Ventilator-Associated Pneumonia in Critically Ill Children: A New Paradigm

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KEYWORDS

• Ventilator-associated pneumonia • Mechanical ventilation • Microbiome
• Metagenomics • Pediatric intensive care

KEY POINTS

- Surveillance definitions for ventilator-associated pneumonia (VAP) are in the process of being updated. Further evaluation is needed to assure that the patients who are most amenable to targeted prevention strategies are identified.
- VAP is the most common indication for antibiotic use in the pediatric intensive care unit. Present approaches to clinical cultures and antibiotic use may actually increase risk for VAP by depleting protective commensal organisms and selecting for antibiotic resistant pathogens.
- Recent metagenomic and proteomic technologies offer the potential to better interrogate the relationships between an intubated individual's respiratory microbiota, the host's immune response, and the underlying disease process to provide important insights into the pathogenesis of VAP.
- The normal lung is colonized with diverse microbial communities. It seems likely that critical illness and its care contribute to a dysbiosis and the selection of a disease-promoting microbiome or pathobiome that increases risk for nosocomial infection, including VAP.

INTRODUCTION

Mechanically ventilated children are at high risk for nosocomial infections, including ventilator-associated pneumonia (VAP). Children who develop VAP have an increased risk of mortality[1] and morbidities such as prolonged intubation and intensive care unit (ICU) stays and the need for extensive rehabilitation.[2] VAP is the most common nosocomial infection in mechanically ventilated patients,[1] occurring in up to 32% of pediatric ICU (PICU) patients who require mechanical ventilation (MV) for more than

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24 hours.[3,4] VAP is associated with a 2-fold to 3-fold increase in mortality in ventilated children,[5,6] and increases total hospitalization costs and resource utilization, increasing duration of MV by 5 to 11 days and PICU length of stay by 11 to 34 days.[3,4,6,7] The suspicion and/or the diagnosis of VAP remain the primary reason for antibiotic administration in the PICU.[8] Thus, VAP remains a significant obstacle to the management of pediatric critical illnesses and injuries.

The traditional view of the pathogenesis of pneumonia was based on the premise that the lung was sterile, and that infection occurred by the introduction of pathogens either by direct inoculation from the environment or through the blood stream. However, recent evidence has revealed that the lungs contain diverse microbial populations.[9,10] The endogenous microbiota are likely critical regulators of both pathogen behavior and host responses in the airways. Infection, therefore, occurs as a result of the combination of dysbiosis and failure of the host immune response. Because the lungs are inhabited by microbial populations (akin to the intestinal tract albeit in far lower density,[9–12]), the simple paradigm of a single pathogen gaining access to a sterile lower respiratory tract to cause infection has evolved. Pathogens are introduced to a pre-existing and often complex microbial community[9,11] that either allows, facilitates, or hinders the potential pathogen, and consequently determines whether progression to VAP occurs. Limited understanding of the microbial and host factors associated with VAP pathogenesis has precluded development of truly effective prevention and treatment strategies.[13,14]

This article briefly discusses the changing criteria by which VAP is diagnosed and the limitations of these definitions for both surveillance and clinical research attempting to identify risk factors for and the pathogenesis of VAP. It also discusses the prospects for a deeper understanding of the pathogenesis of VAP in the new era of metagenomics and proteomics, together with the recent evidence about the role of microbiome in health and disease.

SURVEILLANCE DEFINITION

In the absence of a readily available microbiologic gold standard, standardized clinical criteria for VAP were first developed in 2002 by the Centers for Disease Control (CDC) and National Nosocomial Infections Surveillance (NNIS) to allow for consistent diagnosis and reporting.[15] The CDC/NNIS definitions, which underwent some minor modifications during the subsequent decade, relied on combinations of radiographic, clinical, and laboratory evidence in the consideration of a VAP diagnosis. Because traditional culture from respiratory samples depends on the chosen medium, positive cultures from these methods were optional parts of the pediatric criteria.[16–19] When rigorously applied, CDC/NNIS VAP criteria have been shown to be associated with predictably poor outcomes.[20–22] However, application of these criteria is time-consuming and inconsistent because definitions of components of the criteria are subjective and imprecise.[23,24] Several studies demonstrate this variability. Among 64 PICUs reporting data to CDC's National Healthcare Safety Network (NHSN) between 2007 and 2012, the incidence of VAP decreased from 1.9 to 0.7 per 1000 ventilator-days.[25] However, other published prospective pediatric studies report rates as high as 7.1 per 1000 ventilator-days in the United States.[6] That different studies report markedly different VAP rates suggest that diverse populations of children have unique risk for VAP or that interpretation of the criteria by investigators is subjective. Similarly, from 2006 to 2012, adult medical ICUs reporting data to NHSN demonstrated a decline in VAP rates from 3.1 to 0.9 per 1000 ventilator-days, whereas other evaluations have concluded that VAP rates have not declined during this period with a