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AGRICULTURAL RESEARCH FOR DEVELOPMENT

Antimicrobials in agriculture: reducing their use while limiting health and socioeconomic risks in the countries of the South

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The widespread use of antimicrobials in agriculture is increasing, driven by growth in intensive livestock production and demand for animal products. This is creating a serious problem of antimicrobial resistance: bacteria are developing antimicrobial resistance mechanisms, which spread through populations of bacteria, including those affecting humans. Antimicrobial resistance has a major impact on public health, and its effects on animal health and biodiversity are not yet fully understood. To address this alarming situation, reducing and rationalising the use of antimicrobials is a global priority, in the North and the South alike. This calls for intersectoral actions involving professionals and researchers from many different scientific fields: domestic animals, wildlife, plants, humans and the environment. Implementing such actions is particularly complex in the countries of the South.

Since the mid 20th century, in both the North and the South, radical changes in food production and eating habits have made antimicrobial use commonplace on farms. In the industrialised countries, spurred on by the public authorities, numerous measures are now in place or are being developed to limit this use.

But in some of the countries of the South, antimicrobial use is still increasing, and is accentuated by two contextual factors. First, growing demand for animal protein, especially in the middle-income countries: this translates into an increase in intensive pig, poultry and fish farming, which use antimicrobials routinely as growth promoters and veterinary drugs. Second, the need for tighter regulations and surveillance: regulations on antimicrobials are relatively soft, and controls of their sales as well as surveillance of antimicrobial resistance are often lacking. In addition, health and veterinary advice is generally insufficient. This widespread use of antimicrobials is seen in particular in China, Southeast Asia, India, Brazil and some African countries.

Antimicrobial resistance, a complex problem that knows no boundaries

Antimicrobials, antimicrobial residues and resistance genes know no boundaries, especially as intensive antimicrobial use in livestock production and agriculture also extends to aquaculture, which is set to provide two thirds of all fish consumed in the world by 2030.

Antimicrobial resistance is a highly complex problem. It spreads through natural trophic chains and food supply chains, from a very local scale to the planetary scale. This spread is accentuated by the transmission of certain resistance genes between different bacterial species, pathogenic or otherwise. It occurs in the environment through water and soil, even in ecosystems with little human impact. The aquatic environment further promotes this contamination by resistant bacteria. Antimicrobial resistance can affect human health and also – though this is less quantified – that of terrestrial, aquatic, domestic or wild animals and, more broadly, all biodiversity.

In regions with strong connections between natural zones and those shaped by humans, the use of antimicrobials and the ensuing development of resistance result in the selection of bacterial genetic material that can spread through many different ecosystems. The resistance genes present in the environment may, in turn, spread through domestic animal and human populations. Moreover, the use of certain chemicals in agriculture (biocides) and the associated pollution also impact on this resistance selection.

The dramatic increase in antimicrobial resistance points to the need to address this problem globally in a coordinated manner, ensuring coherent action at different levels as well as at the interface between public health, animal health and environmental issues. Systemic approaches are crucial to achieving this goal: in terms of health, these include initiatives such as One Health and EcoHealth and, where agriculture is concerned, a holistic approach to farms and rural areas is required.

Reducing the use of antimicrobials is therefore critical to reducing the risk of the persistence or emergence of new types of resistance, although it will not undo some of the resistance already observed.

Rationalising the use of antimicrobials and organising surveillance

In both the North and the South, the major challenge is to implement policies enabling the reduction and rationalisation of antimicrobial use, through a set of actions and associated regulatory measures. However, it should be noted that the effective application of these policies is dependent on one key factor: minimising adverse health and socio-economic impacts on the standard of living for farmers, especially in the most vulnerable regions.

Meeting this challenge implies blending a number of complementary approaches:

- assessing agricultural systems, in other words, identifying and understanding the different agricultural production, livestock farming and processing methods, with particular emphasis on practices linked to antimicrobials;
- understanding antimicrobial supply chains and analysing factors influencing decisions about their use;
- stepping up biosecurity on farms: better control of the introduction of animals, inputs and drugs; more effective

Main pathways for the dissemination of antimicrobial resistance in agriculture; research, actions and policies to be implemented.

