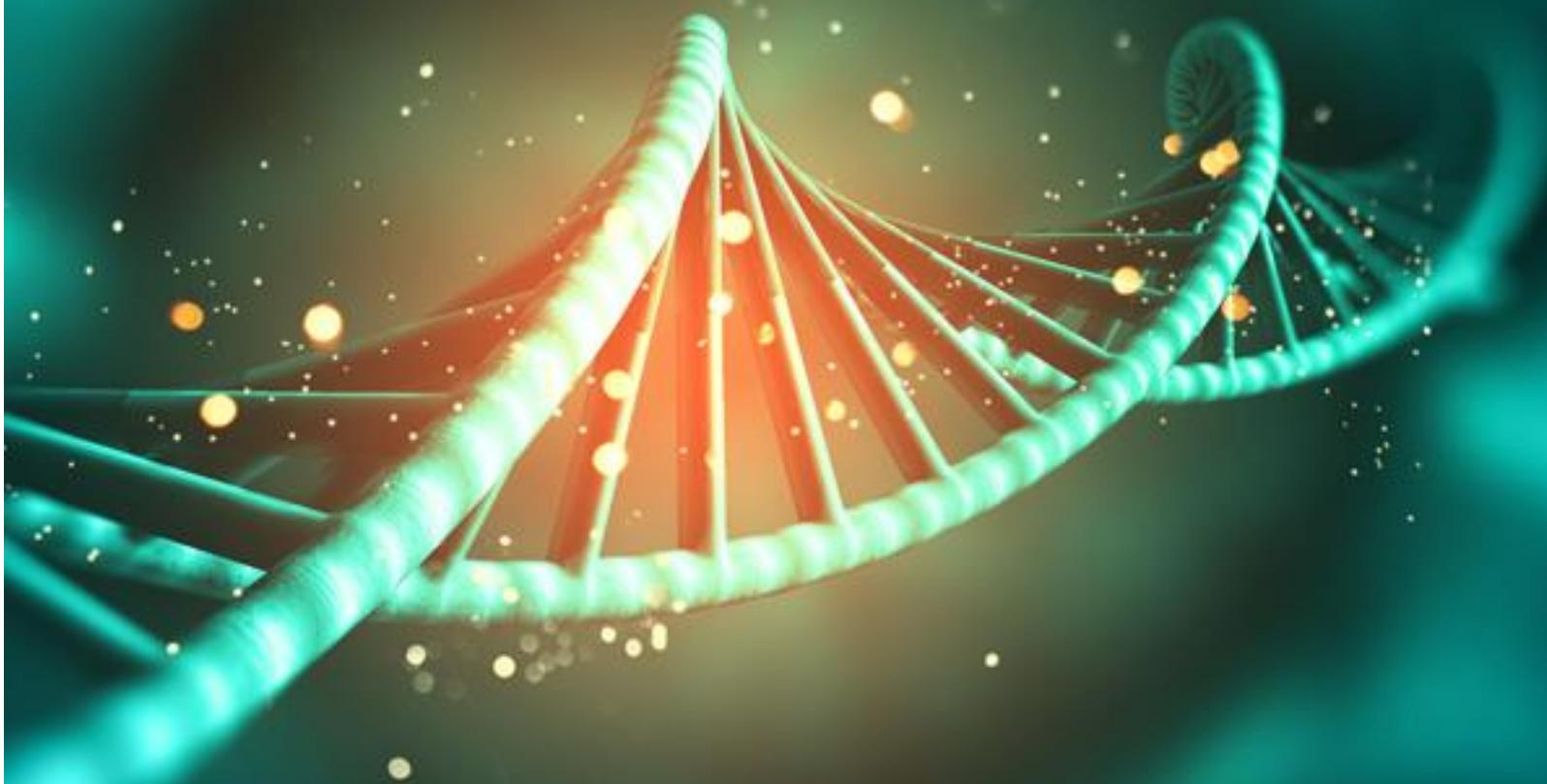


AntiMicrobial Resistance



Manual



Contents

Introduction

What you have to know about AMR

- : [How serious is the current AMR crisis ?](#)

Credit: Neem Summary Report 2015 - Oct FINAL

- : [How does antimicrobial resistance occur in the veterinary field ?](#)
- : [How do people get infections with resistant bacteria from animals ?](#)
- : [Can you give me some examples of resistant bacteria ?](#)
- : [Can you give me some examples of resistant viruses ?](#)
- : [What are the global surveillance measures for AMR ?](#)

interprofessional movement against AMR

- : [What can I do to help tackling AMR in my daily life ?](#)
- : [What can I do to help tackling AMR as a pharmacist ?](#)
- : [What can I do to help tackling AMR as a veterinarian ?](#)
- : [What can I do to help tackling AMR as a human doctor ?](#)
- : [What are the possible solutions to mitigate resistance in those cases ?](#)

