Monitoring of antimicrobial resistance in non-clinical environments with a One Health perspective

There are three pillars in a One Health perspective: human medicine, veterinary medicine and the environment. Monitoring programmes (e.g. NORM) for resistance development to antimicrobial agents have been developed for the first two pillars, yet resistance monitoring lacks a similar environmentally oriented dimension in this perspective.

Background

Antimicrobial resistance (AMR) is a rapidly growing problem throughout the world. AMR can be described as a bacterium's ability to withstand the action of an antimicrobial agent (antibacterial agents, anti-fungal agents, potential toxic metals, disinfectants and other means).

The use of such means is known as the main driving force for the development and spread of antimicrobial resistance. The genetic and phenotypic status of bacteria can adapt to exposure to antimicrobial agents of variable doses, duration and combinations.

Fecal material from the human and veterinary environment containing resistant microbes and remnants of antimicrobial agents will eventually end up in the environment. It is not clear how exposure to such microbes or means promotes the development of antimicrobial resistance in microbial communities. An increase in resistance among bacteria from non-clinical environments such as soil, freshwater, oceans, sedimentary deposits and wild animals can further spread and increase the global incidence of resistance. In addition, resistant genes from pathogenic and clinical isolates that end up in the environment from i.e. sewage and fertilizers, can transfer to environmental bacteria. Environmental bacteria with acquired resistance can be reservoirs for resistance genes over time, where genes in turn can transfer to pathogenic bacteria. Reservoirs of resistant bacteria/resistance genes being built up in the environment create a precarious situation. The size, dynamics and effects of exposure to these resistance reservoirs are little understood.

Investigating available related evidence is necessary in order to propose possible development of systematic environmental monitoring of antimicrobial resistance.

An assessment of the possibility and usefulness of monitoring environmental resistance must take place within the context of other monitoring initiatives, and include considerations of approaches to experimental design, targets, and/or the monitoring rationale, concepts and goals. Furthermore, it is expected that approaches found in different environments vary, including the importance of fecal sources and their treatment in circular models.

Basic challenges include:

1. The lack of methods for standardization of resistance determination of non-clinical microbe isolates, species and populations.

2. The lack of a framework for sampling, handling and analysing in non-clinical environments.

3. Ambiguous resistance definition of non-clinical samples lacking clear methods for distinguishing between acquired, mobile resistance and inherent resistance. Unclear relationship between resistance determination in culturable versus non-culturable specimens.

4. A unified international approach to surveillance and data reporting is lacking but is necessary for comparative analysis of larger datasets sampled over time/space.

5. Time series are missing but are necessary since the change in the resistance situation over time will provide the framework for comparative analysis. Today's fragmented and point-prevalence-based studies do not provide insight into the dynamics of resistance populations over time.

6. Combination toxicology/resistance (mixture toxicology) is more relevant in the environment than in clinics where exposure to different resistance drivers is expected but is methodically underdeveloped.

7. The rate of decomposition and dynamics of resistance (bacteria, genes and selective agents) dispersed from anthropogenic environments is not widely understood, including the long-term effects of continuous discharges (e.g. sewage).

8. The diversity (type, mechanism, concentration) of resistance-driving agents in the environment (e.g. cleaning chemicals, various drugs including antimicrobial agents, etc.) is only described to a limited extent. More knowledge is needed on how these interact in open environments regarding the development and maintenance of antimicrobial resistance.

9. Lack of unified international initiative and framework for the establishment of environmental monitoring (e.g. NORM-ECO) that provides a basis for understanding the relationships between resistance development and the environment, regions, and continents.

10. Undetermined potential in how the rapid development of more cost-effective experimental methods/technologies can be used and put together with model development and machine learning. New technologies and new combinations of technologies including data management and analysis quickly change the prerequisites for effective environmental monitoring of resistance.

The focus of this study on approaches to monitoring resistance in the environment is related to assessments of the knowledge base supporting:

- Definition and description of resistance in the environment (environmental resistance)
- Design and methods available
- Approaches to surveillance/surveillance
- Existing international arenas where approaches to resistance are negotiated/decided

The assessment is undertaken considering the limitations and possibilities as indicated in the 10 points above.

Mandate

1. Summarize the knowledge base supporting the definition and description of environmental resistance and propose a definition of acquired resistance in environmental bacteria based on established clinical definitions.

2. Evaluate available methods for resistance determination and the extent to which these are suitable for environmental samples, including the pros and cons of culture-based methods versus metagenome/whole genome-based methods (phenotype versus genotype).

3. Evaluate possibilities and limitations in sampling design and methods for sampling, sample material and sample selection, including how this is solved in today's NORM/NORM-VET approach.

4. Develop an overview of existing and planned approaches to environmental resistance monitoring nationally and internationally and assess how these can best be used in a potential NORM-ECO approach.

5. Base work on a comprehensive assessment of the knowledge base, identifying the main challenges, opportunities and added value of establishing an ECO NORM monitoring program.

6. After clarifying added value, suggest how further work in VKM can develop the program, including identification of manageable selection of environment, samples, species and methods that can provide a basis for standardization and time series.

Deadline: January 25th, 2022