The transmission pathways for antimicrobials, their residues and antimicrobial resistance are symbolised by arrows from one circle to another and by overlaps between circles.

The circles represent all of the living compartments concerned: agricultural production (agriculture, livestock farming, aquaculture) and its processing sectors, environmental elements, and the human population, within which antimicrobial therapy may be widespread and unregulated.

CIRAD, the French National Institute for Agricultural Research (INRA, France) and their partners in the South and the North are active in the four fields: practices, stakeholder awareness (livestock farmers, consumers, etc.), evidence (studies, surveillance) and governance (health policies, collective action).

Diagram inspired by the two following sources:

– Figure 1 of the open access article: Thanner S, Drissner D, Walsh F. 2016. Antimicrobial resistance in agriculture. mBio 7(2):e02227-15. http://dx.doi.org/10.1128/mBio.02227-15.

Figure 1 of the open access document: FAO, 2016. The FAO Action Plan on Antimicrobial Resistance 2016-2020. FAO, Rome, 25 p. ISBN 978-92-5-209392-3. http://www.fao.org/documents/card/fr/c/2f749e74-5ca8-4934-8762-9fd61ad6935e/.

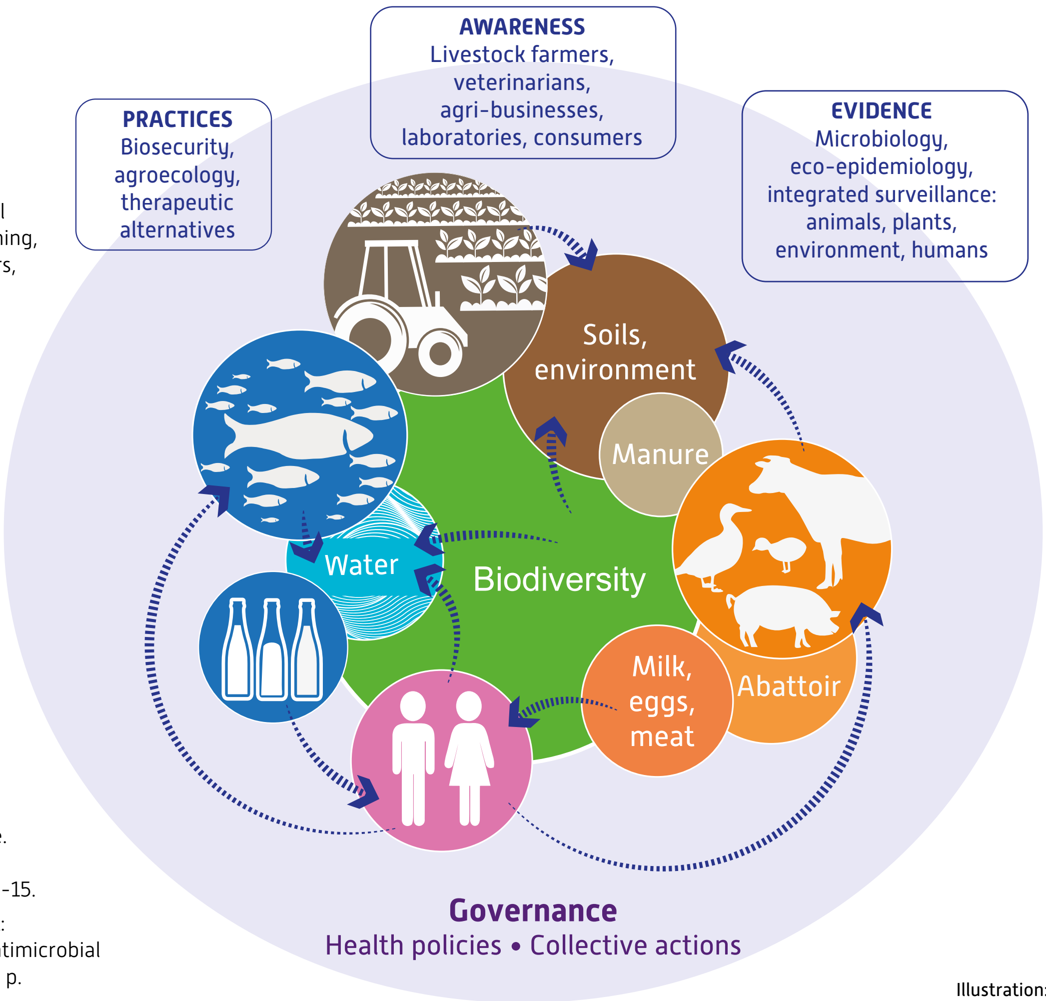

Illustration: Françoise Chirara, ASTRE Joint Research Unit management of contacts between animal species; closer monitoring of conditions in farm buildings (temperature, light, humidity, etc.); and vaccinating against common infectious diseases in order to reduce not only their incidence, but also the antimicrobials used to treat them;

- optimising the use of antimicrobials, which entails developing rapid bacteriological diagnosis tools while bearing in mind that access to medical and veterinary care may be problematic in the countries of the South;
- finding new therapeutic and preventive solutions to replace antimicrobials.

Inventing alternative solutions is a key element in limiting the impacts of a reduction in the use of antimicrobials. Traditional preventive approaches – biosecurity, vaccination, better animal welfare – could thus be consolidated by new treatments using plants and plant extracts. Research promoting plants with specific properties is also of interest in aquaculture, since there is currently no alternative means of effectively combating resistant bacteria, which are capable of wiping out the entire fish population in a given enclosure.

