Strategies on Control of MDRO in Europe

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Outline

• Problems of antibiotic (ab)use and resistance in Europe
• Towards a European antibiotic policy
  - First steps
  - Member States initiatives
• National and European campaigns
  - On prudent antibiotic use
  - On hand hygiene in hospitals
• Towards a Global policy
  - Transatlantic Task Force for Antimicrobial Resistance (TATFAR)
  - World Health Day, April 7th 2011
“If you cannot measure it, you cannot improve it”

Lord Kelvin, 1824-1907
ESAC: European Surveillance of Antimicrobial Consumption

- Launched in November 2001 (Belgian EU Presidency)
- ESAC is an international network of surveillance systems, aiming to maintain a continuous, comprehensive and comparable database on antimicrobial consumption for all Member States, candidate countries and EFTA-EEA countries
- Coordinator: Herman Goossens (UA)
- Transfer to ECDC (Stockholm) in July 2011

http://www.esac.ua.ac.be
Total outpatient antibiotic use in DID in 31 European countries in 2009

* Total care : LT, CY
  MT : 2008 data

Source: ESAC
No statistical Differences in Recovery between those Prescribed Antibiotics and Those Not Prescribed Antibiotics CA-LRTI (survival analysis)

Butler et al., BMJ 2009
Correlation Between Penicillin Use and Prevalence of Penicillin-resistant S. pneumoniae

Consumption of Penicillin (J01C) in DID, AC 2000

<table>
<thead>
<tr>
<th>Organism year of isolation [source of information]</th>
<th>Antibiotic resistance</th>
<th>Antibiotic use - ATC group (year of data)</th>
<th>No. of countries</th>
<th>Spearman correlation (r) (confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae 2001 [7]</td>
<td>Penicillin</td>
<td>Penicillin – J01C (2000)</td>
<td>19</td>
<td>0.84 (0.62-0.94)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Goossens et al., Lancet 2005; 365: 579-87
**MAIN FINDINGS**

- Mean pre-antibiotic (Day 0) carriage of macrolide-resistant streptococci was 28%.

- Use of both macrolides resulted in a huge increase in resistant streptococci, which persisted for at least 6 months ($P \leq 0.01$).

- In the azithromycin group, resistance remained at a higher level than in the clarithromycin group during mid-time points ($P \leq 0.001$).

**E. coli**: Proportion of Invasive FQ Resistant Isolates, 2009

Source: EARS-Net 2010

The symbols **↑** and **↓** indicate a significant increasing or decreasing trend for the period 2006-2009.
**K.pneumoniae: Proportion of Invasive Cephalo-3 Resistant Isolates, 2009**

The symbols ↗ and ↘ indicate a significant increasing or decreasing trend for the period 2006-2009.

Source: EARS-Net 2010
K. pneumoniae: Proportion of Invasive Carbapenem Resistant Isolates, 2009

Source: EARS-Net 2010
Emergence of NDM-1 Producing *Enterobacteriaceae* in Europe

- ECDC conducted a questionnaire survey in all EU Member States, Iceland and Norway.
- By 4 October 2010, a total of 77 cases were reported from 13 countries in 2008-2010.

Struelens M et al, Euro Surveill, November 2010
### Survey Results on ICU Patients Infected with Resistant Bacteria

**Gram-positive bacteria**
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-resistant *Enterococcus spp.* (VRE)
- Penicillin-resistant *Streptococcus pneumoniae* (PRSP)
- Vancomycin-resistant/intermediate *S. aureus* (VRSA/VISA)

**Gram-negative bacteria**
- Third-generation cephalosporin-resistant *Enterobacteriaceae*
- Carbapenem-resistant *Pseudomonas aeruginosa*
- Carbapenem-resistant *Acinetobacter spp.*
- Carbapenem-resistant *Enterobacteriaceae*

**Bacteria totally or almost totally resistant to available antibiotics**

![Bar chart showing percentage of respondents](chart.png)

*Note: The bar chart shows the percentage of respondents who reported various levels of infection with different types of resistant bacteria.*

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Lepape A & Monnet DL, Euro Surveill, November 2009
Prevalence of HAI by Hospital

Mean prevalence: 7% [0%-23%]

Hospital number

% patients with HAI

0%
5%
10%
15%
20%
25%
Prevalence of AM Use by Hospital

Mean: 38% [2% – 100%]
Net: 35%
Society’s Failure

• Antibiotic sales in the community represent > 90% of all antibiotic use and is, therefore, an important component in the selection pressure.

