Scourge of antimicrobial resistance: Time to act now

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Introduction

Antimicrobial resistance is posing a serious threat to

- human,
- animal and
- environmental health and the
- economy globally, and

the systematic misuse of the antimicrobial drugs in human and veterinary medicine and food production have put every nation at risk, particularly in developing nations.

Introduction

In addition, the availability of

- falsified and
- substandard medicines further contributes to development of antimicrobial resistance.

Introduction

The 4 days International Workshop on Antimicrobial Resistance and Strategis for its mitigation was organized at GADVASU, Ludhiana jointly by:

- ✓ Department of Veterinary Microbiology, Guru Angad Dev Veterinary & Animal Sciences University (GADVASU), Ludhiana (Punjab), and
- ✓ Centre for Science & Technology of the Non-Aligned and Other Developing Countries (NAM S&T Centre) during 10-13 July 2018;
- ✓ Delegates from 15 different countries participated and had discussions.

Delegates were comprising of the

clinicians, microbiologists, veterinarians, pharmacists and experts in allied sciences, public health experts and policy planners working in academic and R&D institutions, govt. departments and ministries, NGOs and industries of the developing countries from Afghanistan, Egypt, India, Indonesia, Iran, Kenya, Malaysia, Mauritius, Myanmar, Nepal, Nigeria, Palestine, South Africa, Sri Lanka and Zambia;

Introduction

International Workshop on Antimicrobial Resistance & Strategies for its mitigation at GADVASU, Ldhiana

Introduction

The successful use of any therapeutic agent is compromised by the potential development of tolerance or resistance to that compound from the time it is first employed. This is true for agents used in the treatment of

- ✓bacterial,
- ✓fungal,
- ✓parasitic, and
- ✓viral infections
- ✓and for treatment of chronic diseases such as
- ✓cancer and diabetes;

Introduction

It applies to ailments caused or suffered by any living organisms, including

- ✓ humans,
- ✓ animals,
- ✓ fish,
- ✓ plants,
- ✓ insects, etc.

It is essential to provide effective antimicrobial drugs for protecting humans & animals from diseases and ensuring the success of surgery, chemotherapy & other medical interventions

Introduction

The most striking examples of resistance, and probably the most costly in terms of morbidity and mortality, concern bacteria.

The discovery of these infectious agents in the late 19th century stimulated the search for appropriate preventative and therapeutic regimens; however, successful treatment came only with the discovery and introduction of antibiotics half a century later.

Introduction

Antibiotics have revolutionized medicine in many respects, and countless lives have been saved; their discovery was a turning point in human history.

