Respiratory Syncytial Virus

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Respiratory syncytial virus (RSV) is a common enveloped, negative-sense, single-stranded RNA virus belonging to the genus *Orthopneumovirus* within the family *Pneumoviridae*. It is a major cause of lower respiratory tract infections worldwide, particularly among infants, young children, older adults, and immunocompromised populations.

respiratory syncytial virus | Orthopneumovirus | Pneumoviridae

1. Taxonomy and Virology

RSV is classified within the *Orthopneumovirus* genus of the *Pneumoviridae* family, which also includes human metapneumovirus. The RSV genome is approximately 15.2 kilobases in length and consists of ten genes encoding eleven proteins. These include surface glycoproteins essential for viral entry and immune recognition: the fusion protein (F) and the attachment glycoprotein (G). The small hydrophobic (SH) protein, nucleoprotein (N), phosphoprotein (P), matrix (M) protein, and large polymerase (L) protein are also critical for replication and assembly. RSV exists as two antigenic subgroups, RSV-A and RSV-B, differentiated by variations in the G glycoprotein.

The viral life cycle begins with attachment to host epithelial cells via the G protein, followed by fusion mediated by the F protein. Viral replication occurs in the cytoplasm, and newly formed virions bud from the host cell membrane. RSV spreads primarily through respiratory droplets and direct contact with contaminated surfaces [1].

2. Historical Background

RSV was first identified in 1956 in chimpanzees suffering from respiratory illness, originally termed the “chimpanzee coryza agent.” In 1957, the virus was isolated from children with lower respiratory tract infections, confirming its significance as a human pathogen. Since then, RSV has been recognized as a major cause of seasonal epidemics of bronchiolitis and pneumonia. Early vaccine development in the 1960s was hampered by the tragic failure of a formalin-inactivated RSV vaccine, which led to enhanced disease upon natural infection in vaccinated children. This historical episode shaped subsequent research approaches and delayed vaccine development for decades.

3. Epidemiology and Global Burden

RSV is nearly ubiquitous, with most children experiencing infection by two years of age. Reinfections are common throughout life due to incomplete immunity. The virus exhibits a pronounced seasonal pattern, peaking during winter months in temperate regions and during rainy seasons in tropical climates [2].

Globally, RSV is responsible for significant morbidity and mortality. A large-scale analysis estimated that in 2015 RSV caused approximately 33 million episodes of acute lower respiratory infection in children under five years old, resulting in 3.2 million hospitalizations and around 59,600 in-hospital deaths. Beyond pediatrics, RSV imposes a substantial burden on older adults and those with chronic cardiopulmonary conditions, with hospitalization rates comparable to influenza in these groups.

4. Pathogenesis and Immune Response

RSV primarily infects epithelial cells of the respiratory tract, inducing cytopathic effects such as syncytium formation, from which the virus derives its name. Disease severity is influenced by viral load, host immune status, and age. In infants, small airway obstruction due to mucus and cellular debris contributes to bronchiolitis.

The host immune response involves both innate and adaptive mechanisms. Innate responses include interferon production, activation of natural killer cells, and recruitment of neutrophils. Adaptive immunity involves neutralizing antibodies against the F and G proteins, as well as cytotoxic T lymphocytes. However, immunity is not sterilizing, allowing reinfections. Importantly, the prefusion (pre-F) conformation of the F protein is highly antigenic and the target of modern vaccine design [3].

5. Clinical Manifestations

RSV infection presents with a spectrum of illness:

- **Upper respiratory tract symptoms**: rhinorrhea, cough, and fever.
- **Lower respiratory tract involvement**: bronchiolitis and pneumonia, especially in infants and elderly.
- **Severe disease**: apnea in very young infants, hypoxemia, and respiratory failure in high-risk groups.

In otherwise healthy adults, RSV typically causes mild, cold-like symptoms, but can exacerbate chronic lung diseases or congestive heart failure in older populations.

6. Diagnosis

Accurate diagnosis is crucial for patient management and infection control.

- **RT-PCR**: The most sensitive and specific method, frequently deployed in multiplex panels.

- **Rapid antigen detection tests**: Useful in pediatric populations but less sensitive in adults.
- **Viral culture**: Historically important but rarely used now due to time constraints.
- **Serology**: Limited utility in acute diagnosis, occasionally used for research purposes.

7. Treatment and Management

No universally approved specific antiviral therapy for RSV exists. Management is largely supportive, including oxygen supplementation, hydration, and mechanical ventilation in severe cases.

- **Ribavirin**, a nucleoside analogue, has limited and controversial use due to variable efficacy and concerns about toxicity and cost.
- **Monoclonal antibodies**:
  - *Palivizumab* is approved for prophylaxis in high-risk infants, though high cost limits widespread use.
  - *Nirsevimab*, a long-acting monoclonal antibody, has demonstrated strong protective efficacy in clinical trials and offers season-long protection with a single dose.

8. Prevention and Vaccination

After decades of unsuccessful attempts, major breakthroughs have occurred in RSV prevention. Stabilization of the prefusion F protein structure enabled the development of effective vaccines.

- In May 2023, the U.S. FDA approved **Arexvy** (GSK) for adults aged ≥60 years.
- In August 2023, the FDA approved **Abrysvo** (Pfizer) for maternal immunization at 32–36 weeks gestation, protecting infants through passive antibody transfer.
- Additional vaccines are under development for infants, older adults, and immunocompromised populations.

These advances mark a turning point in RSV prevention, offering long-awaited tools for global public health.

9. Economic and Public Health Impact

RSV imposes a significant economic burden due to hospitalizations, outpatient visits, and parental work loss. In the United States, RSV-related illness costs are estimated at hundreds of millions annually. The introduction of vaccines and monoclonal antibodies has the potential to reduce healthcare utilization and long-term complications such as recurrent wheezing.

10. Future Directions

Ongoing research focuses on:

- Development of small-molecule antivirals.
- Optimization of vaccine strategies for different age groups.
- Understanding RSV's role in asthma pathogenesis.
- Improving global surveillance to guide vaccination programs.

Integration of novel immunization strategies with established preventive measures is expected to transform the landscape of RSV disease control in coming decades.

References

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