Prevention of RSV
Update for Practitioners

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Medical Director, RSV Prophylaxis clinic CHEO
MOH LTC Ontario RSV Prophylaxis program advisory group member

Conflict of Interest Declaration

• Local investigator on two investigator driven, Abbvie funded trial
• Member of the Canadian Pediatric Society Infectious Diseases Immunization Committee, the Committee to Advise on Tropical Medicine and Travel, and the Ministry of Health and Long Term Care of Ontario RSV Advisory Group

Objectives

• Review the burden of disease associated with RSV
• Present Canadian RSV prophylaxis data
• Present the recent CPS RSV statement
• To review the process for enrolling patients into the provincial RSV Prophylaxis for High-Risk Infants Program for the 2015-16 season

What is RSV?

• RNA paramyxovirus
  – 2 strains – A and B
    • Often circulate concurrently
• Humans are only source
• Almost all children infected at least once by 2 yrs of age
• Re-infection is common
• Presents as a common URI in older children and adults

Epidemiology

• Annual season in Canada
  – November to April
• Viral shedding 3-8 days
  – May be longer in young and immunosuppressed
• Incubation period 2-8 days
• Supportive care, no treatments proven

Burden of RSV in Young Children

• Population based study in children < 5 yrs
• ER (2000-2004); Pediatric offices (2002-2004)
• 5067 enrolled; 919 (18%) RSV infections; RSVH overall (11%)
• RSV associated with: 18% ER visits
• 15% office visits
• Average RSVH: 17/1000 <6 months of age
3/1000 < 5 years of age

Hall CB et al. NEJM 2009;360:588-594
Burden of RSV in Young Children

- Majority of children had no underlying medical illness
- Only risk factors identified: < 2 years of age, history of prematurity
- Under 5 yrs of age RSV results in:
  - 1 of 38 visits to the ER
  - 1 of 13 visits to a primary care (FD) office
- 85% of infants admitted to Ontario hospitals did not have a major risk factor for RSV (manuscript submitted)

Hall CB et al. NEJM 2009;360:588-598

Global Burden

- Global burden of disease related to RSV in children younger than 5 years
- Systematic review 1995-2009
  - 33.8 million new episodes of RSV-associated ALRI occurred worldwide in children younger than 5 years
  - 3.4 million episodes representing severe RSV-associated ALRI necessitating hospital admission
  - 66 000–199 000 children younger than 5 years died from RSV-associated ALRI in 2005
    - 99% of these deaths occurring in developing countries

Lancet. 2010 May 1; 375(9725)

RSV and Seasonality

- Northern Hemisphere temperate zones have mainly winter peak
  - Median February
- Some regions report biennial peaks
  - Sweden, Finland
- Others report semiannual peaks
  - Taiwan
- Tropical zones have broad timing for peak seasons
  - Tend to have more semiannual peaks
- Timing of peak activity weakly associated with latitude with later onset with increased latitude

Prevention – non pharmacologic

- Hand hygiene is simple and effective for reducing transmission of respiratory viruses
  - Jefferson T et al. Physical interventions to interrupt or reduce the spread of respiratory viruses Cochrane Database Syst Rev 2010 Jan 20
- Avoidance
  - Crowding
  - Cigarette smoke
- Support
  - Breastfeeding
Risk factors for RSV hospitalization worldwide

**Exposure**
- Age at start of RSV season
- Siblings
- Crowding at home
- Day care attendance
- Day care attendance of siblings
- Discharge between October and December

**Social Factors**
- Breast feeding

**Physiologic Factors**
- Low birth weight
- Male sex
- Family history of wheezing
- CLD
- Neurologic problems
- Birth order >2

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**Prevention - Palivizumab Efficacy**

- Overall: 55%
- BPD <32 wks: 39%
- 32-35 wks: 47%
- 36-39 wks: 80%

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**CARESS: Data Analysis Overview and Data to Date**

Bosco Paes, Krista L. Lanctôt, Ian Mitchell
Medical Outcomes and Research in Economics (MORE®) Research Group
Sunnybrook Health Sciences Centre, Toronto

**Purpose**
- Document utilization, compliance and health outcomes of all infants receiving palivizumab
- Evaluate the impact of palivizumab on the incidence of RSV infections, minimize healthcare resources, and identify which pediatric subgroups are receiving palivizumab

**Inclusion Criteria**
- Infants who have received at least one injection of Palivizumab
- Have at least one of the following risk factors:
  - Prematurity (<35 completed weeks of gestation)
  - BPD/CLD
  - Hemodynamically significant CHD
  - Other medically approved conditions
    - E.g. Congenital airway anomalies, cystic fibrosis, neuromuscular impairments

**Enrolment**
- A total of 13315 infants have been recruited from 32 sites
- Similar geographical distribution to Canadian population
CARESS Sites - 32

Indications
- 15.8% Premature
- 7.9% Other
- 10.6% BPD/CLD
- 65.7% Other

Compliance
- On average, infants received 93.0% ± 26.6% of their expected number of injections.

