Global Antimicrobial Resistance in the 21st Century

(with a bit of the NDM-1 story)

• H-index 71
• Dean of International Research, Cardiff University
• Director of BARNARDS
• Advisor to UN
• Member of the Fleming Fund (Mott MacDonald/DoH) – Lead for Nigeria, Pakistan and Bangladesh
• Member of PMC for ENABLE (ND4BB)
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• International Engagement Officer for British Society of Antimicrobial Chemotherapy
• MRC (AMR One World Health), Chinese CDC, Chinese DoH and DoA, Advisor to the ECDC; Advisor to the WHO
• Advisor and collaborator with Médecins Sans Frontières
• Advisor to Wellcome Trust Centre, Oxford/Hanoi/Vientiane
Why has it gone so badly wrong?

1. Genetic plasticity of bacteria

2. Stupidity of human behavior
   - arrogance
   - political correctness
   - unbridled greed
   - scientific incompetence
   - short-term thinking (industry and academics)
High income Countries
- Respectable taxation systems
- Controllable corruption
- Appropriate funded healthcare (usually public)
- Decent sanitation
- Clean portable water
- Industrial waste controlled
- Antibiotic stewardship - variable
- Microbiology support – good
- Democratic governments

Low-Middle income Countries
- Broken taxation system
- Corruption is the norm
- Healthcare systems are invariably private (even public hospitals)
- Poor sanitation
- Contaminated portable water
- Industrial waste uncontrolled
- Antibiotic stewardship – poor
- Microbiology support – weak
- Instable governments and war

The Two Worlds?
“Although the scenario where we do not take action is truly frightening, with over 10 million people dying every year by 2050 and a cumulative hit to the world economy of 100 trillion USD, it is sometimes hard to comprehend such large numbers. But these are not just large forecasted numbers; they represent the future for many individuals - all of us. Indeed, at least 700,000 people die every year already from drug-resistant infections. AMR is sometimes compared to a slow motion car crash: sadly, it is one that has already started”

Jim O’Neil 2015
Antimicrobial resistance in the developed world: overall on the rise

Why?

Aggregated data for six high-priority bacterial-AMR combinations

*E. coli (ESBL, FQ)*, *K. pneumoniae* (ESBL, Carba-R), MRSA, PEN-R pneumococci

OECD, 2016

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MRSA in Europe: a remarkable diversity
(EARS-NET 2016 - N=56,606 isolates from invasive infections)
Our growing perception of the obvious!

economic globalisation?
A one-health approach to antimicrobial resistance

While antimicrobial resistance (AMR) is a global concern, its spread in specific settings, such as hospitals, can be exacerbated by factors like poor hygiene practices and the overuse of antibiotics. Understanding the dynamics of AMR can help in developing targeted interventions.

Timothy A. Walsh
What is the pre-antibiotic Era?

- **Multi-drug Resistance (MDR)**
  - e.g. NDM-1 (resistance to carbapenems)

- **Extensively-drug Resistance (XDR)**
  - e.g. MCR-1 (resistance to polymixins/colistin)

- **Pan-drug Resistance (PDR)**
Medical tourism

Naming of NDM-1

Carbapenem-R *K. pneumoniae* in Europe
(EARS-NET – isolates from invasive infections)
Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study

Prof Timothy R Walsh, PhD, Janis Weeks, BSc, David M Livermore, PhD, Mark A Toleman, PhD
Published: 07 April 2011

**Environmental Study**

171 swabs
- 156 grew meropenem resistant Gram-negatives)
- 51/171 (29.8%) were positive for NDM-1

UNDERESTIMATION!

50 water samples
- 14 grew meropenem resistant Gram-negatives)
- 2 out of 50 (4%) were positive for NDM-1
Environmental study in Dhaka

60 samples in six areas of Dhaka

NDM-1 found in 61% of all samples.

Positive isolates included
E. coli
Klebsiella pneumoniae
Citrobacter freundii
Acinetobacter baumanii
Acinetobacter junii
Acinetobacter tandoi
Acinetobacter genomospecies 3
Acinetobacter towneri
Pseudomonas putida
Pseudomonas aeruginosa
Pseudomonas otitidis
Pseudomonas mendocina
Pseudomonas fulva
Stenotrophomonas maltophilia.
World map of poverty represented as size
Our work in the Murtala Hospital, Kano
AMR genes in baby rectum (LOS)

AMR genes in mother’s rectum
The notion that the human gut contains $10^{14}$ bacteria, many of which are Enterobacteriaceae, non-clinical questions started to emerge, not least of which was how do we globally manage human and animal waste now that it contains XDR Enterobacteriaceae?

Deaths from unsafe water, sanitation and hygiene


Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis

Source: The World Health Organization. © WHO 2005. All rights reserved.
Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis

Corruption and governance

Infrastructure
Number of people in countries without adequate sanitation

1. India (818 million)
2. China (607 million)
3. Indonesia (109 million)
4. Nigeria (103 million)
5. Pakistan (98 million)
6. Bangladesh (75 million)
7. Ethiopia (71 million)
8. Congo, DR (50 million)
9. Brazil (39 million)
10. Tanzania (32 million)
11. Sudan (27 million)
12. Kenya (27 million)
13. Philippines (22 million)
14. Vietnam (22 million)
15. Ghana (20 million)
16. Nepal (20 million)

World Bank Data - 2014

January 2017
#HandHygiene  #Sepsis

IT'S IN YOUR HANDS

PREVENT SEPSIS IN HEALTH CARE

How to prevent sepsis
The role you can play in health care and communities

What is sepsis?

Every year sepsis affects...

Who is at risk?

Evolution of an infection to sepsis can be prevented by:

Together we can help prevent sepsis and save millions of lives every year
What is the pre-antibiotic Era?

