ECRONICON OPEN ACCESS

EC PULMONOLOGY AND RESPIRATORY MEDICINE

Review Article

Respiratory Syncytial Virus (SRV) Mechanism of Infection, Symptoms, Diagnostics and Prevention

Osama O Ibrahim*

Consultant Biotechnology, Bio Innovation, Gurnee, IL, USA

***Corresponding Author:** Osama O Ibrahim, Consultant Biotechnology, Bio Innovation, Gurnee, IL, USA.

Received: September 10, 2023; **Published:** September 29, 2023

Abstract

Respiratory Syncytial Virus (RSV) is belonged to the family paramyxoviridae. This family are enveloped viruses with a single-stranded, negative-sense RNA genome (-RNA) directed by RNA polymerase. RSV is a common infection that spread by air droplets, and close contact. Mainly, infects nose, throat, lungs, and breathing passages causing mild cold-like symptoms, with short breath that are clinically indistinguishable from other viral respiratory infections. The virus infects infants, young children, immunocompromise patients and old people (over 60 years and older). Most patients recover in a week or two, but sometimes it can be serious with severe infections such as bronchiolitis and pneumonia that might cause morbidity and mortality. RSV is epidemic infection occurred in winter and early spring. RSV infection can be detected by culture methods of fluid sample (respiratory specimen), and can be detected in blood sample after the infection by measuring the level of antibodies (immunoglobulins), this is in addition to rapid detection methods. Over-the-counter fever reducers and pain relievers, such as acetaminophen or ibuprofen are commonly used for managing the fever and pain. This is plus drinking enough fluids to prevent dehydration. Some medications to ease breathing such as bronchodilators are commonly used to treat long term RSV infection where the patient airways (bronchi) become narrow and inflamed. These bronchodilators medicines are muscle relaxation that widen the lung airway. Food and Drug Administration (FDA) approved antiviral medication Ribavirin for pediatric patients with severe lower respiratory infections. This is in addition to the early approved antiviral medication Palivizumab. Recently FDA approved RSV vaccines ABRYSVO and AREXVY for 60 years and older for the prevention of lower respiratory tract disease (LRTD) caused by this RSV infection.

Keywords: *Viral Lung Disease; RSV; Pediatrics Infections; Adult Infection; Bronchiolitis; Lower Respiratory Tract Disease (LRTD); Mucosal Immunity; RSV Diagnostics; Mono Clonal Antibody; Polyclonal Antibody; Nirsevimab; Palivizumab; RSV Vaccine; ABRYSVO Vaccine; AREXVY Vaccine*

Introduction

The family Paramyxoviridae [1] consists of three genera. These three genera are Paramyxovirus, Pneumovirus, and Morbillivirus. The genera Paramyxovirus includes the parainfluenza viruses and mumps virus, while the genera Pneumovirus [2], includes respiratory syncytial virus (RSV), and the third genera Morbillivirus, includes the measles virus. Human respiratory syncytial virus (RSV) is an enveloped, non- segmented negative-sense RNA (-RNA), and is the most complex member of this Paramyxoviridae family in terms of the number of genes and proteins [3]. RSV genome (Figure 1) encodes multiple proteins, includes structural proteins (G, F, M, P, and L) and nonstructural proteins (N, and SH). The three integral cell membrane proteins are the (G) glycoprotein [4] involved in viral attachment

to the host cell receptor, the prefusion (F) glycoprotein [5] control the initial phases of the host cell cytoplasm infection, and the (SH) glycoprotein a nonstructural short hydrophobic protein with unknown function. Both viral cell membrane structural glycoproteins (G) and (F) are protective antigens stimulate the production of neutralizing antibodies via humoral and cellular immunity upon the host infection [6]. These three viral cell membranes (G, F, and SH) glycoproteins are transmembrane surface proteins. The matrix protein (M) is positively charged hydrophobic domains that is essential for virus particle formation, plus protein (M) is important for cytoplasmic membrane binding, and is the main force that drives RSV assembly and budding after host cell infection and virus replication [7]. The virus single-stranded negative sense RNA (-RNA) forms a helical assembly termed the ribonucleoprotein complex (RNP) with three structural proteins consists of nucleoprotein (N), phosphoprotein (P), and RNA-dependent RNA polymerase (L). These three structural nucleoproteins protect the negative sense RNA (-RNA) and forms the minimal replication machinery [8].

