

# The startups waging war against superbugs

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Anand Anandkumar's father was a physician who spent his career fighting infectious diseases in the South Indian city of Chennai. It was an infection that killed him.

In and out of hospital for a failing heart, he picked up a bug resistant to most antibiotics and died of complications from sepsis.

His story is common in India, where so-called superbugs kill nearly 60,000 newborns every year. The rapid spread of resistant bacteria has made India the epicenter of a war to prevent a post-antibiotic world, where people would once again die in the thousands of commonplace infections.

"We're on the front line," said Anandkumar, who a year after his father's death co-founded Bengaluru-based startup Bugworks Research India, to develop new antibiotics.

"We're creating a bullet against organisms that are taking out humanity. Wouldn't it be nice to get a battleground to test it on that's really tough?"

The theater of war is all around him. India has few weapons to fight infection after years of poorly controlled antibiotic use in humans and animals, combined with effluent from the local drug industry that turned lakes and streams into breeding grounds for resistance. A study of one hospital in South India found half the patients acquired at least one

infection during their stay, with about 74 percent of those infections showing resistance to multiple drugs.

The Indian government has begun to provide early research funding, advice and support to startups like Bugworks. It also funds the startup incubator that Bugworks shares with 21 other biotech firms.

Last year, Bugworks became the first company in Asia to receive investment from CARB-X, the U.S. government's main funding vehicle for the fight against superbugs.

“The science is as good as anywhere else,” said Ramanan Laxminarayan, a professor at Princeton University and director of the Center for Disease Dynamics, Economics & Policy, based in Washington and New Delhi. “On a per-dollar basis, I think the chance of a new antibiotic discovery is as great or higher in India as anywhere.”

Governments have begun to take concerted action in the last few years. In 2015 the U.S. launched its Combating Antibiotic Resistant Bacteria initiative. The next year the British government commissioned a report that found superbugs kill about 700,000 people around the world each year, a figure that could rise to 10 million a year by 2050 if nothing is done.

Bugworks' answer is an antibiotic that attacks bacteria in two ways at once rather than the single target approach of traditional drugs, making it harder for the bug to develop resistance. The drug also evades the bacteria's own defenses, giving it more time to kill the infection.

Anandkumar says the compound has shown effectiveness against lung, blood and urinary tract infections in animals.

In about two years, he says, it should be ready for human trials.

India's low research costs and deep pool of biotech graduates mean Bugworks isn't alone in trying to stem the superbug tide. In the same building, Biomoneta is focusing on an air purification system that kills bacteria in hospitals before they can infect patients.

In a nearby industrial zone is GangaGen Inc., named in honor of the founder's mother, who was killed by an infection. The startup is working with bacteria-eating viruses called phages to isolate proteins that can make superbug-killing drugs. It has developed a drug that targets staph infections and is seeking more drugs that treat other infections using the same method.

Other companies from the nearby city of Hyderabad and the capital, New Delhi, have joined the fight.

"You're probably sitting in the epicenter of the problem," said Janani Venkatraman, Biomoneta's founder. "But there are also so many people working to solve the problem, and that makes for an extremely exciting and collaborative ecosystem."

But turning the ideas into safe, available drugs requires a lot of money and expertise in human testing and approvals. And that means enlisting the big pharmaceutical companies that haven't brought a new antibiotic to market for 30 years.

Investing in treatments for diseases that last a lifetime, like diabetes or hypertension, was better business than a drug the patient takes once. And increasing regulation of antibiotics by governments that might insist any new

treatment be used only as a last resort, make it even less financially attractive.

Nevertheless, the tide is turning. More than 80 health-care companies, including Pfizer, Novartis and GlaxoSmithKline, pledged to help fight antimicrobial resistance at the World Economic Forum in 2016. Governments are providing subsidies, fast-tracking approvals and extending patent protection.

The big pharmaceutical companies are also slowly bringing their antibiotic research pipelines back to life, led by U.K.-based Glaxo. Pfizer announced a program earlier this year with the Indian Council of Medical Research.

In the meantime, the fight revolves around efforts to slow the development of resistance by tightening rules on how antibiotics are dispensed, especially in livestock farming, where widespread misuse of the drugs has been one of the biggest contributors to the rise of superbugs.

One thing that drives the effort in India is the personal experience of so many researchers. Staff at Bugworks recount stories of friends in their forties dying in hospital from pneumonia, or from a urinary tract infection that lasts months as one antibiotic after another fails to work.

T.S. Balganesh, president of GangaGen, tells of the wife of a close friend who went to hospital for a stomach operation and died of pneumonia within a fortnight, and an aunt who went in to treat a burn and died from an infection a week later.

“Friends go to hospital and don’t come back,” he said.