GARDP
Global Antibiotic Research & Development Partnership
A joint DNDi / WHO initiative

Antimicrobial resistance (AMR) is a major and rapidly growing global public health challenge. Responsible for more than 700,000 deaths a year[1], it poses a significant threat to achieving the Sustainable Development Goals (SDGs), in particular SDG 3, which aims to ensure healthy lives and promote wellbeing for all[2].

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavouring to ensure their sustainable access.

Initiated by the World Health Organization (WHO) and the Drugs for Neglected Disease initiative (DNDi) in May 2016, GARDP is an important element of WHO's Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships to encourage research and development of new antimicrobial agents and diagnostics.

GARDP's programmes – sexually-transmitted infections, neonatal sepsis, paediatric antibiotics and antimicrobial memory recovery, evaluation and exploratory research – are designed to address global public health priorities. Each programme incorporates sustainable access and stewardship strategies to ensure treatments are affordable and available to all those who need them.

Partnerships are central to GARDP's model and include WHO, pharmaceutical and biotechnology companies, academia, governments, health authorities, philanthropic organisations and civil society from across the world.

Neonatal sepsis

Although the world has seen significant progress made to improve child health, including a 50 percent reduction in child mortality since 1990, the number of preventable deaths in neonates (newborn babies up to 28-days-old) remains unacceptably high. Globally, neonatal deaths account for 44 percent of all deaths in children under-five[3].

Newborns are at significant risk from serious blood-stream infections, such as sepsis, as well as other serious bacterial infections such as pneumonia and meningitis. The situation is aggravated by AMR, as currently available treatments become less effective. Of great concern are the 214,000 neonatal sepsis deaths estimated to result from drug-resistant infections across the world in 2015.

Drug-resistant neonatal sepsis is often associated with high-mortality rates in hospital settings. When healthcare systems are overwhelmed hospitals may not have sufficient resources to ensure medical care, let alone infection control. In such settings, the Gram-negative bacteria which lead to drug-resistant infections can thrive.

A major challenge is the knowledge gap, as there is very little evidence to support the appropriate treatment of serious and drug-resistant infections in neonates. Despite increasing rates of resistance to the WHO recommended treatment regimen, up to 80 percent[4] in some cases, the lack of evidence on potential alternatives means the guidelines have not been updated for more than 50 years.

GARDP'S NEONATAL SEPSIS PROGRAMME

GARDP's neonatal sepsis programme aims to develop new antibiotic treatments and provide an evidence base for the use of antibiotics, both old and new, in neonates with confirmed or suspected sepsis.

OBJECTIVES

By 2023

- Develop and deliver a new first-line antibiotic treatment for clinically-diagnosed neonatal sepsis (i.e. where the signs and symptoms indicate sepsis, but it is not possible to identify the bacteria) in areas experiencing high levels of drug-resistance to the current WHO recommended treatment regimen (ampicillin and gentamicin).
- Develop evidence-based treatment(s) for neonatal sepsis caused by (highly-suspected or confirmed) multidrug-resistant Gram negative pathogens.

To ensure sustainable capacity to tackle these issues into the future, the programme will incorporate a research network to design, implement and interpret clinical trials for neonatal sepsis. That network will significantly contribute to plans for a global paediatric antibiotic platform. The platform will collaborate and build partnerships with institutions and experts from across the world to systematically assess and develop new and re-purposed antibiotics for babies and children of all ages.

TO DATE, GARDP HAS

- Started a multi-country observational study to increase understanding about neonatal sepsis which began in Delhi, India in July 2018. The study will collect clinical information on suspected (clinically-diagnosed) sepsis in up to 3,000 newborns in hospitals and / or neonatal units in 11 countries.

  Outcomes such as antibiotic use, duration of treatment and mortality rates will be recorded and analysed. The study will help to build the evidence-base needed to evaluate future interventions to treat neonatal sepsis.

- Developed a target product profile (TPP) to re-purpose an existing antibiotic for use – in a combination regimen – for the treatment of clinically diagnosed neonatal sepsis and identified an antibiotic (fosfomycin) as meeting the criteria of the TPP.

  A clinical trial is underway in Kenya to assess the safety of, and determine the correct dose for, fosfomycin in neonates. It is due to finish in early 2019.

- Developed a second TPP for an antibiotic to treat confirmed or highly-suspected neonatal sepsis caused by multidrug-resistant Gram-negative pathogens.

LOOKING AHEAD

In 2019, GARDP will use the data the fosfomycin clinical trial, the observational study and ongoing evaluations and other published data to choose which antibiotic candidates to take forward into a large-scale clinical trial. This will help to increase the evidence-base needed to develop and deliver a new first-line antibiotic treatment for clinically-diagnosed neonatal sepsis.

A GLOBAL COLLABORATION

The neonatal sepsis programme is made up of an international, multidisciplinary partnership of experts, institutions and research centres from Bangladesh, Belgium, Brazil, China, Greece, India, Italy, Kenya, South Africa, Thailand, Uganda, United Kingdom and Vietnam, highlighting neonatal sepsis' truly global burden.

Partners include: St George's University and the Medical Research Council – Clinical Trial Unit, UK, PENTA-ID Foundation, Italy, University of Antwerp, Belgium, Chris Hani Baragwanath Hospital and Tygerberg Hospital, South Africa, the All India Institute of Medical Sciences, Lady Hardinge Medical College, India.

1 Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. The Review on Antimicrobial Resistance Chaired by Jim O'Neill, 2014
2 Sustainable Development Goals sustainabledevelopment.un.org/SDG3 3
3 Reducing Child Mortality Factsheet, World Health Organization, September 2018
4 *A 2015 review of studies in Africa the Middle East and Southeast Asia, found 80 percent resistance to ampicillin and 22 percent to gentamicin, (the current WHO recommended regimen) as well as 74 percent resistance to ceftriaxone, another commonly-used treatment.*
Le Doare, et al. Systematic Review of Antibiotic Resistance Rates Among Gram-Negative Bacteria in Children With Sepsis in Resource-Limited Countries, Journal of the Pediatric Infectious Diseases Society, March 2015