Resources for further information

- : [Links to information about AMR](#)
- : [Links to national & global action plans](#)
- : [Links to infection prevention](#)
- : [Links regarding surveillance of resistance](#)

References





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INTRODUCTION

Dear all,

We are very excited to present this manual to you, which is the result of a joint effort between representatives of the International Federation of Medical Students' Association (IFMSA), the International Pharmaceutical Students' Federation (IPSF), and the International Veterinary Students' Association (IVSA). These organizations have been collaborating for months on this project with the common goal of raising awareness about antimicrobial resistance as well as encouraging students all over the world to take an active role in the fight against antimicrobial resistance. The primary object of this manual is to provide a concise overview of antimicrobial resistance through the One Health approach. Please feel free to share this manual with as many people as you would like, and remember that we all can make a difference.

Enjoy reading!

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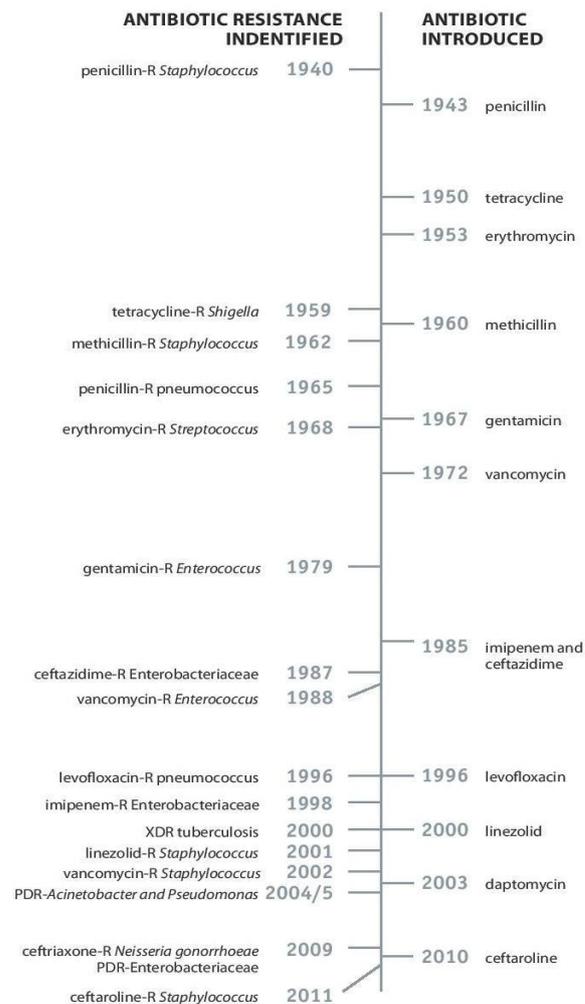
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WHAT YOU HAVE TO KNOW ABOUT AMR

● What is antimicrobial resistance?

According to the World Health Organization (WHO), antimicrobial resistance happens when microorganisms (including bacteria, fungi, viruses and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarial and anthelmintic) used to treat the infections they cause. These are sometimes referred to as “superbugs”. As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others.



