AMR Surveillance
Past, Present, and the Future

Fleming Fund RADAAR Project

September 23, 2021

John Stelling

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Part 1 – Past

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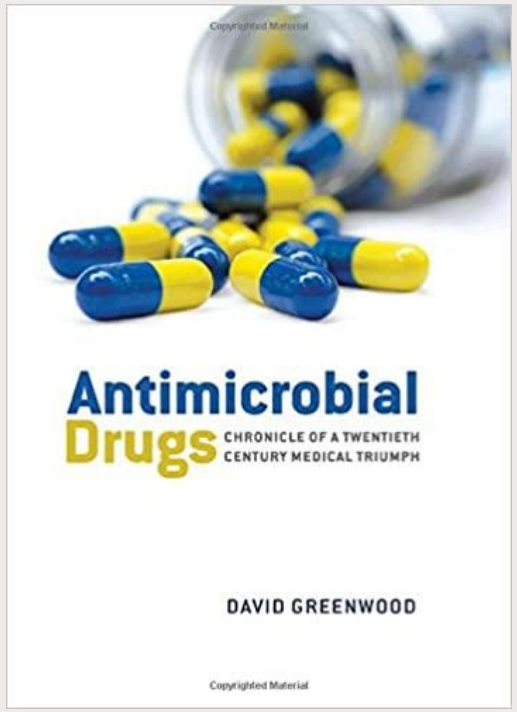
Background

Antimicrobials, Antimicrobial resistance, Antimicrobial susceptibility testing



Social History of Medicine Advance Access published May 12, 2013

Social History of Medicine page 1 of 20

Sensitive Matters: The World Health Organisation and Antibiotic Resistance Testing, 1945–1975

Christoph Gradmann*

Antibiotic sensitivity testing. Report of an international collaborative study.

H. Ericsson, J. Sherris · Published 1971 · Business, Medicine ·
Acta pathologica et microbiologica Scandinavica. Section B: Microbiology and immunology

A working party of people well known internationally in the field of was set up under World Health Organization sponsorship in 1961 to study the reproducibility of antibiotic sensitivity testing. Their aim was to investigate the possibility of introducing standard techniques which might become universal reference methods. The work involved 16 laboratories. Each was provided with the same 16 organisms, supplies of standard media and antibiotics and precise instructions for their use. The Other CABI sites Collapse

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Antimicrobial disk diffusion testing in Boston

Bauer, A. W., W. M. M. Kirby, J. C. Sherris, and M. Turck. 1966. Antibiotic susceptibility testing by a standardized single disk method. Am. J. Clin. Pathol. 36:493-496

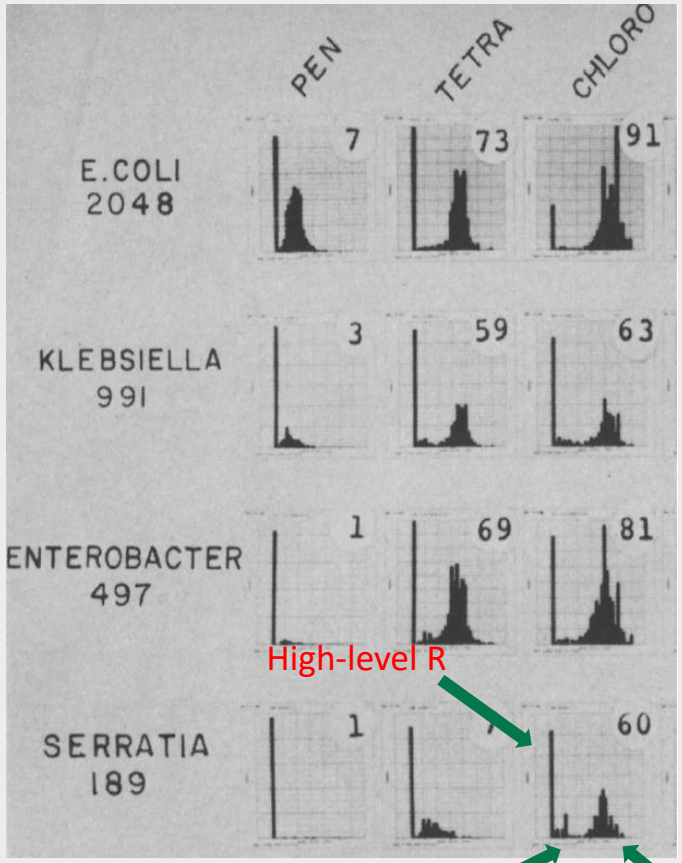
In 1962, Dr. Thomas F. O'Brien was appointed Director of the Division of Infectious Diseases and the Clinical Microbiology Laboratory of the Peter Bent Brigham Hospital in Boston.

In 1963, he trained at the University of Washington to learn microbiology, including a new standardized disk diffusion method developed by William M.M. Kirby (Infectious Diseases), A.W. Bauer (Research Fellow), John C. Sherris (Microbiology) and M. Turck.

In 1963, Dr. O'Brien introduced this new method to the clinical laboratory in Boston.

In 1964, Dr. O'Brien's team initiated a mainframe-based data management system for storing and analyzing disk diffusion zone diameter results.

