

Respiratory Syncytial Virus Infection (RSV)



With Theresa Lowry Lehnen, GPN, RNP, PhD. Clinical Nurse Specialist and Associate Lecturer at Institute of Technology Carlow

Respiratory syncytial virus (RSV) is a common, ubiquitous and contagious viral pathogen that infects the respiratory tract of most children by 2 years of age. RSV is an RNA pneumovirus of the Paramyxoviridae family, and humans are the only natural host.

Worldwide, it is estimated that RSV is responsible for approximately 33 million lower respiratory tract illnesses, three million hospitalisations, and up to 199,000 childhood deaths.

We recently spoke to Clinical Nurse Specialist and Associate

Lecturer at Institute of Technology, Carlow, Theresa Lowry Lehnen to understand more about this contagious area.

RSV typically spreads via hands, fomites and the airborne aerosol route. Respiratory syncytial virus spreads from person to person by aerosol droplets through coughing or sneezing, and is also spread through direct contact by touch.

Theresa notes that RSV can survive on surfaces and objects for 24 hours and spread can occur indirectly through contact with contaminated hands.

“Respiratory syncytial virus is primarily a childhood infection, however, it may occur at any age and can be most severe in infants under one year of age, the immunocompromised, and in people aged 65 years and older. It infects 90% of children within the first 2 years of life and frequently re-infects older children and adults,” she says.

Respiratory Syncytial Virus infection can present as a variety of clinical syndromes including upper respiratory tract infections, bronchiolitis, pneumonia, exacerbations of asthma and viral-induced wheeze.

Presentation in Children

Theresa says that for most babies and young children, the infection is mild presenting with cold like symptoms which usually last 1 to 2 weeks. “For a small percentage, however, RSV infection can lead to serious and sometimes life-threatening problems such as pneumonia or bronchiolitis,” she adds.

“The chance of developing severe infection is highest for premature babies, children less than 10 weeks old, children less than 2 years of age with congenital heart or chronic lung disease and infants and young children with

a weak immune system or who are immunocompromised. Adults with weakened immune systems and those aged 65 years and older are also at increased risk of developing severe RSV disease.”

Respiratory Syncytial Virus infection has been a notifiable disease in Ireland since January 2012, and RSV activity in Ireland is monitored by the HSE-Health Protection Surveillance Centre (HPSC).

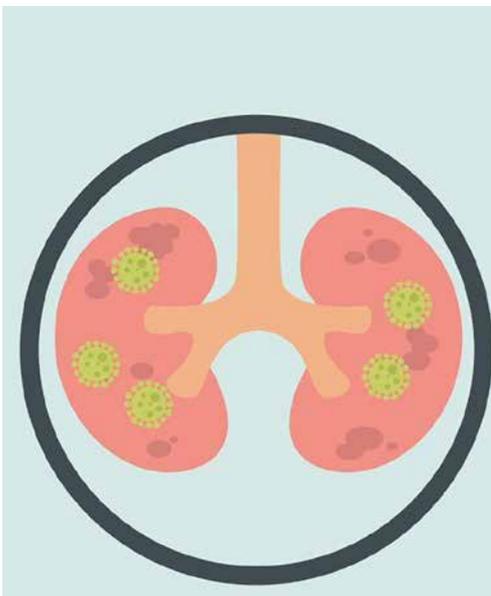
Respiratory Syncytial Virus infections occur in a seasonal pattern in temperate climates with epidemics from October to April. Outbreaks typically occur in the winter months with the highest numbers of infections usually reported in December and January every year. The sharp winter peak varies little in timing or size from year to year, in contrast to influenza.

Incubation Period and Symptoms

Theresa continues, “The incubation period for RSV is usually 4 - 6 days, but ranges from 2 to 8 days depending on host factors such as the age of the patient and whether it is the patient's primary infection with RSV. After inoculation into the nasopharyngeal or conjunctival mucosa, the virus rapidly spreads into the respiratory tract, where it targets its preferred growth medium, apical ciliated epithelial cells. There it binds to cellular receptors using the RSV-G glycoprotein and uses the RSV-F fusion glycoprotein to fuse with host cell membranes and insert its nucleocapsid into the host cell to begin its intracellular replication.”

Symptoms include; fever, rhinorrhoea, pharyngitis, nasal congestion, sneezing, coughing which can be croupy or barking in nature, tachypnoea, sore throat, wheeze, decreased appetite and ear infections in children.

In very young infants, irritability, decreased activity and breathing difficulties may be the only symptoms of infection. Lower respiratory tract infections, such as pneumonia or pneumonitis, are most likely to occur during a child's first infection with RSV and



What is respiratory syncytial virus (RSV) infection?

The respiratory tract is the parts of the body related to breathing—including the nose, windpipe, air passages in the lungs, and the lungs. RSV is a virus that infects the respiratory tract.



The development of a successful treatment or prophylactic agent has the potential to revolutionise the care and outcome for severe RSV infections in the world's most vulnerable infant population."

may develop in 30-70% of first infection. Typically, only between 1% and 3% of infected infants require hospitalisation.

Bronchiolitis is an inflammatory process in the small airways of the lungs and is the most common clinical syndrome associated with RSV infection. Theresa adds, "This typically presents in infants under 1 year of age but may be diagnosed in children up to 2 years old, and is characterised by a short history of low-grade fever, cough, coryza, dyspnoea and reduced feeding. The symptoms usually peak in clinical severity between day 3 and 5 of the illness. RSV bronchiolitis presents a significant clinical burden. In the UK, infection with RSV is responsible for up to 80% of all cases of bronchiolitis, similar to that of 65-70% in the US.