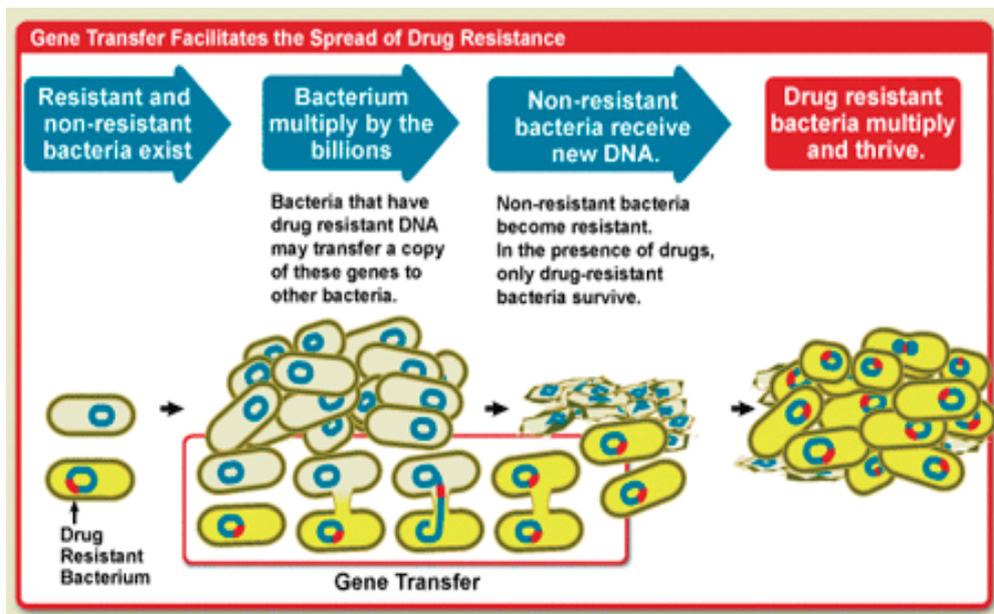


- **What is the difference between antibiotic resistance and antimicrobial resistance?**

Antibiotic resistance refers specifically to the resistance to antibiotics that occurs in common bacteria that cause infections. Antimicrobial resistance is a broader term, encompassing resistance to drugs to treat infections caused by other microbes as well, such as parasites (e.g. malaria), viruses (e.g. HIV) and fungi (e.g. Candida).

- **How does antibiotic resistance occur?**

The two following illustrations shows how it can happen and spread.

