Expert Perspectives on Safeguarding Infants and Children from Respiratory Syncytial Virus

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Interview Summary

For this article, EMJ conducted an interview with key opinion leader, João Farela Neves, who currently holds the positions of Paediatrician and Director of the Department of Paediatrics at the Hospital da Luz, Lisbon, Portugal. He also serves as an Associate Professor/Invited Assistant and researcher at NOVA Medical School, NOVA University of Lisbon, Portugal. Neves specialises in paediatric immunology, with a specific focus on primary immunodeficiencies, paediatric infectious diseases, paediatric intensive care, and clinical immunology.

In this interview, Neves discussed the importance of safeguarding infants and children from respiratory syncytial virus (RSV) due to the associated risk factors, particularly among infants under the age of 2 years. This discussion highlighted that RSV can impose a significant burden on healthcare systems, families, and infants alike, while also addressing the potential strategies for prevention to safeguard vulnerable populations. Neves provided insights into the importance of implementing preventive measures, which encompass both non-pharmacological interventions and pharmaceutical measures. These interventions are aimed at mitigating hospitalisations, and alleviating the burden of long-term respiratory conditions in infants. Furthermore, Neves highlighted the importance of improving health education and fostering awareness regarding the potential severity of RSV. This awareness is needed among the general public, caregivers, and healthcare professionals.

INTRODUCTION

RSV is a single-stranded, negative-sense RNA virus, that belongs to the *Paramyxoviridae* family.^{1,2} RSV is highly infectious, is primarily transmitted through respiratory droplets and contaminated surfaces, and spreads rapidly within crowded environments, such as households, schools, nurseries, and hospitals.^{2,3} RSV instigates infections in the respiratory tract, inducing inflammation, cellular damage, and airway obstruction.^{3,4}

THE ENDURING IMPACT OF RESPIRATORY SYNCYTIAL VIRUS ON INFANTS

RSV continues to impose a major burden on healthcare systems, contributing annually to approximately 33 million infection episodes, resulting in 3.2 million hospital admissions, and 118,200 deaths among children under 5 years old worldwide.⁵ Infants, particularly those under the age of 2 years old, remain highly vulnerable to the threat imposed by RSV.^{6,7} Notably, RSV can cause bronchiolitis in infants, which is a leading cause of hospitalisation in children under 12 months of age worldwide.^{8,9}

Neves also identified that infants considered at 'high-risk' from RSV encompass those born prematurely, or with underlying medical conditions, such as heart disease and chronic pulmonary diseases, who may be predisposed to severe RSV-associated illnesses.¹⁰ However, most RSV-related hospitalisations (approximately 80–90%) occur in previously healthy infants without underlying medical conditions.¹¹⁻¹⁵ Furthermore, those who have a severe burden of disease may encounter other long-term respiratory conditions in later life.¹⁶ For example, Neves identified that children (up to 5 years old) infected with RSV during early infancy may go on to develop recurrent wheezing,¹⁷ where studies have associated a link with asthma and genetic predisposition, all of which collectively contribute to the burden on the healthcare system.^{16,18}

The Immune Challenges of Respiratory Syncytial Virus in Infants

As highlighted by Neves, a key risk factor contributing to severe RSV disease in infants

is their immature immune systems, and small respiratory tracts.¹⁹ The virus undergoes its life cycle within infected epithelial cells of the airway, thereby hindering the effective clearance of RSV by hampering the establishment of a well-balanced Th1-type immune response.² This response involves the activation of cytotoxic T-cells that secrete interferon y.² Neves elucidated that this response is "not very robust," indicating a relatively mild Th1 response. Consequently, RSV evades the human adaptive immune response, leading to an imbalance,² favouring a Th2-type immune response that is responsible for enduring immunity through the production of neutralising antibodies against reinfection.^{6,20} This implies that RSV fails to induce a robust, long-term immune defence. As stated by Neves, individuals "can get reinfected in the same RSV season, because they don't get durable and enough protection from the immune system," therefore rendering individuals susceptible to recurrent infection by the same or distinct RSV strains.6,21

THE PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS IN INFANTS

Preventing the impact of RSV infections is of key concern, noted Neves, due to its significant implications for infants, families, and healthcare systems. Neves explored preventive measures, including non-pharmacological interventions, as well as pharmacological options. Neves noted that previously, there were gaps in immunisation schedules regarding protection against RSV disease, highlighting the challenges in developing preventive options for RSV, due to the virus' unique characteristics, and the difficulty in mounting a strong immune response.

