

SCIENTIFIC BASIS FOR INDIVIDUALIZATION AND OPTIMIZATION OF THERAPY FOR AIRBORNE DISEASES IN CHILDREN: A COMPREHENSIVE REVIEW

Oripova Jamila Nematovna,
Department of Infectious diseases,
Andijan State Medical Institute,
Andijan, Uzbekistan

ABSTRACT: Airborne diseases represent one of the most significant causes of morbidity and mortality in pediatric populations worldwide, imposing a substantial burden on healthcare systems. The conventional "one-size-fits-all" therapeutic approach to managing these infections, including pneumonia, bronchitis, influenza, and respiratory syncytial virus (RSV), is increasingly being challenged by the rise of antimicrobial resistance (AMR), high rates of treatment failure, and the potential for adverse drug reactions in children. The unique physiological and immunological characteristics of children, which undergo dynamic changes from infancy to adolescence, necessitate a more nuanced and personalized treatment strategy. This review article aims to provide a comprehensive scientific rationale for the individualization and optimization of therapy for airborne diseases in children. We explore the critical interplay of host factors (genetics, age-related pharmacokinetics/pharmacodynamics (PK/PD), immune status, microbiome) and pathogen characteristics (genotype, resistance patterns) in determining clinical outcomes. The paper synthesizes current evidence on advanced diagnostics, biomarker-guided therapies, pharmacogenomics, and therapeutic drug monitoring as key pillars for developing tailored treatment regimens. The central thesis is that a shift from empirical to precision-based therapy is not merely an academic pursuit but a clinical imperative to enhance therapeutic efficacy, minimize toxicity, and combat the growing threat of AMR. We discuss the integration of multi-omics data and computational modeling as future directions for creating dynamic, adaptive treatment protocols that can significantly improve the standard of care for children suffering from airborne infections.

Keywords: Airborne Diseases, Pediatrics, Personalized Medicine, Therapy Optimization, Pharmacogenomics, Antimicrobial Resistance, Biomarkers, Pharmacokinetics, Individualized Therapy.

INTRODUCTION

Airborne infections, transmitted through droplets or aerosols, remain a leading cause of pediatric hospitalization and mortality globally. The spectrum of these illnesses ranges from self-limiting viral upper respiratory tract infections (URTIs) to life-threatening bacterial pneumonia and bronchiolitis. The World Health Organization (WHO) identifies pneumonia alone as the single largest infectious cause of death in children worldwide, accounting for approximately 15% of all deaths of children under 5 years old.

The current paradigm for managing these conditions often relies on empirical treatment guided by standardized clinical protocols. While these guidelines are essential for ensuring a baseline level of care, they are inherently limited as they do not account for the vast inter-individual variability in both the host and the pathogen. A child's response to an infection and to a specific therapeutic agent is a complex multifactorial process influenced by: Age and Developmental Stage: Organ maturation, particularly of the liver and kidneys, profoundly affects drug metabolism and elimination. Genetic Predisposition: Polymorphisms in genes encoding drug-metabolizing enzymes, transporters, and therapeutic targets can lead to significant variations in



drug efficacy and toxicity. Immune System Maturity: The developing immune system of a child may respond differently to pathogens and therapies compared to an adult's. Nutritional Status and Co-morbidities: Underlying conditions such as malnutrition, asthma, or congenital heart disease can alter disease severity and drug disposition. Pathogen Variability: The causative agent's species, strain, virulence factors, and antimicrobial susceptibility profile are critical determinants of the appropriate treatment.

The indiscriminate use of broad-spectrum antibiotics, often a cornerstone of empirical therapy, is a major driver of antimicrobial resistance (AMR), which has been declared a global health crisis. Consequently, there is an urgent and compelling need to move towards a more sophisticated, individualized approach. This paper will systematically review the scientific foundations that underpin the optimization and personalization of therapy for airborne diseases in the pediatric population, arguing for a paradigm shift towards precision medicine in pediatric infectious disease management.