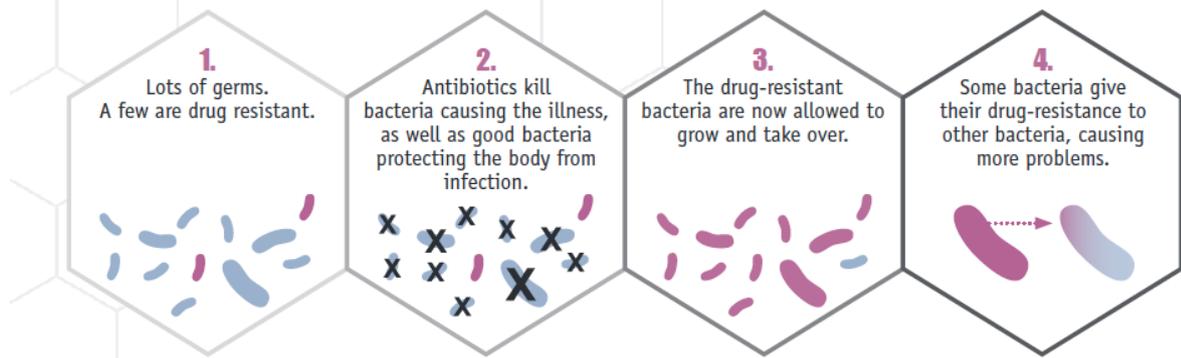


Credit: Centers for Disease Control and Prevention

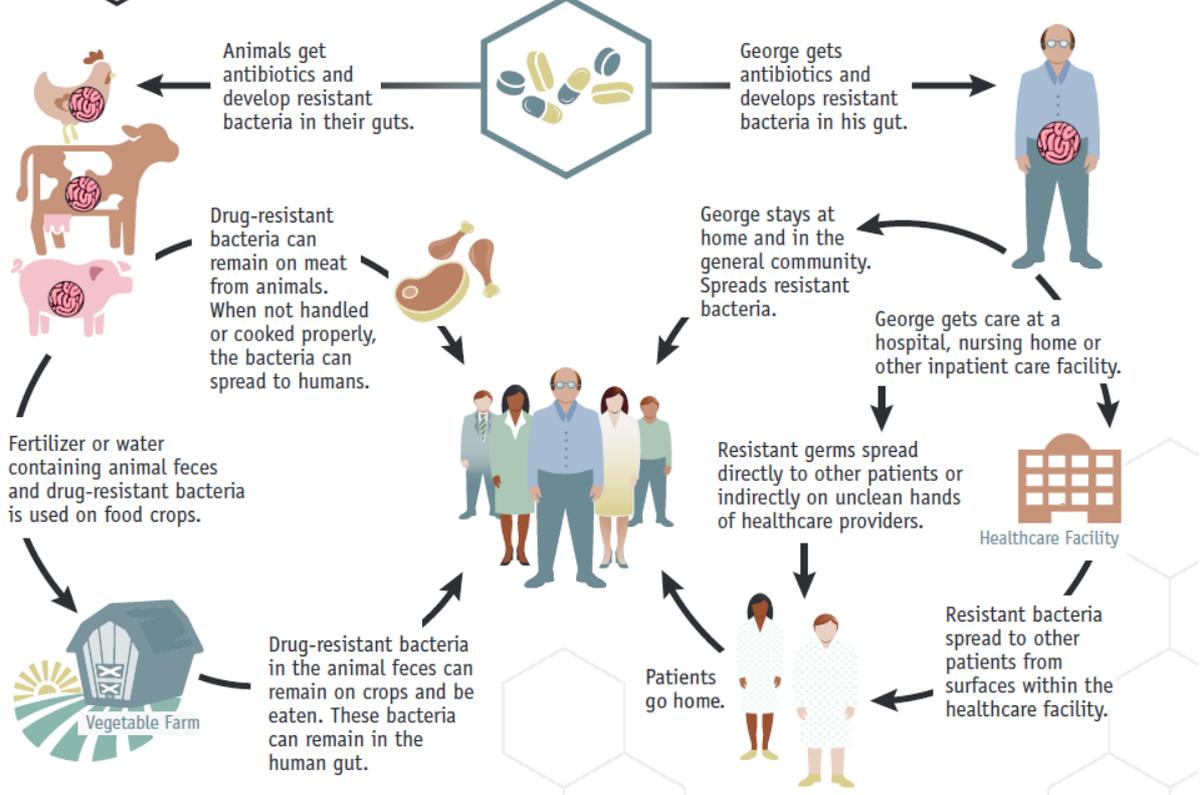




How Antibiotic Resistance Happens



Examples of How Antibiotic Resistance Spreads



Simply using antibiotics creates resistance. These drugs should only be used to treat infections.



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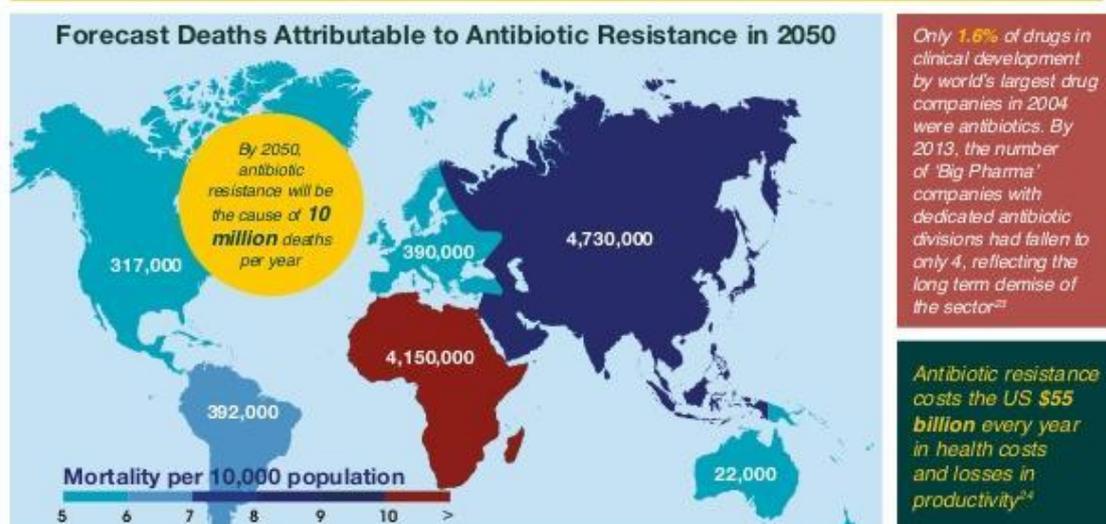
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- **How serious is the current AMR crisis?**

Without effective treatment, many standard medical treatments will fail or turn into very high risk procedures. Consider that people may die from common bacterial infections again! Antimicrobial resistance causes prolonged diseases –and so increases the risk of spreading to others; it also increases probability to death and leads to greater health care costs and expenses.

A Return to the Dark Age of Medicine?



Source: Review on Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations (2014)

Credit: Neem Summary Report 2015 - Oct FINAL

Among the different antimicrobial resistances, antibiotics are the most widely and irrationally used, making it the most urgent trend. Antibiotic resistance is getting increasingly worse, as you can see on the graph below. The issue is so crucial that WHO developed a global action plan on antimicrobial resistance, which was adopted by Member States at the Sixty-Eighth World Health Assembly and supported by the FAO and OIE governing bodies in May and June 2015. The goal of the global action plan is to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them.