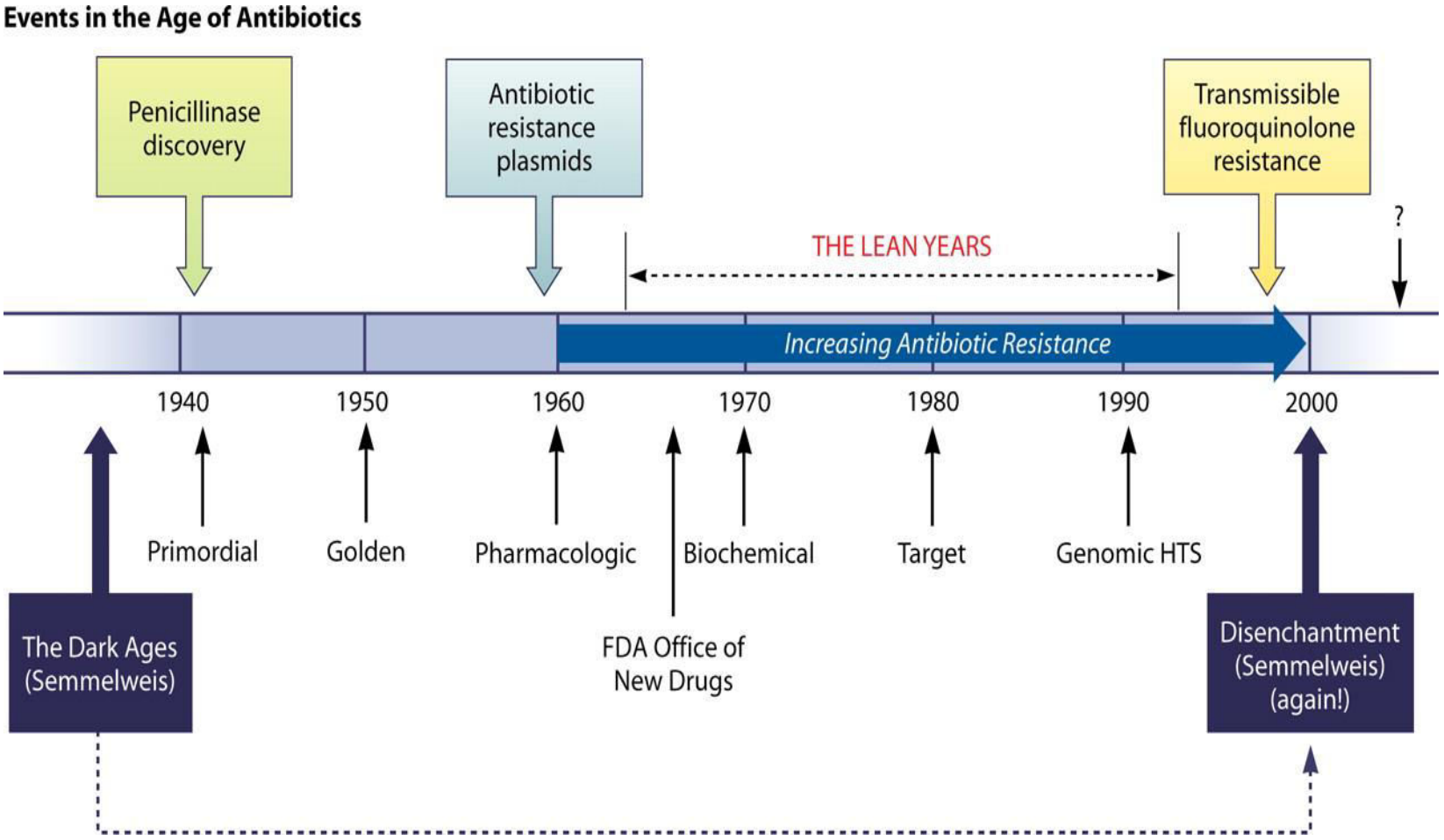
Regrettably, the use of these wonder drugs has been accompanied by the rapid appearance of resistant strains.

Introduction

- Medical pundits are now warning of a return to the preantibiotic era; a recent database lists the existence of more than 20,000 potential resistance genes (r genes) of nearly 400 different types, predicted in the main from available bacterial genome sequences (**Liu, B., and M. Pop.** 2009. ARDB—Antibiotic Resistance Genes Database. *Nucleic Acids Res.* **37:**D443-D447)
- Fortunately, the number existing as functional resistance determinants in pathogens is much lower.

Introduction

History of antibiotic discovery & concomitant development of antibiotic resistance.



Julian Davies, and Dorothy Davies Microbiol. Mol. Biol. Rev. 2010; doi:10.1128/MMBR.00016-10

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Modes of action and resistance mechanisms

They vary with the type of antibiotics and include one or the other of the following:

- efflux,
- phosphorylation,
- altered target,
- hydrolysis,
- acetylation,
- glycosylation,
- nucleotidylation,
- ADP-ribosylation.

Causes of Antibiotic Resistance

The development of generations of antibiotic-resistant microbes and their distribution in microbial populations throughout the biosphere are the results of many years of selection pressure from human applications of antibiotics, via

- ✓ underuse,
- ✓ overuse, and
- ✓ misuse.