LITERATURE REVIEW

The concept of personalized medicine, while well-established in fields like oncology, is gaining traction in infectious diseases. The literature reveals several key domains that form the scientific basis for individualizing therapy in children.

Pharmacokinetic and Pharmacodynamic (PK/PD) Variability in Pediatrics The pediatric population is not a homogenous group. It encompasses distinct developmental stages (neonates, infants, children, adolescents), each with unique physiological characteristics affecting drug disposition. Maturation of absorption, distribution, metabolism, and excretion (ADME) processes is non-linear. For instance, gastric acid secretion is lower in infants, affecting the absorption of acid-labile drugs. Total body water content is higher in neonates, increasing the volume of distribution for hydrophilic drugs like beta-lactams and aminoglycosides, often necessitating higher weight-based doses. The activity of cytochrome P450 (CYP) enzymes, crucial for metabolizing many drugs, changes dramatically throughout childhood. For example, CYP3A4 activity is low at birth but matures to adult levels within the first year. Understanding these PK/PD changes is fundamental to dose optimization and preventing sub-therapeutic or toxic drug concentrations.

The role of pharmacogenomics (PGx) Pharmacogenomics studies how an individual's genetic makeup influences their response to drugs. Genetic variations can alter the function of metabolic enzymes, leading to different drug exposure levels. A classic example is the variation in the *CYP2C19* gene, which affects the metabolism of proton pump inhibitors, sometimes used as adjunctive therapy in respiratory conditions. More relevant to infectious diseases are variations in genes related to immune response (e.g., *TNF- α* , *IL-6*) which might predict disease severity, and genes encoding drug transporters that affect antibiotic concentrations at the site of infection. PGx testing has the potential to pre-emptively identify patients at risk for adverse effects or treatment failure, allowing for dose adjustments or selection of alternative drugs.

Biomarker-Guided therapy and antimicrobial stewardship Biomarkers are objective indicators of a biological state or process and can be invaluable tools for personalizing therapy. In the context of airborne infections, biomarkers can help:

Differentiate between bacterial and viral etiologies: Procalcitonin (PCT) and C-reactive protein (CRP) are widely used to guide antibiotic initiation and cessation. Elevated PCT is more specific for bacterial infections, and its serial measurement can help shorten the duration of antibiotic therapy, a key principle of antimicrobial stewardship.



Assess disease severity and prognosis: Levels of certain cytokines (e.g., IL-6, IL-10) and endothelial markers can correlate with the severity of sepsis or acute respiratory distress syndrome (ARDS) secondary to pneumonia.

Monitor treatment response: A rapid decline in CRP or PCT levels following treatment initiation can indicate therapeutic efficacy.

Advanced Molecular Diagnostics The optimization of therapy begins with accurate and rapid identification of the causative pathogen and its resistance profile. Traditional culture-based methods are slow and have limited sensitivity, especially if antibiotics have been administered. The advent of molecular diagnostics, such as multiplex PCR panels, has revolutionized the field. These panels can simultaneously detect dozens of viral and bacterial respiratory pathogens within hours. Furthermore, next-generation sequencing (NGS) and metagenomics offer the potential for unbiased pathogen detection, discovery of novel pathogens, and comprehensive antimicrobial resistance gene profiling directly from clinical samples. This level of diagnostic precision is crucial for transitioning from broad-spectrum empirical therapy to targeted, narrow-spectrum treatment.

MATERIALS AND METHODS

This article is a comprehensive narrative review of the scientific literature. A systematic search was conducted using the following electronic databases: PubMed/MEDLINE, Scopus, Google Scholar, and Web of Science for articles published between January 2000 and September 2025. The search strategy included a combination of Medical Subject Headings (MeSH) terms and keywords such as: ("airborne diseases" OR "respiratory tract infections" OR "pneumonia") AND ("pediatrics" OR "children") AND ("personalized medicine" OR "individualized therapy" OR "precision medicine") AND ("pharmacogenomics" OR "pharmacokinetics" OR "biomarkers" OR "molecular diagnostics").

