The Antibiotic Pipeline is Running Dangerously Dry

EXPERT EXPLAINS

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OVER THE last few weeks, Prime Minister Narendra Modi, Union Home Minister Amit Shah and Union Health Minister J P Nadda have all spoken publicly about a growing public health threat — anti-microbial resistance (AMR) because of antibiotic overuse.

According to the Institute of Health Metrics and Evaluation, Washington University, an estimated 2.67 lakh deaths were attributable to AMR in 2021.

Key statistics highlight high resistance rates (one study, for instance, shows 83% of Indians carrying resistant bacteria), treatment gaps and heavy misuse of antibiotics, making common infections untreatable and jeopardising modern medicine.

"In one of the studies, which we are conducting right now, we are seeing that one in 10 patients in India who are admitted to hospitals with some kind of infection are resistant to last-resort antibiotics," says Dr Kamini Walia, senior scientist at ICMR (Indian Council of Medical Research), who coordinates its Antimicrobial Resistance and Diagnostics initiatives. Speaking to Rinku Ghosh, she says: "Globally, the antibiotic pipeline is running dangerously dry. While a few antibiotics have been approved over the past two decades, almost none represent truly new classes or mechanisms of action. As antibiotics are overused, we risk exhausting the limited effectiveness of the drugs we already have — without adequate replacements in sight."

What is the extent of antimicrobial resistance in India now?

Antimicrobial resistance is a silent pandemic. Often dismissed as a hospital-acquired infection or complication, its impact was felt during Covid when patients were impacted by drug-resistant infections. In hospitals, where there is high use of antibiotics, that pressure forces the bacteria to develop ways to survive them primarily through genetic mutations. Then they pass on resistance genes to other bacteria, accelerated by the overuse and misuse of antibiotics in humans.

The patient gets admitted with one problem, which could be a myocardial infarction or kidney disease. But during the course of hospitalisation or treatment, they acquire drug-resistant pathogens, which cause infections, some of which claim lives. It is because of this invisible reason that we don't have a quantifiable burden of drug-resistant infections in our country or globally. The first figures actually came in 2021... We still need a more reliable number.

Apart from hospital-acquired infections, there are community-acquired infections which are becoming drug-resistant, like typhoid, diarrhoea and pneumonia. We do not yet have an exact figure, considering we have 18% of the world's population. So of the total infections which were estimated, almost 20% happens in India broadly.

How much antibiotic overuse is behavioural?

In India, there is learned behaviour that has happened over time. Whenever Indians have a cough, cold or diarrhoea, they reach for an antibiotic. Some wouldn't wait to find out if their infection is viral or bacterial, not knowing antibiotics don't work for viral infections. Sometimes, people rely on

pharmacists for what they perceive are seasonal infections. Physicians, themselves, prescribe them for prophylactic use.

In India, there is a need to unlearn the behaviour of immediately reaching for an antibiotic without finding out the nature of the infection.

Bitter pill

While a few antibiotics have been approved over the past two decades, almost none represent truly new classes or mechanisms of action.

Without replacements in sight, there is a risk of exhausting the limited effectiveness of current drugs.

Does antibiotic stewardship work?

It is more effective than an overnight ban on over-the-counter (OTC) sales. Take the case of Kerala, the first state to launch the antimicrobial stewardship programme in 2015, which focuses on rationalising antibiotic prescription and awareness at all levels. They banned OTC sales only last year with a reasonable amount of success. It took 10 years. We have a knife at home but do we use it to kill people? Similarly, we must first internalise what antibiotics are meant for. Only then can we be responsible.

How difficult has it become to treat routine infections?

There are two sides to this. One is getting infected with the drug-resistant bug that requires a next-level antibiotic. The other is a community-acquired infection, for example UTI, becoming complicated because of improper and inappropriate use of antibiotics over a period. Salmonella typhi strains are becoming resistant to fluoroquinolones. Drugs like ceftriaxone and azithromycin are being overused and risk becoming ineffective for treatment of typhoid.

But the good news is that when you stop using the drugs for a short while, the sensitivity also comes back. For example, in the 1990s, typhoid was resistant to three commonly-used drugs — co-trimoxazole, chloramphenicol and amoxycillin. Then we stopped using these drugs and shifted to fluoroquinolones. Fifteen years later, research has shown that the old drugs are regaining effectiveness.

Is antibiotic use in livestock, agricultural practices and the environment complicating AMR?

First, we must find the attributable risk to humans from the antibiotics being used in animals. Some of the antibiotic classes to which we are seeing very high levels of resistance in humans are not used in animals. If we are seeing 60–70% resistance to the drugs used by humans, then the root cause is human behaviour.

ICMR did a study at two sites in Delhi and Vellore with two pathogens, E coli and Klebsiella pneumoniae, drawn from veterinary, environmental and clinical samples. We found a sizeable overlap of antibiotic resistance genes between human and environmental isolates from hospital surroundings, but very minimal overlap between the human and the animal. What we need to be vigilant about is antibiotic residues from food which continue to persist in your gut microbiome. The gut microbiome functions as a hidden reservoir of antimicrobial resistance, especially under antibiotic pressure.

What are the challenges in data collection?

At ICMR, our network is limited to 25 tertiary care hospitals, all of which have well-functioning clinical microbiology labs. We publish the data every year, this being our eighth edition. The reason this cannot be taken as representative of the entire country is that this data is coming from tertiary care hospitals

where patients come with a previous history of hospitalisation and excessive antibiotic usage. That's why the data that we present has a very high level of resistance. We need to widen the circle of authentic data collection. The Japan Nosocomial Infections Surveillance has data from around 2,000 hospitals.

What are the alternative therapies that can beat AMR?

One is phage therapy, which involves bacteria-eating viruses. It is effective in treating UTIs. But it requires a kind of precision to identify which phages will work for your infection. Resistance develops even to phages. Then you have to use a cocktail of viruses. This is an evolving field and needs customisation for patients depending upon the nature of infection. There are monoclonal antibodies but they are at an ascent stage.