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A Review on Antibiotic Resistance in Peadiatric Population

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ABSTRACT: Antibiotic resistance is a public health threat of the utmost importance, especially when it comes to children: according to WHO data, infections caused by multi-drug resistant bacteria produce 700,000 deaths across all ages, of which around 200,000 are newborns. This surging issue has multi pronged roots that are specific to the k age. For instance, the problematic overuse and misuse of antibiotics (for wrong diagnoses and indications, or at wrong dosage) is also fueled by the lack of pediatric-specific data and trials. The ever-evolving nature of this age group also poses another issue: the partly age-dependent changes of a developing system of cytochromes determine a rather diverse population in terms of biochemical characteristics and pharmacokinetics profiles, hard to easily codify in an age- or weight-dependent dosage. The paediatric population is also penalized by the contraindications of tetracycline's and fluoroquinolones, and by congenital malformations which often require repeated hospitalizations and pharmacological and surgical treatments from a very young age. Emerging threats for the paediatric age are MRSA, VRSA, ES-BL-producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae and the alarming colistin resistance. Urgent actions need to be taken in order to step back from a now likely post-antibiotic era, where simple infections might cause infant death once again.

Key words: multi-drug resistance, antibiotic resistance, childhood infections,

I. INTRODUCTION:

Antibiotic resistance in children is a critical and growing concern for global public health. Just like adults, children can develop infections caused by bacteria, and when these infections are treated with antibiotics, the bacteria may evolve resistance. However, children are particularly vulnerable to the consequences of antibiotic resistance due to their developing immune systems, and they often require antibiotics for common childhood illnesses such as ear infections, pneumonia, and urinary tract infections (UTIs).

Increased Risk for Antibiotic Resistance:

1. High Frequency of Infections: Children, especially in their early years, experience frequent respiratory and ear infections, which are often treated with antibiotics. Overuse or misuse of antibiotics for these conditions, many of which are viral and do not require antibiotics, can contribute to resistance.
2. Immature Immune Systems: Children's immune systems are still developing, making them more susceptible to infections. When these infections are treated with antibiotics, it can increase the risk of antibiotic-resistant bacteria taking hold in their bodies.
3. Overuse of Antibiotics: In many parts of the world, antibiotics are commonly prescribed for common childhood illnesses that are viral in nature (e.g., colds, most cases of sore throats, and viral ear infections), even though antibiotics are ineffective against viruses. This over prescription fosters resistance in bacteria.
4. Vulnerability to Hospital-Acquired Infections: Children, especially those with chronic conditions, weakened immune systems, or those who are hospitalized, are more likely to acquire healthcare-associated infections. These infections are often caused by resistant bacteria, which can be harder to treat and more dangerous for young children.

Common Infections in Children Affected by Antibiotic Resistance:

1. Ear Infections (Otitis Media): Middle ear infections are very common in children, and antibiotics are often prescribed for them. However, many cases are viral, and overuse of antibiotics for these infections has led to the

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emergence of resistant bacteria, such as Streptococcus pneumoniae and Haemophilus influenzae.
2. Respiratory Infections: Pneumonia and bronchitis are frequent causes of illness in children. Antibiotic resistance in bacteria such as Streptococcus pneumoniae and Mycoplasma pneumoniae can make it harder to treat these infections effectively.
3. Urinary Tract Infections (UTIs): UTIs are common in children, particularly in young girls. Antibiotic resistance in the bacteria that cause UTIs, such as Escherichia coli (E. coli), is becoming more widespread. This can result in longer hospital stays and the need for stronger or more toxic treatments.
4. Gastrointestinal Infections: Diarrheal diseases caused by bacteria like Salmonella and Campylobacter are common in children. Antibiotic-resistant strains can lead to more severe illness and longer recovery times.

Consequences of Antibiotic Resistance in Children:

1. Longer and More Complicated Illnesses: Infections that are resistant to standard antibiotics are harder to treat, leading to longer illnesses. This can be particularly problematic for children, who may need more time to recover and can miss more school or experience disruptions in their development.
2. More Severe Infections: When antibiotics are ineffective, infections can become more severe. For example, a mild urinary tract infection that would have been treated with a simple course of antibiotics may progress to a kidney infection or sepsis if left untreated or if more potent antibiotics are required.
3. Increased Risk of Hospitalization: Resistant infections can lead to hospital stays that are longer and more complicated. Children with chronic health conditions, premature infants, or those in neonatal intensive care units (NICUs) are particularly vulnerable to these infections.
4. Higher Mortality Rates: In severe cases, antibiotic resistance can lead to infections that are difficult to treat, resulting in a higher risk of mortality, particularly for vulnerable children.

