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Editorial

Superbugged

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We thought that with the decline of the Covid-19 pandemic the worst had gone and that we could go back to normal life, maybe keeping one eye open on the evolution of the virus variants from time to time. Suddenly almost any news on TV about the pandemic has disappeared.

But we are not aware of the threatening risk of a super-pandemic for which we won't have powerful weapons: antimicrobial resistance (AMR).

The phenomenon is well known in the scientific community but citizens are not informed that they can play a crucial role in avoiding this disaster.

Briefly, bacteria produce natural antibiotics to fight against other strains, and some develop resistance. When we use antibiotics without a real need, they kill good and bad bacteria, but those that develop resistance are free to proliferate. AMR can be transferred to deadly pathogens and we will not have any tool to control or limit infections. At the end, humans will not have efficient bullets against superbugs as they will have already mutated and become resistant to the most powerful antibiotics.

We (humans) are responsible for AMR. The wrong use of antibiotics is a common practice all over the world, in all countries. Often people take these drugs even in the case of diseases that are not related to bacteria, e.g. cold, flu and other infections like dengue and malaria. In other cases the patient stops assuming the antibiotic before the sickness and the infection are totally eradicated, with a potential relapse of the illness. We must not forget that expired antibiotics are often dispersed in the environment and not disposed of in the proper way.

Another terrific source of AMR comes from large livestock farms, where the animals are administered huge amounts of antibiotics to "improve" their health. While urban sites possess sewer ducts to collect waste waters and bring them to the treatment plants, the waste waters in animal farms are dispersed in the soil and can reach the groundwater streams without any control. In general, AMR in soils represents a serious risk to human health through the food chain and human–nature contact.[1]

Some data.

A recent World Health Organization (WHO) document reports high levels of AMR in 87 countries in 2020. The study concerns both bacteria that cause infections in the bloodstream, for example *Klebsiella pneumoniae* and *Acinetobacter spp* that become insensitive to carbapenems.[2] The same phenomenon occurs with more common bacteria, in fact more than 60% of *Neisseria gonorrhoea* isolates, a common sexually transmitted disease, have shown resistance to ciprofloxacin and more than 20% of *E.coli* isolates – the most common pathogen in urinary tract infections – became resistant to first-line drugs (ampicillin and co-trimoxazole) and to second-line treatments (fluoroquinolones).

In the past four years most AMR trends have remained stable, but bloodstream infections due to resistant *Escherichia coli* and *Salmonella spp.* and resistant gonorrhoea infections increased by at least 15% compared to 2017. More research is needed to identify the reasons behind the observed AMR increase and to what extent it is related to raised hospitalizations and increased antibiotic treatments during the Covid-19 pandemic.

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[2] Report signals increasing resistance to antibiotics in bacterial infections in humans and need for better data. https://www.who.int/news/item/09-12-2022-report-signals-increasing-resistance-to-antibiotics-in-bacterial-infections-in-humans-and-need-for-better-data (last accessed: 25/02/2023).

Antibiotics continue to be prescribed for diarrheal diseases and upper respiratory infections for which they have limited value.

During the chaotic treatment of Covid-19, patients were treated with antibiotics which resulted in more adverse effects.

A recent study carried out at the Indian Council of Medical Research showed that out of about 17,000 patients in Indian hospitals, more than half of them who acquired drug-resistant infections died.[3] The problem is extremely serious and is affecting Western countries as well.

In spite of all these warnings, broad-spectrum antibiotics – i.e. drugs that should be reserved for tackling the hard-to-treat bacterial infections – represent 75% of all prescriptions issued in India's hospitals.[4]

Of course, the environmental regulations that every single country adopt (or should do so) play another crucial role. Recently it was reported that several big pharmaceutical industries delocalized their plants in China and in India for the production of antibiotics, including the generic brands. Well, it was found that – astonishingly – the industrial waste waters carrying antibiotics and byproducts discarded their junk in the same stream where untreated raw sewage was released! Nobody could ever build a better bioreactor for the production of antibiotic resistance bacteria! In this case the responsibility of the companies to press and obtain from the governmental agencies the respect of the procedure to properly treat the industrial and urban wastes is clear.[5]

Even more recently scientists confirmed or realized that other chemicals can induce resistance in pathogens. This is the case of cationic surfactants,[6,7] often used as antimicrobial agents for example in household detergents, and antidepressants.[8]

The goal of this brief document is to recall how the problem is serious and to show that it must be treated efficiently and rapidly.[9]

The next (super)pandemic has already been announced, the perfect storm is approaching.

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[4] India facing a pandemic of antibiotics-resistant superbugs. https://www.bbc.com/news/world-asia-india-63059585 (last accessed: 25/02/2023).

[5] Waste from pharmaceutical plants in India and China promotes antibiotic-resistant superbugs. https://www.statnews.com/2016/10/14/superbugs-antibiotic-resistance-india-china/ (last accessed: 25/02/2023).

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[8] How antidepressants help bacteria resist antibiotics. https://www.nature.com/articles/d41586-023-00186-y (last accessed: 25/02/2023).

[9] C. Lübbert, C. Baars, A. Dayakar, N. Lippmann, A. C. Rodloff, M. Kinzig, F. Sörgel. Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended-spectrum beta-lactamase and carbapenemase-producing pathogens. Infections 45 (2017) 479-491.