THE NORTHERN HOSPITAL

RESPIRATORY SYNCYTIAL VIRUS (RSV)

Introduction

Respiratory syncytial virus (RSV) is a pathogen of global importance and is currently a World Health Organization priority for the development of an effective vaccine and/ or monoclonal antibody treatment.

It is a **ubiquitous** cause of both **upper** and **lower respiratory tract infections**.

It is estimated that RSV may be responsible for as much as 25% of excess wintertime mortality, previously attributed solely to influenza.

Severe disease is most commonly seen in **infants** and **young children** or in the **elderly.**

It should be noted that acute respiratory disease caused by RSV is not simply restricted to paediatric and high-risk adult populations. Healthy adults are infected repeatedly throughout their lives and typically have symptoms restricted to the upper respiratory tract.

In children it may manifest as:

1. Upper respiratory tract infection
2. Bronchiolitis (most common cause)
3. Croup (along with parainfluenza viruses, influenza and adenoviruses)
4. Viral bronchitis / pneumonia

In adults it may manifest as:

1. Upper respiratory tract infection
2. Viral bronchitis / pneumonia

Diagnosis can be made in the **ED** by **rapid PCR testing**.

Usually this virus causes only mild respiratory tract infection, but occasionally infection can be severe, especially in:

1. The very young

2. The elderly

3. The immunocompromised

4. Those with significant comorbidities.

History

Respiratory syncytial virus was originally recovered from a colony of chimpanzees with coryza in 1956.

It was designated, “chimpanzee coryza agent”.

Epidemiology

Illness is very common in **children < 3 years of age**, although it can occur in **any age**.

Respiratory syncytial virus is a pathogen of global importance, thought to be responsible each year for more than 33 million infections

This includes around 60,000 in-hospital deaths of children < 5 years of age.

The full burden of disease however is likely to be much higher, as 50% of deaths occur outside hospitals.

It is estimated that RSV may be responsible for as much as 25% of excess wintertime mortality, previously attributed solely to influenza.

The World Health Organization now regards RSV vaccine development as a global priority, and RSV vaccines have been short-listed for the Global Vaccine Alliance (Gavi) vaccine investment strategy. Several vaccine candidates and monoclonal antibodies are being investigated, and it is anticipated that commercial vaccines will be available by 2025. [4]

RSV causes **seasonal** outbreaks throughout the world

In the southern hemisphere, wintertime epidemics occur from May to September, with a peak in May, June, or July.

Pathology

Organism

Human **Respiratory syncytial virus (RSV)** is a medium-sized (120 - 200 nm) enveloped virus that contains a linear negative-sense RNA genome

It belongs to the family Pneumoviridae.

Its name comes from the fact that F proteins (or fusion proteins) on the surface of the virus cause the cell membranes on nearby cells to merge, forming syncytia (or multinucleated cells)

There are two subtypes of RSV, Types A and B. They differ primarily in the composition of the G protein, (an attachment protein) while the F protein is conserved between the two strains. The two subtypes, A and B, are simultaneously present in most outbreaks. Type A subtypes typically causes more severe disease.

Reservoir

- Humans

Transmission

- Transmission of RSV is primarily by inoculation of nasopharyngeal or ocular mucous membranes after contact with virus-containing secretions or fomites.

  Direct contact is the most common route of transmission.

  Aerosol droplets spread also occurs.

  RSV can survive for several hours in the environment.

Incubation Period

- Incubation period is generally 2 - 8 days.

Period of communicability

- A person is usually infectious for up to **10 days** after symptoms begin.

Susceptibility & resistance

- Almost all children will have been infected by the age of 3 years

- RSV infection does **not** induce complete or long term immunity and people may be repeatedly infected with the same and different strains of RSV.

- Transplacentally acquired antibody against RSV does not protect infants against infection. However, infants with high antibody titers usually have milder symptoms restricted to the upper respiratory tract

Clinical Features

Symptoms are often only mild and usually resolve within **1 - 2 weeks**.

