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Antimicrobial resistance (AMR) - Antimicrobial Resistance (AMR) in relation to plant health aspects
Agenda item 8.9
Prepared by the IPPC Secretariat
English only

This paper has been developed by the IPPC Secretariat and Commission on Phytosanitary Measures (CPM) Bureau members in cooperation with the FAO Task Force on Antimicrobial Resistance (AMR) to raise awareness of AMR as a threat to health and global development. The Strategic Planning Group (SPG) (October 2018) and the CPM Bureau agreed to include AMR in the agenda of the 14th Session of the Commission for Phytosanitary Measures (CPM-14) with an information paper that explores plant health aspects relevant to the risks, impact and implications of AMR.

Summary

- AMR occurs when microbes become resistant to antimicrobials. Bacteria, viruses, and other microbes mutate to survive antimicrobials that are given to treat diseases.
- AMR is a natural phenomenon. It cannot be eliminated but it must be controlled.
- AMR is a huge threat - to health (humans and animals), food security and to global development. Imagine a world without effective antibiotics.
- The more antimicrobials are used inappropriately – the more resistance is triggered.
- Foods of plant origin play a role in the food-borne transmission of resistant microorganisms.
- Antibiotic resistance is of particular concern given that bacterial infections are common in humans and animals and the range of available antibiotics and their development is limited.
- The mandate to prevent and control the introduction and spread of pests means that IPPC is uniquely placed to implement effective measures to contribute to the global AMR efforts.

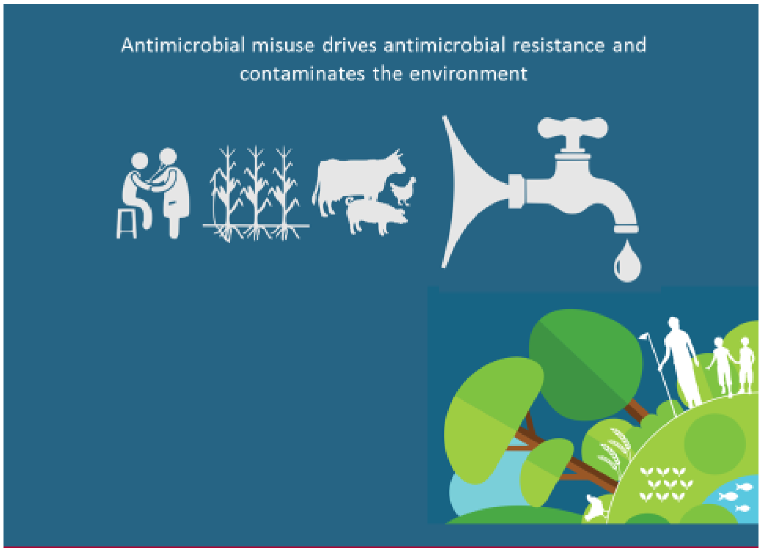
What is antimicrobial resistance?

AMR is about microbes becoming resistant to antimicrobials. This occurs when bacteria, viruses, and other microbes mutate to survive antimicrobials given to treat disease in humans and animals.

Antibiotic resistance is the current focus of AMR efforts given that bacterial infections are common in humans and animals. Until recently, AMR has mainly been addressed from a human and animal health perspective, but more attention is now being drawn to the environment, including plants.

Bacteria and fungi are important causes of plant disease and production losses worldwide. Climate change is predicted to exacerbate this problem through the occurrence of extreme weather events that damage and stress plants, and shifts in climatic conditions that impact the distribution and spread of pest populations into new areas.

Antimicrobials play a critical role in plant production to treat diseases and reduce their impact on production, food safety and food security.



Antimicrobials play a critical role in human health, plant production and in veterinary medicine to treat diseases ensuring good health, food safety and food security. However, overuse or misuse of antimicrobials in all sectors triggers resistance and increases the risk of polluting the environment with antimicrobial residues, resistant genes and pathogens.

While there is not a significant body of information that indicates plant production systems as a major risk in the development and proliferation of AMR, large volumes of antimicrobials are applied to crops to control plant pests.

Pesticide resistance can lead to reduced plant yields and economic losses to the producer. Agrochemical companies have long been aware that plant pests can develop resistance to crop protection chemicals and have developed strategies to reduce this risk and extend the life of their products. For example, many disease control strategies that use a systemic eradicant fungicide will include a protectant chemical to reduce disease pressure and improve both the efficacy and longevity of the eradicant product. Insect resistance to insecticides and fumigants has been widely studied and documented.