Causes of Antibiotic Resistance in Children

1. Overprescription of Antibiotics: Antibiotics are frequently prescribed for conditions that don't require them, such as viral infections like the flu, colds, or viral sore throats. In many cases, parents may request antibiotics, and healthcare providers may feel pressure to prescribe them even when they are not necessary.
2. Incomplete Courses of Antibiotics: When children don't finish their full course of prescribed antibiotics, or when the dosage is skipped or reduced, it can encourage bacteria to develop resistance.
3. Self-medication and Sharing of Antibiotics: In some settings, parents may use leftover antibiotics from previous treatments or share them between children, which can contribute to resistance. This is more common in lower-income countries where antibiotics may be available over-the-counter without a prescription.
4. Poor Infection Control in Healthcare Settings: Children who are hospitalized or receive medical treatments are at risk of exposure to resistant bacteria. If infection control practices in hospitals are not stringent, resistant strains can spread easily among patients.

Addressing Antibiotic Resistance in Children:

1. Antibiotic Stewardship: Implementing antibiotic stewardship programs in pediatric care settings is essential. These programs focus on ensuring that antibiotics are prescribed only when necessary, at the correct dosages, and for the right duration. Healthcare providers must differentiate between viral and bacterial infections to avoid unnecessary antibiotic use.
2. Parental Education: Educating parents about the dangers of overusing antibiotics is critical. Parents need to understand that many common childhood illnesses, such as colds and ear infections, are caused by viruses and do not require antibiotics.
3. Improved Diagnostic Tools: Better diagnostic tests can help healthcare providers identify bacterial infections that require antibiotics and differentiate them from viral infections, which do not need antibiotic treatment.
4. Vaccination: Vaccination plays an important role in preventing infections that may otherwise require antibiotics. Vaccines against diseases like pneumococcal pneumonia, Hib (Haemophilus influenzae type b), and pertussis (whooping cough) help reduce the need for antibiotics and the spread of resistant bacteria.
5. Infection Prevention: Teaching children and caregivers good hygiene practices, such as

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regular hand-washing, and ensuring that children receive proper nutrition and immunizations, can reduce the likelihood of infection and the need for antibiotics.

6. Research and Development: Research into new antibiotics and alternative therapies for resistant infections is vital to staying ahead of the evolving bacteria. This includes the development of vaccines, antimicrobial peptides, and phage therapies.

II. ROOTS OF ANTIBIOTIC RESISTANCE IN CHILDHOOD:

Antibiotic resistance in children is a complex, multifaceted issue that originates from a variety of practices and behaviors. It is rooted in the ways antibiotics are used and misused, both in healthcare settings and in the community. Below are the key roots of antibiotic resistance in childhood:

1. Overuse and Misuse of Antibiotics

One of the primary contributors to antibiotic resistance in children is the overuse and misuse of antibiotics. This happens in various ways:

- **Unnecessary Prescriptions**: Antibiotics are often prescribed for viral infections, such as the common cold, flu, or most sore throats, which are not affected by antibiotics. However, parents may expect antibiotics for these conditions, and healthcare providers might prescribe them to meet these expectations.
- **Inappropriate Use for Mild Bacterial Infections**: Sometimes, antibiotics are prescribed for mild bacterial infections, like ear infections (otitis media), which may resolve on their own without medication. The unnecessary use of antibiotics increases the risk of developing resistant bacteria.
- **Incorrect Dosages and Duration**: Even when antibiotics are prescribed appropriately, incorrect dosages or not completing the full prescribed course can contribute to resistance. If the full course is not completed, some bacteria may survive and develop resistance to the antibiotic.

2. Parental Pressure and Expectations

Parents sometimes pressure healthcare providers to prescribe antibiotics for their children's illnesses, especially when they are anxious about their child’s health or if they expect fast results. In some cases, parents may not understand the difference between viral and bacterial infections, leading them to request antibiotics for conditions that do not require them. This pressure can lead to:

- **Inappropriate antibiotic use**: When doctors succumb to patient or parental pressure, antibiotics are given for viral infections, perpetuating the cycle of misuse.
- **Self-medication**: In some regions, parents may give their children leftover antibiotics from previous treatments or share antibiotics between children, which is both unsafe and ineffective.

3. Frequent and Repetitive Use of Antibiotics

Children are particularly susceptible to infections because of their developing immune systems. They may experience multiple rounds of antibiotics during their early years for common infections like:

- **Ear infections (Otitis Media)**
- **Respiratory infections (pneumonia, bronchitis)**
- **Urinary tract infections (UTIs)**

Frequent use of antibiotics can increase the chance of bacteria developing resistance. Repeated exposure to antibiotics allows bacteria to gradually evolve mechanisms that protect them from the drug's effects, such as:

- **Mutations in bacterial DNA**
- **Horizontal gene transfer** (the exchange of resistance genes between different bacteria)
- **Selection of resistant strains**: Over time, the resistant bacteria survive and multiply, leading to more difficult-to-treat infections.