• The largest use of these antibiotics is towards minor respiratory tract infections which are often self-limiting and self-healing and for which AB real usefulness is dubious
  - pharyngitis
  - bronchitis
  - flu-like syndrome, ... 

• Antibiotic use will select for antibiotic resistance
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First Steps Towards a European Antibiotic Policy


- September 1998: EU Conference on the Microbial Threat, Copenhagen & “Copenhagen Recommendations”
  [http://www.im.dk/publikationer/micro98/index.htm](http://www.im.dk/publikationer/micro98/index.htm)

- May 1999: “Opinion of the Scientific Steering Committee on Antimicrobial Resistance”

Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections (2009/C 151/01)
Country Visits Organised by ECDC to Discuss Implementation of Council Recommendations, 2006-2011

Country visits to discuss AMR issues (as of February 2011)

Based on Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC)

Reports (observations, conclusions, suggestions, examples of best practice)

14 initial visits (see map)
5 follow-up visits (Czech Rep., Greece x 2 and Hungary x 2)
5 visits budgeted for 2011
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Belgian National Public Campaigns

- **When:** since November 2000, annually during winter season
- **Organised by:** BAPCOC (Belgian Antibiotic Policy Coordination Committee)
- **Budget:**
  - 400,000 EUR/annual campaign
- **Interventions targeting the public:**
  - Ads on TV, radio and newspaper
  - Information booklets
  - Folders
  - Posters
  - Internet campaigns: www.antibiotics-info.be
BAPCOC Organised
Three Different Awareness Campaigns

2000 – 2003 (3 winters)

2004 – 2008 (4 winters)

2008 – … (launched 18.11.08)
OPGELET: ALLEEN GEBRUIKEN INDEN NODIG.
ANTIBIOTICA HEBBEN GEEN ZIN BI GRIEP, BRONCHITIS OF EEN VERKOUHDEIH.

BAAT HET MET, DAN SCHRAAT HET WIL

Tijgsussen
Kinderen zijn vaak te vroeg opgemaakt. Vermijd daardoor een patiënt die (in elke geval) wordt opgezet. Genoemde antibiotica hebben weinig effect op een patiënt die al op zijn eigen weeg is. Kinderen hebben des te meer sensibiliteit voor antibiotica en sensibiliteit is een belangrijk criterium bij de keuze van antibiotica.

Wanneer zijn antibiotica des te nodig?

Infecties zoals grijp, bronchitis of een verkoudeih genoemd sportaan.

Vind ik niet nodig
Kinderen met ademhalingsproblemen zoals grijp of bronchitis hebben weinig sensibiliteit voor antibiotica. Kinderen met ademhalingsproblemen hebben weinig sensibiliteit voor antibiotica.

WAT IS RESISTENTIE?
Kinderen met ademhalingsproblemen zoals grijp of bronchitis hebben weinig sensibiliteit voor antibiotica. Kinderen met ademhalingsproblemen hebben weinig sensibiliteit voor antibiotica.

BELANGRIJK: GEbruik antibiotica AAN DEZALEN
Als je voor een infectie antibiotica gebruikt, is het belangrijk dat je de juiste dosering en het juiste type antibiotica gebruikt. Kinderen met ademhalingsproblemen hebben weinig sensibiliteit voor antibiotica. Kinderen met ademhalingsproblemen hebben weinig sensibiliteit voor antibiotica.
OPGELET:
ALLEEN GEBRUIKEN INDEN NODIG

Gebruik antibiotica alleen als het nodig is
www.gebruik.nl/epidemiologie/epidemiologie.html