Boston zone diameter distributions – 1966 to 1969

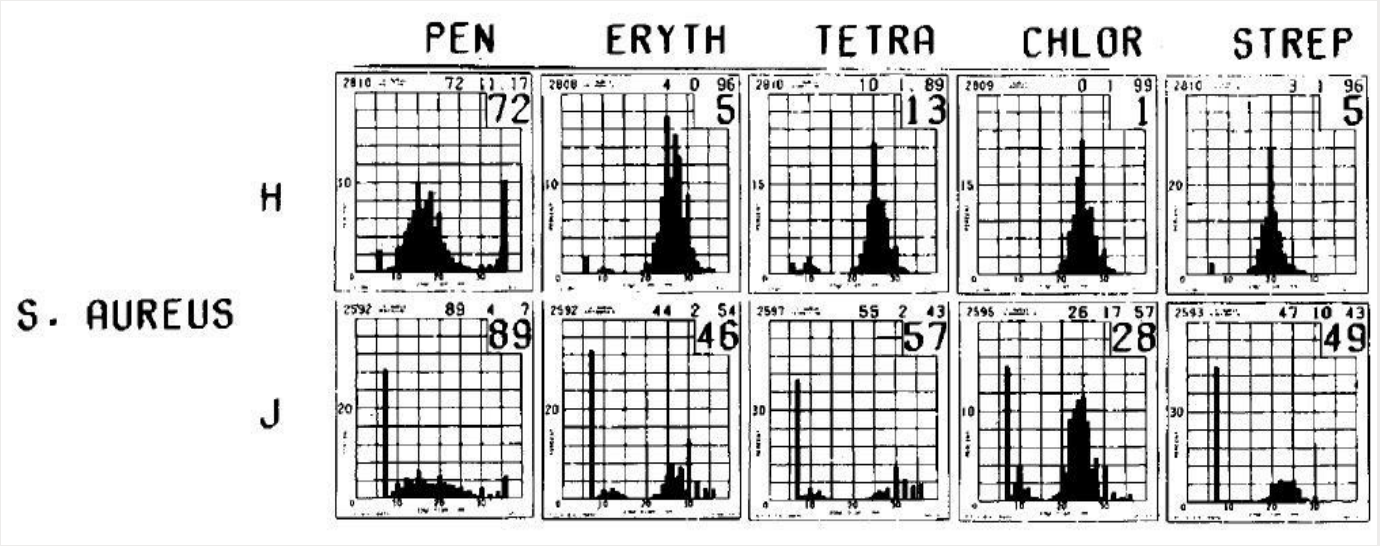


- Mainframe database created in 1964
- Circled numbers indicate %S
- Inhibition zones permit discrimination of distinct resistant subpopulations
- Similar subpopulations exist in all species but in very different proportions

O'Brien TF, Kent RL, Medeiros AA. Computer-generated plots of results of antimicrobial-susceptibility tests. JAMA. 1969 Oct 6. 210(1):84-92.

Early U.S. and international Collaborations

In the 1960s the focus was on local Boston data, but in the 1970s, Dr. O'Brien's team worked with the U.S. Food and Drug Administration to develop collaborations with U.S. hospitals, U.S. food and veterinary laboratories, and laboratories in Europe, Latin America, Africa, and Asia.



%Resistant

U.S. Hospital
(low resistance rates)

European hospital
(high resistance rates)

O'Brien TF, Acar JF, Medeiros AA, Norton RA, Goldstein F, Kent RL. International comparison of prevalence of resistance to antibiotics. JAMA. 1978 Apr 14. 239(15):1518-23.

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WHONET Software development history

- 1960s: Mainframe computers with Fortran punch cards at one Boston hospital
- 1970s: Mainframe computers with a move to optical scan sheets. Several U.S. and international laboratories
- 1980s: Migration to Personal Computers (PCs) using GWBASIC and eventually DOS
  - Distributed data entry and data analysis were now possible in collaborating laboratories around the world
  - The name WHONET was given in 1989 to support the proposed WHO Network for Surveillance of Antimicrobial Resistance
- 1990s: Migration to Quick Basic for DOS, then Visual Basic 4 to Visual Basic 6 for Windows
  - Innovations included a universal file structure, a laboratory configuration module, and the BacLink data import utility
  - DOS versions of WHONET used simple text files. Windows used dBASE files.
- 2000s: Integration of SaTScan for cluster detection. Migration to Visual Studio 2008
- 2010s: Migration to Visual Studio 2015/2017/2019
- 2020s: Migration to SQLite data file structure and Visual Studio .NET 5

The Vision of WHONET

Clinical microbiology laboratories generate routine data daily that could be utilized to provide a detailed view of evolving microbial populations in real-time. Yet this resource remains largely untapped and underutilized.

The use of a common software supports local, national, regional, and global collaboration and analyses to support:

- recognition, tracking, and containment of emerging threats
- cost-effective care and treatment guidelines
- public health policy, interventions, and advocacy
- laboratory capacity-building