Articles were included if they were published in English and focused on the scientific basis or clinical application of personalizing treatment for respiratory infections in children. The review prioritized systematic reviews, meta-analyses, randomized controlled trials, and seminal cohort studies. The gathered information was synthesized and structured to build a coherent argument for the individualization and optimization of therapy.

To illustrate the practical application of these principles, we present hypothetical data and frameworks in the results section, including comparative tables based on the synthesized evidence from the literature.

RESULTS AND DISCUSSION

The synthesis of available evidence points to a multi-pronged strategy for individualizing therapy for pediatric airborne diseases. The core components of this strategy are precision diagnostics, tailored pharmacotherapy, and host-response modulation.

Pillar 1: Transitioning from syndromic to precision diagnosis the traditional approach often treats based on a clinical syndrome (e.g., community-acquired pneumonia). However, the etiology can be vastly different, ranging from *Streptococcus pneumoniae* to Mycoplasma, to viral agents like RSV or influenza. Optimization requires moving beyond this syndromic approach.

Table 1: Comparison of diagnostic approaches for pediatric pneumonia

Feature	Traditional approach	Optimized/individualized approach
Diagnostic method	Chest X-ray, blood culture, sputum culture	Multiplex PCR panels, next-generation sequencing (NGS), host-gene expression



		classifiers
Time to result	24-72 hours for culture results	1-6 hours for PCR; 24-48 hours for NGS
Pathogen identification	Low sensitivity, especially for atypical and viral pathogens	High sensitivity and specificity; detects co-infections and resistance genes
Treatment decision	Empirical, broad-spectrum antibiotics	Targeted therapy (narrow-spectrum antibiotic or antiviral), de-escalation based on results
Impact on stewardship	Promotes overuse of broad-spectrum antibiotics	Facilitates antibiotic stewardship, reduces unnecessary antibiotic use for viral infections
Example	A 3-year-old with fever and cough is started on amoxicillin + azithromycin empirically. Blood culture is negative.	A PCR panel on a nasopharyngeal swab reveals RSV and <i>Bordetella pertussis</i> . Azithromycin is continued, amoxicillin is stopped.

Discussion: The use of rapid molecular diagnostics is a cornerstone of individualized therapy. By quickly identifying the pathogen, clinicians can select the most effective, narrow-spectrum antimicrobial agent. This not only improves the likelihood of a positive clinical outcome but is also a critical tool in combating AMR. For instance, identifying influenza A allows for the timely administration of neuraminidase inhibitors, while detecting RSV confirms that antibiotics are futile and care should be focused on supportive measures. Host-gene expression classifiers represent a further step, analyzing the patient's own gene activity to differentiate between bacterial and viral responses with high accuracy, even when a pathogen is not detected.

Pillar 2: Individualized pharmacotherapy once the right drug is selected, the right dose must be administered. This is particularly challenging in pediatrics due to dynamic PK/PD.

Dose optimization via PK/PD Modeling and TDM Weight-based dosing is a starting point, but it fails to account for variability in organ function and maturation. Population PK (PopPK) modeling, which uses sparse data from patients to model how a drug behaves in a specific population (e.g., 2-5-year-old children), can lead to more accurate dosing nomograms. For drugs with a narrow therapeutic index (e.g., vancomycin, aminoglycosides), Therapeutic Drug Monitoring (TDM) is essential. TDM involves measuring drug concentrations in the blood to ensure they are within the target range for efficacy while minimizing toxicity.

The impact of pharmacogenomics Genetic testing can guide drug selection and dosing. For example, oseltamivir (Tamiflu) is a prodrug converted to its active form by carboxylesterase 1 (CES1). Genetic variants in *CES1* that reduce its activity could lead to lower concentrations of the active metabolite, potentially causing treatment failure.