18 November
Eerste Nationale Reef

10.30 uur eindredactie
Belgian Campaigns 2002-2010
Outpatient antibiotic use in Belgium in packages per 1,000 inhabitants per day – July - June
Belgian Campaigns 2002-2007
Outpatient antibiotic Use in Belgium in EUR,
January - December

State
Patients

EUR, million

Antibiotic Resistance of *S. pneumoniae* in Belgium 1985 - 2009

National Reference Centre *S. pneumoniae* (University Leuven)
French Awareness Campaigns

- **When:** since November 2002, annually during winter season
- **Organised by:** French Social Insurance System
- **Budget:**
  - 4 million EUR/annual campaign
- **Interventions targeting the public:**
  - Ads on TV, radio and newspaper
  - Information leaflets
  - Folders
  - Travelling exhibition around France
  - Internet campaigns:
    - www.antibiotiquespasautomatiques.com
French Campaigns 2002-2007
Outpatient antibiotic use in France in prescriptions per inhabitant – October to March

Sabuncu et al., PloS Medicine; June 2009
Antibiotic Use by Age Group in France

Conclusions

• National public campaigns have been very successful to reduce antibiotic use and resistance in Belgium and France
• Huge cost savings: for 1 € invested, about 8 were saved
  • Belgium: 250 million EUR 2000-2010
  • France: 845 million EUR 2002-2010
• Decrease of antibiotic use amplified by the effect of the 7 valent conjugated pneumococcal vaccine
• In both countries actions were also directed towards the prescribers:
  - academic detailing
  - distribution of guidelines
  - individual feedback of antibiotic prescriptions
  - promotion of streptococcal antigen tests (only France)

The burden of antibiotic resistance warrants a multifaceted approach
18 November 2008

EUROPEAN ANTIBIOTIC AWARENESS DAY

A European Health Initiative
• Establishment of Technical Advisory Committee (national experts, Commission, WHO EURO, CPME, ESCMID)
• Focus on awareness raising amongst general public about not using antibiotics when not necessary, e.g. for colds and flu
• Based on successful national campaigns (Belgium and France)
COLD? FLU?
TAKE CARE
NOT ANTIBIOTICS

A European Health Initiative

COLD? FLU?
GET WELL
WITHOUT ANTIBIOTICS

COLD? FLU?
TAKE CARE
NOT ANTIBIOTICS

A European Health Initiative
Images from National Campaigns on Prudent Use of Antibiotics
Images from National Campaigns: Belgium, Cyprus, Poland, England, Luxembourg, Greece
EAAD, 2008-2011

2008
Materials for general public
32 countries participated

2009
- Article in Eurosurveillance
- Materials for primary care prescribers
- Website translated in all EU languages, three TV spots developed
- 34 countries participated

2010
- 36 countries participated
- Materials for hospital prescribers
- Matched Get Smart week in the United States and the campaign in Canada

Toolkit for Hospital Prescribers

Advertorial
Fact sheet
Check list
PPT Presentation
Screen saver

Web banner
**EAAD 2010**

**Media coverage**

- **Key Figures**
  - Number of clippings: 476
  - Reach (print): 51,334,208
  - Circulation (print): 17,152,770
  - Visits (online): 54,241,600

- **Media Type**
  - Print: 49%
  - Online: 47%
  - Newsagency: 4%
  - Local: 33%
  - Regional: 17%
  - National: 2%
  - International: 41%

- **Peak Week 46**

- **Coverage in the Course of Time**
Antibiotics kill viruses. True or false? % respondents with correct answer (i.e., “false”): 36% (range: 14 – 73%)
Why is the EAAD so successful?

- Strong upfront political support and commitment at European and national level;
- Planning well ahead;
- Building on existing success stories of countries;
- Early establishment of a Technical Advisory Committee with dedicated experts;
- Briefing of national communications contact points prior to the campaign and sharing contact information;
- Initiation of a broad stakeholder contact programme to inform interest groups and invite contributions;
- Good support from professional organisations,
- Development of campaign key messages and visuals with the support of experts in social marketing.
FIRST GLOBAL PATIENT SAFETY CHALLENGE

To reduce health care-associated infections

**Hand hygiene as the cornerstone**
“The 5 Moments of Hand Hygiene”

1. Before touching a patient
2. Before clean / aseptic procedure
3. After body fluid exposure risk
4. After touching a patient
5. After touching patient surroundings

Sax et al, J Hosp Infect 2007;67:9-21
Hygiène des mains

Quand ?

