Challenges and Successes in AMR Global Action Plan Implementation

Dr. Marc Sprenger, director AMR

14 September 2017
Canadian Academy of Health Sciences

Overview

1. Global Impact of AMR
2. Use of Antibiotics
3. WHO and the Global Action Plan
5. One Health
6. Moving Forward
AMR is the Greatest Threat to Modern Medicine

Antibiotic resistance is a global health crisis that should be addressed with the utmost urgency.

-Dr. Tedros Adhanom,
Director General
World Health Organization

AMR is the Greatest Threat to Modern Medicine

Profound health consequences
- Individuals, health systems, food systems, and practice of medicine

Economic and other intersectoral implications
- Development, agriculture, food, business, etc.

Long-term threat with no end in sight unless fundamental changes are made
AMR Over Time

Factors Contributing to AMR

Holmes et al., 2016
WB Projects the Global Implications of AMR

Focusing In: AMR in Thailand

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Focusing In: AMR in Thailand
Notified MDR-TB cases, 2014

- 123,000 pt MDR-TB detected & reported, 111,000 pt were started on second-line treatment
- 480,000 cases of MDR-TB estimated among TB patients

AMR and SDGs

- AMR strikes hardest on the poor
  → Rate of resistance is high
  → Lack of affordable treatment
  → Poor infection prevention
- Antibiotic residues from hospitals, pharmaceutical companies and agriculture contaminate the water
- Untreatable infections in animals threaten sustainable food production for our population
- Antimicrobials are fundamental components of all health systems
- It is crucial to balance access, innovation and conservation of antimicrobials to contain AMR

*Cumulative costs of AMR is predicted to be US $120 trillion by 2050

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Use of Antibiotics Is On The Rise

Total global antibiotics consumption increased 30%

Van Boechol et al. The Lancet Infectious Diseases 2014 14, 742-750 DOI: 10.1016/S1473-3099(14)00780-7
The More We Use Antibiotics, The More We Lose

From Albrich et al EID 2004

The More We Use Antibiotics, The More We Lose


JIACRA 2017 ECDC/EFSA/EMA
Antibiotic Consumption in Animals/Humans

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Global Action Plan Antimicrobial Resistance

Adopted by World Health Assembly in 2015

Recognized & supported by FAO (Resolution 4/2015) and OIE (Resolution 26) governing bodies in 2015

Bring AMR to UNGA!

Global Action Plan’s 5 Strategic Objectives

1. Improve awareness and understanding (WAAW & behaviour change)
2. Strengthen knowledge through surveillance & research (GLASS)
3. Reduce the incidence of infection (IPC)
4. Optimize the use of antimicrobial medicines (stewardship)
5. Ensure sustainable investment (R&D)
GAP Implementation

Objective 1: “Improve awareness and understanding of AMR through effective communication, education and training.”

A) World Antibiotic Awareness Week
B) Behaviour Change Group
C) Health Workforce Education

Antibiotics Consumption in Humans

(JACRA ECDC/EFSA/EMA, 2017)
Patient Pressure to Prescribe Antibiotics

Figure 4.15. The percentage of GPs who feel under pressure to prescribe antibiotics when not indicated, total and by Member State (as a percentage of all GPs; n = 518 GPs). (Source: ARNA GP survey.)

World Antibiotic Awareness Week

Annual campaign to educate the public and health professionals on AMR

13-19 November 2017
Behaviour Change Expert Group

Will provide guidance to WHO on best practices within behavior change

Health Workforce Education & AMR

Consultation on health workforce education in March 2017

Defined tools/resources needed to ensure health workers are educated and trained on AMR
Strengthening Educational Materials on AMR

New Materials Include

- Courses and educational materials in ALL regions
- In-service and pre-service training
- Focus on physicians and pharmacists

WHO is Leading

- Competency framework
- Curricula development
- Survey of health workers’ knowledge and attitudes

Academia are crucial

GAP Implementation

Objective 2: Strengthen the knowledge and evidence base through surveillance & research
Resistant Pathogens in SE Asia

<table>
<thead>
<tr>
<th>Organism</th>
<th>Resistance</th>
<th>National resistance data (%)</th>
<th>Published resistance data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>3rd generation cephalosporins</td>
<td>16.6%</td>
<td>15.8%</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolones</td>
<td>37.6%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>3rd generation cephalosporins</td>
<td>37.4%</td>
<td>5.4%</td>
</tr>
<tr>
<td></td>
<td>Carbenicillin</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Methicillin resistant</td>
<td>ß-lactams</td>
<td>10.3%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Staphylococcus aureus (MRSA)</td>
<td>Penicillin</td>
<td>47.8%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Non-typhoidal Salmonella</td>
<td>Fluoroquinolones</td>
<td>0.2%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Shigella sp</td>
<td>Fluoroquinolones</td>
<td>–</td>
<td>0.8%</td>
</tr>
<tr>
<td>Netericola meningitensa</td>
<td>3rd generation cephalosporins</td>
<td>0.5%</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

Source: WHO. Antimicrobial resistance: global report on surveillance. *Percentage of resistant isolates out of total isolates of bacteria that were analysed for antimicrobial susceptibility testing.