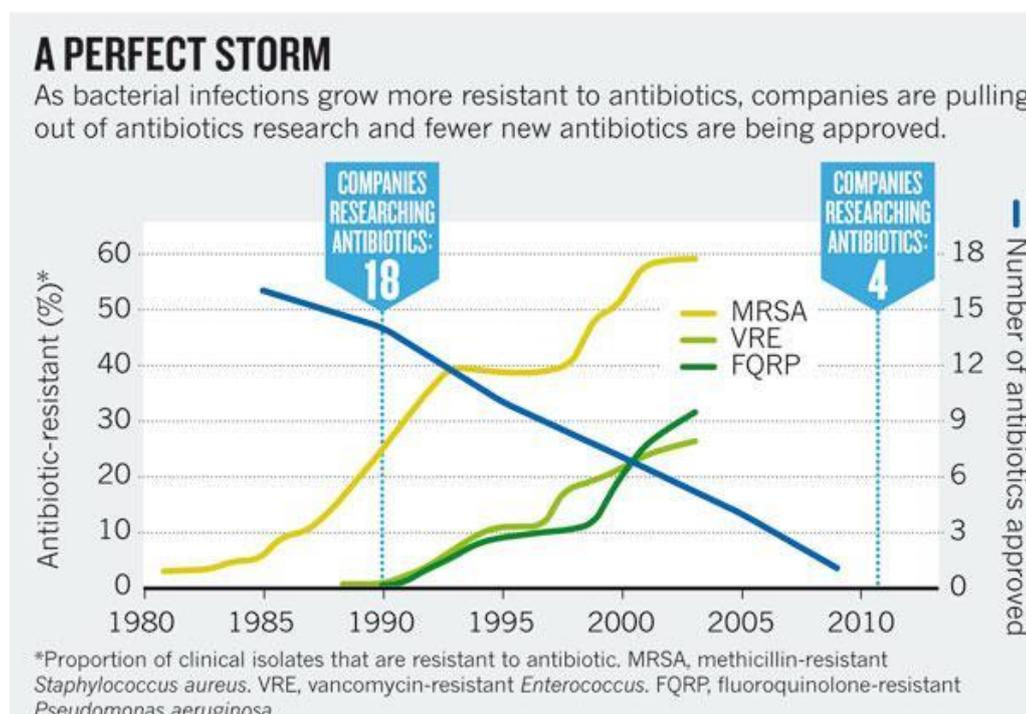
Later that year WHO launched the first World Antibiotic Awareness Week to raise awareness of antibiotic resistance. The week now takes place annually in November.





Over the years, developing a new antibiotic has become very expensive and difficult, which increases the gravity of the crisis.

Sometimes the bacteria causing infections are resistant to the first-choice drug and this one doesn't work. Physicians must then recommend second or third-choice drugs for treatment, but these drugs might be less effective, more toxic, and more expensive. Preserving the effectiveness of antibiotics is vital to protect human and animal health.



Credit: Centers for Disease Control and Prevention

● How does antimicrobial resistance occur in the veterinary field?

In the veterinary field, different practices are responsible for facilitating antimicrobial resistance.

For instance, in production animals, it is still common to use antibiotics not only for treatments, but also as growth promoters. It means that the breeder uses the antibiotics at a low, sub-therapeutic dose so as to limit the development of bacteria. The interest for the breeder to do that is to help his animals growing faster. Indeed, antibiotics may decrease the production of toxins by intestinal bacteria and improve the absorption of nutrients due to thinning of small intestinal barrier. The issue is that this method contributes to the selection of resistant bacteria.





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Another example, this time with companion animals, is the unnecessary medical prescription of antibiotics, sometimes prescribed just in case, when nothing was diagnosed.

- **How do people get infections with resistant bacteria from animals?**

People can get exposed to resistant bacteria from animals when they handle them or when they come into contact with the animal faeces. They can also get exposed when they eat meat or any other products contaminated with resistant bacteria.

Another way is through contaminated food. All animals, just like all humans, carry bacteria in their intestines. Giving antibiotics to animals will kill most bacteria, but resistant bacteria can survive and multiply. These bacteria can contaminate the meat or other animal products when the animals are slaughtered and processed. They can also get into the environment through the excrements of the animals and then contaminate the water used for other productions.

- **Can you give me some examples of resistant bacteria?**

- **Staphylococcus aureus** - People suffering from **MRSA**, that is to say **Methicillin-Resistant *Staphylococcus aureus***, are estimated to be **64% more likely to die** than people with a non-resistant form of the infection. *Staphylococcus aureus* is a common source of severe infections in the community and in hospitals.

- ***Escherichia coli*** – This bacterium is widely resistant to fluoroquinolone, the most common antibiotic used for the oral treatment of urinary tract infections caused by it.

Resistance in *E. coli* to one of the most widely used medicines for the treatment of urinary tract infections (fluoroquinolone antibiotics) is very widespread. There are countries in many parts of the world where this treatment is now ineffective in more than half of patients.