Local data to support local needs

Promote national and international collaborations

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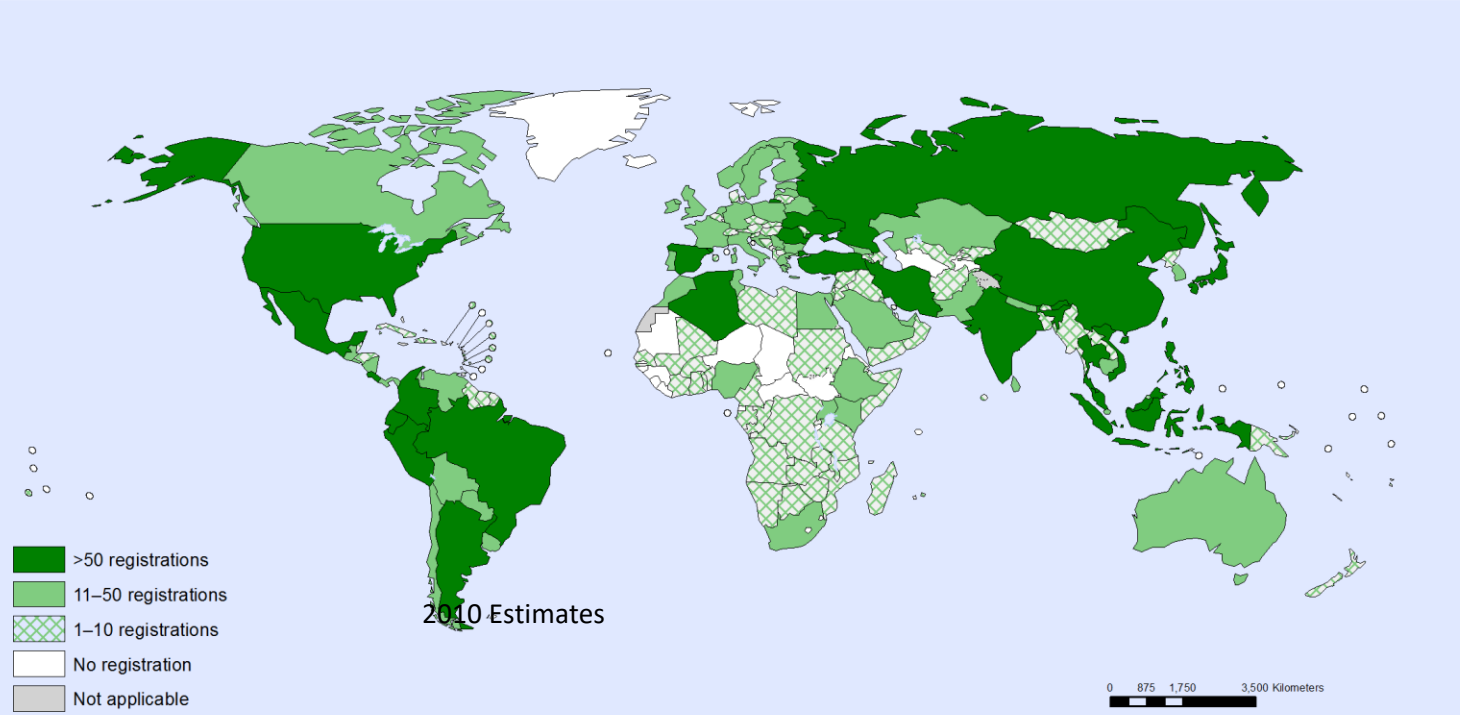
WHONET Registrations



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

World Health Organization

Early WHO Meetings on antimicrobial susceptibility testing and resistance

- Ericsson HM, Sherris JC. Antibiotic sensitivity testing. Report of an international collaborative study. Acta Pathol Microbiol Scand B Microbiol Immunol 1971; 217 (suppl): 1, representing the WHO International Collaborative Study on Antibiotic Sensitivity Testing

- World Health Organization. Surveillance for the prevention and control of health hazards due to antibiotic-resistant enterobacteria : report of a WHO meeting held in Geneva from 18 to 24 October 1977

- World Health Organization. Antimicrobial Resistance: Report of a scientific working group, Geneva 23-27, November 1981

- World Health Organization. Surveillance of antimicrobial resistance: Report of a consultation, Geneva 22-26, November 1982

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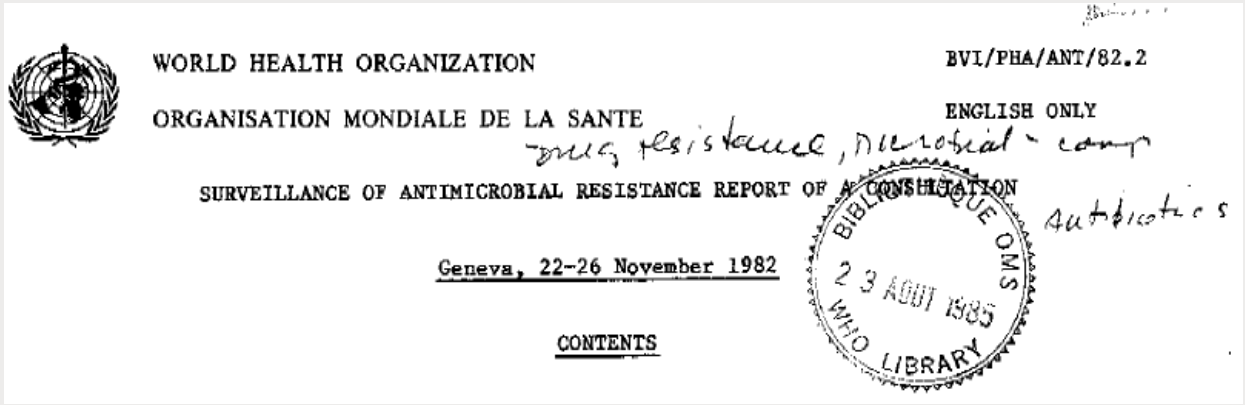
WHO Consultation on Surveillance of Antimicrobial Resistance – 1982
-- Emphasis on the local, national, and global needs for surveillance and for action