Table 2: Examples of pharmacogenomic associations relevant to pediatric airborne diseases

Gene	Drug class/agent	Clinical implication in pediatrics	Recommendation
CYP2C9	Ibuprofen	Poor metabolizers may have increased exposure, raising the risk of gastrointestinal or renal toxicity.	Consider dose reduction or alternative non-steroidal anti-inflammatory drugs (NSAIDs).
SLCO1B1	Oseltamivir	Transporter gene variants may influence drug distribution and efficacy. Research is ongoing.	Currently for research; potential future relevance for dose optimization.
TPMT, NUDT15	Azathioprine	Used in severe, steroid-dependent asthma. Poor	Genotype-guided dosing is the standard of care



		metabolizers have a high risk of life-threatening myelosuppression.	before initiating therapy.
IL-6, TNF-α	Systemic Corticosteroids	Polymorphisms in inflammatory cytokine genes may predict response to steroids in severe respiratory disease like ARDS or croup.	Potential to identify patients who would benefit most from adjunctive immunomodulatory therapy.

Discussion: While routine preemptive pharmacogenomic testing is not yet standard practice in most pediatric infectious disease settings, its utility is growing. The primary barriers are cost, turnaround time for results, and the need for more robust clinical guidelines for interpretation. However, as the cost of genotyping decreases, integrating PGx data into the clinical workflow will become increasingly feasible. This represents a proactive approach to prevent adverse drug events and improve efficacy.

Pillar 3: Biomarker-Guided Disease Management Biomarkers provide a real-time snapshot of the host's response to infection, offering critical information beyond pathogen identification.

Table 3: Key biomarkers for individualizing therapy

Biomarker	Biological role	Clinical application in pediatric airborne disease
Procalcitonin (PCT)	Precursor of calcitonin, highly upregulated in bacterial infections.	- Differentiate bacterial vs. viral pneumonia. - Guide antibiotic initiation and duration.
C-Reactive protein (CRP)	Acute-phase reactant produced by the liver in response to inflammation.	- Monitor response to therapy (levels should fall). - Less specific than PCT for bacterial infection.
Interleukin-6 (IL-6)	Pro-inflammatory cytokine.	- Marker of systemic inflammation and severity. - Potential target for immunomodulatory therapy in ARDS.
Endothelial markers (e.g., angiopoietin-2)	Reflect endothelial activation and injury.	- Predict severity and development of ARDS in pneumonia and sepsis.

Discussion: The most impactful use of biomarkers has been in antibiotic stewardship. Several randomized controlled trials have shown that using PCT algorithms to guide the duration of antibiotic therapy in lower respiratory tract infections can reduce antibiotic exposure by several days without negatively impacting clinical outcomes. This is a powerful, evidence-based optimization strategy that can be implemented in many hospital settings. The future lies in combining multiple biomarkers into a predictive panel. For example, a combination of pathogen load (from PCR), host inflammatory markers (PCT, IL-6), and endothelial injury markers could be used in a machine learning algorithm to predict which child with pneumonia is likely to deteriorate and require intensive care, allowing for early intervention.

CONCLUSION

The scientific foundation for individualizing and optimizing therapy for airborne diseases in children is robust and rapidly expanding. The traditional empirical model is no longer sufficient in an era of rising antimicrobial resistance and with our deepening understanding of human biological variability. The future of pediatric infectious disease management lies in the



thoughtful integration of advanced molecular diagnostics, pharmacogenomic data, PK/PD modeling, and biomarker-guided strategies.

This personalized approach allows clinicians to answer three critical questions with increasing precision:

What is the cause? (Answered by rapid molecular diagnostics).

What is the best drug and dose for *this* child? (Answered by PK/PD modeling, TDM, and pharmacogenomics).

How is *this* child responding to the infection and treatment? (Answered by serial biomarker measurement).

Implementing this paradigm shift presents challenges, including the need for new infrastructure, clinician education, and addressing the cost-effectiveness of these advanced technologies. However, the potential benefits are immense: improved cure rates, reduced adverse drug events, preservation of antimicrobial efficacy for future generations, and shorter hospital stays. Continued research, particularly prospective clinical trials validating these personalized strategies in diverse pediatric populations, is essential. Ultimately, by embracing the principles of individualized therapy, we can move closer to providing the right treatment, at the right dose, for the right child, at the right time.

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