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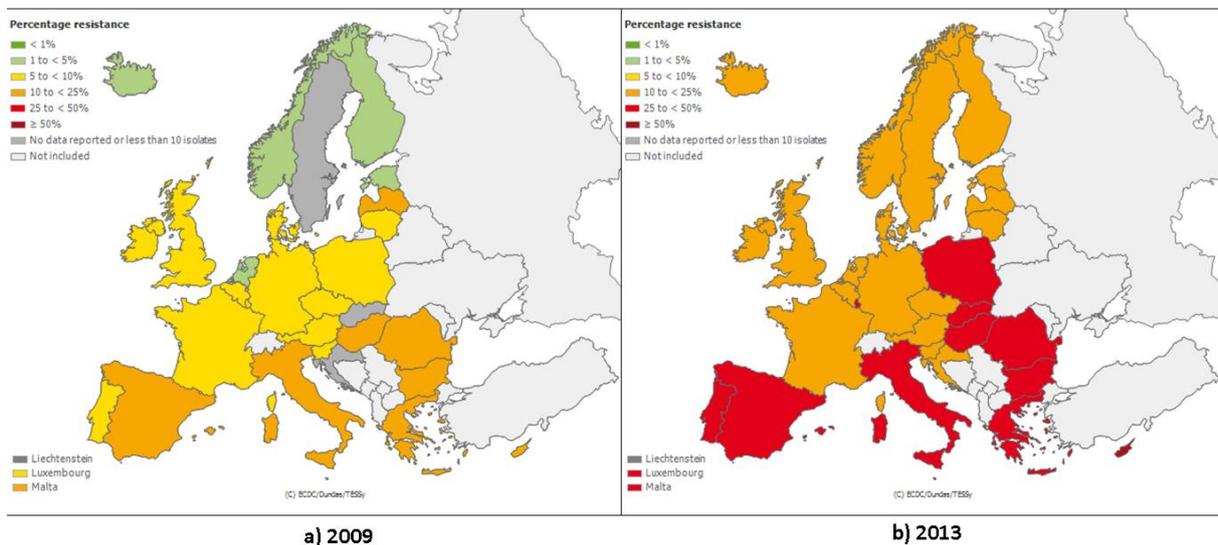
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WHO recently updated the treatment guidelines for gonorrhoea to address emerging resistance. The new WHO guidelines do not recommend quinolones (a class of antibiotic) for the treatment of gonorrhoea due to widespread high levels of resistance. In addition, treatment guidelines for chlamydial infections and syphilis were also updated.

- **Enterococcus sp** – Lots of them are resistant to Vancomycin and are called Vancomycin Resistant Enterococcus (VRE).
- **Mycobacterium tuberculosis** – This bacterium, responsible for **tuberculosis**, can be Multidrug-resistant (MDR-TB), that is to say resistant to at least isoniazid and rifampin; and can be sometimes even Extensively Drug-Resistant (XDR-TB), that is to say additionally resistant to any fluoroquinolone and at least one of three injectable second-line drugs (amikacin, kanamycin or capreomycin). In 2013, there were an estimated 480 000 new cases of MDR-TB in the world, and XDR has been identified in **100 countries**, in all regions of the world. It has also become an important worrisome.

Escherichia coli resistant to cephalosporins across Europe in a) 2009 and b) 2013





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- **Can you give me some examples of resistant viruses?**

- **HIV drug resistance** - HIV drug resistance emerges when HIV replicates in the body of a person infected with the virus who is taking antiretroviral drugs. HIV drug resistance may rise to such a level that the first-line and second-line anti-retroviral therapy regimens currently used to treat HIV become ineffective.

- **Influenza drug resistance** - Antiviral drugs are important for treatment of epidemic and pandemic influenza. So far, virtually all influenza A viruses circulating in humans were resistant to one category of antiviral drugs – M2 Inhibitors (amantadine and rimantadine). However, the frequency of resistance to the neuraminidase inhibitor oseltamivir remains low (1-2%). Antiviral susceptibility is constantly monitored through the WHO Global Influenza Surveillance and Response System.

- **What are the global surveillance measures for AMR?**

- WHO has a surveillance system for AMR. For the specific case of Salmonella sp, for instance, a worldwide network of institutions and individuals consisting of 156 countries and 1185 members are helping to the detection, control and prevention of foodborne illness and infections. Through this surveillance program, Salmonella typhimurium DT104 appears to be resistant to more than 5 antibiotics tied to genomic evolution.

- One of the tools for the AMR surveillance is the Global Antimicrobial Resistance Surveillance System (GLASS), launched by the WHO to support a standardized approach to the collection, analysis and sharing of data on AMR at a global level. GLASS aims to combine clinical, laboratory and epidemiological data on pathogens that pose the greatest threats to health globally.



