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Snapshot of RSV

Urvashi Mathur
The University of Texas Rio Grande Valley, urvashi.mathur01@utrgv.edu

Barbara Stewart
The University of Texas Rio Grande Valley

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Urvashi Mathur[1], Barbara Stewart MD[1,2]
[1]University of Texas Rio Grande Valley School of Medicine
[2]University of Illinois College of Medicine Peoria

Background

Respiratory syncytial virus (RSV) is known to cause bronchiolitis and other upper respiratory infections (URIs) in children <1 year old predictably around fall and winter seasons. However, given the COVID-19 pandemic and the resultant lockdowns, circulation of other respiratory viruses was uncharacteristically low. Restrictions are quickly falling and with increased interaction there has been an uncharacteristic jump in cases.

Purpose

To summarize the pathogenesis of RSV and the mechanisms the virus uses to evade immune responses. Additional discussion of the increased rates of RSV hospitalizations as well as the role of vaccinations in controlling infection.

Method

A literature review on PubMed was done including keywords “RSV” “COVID” “immunogenicity” “pathogenesis”. Retrospective cohort studies and overviews of infectivity were included in discussion. CDC data regarding RSV hospitalizations was also used.

Pathogenesis

RSV largely affects children less than 2 years old, with the majority being <1-year-old. The virus infects respiratory ciliated epithelia, starting with the nasal passages, that then secrete proinflammatory cytokines and recruit an array of immune cells. Lower down the respiratory pathway, the virus also infects type II alveolar cells. The naivete of the immune systems of <1 year-old children helps illuminate how this virus disparately affects this demographic.

Increased RSV Hospitalizations

According to CDC preliminary data, RSV hospitalizations for the 2022-2023 year starting in October have already more than doubled case numbers from previous years. As per Figure 1, October and November 2022 reported cases at 11.8 and 19.0 per 100,000 people, respectively, across all ages compared to a 4.2 and 4.8 in October and November 2021. As seen in 2018-2019 and 2019-2020 most cases occurred in the fall and winter (October-February), a stark contrast to the nearly nil cases in those same months of 2020-2021. The strictest social distancing restrictions were uplifted by summer 2021, and consequently the rates in 2021-2022 show the highest rate of hospitalizations among the summer months. These then reach the overall peak in November 2022. As seen in Figure 2, the number of hospitalizations in children <4 years, 64.2 per 100,000, was 6x higher any other age range.

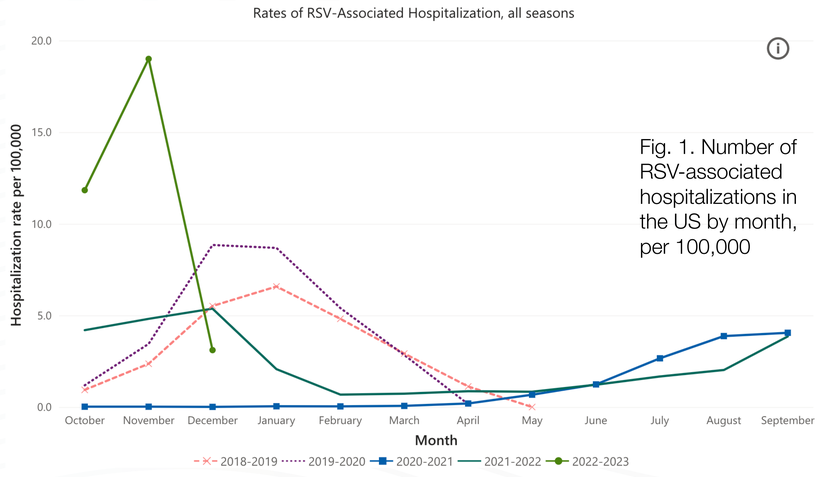

Fig. 1. Number of RSV-associated hospitalizations in the US by month, per 100,000

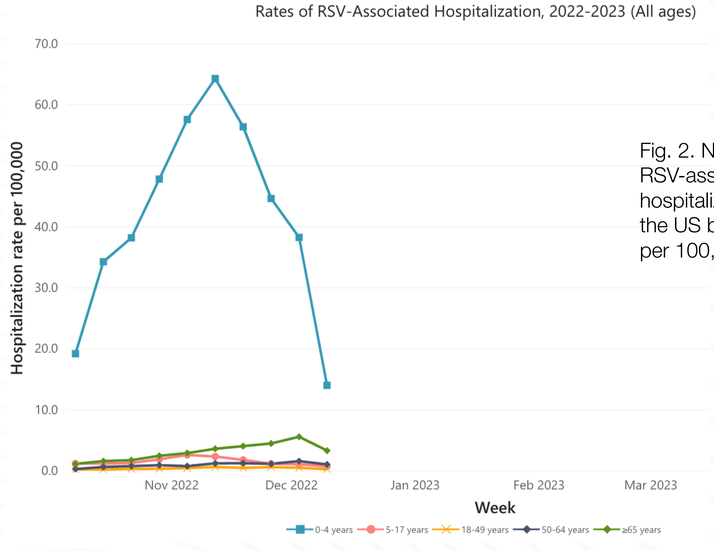

Fig. 2. Number of RSV-associated hospitalizations in the US by age, per 100,000

Pathogenesis (cont.)

G protein is a transmembrane protein that governs much of the infectivity through various methods, including assisting virus attachment to cells, binding to cytokines that then induce innate immune cells, disrupting antibody recognition due to its heavy glycosylation, and creating truncated G proteins that act as decoys for antibodies.

F protein is another transmembrane protein that works with G protein to facilitate fusion of the viral particle to respiratory cells. The G and F proteins are by far the largest proteins of RSV, displaying 230 and 270 epitopes, respectively, with the next largest protein having 100 epitopes and the rest with less than 50.

NS2 protein (non-structural 2 protein) which induces shedding of the infected respiratory cells, clearing some infection, but in turn results in obstructed airways.

Role of Vaccinations

As recent as 2014, the development of a vaccine against RSV was elusive due to the difficulty in balancing immunogenicity and attenuation. Palivizumab, an antibody against RSV, has been used since its approval in 1998 to prevent infection only in high-risk babies. Current vaccine development is underway with the goal of providing all children with immunity to developing disease, not just controlling severity. Given their vital roles in achieving infection, F and G proteins will likely have a part to play in an effective vaccine.

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