This is not a natural process, but a man-made situation superimposed on nature; there is perhaps no better example of the Darwinian notions of selection and survival.

Causes of Antibiotic Resistance

- Human activity shapes the microbial communities residing in urban environments.
- In particular, urban sewage systems are designed to evacuate human wastes from the houses to areas of low human exposure and gradually reinstate them into natural watercourses such as creeks, beaches, or the sea.
- This cycle is of tremendous importance for public health as waste waters can be a reservoir and vehicle for the transmission of pathogenic bacteria and antibiotic resistance mechanisms.

Causes of Antibiotic Resistance

- Indeed, the rapid emergence and spread of pathogenic bacteria with extensive antibiotic resistance has been recognized by the WHO as a top health issue since water can easily move microorganisms between humans and other animal species.
- Accordingly, the analysis of environmental waters is being adopted as an effective method to monitor the dynamics of antibiotic-resistant pathogens as this kind of environments can play a role as important as clinical settings for the selection of antibiotic resistance.

Causes of Antibiotic Resistance

- Recent advances in high-throughput sequencing (HTS) and computational biology now allow the exploration of microbial communities based on culture-independent approaches using metagenomics.
- This enables us to quantify & functionally characterize environmental microbiomes with unprecedented precision and comprehensiveness.

Causes of Antibiotic Resistance

In summary, there are **6 main causes**:

- Over-prescription of antibiotics
- Patients not finishing entire antibiotic course
- Overuse of antibiotics in livestock & fish farming
- Poor infection control in health care settings
- Poor hygiene and sanitation
- Absence of new antibiotics being discovered