RSV is considered highly seasonal, predominately occurring from October–March in temperate climates,²² while the pattern is more diverse in tropical countries.²³ Notably, the epidemiological landscape of RSV underwent a marked shift during the COVID-19 pandemic, leading to a substantial reduction in transmission.²⁴ Neves highlighted how this change demonstrated the importance and efficacy of non-pharmacological measures, such as diligent handwashing and mask utilisation in crowded settings, to reduce the spread of respiratory viruses, including RSV. However, following the relaxation of COVID restrictions, there was a resurgence of RSV, as noted by an increase in RSV cases. $^{\rm 25\mathchar`27}$

During the COVID-19 pandemic, the epidemiology and behaviour of RSV altered, leading to more cases seen in older children.^{26,27} Neves identified that pregnant females were not being infected with RSV during their pregnancy, therefore resulting in limited antibody responses, and subsequently contributing to an increase in RSV cases in infants under 3 months old.^{28,29} Neves stated that this pattern highlighted the importance of passive immunity to help protect infants against RSV-related illness.

Prior to 2022, protection from RSV lower respiratory tract infection was limited to only infants with a higher individual risk. However, Neves noted that "we all live in very exciting times," where prevention of RSV lower respiratory tract infection is now possible for groups at risk of severe RSV disease, including the infant population and older adults.

FOSTERING AWARENESS AND EFFECTIVE MANAGEMENT OF RESPIRATORY SYNCYTIAL VIRUS EPIDEMIC

Neves also highlighted the responsibility of healthcare professionals to increase the understanding of parents and caregivers, stating that there is a need for greater health education and heightened awareness regarding the potential seriousness of RSV among the general public, caregivers, and healthcare professionals. Neves emphasised the importance of raising awareness about the significant burden of RSV on both infants and healthcare systems, while also providing insights into potential preventive measures. The objective is to inform and educate the audience, particularly parents, caregivers, and healthcare professionals, regarding the critical importance of understanding, and effectively preventing, RSV in infants.

CONCLUSION

Neves identified the significant impact of RSV on infants and healthcare systems, offering insights into its patterns and preventive measures. This interview explored the current preventive measures encompassing both non-pharmacological interventions and pharmaceutical measures. Neves identified the importance and need for implementing preventive measures, and their potential implications for infants, families, and healthcare systems, which Neves stated requires further investigation. Neves noted the importance of educating stakeholders, particularly parents, caregivers, and healthcare professionals, to ensure vital understanding and effective management of RSV in infants. This collective responsibility aims to alleviate the burden of RSV, and to foster a well-informed, proactive approach towards its management.

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References

- Collins PL et al. Respiratory syncytial virus: virology, reverse genetics, and pathogenesis of disease. Curr Top Microbiol Immunol. 2013;372:3-38.
- Collins PL, Graham BS. Viral and host factors in human respiratory syncytial virus pathogenesis. J Virol. 2008;82(5):2040-55.
- Carvajal JJ et al. Host components contributing to respiratory syncytial virus pathogenesis. Front Immunol. 2019;10:2152.
- González PA et al. Respiratory syncytial virus infection and immunity. Rev Med Virol. 2012;22(4):230-44.

- Shi T et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet. 2017;390(10098):946-58.
- Glezen WP et al. Risk of primary infection and reinfection with respiratory syncytial virus. Am J Dis Child. 1986;140(6):543-6.
- Esposito S et al. RSV prevention in all infants: which is the most preferable strategy? Front Immunol. 2022;13:880368.
- 8. Suh M et al. Respiratory syncytial virus is the leading cause of United States infant hospitalizations,

2009-2019: a study of the national (nationwide) inpatient sample. J Infect Dis. 2022;226 (Suppl 2):S154-63.

