Use of Antimicrobials and Antimicrobial Resistance – WHO initiatives on Risk Assessment and Surveillance

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Antimicrobial resistance: a public Health concern

- Antimicrobials are essential drugs for treatment of infectious diseases in Human and Animals, and must be preserved.
- Discovery of antibiotics is one of the most important achievements of the 20th century.
- Resistance has developed soon after and new drugs has been developed to replace older ones as resistance emerged...
- BUT today, Resistance is emerging and spreading faster than new drugs are being developed;
- AMR a priority for WHO and was the topic of World Health Day 2011 on April 7th 2011.
COMBAT DRUG RESISTANCE

No action today, no cure tomorrow

7 APRIL 2011 WORLD HEALTH DAY

World Health Organization
Why AMR is a global concern?

- Antimicrobial resistance (AMR) kills
- Challenges care and control of infectious diseases
- Greatly increases care costs
- Threatens a return to the pre-antibiotic era
- Jeopardizes healthcare gains for individuals and society
- Compromises health security, damages trade and economy
Highly resistant *Escherichia coli*

Proportion of invasive isolates with resistance to fluoroquinolones in 2009

Proportion of 3\textsuperscript{rd} generation cephalosporins resistant isolates in 2009

Source: ECDC, Antimicrobial resistance surveillance in Europe 2009
Distribution of NDM-1 producing *Enterobacteriaceae* strains

*Strains in Bangladesh, India, Pakistan and UK*

Source: Lancet ID, 2010
What drives AMR?

- Plans and resources not comprehensive or coherent; poor accountability
- Consumers and communities not engaged
- Surveillance systems weak or absent
- Systems for ensuring quality and supply of medicines inadequate
- Use of medicines inappropriate and irrational, including in animal husbandry
- Infection prevention and control poor
- Antimicrobials and diagnostics arsenal limited
- Research and development for diagnostics and medicines insufficient
Global policy response to AMR

  - Surveillance systems and response strategies being pursued
  - Task Force and informal network at global and regional levels

- Regional Action: WHO Regional Committee Resolutions (e.g. AFRO, PAHO, SEARO)

- Political will: World Health Assembly Resolutions
  - 1998 – Emerging and other communicable diseases AMR
  - 2005 – Improving the containment of AMR
  - 2009 – Prevention and control of MDR-TB and XDR-TB

Despite progress, strategies for AMR containment have not been widely implemented
AMR: What is blocking progress?

- Complex problem requiring a comprehensive response among and between Member States across different sectors

- Actions needed are clear – but there is a failure of commitment, implementation and accountability

- Preventing AMR is a "public good" which strengthens health security – but financing is insufficient
WHD 2011: What did we achieve?

- **Goal:**
  
  To save lives and protect health by keeping precious, lifesaving medicines effective and useful to combat disease

- **Aims:**
  
  To raise awareness on what drives AMR
  
  To build commitment for effective policies and practices and their implementation to combat AMR

- **Objectives:**
  
  To introduce a Policy Package for Member States focused on six top priority actions to combat AMR
  
  To reach and engage key stakeholders through innovative communications, advocacy and events
  
  To promote further collaboration across sectors and among stakeholders
WHD 2011 will lead to

- Coherent statement of commitment across stakeholders and by key constituencies
- Comprehensive, financed national plans and clearer accountability lines
- New national, regional and global initiatives, such as collaboration across AMR surveillance networks
- Coordinated NGO action
- Sustained information campaigns
- Incentives for more R&D for new diagnostics and medicines
WHO Initiatives on AMR use in food-producing animals and Antimicrobial Resistance
AMR and Animal Husbandry

- Widespread use of antimicrobials in livestock production … not only from therapeutic purposes

- Same classes of antimicrobials are used both in humans and food-producing animals…

- Food is generally considered to be the most important vector for spread of resistance between humans and animals

- Globalization of food trade, need for international action
1998 WHA Resolution

WHA 51.17

- Concerned by the extensive use of antibiotics in food production, which may further accelerate the development of antimicrobial resistance rendering treatment ineffective,