The overuse or misuse of antimicrobials can also trigger development of resistant microorganisms relevant to human and animal health. There is scientific evidence that foods of plant origin serve as a vehicle for food-borne exposure to resistant bacteria (Bezanson et al., 2008; Boehme et al., 2004; Hassan et al., 2011; Raphael et al., 2011; Rodríguez et al., 2006; Ruimy et al., 2010; Schwaiger et al., 2011; and Walia et al., 2013).

AMR Awareness and Action

AMR has gained increasing attention at the international level due to its impact on humans and animals, as well as on global economics. The costs of AMR are significant. Globally, it is estimated that about 700,000 people die each year from infections caused by antibiotic resistant bacteria. The corresponding estimate for the European Union (EU) is about 33 000 (European Centre for Disease Prevention and Control). By the year 2050, AMR may strip the global economy of more than $6 trillion dollars annually, corresponding to nearly 4% of global Gross Domestic Product. These impacts are predicted to hinder countries from reaching the Sustainable Development Goals by 2030, in particular goals realizing food security, good health and wellbeing. The World Health Assembly (WHA) adopted a global action plan (GAP) to tackle AMR in 2015[1], where all member states committed to develop their own national action plans on AMR in line with the GAP by 2017. The UN General Assembly then adopted a resolution[2] in 2016 to ensure sustained and effective global action to address AMR.

[1] http://www.wpro.who.int/entity/drug_resistance/resources/global_action_plan_eng.pdf
[2] A/RES/71/3

AMR awareness is steadily increasing in the pesticide management community. For example, the FAO/WHO Joint Meeting on Pesticide Management (JMPM) agreed in October 2018 that:

- Antimicrobial resistance issues should to be integrated into technical guidelines, where relevant, and,
- Antibiotics used for human and animal health should not be registered as pesticides by countries.

Different sectors, however, have different definitions of the same antimicrobial agents. The International Code of Conduct on Pesticide Management[3] for example, defines a pesticide as “any substance, or mixture of substances of chemical or biological ingredients intended for repelling, destroying or controlling any pest, or regulating plant growth”, thereby including agents such as streptomycin. Streptomycin belongs to the antibiotic class of aminoglycosides and is defined by WHO as a critically important antimicrobial (CIA) for human medicine[4].

AMR, Plant Production and Crop Protection

Pathogens and genes resistant to antimicrobials used in human and animal medicine have been detected on plants. Soil, irrigation water, insects, animal intrusion, manure as fertilizer, and human handling are probable contamination sources.

There is increasing concern that overuse or misuse of antimicrobials to manage plant pests is creating a selection pressure in the production environment. This selection pressure can accelerate the development and spread of AMR for example from soil bacteria to human pathogens present in the natural environment. As such, it is not only the antimicrobials that should be regarded as environmental contaminants, but also the genes that confer AMR.

Antimicrobials present in the environment create a selection pressure that leads to the development of AMR. Antibiotics and copper formulations are used to treat and control plant diseases. Evidence indicates that contamination of soil with copper promotes AMR in soil bacteria. Bacteria exposed to a combination of antibiotics and pesticides develop resistance faster. Contamination of soils with these products following crop application leads to enrichment of AMR bacteria and AMR genes in the environment.

Bacteria resistant to both metal ions and antimicrobials are more commonly present in bacteria of plant origin compared to bacteria from animals or humans (Pal et al., 2015). Other studies show that bacteria develop antibiotic resistance up to 100,000 times faster when exposed to pesticides and antibiotics in combination compared to when exposed to antibiotics alone (Kurenbach et al 2018). Thus, the use of antimicrobials in plant production provides a potentially important risk factor for selection and dissemination of resistant microorganisms and genes from plants to humans and animals.

> Approximately 25% of plant origin food products were contaminated with antibiotic resistant bacteria in a scoping review of the literature. Because fruits and vegetables are frequently eaten raw or with minimal processing, fresh produce may serve as a source of dietary exposure to resistant bacteria and resistance genes.

Foods of plant origin serve as a vehicle of food-borne exposure to resistant bacteria. However, the relative importance of AMR in the plant production environment is not fully understood and needs to be defined.

