistant infections cost the U.S. healthcare system **an excess of $20 billion annually**

- These avoidable infections result in more than **8 million additional days** spent in the hospital

  (Extrapolations based on Roberts et al CID 2009)
Modern medicine is built on access to effective antibiotics.....
ANTIBIOTICS

- Major surgery
- Care of preterm babies
- Cancer chemotherapy
- Organ transplants

Intensive care
How did we end up here?
“It is not difficult to make microbes resistant to penicillin …

…. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.”

*Alexander Fleming’s Nobel Lecture, 1945*
The misuse of a miracle
Antibiotic sales without prescription in the EU

Athens, Greece 2008 (174 pharmacies)
2008:

- 100% of all visited pharmacies sold Amoxicillin/clavulanate acid OTC
- 53% sold Ciprofloxacin OTC, despite extra restrictions for fluoroquinolone prescriptions

Plachouras et al. Euro Surveill. 2010
70 years of antibiotic use....
We have wasted a precious resource by not rendering antibiotics the respect they deserve

Duration of cough after physician visit until patient is feeling better

From Little, JAMA 2005;293:3029-3035
ESBL (CTX-M) producing *Enterobacteriaceae*

2001-2002

2007

Endemicity

Sporadic reports
Clonal outbreak of multiresistant *Klebsiella pneumoniae*, Uppsala University Hospital
## Antibiotic susceptibility proportions for NDM-1-positive Enterobacteriaceae isolated in the UK and India

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>UK (n=37)</th>
<th>Chennai (n=44)</th>
<th>Haryana (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipenem</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Meropenem</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Piperacillin-taz</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Cefpirome</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>11%</td>
<td>0%</td>
<td>8%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>8%</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Amikacin</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Minocycline</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>64%</td>
<td>56%</td>
<td>67%</td>
</tr>
<tr>
<td>Colistin</td>
<td>89%</td>
<td>94%</td>
<td>100%</td>
</tr>
</tbody>
</table>

From Kumarasamy et al. Lancet Infect Dis 2010
Introduction of New Antibiotic Classes

- Sulphonamides
- Penicillins
- Aminoglycosides
- Macrolides
- Glycopeptides
- Tetracyclines
- Chloramphenicol
- Lincosamides
- Quinolones
- Streptogramins
- Trimethoprim

Timeline:
- 1930’s
- 1940’s
- 1950’s
- 1960’s
- 1970’s
- 1980’s
- 1990’s
- 2000’s

New classes:
- Oxazolidinones
- Lipopeptides
We are facing a threat to public health security

Antibiotic Resistance

Drug Development

Morbidity
Mortality
Costs
Confidence
The challenge
Bridging the gap between science and policy

Number of articles in the medical database Pub-MED
(Antibiotic or antibacterial+ resistance) per 5 years period
FIFTY-EIGHTH WORLD HEALTH ASSEMBLY

WHAS.27

Agenda item 13.10

25 May 2005

Improving the containment of antimicrobial resistance

The Fifty-eighth World Health Assembly,

Having considered the report on rational use of medicines by prescribers and patients;

Acknowledging that the containment of antimicrobial resistance is a prerequisite for attaining several of the internationally agreed health-related goals contained in the United Nations Millennium Declaration;

Recalling the recommendations of the Second International Conference on Improving Use of Medicines (Chiang Mai, Thailand, 2004);

Recalling also the findings of relevant WHO reports, including “Priority medicines for Europe and the world” 1 and the Copenhagen Recommendations from the European Union conference on “The Microbial Threat” (Copenhagen, 1998);

Aware that the spread of antimicrobial resistance recognizes no national boundaries and has reached proportions that require urgent action at national, regional and global levels, especially in view of the increasing development of new antimicrobial agents;

Recalling previous resolutions WHA48.27 and WHA47.11 on the rational use of drugs, WHA51.17 on antimicrobial resistance, and WHA54.14 on global health security;

Recognizing the efforts of WHO in collaboration with governments, universities, the private sector and non-governmental organizations to combat antimicrobial resistance, thereby contributing to prevention of the spread of infectious diseases;

Noting, however, despite some progress, the strategy for containment of antimicrobial resistance has not been widely implemented; 2

Wishing to encourage efforts to contain antimicrobial resistance and to promote rational use of antimicrobial agents by providers and consumers in order to improve global health security;

1 Document WHA48.27
2 Document WHA47.11
Antibiotic Resistance - a collective failure of

- public policy & global governance

- research prioritization

- the current market system
The Global Need for Effective Antibiotics
- moving towards concerted action

September 6–8, 2010 Uppsala, Sweden