Antimicrobial Resistance

Independent Analysis

Antimicrobial-resistant populations are present everywhere in all bacterial communities. Their expansion follows complex pathways through environmental systems, people, animals, food and water (Acar & and Moulin, 2013). The complexities of antimicrobial resistance (AMR) are not completely understood, but as more surveillance programs are developed and additional research is performed in the area, health professionals continue to gain understanding. Studies on bacterial resistance have shown that there is a huge diversity of resistance mechanisms, the distribution and mechanism of which is complex and largely unknown (Acar & and Moulin, 2006) (Franklin, et al., 2001).

The farm ecosystem is open, so there is an exchange of bacteria both resistant and susceptible to antibiotics occurs at regional, national and international levels as a result of export and modern farming systems (Acar & and Moulin, 2006) (Robinson, et al., 2016). New strains are transported and introduced by normal transmission modes including people, new stock, pests e.g. birds and rodents, insects, water (surface water particularly), and feed (Acar & and Moulin, 2006). The dissemination and incorporation of these bacterial genes follow many pathways where bacteria may meet antibiotic residues. This is important to note because even farms that have little to no use of antimicrobials, may still have cultures of bacteria that are resistant to antibiotics. This is pictured in Figure 1, which aims to represent residue dispersion and potential points of surveillance for antimicrobial resistant organisms.

Surveillance for AMR is an area that is growing, and several countries have commenced programs to monitor AMR. The sample size required for accurate surveillance is detailed in Figure 2 for meaningful results in a true prevalence survey. The CBC Marketplace survey selected very few samples for testing, and the results could have indicated (Marshall & and Levy, 2011):

1. Bacteria picked up during handling/processing by human contamination, environment or processing water-source
2. Bacteria from farming environment, or water source
3. Bacterial entry from near-by industry, sewage, terrestrial farming, municipalities

There is not a clear relationship that can be established between antimicrobial use on farm, and the end-product testing positive for antimicrobial resistant bacteria.

Challenges: What to include?

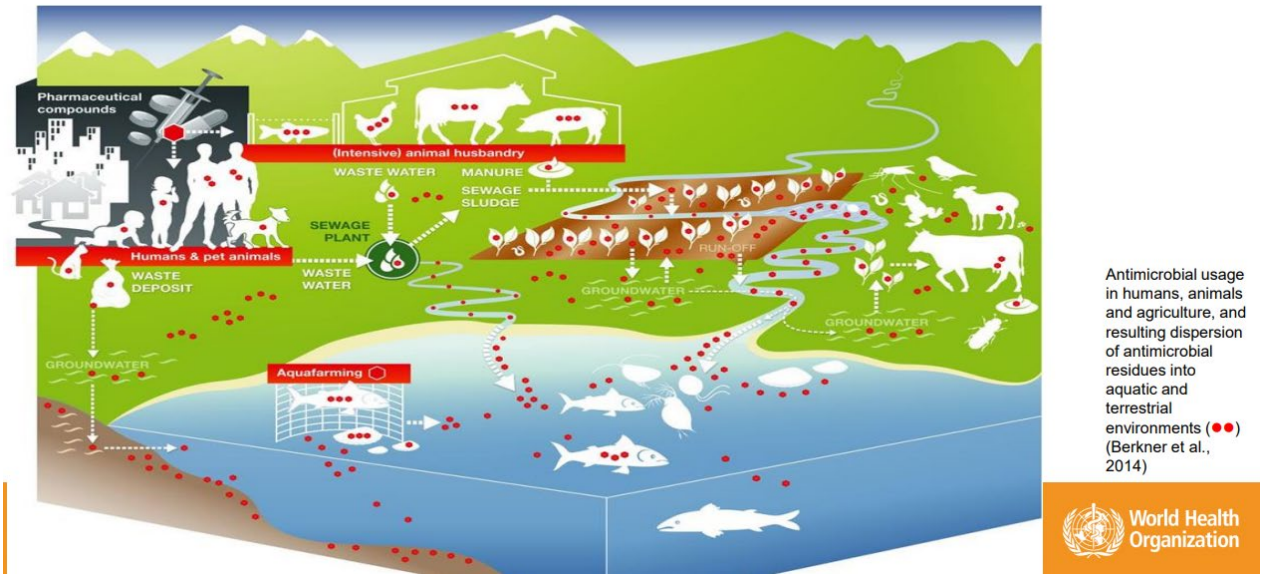

Figure 1: Schematic of the presence of AMR organisms in human and health and their interactions (Cahill, 2018)

Sample size estimates for prevalence of antimicrobial resistance in a large population

Expected prevalence	Level of confidence 90% Desired precision 10%	5%	1%	95% Desired precision 10%	5%	1%
10%	24	97	2,429	35	138	3,445
20%	43	173	4,310	61	246	6,109
30%	57	227	5,650	81	323	8,003
40%	65	260	6,451	92	369	9,135
50%	68	270	6,718	96	384	9,512
60%	65	260	6,451	92	369	9,135
70%	57	227	5,650	81	323	8,003
80%	43	173	4,310	61	246	6,109
90%	24	97	2,429	35	138	3,445