4. Antibiotic Use in Agriculture and Livestock

A major, often overlooked, source of antibiotic resistance is the use of antibiotics in agriculture, including livestock farming. Antibiotics are used in healthy animals to promote growth or prevent infections in crowded conditions. While this may not directly affect humans, it contributes to resistance in the environment. Key ways this happens include:

- **Antibiotic-resistant bacteria in food**: Antibiotic-resistant bacteria from animals can transfer to humans through the consumption of contaminated meat, milk, or eggs.
- **Environmental spread**: Resistant bacteria can also spread from farm environments to nearby communities through water, soil, or air.

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Children, especially those who consume a lot of animal products, may be at risk of ingesting antibiotic-resistant bacteria.

5. Incomplete Courses of Antibiotics

Another root cause of antibiotic resistance in childhood is when children do not complete their prescribed antibiotic regimen. Parents may stop giving antibiotics when their child starts feeling better, even though the bacteria might not have been completely eradicated. This incomplete treatment allows some bacteria to survive and evolve resistance to the antibiotic.

- **Premature discontinuation of antibiotics**: Stopping antibiotics too soon can lead to the development of more resistant bacteria that are harder to treat with the same or different antibiotics in the future.

6. Infection Control Failures in Healthcare Settings

Healthcare-associated infections are a significant source of antibiotic-resistant bacteria. Hospitals, clinics, and daycare centers where children are treated or congregate can become breeding grounds for resistant pathogens. Several factors contribute to this:

- **Cross-contamination**: In healthcare settings, where children with compromised immune systems or serious conditions are treated, resistant bacteria can spread from one child to another.
- **Improper hand hygiene**: Inadequate infection control practices, such as not washing hands properly between patient interactions, can allow resistant bacteria to spread.
- **Inconsistent sanitation**: Failure to disinfect surfaces, medical instruments, or toys in childcare centers can lead to the spread of resistant bacteria.

7. Global Spread of Resistance Through Travel and Migration

As resistant bacteria are often not confined to one location, travel between countries or regions can contribute to the global spread of antibiotic resistance. Families who travel or migrate may unknowingly carry resistant bacteria across borders, potentially exposing children to infections that are resistant to antibiotics commonly used in their home country.

- **Global trade and travel**: Resistant strains of bacteria spread from one country to another through people, animals, and food products.

8. Lack of Awareness and Education

Many parents and caregivers lack knowledge about the proper use of antibiotics. The misconception that antibiotics are needed for all infections or that they should be taken "just in case" is widespread. Without proper education, parents may:

- **Request unnecessary antibiotics**: Even if the doctor doesn't prescribe antibiotics, some parents insist on them, especially if they see no immediate improvement in their child's condition.
- **Not follow instructions**: Parents might not understand the importance of taking the full course or giving antibiotics at the right times, leading to misuse.

III. DOSE APPROPRIATENESS FOR THE PEDIATRIC AGE:

Appropriate dosing of antibiotics in children is critical not only for effectively treating infections but also for minimizing the risk of developing antibiotic resistance (AMR). The improper use of antibiotics—whether through incorrect dosages, inappropriate drug selection, or incomplete courses—can contribute to the emergence and spread of resistant bacteria. In the context of childhood infections, ensuring the correct dose is especially important given the differences in physiology, age, weight, and development of children's bodies compared to adults.

1. Weight-Based Dosing

Children's pharmacokinetics (absorption, distribution, metabolism, and excretion of drugs) differ significantly from adults, meaning they often require different dosages based on their weight, age, and developmental stage.

- **Weight-based dosing** is essential, especially for antibiotics with a narrow therapeutic index or a significant risk of adverse effects. For example, antibiotics like **amoxicillin**, **cephalosporins**, and penicillin are commonly prescribed to children, and the dose should be carefully adjusted based on the child's body weight.
- **Inaccurate dosing** (too low or too high) can lead to ineffective treatment or toxicity, and in the case of under dosing, it can also contribute to sub-optimal **bacterial killing**. This allows bacteria to survive and develop resistance.

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For instance:

- **Amoxicillin**: For a child aged 2-5 years with a mild to moderate infection, the usual dose is 20-40 mg/kg/day in divided doses. For a child with a more severe infection, the dose may be adjusted, but it must not exceed the recommended maximum daily limit to avoid adverse effects.

