

Guest Editorial

Antimicrobial resistance in paediatric medicine

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We are approaching the important deadline of the Millennium Development Goals (MDG) and we have to celebrate the achievements in child mortality reduction. Whilst between 1990 and 2000 childhood mortality declined only marginally from 12.4 million to 10 million deaths per year, the subsequent decade, with renewed focus on child health through MDG 4, has seen a much steeper decrease of child mortality down to 6.4 million deaths per year, almost half of the 1990s figure [1].

However this achievement is somewhat less ambitious than originally proposed. With less than one year from the deadline, the current mortality figure is 2 millions off the MDG 4 target (to reduce childhood mortality by 2/3 compared with the 1990s figures) [2]. It is therefore important not to lose the drive and continue to keep child health high on the global agenda.

We know that the burden of mortality is now mostly due to neonatal deaths, accounting for almost half of the global child deaths. Of those at least 20–25% are infection-related. These figures do not include stillbirths which mostly remain uncounted and are probably as many in number as neonatal deaths [3]. Beyond the neonatal period the majority of child mortality is due to respiratory tract infections and diarrhoea [1].

Neonatal infections and childhood pneumonia alone account for over 1.2 million deaths per year [1]. To treat these infections there are a relatively small number of affordable antimicrobials for use in children and neonates, particularly in developing countries. The backbone of treatment for neonatal infections, for example, is limited to penicillins and ami-

noglycosides. Cephalosporins are expensive and resistance is developing quickly, and carbapenems are even more expensive and not widely available. Since the discovery of antimicrobials, a relatively small number of new classes have been produced and investments on antimicrobial research have been and still are largely inadequate in terms of development of new molecules, and basic science research, for example, on resistance mechanisms is also weak [4]. This is especially the case in paediatrics, because of the inherent complexity of setting up clinical trials in this population.

In the meanwhile the development of antimicrobial resistance is inevitable, as already predicted by Fleming [5], and is progressing at a faster pace than the development of new antimicrobials. Multi-resistant organisms can no longer be contained and over the last 10 years increasing attention has been given to antimicrobial resistance (AMR) worldwide. The World Health organisation in 2014 has published the first report on antimicrobial resistance (AMR) [5]. The document collected data on 7 bacteria causing high burden of disease worldwide and reported a high level of resistance, both in hospital and community acquired infections, to commonly used antibiotics, such as third generation cephalosporins. For example significant resistance (in more than 50% of national reports) was detected in all 6 WHO regions for *Klebsiella pneumoniae* and in 5 out of 6 for *E. coli*. The report also highlights a number of gaps in knowledge: the lack of data from countries with the highest mortality; the lack of agreement on methodologies to measure and record antimicrobial resistance for data comparison within and between countries; and the lack of data for specific bacteria and for specific populations, such as children [6].

The JPID AMR special issue focuses on the in-

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formation gap in paediatrics, bringing together a number of authors from different European and non-European countries to share their research on different aspects of antimicrobial resistance, use and prescribing in children.

This issue starts with an overview of the European strategy to contain antimicrobial resistance (AMR), written by Dr. Nienke van de Sande-Bruinsma and Dr. Danilo Lo Fo Wong from the WHO Communicable Diseases, Health Security and Environment Regional Office for Europe.

The authors explain the WHO strategic objectives to fight antimicrobial resistance adapted to the European region, with details of the activities and challenges linked to this theme. Fighting AMR is a complex task requiring coordinated action of different agencies. WHO Europe offers support to European countries to develop national AMR strategies through the implementation of a number of objectives such as the development of national committees to coordinate AMR activities; developing awareness amongst the public and health professionals about AMR; supporting or encouraging the development of national surveillance systems for monitoring resistance; setting up systems to measure antimicrobial consumption and promote rational antimicrobial use in human medicine; implementing infection control measures in health care settings; regulating antimicrobials use in veterinary medicine; and promoting research into basic science, drug development and diagnostics.

The editorial from the UK Paediatric Infectious Diseases Research Group lead by Professor Sharland, describes the success of an European programme aimed at understanding antimicrobial resistance and prescribing in the paediatric population, and gives an overview of the different components of the ARPEC project (Antimicrobial Resistance and Prescribing in European Children).

This project combined several streams and produced data on antimicrobial use in neonates and children in hospital and in primary care across several European and non-European countries; measured antibiotic resistance for a number of sentinel pathogens; laid the basis to establish an appropriate methodology for measuring antibiotic consumption in children; collected existing antimicrobial guidelines and policies across the participating countries; and finally developed educational materials for better paediatric antibiotic prescribing. ARPEC also resulted in the formation of networks of committed paediatricians

interested in research to reduce AMR in paediatrics both within Europe and globally.

The first original article from Prof Milan Čižman and colleagues from Slovenia illustrates the large variation in antibiotic consumption within a small country illustrating the need to improve prescribing practices. Interestingly the high use of antimicrobials was correlated with the incidence of upper respiratory tract infections, which are mostly viral. The article nicely shows a trend between pneumococcal resistant strains and high antimicrobial consumption.

Two manuscripts illustrate examples of the ARPEC point prevalence survey (PPS) methodology, used to measure antibiotic prescribing in children admitted to hospitals over a pre-defined day in two different countries.

In the first case, Dr. Gabriela Tavchioska and her group highlight a very high number of paediatric inpatients treated with antibiotics and show the importance of initiatives such as ARPEC to benchmark practice across European countries.

The second ARPEC PPS study from Dr. Sanjeev Singh and colleagues from India reports data from 8 hospitals treating neonates and children. The manuscript demonstrates high use of multiple antimicrobials and inappropriately long courses of prophylactic antibiotics use. The authors advocate for the establishment of antimicrobial stewardship programmes to improve prescribing practices in paediatrics.

The special issue closes with an article from Romania, where Dr. Simona Claudia Cambrea reports antimicrobial susceptibility patterns of *E. coli* isolated from paediatric patients in Constantia and shows a high level of resistance to penicillins.

To conclude, while it is imperative to increase investments on antimicrobial research and development, it is equally essential to work on preserving the available preparations through antimicrobial surveillance and stewardship programmes in paediatrics, and on novel methods for the prevention and containment of hospital acquired infections applicable not only in high, but also in low and middle income countries. This is fundamental to slow down the spread of resistance. These need to be joined efforts of large networks of paediatricians collaborating both in research and implementation of effective measures to reduce the spread of resistance. This JPID AMR special issue shows several examples of the results of productive collaborations. The ARPEC project is an excellent model of how these can be functional out-

side national borders and from them an even bigger project, GARPEC, looking at measuring the global burden of antimicrobial resistance and consumption is taking shape, and will try to address the problem of hospital acquired infection and resistance in paediatrics globally.

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