However, in order to implement this package of complementary approaches, the countries of the South need to organise surveillance systems enabling them to detect the emergence of resistance on farms and in the environment, and to assess the effectiveness of measures taken to reduce antimicrobial use. Developing integrated surveillance systems (such as One Health) would make it possible to jointly assess the impacts of measures on humans, animals and the environment.

Moreover, without these surveillance systems it is difficult to develop collective actions that take account of the different types of farms and practices, for two reasons: these actions simultaneously concern several levels – cooperatives and health protection groups, veterinary services, the private sector; and the legislation varies considerably in terms of content and application depending on the country in which the action is conducted.

Where surveillance is concerned, it is therefore necessary to identify and propose suitable, applicable approaches, associating public health, animal health and environmental surveillance. For example, in areas that have both fish farms and other types of livestock production, such as pigs or poultry, "sentinel" resistance detection networks could be merged by incorporating all of these sectors within a single surveillance system.

Promoting action research

Developing programmes of action aimed at rationalising the use of antimicrobials requires a participatory approach associating researchers and all of the stakeholders involved. The goal is to target priority actions according to sectors and geographical areas. This may involve preventing infectious diseases treated with the repeated use of antimicrobials, reducing the misuse of antimicrobials, or developing therapeutic alternatives.

The participatory approach facilitates the development of coherent measures that take into account the vulnerability of some rural communities to changes in legislation. Thus, for a given territory, a geographical approach to health may help to align health governance with stakeholders' interests, and to define policies that are appropriate to the specific context.

Some research teams, for example, are developing methods that combine participatory modelling with role-playing to encourage stakeholders to identify the problems and to work together to develop a shared vision. These methods can be applied to issues linked to antimicrobial resistance. The participants may be those involved in the use of antimicrobials: policy makers, agribusinesses, health practitioners and livestock farmers. Researchers can thus analyse the position and interests of these stakeholders and characterise the interactions between sectors and levels of policy-making: collaboration, communication and decision-making mechanisms.

