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The presence of antibiotic resistance in the environment should worry us

Until now, India's fight against antibiotic-resistance was focussed on getting people to cut down on unnecessary antibiotic consumption. Having too many antibiotics causes bodily pathogens to resist these miracle drugs. But, for the first time, the 2017 National Action Plan on Antimicrobial Resistance talks about limiting antibiotics in effluent being dumped by drug makers into the environment. This is because when these drugs taint soil and water, the scores of microbes that live there grow drug-resistant. But only a tiny proportion of these environmental microbes trigger disease in humans. So why is resistance among them a problem?

Environment-pathogen link

The answer lies in the intimacy shared between environmental bacteria and human pathogens. Typically, a pathogen, say *Klebsiella pneumoniae* (*K. pneumoniae*), that causes pneumonia, can take two routes to antibiotic resistance. The first is for its own genes to mutate spontaneously to help fight the drug. This is a long-winded route, because mutations take time to spread through a bacterial population. The second route, a shortcut known as horizontal gene transfer, is for the bug to borrow resistance genes from its neighbours.

Scientists believe that many human pathogens today picked up their resistance genes from the environment through this shortcut. Take ciprofloxacin, an antibiotic launched by the German company Bayer in the mid-1980s. Ciprofloxacin was the most effective among the quinolone class of antibiotics in fighting gram-negative bacteria such as *K. pneumoniae*. But cipro also had another ace up its sleeve. Because bacteria would need multiple resistance mutations to fight cipro, and because such multiple mutations are rare, scientists thought resistance was unlikely.

In fact, phylogenetic studies suggest that the earliest antibiotic-resistance genes in nature are millions of years old. But when humans starting manufacturing antibiotics in the 1950s, a dramatic shift occurred. Large doses of these drugs seeped into the environment through poultry and human excreta, and waste water from drug makers and hospitals. This led to an explosion of resistance genes in soil and water microbes.

This is the context in which the antibiotic-tainted wastewater from pharma companies in Hyderabad must be seen (*The Hindu*, 'Ground Zero' page – "The superbugs of Hyderabad", November 18, 2017). In 2007, Swedish investigators found that water in a pharma effluent treatment plant had both high levels of ciprofloxacin as well as novel resistance genes, never seen in microbes elsewhere. Such genes were also found in effluent from a hospital in Pune.

How likely are these genes to make the journey from living harmlessly in environmental bacteria to human pathogens that sicken people? "That is the question, and we do not know the answer," says Luigi Rizzo, an environmental engineer who studies technologies to remove antibiotic-resistance germs from wastewater for a European project called ANSWER or 'Antibiotics and mobile resistance elements in wastewater reuse applications: risks and innovative solutions'.

When the Swedish researchers compared the numbers of qnr genes in the faeces of people living in Hyderabad's antibiotic-polluted regions and elsewhere, they found no difference. This seems to imply that the flow of genes from the environment to humans is a rare event. Instead, most transmission happens from one human to another. "Indeed, if it was not (a rare event), given the fact that there is so much resistance in environmental bacteria, we never would have enjoyed the use of antibiotics over the past six decades," says Gerard D. Wright, director of the Michael G. DeGroote Institute for Infectious Disease Research in Canada.

But the rarity isn't reason to lower our guard. We live in unprecedented times where environmental bacteria, pathogens and antibiotics are mixing like never before. This means such rare events are almost inevitable, says Prof. Wright. Once they jump to human bugs, resistance-genes can spread across continents in a few days, thanks to international air travel.

In 2009, when a deadly resistance gene was discovered in a Swedish patient who had recently travelled to New Delhi, researchers assumed the gene was picked up in India and named it the New Delhi metallo-beta-lactamase 1 (NDM-1). The Indian government saw this nomenclature as a public relations disaster, arguing that there was no evidence of the gene's Indian origin. Whether NDM-1 came from New Delhi or not is still a bone of contention. But the worry is that if India doesn't move quickly, wastewater in pharma clusters could give rise to new genes as dangerous as NDM-1. Once such genes jump to humans, they will, no doubt, blaze their way across the planet. When this happens, it will be more than a public relations disaster for India. It will be a death sentence for Indians as well as thousands across the globe.

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