Shah et al., 2017

Surveillance of Human Pathogens

Global Antimicrobial Surveillance System (GLASS) - 43 countries
- IT platform: aggregated & individual data
- WHONET adapted for GLASS

Implementation package developed (with focus on LMICs)

Rapid alert portal being developed
GLASS Priorities

Table 2. Priority specimens and pathogens for surveillance of AMR.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Laboratory case definition</th>
<th>Surveillance type and sampling setting</th>
<th>Priority pathogens for surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Isolation of pathogens from blood*</td>
<td>Selected site or national coverage, continuous, Patients in hospital and in the community</td>
<td>E. coli, K. pneumonia, A. baumannii, E. aerogenes, S. pneumoniae, Salmonella spp.</td>
</tr>
<tr>
<td>Urine</td>
<td>Significant growth in urine specimen*</td>
<td>Selected site or national coverage, continuous, Patients in hospital and in the community</td>
<td>E. coli, K. pneumonia</td>
</tr>
<tr>
<td>Feces</td>
<td>Isolation of Salmonella spp. or Shigella spp. from stools</td>
<td>Selected site or national coverage, continuous, Patients in hospital and in the community</td>
<td>Salmonella spp., Shigella spp.</td>
</tr>
<tr>
<td>Urethral and cervical swabs</td>
<td>Isolation of N. gonorrhoeae</td>
<td>Selected site or national coverage, continuous, Patients in hospital and in the community</td>
<td>N. gonorrhoeae</td>
</tr>
</tbody>
</table>

* Call for country enrolment issued on 21 March 2016

Status of countries enrolled in GLASS
As of 21 July 2017*

Enrolment completed (n=47)
Enrolment in progress (n=9)
GLASS Future Directions

Integrated foodborne AMR surveillance
- Food-animals
- Food
- Humans

Monitoring of antimicrobial use or consumption

Surveillance of bacterial resistance in humans

Environmental AMR surveillance

... other types of AMR surveillance

GAP Implementation

Objective 3: Reduce incidence of infection through effective sanitation, hygiene and infection prevention measures
Preventing Infections: Semmelweis pioneer!

Preventing Infections
Hand Hygiene Day - 5 May 2017

"Fight antibiotic resistance: it's in your hands"

- The “5 Moments for Hand Hygiene” guidelines

Preventing Infections

Infection Prevention and Control
- Core Components implementation manuals and assessment framework
- Hand Hygiene Day
- Guidelines

Vaccines
- AMR in new vaccine development
Vaccine Uptake Is Important for AMR

Vaccine uptake reduces the number of unnecessary antibiotic prescriptions.

GAP Implementation

Objective 4: Optimize the use of antimicrobials in human and animal health
WHO Guidelines and Resources

WHO Model List of Essential Medicines

- Updated in 2017
- Added 30 medicines for adult and 25 for children
- Antibiotics are now grouped to 3 categories:
  - ACCESS Antibiotics that should be available at all times (29 AB)
  - WATCH Antibiotics recommended as first- or second-choice (7 AB) treatments for a small number of infections
  - RESERVE Antibiotics that are last-resort options (8 AB)

WHO is creating an analysis of the antibiotic pipeline

- Will be released September 2017

EML A-WA-RE index uses in DU
PPS in >20.000 patients

Mike Sharland, personal communication, Penta-id.org
Antibiotic Use in Primary Care Facilities

Antibiotic stewardship programs reduce incidence of infections in hospitals, especially for MDR gram-negative bacteria

When paired with IPC methods, AB stewardship is highly effective, and the combination reduces AMR more than just AB stewardship alone.

Magnitude of effect depends on the type of AB stewardship programme implemented.

Implementing Antibiotic Stewardship with IPC

AB stewardship and IPC should be integrated in national action plans.

Financial restrictions pose as a challenge for some countries.

- Important to consider non-traditional stewards (e.g. community health workers) in resource-limited settings.

