
**Severity of viral coinfection
in hospitalized infants with
respiratory syncytial virus infection**

Dear Editor,

We have read with special interest the article by De Paulis et al.¹ on viral co-detection in hospitalized infants with bronchiolitis. The authors studied a cohort of hospitalized infants in São Paulo and found high rates of viral co-detection, which were not associated with disease severity. In the editorial published in the same issue of *Jornal de Pediatria*, Sly and Jones² highlight that previous clinical studies are contradictory regarding the association between co-detection and severity of viral infections of the lower respiratory tract. In Recife, we had the opportunity to prospectively follow 407 children under five years of age with acute respiratory infection (ARI) who received emergency care at Instituto de Medicina Integral Prof. Fernando Figueira (IMIP) between April 2008 and March 2009.³ The disease severity spectrum was categorized as very mild (upper ARI), mild (lower ARI without hospitalization), moderate (lower ARI with hospitalization, but no need for supplemental oxygen), and severe (lower ARI with hospitalization and need for oxygen). Nasopharyngeal aspirate samples were collected from all children during the acute phase of disease, and 17 respiratory pathogens were investigated using molecular diagnostic techniques (multiplex RT-PCR): respiratory syncytial virus (RSV), metapneumovirus, parainfluenza viruses 1, 2, 3, 4, influenza viruses A and B, bocavirus, adenovirus, coronavirus- 229E, NL63, OC43, KHU1, rhinovirus, *Mycoplasma pneumoniae* (*Mpp*), and *Chlamydia pneumoniae* (*Cpp*). One or more pathogens were detected in 85.5% of samples, with a co-detection rate of 39.6%. The most common co-detections included adenovirus, RSV, bocavirus, and rhinovirus. While children with RSV and *Mpp* infection were more likely to be hospitalized than children without these pathogens, the proportion of children in whom a pathogen was detected was similar across the disease severity groups and between ambulatory and hospitalized patients. Similarly, no difference in disease severity was found in children in whom one, two, three or four pathogens were detected. Although our study did not have statistical power to detect whether particular pathogen combinations were associated with more severe disease, our findings corroborate those of De Paulis et al.¹

Detection of pathogens by molecular methods provides a major advance in understanding the epidemiology of ARI in childhood, but the interpretation of results has some limitations, as indicated by Sly and Jones² and De Paulis et al.¹ We agree with those authors that there is no clear advantage in detecting viral coinfection to determine the appropriate treatment for the individual child. From an academic standpoint, however, the use of quantitative PCR techniques may allow a better assessment of the role of co-detection in the induction of immune response and respiratory symptoms. By allowing us to establish the viral load in nasopharyngeal aspirate samples, quantitative PCR techniques could, in theory, help identify cases with high acute-phase viral replication of the agent responsible for symptoms or contribute to relativize the finding of trace amounts of DNA or RNA present in the sample. Future research on viral load, host genetic polymorphism and epigenetics may clarify the importance of different viral pathogens on disease severity in children with ARI.

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doi:10.2223/JPED.2149

No conflicts of interest declared concerning the publication of this letter.

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2. Sly PD, Jones CM. *Viral co-detection in infants hospitalized with respiratory disease: is it important to detect?* *J Pediatr* (Rio J). 2011;87:277-80.
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Authors' reply

Dear Editor,

The discussion about the role and impact of viruses on the respiratory health of children is not only important, but always stimulating and instigating.

New knowledge accumulates and changes concepts, as indicated in the editorial published in *Jornal de Pediatria* (Vol. 87, No. 4, 2011) by Sly and Jones,¹ which may or may not produce changes in clinical practice. It is worth remembering that both situations have consequences and should therefore be ideally based on the best available scientific evidence.

A letter to the Editor published in this issue of *Jornal de Pediatria* cites the study by Bezerra et al.,² which is in some aspects different from our study.³ While our results relate to viral investigation in hospitalized infants with infections of the lower respiratory tract, those of Bezerra et al.² refer to children under five years of age who received ambulatory care or were hospitalized due to upper and/or lower respiratory tract infections. Even so, the results are in agreement about the lack of influence of viral co-detection on the severity of infection.^{2,3}

Several factors may contribute to the current controversy about the clinical relevance of viral co-detection in nasopharyngeal aspirates of children, including characteristics of the study population (age, clinical presentation, and others) and outcomes studied. Differentiating age groups is therefore important. Respiratory syncytial virus (RSV), for example, is associated with more severe symptoms in the first contact with the child, which usually occurs during the first year of life. In addition, RSV reinfections are frequent and associated with milder cases. Therefore, it may be assumed that finding RSV in respiratory secretions of children under one year or up to

five years of age may represent different clinical situations that reflect different etiopathogenic mechanisms. The same is valid for the co-detection of RSV associated with other viruses.

The molecular methods for viral diagnosis increasingly enable the detection of agents with or without a pathogenic role, underscoring the clinical importance of questioning the role of each agent detected and of viral co-detection, as well as the importance of studies such as those mentioned above, which evaluate actual and usual clinical situations. Techniques that allow the quantification of viral load may contribute to the diagnosis of active infection in the presence of virus in the respiratory tract, but further studies involving relevant clinical situations, such as acute bronchiolitis or different types of asthma attacks, are still needed.

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doi:10.2223/JPED.2150

No conflicts of interest declared concerning the publication of this letter.

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