[3] http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Code/Code_ENG_2017updated.pdf

[4] https://www.who.int/foodsafety/publications/cia2017.pdf

Antimicrobial use in plant production

There is currently no robust data on the volume of antimicrobial use by the plant sector worldwide. However, as an example, at least 20 countries outside the EU authorise antibiotic use to control fire blight and citrus greening disease in plants. In some countries, streptomycin is authorized to control certain bacterial diseases in pip fruit, stone fruit, seedling tomatoes and kiwifruit. Kasugamycin, oxytetracycline and oxolinic acid are other antibiotics used to control plant pests (de León et al., 2008; Stockwell and Duffy, 2012. These and others, including aminoglycosides, quinolones and tetracycline, are used in human and veterinary medicine.

Many countries do not approve any antibiotic as active ingredients in pesticides. Others may approve them for emergency use only and apply strict regulatory controls on their use. Commercial factors, such as availability, efficacy and cost also impact the use of antibiotics in crop production systems.

Triazole antifungals/fungicides are widely used for the control of infectious diseases of both humans and plants. The emergence of azole resistance is now challenging the management of human aspergillosis, a life-threatening infection if invasive (Rivero-Mendez et al 2016). Strategies have also been developed by chemical companies to prevent the development of plant pathogen resistance to azoles.

Focusing on preventative measures

Neither reducing the use of antibiotics nor the discovery of new ones may be sufficient strategies to avoid a post-antibiotic era. This is because bacteria may be exposed to other non-antibiotic chemicals, like pesticides or biocides that can increase selective pressure for the development of antibiotic resistance.

By preventing disease in all sectors, the need for all types of antimicrobials could be greatly reduced. International AMR focus has shifted from antimicrobial management and use towards implementing good agricultural and production practices, biosecurity, and infection control, thereby reducing the need for antimicrobials and the selective pressure for developing AMR.

In the animal sector, the World Organisation for Animal Health (OIE) is increasingly focusing on preventative measures instead of using antimicrobials to combat animal diseases. Preventative measures include guidance on improved hygiene and biosecurity, boosting immunity with high quality feed and vaccination programs, and breeding programs for more robust animals.

The Codex Alimentarius Commission (CAC) has re-established the ad hoc Codex Intergovernmental Task Force on Antimicrobial Resistance (TFAMR)[5] with the objective to develop science based guidance on the management of food-borne AMR by 2021. The CAC has previously published guidelines for risk analysis of food-borne AMR, which provide a structured framework to address the risks to human health from AMR in food, including food of plant origin[6].

In this context, International Standards for Phytosanitary Measures (ISPMs) adopted by the CPM play a significant role by helping countries to prevent the introduction of pests, improve and maintain their plant health, and thereby reduce the need for antimicrobials use and the risk of AMR development. Implementation of good agricultural practices and integrated pest management (IPM), as described in the

[5] http://www.fao.org/fao-who-codexalimentarius/committees/committee/en/?committee=TFAMR

[6] file:///C:/Users/EKLUND/Downloads/CXG_077e%20(4).pdf

International Code of Conduct on Pesticide Management[7] will also help greatly to reduce the reliance on pesticides including antibiotics. Harmonized systems for recording antimicrobial use and resistance in crops would provide guidance to producers and inform policy work.

What can the international plant health community do?

The full extent to which antimicrobial use in plant production selects for the emergence of AMR in plant pathogens, soil or spoilage organisms and in zoonotic pathogens present on foods of plant origin is not fully understood. AMR is detected in plants and their immediate environment, and antimicrobials enhance the selection pressure for resistance development.

While more information is needed to quantify the relationship between the use of antimicrobials and other disease preventative measures on the selection, transmission, and persistence of AMR in the surrounding plant production environment, the IPPC community could play an important role in multi-sectoral efforts to decrease the risks with AMR.

In the short term, prevention is a primary focus for the plant production and protection sector in reducing plant associated development and proliferation of AMR. Preventative actions include many elements essential to the effective prevention, control and management of plant pests.

Contracting parties are encouraged to:

1. Restrict the use of antibiotics in crop production and plant protection, and particularly those that are used in animal and human disease control.
2. Develop and implement integrated production processes that prevent or reduce the incidence and severity of plant pests and diseases, and with it, the need to apply pesticides. This might include good agricultural practices, such as crop rotation, or pest impact reduction strategies using host resistance – whether this is achieved through conventional breeding, gene editing or genetic modification; induced resistance; integrated pest management; and biological controls.
3. Apply strategies to minimize the development of pest resistance to pesticides.
4. Develop and implement strategies to minimize the contamination of plants and plant products with bacteria that cause food-borne illnesses, including faecal bacteria.
5. Continue working together through the IPPC to prevent the international movement of pests.

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[7] http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Code/Code_ENG_2017updated.pdf

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