Collaboration among countries and taking a multidisciplinary approach to AB stewardship is crucial.

**NL: high AB use in Agriculture**

![Antibiotic Usage in Animals in NL](chart)

**Netherlands: political commitment**

- **Minister of Public Health**
  - Ban Critically Important Antimicrobials for human use
  - Redefine 1st, 2nd, 3rd choice antimicrobials (selection for ESBLs)

- **Minister of Agriculture**
  - take your own measures, or I have to make new laws!
Netherlands: results so far

- Developments in sales of antimicrobial agents between 1999 and 2015, in number of kilograms of active substances sold (x1000) (source: FIDIN), by main pharmacotherapeutic group in 2015.

Benchmarking of broiler farms

Figure 1: Benchmarking broiler farms 2012 (upper figure) and 2015 (lower figure) with target (→), signaling (←) and action (⇒). Key points: number of farms (Y-axis) and Defined Daily Dose Animal/year (X-axis). Shows change in distribution of farms over the years.
Removing ABX From Food Producing Animals

Total sales, in kilograms of active substance, of antimicrobials for therapeutic use in farmed fish in Norway

British Poultry Council

BPC reduced antibiotic use by weight by 71%

Poultry meat production increased by 11%
Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines, and other interventions.

'Magical' antibiotic brings fresh hope to battle against drug resistance

It has taken 60 years for bacteria to become resistant to vancomycin; modified drug now works in three ways, making it harder for bugs to develop resistance.

© The WHO has warned that antibiotic resistance is one of the biggest threats to global health, food security and development. Photograph: David Goldman/AP
Researchers amplify antibiotic of last resort hoping to halt superbugs

By Elizabeth Roberts, CNN
© Updated 14:04 GMT (22:04 EDT) May 30, 2017

New "superbug" no antibiotic can combat arrives in U.S. 03:23

WHO Priority Pathogens List for R&D

**Priority 1: CRITICAL**
- Acinetobacter baumannii carbapenem-resistant
- Pseudomonas aeruginosa carbapenem-resistant
- Enterobacteriaceae carbapenem-resistant, ESBL-producing

**Priority 2: HIGH**
- Enterococcus faecium vancomycin-resistant
- Staphylococcus aureus methicillin-resistant, vancomycin-intermediate and resistant
- Helicobacter pylori clarithromycin-resistant
- Campylobacter spp. fluoroquinolone-resistant
- Salmonella fluoroquinolone-resistant
- Neisseria gonorrhoeae cephalosporin-resistant, fluoroquinolone-resistant

**Priority 3: MEDIUM**
- Streptococcus pneumoniae penicillin-non-susceptible
- Haemophilus influenzae ampicillin-resistant
- Shigella spp. fluoroquinolone-resistant

Source: WHO globalatlas.org
GARD-P

Partnership to Develop New Antibiotics

- WHO and DNDi collaboration; May 2016
- Assist with drug approval process, manufacturing, and stewardship

Programme Areas:

1. Sexually Transmitted Infection
2. Antimicrobial Memory Recovery and Exploratory Programme
3. Neonatal Sepsis
4. Paediatric Antibiotic Platform

GARD-P Update

More than EUR 56 million raised to fund initiative to fight antibiotic resistance

(Berlin - 4 September 2017)

Germany hosts pledging event for GARDP, a new initiative to develop new antibiotic treatments

Germany, together with a number of countries and foundations, today pledged EUR 56.5 million to help develop new treatments to fight against antibiotic resistance, during a fundraising event for the Global Antibiotic Research and Development Partnership (GARDP), hosted in Berlin by the German Federal Ministry of Health and the German Federal Ministry of Education and Research.
**GARD-P**

**Partnership to Develop New Antibiotics**
- WHO and DNDi collaboration
- Assist with drug approval process, manufacturing, and stewardship

**In Action: Gonorrhoea pipeline (Zoliflodacin, Phase 3)**
- GARDP is helping Entasis Therapeutics with nonclinical activities

**When the medication reaches the market**
- Entasis will sell to 44 countries (high income countries + China)
- GARDP will manufacture and sell to the rest of the world (mostly LMICs)

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**Point of Care Diagnostics**

Point-of-care diagnostics are essential for appropriate treatment and surveillance

WHO is working on target product profiles for diagnostics and developing guidelines
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## Global Action Plan is the Model for NAPs

Countries committed to developing National Action Plans

Currently 82 countries have NAP

52 countries are developing their NAP
National multisectoral workshop 5d

Integrated approach
Country Progress with NAP Development

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"One Health" Approach

AMR affects humans, animals, and the environment

Partnering with FAO and OIE on a comprehensive approach

WHO is collaborating with UNEP to develop evidence base on AMR’s impact on the environment

AMR and One Health

“When we treat animals with antibiotics, we are treating the microflora in the rivers, the fish and aquatic life in those rivers, the animals that drink from those rivers and the humans that get their drinking water from those rivers. We are all very interconnected.”