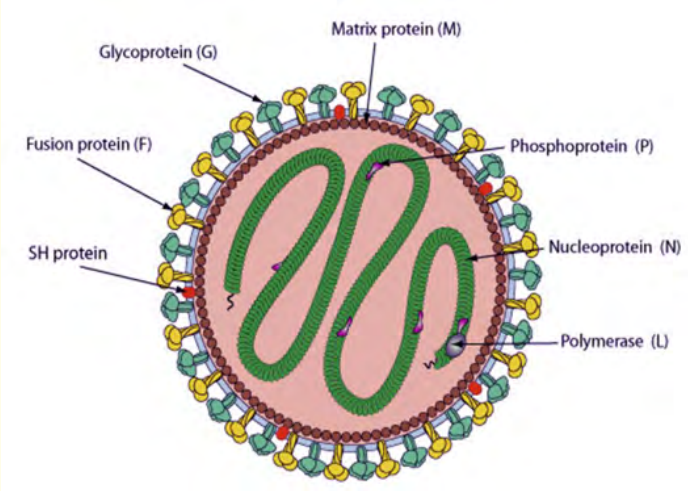

Figure 1: *Human respiratory syncytial virus (RSV). RSV is an enveloped, nonsegmental negative-strand RNA (-RNA) virus of Paramyxoviridae family. RSV is the most complex member of the family in terms of the number of genes and proteins. It is also relatively divergent and distinct from the prototype members of the family. [CD: Creative Diagnostics].*

Mechanism of infection

RSV infection begins in the nasal epithelial cells (Figure 2), preferentially targets the ciliated cells of the airway epithelium via the attachment of RSV (G) glycoprotein to the host cell receptor CX3C Chemokine Receptor 1 (CX3CR1). This host cell receptor CX3CR1 express on various cell types including epithelium cells of human respiratory system [9]. The interaction between RSV (G) glycoprotein and host cell receptor CX3CR1 plays the crucial rule in RSV pathogenesis. It is important to highlight that RSV (G) glycoprotein can interacts with other host cell membrane receptors such as Insulin-Like Growth Factor-1 Receptor (IGF1R), Epidermal Growth Factor (EGFR), Heparan Sulfate Proteoglycans (HSPGs), and Intercellular Adhesion Molecule-1 (ICAM-1) also known by (CD54). This interaction (attachment) between viral (G) glycoprotein, and host epithelial cell receptor (CX3CR1). induces the secretion of multiple cytokines and chemokines [10]. These secreted cytokines and chemokines play a role in the orchestration of inflammation in inflammatory airway diseases, such as chronic obstructive pulmonary disease that cause due to the recruitment, and activation of inflammatory cells [11]. RSV prefusion (F) glycoproteins also promotes virus attachment to host epithelial cell receptor (CX3CR1) but to a much lesser extent than RSV (G) glycoprotein. The key function of SRV perfusion (F) glycoprotein is the fusion between the virus envelop and host epithelial cell

membrane to enables the release of the virus nucleocapsid and the single strand negative sense RNA (-RNA) into the host cell cytoplasm [12]. Inside the infect cell cytoplasm the RSV nucleocapsid protein mediate the virus single strand negative sense RNA (-RNA) to reverse transcript into complement DNA (cDNA) to replicate into positive double strand DNA (dsDNA). One the positive double strand DNA is transcript into mRNA for synthesis (translation) virus proteins utilizing host cell translation machinery consists of host cell transfer RNA (tRNA), host cell Ribosomal RNA (rRNA) in the presence free amino acids [13]. These translation processes for virus proteins synthesis initiated from the transcription of virus single strand negative sense RNA (-RNA), and requires a single polymerase complex comprising of the virus ribonucleoprotein (RNP) consists of nucleoprotein (N), phosphoprotein (P), and RNA polymerase (L). Synthetized (translation) virus proteins G and F glycoproteins are glycosylated in the host cell endoplasmic reticulum (ER) and Golgi apparatus [14]. Synthesized (translated) virus structure and nonstructural proteins, including (G) and (F) glycoprotein, plus the replicated virus single strand negative sense RNA (- RNA) are assembled into mature viruses (RSVs) inside infected host cell and released through budding process [15]. This budding process is coordinated by the virus matrix (M) protein incorporated into the host cytoplasmic inclusion bodies [16]. In this RSVs budding process, the mature virus obtains its lipid envelope from the host cell plasma membrane. The host cell plasma membrane of epithelial cell is differentiated into two domains apical membrane highly enriched in glycosphingolipids, and basolateral membrane highly enriched in phosphatidyl choline and sphingomyelin. The released mature RSVs membrane is preferentially from the apical surface of infected epithelial cells [17]. Released mature RSVs from infected host epithelium cell infect neighboring healthy respiratory epithelial cells and the mechanism of infection cycle continue. The spread of RSV from the upper respiratory tract to the lower airways is not yet clear, but it is presumed to be via direct spread along the respiratory epithelium cells as well.