- the World Health Assembly urges Member States

  • to develop programs for monitoring and containment of antimicrobial resistance

  • to take measures to encourage the reduced use of antimicrobials in food-animal production
AMR and the Food Chain = AMU in the Food Chain

- In Food Animal Production
  - Terrestrial animal
  - Aquaculture

- In Horticulture
  - Plant production

Others: Environment, Waste management….One Health!
Use of Antimicrobials in one ecosystem or geographic area can lead to resistance in another ecosystem or geographic area.
One Health
it all goes around, and around, and around
International activities on AMR
What has happened over the 2 decades

- Scientific agreement – enabling all schools of thought
  - Call for experts, call for data

- Partner participation
  - Farm-to-Fork

- Stakeholder participation
  - All parties have a voice

- Separating assessment and management
Addressing the public health impact of use of antimicrobials in food-producing animals - WHO Achievements 1990-2011

- International collaboration established
  - Codex, FAO, OIE, WHO

- 18+ expert meetings and consultations

- Codex Ad Hoc Intergovernmental task Force on Antimicrobial resistance (2007-2010)

- WHO list of Critically Important Antimicrobials for Human Heath developed

- Establishment of an Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)

- WHD 2011 : Joint WHO and OIE Call for reduction of use of AMU in Animal Husbandry
Antibiotic Resistance in people
Are Food-Producing Animals involved?
Risk Assessment

- Berlin 1997: WHO Expert Meeting on The Medical Impact of Use of Antimicrobials in Food Producing Animals
Food as a source of antimicrobial resistance

- Resistant bacteria: *direct hazard*
  - Humans can be infected after food ingestion or handling
    - Zoonotic bacteria e.g. *Salmonella*, *Campylobacter*
    - Non-zoonotic bacteria e.g. *Shigella*, *Vibrio*

- Resistance genes: *indirect hazard*
  - Transfer of resistance genes from a resistant bacterium to a pathogenic bacterium, directly, or via another commensal
  - Mobile genetic elements harboring resistance determinants can readily be transferred horizontally between bacteria from terrestrial animals, fish and humans
    - Can also take place in natural environments
    - *E. coli* and *Enterococcus* spp.
Foodborne disease caused by resistant *Salmonella* well documented

- Through beef, pork, poultry, dairy products, eggs, fresh produce
- The most common resistances observed are typically to those antibiotics that are frequently used in animal husbandry
- Antibiotic use in animals selects for antibiotic resistant non-typhoid *Salmonella* serotypes
  - Transmitted to humans in food, or through direct contact with animals
  - ESBL resistant *Salmonella* from humans has been associated with ceftiofur use in poultry
Ceftiofur in ovo use and prevalence of ceftiofur resistance among retail chicken *Escherichia coli*, and retail chicken and human clinical *Salmonella enterica* serovar Heidelberg isolates during 2003–2008 in Québec, Canada

Resistant *Campylobacter*

- Food, in particular poultry meat, is considered the most common infection route for *Campylobacter*, including resistant strains.

- Resistance emergence and its increase in *Campylobacter* from animals and humans linked to the introduction of the antibiotic in food animal.

- *Campylobacter* from poultry meat is frequently resistant, in many countries also to fluoroquinolones.

- Concluded that:
  - There is clear evidence of adverse human health consequences due to resistant organisms resulting from use of antibiotics in food-producing animals
    - Increased number of infections, increased treatment failures, increased (in some cases death) severity of infections
    - The consequences of antimicrobial resistance are particularly severe when pathogens are resistant to antimicrobials critically important in humans

- Recommended that
  - An expert clinical medical group appointed by WHO define the antimicrobials that are considered critically important in humans
World Health Organization Ranking of Antimicrobials According to Their Importance in Human Medicine: A Critical Step for Developing Risk Management Strategies for the Use of Antimicrobials in Food Production Animals

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The use of antimicrobials in food animals creates an important source of antimicrobial-resistant bacteria that can spread to humans through the food supply. Improved management of the use of antimicrobials in food animals, particularly reducing the usage of those that are “critically important” for human medicine, is an important step toward preserving the benefits of antimicrobials for people. The World Health Organization has developed and applied criteria to rank antimicrobials according to their relative importance in human medicine. Clinicians, regulatory agencies, policy makers, and other stakeholders can use this ranking when developing risk management strategies for the use of antimicrobials in food production animals. The ranking allows stakeholders to focus risk management efforts on drugs used in food animals that are the most important to human medicine and, thus, need to be addressed most urgently, such as fluoroquinolones, macrolides, and third- and fourth-generation cephalosporins.
The expert panel pointed out that the development of this list is one part of a more comprehensive overall approach to the public health issues of antimicrobial resistance in both animals and humans.