- Dr. Herman Barkema, University of Calgary
Countries with One Health Programs

WHO Critically Important Antimicrobials List

Food and Safety Department developed guidelines for antimicrobials important for human medicine in food animals

5th Critically Important Antimicrobials for Human Medicine List was published in April
WHO Guideline for Use of Medically Important Antimicrobials in Food-Producing Animals

Goals:
Help preserve the effectiveness of medically important antimicrobials, particularly those antimicrobials judged to be critically important to human medicine.

Provide formal recommendations for limitations of specific uses of medically important antimicrobials in food-producing animals, particularly antimicrobials judged to be critically important for humans.

Supports the Global Action Plan on Antimicrobial Resistance

Restriction in the use of antibiotics in food animals and antibiotic resistance in food animals and humans:
A Systematic Review and Meta-Analysis

Dr. Karen Tang and Dr. Paul Ronksley
On Behalf of the Systematic Review Team
University of Calgary

March 27th, 2017
2nd WHO Guideline Development Meeting
Increasing Consumer Demand…

Public Interest Research Group, 2015

Public Interest Research Group, 2016
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Framework for Monitoring GAP

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<th>Activities/Outputs</th>
<th>Outcomes</th>
<th>Impact</th>
<th>Goal</th>
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<tbody>
<tr>
<td>Country stakeholder engagement</td>
<td>Develop &amp; implement national AMR plans in line with GAP</td>
<td>Better data on prevalence, AM use and resistance</td>
<td>More appropriate consumption of antimicrobials</td>
<td>Effective &amp; safe medicines are available for infectious diseases</td>
</tr>
<tr>
<td>Situation analysis</td>
<td>Surveillance &amp; research on resistance, infections and consumption</td>
<td>Behaviour changes in antibiotic demand (in health &amp; food chain)</td>
<td>Slower development of resistance</td>
<td>Lower mortality &amp; morbidity from infectious diseases</td>
</tr>
<tr>
<td>WHO support &amp; guidance</td>
<td>Raise awareness &amp; educate policy makers, farmers, vet &amp; health workers, general public</td>
<td>Appropriate prescribing of AMs by professionals (health workers &amp; vets, public &amp; private)</td>
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<td></td>
</tr>
<tr>
<td>FAO &amp; OIE guidance &amp; standards</td>
<td>AM stewardship (resistance, quality, regulations, treatment guidelines)</td>
<td>AMs available are of assured quality, on approved list, growth promotion phased out</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other international &amp; national partners’ action</td>
<td>Infection prevention &amp; control in facilities, farms &amp; community</td>
<td>Lower incidence of infection in health facilities, higher WASH and vaccine coverage</td>
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</tr>
<tr>
<td>Funding</td>
<td>R&amp;D incentives, R&amp;D Facility, additional funding, coordination</td>
<td>Increased R&amp;D related to priority infections including diagnostics, vaccines, meds</td>
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<tr>
<td>Technical expertise &amp; support</td>
<td></td>
<td>New treatments, diagnostics and vaccines developed</td>
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UNGA High-Level Meeting 21 Sept 2016

AMR Inter-Agency Coordination Group

Chaired by UN Deputy Secretary-General and WHO DG
  – Secretariat housed at WHO

Composed of individual experts/representatives of agencies
  – Responsible for global coordination of AMR activities; determining commitments and gaps of activity

Upcoming: Teleconference in Sep; Meeting in Oct in Paris
After 20h flight: reality check

No prescription needed, just take 2
**Limited staff, 10 fte 3000 beds**

[Image of a laboratory setting with staff]

**No prescription needed, just take 2**

[Image of a laboratory setting with staff]
Home made disks

Pleased to see a dispenser…
Moving Forward

Scientific Academies do play a crucial role in AMR research

This research is the foundation of future policies for AMR stewardship

We appreciate Canada’s engagement and look forward to its continued leadership in this space

My dream: Preserve AB 4 future generations!
For More Information

Please visit: http://www.who.int/antimicrobial-resistance/en/

On Twitter: @Marcsprenger4PH