Finally, another key element of these programmes is training at all levels: farmers, doctors, veterinarians, researchers and consumers. Teaching approaches associating livestock farmers, practitioners and private sector actors are needed to raise awareness about the prudent use of antimicrobials and to enable these stakeholders to work together to develop alternative solutions. Efforts also need to focus on ongoing training for doctors and veterinarians. Another challenge is training the next generations of researchers by integrating the issue of antimicrobial resistance into a more systemic health curriculum, along the lines of the One Health approach.

Interdisciplinarity is essential in research

The issue of antimicrobial resistance calls for interdisciplinary efforts on subjects ranging from genes to socio-ecosystems (the human society in its environment). A number of disciplines are useful in understanding the scale and distribution of antimicrobial use, analysing the evolution of resistance and proposing practice changes with the stakeholders concerned.

Systemic approaches are required in order to tackle antimicrobial resistance. First, plant health must be included, since antimicrobials are widely used in plant pathology in some countries, especially in Asia. Second, the human and social sciences are critical in raising awareness among stakeholders, analysing their viewpoints and exploring courses of action with them. They also incorporate economic aspects, to assess the impacts of practice changes on the standard of living for the stakeholders concerned. Third, the modelling sciences are important in studying the transmission of resistance genes at various levels, understanding practices, simulating actions to reduce antimicrobial use and assisting policy makers. Fourth, a number of collaborations need to be consolidated: between the different agricultural sectors, but also between these sectors and those involved in the management of natural areas and of public health.

To address the complexity of these issues, we can draw on data obtained by research teams in the South and the North, which reflect the diversity of agricultural contexts and livestock farming systems. This research focuses on the implementation of technical solutions, methodological approaches and innovative surveillance mechanisms in different areas. It informs the stakeholders concerned about public health issues in these areas. More generally, it fuels the debate between researchers and field operators and can thus contribute to the co-development of new practices that are adapted to the challenges faced in other contexts. ■

Perspective n° 39 is the result of research conducted by teams at CIRAD in the Joint Research Units ASTRE (Animals, Health, Territories, Risks and Ecosystems - http://umr-astre.cirad.fr/), ISEM (Institute of Science of Evolution - Montpellier - http://www.isem.univ-montp2.fr/) and SELMET (Tropical and Mediterranean Animal Production Systems - http://umr-selmet.cirad.fr/), the Animal Health Division (http://www.sa.inra.fr/) at the French National Institute for Agricultural Research (INRA, France), and their partners in the South and the North.

Eventually, the teams at CIRAD may develop interdisciplinary research services, including studies on plants (the phyllosphere) and on agricultural waters and soils as reservoirs of bacterial resistance to antimicrobials, while strengthening partnerships with the public health sector.

This research has resulted in several publications, including:

Adam C., Ducrot C., Paul M., Fortané N., 2017. Autonomy under contract: the case of free-range poultry farmers. *Review of Agricultural, Food and Environmental Studies*. http://dx.doi.org/10.1007/s41130-017-0044-7.

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Rakotoharinome M., Pognon D., Randriamparany T., Ming J.C., Idoumbin J.P., Cardinale E., Porphyre V., 2014. Prevalence of antimicrobial residues in pork meat in Madagascar. *Tropical Animal Health and Production* 46(1): 49-55. http://dx.doi.org/10.1007/s11250-013-0445-9..

A few words about...

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A few links

World Bank, 2013. Fish to 2030. Prospects for Fisheries and Aquaculture. Report number 83177-GLB.
http://hdl.handle.net/10986/17579

European Food Safety Authority (EFSA). Topic: Antimicrobial Resistance.
https://www.efsa.europa.eu/en/topics/topic/antimicrobial-resistance

World Organisation for Animal Health (OIE). Antimicrobial Resistance (AMR).
http://www.oie.int/en/for-the-media/amr/

Réseau Recherche Antibiotiques Animal (R2A2 - Research network on reduced use of antimicrobials and resistance to antimicrobials in animal production) within the GISA metaprogramme (Integrated management of animal health, INRA).
https://www6.inra.fr/r2a2

Review on Antimicrobial Resistance (Wellcome Trust, HM Government).
https://amr-review.org

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