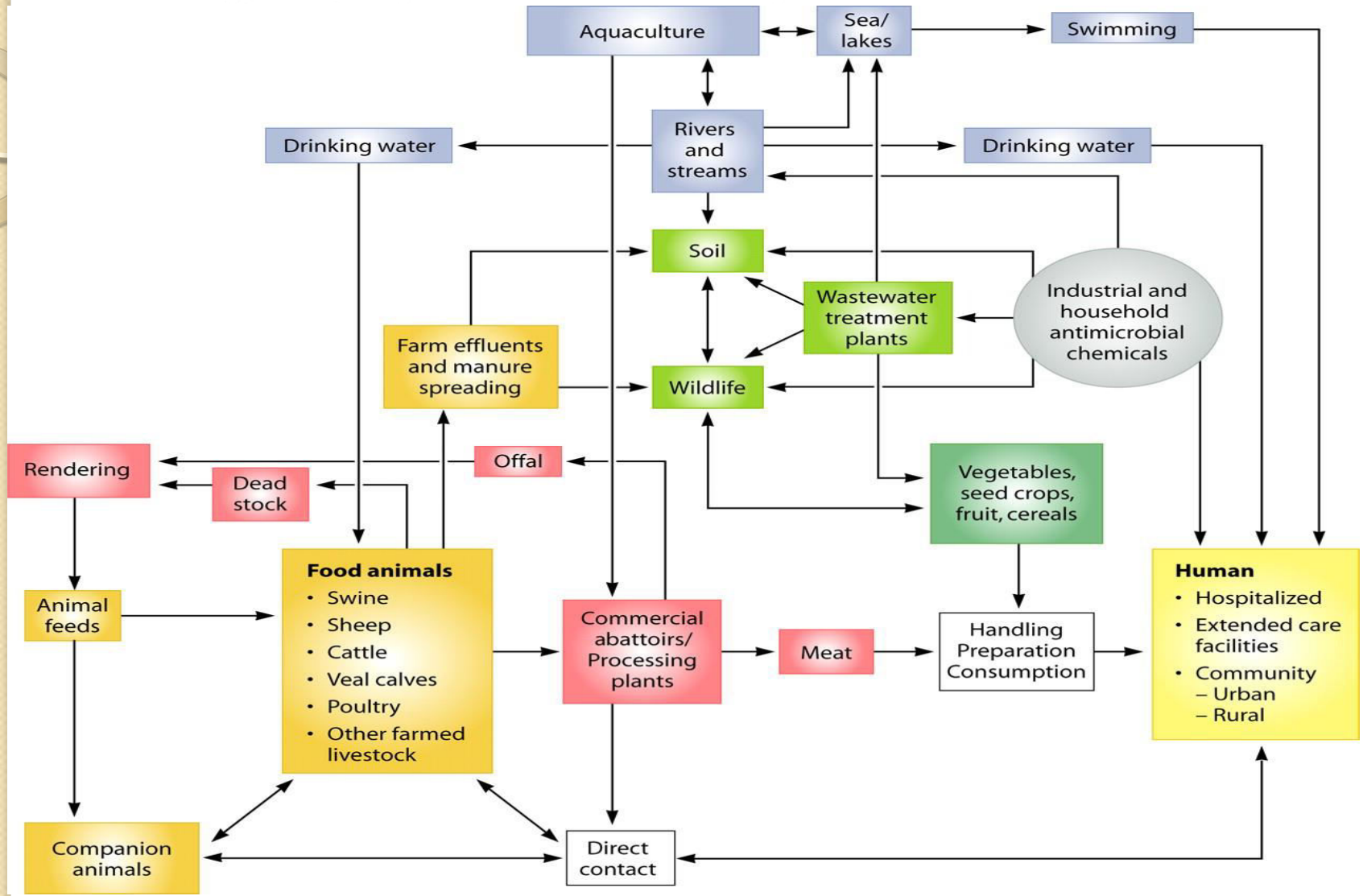
Superbugs and Super-resistance

- Many of the bacterial pathogens have evolved into multidrug-resistant (MDR) forms subsequent to antibiotic use e.g. MDR *M. tuberculosis*. Even from MDR to XDR (extremely drug resistant) and to TDR (totally drug resistant).
- The term "superbugs" refers to microbes possessing enhanced morbidity and mortality due to multiple mutations endowing high levels of resistance to the antibiotic classes. Realistically, antibiotic resistance is just like a virulence factor.

Superbugs and Super-resistance

- Other serious infections include nosocomial (hospital-linked) infections with bacteria like*: Acinetobacter baumannii, Burkholderia cepacia, Campylobacter jejuni, Citrobacter freundii, Clostridium difficile, Enterobacter spp., Enterococcus faecium, Enterococcus faecalis, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella spp., Serratia spp., Staphylococcus aureus, Staphylococcus epidermidis, Stenotrophomonas maltophilia, and Streptococcus pneumoniae, Vibrio cholerae.*
- *In these bacteria, horizontal gene transfer (HGT) plays an important part in creating superbugs.*

Dissemination of antibiotics and antibiotic resistance within agriculture, community, hospital, wastewater treatment, and associated environments.



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Mitigation Strategies

- It is clear that antibiotic resistance seems inevitable.
- What steps can be taken to prevent or at least delay this process?
- Over the years, many different solutions have been proposed by knowledgeable experts and all the major international health groups (e.g., WHO and the CDC).

Mitigation Strategies

Among the proposals for action are

- Strict controls on antibiotic use by humans, requiring accurate prescriptions (no use of antibiotics to treat colds and other viral infections),
- No delivery of antibiotics without a doctor's prescription (reducing needless use of antibiotics), and
- Controlled therapeutic use in animal husbandry and agriculture.

