Penicillin increased the chance of survival from 10% to 90%
Antibiotic resistance -
The extent of the problem

- Infections by multidrug-resistant bacteria are in the EU associated with 25,000 extra deaths per year.

- These infections cost about 1.5 billion Euros of extra economic burden per year.

- There are many reasons to believe that these figures correspond to an underestimate of the human and economic burden.
Modern medicine is built on access to effective antibiotics

- Hip replacement
- Organ transplants
- Cancer chemotherapy
- Care of preterm babies
Orphanage in Bamako, Mali
ESBL colonized 100% of the children and 63%, of the adult staff studied.

Mumhibili hospital, Tanzania
The mortality rate from Gram-negative bloodstream infection was 43 %, more than double that of malaria.
Blomberg et al. BMC Infect Dis. 2007 May 22;7:43.
Third-generation cephalosporin-resistant *Escherichia coli*, blood and CSF, 2008

- **<1%**
- **1–5%**
- **5–10%**
- **10–25%**
- **25–50%**
- **>50%**
- **No data/low number**
- **Other countries**

Country with:

- **↑** Significant increase (2005-2008)
- **↓** Significant decrease (2005-2008)

Source: European Antimicrobial Resistance Surveillance System (EARSS), 2009
# 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
Antibiotic resistance: The causes

• The indiscriminate effects of antibiotics

• The indiscriminate use of antibiotics

• The rapid dynamics of gene transfer between bacteria and the global spread of resistance

• Poor sanitation and hygiene

• Alarming decline in drug development
Illegal OTC antibiotic sale 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
Strategies to stop **manage** antibiotic resistance

Prolong the lifespan of existing drugs
   *Rational Use, Optimization of dosage, Better diagnostics*

Prevent the spread of **resistant** bacteria
   *Improved hygiene, Infection control, Hospital structure*

Development of new antibiotics
Antibacterials in the Pipeline

New Molecular Entities Publicly Disclosed in R&D Programs of the World’s 15 Largest Pharmaceutical Companies

90.2% Other drugs
1.6% Antibacterials
8.2% Other Anti-Infectives

Adapted from Spellberg, 2004
New antibiotic approvals in decline

Ref: http://www.idssociety.org/10x20.htm
Pipeline Analysis

90 agents with direct activity on multidrug-resistant bacteria

66 agents were new active substances

15 “novel” agents with systemic administration
The pipeline is empty!
Innovative Incentives for Effective Antibacterials

Council Conclusions on innovative incentives for effective antibiotics
2986th EMPLOYMENT, SOCIAL POLICY, HEALTH AND CONSUMER AFFAIRS Council meeting
Brussels, 1 December 2009

The Council adopted the following conclusions:

Note: In this document, the term "antibiotics" encompasses medicinal products produced either synthetically or naturally used to kill or inhibit the growth of bacteria as well as those with alternative mechanisms of action e.g. effect on bacterial virulence. In this context, alternative methods for prevention and control of infections should also be taken into account.

2. RECALLS the Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine.
3. RECALLS the Council Conclusions on antimicrobial resistance of 10 June 2008.
4. RECALLS the Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections.

Press

Rue de la Loi 175 B - 1040 BRUSSELS Tel.: +32 (0)2 281 8289 / 8318 Fax.: +32 (0)2 281 8826 press.office@conclaves.europa.eu http://www.conclaves.europa.eu/
ReAct and Uppsala University hosted the conference “The Global Need for Effective Antibiotics” in 2010
Some causes for lack of antibiotic innovation

- **Return of Investment** is much safer from medicines for treatment of chronic diseases
  - antibiotics given in short courses
  - new products must be conserved
- **Pharma industry consolidation** - fewer people in fewer companies doing antibiotic research
- **Highly genericised market** – overall price is low
- **Clinical drug development costly** for antibiotics
- **Inevitability of resistance** limits antibiotic lifespan – limits duration in market place
- **Unclear regulatory demands** on antibiotics – creates uncertainty
- **Major scientific challenges**
There have been numerous initiatives to promote action to stimulate R&D for novel antibiotics in the US....
In the EU.....
Establishment of a transatlantic taskforce on urgent antimicrobial resistance issues
Agreed at the EU-US Summit on the 3rd of November. The task force is to focus on appropriate therapeutic use of antimicrobial drugs in the medical and veterinary communities, prevention of both healthcare- and community-associated drug-resistant infections, and strategies for improving the pipeline of new antimicrobial drugs.
A new business model must be built on the **global needs** and secure **access and affordability** as well as rational use.
The solution: collaboration for innovation

New Antibiotics

Civil society
Pharm. industry
Academia
WHO

DG Enterprise
DG Research
DG SANCO

Regulatory agencies
National Govt’s