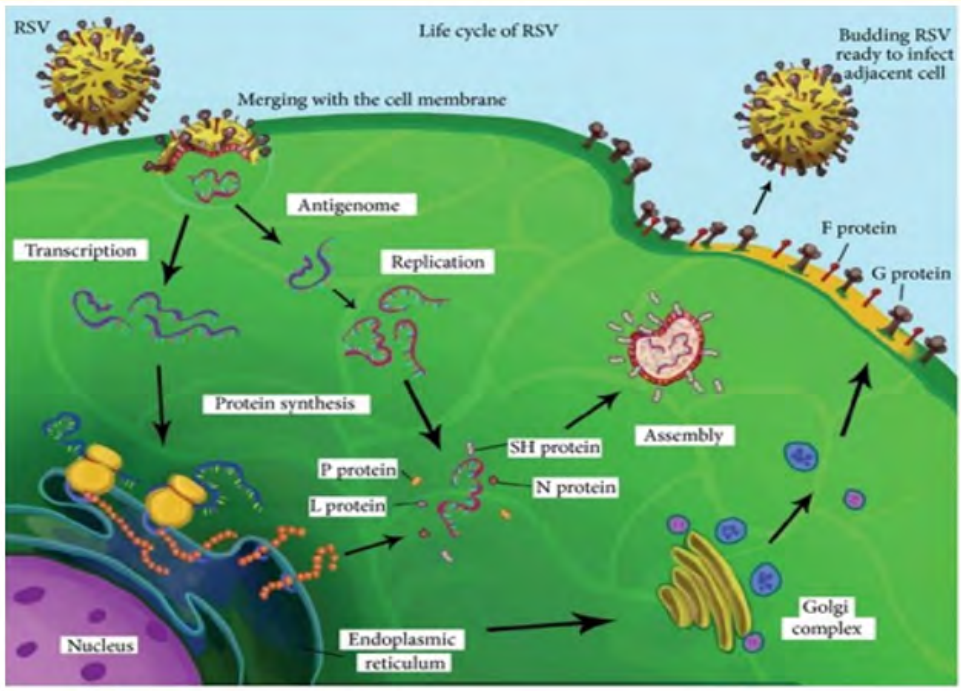

Figure 2: *Respiratory Syncytial Virus (RSV) mechanism of infection. RSV has two antigenic subgroups: type A and type B, their genome encodes ten proteins, including seven structural proteins (G, F, M1, M2, P, L, N) and three nonstructural proteins (NS1, NS2, SH). [CD: Creative Diagnostics].*

RSV infection symptoms

The incubation period for RSV after the infection is about four to six days and appears first as mild cold-like sign. In adults and older children' RSV symptoms includes congested or runny nose, dry cough, low-grade fever, sore throat, sneezing, and headache. The infection spread to the lower respiratory tract, causing pneumonia or bronchiolitis. RSV infection cause inflammation in the small airway passages and lungs [18]. Most children and adults recover in one or two weeks. Severe illness symptoms in adults and young children may include fever, severe cough, wheezing, rapid breathing or difficulty breathing, and bluish color of the skin due to lack of oxygen. Severe illness in infants include short, shallow and rapid breathing, struggling to breath, cough, unusual tiredness, irritability, and poor feeding. These severe illness symptoms are life-threatening and require hospitalization for few days. RSV patient in hospital usually require oxygen supply, IV fluids and mechanical ventilation, tube feeding, and suction of mucus is usually applied [19]. Hospitalization due to RSV sever illness are mostly occurs for premature infants, and children or adults suffering from chronic heart or lung problems.