WORLD HEALTH ORGANIZATION

BVI/PHA/ANT/82.2

ORGANISATION MONDIALE DE LA SANTE

ENGLISH ONLY

drug resistance, microbial - comp

SURVEILLANCE OF ANTIMICROBIAL RESISTANCE REPORT OF A CONSULTATION

antibiotics

Geneva, 22-26 November 1982

CONTENTS

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LEVEL	OBSERVATION	USE
LOCAL	Frequency of resistance to each antibiotic	Aid selection of antibiotics for individual patients.
	Frequency of resistance to each combination of antibiotics	Identify cross-infecting strains, locally endemic resistance plasmids
	Local trends in resistance	Aid reevaluation of local antibiotic usage and infection control practices
NATIONAL	More resistance to one antibiotic than usual in other countries.	Decrease use of the antibiotic, introduce alternative agents.
	Variation in antibiotic resistance in different regions of the country.	Seek regional differences in usage, vehicles of resistance spread, e.g. food or water, hygienic practices.
	General level and trend of national resistance overall in comparison with other countries	Review, revise national antibiotic usage strategy to increase its effectiveness, reduce costs and resistance.
GLOBAL	Global trends in resistance to various antibiotics, prevalence of different bacterial genera.	Guide development, use of new antibiotics, ways of preserving efficacy of older ones. Compare practices in different countries.
	Early detection of new resistance to an antibiotic in a particular strain in a particular area.	Global warning to detect, contain treat the emerging strain, examine circumstances preceeding its emergence.
	Global trends in prevalence of distinctive combinations of resistance or resistance genes	Detection, prevention of international spread of particular resistance plasmids or resistant strains.

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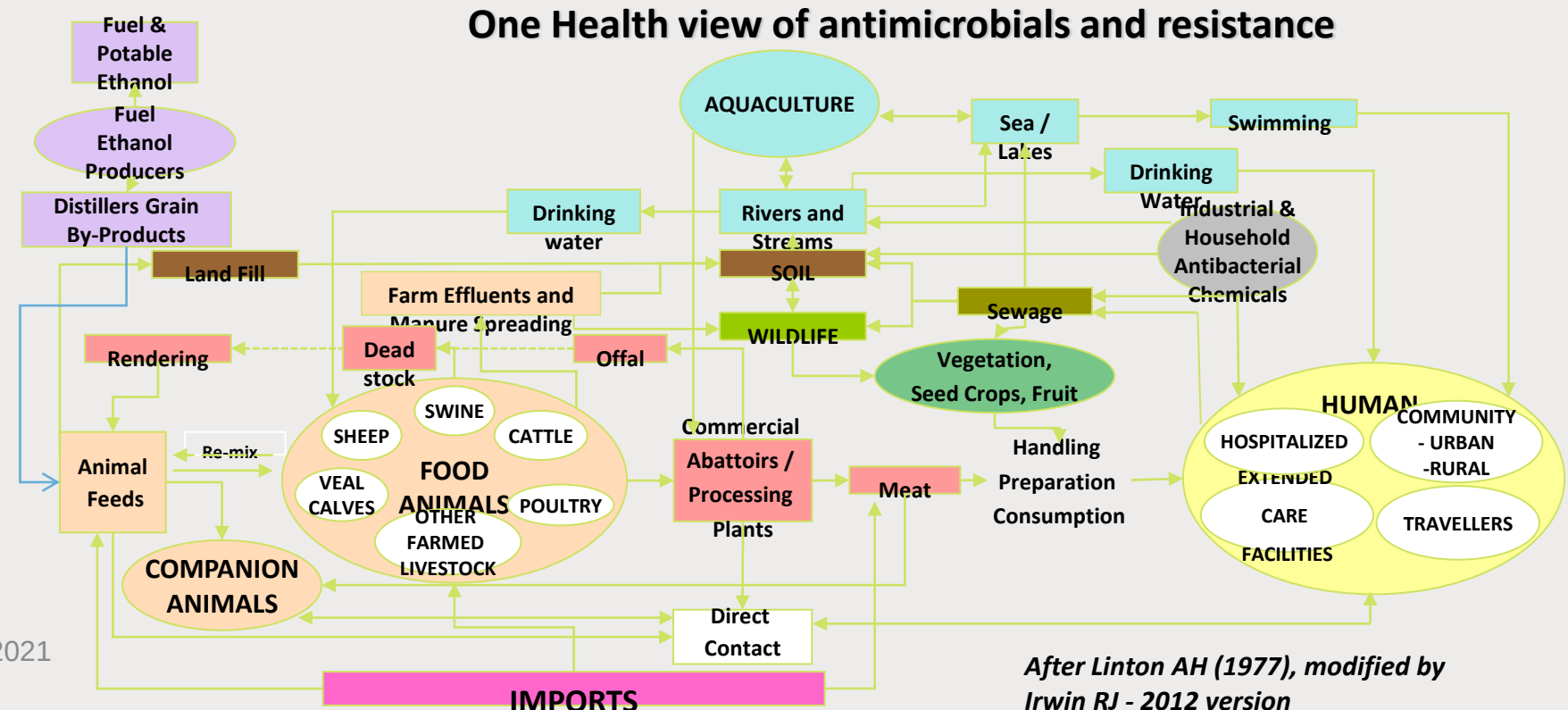
AMR Surveillance objectives

Objectives	Local	National	Regional	Global
Policy and advocacy				
Priority setting and funding	X	X	X	X
Awareness and education	X	X	X	X
Legislation and regulation			X	X
Epidemiology of resistant microbes				
Pathogen and resistance trends	X	X	X	X
Recognition of emerging threats	X	X	X	X
Disease and economic burden	X	X	X	X
Benchmarking		X	X	X
Resistance containment				
Treatment guidelines	X	X		
Response to emerging threats	X	X	X	X
Assessment of interventions	X	X	X	X
New diagnostics and therapeutics			X	X
Capacity-building				
Laborotory capacity	X	X	X	X
Epidemiological capaciy	X	X	X	X

