

IN FOCUS

MAKING CHILDREN'S ANTIBIOTICS A PRIORITY

Children under the age of five, and newborns in particular, are among the most vulnerable to drug-resistant infections. The lack of research and development to develop new treatment options for this group is putting their lives at risk. Through public and private partnerships, the Global Antibiotic Research and Development Partnership (GARDP) is working to reach its 5 BY 25 goal to deliver five new treatments for drug-resistant infections by 2025, with children's antibiotics being a key area of focus.

SERIOUS & GROWING THREAT

Infectious diseases, including pneumonia and sepsis, are a leading cause of death and disability in children under the age of five. Most childhood deaths due to bloodstream infections occur in newborns up to 28 days old; since children of this age do not have a functioning immune system, they are more prone to developing infections and less able to overcome them.

Up to 40 percent of bacterial infections in newborns are resistant to standard treatments¹, leading to an estimated 214,000 newborn deaths each year from drug-resistant infections². Most of these deaths occur in resource-constrained countries³ and could be prevented through the availability of effective antibiotics. Unfortunately, antibiotics to treat drug-resistant infections in children are extremely limited, and even more so in low- and middle-income countries.

A GAP IN ALTERNATIVE ANTIBIOTIC TREATMENTS

To ensure effective antibiotics are available for children when they are needed, regulatory agencies require pharmaceutical companies to evaluate new treatments for use amongst this group. However, these programmes are usu-

ally delayed for years after licensing in adults, if undertaken at all. A recent study found that out of 37 new antibiotics being developed in adults, just two were being studied in children⁴. Furthermore, the lack of data on potential new treatment options means treatment guidelines for childhood infections such as neonatal sepsis have not been updated for 50 years.

As part of an urgent global response to this issue, GARDP is currently working with more than 50 public and private sector partners in 20 countries to address the need for new antibiotic treatments, with children's antibiotics as one of its key areas of focus.

GARDP IS WORKING WITH PARTNERS TO DEVELOP NEW ANTIBIOTICS FOR CHILDREN AND BABIES

GARDP's progress in the development and delivery of lifesaving treatments for drug-resistant infections in children and babies is made possible through effective public-private partnerships.

- PENTA FOUNDATION**
 GARDP is partnering with Penta, the paediatric infectious diseases research network in Italy, to build on existing infrastructure to further

develop a global children's antibiotic platform. This platform consists of Penta's international network of expert neonatologists, paediatricians and microbiologists and other experts working in hospitals and academic institutions ranging from tertiary care hospitals in high-income countries to district general hospitals in low- and middle-income countries. These settings are focused on paediatric infection, including neonatal sepsis and pneumonia.

- OBSERVATIONAL STUDY OF BABIES WITH SEPSIS**

In early 2020, GARDP completed enrolment into one of the largest ever observational studies on the care of babies with sepsis. This project is coordinated through a strategic partnership with the Penta Foundation, the Medical Research Council Clinical Trials Unit at University College London, St George's University of London and the University of Antwerp and 19 hospitals in 11 countries. The purpose of this study, which is following approximately 3,200 newborns, is to provide the evidence needed to fill knowledge gaps to inform future evaluation of potential treatments for neonatal sepsis.

¹Costello, A. and Peterson, S.S. (2016). Birth in a time of antibiotic-resistant bacteria. *WHO Media Center* / ²Balasegaram M, Pécoux B, Gray G, Sharland M, Swaminathan S. *The Lancet Infectious Diseases* 2019, 19(6):573-574. doi: 10.1016/S1473-3099(19)30214-2 / ³S Vergnano, M Sharland, P Kazembe, C Mwansaambo, PT Heath. *Review: Neonatal sepsis: an international perspective. BMJ journals. ADC Fetal and Neonatal Edition* <https://fn.bmj.com/content/90/3/F220> / ⁴Thompson G, Barker CI, Folgori L, et al Global shortage of neonatal and paediatric antibiotic trials: rapid review - *BMJ Open* 2017;7:e016293. doi: 10.1136/bmjopen-2017-016293

• **VENATORX PHARMACEUTICALS**

GARDP is collaborating with Venatorx Pharmaceuticals to develop a novel antibiotic to treat serious bacterial infections. Cefepime-taniborbactam is an investigational combination of the fourth-generation antibiotic cefepime with taniborbactam, a novel, broad-spectrum beta-lactamase inhibitor that restores the activity of cefepime against carbapenem-resistant *Enterobacteriaceae* (CRE) and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA). The World Health Organization has identified CRE and CRPA as ‘critical-level’ pathogens posing the greatest threat to global health and urgently requiring new antibiotics. This collaboration will expedite a paediatric programme for cefepime-taniborbactam.

GARDP IS MAKING EXISTING ANTIBIOTICS SUITABLE FOR USE IN CHILDREN AND BABIES

Along with the development of new treatments, **GARDP** is also providing evidence to support the use of existing antibiotics for babies and children.

• **FOSFOMYCIN**

In collaboration with KEMRI-Wellcome Trust Research Programme in Kenya and the Centre for Tropical Medicine and Global Health at the University of Oxford, **GARDP** completed a study to assess the blood levels (pharmacokinetics) of the antibiotic fosfomycin. This research will help to establish a safe dose of fosfomycin that can be used in combination with other antibiotics to treat newborns with sepsis.

• **COMBINATION(S) TO TREAT NEONATAL SEPSIS**

GARDP has successfully identified one antibiotic combination of fosfomycin and amikacin and continues to evaluate others, with the objective of developing an alternative to ampicillin-gentamicin, the current **WHO** recommended treatment for sepsis in newborns. Half of the infections that cause neonatal sepsis are now reported to be resistant to ampicillin-gentamicin, which means an alternative is urgently needed⁵.

• **POLYMYXIN B**

As part of its paediatric programme, **GARDP** aims to develop a paediatric investigation plan for polymyxin B in the treatment of neonatal sepsis caused by confirmed (or highly suspected) multidrug-resistant Gram-negative bacteria. Polymyxin B has a US FDA license, but the evidence for the paediatric dose is limited. **GARDP**'s paediatric programme will help address this gap.

5 BY 25

GARDP is calling on the world to support the delivery 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. It's an ambitious goal, but one that we can achieve if we act now, collectively and with urgency.

NEONATAL SEPSIS OBSERVATIONAL STUDY

GARDP and its partners have completed enrolment for one of the world's largest neonatal sepsis observational studies

They have recruited more than 3,200 newborns across 11 countries.

- | | | |
|------------|--------------|----------|
| Bangladesh | India | Thailand |
| Brazil | Italy | Vietnam |
| China | Kenya | Uganda |
| Greece | South Africa | |



⁵[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(17\)30362-5/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(17)30362-5/fulltext)