Mitigation Strategies

- Deception has played a role in this failure; many of the antimicrobials approved for treatment of humans are given to animals under the cover of different names for different uses, as described in the *Report of the Advisory Committee on Animal Antimicrobial Use Data Collection in the United States of the Alliance for the Prudent Use of Antibiotics.*

(DeVincent, S. J., and C. Viola. *2006. Deliberations of an advisory committee regarding priorities, sources, and methods for collecting animal antimicrobial use data in the United States. Prev. Vet. Med. 73:133-151.)*

Cross Ref. PubMed Google Scholar

Mitigation Strategies

- Interestingly, the Swann recommendations of 1969 were the first to call for a ban on non-therapeutic use in animals and agriculture, a reasonable but highly contentious suggestion that has been impossible to enforce in many countries to this day. (***Swann, M.*** *1969. Report of the joint committee on the use of antibiotics in animal husbandry and veterinary medicine. Her Majesty's Stationery Office, London, United Kingdom.*Google Scholar)

Mitigation Strategies

The antimicrobial resistance is emerging and spreading at a threateningly fast pace through microbial populations and even though the development of resistive strains is a normal evolutionary process, it is getting accelerated by the selective pressure exerted by widespread use of various antimicrobial drugs;

Mitigation Strategies

There is an urgent need to strengthen the existing strategies and develop innovative and alternative strategies to combat the detrimental effect of antimicrobial resistant micro-organisms under the One Health approach; (taking into fold the pathogens from humans, animals and environment sources)

Mitigation Strategies

There is dire need to achieve development goal set forth to evolve strategies for the mitigation of resistance to antimicrobial agents and foster

- international,
- regional,
- sub regional,
- multilateral and
- bilateral collaboration in evolving and implementing the same;

Mitigation Strategies

Accelerated efforts should be made to comprehensively examine the current status and understand the real extent of antimicrobial resistance in

- human and
- animal pathogens and
- environmental micro-organisms.

Mitigation Strategies

- More basic and applied research work should be directed towards evolving newer and effective strategies for prevention and containment of antimicrobial resistance, particularly in pathogenic micro-organisms.

Mitigation Strategies

- Ministries and agencies concerned with the human and animal health and environment should constitute scientific groups comprising the experts and practicing professionals of the NAM member countries and other developing countries to address the problems from various angles and also to exchange technological advancements available to mitigate antimicrobial resistance problems.

Mitigation Strategies

Specialised centres and research laboratories exclusively for the identification and surveillance of antimicrobial resistance in humans, animals and environment should be set up in each country or region to facilitate exchanging their antibiotic resistance data on a common platform like Global Antimicrobial Resistance Surveillance System (GLASS) by WHO, on a regular basis to enable interventions as well as knowledge sharing and networking.

Mitigation Strategies

Concerted efforts should be made

- to build strong, sustainable quality systems to eliminate falsified and substandard antimicrobials and
- ensure the supply of quality medicines, while strengthening post-market quality surveillance to guarantee their accessibility to the end users.

Mitigation Strategies

Research should be focused on finding new and innovative alternatives, including but not limited to,

- ✓ bacteriophages,
- ✓ antibodies,
- ✓ herbal medicines or
- ✓ newer and safer antibiotics to address the problem of antimicrobial resistance.

Mitigation Strategies

Specialized centres and research laboratories exclusively for the development of mitigation strategies against antimicrobial resistance like

- ✓ novel therapies,
- ✓ prophylactics and
- ✓ diagnostics should be set up by the governments of the different countries for mutual cooperation and networking among the institutions and nations.

Mitigation Strategies

- Established specialised centres and research laboratories should work in close tandem with the government agencies to formulate appropriate policies and guidelines to prevent escalation of menace of antimicrobial resistance.
- Emphasis should be laid on devising and enforcing appropriate legislative control measures to avoid the misuse of the antimicrobials in both human & vety sectors.

Mitigation Strategies

- The implementation of Antimicrobial Stewardship and infection prevention and control programme in
- human and
- veterinary medicine

should be accelerated to reduce the development of antimicrobial resistance and its spread.

Mitigation Strategies

- The Governments and NGOs should be actively involved in the creation of public awareness through
- knowledge transfer,
- including but not limited to print and
- mass media,

regarding judicious use of antimicrobials.

THANK YOU