Antimicrobial resistance surveillance models

- Alert organism surveillance
- Enhanced routine surveillance
- Targeted surveillance protocols and surveys



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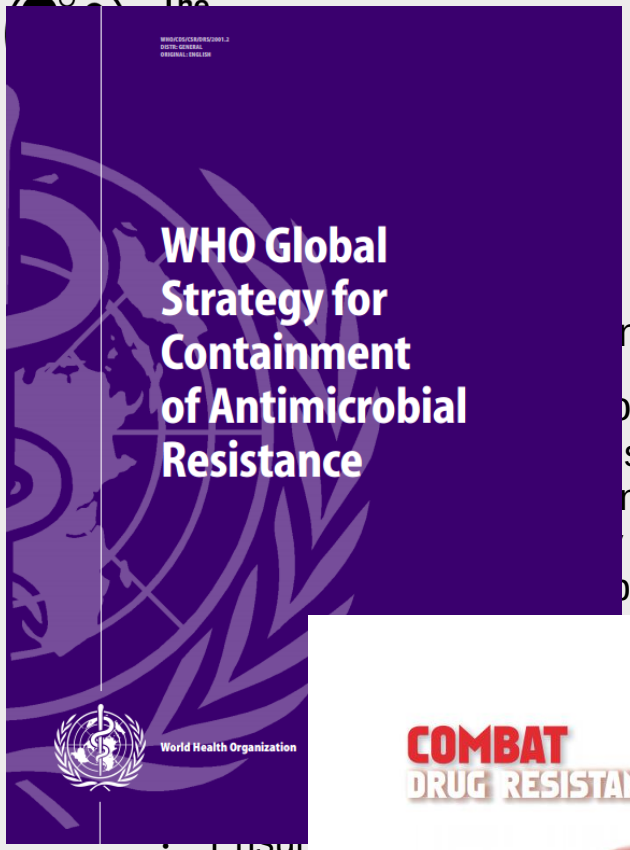

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Integrated AMR surveillance and containment

- Meetings and reports
  - 2014 Antimicrobial resistance: global report on surveillance 2014
  - 2013 Integrated surveillance of antimicrobial resistance
  - 2012 WHO advisory group on integrated surveillance of antimicrobial resistance: 3rd meeting report
  - 2012 Critically important antimicrobials for human medicine
  - 2011 WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance: 2nd meeting report
  - 2011 Critically important antimicrobials for human medicine
  - 2010 Report of the 3rd session of the CODEX Ad HOC intergovernmental task force on antimicrobial resistance
  - 2009 WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance: 1st meeting report
  - 2008 Report of the 2nd session of the CODEX Ad HOC intergovernmental task force on antimicrobial resistance
  - 2007 Report of the 1st session of the CODEX Ad HOC intergovernmental task force on antimicrobial resistance
  - 2007 Critically important antimicrobials for human medicine
  - 2005 Critically important antibacterial agents for human medicine for risk management strategies of non-human use
  - 2002 WHO consultation on monitoring antimicrobial usage in food animals for the protection of human health
  - 2002 Methods for foodborne disease surveillance in selected sites
  - 2000 WHO global principles for the containment of antimicrobial resistance in animals intended for food
  - 1997 WHO meeting on the medical impact of the use of antimicrobials in food animals

Role of governmental authorities in AMR Surveillance in human health

- AMR in pathogens with disease control objectives since decades
  - *Mycobacterium tuberculosis*, *Plasmodium falciparum,* HIV, *Neisseria gonorrhoeae*

- AMR for routine community and hospital pathogens
  - 1980s: Few examples of involvement by governmental authorities. In absence of national disease control objectives, resistance was considered to be an important “clinical”, but not a “public health” issue. Activities were led by research organizations, university hospitals, and clinical societies. Significant concerns by governmental authorities on data quality and data biases.
  - 1990s: A growing number of national surveillance initiatives led by reference laboratories, but often without a tie to governmental policymaking. There was recognition in a growing number of countries in the role of government authorities in assuring patient care quality, for example in the prevention and treatment of hospital infections. Regional AMR surveillance initiatives established in WPRO, EURO, and PAHO.
  - 2000s: WHO Global Strategy for Containment of Antimicrobial Resistance. World Health Assembly on the threat of antimicrobial resistance AND antimicrobial use/misuse. Increasing evidence on the Awareness of economic and health burden of resistance.
  - 2010s: World Health Day, UK AMR Review reports, World Bank report, World Antibiotic Awareness Week, etc.

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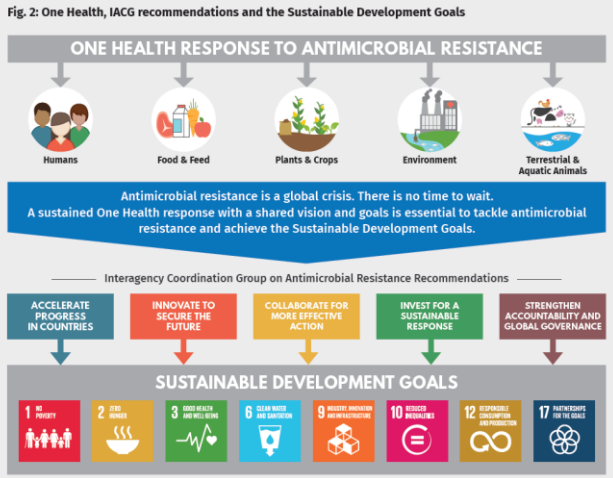
United Nations