Calculations based upon Epi Info v6.04b to c Upgrade, October 1997, Centers for Disease Control (public domain software available at http://www.cdc.gov/epo/epi/epiinfo.htm)

Figure 2: Sample size for surveillance (Franklin, et al., 2001)

There are several comments pertaining to the results submitted by the CBC Marketplace:

1. The presence of antimicrobial resistant bacteria is naturally occurring. What is important, is the prevalence and the trends over time. The sample size was too small to determine prevalence (Franklin, et al., 2001). These long-term trends also need to be compared to

antibiotic use data in both humans and animals. This is not possible with the results presented by the CBC.

2. The spread of resistant clones is never monodirectional, and it occurs between different compartments as they overlap (Acar & and Moulin, 2006). Therefore, it is not scientifically correct to say that the presence of AMR bacteria is linked back solely to farming practices.
3. Resistant bacteria can be passed along the chain by contact with processed or live animals, or by consumption. A risk assessment should be carried out to understand the risk to the consumer. Upon cooking or freezing the product, the risk of bacterial contamination greatly reduces.

The use of antibiotics is an animal welfare issue and thus an important aspect of production animal medicine, for the treatment of diagnosed bacterial infections when there are welfare indications to support treatment. Prudent use of antibiotics is listed in the World Organization for Animal Health (OIE) Aquatic Animal Code (Chapter 6)[1].

Of the countries listed in the sample origins, China, India and Thailand are member countries of the OIE[2]. In these countries, the development of a national AMR surveillance program has been recent. Therefore, in time, it is expected that a greater understanding of national antibiotic use in human and animal medicine will be gained. In 2018, the "2nd OIE Global Conference on Antimicrobial Resistance and Prudent Use of Antimicrobial Agents" was held in Marrakesh, Morocco with the following recommendations:

[1] http://www.oie.int/index.php?id=171&L=0&htmfile=titre_1.6.htm

[2] http://www.oie.int/en/about-us/our-members/member-countries/

2nd OIE Global Conference on Antimicrobial Resistance and Prudent Use of Antimicrobial Agents

Putting Standards into Practice

Marrakesh (Morocco), 29-31 October 2018

RECOMMENDATIONS

CONSIDERING THAT:

1. Antimicrobial resistance (AMR) is a serious global threat to human health, animal health and welfare, plant health, food security, and also impacts to the environment throughout the world and cannot be successfully tackled without multi-sectoral cooperation;

2. The Tripartite (Food and Agriculture Organization of the United Nations (FAO), World Organisation for Animal Health (OIE), World Health Organization (WHO)) are collaborating with the United Nations Environment Programme (UN Environment) to ensure the development and implementation of global strategies and measures designed to control the development and spread of AMR, and contribute to the fulfilment of the United Nations Sustainable Development Goals;

3. The Tripartite is developing frameworks on AMR Stewardship and the Monitoring and Evaluation of the implementation of National Action Plans and has recently been strengthened through the signing of a Memorandum of Understanding (MoU) with a strong focus on AMR including the development of a detailed workplan for the coming years in collaboration with UN Environment;

4. The OIE establishes global standards and guidelines and provides assistance and leadership to Member Countries to strengthen Veterinary Services and capacities to support their implementation at national level;

5. The OIE is implementing its Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials, improving awareness and capacity through monitoring and training; in line with the Global Action Plan on AMR developed by the WHO in collaboration with FAO and OIE;

6. Following the Political Declaration of the High Level Meeting of the United Nations General Assembly on Antimicrobial resistance in 2016, the UN Interagency Coordination Group (IACG) on AMR with the support of the Tripartite secretariat is preparing a report to the UN Secretary General by May 2019;

AND CONSIDERING

The commitment expressed by Ministers attending the conference, who confirmed their support to the Global strategies and initiatives developed under the leadership of the Tripartite OIE-FAO-WHO, as well as their political will to allocate the adequate resources for the implementation of those strategies at national level,

THE PARTICIPANTS OF THE OIE GLOBAL CONFERENCE ON ANTIMICROBIAL RESISTANCE AND PRUDENT USE OF ANTIMICROBIAL AGENTS

RECOMMEND TO THE TRIPARTITE (FAO, OIE, WHO)

1. To further strengthen international collaboration and coordination, for surveillance and monitoring of AMR and antimicrobial use in different sectors and support implementation of standards and guidelines related to responsible and prudent use of antimicrobial agents in animals in partnership with relevant professional organisations;

2. To collaborate with the World Bank, the Organisation for Economic Co-operation and Development and other related institutions on the strengthening of the economic case for sustainable investment in the prevention and control of AMR, and providing appropriate economic and social analysis, that can be considered by policy makers and risk managers and help countries to prioritize their investment;

