IN FOCUS

SERIOUS BACTERIAL INFECTIONS

Every year, drug-resistant infections are responsible for 700,000 deaths worldwide; without urgent action this number is projected to increase exponentially. The impact of these infections is especially severe in hospital and healthcare facilities, where bacteria spread easily and can enter the body through wounds, surgery sites, ventilators and catheters, impacting medical and surgical procedures and leading to disability and death.

The Global Antibiotic Research and Development Partnership (GARDP) is working to develop new treatments for these serious bacterial infections, with a focus on those caused by Gram-negative bacteria on the World Health Organization's (WHO) priority pathogens list.

HUMAN & FINANCIAL COST

In Europe, hospital infections cause 37,000 deaths and contribute to an additional 110,000 deaths every year; in the US they are responsible for 98,000 deaths every year. Hospital infections also hurt economic growth, costing the European economy €7 billion and US economy $6.5 billion annually. In low- and middle-income countries, where less data is available, indicators point to a more severe human and economic impact. The WHO estimates the rate of hospital infections among newborns in low-income countries is up to 20 times higher than in economically developed countries.

Drug resistance means these infections are becoming more difficult to treat. Even routine surgery, as well as treatments like chemotherapy, carry greater risk. Between 39% and 51% of bacteria causing surgical site infections, and 27% causing infections after chemotherapy, are now resistant to standard antibiotics.

THE RISE OF INFECTIONS

The most serious infections in healthcare settings are caused by members of the Enterobacteriaceae family of bacteria, as well as the Pseudomonas aeruginosa and Acinetobacter species. These bacteria are known as Gram-negative due to the structure of their cell wall, which generally makes them more resistant to antibiotics.

Some Enterobacteriaceae produce enzymes called extended-spectrum beta-lactamases (ESBLs) that break down and destroy commonly used antibiotics, including penicillin and cephalosporins.

Many of these bacteria are also resistant to carbapenems, a group of antibiotics that are usually reserved for the most serious infections, including multi-drug-resistant infections. It is estimated that carbapenem-resistant Enterobacteriaceae are harboured in the intestines of around 200 million people in South Asia. While aminoglycosides and some other antibiotics have been used against carbapenem-resistant Enterobacteriaceae, they are increasingly losing their effectiveness due to resistance.

This leaves colistin as the antibiotic of last resort, which due to its extreme toxicity is only used when there are no other options. Even this drug’s days may be numbered as research shows bacterial resistance to colistin is spreading worldwide and its effectiveness in treating infections is being questioned.

THE CHALLENGE

Bacteria change naturally in response to medicines, developing the ability to defeat drugs. However, the overuse and misuse of antibiotics is accelerating the process. While new drugs have been made available, the pace of development has not kept up with the pace of resistance. Even when new antibiotics are developed, they rarely target priority drug-resistant bacteria and are only registered for use in a small number of countries. In the past 20 years, no new antibiotic class against Gram-negative bacteria has been approved.

THE GARDP RESPONSE

GARDP is bringing together partners in the public and private sectors to address critically underfunded and unfilled gaps in the development of treatments for drug-resistant serious bacterial infections. This includes partnering to support early-stage exploratory activities, alongside clinical and pharmaceutical development of treatments, with a focus on sustainable access. GARDP’s work on serious bacterial infections includes ensuring new treatments are evaluated for use with children, who are too often overlooked during the development of treatments.
A NEW TREATMENT
GARDP is partnering with Venatorx Pharmaceuticals to co-develop cefepime-taniborbactam, a novel treatment effective against carbapenem-resistant infections for which there are limited or no treatment options. As part of the collaboration, GARDP is leading clinical trials in adults with multidrug-resistant infections, alongside development activities and trials to ensure this treatment is safe and effective for use with children and babies.

“Hospitals should be places where people go to heal, but around the world many patients acquire life-threatening infections in hospitals. WHO is delighted that GARDP is entering into this new partnership to drive the development of urgently needed new antibiotics for such drug-resistant hospital-acquired infections.”

DR TEDROS ADHANOM GHEBREYESUS
DIRECTOR-GENERAL OF THE WORLD HEALTH ORGANIZATION

5 BY 25
GARDP is calling on the world to support the development of five new treatments by 2025 to tackle the drug-resistant infections that pose the greatest threat to global health and economic security. GARDP is seeking €500 million to develop these treatments. If we act now, collectively and with urgency, we can prevent a post-antibiotic era.

THE 3 MOST CRITICAL BACTERIA
The WHO priority pathogens list identifies families of drug-resistant bacteria that pose the greatest threat to health and development and are in critical need of new antibiotics. These pathogens form the focus of GARDP’s work on serious bacterial infections:

- **Acinetobacter baumannii** (carbapenem-resistant) – can cause infections in the blood, urinary tract, lungs and wounds. It can also colonize the body without causing infections or symptoms.
- **Pseudomonas aeruginosa** (carbapenem-resistant) – affects up to 10% of all hospital patients in high-income countries and can result in pneumonia and infections of the skin, bones, blood, joints and urinary tract.
- **Enterobacteriaceae** (carbapenem-resistant, ESBL producing) – a family of bacteria that includes Escherichia coli and Klebsiella pneumonia, both of which commonly cause infections in healthcare settings and communities.

1 Gram-negative bacteria cause infections including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis in healthcare settings. Gram-negative bacteria can be resistant to one or many drugs and are increasingly resistant to most available antibiotics. Bacteria are often easily able to become drug-resistant and can pass along many drug-resistance genes to other bacteria so that they too become drug-resistant.