- High-Level Meeting on AMR - 2016
- Inter-Agency Collaborative Group on AMR (IACG)
- One Health Global Leaders Group on AMR (GLG)
- Sustainable Development Goals
  - New indicators for MRSA and ESBL *E. coli* in blood



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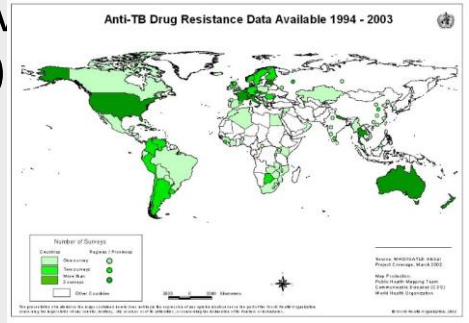
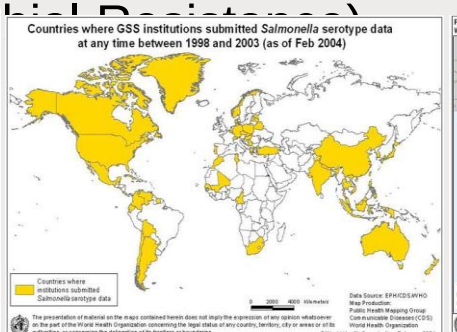
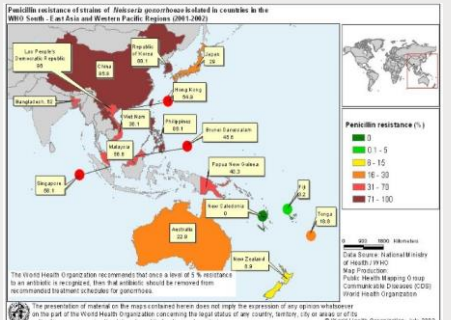
World Health Organization

- World Health Day, World Antimicrobial Awareness Week
- WHO Global AMR Report, WHO Global Antimicrobial Action Plan
- WHO GLASS modules
  - Core AMR surveillance
  - Core AMC surveillance
  - EAR – Emerging Antimicrobial Resistance
  - EGASP – AMR in *Neisseria gonorrhoeae*
  - AMR in Candidemia
  - Attributable mortality in bacteremia
  - Hospital Antimicrobial Use Point Prevalence Study
  - ESBL *E. coli* TriCycle
- Pathogen- or subject-specific programs
  - AGISAR (Advisory Group for Integrated Surv[illance] [of] Antimicrobial Resistance)
  - Global Foodborne Infections Network (GFN)
  - WHO/IUTLD TB
  - HIVResNet
  - Malaria

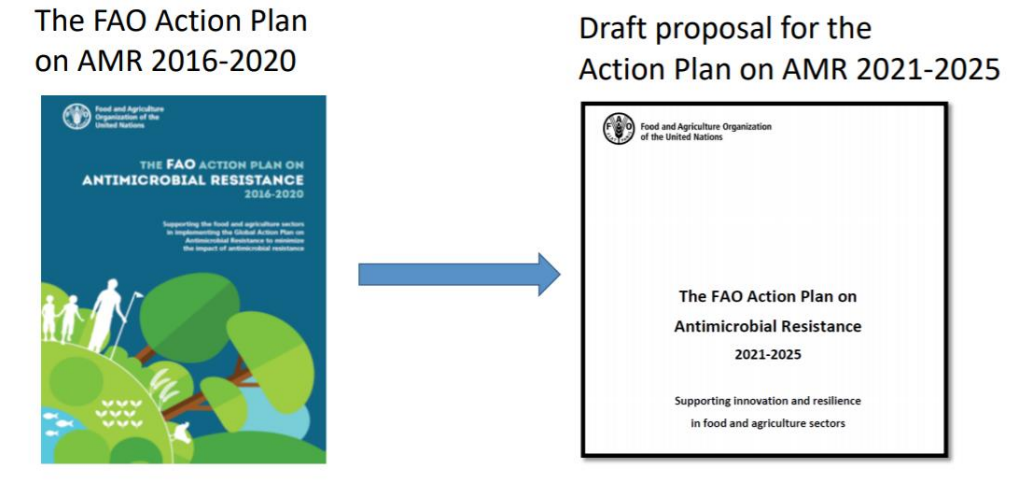


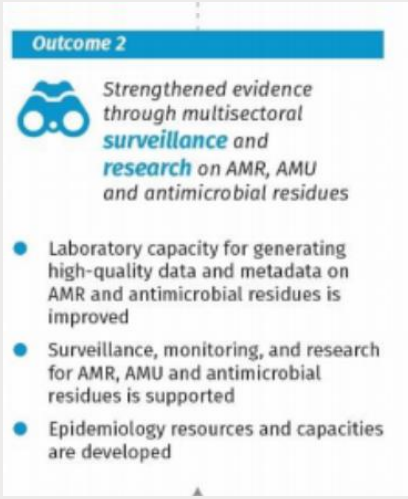




Food and Agriculture Organization of the UN

- FAO AMR Surveillance guidelines
  - Published: AMR in healthy animals
  - Advanced draft: AMR in diseased animals and in aquiculture
  - In development: AMR in animal environment and Antimicrobial use
- FAO-ATLASS: FAO Assessment Tool for Laboratories and AMR Surveillance Systems
- FAO-PMP-AMR: FAO Progressive Management Pathway for AMR
- FAO Technical Working Group on AMR Data Management