Les 5 indications

1. AVANT contact patient
   Avant tout contact direct avec un patient
   Un contact social court (par ex. serrer la main) est probablement associé à un risque de transmission moindre

2. APRES contact patient
   En quittant un patient après un ou des contacts directs

3. AVANT acte propre/invasif
   Immédiatement avant un sein propre
   Immédiatement avant un geste invasif

4. APRES exposition aux liquides biologiques
   Après un acte comportant un risque d'exposition à des liquides biologiques qui normalement s'anticipe par le port de gants

5. APRES contact avec l'environnement du patient
   En cas de souillures visibles, se laver les mains, les sécher puis les désinfecter avec la solution hydro-alcoolique

Conformément aux programmes de l'ICU et de CES

Une initiative du Service Public Fédéral Santé Publique Sécurité de la Chaîne Alimentaire et Environnement / Réalisation Plate-forme Fédérale pour l'hygiène / Hôpital, AP-HP, SICS, MMXY, IP / Avec le soutien de BAPDC et de la Direction générale Organisation des Établissements de santé.
Methodology

Nation-wide campaign:

- **2004**: preparation of first campaign by working group of federal platform of hospital hygiene with the financial support of the ministry of Health

- **Objective**: Raising awareness on good hand hygiene practices and promote use of alcohol handrubs

- **Target population**:
  - HCW having contact with patients in hospitals
  - And hospitalised **patients**
  - In acute, chronic and psychiatric hospitals
Methodology: Two components

1. **Awareness campaign** with standardised material to improve Hand Hygiene compliance distributed to participating institutions

2. **Measuring** impact of the campaign
   - Hand Hygiene compliance (soap and/or alcohol / Hand Hygiene opportunities)
   - Alcohol rub consumption (liters alcohol rub / 10,000 patient days)
   - Respect of basic hygiene conditions (optional, only 3rd campaign)
Planning of Campaigns

- **First campaign:** 2005
- **Second campaign:** 2006-2007
- **Third campaign:** 2008-2009
- **Fourth campaign:** 2010-2011

1. **During 1 month**
   - Invitation to participate

2. **1 month later and for 1 month**
   - Measurement of Hand Hygiene indicators

3. **1 month later and for 1 month**
   - Awareness Campaign + press conference

4. **9 months later campaign**
   - Measurement of Hand Hygiene indicators

5. **Post-campaign**
   - National Feedback session
Awareness Campaigns: Multi Modal

• Reminders (posters) in accordance with the WHO guidelines
• Education of Healthcare workers
  - Standardised powerpoint presentation
  - Interactive quiz
• Distribution of gadgets for Healthcare workers or patients
• Promotion of hand rub (posters, black light)
• Implication of patients (leaflets, gadget)
• Feedback of measurement results before and after campaign
Campaign Messages and Targets Varied!

- **First campaign:**
  - Hand hygiene, just do it … and with alcohol rubs

- **Second campaign:**
  - Hand hygiene, do it correctly

- **Third campaign:**
  - Do not wear jewellery or artificial nails and keep your nails clean
  - Use gloves correctly

- **Fourth campaign:**
  - Patient empowerment: “Did you disinfect your hands” to increase the compliance before patient contact and to try to exceed the 70% compliance after campaign
### Distribution of Average Hand Hygiene Compliance

<table>
<thead>
<tr>
<th>Campaign Year</th>
<th>N hop</th>
<th>Before Campaign</th>
<th>After Campaign</th>
<th>Compliance HH (%)</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st campaign (2005)</td>
<td>n=148</td>
<td>48%</td>
<td>68%</td>
<td>+20%</td>
<td></td>
</tr>
<tr>
<td>2nd campaign (2006)</td>
<td>n=127</td>
<td>48%</td>
<td>69%</td>
<td>+16%</td>
<td></td>
</tr>
<tr>
<td>3rd campaign (2008)</td>
<td>n=178</td>
<td>48%</td>
<td>69%</td>
<td>+11%</td>
<td></td>
</tr>
</tbody>
</table>
MRSA in Belgian acute care hospitals:
proportion of *S. aureus* clinical isolates and incidence of nosocomial acquisition