RSV test diagnostics

Many respiratory viruses cause the same symptoms as RSV specially in the early stage of the infection and physicians needs laboratory testing to identify the virus that cause the infection to prescribe the appropriate treatment. The most common diagnostic methods for the detection of RSV virus (Type A or type B) in the respiratory specimen (fluid from nose swab) are Reverse transcription-polymerase chain reaction (rRT-PCR), Raped antigen detection tests (RADTs), and Direct fluorescent antibody (DFA).

Reverse transcription-polymerase chain reaction (rRT-PCR): This is the most sensitive test method comparing to other methods [20]. This method is designed to detect the virus RNA from the patient respiratory specimen. Reverse transcription-polymerase chain reaction (rRT-PCR) method involves (Figure 3) the conversion of the extracted virus RNA into the virus complement double strand DNA (cDNA) sequence using the enzyme reverse transcriptase [21], following by the generation (amplification) of double strand complement DNA (ds cDNA). This amplification process is performed in polymerase chain reaction machine (PCR). This PCR method is based on enzymatic replication of the nucleic acids sequence from few copies of the virus complement dsDNA (cDNA) using very specific primers for cDNA replication into thousands or millions copies of a particular virus cDNA sequence. These Amplified cDNA are carried out by agarose gel electrophoresis for identification. The virus cDNA identification is by using standard markers and revealed by ethidium bromide staining [22].

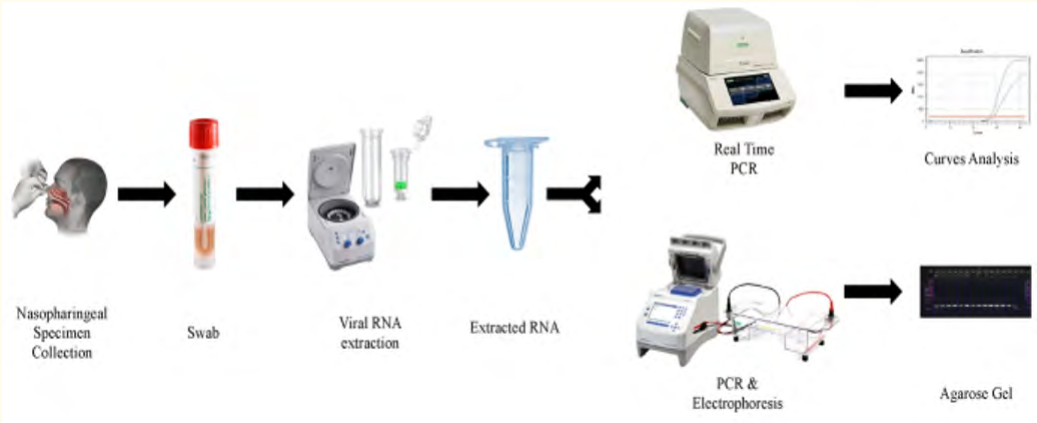

Figure 3: *Reverse transcription-polymerase chain reaction (rRT-PCR). Flow chart (two steps processing) for RSV detection by rRT-PCR protocol. The first step is reserve transcript RNA into ds cDNA, second step is PCR for RSV ds cDNA replication. The detection can be by curve analysis method, or by Agarose Gel electrophoresis. The RSV cDNA identification is by using standard markers and revealed by ethidium bromide staining.*

Rapid antigen detection tests (RADTs): This test method is based on antigen/antibody interaction (Figure 4) to detect the presence or absence the virus (G) or (F) glycoproteins located on the surface of the virus cell membrane [23]. A positive antigen test result indicates the patient infection with RSV. The best sampling method for this test is nasal aspirate or wash comparing not sampling by inserting nasal swab in the nose. This rapid test gives a result in 5 to 30 minutes, and require minimal training. There are test kits in the market with instruction for RSV test that are approved by FDA. This RADT test method has significant cost advantages comparing to rRT-PCR test method.

