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BRIEF REVIEW

What? Now a Respiratory Syncytial Virus Epidemic

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Just when we were celebrating some attenuation of COVID-19 contagion, there are resurgent, new outbreaks of respiratory syncytial virus (RSV) and influenza infections. Our previous coronavirus precautions might have predisposed our population to a higher incidence of illness now. These three respiratory ailments initially present in a similar fashion, and each of them might, via lowered immunity, augment the chances of contracting the other infections.

RSV is a single-stranded RNA virus belonging to the Paramyxoviridae family. It was discovered in chimpanzees in 1955 and was later confirmed to be a human pathogen. The RSV structure is that of a bilipid layer envelope surrounding a ribonucleoprotein core, with several membrane proteins that aid attachment and fusion to host cells.[1]

Serious illness associated with RSV infection occurs mainly in young children. Symptoms of infection most commonly appear around four to six days after exposure to the virus and may include dry cough, congested runny nose, sneezing, sore throat, headache, and fever.[2]

Infants are those most dangerously affected by RSV, especially premature ones and those with other medical complications. Severe cases present with fever; cough; dyspnea with short, shallow, and rapid breaths; lethargy; irritability; and feeding difficulties. In healthy older children and adults, RSV illness is milder and typically mimics a "common cold." However, contagion and severity of disease increase with coexisting cardiopulmonary disease and compromised immunity.[3]

Most people, even children, recover within about two weeks with hydration and little or no additional care; however, some individuals might exhibit sustained wheezing or cough. Severe or life-threatening RSV infections require hospital treatment with supportive measures, intensive care, and other interventions as clinically indicated.[3]

After replicating in the nasopharynx, RSV affects the small bronchiolar epithelium and extends to alveolar pneumocytes in the lung, presumably by cell-to-cell spread or aspiration. RSV is usually restricted to the respiratory epithelium and less often into the lumen of the airways. Lower respiratory tract infection may follow a few days later. The pathology may include epithelial cell necrosis, bronchiolar epithelium proliferation, monocyte infiltration with T-cells at bronchial and pulmonary arterioles, and neutrophil infiltration between vascular structures and small airways. This can cause airway obstruction, air trapping, and airway resistance. Neutrophilia is documented upon bronchoalveolar lavage. Pneumonia, bronchiolitis, and further inflammation can result, causing pulmonary and general clinical deterioration.[4]

The immune response, especially from cytokine and chemokine release, can induce severe bronchiolitis. The cytokines interleukin (IL)-8, IL-6, tumor necrosis factor (TNF)-alpha, and IL-1 beta may be detected in the airway secretions of infected children, and IL-6 levels correlate with severe disease. Respiratory tract secretions include chemokines, proteins, cells, and other inflammatory markers, and these are associated with serious illnesses. It remains unknown whether the cytokines and chemokines associated with severe cases are the cause or are the byproduct of a high RSV antigen load that stimulates an inflammatory response.[4]

Supportive care is the usual treatment for patients ill with RSV. Hospitalization is recommended for those who are experiencing or are at risk for moderate to severe disease, anyone requiring parenteral fluids, and persons requiring respiratory support. There are as yet no FDA approved vaccines in adults or infants [4]; however, the FDA is expected to make a final decision on whether to approve the Pfizer vaccine for older adults by May 2023. Effective passive immune prophylaxis for RSV exists in the form of palivizumab, a humanized murine monoclonal antibody with activity against the RSV membrane proteins required for fusion with host cells. Palivizumab is administered monthly for the duration of the RSV season. Palivizumab is expensive; thus, it is also subject to cost-effectiveness debate.[5]

Ribavirin is an antiviral medication approved for RSV interventions. It is an effective nucleoside RSV analog drug with *in vitro* activity, administered in aerosolized form. It is available in multiple forms: tablets, oral solution, and inhalation solution. The inhaled form is superior to oral; however, the inhaled form is rarely used for immunocompromised adults because of limited evidence for its efficacy in these patients and the occupational risk to health care workers exposed to ribavirin aerosols.[6] Prescribing it during RSV infections is controversial due to expense, efficacy questions regarding mortality and hospital stay, and concerns about risk to persons exposed to this medicine. Adverse events associated with administration of aerosolized ribavirin include headache (51%); conjunctivitis (32%); and rashes, dizziness, nausea, rhinitis, pharyngitis, and lacrimation (10–20% each).[5]

In our opinion, we are still in need of well-designed randomized controlled trials to determine the benefit of a short course of oral ribavirin for RSV in immunocompromised and elderly patients; hopefully, we could avoid the risk of exposure to aerosolized ribavirin.

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