Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Respiratory syncytial virus: promising progress against a leading cause of pneumonia

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This World Pneumonia Day, as the global COVID-19 pandemic persists, another deadly and familiar, although under-recognised, respiratory virus requires attention: respiratory syncytial virus (RSV). RSV is responsible for acute respiratory illness, including pneumonia, in people of all ages. Globally, RSV is the most common cause of severe lower respiratory tract infection (LRTI) among infants younger than 6 months, almost all children are infected by age 2 years, and reinfection is common.[1] Severe RSV can increase risk of bacterial coinfections and subsequent LRTI, particularly in young infants.[2] The global burden of RSV disease is greater than previously estimated, in large part because of unmeasured mortality in community settings in low-income and middle-income countries (LMICs), particularly among infants younger than 6 months.[3]

Although RSV is recognised as a common cause of childhood pneumonia and an increasingly important cause of acute LRTI in older adults (aged ≥65 years), research and development, particularly around prevention, had lagged for decades.[1,4] In the 1960s, a formalin-inactivated whole virus vaccine resulted in enhanced respiratory disease in RSV-naive children after primary infection with RSV, delaying subsequent vaccine efforts.[5] Currently, no RSV vaccine is licensed or available for use in humans. Palivizumab, a monoclonal antibody (mAb) targeting the RSV surface fusion glycoprotein (F protein) that confers protection against severe disease, has been licensed for over two decades. However, palivizumab must be administered in 5-monthly intravenous doses and is extremely costly, and so has only been approved for use in some high-risk preterm infants in high-income and some middle-income countries.[1]

Improved understanding of the RSV F protein has enabled rapid advances in vaccine and mAb development. Two second-generation, long-acting, single-dose mAbs and 22 candidate RSV vaccines, including protein-based, live-attenuated or chimeric, recombinant vector-based and nucleic acid-based vaccines are in clinical development, targeting disease in infant, paediatric, and older populations.

Momentum in product development to prevent RSV disease in infants is accelerating, with two maternal vaccines (NCT04424316, NCT04605159) and two infant mAbs (NCT03979313, NCT04767373) currently in phase 3 clinical trials. The mAb nirsevimab has shown 70% protection against medically attended RSV LRTI and 78% protection against RSV LRTI hospitalisations for 150 days after administration in a phase 2b trial of healthy preterm infants, and reportedly met prespecified endpoints in an ongoing phase 3 trial among healthy term infants.[6,7] Notably, nirsevimab and an earlier maternal vaccine candidate that did not achieve licensure both conferred protection against all-cause LRTI hospitalisation in the first 6 months of life, highlighting that prevention of RSV in early infancy could bestow broader benefits to infant health.[6,8]

RSV vaccine development is also poised to leverage the successful COVID-19 mRNA vaccine experience, which continues to show high safety and protection in large and diverse populations including pregnant women and children.[9] RSV mRNA vaccines, which encode the RSV F protein stabilised in the prefusion conformation and induce a T-cell response mimicking the response to live virus infection, have been shown to increase neutralising antibody titres among healthy adults, and older, maternal, and paediatric populations are currently being enrolled into early phase clinical trials.[10] The potential to address the RSV burden with an mRNA vaccine approach that targets infants through maternal vaccination and infants and children aged 6 months to 3 years through direct vaccination–the populations that are probably responsible for the majority of disease transmission–further opens the possibility to substantially reducing the burden of RSV disease among other vulnerable populations.

Challenges to RSV vaccine and mAb development remain. Without a definitive immunological correlate of protection against clinically relevant RSV infection, cell-mediated immunity, mucosal IgA, and potent neutralising antibodies have been used as surrogate indicators because of their association with decreased disease severity. Expanded efforts for RSV genomic surveillance, including in LMICs, are also needed to assess for the emergence and circulation of antigenically divergent strains, which might be of particular relevance for mAb-based prophylaxis strategies.

For more on **RSV vaccine and mAb development** see https://www.path.org/resources/rsv-vaccine-and-mab-snapshot

The RSV prophylaxis pipeline is robust with encouraging safety and efficacy profiles. Further innovation and evaluation are needed to tackle this deadly respiratory virus, yet there is much to be hopeful for as promising clinical development progresses. Introduction of an RSV vaccine or mAb in the near-term to mid-term highlights the importance of increasing awareness of RSV as a leading cause of infant pneumonia and death in LMICs, where RSV burden is greatest and vulnerable populations would benefit the most from advances in product development. The full public health impact of RSV prophylaxis in these locations and populations will depend not only on immunological and clinical efficacy of a given vaccine or mAb, but also on appropriate support to effectively deliver these products through infant and maternal antenatal care immunisation platforms.

We declare no competing interests.

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