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- **INTERPROFESSIONAL MOVEMENT AGAINST AMR**

Interprofessional collaboration is effective in every mechanism related to spread of AMR. By improving awareness about AMR among our association members and by defining their specific roles as future doctors, pharmacists and veterinarians and their roles in collaboration with each other, future generations will be having a greater understanding of how to act to diminish the spread of AMR worldwide. Here we recommend four different mechanisms of interprofessional collaboration:

- ① One of the most effective strategies to control AMR in hospitals is providing **stewardship programs** and creating **guidelines** on rational use of antibiotics. Those guidelines are provided within Drug and Therapeutic Committee (DTC) in hospitals. In those DTCs, medical doctors and pharmacists work through an interprofessional collaboration to create those guidelines.
- ② One important reason of AMR spread is the irrational use of antibiotics for breeding animals. This is where veterinarians and pharmacists should collaborate closely with each other. Pharmacists should not provide over-the-counter antibiotics to farmers who do not have a veterinarian consent or prescription while veterinarians should have strict guidelines for providing animals with antibiotics.
- ③ Improper drug disposal leading to AMR is another concern. Pharmaceuticals disposing their products waste into water and to a lesser extent medications flushing can pollute the water which can be used in livestock and farmers. Here is also where pharmacists and veterinarians should work together. Pharmaceuticals should obey the proper guidelines for disposing the waste and make sure the antimicrobial products are not released into the water while veterinarians should monitor that animals are not watered with improper unstandardized water.
- ④ Irrational prescription of antibiotics for patients should be restricted by doctors. It should be explained to the patients that antibiotics are not the first choice in treatment of the flu and most cases are viral. Patients won't trust pharmacists if they see their requested over-the-counter antibiotics easily prescribed by their medical doctor. Medical doctors and pharmacists should work on people awareness on rational use of antibiotics.



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- **What can I do to help tackling AMR in my daily life?**

A first easy and very good way to start helping is sticking to healthy habits so as to avoid infections as much as possible:

- **Clean your hands** - Regular hand cleaning, particularly before and after certain activities, is one of the best ways to remove germs, avoid getting sick, and prevent the spread of germs to others.

- **Stay up-to-date with vaccines** - Disease prevention is key to staying healthy. It is always better to prevent a disease than to treat it. Vaccines can protect both the people who receive them and those with whom they come in contact. Vaccines are responsible for the control of many infectious diseases that were once common around the world, including polio, measles, diphtheria, pertussis (whooping cough), rubella (German measles), mumps, tetanus, and Haemophilus influenzae type b (Hib). Over the years' vaccines have prevented countless cases of infectious diseases and saved millions of lives.

- **Pay attention to keeping your food and your water safe**

- **Prevent the spread of sexually transmitted diseases** - Take control and learn effective strategies to reduce STD risk. Know the facts and protect yourself and your partner.

Of course, even doing your best, you may get sick at some point. In this case, you can still act to help tackling AMR:

- **Learn when illnesses need antibiotics and value symptom treatment** - Are you aware that colds, flu, most sore throats, and bronchitis are caused by viruses, on which antibiotics are ineffective? They aren't always the answer for common respiratory infections. Symptom relief, with over-the-counter medicines, might be the best treatment option. With a cold, a type of viral infection, you will recover when the illness has run its course within two weeks. You should keep your healthcare provider informed if you or your child's illness gets worse or lasts longer than expected, that may be then the signal for a bacterial infection.

1. **Respect the recommendations of your practitioner.** Only use antibiotics when prescribed by a certified health professional and don't demand antibiotics if your health worker says you don't need them.
2. Always follow your health worker's advice when using antibiotics
3. Never share or use leftover antibiotics
4. Prevent infections by regularly washing your hands, avoiding close contact with sick people, practise safer sex and keeping your vaccinations up to date



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● What can I do to help tackling AMR as a pharmacist?

As a pharmacist and the last member of healthcare chain, you can have a great impact on reducing the rate of AMR prevalence by simply talking to your patients. By taking to action these 7 statements, be a 7-star pharmacist:

1. Ask patients to **wash their hands** and care for their hygiene.
2. Ask patients to **complete their vaccination program** properly.
3. Ask patients **not to be in close contact** with people who suffer from communicable diseases.
4. Ask patients not to get over-the-counter **antimicrobial medicines** and stop giving over-the-counter antibiotics to patients.
5. Ask patients to **complete the duration of their treatment** with antibiotics, each day at the exact times according to doctor's prescription till the final day.
6. For common cold, ask patients to **take rest and wait for 2-3 days** for their symptoms to improve. In most cases, common cold is viral and doesn't need antibiotics.
7. **Raise awareness** about AMR within your pharmacy and also as a person who cares for AMR elsewhere.