Children:

In children it may manifest as:

1. Upper respiratory tract infection
    - Cough, coryza, rhinorrhea, sore throat, conjunctivitis.
2. Bronchiolitis (most common cause)
3. Croup (along with parainfluenza viruses, influenza and adenoviruses)
4. Viral bronchitis/ pneumonia
    - Chest pain, dyspnea, productive, reduced oxygen saturations.
5. Apnea:
    - RSV infection has been postulated as one cause of **sudden infant death syndrome**.

Infants and young children with RSV infection may have rhinorrhea and a decrease in appetite before any other symptoms appear.

Cough usually develops one to three days later.

Soon after the cough develops, sneezing, fever, and wheezing may occur.

In very young infants, irritability, decreased activity, and **apnea** may be the *only* symptoms of infection.

Adults:

In adults it may manifest as:

1. Upper respiratory tract infection
    - Cough, coryza, rhinorrhea, sore throat, conjunctivitis.
2. Viral bronchitis / pneumonia:
    - Chest pain, dyspnea, productive, reduced oxygen saturations.

Complications:

Secondary complications can include:

1. Bacterial otitis media/ sinusitis.

2. Bacterial pneumonia

3. Bronchospasm

4. Exacerbation of serious conditions such as:

    - Asthma
    - COPD
    - Heart failure

Risk factors for severe illness:

Those who have a higher risk for s**evere** illness caused by RSV include:

1. Children < 3 years

    - Especially infants < 6 months and premature babies.

2. Older adults, especially those > 65 years

3. Those with significant comorbidities:

    - Chronic lung disease or heart disease.
    - Those with neuromuscular disorders, including those who have difficulty swallowing or clearing mucus secretions.

4. The immunosuppressed, including:

    - HIV infection
    - Patients with organ transplants
    - Patients on chemotherapy

Investigations

PCR:

Clinical symptoms of RSV are nonspecific and can overlap with other respiratory infections.

Definitive clinical diagnosis is not possible and is usually confirmed with PCR testing.

Diagnosis can be made in the ED by taking nose or throat swabs for **rapid PCR testing**

Serology

Diagnostic serology is not helpful in infants because of maternal antibody.

Serology is unhelpful in adults because repeated infections throughout a person's life result in a stable and sustained level of RSV-specific antibody.

CXR:

CXR is done when viral pneumonia or secondary bacterial infection is suspected.

Management

Treatment:

Treatment is predominantly supportive

1. Oxygenation:
    - Supplemental oxygen as required

      For unwell infants high flow oxygen or NIV may be required

      Rarely mechanical ventilation may be required
2. Fluids:
    - Fluids should be encouraged

      NG or IV fluids may be required in more severe disease
3. Steroids:
    - These are given in cases of Croup
4. Salbutamol:
    - This may be required in children with bronchiolitis
5. **Ribavirin**:
    - This is a synthetic guanosine analogue.

      It is a **broad-spectrum antiviral agent** that is approved can be delivered by aerosol.

      It may be considered in severe cases or in those at high risk, but its efficacy in RSV infection is uncertain.

Prevention:

Currently there is no vaccine to prevent RSV infection

Immunoglobulin for children: [3]

- RSV Immunoglobulin (Ig) can provide passive immunity against RSV infection and has been shown to decrease hospitalisation for RSV related illness.

  For patients who have been admitted to hospital for RSV infection, the incidence of an ICU admission related to RSV infection is decreased in patients receiving 4 weekly RSV Ig.

  Criteria for use can include:

  - ♥ Preterm infants with or without chronic lung disease of prematurity or congenital heart disease.
  - ♥ Infants with haemodynamically significant congenital heart disease.
  - ♥ Children with anatomic pulmonary abnormalities or neuromuscular disorder.
  - ♥ Immunocompromised children assessed on an individual basis.

- The recommended dose of RSV Ig is 15mg/kg IM and can be given from birth

  Dose 2 is given 3 weeks after dose 1 and then 4 weekly for the remainder of RSV season.

  A total of 5 doses are given.

Notification:

RSV infection is not a notifiable disease.

School exclusion:

Infected children should stay away from childcare until their symptoms have resolved.

References

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5. Frederick E Barr et al. Respiratory syncytial virus in Up to Date Website, June 2019.

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