1994 - 2009

Source: National surveillance, B. Jans
Mean of rates in cohort of hospitals with min. 5 participations since 1994
Conclusion: Campaigns Were Successful

- High participation rate
- Increase of Hand Hygiene compliance at short and long term
- Alcohol rub widely used

➔ Key factors for success:
  - Multi modal awareness campaign
  - Repetition of campaign
  - National implication
  - Political and financial support
Counts of MRSA Bacteraemia
Oct 2005 to June 2009

A. Pearson and colleagues (HPA, Sept 2009)
Estimated average procurement of Alcohol Hand Rub and Liquid Soap in mls per bed-day July 2004-December 2007 in 148 acute NHS Trusts

- 3-fold increase in combined use to 60 mls per pt-day
- Analysis shows highly significant association between each ml of AHR used and 1% drop fall in MRSA BSI

Stone S et al. ECCMID 2009 (abstract O140)
% MRSA and incidence per 100 admissions or 1000 days of hospitalisation.
Univ. hospitals of Paris (n=39) 1993-2007

V. Jarlier, D. Trystram 2008
Many Success Stories in Europe: MRSA Bacteraemia Trends in Europe, 2007

Country code (average number of isolates reported per year) & year of start surveillance

% MRSA


Courtesy: Grundmann et al. (EARSS)
Expert-Proposed European Strategies to Monitor and control Infection, Antibiotic Use and Resistance in Health-care Facilities

- Initiate or continue hand hygiene campaigns and use hand hygiene as a quality indicator
- Collection and monitoring of structure-of-care quality indicators and indicators of good practice (e.g. consumption of alcohol solution)
- ECDC Point Prevalence Surveys on HAI and AB Use (completed in all Member States by November 2012; repeated at least once every 5 years)
- National LTCF resident safety programmes, external audits of LTCF and monitoring

Goossens, Lancet Infect Dis 2011, April 7th
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The EU-US Summit Declaration called for the establishment of “...a transatlantic task force on urgent antimicrobial resistance issues focused 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, which could be better addressed by intensified cooperation between us”.
Organisations - US

United States Department of Health and Human Services:

- Office of Global Health Affairs (OGHA)
- Centers for Disease Control and Prevention (CDC)
- Food and Drug Administration (FDA)
- National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID/NIH)
Organisations - EU

**European Commission:**
EC-Directorate General for Health and Consumers
EC-Directorate General for Research
European Centre for Disease Prevention and Control (ECDC)
European Medicines Agency (EMA)
European Food Safety Authority (EFSA)

**Council of the European Union:**
Represented by the TRIO Presidency (Spain, Belgium, Hungary)
The expected outcome of the TATFAR is a review of ongoing and planned activities and a proposal with suggestions for areas of future collaboration between the EU and the US.

**September**
Launch of EU interaction with third parties based on Commission website consultation

**December**
Interim draft reports from working groups (including input from public consultations)

**31 March**
Final report

**2010**
- June
  TATFAR face to face meeting, US
- October - November
  U.S. stakeholder meeting

**2011**
- January
  Final draft reports from working groups
- March
  Face to face meeting, EU
And Now....
World Health Day, 7 April, 2011

COMBAT DRUG RESISTANCE

No action today, no cure tomorrow
Conclusion

“We have watched too passively as the treasury of drugs that has served us well has been stripped of its value. We urge our colleagues worldwide to take responsibility for the protection of this precious resource. There is no longer time for silence and complacency”.

Acknowledgement

Anne Simon and many other colleagues of the Belgian Antibiotic Policy Coordination Committee (BAPCOC)
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Dominique Monnet and Sarah Earnshaw of ECDC, Stockholm