RECOMMEND TO THE OIE

1. To continue updating OIE standards in the OIE Terrestrial and Aquatic Codes relevant to AMR and needed capacities of Member Countries and to complete standards in the OIE Terrestrial and Aquatic Manuals,

2. To provide OIE Member Countries, through activities undertaken under the PVS Pathway, with tools and capacity-building activities, with a greater focus on AMR including update of policy and legislation;

3. To continue to develop the OIE List of Antimicrobial Agents of Veterinary Importance, considering a) the inclusion of antimicrobials only used in companion animals, b) the sub-division of the List in the different animal species, and c) the expansion of the List, to include over time antiparasitic agents of veterinary importance such as anthelmintics, insecticidal and acaricidal;

4. To further develop the OIE data collection on Antimicrobial Agents Intended for Use in Animals, converting the current spreadsheet format to a database system, able to accommodate data submissions by animal species, and its connection to the World Animal Health Information System (WAHIS) and also allowing addition of data from field studies;

5. To work with Animal Food Production sectors and institutions such as the World Veterinary Association and related professional bodies for supporting the development of species specific treatment guidelines to be used at sub-regional and national level and the establishment of a global repository of existing clinical treatment guidelines and tools;

6. To explore the possibility of building an information system of falsified or substandard drugs in the animal sectors illegally circulating within and between countries and building on the experience of the monitoring systems set up by WHO for drugs designated for human use taking a "One Health" approach;

7. To encourage research based on robust methodologies, aiming at comparison of results, that focuses on a better understanding of the dynamics and epidemiology of AMR, from an integrated "One Health" perspective, on the development of priority vaccines and other alternatives to antimicrobials, of proven safety, efficacy and quality and on rapid diagnostic and sensitivity tests specific for veterinary medicine, building on public-private partnerships;

8. To explore the opportunity to develop standards or guidelines related to autogenous vaccines and other alternatives to antimicrobials, including guidance for quality, safety and efficacy, as tools to reduce the need to use antimicrobials;

9. To develop a Monitoring and Evaluation (M&E) framework to monitor the progress of the implementation of the OIE Strategy on AMR and the Prudent Use of Antimicrobials, adopted by Resolution No. 36 by the OIE World Assembly of Delegates at the 84th General Session of the OIE in 2016;

10. To continue to support OIE Member Countries in the development of their communication activities and national action plans involving all animal health stakeholders, specifically supporting capacity building activities for behaviour change initiatives tackling antimicrobial resistance;

RECOMMEND TO OIE MEMBER COUNTRIES

1. To continue the implementation of the OIE Strategy on AMR and the Prudent Use of Antimicrobials, adopted by Resolution No. 36 by the OIE World Assembly of Delegates at the 84th General Session of the OIE in 2016; and strengthen their national legislation and human capacity if needed;

2. To develop, approve and implement national action plans for AMR under a "One Health" approach, taking into account multi-sectoral and multinational experience and aligned with the Global Action Plan developed by WHO and formally endorsed by OIE and FAO;

3. To follow the recommendations in the OIE List of Antimicrobial Agents of Veterinary Importance, in particular regarding restrictions on the use of fluoroquinolones, third and fourth generation cephalosporins and colistin, and to phase out the use of antibiotics as growth promoters, in the absence of risk analysis, giving priority to the classes in the WHO category of Highest Priority Critically Important Antimicrobials;

4. To contribute to the OIE annual collection of data on antimicrobial agents intended for use in animals, and to publish, whenever possible, their own national reports on the sales or use of antimicrobial agents in relation to the animal population of the country;

5. To promote a strong collaboration between the public and private sectors, in particular veterinarians, veterinarians paraprofessionals, and farmers in order to implement the principles of good animal health/husbandry practices including biosecurity measures to reduce the need for antimicrobials and take steps to ensure that, when their use is unavoidable, they are used in a responsible and prudent manner in accordance with relevant international standards, including Chapter 6.10 of the *Terrestrial Animal Health Code* and Chapter 6.2 of the *Aquatic Animal Health Code*;

6. To support National Focal Points for Veterinary Products active participation in training seminars and take advantage of their expertise to support the implementation of national AMR-related activities and regional and global projects in collaboration with all interested parties and sectors;

7. To mobilise adequate resources to develop sustainable communication and behaviour change activities targeting AMR in line with OIE international Standards, and ensuring the strategic development of activities that include all relevant animal health stakeholders.

8. To strengthen curricula of veterinarians and veterinary para-professionals on antimicrobial resistance based on OIE guidelines and following a "One Health" approach.

In conclusion, BAP standards support initiatives to reduce AMR worldwide. However, the results of the study, indicating the presence of antimicrobial resistant bacteria on product cannot be definitively linked to the misuse of antimicrobials on the farms of origin, and it is concerning that misrepresentation of the results published by the CBC could be be detrimental to the seafood industry.

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