RSV Bronchiolitis: Preventive measures and new guidelines

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Disclosures

• Conflicts of interest: Recipient of research support /honoraria from AbbVie and Abbott pharmaceuticals in the past.

• Communications: Voice views through Social / Professional media including.
Scheme & Scope

- RSV virus
- RSV infection
- Spectrum of severity
- Preventive approach
- Guidelines
- Evidence base
- Management approaches
- Take ‘to practice’ points
Causes of deaths among children under 5 years, 2012

- Postneonatal: 1-59 months
  - Other group 1 conditions: 10%
  - Congenital anomalies and other non-communicable diseases: 7%
  - Injuries: 5%
  - HIV/AIDS: 2%
  - Malaria: 7%
  - Measles: 2%
  - Diarrhoea: 9%
  - Prematurity: 15%

- Neonatal: 0-27 days
  - Pneumonia: 2%
  - Intrapartum-related complications, including birth asphyxia: 10%
  - Neonatal sepsis: 7%
  - Congenital anomalies: 4%
  - Neonatal tetanus: 1%
  - Other: 4%
  - Prematurity: 15%

RSV is a single-stranded RNA virus of the family Paramyxoviridae, which includes common respiratory viruses such as those causing measles and mumps.

Its name comes from the fact that F protein on the surface of the virus cause the cell membranes on nearby cells to merge, forming syncytia.
>3.5 million infections in children under 2 years of age

175,000 hospitalized adults

125,000 hospitalized infants

90,000 Premature infants

Nature Reviews Drug Discovery 9, 15-16 (January 2010)
Most RSV-infected infants experience upper respiratory tract symptoms, and 20% to 30% develop lower respiratory tract disease (eg, bronchiolitis and/or pneumonia) with their first infection.

Most previously healthy infants who develop RSV bronchiolitis do not require hospitalization, and most who are hospitalized improve with supportive care and are discharged in fewer than 5 days.

Approximately **1% to 3% of all children in the first 12 months** of life will be hospitalized because of RSV lower tract disease.
Duration of RSV Season, by U.S. Department of Health and Human Services Region* and Florida, July 2011–June 2012

Florida
Region 3 (Philadelphia)
Region 2 (New York)
Region 6 (Dallas)
Region 1 (Boston)
Region 4 (Atlanta)†
Region 5 (Chicago)
Region 9 (San Francisco)
Region 10 (Seattle)
Region 8 (Denver)
Region 7 (Kansas City)

†Excludes data from Florida
RSV spreads easily by direct contact, and can remain viable for a half an hour or more on hands or for **up to 5 hours on countertops***. 

My 5 moments for **HAND HYGIENE**

1. **Before touching a patient**
2. **Before clean/aseptic procedure**
3. **After body fluid exposure risk**
4. **After touching a patient**
5. **After touching patient surroundings**
First vaccine!

It's Breast Milk.
It's named Liquid Gold.
It builds immunities.
It has never been recalled.
It fights cancer.

It's organic.

And no matter where it is; Who's making it,
Respect The Breast

IT'S BEAUTIFUL.
Carbon Monoxide
Gas from car exhausts

Tar
Road surfaces

Nicotine
Pesticide

Butane
Lighter fuel

Acetone
Nail Varnish Remover

Ammonia
Cleaning products

Arsenic
Rat poison

Methanol
Rocket Fuel

Hydrogen Cyanide
Poison used on death row

Formaldehyde
Used to pickle dead bodies

Radon
Radioactive gas

Cadmium
Batteries
Respiratory syncytial virus (RSV) causes bronchiolitis and pneumonia. RSV infections are the leading cause of viral death in infants, although RSV-related mortality has decreased since the development and approval of prophylactic antibodies.