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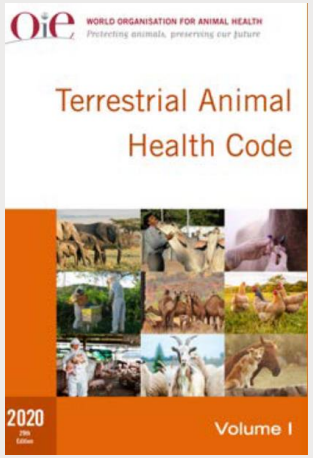
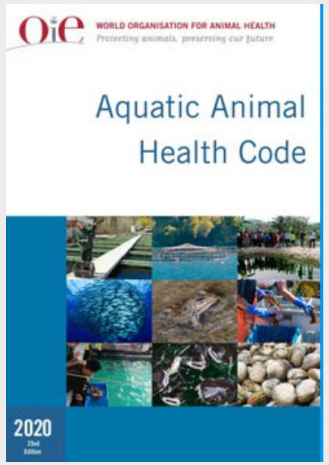
World Organisation for Animal Health



CHAPTER 6.8.

HARMONISATION OF NATIONAL ANTIMICROBIAL RESISTANCE SURVEILLANCE AND MONITORING PROGRAMMES



CHAPTER 6.4.

DEVELOPMENT AND HARMONISATION OF NATIONAL ANTIMICROBIAL RESISTANCE SURVEILLANCE AND MONITORING PROGRAMMES FOR AQUATIC ANIMALS

United Nations Environment Programme

UN environment programme

What are priority areas for management of Antimicrobial Resistance (AMR) in the Environment?

Advancing the One Health Response to Antimicrobial Resistance

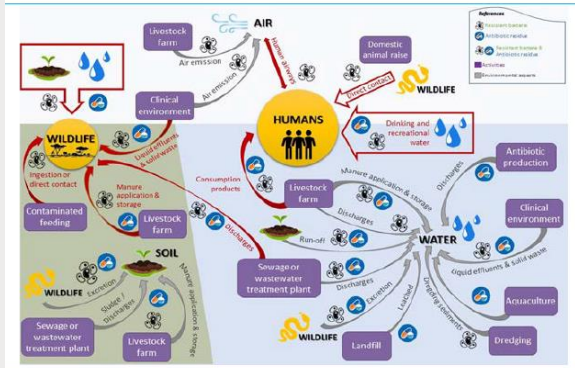
7) Discovery, Knowledge Sharing

Address knowledge gaps and improve monitoring and surveillance to identify and quantify primary sources of environmental pollution that contribute to the spread and emergence of antimicrobial resistance and share findings globally.

- Good quality data collection and management
- Best practices for laboratories to detect AMR threats
- Coordinated data sharing and harmonized analysis
- Expert consultations

Priority Areas for Management of AMR in the Environment

Entry of residues, resistant microorganisms and antimicrobial resistant genes into the environment



- Antimicrobial Resistance in the Environment is a complex problem, and it will require coordinated solutions.
- The source of AMR in soil and water are numerous and extend from production of antimicrobials, through usage and waste management.
- Every identified pathway (arrows) of contamination also present a target for intervention and measures for mitigation.
- UNEP is increasing coordination and cooperation efforts.

Image source:
https://www.unenvironment.org

UN environment programme

Antimicrobial Resistance is a Global Human, Animal and Environment Health Crisis.

There is no time to waste.

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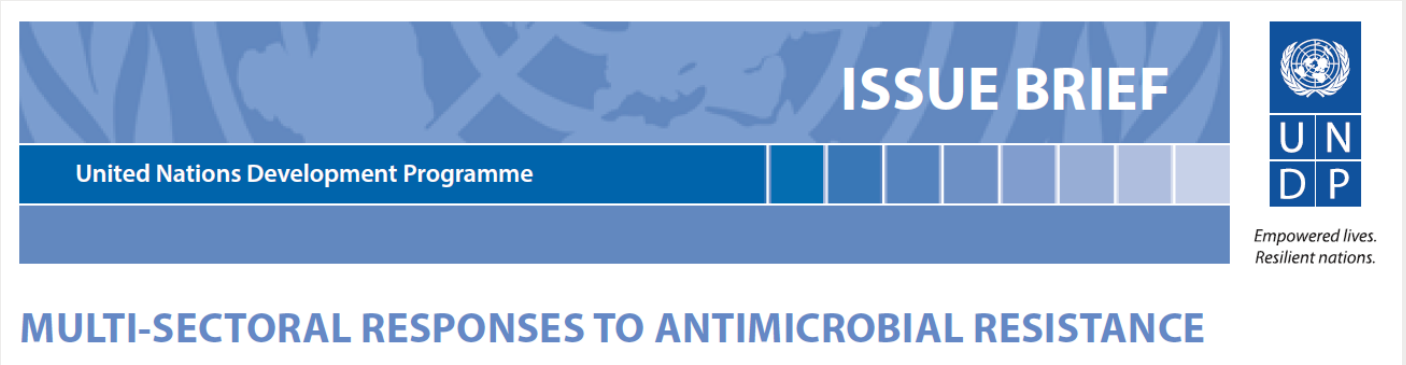
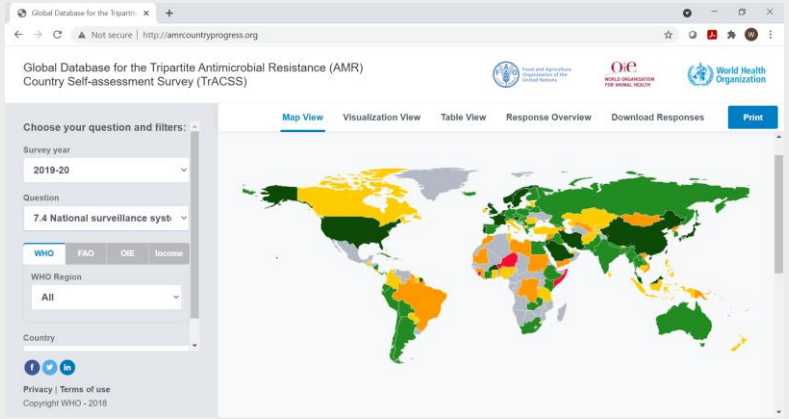
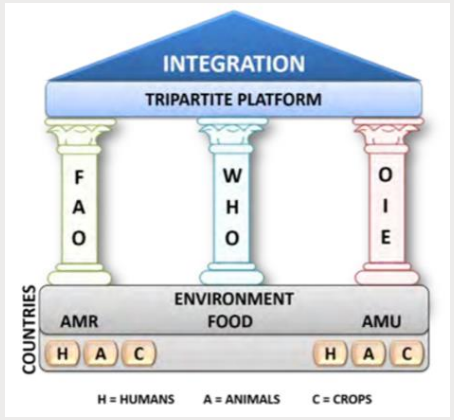
United Nations Development Programme