- Del Riccio M et al. Burden of respiratory syncytial virus in the European Union: estimation of RSV-associated hospitalizations in children under 5 years. J Infect Dis. 2023;228(11):1528-38.
- Sommer C et al. Risk factors for severe respiratory syncytial virus lower respiratory tract infection. Open Microbiol J. 2011;5:144-54.
- Thwaites R et al. Clinical burden of severe respiratory syncytial virus infection during the first 2 years of life in children born between 2000 and 2011 in Scotland. Eur J Pediatr.



2020;179(5):791-9.

- Demont C et al. Economic and disease burden of RSV-associated hospitalizations in young children in France, from 2010 through 2018. BMC Infect Dis. 2021;21(1):730.
- Sanchez-Luna M et al. Trends in respiratory syncytial virus bronchiolitis hospitalizations in children less than 1 year: 2004-2012. Curr Med Res Opin. 2016;32(4):693-8.
- Mendes-da-Silva A et al. Trends in hospitalization for acute bronchiolitis in Portugal: 2000-2015. Pulmonology. 2019;25(3): 154-61.
- Kobayashi et al. Epidemiology of respiratory syncytial virus in Japan: a nationwide claims database analysis. Pediatr Int. 2022;64(1):e14957.
- Fauroux B et al. The burden and long-term respiratory morbidity associated with respiratory syncytial virus infection in early childhood. Infect Dis Ther. 2017;6(2):173-97.
- Shi T et al. Association between respiratory syncytial virusassociated acute lower respiratory infection in early life and recurrent wheeze and asthma in later childhood. J Infect Dis. 2020;222(Suppl 7):S628-33.

- Kabego L, de Beer C. Association between respiratory syncytial virus infection in infancy and subsequent asthma: a metaanalysis of observational studies. JSM Allergy Asthma. 2017;2(1):1009.
- Fonseca W et al. Factors affecting the immunity to respiratory syncytial virus: from epigenetics to microbiome. Front Immunol. 2018;9:226.
- Bueno SM et al. Protective T cell immunity against respiratory syncytial virus is efficiently induced by recombinant BCG. Proc Natl Acad Sci USA. 2008;105(52):20822-7.
- 21. Zhang W et al. Respiratory syncytial virus: immunopathology and control. Expert Rev Clin Immunol. 2006;2(1):169-79.
- Obando-Pacheco P et al. Respiratory syncytial virus seasonality: a global overview. J Infect Dis. 2018;217(9):1356-64.
- Bloom-Feshbach K et al. Latitudinal variations in seasonal activity of influenza and respiratory syncytial virus (RSV): a global comparative review. PLoS One. 2013;8(2):e54445.
- 24. Sanz-Muñoz I et al. Social distancing, lockdown and the wide use of mask; a magic solution

or a double-edged sword for respiratory viruses epidemiology? Vaccines (Basel). 2021:9(6):595.

- Movva N et al. Respiratory syncytial virus during the Covid-19 pandemic compared to historic levels: a retrospective cohort study of a health system. J Infect Dis. 2022;226(Suppl 2):S175-83.
- van Summeren J et al. Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter? Euro Surveill. 2021;26(29):2100639.
- 27. Foley DA et al. The interseasonal resurgence of respiratory syncytial virus in Australian children following the reduction of coronavirus disease 2019-related public health measures. Clin Infect Dis. 2021;73(9):e2829-30.
- Messacar K et al. Preparing for uncertainty: endemic paediatric viral illnesses after COVID-19 pandemic disruption. Lancet. 2022;400(10364):1663-5.
- 29. Johannesen CK et al. Age-specific estimates of respiratory syncytial virus-associated hospitalizations in 6 European countries: a time series analysis. J Infect Dis. 2022;226(Suppl 1):S29-37.