Figure 4: *Rapid antigen detection tests (RADTs). The RSV (RADTs) is rapid antigen /antibody test cassette qualitatively detects the presence of RSV antigen in nasopharyngeal swab or nasal aspirate specimens. This test providing results after 15 minutes, allowing the decision sooner comparing to other alternative methods. (Path Flow® RSV).*

Direct fluorescent antibody (DFA): This test method is also based on antibody/antigen Interaction to detect the presence or absence the virus (G) or (F) glycoproteins located on the surface of the virus cell membrane. This DFA test method is based on using conjugated (tagged or labeled) monoclonal or polyclonal antibody with fluorescently stain [24]. When patient specimen incubated with conjugated antibody on microscopic slide, and the unbound antibody to the virus (G) or (F) glycoprotein (antigen) washed away the conjugated antibody/RSV antigen interaction form complex that can be visualized as fluorescent using a fluorescence microscope (Figure 5). This interaction indicates the patient is infected with RSV. This DFA test method allows the detection of the virus (RSV) within 2 - 3 hours [25]. This test method is labor intensive and requires considerable experience comparing to Rapid antigen detection (RATs) test method that require minimum training. This DFA test method is reliable in infants and young children, but its sensitivity for adults and younger children is less sensitive due to the lower viral shedding in adult and young children comparing to infants.

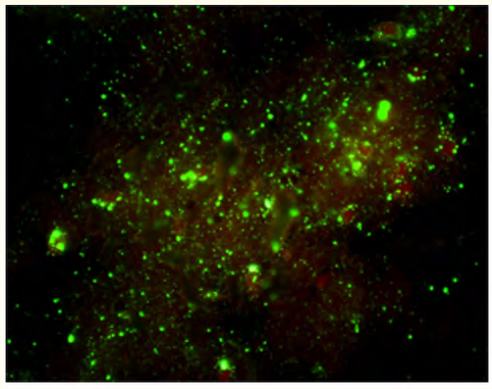

Figure 5: *Direct fluorescent antibody (DFA). When labeled antibody is incubated with RSV it will bind to RSV antigen. Unbound free labeled antibody is washed away, the antigen/antibody complex can be visualized as fluorescent using a fluorescence microscope if the patient is infected. If RSV is absent in the specimen there will be no fluorescent indicted the patient is not infected.*

RSV prevention and treatments

RSV can survive for hours on dry surface, plus it is highly contagious. There are common steps that helps limiting RSV spreading. These common steps are avoiding close contact with infected people, wash hands with disinfectants or with soap and water after contact infected person, and avoid sharing items that being used by infected person. Recently, Center for Diseases Control and Prevention (CDC) recommended the use of a new approved FDA monoclonal antibody Nirsevimab under the trade name Beyfortus for RSV treatment [26]. Nirsevimab is recommended for infants younger than eight months in their first infection season, and for highly RSV risk 8-19 months old children in their second infection season. This monoclonal antibody Nirsevimab is available in the fall (RSV season) and is given by intramuscular injection into the thigh muscle, The efficacy of Nirsevimab is expected to last during the RSV season (5 months). In addition, other FDA recently approved humanized monoclonal antibody (IgG) Palivizumab under the trade name Synagis produced by recombinant DNA technology [27]. This Palivizumab is also available in the fall (RSV season) and must be given intramuscular monthly (five times) during the RSV season. This Palivizumab is recommended for infants at high-risk of infection due to conditions such as prematurity or other medical problems including heart or lung diseases [28]. In addition, to these two monoclonal antibodies for injection to give the person immunity during RSV season for the prevention from respiratory syncytial virus infection, a newly developed RSV vaccine called ABRYSVO has been approved by FDA for immunization all healthy 60 years of age and older to trigger immune response for the prevention from lower respiratory tract disease (LRTD) caused by RSV infection [29]. There is second vaccine ABRYSVO is also approved for pregnant women in their 32 to 36 weeks' gestation to protect new born babies from RSV infection [30]. This newly developed vaccines are RSV antigen components containing recombinant virus prefusion (F) glycoprotein for both RSV type A and type B. The mechanism of these recombinant virus prefusion (F) glycoprotein as vaccines are to trigger host immune response to develop antibody against RSV prefusion protein. Antibody against RSV prefusion (F) glycoprotein in the host blood circulation will inhibit the RSV upon infection to inter host cell cytoplasm for virus replication and cause the infection symptoms [31]. The idea of giving this ABRYSVO vaccine to women in their third trimester of pregnancy is to build immunity against RSV and pass this immunity (antibody) to their baby before birth [32]. It is important to highlight that mild RSV infection always go away in less than two weeks without medications, and only over-the- counter fever reducers and pain relievers are enough to manage RSV symptoms. In the case of hospitalization oxygen supply, IV fluids and mechanical ventilation, tube feeding, and suction of mucus are usually applied. Generally, in most cases, hospitalization is only for few days.