*Nature Reviews Drug Discovery* 9, 15-16 (January 2010) | doi:10.1038/nrd3075
Vaccine

- A vaccine trial in 1960s using a formalin-inactivated vaccine (FI-RSV), increased disease severity in children who had been vaccinated.
- There is much active investigation into the development of a new vaccine, but at present no vaccine exists.
- Some of the promising candidates are based on temperature sensitive mutants which have targeted genetic mutations to reduce virulence.
Passive immunization with humanised RSV specific monoclonal antibodies (Palivizumab) prophylaxis is given during the expected annual RSV outbreak season and is effective in reducing the incidence of hospitalization and severe respiratory disease in infants in the high-risk categories.
Palivizumab

- Humanized monoclonal antibody against RSV
- Fab section directed against the F protein of the virion
- Monthly IM injections during RSV season
Palivizumab Pharmacokinetics

Levels obtained with monthly doses of 15 mg/kg IM

* Error bars are ± 1 SD

Is It Time for Vaccination to "Go Viral"?

Philip RK, Shapiro M, Paterson P, Glismann S, Van Damme P.

Other pathogens

- Human metapneumovirus
- Rhinovirus
- Adenovirus
- Influenza
- Parainfluenza
- Mycoplasma pneumoniae
- Chlamydia pneumoniae
Respiratory Syncytial Virus

Recommendations for respiratory syncytial virus (RSV) prophylaxis from the American Academy of Pediatrics [1,2]

- Palivizumab prophylaxis for RSV should be limited to infants born before 29 weeks' gestation and to infants with chronic illness such as congenital heart disease or chronic lung disease.
- Give infants who qualify for prophylaxis in the first year of life no more than 5 monthly doses of palivizumab (15 mg/kg per dose) during the RSV season.
- Qualifying infants born during the RSV season may require fewer doses.
- In the second year of life, palivizumab prophylaxis is recommended only for children who needed supplemental oxygen for 28 days or more after birth and who continue to need medical intervention (supplemental oxygen, chronic corticosteroid therapy, or diuretic therapy).
- Discontinue monthly prophylaxis in any child who is hospitalized for RSV.
- Clinicians may consider prophylaxis for children younger than 24 mo if they will be profoundly immunocompromised during the RSV season.

Continued on next slide
Recommendations for respiratory syncytial virus (RSV) from the American Academy of Pediatrics\textsuperscript{[1,2]}

- Broader use of palivizumab for RSV prevention may be appropriate in Alaska Natives and, possibly, in selected other Native American populations, given the burden of RSV disease and costs associated with transport from remote locations.
- The AAP does not recommend palivizumab prophylaxis to prevent healthcare-associated RSV disease.
- To reduce the risk of RSV and other viral infections, all infants, especially preterm infants, should be offered breast milk and should avoid smoke exposure, attendance in large-group child-care settings during the first winter season, and contact with ill people.
- Household members should be immunized against influenza and practice good hand and cough hygiene.
<table>
<thead>
<tr>
<th>TABLE 2.</th>
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</thead>
</table>

**Guidelines for Administration of Palivizumab**

**Infants eligible for palivizumab in the 1st year of life**
- All infants < 29 weeks gestational age at birth
- Infants < 32 weeks gestational age with chronic lung disease of prematurity, defined as > 21% oxygen for at least 28 days after birth
- Infant, with hemodynamically significant cardiac disease

**Infants eligible for palivizumab until 2nd year of life**
- Infants on supplemental oxygen for at least first 28 days of life and continuing to require medical intervention such as supplemental oxygen, steroid, and/or diuretic therapy

**Infants in whom palivizumab should be considered**
- Infants with pulmonary abnormality
- Infants with neuromuscular disability with inability to clear secretions in lower airways
- Children < 2 years of age who will be severely immunocompromised during respiratory syncytial virus season

**Infants not eligible for palivizumab**
- Infants ≥ 29 weeks and otherwise healthy
- Any infant who experiences breakthrough respiratory syncytial virus infection despite vaccination

*Adapted from Lieberthal and Meissner.*
Mom told me not to touch it
Risk Factors for Hospital Admission with RSV Bronchiolitis in England: A Population-Based Birth Cohort Study


- A population-based birth cohort with follow-up to age 1 year, using Hospital Episode Statistics database.

- 71 hospitals across England.

