Tunisian antibiotic resistance problems: three contexts but one health

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Dear Editor,

Antimicrobial resistance is a serious threat to global public health. Effectiveness of antibiotics in treating common infections is decreasing and has quickened in the past few years, leading to an increase in the cost of health care in terms of days of hospitalization and required intensive care. The infrastructure dedicated to antibiotic discovery is inadequate and needs to be rebuilt. In addition, more research efforts need to be dedicated to antibiotic discovery in order to maintain the efficacy of current antibiotics[1].

Several international reports document the dramatic increase and spread of multidrug resistant organisms, mainly among Gram negative *bacilli* and the *enterobacterial* family. These microbes can spread throughout globe faster than their incubation period. They are also related to the different situations in life: people, animals and the environment which are interconnected. For this, they have created a new dynamic in which the health of each group is profoundly linked and connected to the rest.

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In Tunisia, a Northern African country, information on the occurrence of anti-microbial resistance is needed at the local, national and international levels and should be linked to three situations: human, animals and the environment. Over the past 20 years, epidemiology of the antibiotic resistance in Tunisia in *Enterobacteriaceae* mainly *Escherichia coli* and *Klebsiella pneumoniae* was very dynamic and the number of journal articles describing resistance mechanisms increased considerably. In the 2000's, we began to talk about extended spectrum *beta-lactamases* (ESBL) and resistance to cephalosporin in clinical specimen[2]; TEM and SHV type ESBL were the most dominant ones. In the last few years a novel ESBL named CTX-M15 occurred and replaced the TEM and SHV types. In Tunisian animals, ESBL-producers were initially reported from food samples such as raw chicken meat[3]. More recently, ESBL-producing *E. coli* were described in healthy food animals at the farm level[4].

Carbapenemase producing *Enterobacteriaceae* were detected in clinical specimens since 2010. Those enzymes belong to the Ambler class A (bla_{KPC}), class B (bla_{IMI}, bla_{VIM}, bla_{NDM}) and class D (bla_{OXA-48}, bla_{204} and $bla_{OXA-232}$) *beta-lactamases*.

To face carbapenem-resistant isolates, colistin was considered one of the last resort molecules. Unfortunately, reports indicate colistin resistant strains. However, we should note that despite the scarcity of information about this kind of resistance in Tunisia, some of the available data gives insights of an alarming situation. Indeed, after its first report in 2015, numerous retrospective studies were conducted and we describe for the first time in Tunisia the occurrence of mcr-1 positive *E.coli*[5].

After all these descriptions, it is therefore not surprising that Nasri et al. discovered the presence of carbapenemase gene (*bla*$_{KPC}$, *bla*$_{NDM}$ and *bla*$_{OXA-48}$) in *Enterobacteriaceae* in waste water effluents from Tunisian hospitals. Other studies have described the emergence of ESBL in *enterobacterial* isolates obtained in environmental samples, in vegetables, soil and water of the farm environment. Metallo-*beta-lactamases* were also described in bacterial isolates from Tunisian rivers[6].

The food chain remains a key element to prevent the dissemination of anti-microbial resistance. Lauren Carruth and colleagues stipulate that regulation on anti-microbial use in human health and agricultural systems is not sufficient. In fact, understanding how people prepare and store food as well as how they use various anti-microbials throughout the food chain is another key factor in the control of anti-microbial resistance.

According to the Tunisian National Institute of Consumption, the use of antibiotics in Tunisia increased by 38% during the period between 2005 and 2013 and can increase to superior levels in the near future. So, continuous and updated information on the occurrence of the anti-microbial resistance between different reservoirs, the drug use, the spread of bacterial clones and genes are essential elements for efficient risk management.

Finally, we stress the fact that the detection, prevention as well as the control of antibiotic resistance should be a national concern. For this, governmental strategies should be well designed and implemented as soon as possible and should engage several actors including health care agencies, agricultural agencies as well as the public community.

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