Discussion

Respiratory syncytial virus (RSV) is belonged to Pneumoviridiae family. It is an enveloped virus, nondemented single strand negative sense RNA (-RNA), and there are. 2 antigenic subgroups, type A and type B, for RSV that are cocirculate in the same season. RSV is one of pulmonary diseases infect all ages. Infants, young children and old ages are the most susceptible for RSV infection. Infants and older adults with heart disease, or lung disease, or suffering from weakened immune systems are the highest risk for RSV infection that are sometimes serious and require hospitalization. World Health Organization (WHO) estimated that RSV infection cause annually about 34 million cases of acute lower respiratory tract infections (LRTI) specially in young children. From these 34 million cases per year over 3 million (10%) are severe cases and require hospitalization resulted to about 66,000 - 199,000 fatalities specially in poor countries [33]. In the United States (U.S.) most children by the age two years old are, infected by this virus (RSV) annually with mild symptoms, and recovered within a week or two. However, RSV infection can be serious specially for vulnerable children including premature, very young infants, and old ages with estimated 14,000 annual deaths per year in U.S [34].

Respiratory syncytial virus (RSV) is usually spread through direct contact healthy person to infected person. Droplets from infected person's cough or sneeze can reach healthy person eyes, nose, or mouth and cause the infection. This virus also infects healthy person after touching dry surface area such as doorknob contaminated with viable virus, and then the person touches the face before washing hands.

RSV Symptoms includes runny nose, coughing, sneezing, fever, or wheezing, and decrease appetite. Most people recover in a week or two, but sometime this infection can cause shortness in breath, low oxygen levels, and could lead into sever medical conditions such as asthma, chronic pulmonary disease of the lungs that makes the person hard to breathe, or cause congestive heart failure when the heart can't pump enough blood and oxygen through the body.

RSV mechanism of infection can be summarized into three major steps. These steps are viral attachment and host cell entry, viral transcription and replication inside host cell cytoplasm, and viral assembly, and finally exiting infected host cell by budding mechanism to infect other cells. In the first step of infection the virus (G) glycoprotein, and perfusion (F) glycoproteins on the virus cell membrane plays an important, rule in virus pathogenicity. Understanding the virus structure, and immunogenic properties of the virus (G) and perfusion (F) glycoproteins assist scientists in developing antibody/antigen interaction assay methods for RSV diagnostic in patient specimen. These diagnostic methods are Rapid antigen detection tests (RADTs), and Direct fluorescent antibody (DFA). Also, understanding the virus nucleotides sequence of the virus single strand negative sense RNA (-RNA), and the method of transcribed RNA into double strand complement DNA (ds cDNA) assist scientists in developing RSV diagnostics test method based on molecular assay (rRT-PCR). These three diagnostic methods for RSV diagnostic are highly sensitive and very reliable for RSV identification in patient respiratory specimen and for therapeutic treatments. Other non-sensitive diagnostic methods that are not highly reliable are X ray, culture methods, and detection of RSV antibodies (immunoglobulins) after the infection.