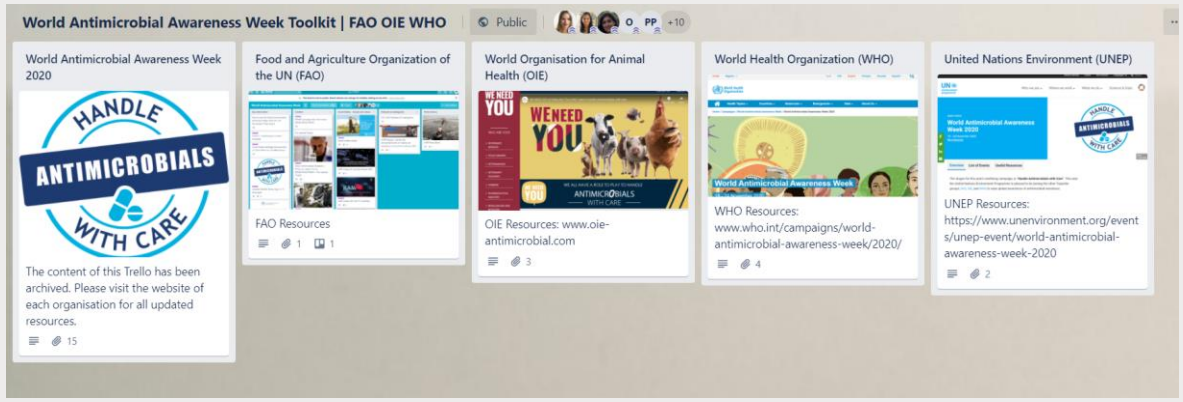


FAO-OIE-WHO Tripartite collaborations

- TrACCs: Tripartite AMR Country Self-assessment Survey, http://amrcountryprogress.org
- TISSA: Tripartite Integrated Surveillance System on AMR and AMU
- World Antimicrobial Awareness Week coordinated messages and activities







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Antimicrobial resistance: a public health priority for G20 countries

INTERNATIONAL CENTRE FOR
ANTIMICROBIAL RESISTANCE
SOLUTIONS

ANTIMICROBIAL
RESISTANCE
Hub

ReAct - Action on Antibiotic Resistance

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Part 3 – Future

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Priority action areas

- Translating data into action for capacity and continuous quality improvement
  - Advocacy and awareness for health services delivery
  - Improved capacity for clinical and laboratory diagnostic services
  - Improved capacity for data management, analysis, and interpretation

- Translating data into action for resistance containment
  - Advocacy and awareness for antimicrobial resistance containment
  - Disease prevention
  - Improved use of existing antimicrobials and treatment options
  - Decreased transmission of resistant pathogens

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Priorities

- What actions are needed?
  - What data are needed to support those actions?
- What data exist?
  - What can be done with these data? Strengths, deficiencies?
- What are the information gaps?
  - What are possible strategies to address these gaps?
- What partners and skillsets are needed?
- What are the costs of inaction? Of action?

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Regional approach to AMR containment

- Value of the regional approach
  - Advocacy: Ownership, relevance, and sustainability
  - Epidemiology: Regional view and benchmarking of antimicrobial use and resistance trends
  - Resistance containment: Regional coordination of response strategies and initiatives and cooperation with national authorities
  - Capacity-building: National strengthening and standardization of approaches, best practices, lessons learned, mentoring, technical support, feedback
- Need for two regional frameworks
  - Framework for data collection, sharing, and analysis
  - Framework for translating data into action

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Some current and developing IT initiatives

- Global initiatives
  - WHO GLASS, OIE WAHIS, FAO, TISSA, TrACSS
  - Integration of Next-Generation Sequencing technologies into routine surveillance
- Microbiology laboratory information systems
  - Free systems: LabBook (Fondation Merieux), BLIS, Bika
  - Free systems in development: Mini-LIMS (Doctors Without Borders), SEDRI-LIMS (SEDRIC, Wellcome Trust), SENAITE, OpenELIS
  - Veterinary LIMS: SILAB (IZSAM with support from FAO)
  - Commercial systems
- Data analysis and public health reporting
  - WHONET and SaTScan, migration to .NET 5
  - DHIS2 and AMR: WHONET, Norway, India, WAHIT, Senegal
  - SORMAS, OpenLDR, AMASS
  - mHealth development, Artificial intelligence/Machine learning/Data mining
- WHO AMR Collaborating Center Network
  - Coding and antibiotic interpretation standards

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Thank you!