For further information, the **Antimicrobial Stewardship Program** may interest you. It compels all guidelines for prescription and use of antibiotics designed by healthcare facilities. According to the situation of a country, antibiotic prescription pattern for any related indication is determined and ascertained within the Drug and Therapeutic Committee (DTC) of the hospital. Doctors and specialists of each hospital are all obliged to obey the guidelines and not allowed to prescribe antibiotics which are on the prohibited list. General and clinical pharmacists are involved in DTC to specify the right dosage and duration of therapy for each indication of each drug on the list.

You can find the link of John Hopkins Antimicrobial Stewardship Program:

<http://www.hopkinsmedicine.org/amp>



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- **What can I do to help tackling AMR as a veterinarian?**

As a veterinarian, you should ensure that antibiotics given to animals are only used to treat infectious diseases and not as growth promoters. You should vaccinate animals to reduce the need for antibiotics. You can promote and apply good practices at all steps of production and processing of foods from animal sources.

- **What can I do to help tackling AMR as a human doctor?**

As a human doctor, you can have a great impact during your consultations with your patients. You can remind them the importance of cleaning hands, checking if they are up to date with their vaccines. You can also act by only prescribing antibiotics when they are truly needed and by choosing the right antibiotic at the right dose and for the right duration.

1. Prevent infections by ensuring your hands, instruments and environment are clean
2. Keep your patients' vaccinations up to date
3. Talk to your patients about antibiotic resistance and dangers of unnecessary use
4. Only prescribe and dispense antibiotics when they are truly needed
5. Prescribe and dispense antibiotics according to current guidelines

- **What are the possible solutions to mitigate resistance in those cases?**

For the instance of growth promoters in production animals, the idea is to introduce alternative strategies. Some possibilities may be fatty acids, essential oils such as clove / cinnamon / citrus, which helps reducing the host association. Some complex oligosaccharides and glycans prevent the binding of bacteria to the cell surface. Growth promoters are already banned in the European Union, and potentially in California.

For the instance of unnecessary prescription of antibiotics in companion animals, an option is to really think before prescribing and explaining our choice of not doing anything to the owner – which is sometimes the best thing to do.



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RESOURCES FOR FURTHER INFORMATION

Links to information about AMR

- Centre for Disease Control - <http://www.cdc.gov/drugresistance/>
- World Health Organization

<http://www.who.int/drugresistance/en/>

Antimicrobial resistance: global report on surveillance, 2014

Worldwide country situation analysis: response to antimicrobial resistance, 2015

Links to national & global action plans

- WHO Global plans

Global action plan on antimicrobial resistance

Global action plan to control the spread and impact of AMR in *Neisseria gonorrhoeae*

WHO global strategy for the surveillance and monitoring of HIV drug resistance

Global plan for artemisinin resistance containment

- National action plans - <http://www.who.int/drugresistance/action-plans/en/>

Links to infection prevention

- Infection Prevention Homepage
- WHO Patient Safety Homepage
- WHO Global Patient Safety Challenge - Tracking antimicrobial resistance
- World Alliance for Patient Safety
- WHO Documents for Infection Control in Health Care

Links regarding surveillance of resistance

- WHO

Surveillance of antimicrobial use

European Surveillance of Antimicrobial Consumption

European Antimicrobial Resistance Surveillance System (EARS-Net)

WHO advisory group on integrated surveillance of AMR: 6th meeting report



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http://www.cdc.gov/drugresistance/pdf/hai-patient-empowerment_dpk.pdf

Adult treatment recommendations

<http://www.cdc.gov/getsmart/community/for-hcp/outpatient-hcp/adult-treatment-rec.pdf>

Materials for healthcare professionals

<http://www.cdc.gov/getsmart/week/downloads/getsmart-penicillin-factsheet.pdf>

Materials for medical students:

<http://www.wakehealth.edu/School/CAUSE/Get-Smart-About-Antibiotics.htm>

For pharmacists

<http://www.cdc.gov/getsmart/community/for-hcp/pharmacists-ce-courses.html>

Antibiotic and food safety

<http://www.hopkinsmedicine.org/amp>

<http://www.cdc.gov/foodsafety/challenges/from-farm-to-table.html>

<http://www.who.int/salmsurv.en/>

<http://www.who.int/drugresistance/surveillance/en/>



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