The theory behind developing antiviral drugs to suppress the virus ability to infect or replicate inside host cell is based on understanding the mechanism of the RSV (G) and perfusion (F) glycoproteins in attachment and internalize the virus into host cell to cause virus pathogenicity. This mechanism of attachment and internalization assisted scientists in developing antiviral for RSV based on inhibit the virus (G) glycoprotein to attach to the host epithelial cell chemokine receptor CX3CR1, and to inhibit the perfusion (F) glycoprotein protein to fuse in host cell membrane for the virus internalization into host cell cytoplasm. Currently, there are two developed antivirals to protect the person from RSV infection. These two antivirals are Nirsevimab under brand name Beyfortus, and palivizumab under brand name Synagis. Both are monoclonal antibodies approved by FDA not for treatment after infection, but to protect infants and adults from RSV infection and causing lower respiratory tract infection (LRTI). The mechanism of these two antivirals (monoclonal antibodies) is to provide the healthy person with monoclonal antibodies for the protection from RSV infection by inhibiting the virus attachment to the host cell receptor and internalize into the host cytoplasm for replication.

In addition, there is newly U.S. developed two vaccines that are approved by FDA both with trade name ABRYSVO to trigger immune response in healthy person (infant or adult) against RSV infection. These two vaccines are genetically engineered perfusion (F) glycoprotein construct. One for adults specially for 60 year and older available for this year for annual vaccination and the second ABRYSVO is for pregnant women at 32 - 36 weeks gestational to protect infant before birth. This ABRSVO for pregnant women to protect infants before birth is not available this year. Both vaccines demonstrated in clinical trials to be active immunization for the prevention from lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV). In addition, a second RSV vaccine AREXVY also a recombinant perfusion (F) glycoprotein was developed in U. K. is recently approved by FDA for adults 60 years and older.

Conclusion

Respiratory syncytial virus (RSV) is a contagious virus disease more common in winter and early spring months. The new developed ABRYSVO and AREXVY vaccines for adult are available this RSV season to vaccinate healthy adults specially 60 years of age and older.

Bibliography

1. Gisela Enders. "Paramyxoviruses Chapter 59 Medical Microbiology". 4th edition. Baron S, editor. (1996).

2. Bernadette G., *et al*. "A newly discovered human pneumovirus isolated from young children with respiratory tract disease". *Nature Medicine* 7.6 (2001): 719-724.

3. N James MacLachlan and Edward J Dubovi. "Paramyxoviridae". *Fenner's Veterinary Virology* (2011): 299-325.

4. Jason S McLellan., *et al*. "Structure and function of respiratory syncytial virus surface glycoproteins". *Current Topics in Microbiology and Immunology* 372 (2013): 83-104.

5. Jason S McLellan mclellanja., *et al*. "Structure of Respiratory Syncytial Virus Fusion Glycoprotein in the Postfusion Conformation Reveals Preservation of Neutralizing Epitopes". *Journal of Virology* 85.15 (2011).

6. Joseph B Domachowske and Helene F Rosenberg. "Respiratory Syncytial Virus Infection: Immune Response, Immunopathogenesis, and Treatment". *Clinical Microbiology Reviews* 12.2 (1999): 298-309.

7. Fyza Y Shaikh and James E Crowe Jr. "Molecular mechanisms driving respiratory syncytial virus assembly". *Future Microbiology* 8 (2013): 123-131.

8. Aartjan JW., *et al*. "Structural insights into RNA polymerases of negative-sense RNA viruses". *Nature Reviews Microbiology* 19 (2021): 303-318.

9. Crystal H Johnson., *et al*. "Effect of chemokine receptor CX3CR1 deficiency in a murine model of respiratory syncytial virus infection". *Comprehensive Medical Management* 62 (2012): 14-20.

10. Peter J Barnes. "The Cytokine Network in Chronic Obstructive Pulmonary Disease". *American Journal of Respiratory Cell and Molecular Biology* 41 (2009): 631-638.

11. Y Gernez., *et al*. "Neutrophils in chronic inflammatory airway diseases: can we target them and how?" *European Respiratory Journal* 35 (2010): 467-469.

12. C Cadena-Cruz., *et al*. "Respiratory syncytial virus entry mechanism in host cells: A general overview". *Molecular Microbiology* (2023): 1-10.

13. Christine M Oshansky., *et al*. "The host response and molecular pathogenesis associated with respiratory syncytial virus infection". *Future Microbiology* 4 (2009): 279-297.