- Identified 296618 individual birth records from 2007/08 and linked to subsequent hospital admission records during the first year of life.
Cohort study - cont

- 7189 hospital admissions with a diagnosis of bronchiolitis, 24.2 admissions per 1000 infants under 1 year (95% CI 23.7–24.8), of which 15% (1050/7189) were born preterm (47.3 bronchiolitis admissions per 1000 preterm infants (95% CI 44.4–50.2)).

- The peak age group for bronchiolitis admissions was infants aged 1 month and the median was age 120 days (IQR = 61–209 days).

- The median length of stay was 1 day (IQR = 0–3).

- The relative risk (RR) of a bronchiolitis admission was higher among infants with known risk factors for severe RSV infection, including those born preterm (RR = 1.9, 95% CI 1.8–2.0) compared with infants born at term.

- Other conditions also significantly increased risk of bronchiolitis admission, including Down's syndrome (RR = 2.5, 95% CI 1.7–3.7) and cerebral palsy (RR = 2.4, 95% CI 1.5–4.0).
Cohort study - cont

• Most (85%) of the infants who are admitted to hospital with bronchiolitis in England are born at term, with no known predisposing risk factors for severe RSV infection, although risk of admission is higher in known risk groups.

• The early age of bronchiolitis admissions has important implications for the potential impact and timing of future active and passive immunisations.
<table>
<thead>
<tr>
<th>Risk Group†</th>
<th>Number of bronchiolitis admissions (% of infants in risk group)</th>
<th>Total number of infants in risk group (% of whole birth cohort)</th>
<th>Median length of stay in days (IQR)</th>
<th>Rate of bronchiolitis admission per 1000 infants under 1 year (95% CIs)</th>
<th>RR† (95% CIs)</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Born at term</td>
<td>6139 (2-2)</td>
<td>274403 (92-5)</td>
<td>1 (0 to 3)</td>
<td>22-4 (21-8 to 22-9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Premature birth</td>
<td>1050 (4-7)</td>
<td>22215 (7-5)</td>
<td>1 (0 to 3)</td>
<td>47-3 (44-4 to 50-2)</td>
<td>2-11 (1-98 to 2-26)</td>
<td>1-89 (1-77 to 2-02)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>11 (6-4)</td>
<td>171 (0-1)</td>
<td>2 (0 to 14)</td>
<td>64-3 (32-1 to 115-1)</td>
<td>2-66 (1-33 to 4-76)</td>
<td>2-45 (1-36 to 4-43)</td>
</tr>
<tr>
<td>Congenital heart Disease</td>
<td>272 (12-1)</td>
<td>2239 (0-8)</td>
<td>2 (0 to 5)</td>
<td>121-5 (107-5 to 136-8)</td>
<td>5-17 (4-56 to 5-84)</td>
<td>3-35 (2-92 to 3-84)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>282 (5-6)</td>
<td>5016 (1-7)</td>
<td>2 (0 to 4)</td>
<td>56-2 (49-9 to 63-2)</td>
<td>2-37 (2-10 to 2-67)</td>
<td>1-61 (1-42 to 1-82)</td>
</tr>
<tr>
<td>Immunodeficiency</td>
<td>7 (11-7)</td>
<td>60 (0-0)</td>
<td>8 (1 to 58)</td>
<td>116-7 (46-9 to 240-4)</td>
<td>4-82 (1-94 to 9-93)</td>
<td>1-69 (0-80 to 3-58)</td>
</tr>
<tr>
<td>Nervous system congenital anomalies</td>
<td>42 (8-6)</td>
<td>489 (0-2)</td>
<td>2 (1 to 4)</td>
<td>85-9 (61-9 to 116-1)</td>
<td>3-56 (2-56 to 4-82)</td>
<td>1-73 (1-26 to 2-36)</td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>28 (15-4)</td>
<td>182 (0-1)</td>
<td>3 (0 to 9)</td>
<td>153-9 (102-2 to 222-4)</td>
<td>6-37 (4-23 to 9-21)</td>
<td>2-53 (1-72 to 3-72)</td>
</tr>
<tr>
<td>Cerebral Palsy</td>
<td>16 (10-7)</td>
<td>149 (0-1)</td>
<td>3 (1 to 5)</td>
<td>107-4 (61-4 to 174-4)</td>
<td>4-44 (2-54 to 7-21)</td>
<td>2-43 (1-48 to 3-99)</td>
</tr>
</tbody>
</table>

†Relative risk compared with infants without risk factor of interest.

doi:10.1371/journal.pone.0089186.t001
ALCAPA presents predominantly in infancy with features of myocardial ischaemia or cardiac failure and may be mistaken for common paediatric conditions such as colic, reflux or bronchiolitis.
Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis

Abstract

This guideline is a revision of the clinical practice guideline, “Diagnosis and Management of Bronchiolitis,” published by the American Academy of Pediatrics in 2006. The guideline applies to children from 1 through 23 months of age.

