





# Fighting the hidden pandemic of antimicrobial resistance in paediatrics: recommendations from the International Pediatric Association

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## THE IMPACT OF ANTIMICROBIAL RESISTANCE (AMR) IN PAEDIATRICS

The 'masked' or the 'silent' pandemic of AMR is one of the biggest emerging threats to global health. The global burden of resistant infections during the neonatal and paediatric period is currently alarming. According to a recent report, infections attributing to multi-drug resistant bacteria may account for up to 30% of the total cases,<sup>1</sup> while in specific areas, like in Middle East region, almost 90% of sepsis cases during the neonatal period in neonatal intensive care units were associated with resistant bacteria.<sup>2</sup> In the sub-Saharan Africa region, a recent meta-analysis in neonates showed that resistance to WHO recommended  $\beta$ -lactams was observed in 68% cases.<sup>3</sup> Several paediatric-related issues have been identified, such as the lack of paediatric antibiotic drug development, the limited paediatric clinical studies and therefore the lack of paediatric-specific data, the limited drug options to treat MDR (multi-drug resistant) paediatric infections and the

misuse or overuse of antibiotics. The 2016 Antibiotic Resistance and Prescribing in European Children (ARPEC) Study reported a list of quality indicators to enhance the appropriate and prudent paediatric antimicrobial use.<sup>4</sup> The WHO report has identified for the first-time priorities for research and development of age-appropriate antibiotics in children. In response to the WHO global action plan to optimise the use of antimicrobial drugs both in adults and paediatrics, WHO has prepared and launched the updated WHO Model List of Essential Medicines (EML). The latter includes a paediatric section aiming to increase literacy and awareness related to the epidemiology, common infectious agents, diagnostic strategies and the impact of AMR. Most importantly, the EML-C includes guidance on antibiotic prescribing for the empiric treatment of common infections in children.

## THE NEED TO SUPPORT INITIATIVES RELATED TO INFECTION CONTROL, INFECTION PREVENTION AND ANTIMICROBIAL STEWARDSHIP IN PAEDIATRICS

A concerted, massive global awareness campaign targeting all healthcare workers, the regulatory authorities as well as the public is urgently needed to combat this AMR pandemic. This is one face of the coin. The second face of the coin is another concerted, massive global campaign in expanding infection prevention strategies, including the vaccination coverage in both developed and developing countries. As a result of vaccination, antibiotic usage will reduce selection pressure that favours resistant organisms.

One key aspect of AMR and hospital-acquired infections (HAIs) associated with AMR is that through specific actions, these

infections can be prevented (preventable harm and waste). It is estimated that up to 60%–70% of HAIs are considered avoidable through the improvement of infection prevention, infection control and antimicrobial stewardship multimodal strategies. Infections can be prevented by implementing a series of measures (known as bundles). The implementation of infection control and prevention strategies in paediatric healthcare remains worldwide a critical quality safety indicator that improves patient outcomes and reduces preventable harm in children, such as the incidence of paediatric infections due to AMR in both inpatient and outpatient settings.

Strict legislation and monitoring regarding the over-the-counter availability of antibiotics are also important infection control pillars in combatting AMR. Unfortunately, acquisition of antibiotics without prescriptions is a global phenomenon. Even in Sweden, a country with very strong legislation and regulation of antibiotics, a recent survey showed that 2.3% of the respondents had acquired antibiotics without prescription.<sup>5</sup> This will require careful attention to access to healthcare so children who require antibiotics can secure an appropriate drug at the correct dose for the ideal length of time after evaluation by a healthcare provider. An important point is to establish the early diagnosis of the infection, demanding the adequate taking of samples, the request for cultures and the use of molecular tools that identify the aetiology and avoid the inappropriate administration of antibiotics.

Key components of paediatric infection prevention and control programmes both at the national and local levels are the establishment of staff education and training; use of evidence-based guidelines; surveillance, monitoring, audit and feedback regarding antibiotic use in antimicrobial stewardship programmes; workload and staffing; and rigorous maintenance of environmental hygiene. Of importance, priorities should be addressed both at global and national levels in governance, planning, regulatory and legal frameworks with close co-ordination and collaboration among key stakeholders in the public and private sectors to decrease the risk of AMR in paediatrics.

Another important aspect is the investment in the development of antiseptics and anti-infectives for the paediatric population. A major barrier to effective antimicrobial therapy is shortage of key antibiotics (such as amoxicillin). The supply of antibiotics must not be left to the market but requires additionally targeted transnational support from governments, Non-Governmental

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Organization (NGOs) and philanthropy. All new and existing drugs need evidence-based dosage regimens from clinical studies for all age groups (modelling and simulation will be useful to supplement carefully designed clinical studies) and formulations that are appropriate for all age groups in all climatic settings. Drug development of antibiotics in paediatrics should be driven by pharmaceutical policy that ensures that children's needs are included in the development of novel approaches such as the 'subscription model'.

## RECOMMENDATIONS

The International Pediatric Association positions against antimicrobial resistance in paediatrics in the following ways:

1. To the paediatricians and IPA (International Pediatric Association) member societies globally to use all indicators related with the prompt discontinuation or de-escalation of antibiotics according to microbial culture results, the early switch from broad spectrum empiric to narrower spectrum definitive antimicrobial therapy in children when possible.
2. To the pharmaceutical industry to increase their efforts in development of new effective antimicrobial agents and to provide sufficient amounts of appropriate antibiotics in paediatric formulations (the current shortage frequently urges paediatricians to use inappropriate broad-spectrum treatment).
3. To the paediatricians and IPA member societies globally to perform the complete documentation for antibiotic prescription in the patient's medical charts.
4. To the paediatricians and IPA member societies globally that the choice of antibiotic, dose, route of administration and duration of treatment for common infectious syndromes in paediatrics should be in alignment with the recommendations for antibiotics included in the WHO EML-C<sup>13</sup> and Essential Medicines for Children and the WHO AWaRe (Access, Watch, Reserve).
5. Action by multiple stakeholders for rational pharmaceutical policy that addresses AMR. This needs to include reliable global supply of key antibiotics, development of dosage regimens and dosage forms that are appropriate for children and the paediatric-specific elements in incentives and drivers for the development of anti-infectives.
6. IPA supports any initiative driven by any global or national agency that fosters public and healthcare provider awareness and literacy, prioritising the need to advocate with local, national and international governments for legislation to reduce OTC (Over-the-counter drugs) antibiotics.
7. IPA supports the need for paediatric-specific research and more accurate and accessible diagnostics to avoid antibiotic overuse.
8. IPA will collaborate together with global stakeholders, agencies and organisations to enhance public awareness and most importantly leverage high-level scientific and political engagement, financial resources and technical expertise, adapting to country-level needs and demands for tackling AMR with focus on the paediatric population.

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