2. Age-Appropriate Adjustments

- **Neonates and Infants**: Infants, especially neonates (newborns), require special consideration due to immature liver and kidney functions. Drugs that are metabolized or excreted by these organs may accumulate in the bloodstream if dosed incorrectly, leading to toxicity or ineffective treatment. For instance, **gentamicin** (an aminoglycoside) dosing in neonates must be adjusted based on their renal function.
- **Younger Children**: As children grow, their metabolic rate and kidney function improve, and dosages must be adjusted accordingly. The ability to metabolize drugs like **cephalexin** or **trimethoprim-sulfamethoxazole** is different in a 6-month-old versus a 5-year-old, requiring different doses.

3. Correct Dosage Forms

- Children may need special forms of medication, such as **liquid suspensions**, **chewable tablets**, or **sprinkles**, as some may not be able to swallow pills or tablets. This is especially important to ensure that the correct dose is administered. **Incorrect dosing with solid forms** or improper conversion from liquid doses (e.g., using a teaspoon instead of a proper medicine spoon) can lead to under dosing or overdosing.

4. Completing the Full Course

Even when the dosage is correct, **failure to complete the prescribed course** of antibiotics can contribute to resistance. Parents and caregivers may stop administering antibiotics once their child starts feeling better, mistakenly thinking the infection is gone. This incomplete treatment can leave some bacteria alive, allowing them to evolve resistance. It's crucial to educate parents and healthcare providers that children should complete the full course, even if they seem to improve before finishing their medication.

Dose Appropriateness Matters for AMR in Children

1. Avoiding Sub therapeutic Dosing

- **Under dosing** (giving too little of an antibiotic) is a primary driver of resistance. If the dose is too low, it may not be enough to kill the bacteria, allowing them to survive and adapt to the drug.
- For example, giving a child a lower dose of antibiotics for a **urinary tract infection (UTI)** than recommended may allow the causative bacteria, like Escherichia coli, to survive and eventually become resistant.

2. Preventing the Development of Resistant Strains

- Resistant bacteria evolve when exposed to antibiotics over time. **Inappropriate dosing**—either under dosing or overusing antibiotics—can create selective pressure on bacteria. Even when children take the right drug for an infection, incorrect dosing can lead to ineffective treatment and create the conditions for bacteria to develop resistance.
- For instance, bacteria that survive a **low dose** of antibiotics may develop resistance mechanisms, making the infection harder to treat in the future.

3. Reducing the Need for Broad-Spectrum Antibiotics

- When antibiotics are given at sub-optimal **doses**, or inappropriate ones, infections can worsen, and healthcare providers may be forced to resort to stronger, **broad-spectrum antibiotics**. These drugs, which target a wide range of bacteria, are more likely to contribute to AMR because they kill both harmful and beneficial bacteria, promoting the growth of resistant strains.
- By ensuring the proper dose of antibiotics, doctors can help **avoid unnecessary escalation to stronger antibiotics**, reserving broad-spectrum agents for cases where they are absolutely necessary.

Key Strategies to Ensure Appropriate Dosing in Children

1. Adherence to Pediatric Dosing Guidelines

- Healthcare providers should strictly adhere to established pediatric dosing guidelines, which take into account the child's weight, age, and infection severity.

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- Many organizations, such as the **American Academy of Pediatrics (AAP)** and the **World Health Organization (WHO)**, provide comprehensive pediatric dosing recommendations for antibiotics.

2. Use of Age- and Weight-Specific Formulas

- When prescribing antibiotics, especially for **serious infections** (e.g., pneumonia, sepsis), doctors must carefully calculate the correct dose based on the child's weight or body surface area. This ensures that the antibiotic is effective without causing harm.

3. Education for Parents and Caregivers

- It's crucial to educate parents on how to properly administer antibiotics. They should understand the importance of **correct dosages** and **completing the full course** of treatment.
- Parents should also be informed about the risks of using leftover antibiotics or sharing them with others.

4. Monitoring and Adjusting Doses

- Healthcare providers should regularly monitor children for signs of **adverse reactions** or **therapeutic failure** during treatment, adjusting dosages if necessary.
- If a child's condition does not improve as expected, the doctor may need to reassess the diagnosis or change the antibiotic, possibly adjusting the dose based on clinical response.

5. Limiting Unnecessary Antibiotic Prescribing

- Not all childhood infections require antibiotics. **Viral infections**, such as colds or the flu, should not be treated with antibiotics. By **limiting unnecessary prescriptions**, the risk of resistance is reduced, and the appropriate use of antibiotics is promoted.

6. Encouraging Vaccination

- Vaccines play an important role in reducing the number of infections that require antibiotics in the first place. By preventing diseases like pneumonia, meningitis, and otitis media (common childhood infections), the reliance on antibiotics is reduced, thus lowering the risk of resistance.

IV. CONCLUSION :

Antimicrobial steamship programs have been plays a major role to promote the rational of use of antibodies in pediatric patients.