Other exclusions are noted. Each key action statement indicates level of evidence, benefit-harm relationship, and level of recommendation. Key action statements were recommended.
A total of 702 infants were hospitalized with community-acquired RSV disease, of whom an estimated 42% were admitted to the intensive care unit (ICU) and 20% required invasive mechanical ventilation (IMV).

Earlier gestational age and younger chronologic age were associated with an increased frequency of RSV-confirmed hospitalization (RSVH), ICU admission, and IMV. Among infants 29 to 32 wGA and < 3 months of age, 68% required ICU admission and 44% required IMV. One death occurred of an infant 29 wGA.

Among the 212 infants enrolled for in-depth analysis of health care resource utilization, mean and median RSVH charges were $55,551 and $27,461, respectively, which varied by intensity of care required.

Outpatient visits were common, with 63% and 62% of infants requiring visits before and within 1 month following the RSVH, respectively.

Conclusion: Preterm infants 29 to 35 wGA are at high risk for severe RSV disease, which imposes a substantial health burden, particularly in the first months of life.
Clinical and health economic outcomes of infants receiving RSV immunoprophylaxis at home versus hospital in an Irish regional birth cohort.

RK Philip, C Herbert, J Shirley, J Powell, C Quinn, E O’Kelly
Archives of Disease in Childhood 101(Suppl 1):A255-A256 · April 2016
DOI: 10.1136/archdischild-2016-310863.420
Supportive care

- Oxygen / Fluid balance
- Pharmacological agents
- To keep calm / sedation
- Feeding
- Neck position
PCO2 after 12 h fell by 0.92 kPa in children treated with CPAP compared with a rise of 0.04 kPa in those on ST (p<0.015). If CPAP was used first, there was a significantly better reduction in PCO2 than if it was used second. There were no differences in secondary outcome measures. CPAP was well tolerated with no complications identified.

CONCLUSIONS: This study suggests that CPAP compared with ST improves ventilation in children with bronchiolitis and hypercapnoea.

Randomised controlled trial of nasal continuous positive airways pressure (CPAP) in bronchiolitis.
Thia LP, McKenzie SA, Blyth TP, Minasian CC, Kozlowska WJ, Carr SB. Department of Paediatric Respiratory Medicine, Royal London Hospital, London, UK.

Power of numbers versus number of powers.
A Randomized Controlled trial of Nebulized Hypertonic Saline Treatment in Hospitalized Children with Moderate to Severe Viral Bronchiolitis.

Department of Respiratory, Children's Hospital, Chong Qing Medical University, China.

Methods 126 infants were randomized to receive either nebulized 3% HS or 0.9% normal saline (NS) and 112 patients completed the study.

Conclusions Frequently inhaled HS shortened LOS significantly and relieved symptoms and signs faster than NS for moderately to severely ill infants with bronchiolitis without apparent adverse effects.

Hypertonic saline (HS) for acute bronchiolitis: Systematic review and meta-analysis.
Maguire C, Cantrill H, Hind D, Bradburn M, Everard ML.

Fifteen trials were included in the systematic review (n = 1922), Non conclusive…..
High flow nasal cannulae therapy in infants with bronchiolitis.

McKiernan C, Chua LC, Visintainer PF, Allen H.
Department of Pediatrics, Tufts University School of Medicine, Baystate Children's Hospital, Springfield, MA, USA.

We hypothesize that HFNC decreases rates of intubation in infants with bronchiolitis by decreasing the respiratory rate and work of breathing by providing a comfortable and well-tolerated means of non-invasive ventilatory support.