"In older children, Respiratory Syncytial Virus typically presents as an URTI, viral pneumonia, episodic viral-induced wheeze or an acute exacerbation of asthma. Viral pneumonia is a common illness with 5 million cases reported in children annually. A meta-analysis of nine studies involving over 4000 children investigating viruses identified by polymerase chain reaction, found that RSV was the causative organism in 11% of community-acquired pneumonia cases."

Vaccination

There is currently no vaccine available against RSV infection. She continues, "Palivizumab, which is a humanised mouse monoclonal antibody specific for the F protein of RSV, provides passive immunity against RSV. Palivizumab inhibits RSV binding to host cells and prevents fusion of infected cells with adjacent cells. It is authorised in Ireland for the prevention of serious lower respiratory tract disease requiring hospitalisation caused by RSV in children at high risk for RSV disease.

"Differences in epidemiology, practice setting, health care systems and drug cost have resulted in variability in palivizumab recommendations and use nationally and internationally. Palivizumab prophylaxis reduces the absolute risk of RSV hospitalisation from about 10% to 5% for premature babies, infants with chronic lung disease and haemodynamically significant congenital heart disease, particularly when complicated by large left-to-right shunts and pulmonary hypertension. It does not reduce mortality or the need for mechanical ventilation."

Treatment and Prevention

The mainstay of treatment for the vast majority of RSV infections is supportive including rest, fluids and paracetamol, but passive preventive immunisation is available for at-risk children, including premature infants and infants with a history of cardiac, pulmonary, or neuromuscular diseases.

"Those with severe respiratory illness require hospitalisation, oxygen therapy, IV fluids and ventilatory support in the form of a high-flow nasal cannula, CPAP, or intubation, and mechanical ventilation," she says.

"Ribavirin is the only licensed antiviral medication for the specific treatment of RSV infection but due to drug toxicity, including bone marrow suppression and potential carcinogenicity and teratogenicity and minimal clinical benefit, it has not been recommended for routine clinical use. Ribavirin, may be considered for a small number of patients and treatment of RSV with Ribavirin must be done under the supervision of an infection

specialist such as a consultant microbiologist or an infectious disease specialist.

"Other treatment modalities for bronchiolitis have been tried in the past and have failed to show broad, reproducible efficacy on clinically significant outcomes in RSV and bronchiolitis. These include albuterol, epinephrine, steroids, hypertonic saline, antibiotics, and chest physical therapy, and routine use of these interventions is not recommended. Antibiotics are not effective against RSV and it is important that unnecessary antibiotics are discontinued once a diagnosis is confirmed, to avoid adverse drug reactions and antibiotic resistance.

"Although palivizumab may help prevent serious complications of RSV infection, it is not used to treat RSV infection. It has however, been shown to reduce the risk of hospitalisation by 39-78% in various groups of infants predisposed to developing severe RSV disease. Palivizumab is given as an intramuscular injection monthly (up to five doses) during the RSV season. As it is very expensive and has a half-life of 18-21 days, meaning monthly injections are required to maintain protective titres, cost-benefit analyses limit its use to only the most vulnerable infants, those born prematurely with moderate or severe BPD, haemodynamically significant, acyanotic congenital heart disease, severe combined immunodeficiency or infants with other severe chronic lung conditions or requiring long-term ventilation."

Theresa says prevention and patient education is key, and frequent, careful handwashing is the most important measure in preventing the spread of RSV.

"In the hospital setting, RSV transmission can be prevented by managing children with RSV together in the same ward, paying strict attention to handwashing guidelines, using barrier precautions and avoiding overcrowding through restriction of visitors. Several studies have shown that strict infection control practices including hand hygiene, the use of personal protective equipment when necessary, timely detection and isolating or cohorting infants with RSV infection can reduce nosocomial RSV infection rates by 39-67%."

RSV Research and Outlook

Theresa concludes, "The management of Respiratory Syncytial Virus disease in infants and children is primarily supportive with antiviral medications reserved for the most vulnerable. Palivizumab continues to be the only effective prophylactic medication licensed for use, however, its high cost prevents it from being used in all infants.

"The development of a well-tolerated, clinically effective and cost-effective RSV vaccine and therapeutic agent remains a global health priority. It is likely that a licensed RSV vaccine is several years away, however, given the burden of RSV infection and the associated costs globally there is much ongoing research into the development of a well-tolerated and effective vaccine. The main target populations for vaccination include infants, school age children, pregnant women and older adults. Multiple different vaccine approaches are being considered including live-attenuated chimeric, whole-inactivated, particle-base, subunit, nucleic acid and gene-based vectors. There are also ongoing efforts to develop long acting monoclonal antibodies for infants.

"Three agents, ribavirin, IVIG and palivizumab have been extensively used and investigated as antiviral treatments for RSV. To date none have proven unequivocally beneficial, and effective treatments and research continues into future therapies. At least 14 anti-RSV treatment products are undergoing phase I and II clinical trials, of which 5 have included paediatric patients.

"Novel therapeutic molecules developed to date include, fusion inhibitors, non-fusion inhibitors, polymerase inhibitors, antibodies, nucleoside analogues, small-interfering RNAs and a benzodiazepine. They have various targets on RSV such as the F protein, RNA polymerase, nucleoprotein and nucleocapsid mRNA. It is hoped that one of these products will become a licensed treatment for RSV infection in children and adults over the coming years. The development of a successful treatment or prophylactic agent has the potential to revolutionise the care and outcome for severe RSV infections in the world's most vulnerable infant population."

References available on request