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- **Extensively-drug Resistance**
  - e.g. MCR-1 (resistance to polymixins/colistin)

- **Pan-drug Resistance**

**Animal Versus Human Antibiotics –**

**Who is to Blame?**
Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study
The role of ‘filth flies’ is the spread of antimicrobial resistance

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The role of wildlife (wild birds) in the global transmission of antimicrobial resistance genes

Jing Wang, Zhen-Bao Ma, Zhen-Ling Zeng, Xue-Wen Yang, Ying Huang, Jian-Hua Liu
College of Veterinary Medicine, South China Agricultural University, Guangzhou 510642, China
Anthropogenic and environmental factors associated with high incidence of mcr-1 carriage in humans across China

Prevalence of mcr-1-positive carriages
- <9%
- 9–17%
- 17–24%
- ≥24%

Production of freshwater aquaculture (×10,000 tonnes)
- <80
- 80–120
- 120–190
- 190–300
- ≥300
Reported *mcr*-positive clinical isolates from Europe

- *E. coli*
- *Salmonella*
- *K. pneumoniae*

Prima et al – Euro Surveill 2016
Campos et al – Euro Surveill 2016
Di Pilati et al – AAC 2016
Iradelaki et al – JAC 2016
Solheim et al – JAA 2016
Douni et al – JAC 2016
Cannatelli et al – AAC 2016
Coppola et al – EID 2017
Codella et al – Euro Surveill 2017
Hartl et al – AAC 2017
Tordahl et al – JAA 2017
Roer et al – Euro Surveill 2017
Huang et al – Euro Surveill 2017

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A colistin crisis in India

Despite some global progress in limiting the use of antimicrobials in animals, inappropriate colistin use is still widespread. Madlen Davies and Timothy Walsh report.
ANIMALS IN THE USA CONSUME MORE
THAN TWICE AS MANY MEDICALLY
IMPORTANT ANTIBIOTICS AS HUMANS

30% of antibiotics are consumed by animals

ANTIBIOTIC USE IN AGRICULTURE
VARIRES GREATLY BY COUNTRY
Antibiotic consumption used in livestock, 2015

![Map showing antibiotic consumption in livestock worldwide, 2015.](image)

**Continued growth projected in China's per capita meat consumption.**

- **Source:** USDA Production, Supply and Distribution database and projections.

**Figure 2.3: Thailand's Feed Demand**

- **Source:** Thai Feed Mill Association
A one-health approach to antimicrobial resistance

Antimicrobial use in animals and agrofood systems may drive the spread of clinically relevant drug resistance genes and pathogens. New work uncovers drug resistance gene patterns from Swedish animal counseled farms and finds a correlation with agricultural antibiotic use.

Timothy R. Walli.
What are we doing?
"Back to the dark ages of medicine"

Without new antibiotics being Camelot talks to the beast.

By 2050, he will warn that the communicable revolution could make global GDP up to 6% per year a calamitous cost of $20 trillion.

This comes in as a shock to antibiotics as a whole fall due to resistance.

Lately, researchers from Sina University and Imperial College London Israel. The resistance to care of the main target organisms will be to clinical challenges, coming from the famous statement may be weakened, antibiotic.

Mr. Sibson will say, "Trends for large-scale action, antibiotic resistance will become an ever greater threat to national and global health."

High-level Meeting on Antimicrobial Resistance
21 September 2016 @ 10:00 am - 6:00 pm

Draft political declaration of the high-level meeting of the General Assembly on antimicrobial resistance

1. The Heads of State and Government and representatives of States and Governments, meeting in United Nations Headquarters in New York on 21 September 2016, in accordance with General Assembly resolution 70/270, have declared at a high-level meeting in 2016 on antimicrobial resistance.


3. Acknowledged that the 2015 Global Antibiotic Resistance Review, a framework to review human, livestock, and wildlife antimicrobial use and the development and implementation of measures to respond to the problem, its findings and recommendations, and in particular the need for action on resistance to antibiotics both within and across sectors, and in particular the need to address the challenges of antibiotic resistance and the overuse and misuse of antibiotics within the health and food systems.

4. Recognized that the current level of coordinated, inter-sectoral and targeted action to combat antimicrobial resistance is insufficient in the face of the growing and urgent threat to human, veterinary and environmental health and the importance of action in this area.

5. Recognised that the above recommendations are most prevalently challenging to those stakeholders, including the development of world-wide consensus and programme towards the goal of a global health governance framework for AMR, as well as the development of and the implementation of evidence-based, national and international strategies to control the emergence and spread of AMR, and in particular the need for action in the health and food systems.

6. Recognized that the above recommendations are most prevalently challenging to those stakeholders, including the development of world-wide consensus and programme towards the goal of a global health governance framework for AMR, as well as the development of and the implementation of evidence-based, national and international strategies to control the emergence and spread of AMR, and in particular the need for action in the health and food systems.

7. Recognized that the above recommendations are most prevalently challenging to those stakeholders, including the development of world-wide consensus and programme towards the goal of a global health governance framework for AMR, as well as the development of and the implementation of evidence-based, national and international strategies to control the emergence and spread of AMR, and in particular the need for action in the health and food systems.
The Roadmap:

**UNGA / GHSA / Global**

**GAP**

**NAP**

- Country Ownership
- NCoE AMR C/66: One Health group
- M o Finance

**UN**

Declaration or “testimony”

**WHO**

GLASS

**BMGF**

BARNARDS

**EU**

ND4BB

**UK**

Fleming Fund

**US**

CDC

**XDR**

Avert Economic and Social Burden of AMR

Surveillance

Capacity Building

Human Resources

Fleming Fellowship Scheme

Government

Development Partners

Academia

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