The expert panel emphasized that there should be a sense of urgency to the development of such risk management strategies, particularly for quinolones, 3rd/4th generation cephalosporins and macrolides.
Summary on the importance of the animal reservoir

- Larger selective pressure

- Most important reservoir for antimicrobial resistant *Salmonella* and *Campylobacter*.

- An increasingly important reservoir for MRSA

- Important, but not quantified reservoir for E. coli

- Transferable genes
WHO Global strategy for Prevention and Control of Foodborne Antimicrobial Resistance

- National and international interdisciplinary cooperation

- Prudent use of antimicrobial agents in all sectors
  - Phase out use of antimicrobial agents for growth promotion
    - EU already banned all growth promoters as of January 1, 2006
  - A good regulatory system for approval and licensing
  - Prescription-only
  - Practitioners not having economic profit from prescription
  - Routine prophylactic use of antimicrobials should be never be used as a substitute for health management
  - Accurate diagnosis and antimicrobial susceptibility testing
  - Appropriate antimicrobial product and administration route

- Infection control
  - Successful disease control relies on a holistic approach encompassing hygiene, animal husbandry and management, nutrition, animal welfare, and vaccination
WHO Global strategy for Prevention and Control of Foodborne Antimicrobial Resistance-2

- Antimicrobials identified as critically important in human medicine (WHO, 1998, 2005, 2007) to be used in animals only if justified
  - Fluoroquinolones, 3 + 4 generation cephalosporins

- Monitoring of antimicrobial resistance and antimicrobial usage in human and animals
  - Useful information on prevalence and trends
  - Input for risk assessment and risk management
  - A basis for choosing, implementing and evaluating interventions
Integrating Surveillance Systems
AGISAR

A group of experts working in veterinary, food and public health disciplines advising WHO on ensuring globally containment of foodborne antimicrobial resistance through integrated surveillance of antimicrobial usage and antimicrobial resistance in the animal, food and human sectors.
Integrated surveillance a key element of AGISAR-AMR Containment strategy

- Documentation of the situation
- Identification of trends
- Input data for:
  - Establishing associations antimicrobial usage and antimicrobial resistance
  - Risk assessment
  - Evaluation of effectiveness of interventions
- Identify need for interventions
- Basis for focused and targeted research
- Basis for communication
Outputs of AGISAR Meetings
- Annual Meeting Report
- WHO List of Critically Important Antimicrobials for Human Medicine (revised version every 2 years)


Copenhagen, 15 - 19 June 2009

Part 1: 3rd Edition WHO List of Critically Important Antimicrobials

Part 2: Strategic Framework for WHO Activities on Integrated Surveillance of Antimicrobial Resistance

Critically Important Antimicrobials for Human Medicine

3rd Edition

World Health Organization
Conclusion

- A continuing problem… but urgent action needed.
- New challenges will arise, including food safety, trade issues
- Need harmonization of methods and reliable data on antimicrobial use and antimicrobial resistance (capacity building, pilot studies in developing countries)
- Need for holistic approaches
  - WHO-AGISAR
  - Proper prevention and control measures
- Basic and applied research
  - Mechanisms, trends and risk factors
  - New antimicrobials, alternatives to antimicrobials, vaccines
- Need for audacity in solutions – end unnecessary use!
AMR, a Global Threat to Public Health

- It challenges the control of infectious diseases, jeopardizes progress on health outcomes by increasing morbidity and mortality and imposes huge costs on societies.

- Irrational/inappropriate use in human and animal health and animal food chain has accelerated the emergence of AMR, and it has not been matched by development effective drugs.

- Elimination of inappropriate antimicrobial use is key!