68% decrease in need for intubation persisted in a logistic regression model controlling for age, weight, and RSV status.
Introduction

The UK Department of Health defines High Dependency Care (HDC) as,,a level of care intermediate between that on a general ward and intensive care.”1 Since 1997 the UK Department of Health has advocated that district general hospitals are to provide Pediatric HDC.2 HDC has clear cost benefits over intensive care as it has a 2:1 nursing ratio opposed to a 1:1 in the latter. Perhaps the most established benefit of paediatric HDC is in respiratory failure, where the paediatric high dependency unit (PHDU) could offer non invasive ventilation (NIV) which is not only cost affective but also the preferable treatment in ARF.6,7 First purpose-built PHDU outside of Dublin was established in the Children’s Ark of University Hospital Limerick (UHL). This study examines the PHDU in UHL since its commencement in January 2010 until January 2014.

Methods

We have conducted a descriptive observational study that was retrospective and prospective on admissions to the PHDU of UHL. Ethical approval from UHL research ethics committee was obtained. Patient characteristics and treatment information as well as length of stay (LOS) were extracted from the PHDU admissions book, PAS and HIPE database. All 517 admissions were used in the data analysis. The data was analysed using SPSS version 18.

Results

The total number of patient contacts were 517. The median age of contacts was 2.5 years. A trend analysis of the number of contacts in three month intervals shows a flat trend line (Figure 1) with an estimated 32 contacts in a 3 month time period. The minimum number of contacts per quarter was 22 and the maximum 49. There was no obvious seasonal component for the total patient pool however case specific trends were noted.

496 (96%) contacts had information on the time of admission. Of these, 57% were admitted out of hours (defined from 6pm to 8am each day). There were no associations between gender or age group and out of hours admissions.

Table 3: System categories (n=517)

<table>
<thead>
<tr>
<th>System category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory (e.g. bronchiolitis, pneumonia)</td>
<td>195 (38.5%)</td>
</tr>
<tr>
<td>Neurological including seizures, post-ictal and epilepsy</td>
<td>132 (25.5%)</td>
</tr>
<tr>
<td>Endocrine (DKA, hyperglycaemia, Addison’s.)</td>
<td>52 (10.1%)</td>
</tr>
<tr>
<td>Haematological (Leukaemia, aplastic anaemia…)</td>
<td>44 (8.9%)</td>
</tr>
<tr>
<td>Surgical (fractures, appendectomy, laceration)</td>
<td>42 (8.1%)</td>
</tr>
<tr>
<td>Biochemical and metabolic (mitochondrial, hypercalcinemia…)</td>
<td>17 (3.3%)</td>
</tr>
<tr>
<td>Cardiac (flutter, SVT…)</td>
<td>16 (3.1%)</td>
</tr>
<tr>
<td>Gastrointestinal, Renal, MSK, Accidents, other</td>
<td>12 (2.3%)</td>
</tr>
</tbody>
</table>

Figure 1: Trend analysis for the number of contacts per year.

Conclusions

Since the opening of the PHDU in 2010 there have been a steady number of admissions per week and quarter. The average admissions per week was 5.29 for the Mid-West general population of 375,324 and paediatric catchment of nearly 95,000. Most patients were admitted out of hours from the ED and discharged to the paediatric ward.

Most frequent admission was for respiratory system pathology and many benefited from non-invasive ventilatory support such as Nasal CPAP and high flow humidified oxygen therapy (HFT). The level of respiratory care offered in the PHDU avoids the dangerous “under-assistance” in the ward and unnecessary “over-assistance” in ICU. There would also be a cost saving to be obtained by managing patients in the PHDU compared to the general ICU or PICU.

Development of regional PHDU could significantly reduce ICU admissions and transfer to tertiary PICU in Dublin. Model of care as offered by PHDU in Limerick with appropriate guidelines, staffing and facilities could be considered for other regional paediatric units as well, thus promoting the care of sick children in a less hospital-like environment.

References

2. Rushford, K. 2006. Pediatric high dependency care in West, North and East
RSV Bronchiolitis: Preventive measures and new guidelines

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