14. Regina Garciaa-Beato., *et al*. "Host Cell Effect upon Glycosylation and Antigenicity of Human Respiratory Syncytial Virus G Glycoprotein". *Virology* 221 (1996): 301-309.

15. Shadi Shahriari., *et al*. "Host cytoskeleton in respiratory syncytial virus assembly and budding". *Virology Journal* 13 (2016): 161.

16. Andreas Forster., *et al*. "Dimerization of Matrix Protein Is Required for Budding of Respiratory". *Syncytial Virology Journal* 89.8 (2015): 4624-4635.

17. Sean C Brock., *et al*. "Apical recycling systems regulate directional budding of respiratory syncytial virus from polarized epithelial cells". *Proceedings of the National Academy of Sciences of the United States of America* 100.25 (2003): 15143-15148.

18. Raymond J Pickles and John P DeVincenzo. "Respiratory syncytial virus (RSV) and its propensity for causing bronchiolitis". *Journal Pathology* 235.2 (2015): 266-276.

19. A Greenough., *et al*. "Health care utilization of infants with chronic lung disease, related to hospitalization for RSV infection". *Archives of Disease in Childhood* 85 (2001): 463-468.

20. Catherine A Hogan., *et al*. "Rapid and simple molecular tests for the detection of respiratory syncytial virus: a review". *Expert Review of Molecular Diagnostics* 18.7 (2018): 617-629.

21. Ann R Falsey., *et al*. "Diagnosis of Respiratory Syncytial Virus Infection: Comparison of Reverse Transcription-PCR to Viral Culture and Serology in Adults with Respiratory Illness". *Journal of Clinical Microbiology* 40.3 (2002): 817-820.

22. Wayne M Sullender., *et al*. "Analysis of Respiratory Syncytial Virus Genetic Variability with Amplified cDNAs". *Journal of Clinical Microbiology* 13.5 (1993): 1224-1231.

23. Caroline Chartrand., *et al*. "Diagnostic Accuracy of Rapid Antigen Detection Tests for Respiratory Syncytial Virus Infection: Systematic Review and Meta-analysis". *Journal of Clinical Microbiology* 53.12 (2015): 3738-3749.

24. Roopa Bhandary and Rekha Boloor. "Detection of Respiratory Syncytial Virus using Direct Fluorescent Antibody Assay in Paediatric Patients with Acute Respiratory Tract Infection". *Journal of Clinical and Diagnostic Research* 10.6 (2016): DC10-DC12.

25. Roopa Bhandary and Rekha Boploor. "Detection of Respiratory Syncytial Virus using Direct Fluorescent Antibody Assay in Pediatric Patients with Acute Respiratory Tract Infection". *Journal of Clinical and Diagnostic Research* 10.6 (2016): DC10-DC12.

26. Eric AF Simoes., *et al*. "Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomized controlled trials". *Lancet Child Adolescent Health* 7.3 (2023): 180-189.

27. Alexander L Rogovik., *et al*. "Palivizumab for the prevention of respiratory syncytial virus infection". *Canadian Family Physician* 56.8 (2010): 769-772.

28. Evan J Anderson., *et al*. "Effectiveness of Palivizumab in High-risk Infants and Children". *The Pediatric Infectious Disease Journal* 36.8 (2017): 699-704.

29. Edward E Walsh., *et al*. "Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults". *The New England Journal of Medicine* 388.16 (2023): 1465-1477.

30. Beate Kampmann., *et al*. "Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants". *The New England Journal of Medicine* 388 (2023): 1451-1464.

31. Ann R Falsey., *et al*. "Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults". *The New England Journal of Medicine* 388 (2023): 609-620.

32. Shabir A MadhI., *et al*. "Vaccination of pregnant women with respiratory syncytial virus vaccine and protection of their infants". *The New England Journal of Medicine* 383.5 (2020): 426-439.

33. Zhe Zheng., *et al*. Estimated incidence of respiratory hospitalizations attributable to RSV infections across age and socioeconomic groups Pneumonia 14 (2022): 6.

34. Edward Walsh., *et al*. "RSV-associated hospitalization in adults in the USA: A retrospective chart review investigating burden, management strategies, and outcomes". *Health Science Reports* 5 (2022): e556.

Volume 12 Issue 8 August 2023