Antimicrobial resistance global emergence: healthcare facilities or environmental microbiota as the most important reservoir of antibiotic resistant microorganisms?

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The ecosystems contamination caused by drugs and by their biologically active transformation products has become an emerging environmental issue: recently developed analytical and sensitive methods have allowed the detection of these pollutants in different matrices (like water, soil, sediment).

Given that, such molecules are characterised by both a relative persistency in the body and a high biochemical reactivity (most of them are able both to cross the biological membranes and to exert therapeutic action on cellular specific target sites even at very low concentrations), their presence in the environment (although in the range of ng/L to µg/L), could represent a risk to the human and ecosystems health.

In this regard, if certain drugs are of particular concern due to their features as endocrine disruptors (e.g. some synthetic steroid hormones) others, such as antibiotics, are worrisome for their ability to induce drug resistance in clinically relevant microorganisms.

The latter phenomenon is particularly alarming, as it can affect therapeutic treatments in severe patients with the consequent spread of infections in the healthy population.
Understanding the flux of resistance units, throughout the diverse ecosystems, is crucial to assess, prevent and eventually predict emerging scaffolds before their appearance as pathogenic germ in human patients. It is well known that the environment contribution to the enlarging spectrum of antibiotic resistance genes is extremely relevant.

This was the case for *Kluyvera* spp., commensal bacteria of both humans and animals, which went ahead to the mobilization of their chromosomal *bla*CTX-M-type beta-lactamase-encoding genes into plasmids of other bacterial species (4).

Another example in this regard is represented by the OXA-type-beta-lactamases. The first report of *Shewanella xiamenensis* carrying a *bla*OXA-48-like gene suggested that the emergence of different genes from this group had their origin in different *S. xiamenensis* strains (17).

The efficacy of *bla*OXA-48-like gene transfer between bacterial species in human cases has also been reported in food-producing, companion and wild animals, as well as in natural environments (18), thus highlighting the importance of this phenomenon in the dissemination of antibiotic resistance among different biological reservoirs.

The idea that selected resistance mechanisms, such as the production of carbapenemase enzymes, are only linked to infections in humans and in the healthcare facilities is no longer valid (14). Another example of this is the recently emerged plasmid-mediated polymixin resistance mechanism, MCR-1, firstly isolated from an *Escherichia coli* strain SHP45 of animal origin in China and now sporadically reported in *Enterobacteriaceae* from humans (10).

This emerging antimicrobial resistance mechanism has been recently detected also from a patient suffering from urinary tract infection in the USA (11): This fact is somehow worrisome since it means that this highly transferable gene, that has been hypothesized to circulate since a long time in *E. coli*, is widely spread among bacteria infecting animals and humans in Asia, Europe and America (8,15).

It is now overwhelming the evidence that the release of antibiotics into the environment must be minimized in order to decrease the selective pressure on free ranging germs, and thus limit the emergence and selection of new resistance mechanisms: now more than in the past integrated approaches are required for the environmental management in this respect.

The development and implementation of national and international guidelines for the biological risk assessment of the emergence and propagation of antibiotic resistant bacteria in the environment is a strategic priority (3,6).

A major limitation in determining the current risk of transmission of antibiotic resistance genes from the environment to human-associated bacteria is the insufficient knowledge on the distribution and abundance of antibiotic resistant bacteria and antibiotic resistance genes in the environment at national, regional or global levels. (3).

Not only long-term surveillance reports on multi-drug resistant (MDR), clinical-derived strains have to be encouraged in Italy, but also national dimension studies to assess the prevalence of resistance mechanisms in the environmental compartments or ecosystems (beginning from soil and water). The available data, mainly coming from sporadic research studies, are indeed reporting on the worrisome emergence MDR bacteria carrying *bla*CTX-M-type genes in the streams of our countries (5).

In these conditions, the role of Clinical Microbiologist is very important, and from an additional perspective: in acting as a driving force for the implementation of a multidisciplinary international concerted action. Only achieving a better overall epidemiological knowledge and control of environmental and veterinary settings, the antimicrobial resistance vicious circle, that represents a major health concern for the near future, could be really understood and countered.

**References**