RSV Hospitalization Rate

Serious Adverse Events
- Thus far, 249 SAE forms have been submitted:
  - 246 Hospitalizations
  - 36 Positive RSV
  - 2 Allergic reaction
  - 3 Deaths
    - All “probably not related” or “not related”

CPS Recommendations 2015
- CHD or CLD
  - < 12 months of age at start
- Preterm
  - Born before 30 + 0 wks GA and less than 6 months at start of season
- Remote requiring air transport for hospitalization
  - Born before 36 + 0 and less than 6 months at start of RSV season
CPS Recommendations 2015

- No prophylaxis
  - Down syndrome, CF, upper airway obstruction
- Consider prophylaxis
  - < 24 months on home oxygen, prolonged hospitalization for severe pulmonary disease, severely immunocompromised
- Dosing
  - Prophylaxis start on discharge during RSV season
  - No more than 5 doses per season

MOHLTC Ontario RSV Program and new CPS statement

- MOH is reviewing
- No changes until 2016-2017 season

OK, tell me what I need to know!!!!!!

MOHLTC Ontario 2015-2016

Background
- Administered through the Exceptional Access Program (EAP) MOH
- RSV Advisory Group
- RSV Adjudicators
- NO CHANGE!

MOHLTC Ontario 2015-2016

Prematurity
- ≤ 32 completed weeks gestation and aged ≤ 6 months at the start of, or during, the local RSV season;
or
- 33 – 35 completed weeks gestation and aged ≤ 6 months at the start of, or during the local RSV season, who DO NOT live in isolated communities AND have a Risk Assessment Tool Score of 49 to 100; or
- 33 – 35 completed weeks gestation and aged ≤ 6 months at the start of, or during the local RSV season, and who LIVE IN isolated communities where paediatric hospital care is not readily accessible and ambulance transportation for hospital admission is required;

MOHLTC Ontario 2015-2016

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MOHLTC Ontario 2015-2016

CHD/BPD/Down Syndrome
• < 24 months of age with Down Syndrome / Trisomy 21; or
• < 24 months of age with BPD/CLD and who required oxygen and/or medical therapy within the 6 months preceding the RSV season; or
• < 24 months of age with hemodynamically significant (HS) cyanotic or acyanotic congenital heart disease (CHD); requiring corrective surgery or is on cardiac medication for hemodynamic significant disease

These are reviewed by the provincial adjudicator!

Out of Province Patients
• Patients must be enrolled with their home provincial RSV prophylaxis program and assigned an enrolment number
  – Criteria for a specific PT may differ from that of Ontario’s and completion of the home provincial enrolment form is required to request enrolment in their program
  – Likewise an Ontario infant travelling to another PT during the season can be treated by enrolling the patient through Ontario’s RSV Prophylaxis Program
  – The enrolment number can be used at health facilities across Canada that delivers the RSV Prophylaxis Program

MOHLTC Ontario 2015-2016

Out of season process
• From May 1st – November 1st, 2015
• NICUs identify patients that qualify for prophylaxis in a log book and send the referrals to CHEO RSV Coordinator monthly
• Enrolment forms / appointment arrangements completed by CHEO RSV Coordinator
• From November 1st 2015 all NICU’s to enroll their babies all year round and refers approved babies to CHEO RSV clinic prior to beginning of season

Special Requests
• Assessed on an individual basis
• Requires letter from requesting physician and an ID + Respirologist signature
• Potential diagnoses:
  – Upper airway anomalies, severe immunodeficiencies, neuromuscular diseases, etc.
During season (November – March)

- NICUs enroll their own patients with Abbvie
- First dose of Synagis® is administered prior to discharge from NICU
- Follow up appointments may be made by NICUs by directly contacting CHEO’s Ambulatory Care (613-737-7600 x4105)
- NICUs fax / email Abbvie reference no. and patient info to CHEO RSV Coordinator

Summary: 2015-16

1. Enrolment process
2. Enrolment forms
3. Drug ordering process
4. Dosing schedule

ENROLMENT PROCESS

- All enrolments will be processed and reference numbers provided by Abbvie
- The ministry’s coordinator will review all those with BPD/CHD criteria and the special requests
- Enrolment forms are faxed directly to the Synagis® Coordinator at Abbvie Canada (1-888-703-6967)

ENROLMENT

- Turn around time is usually one business day (prematurity criteria)
- For enrolments under the BPD / CLD and CHD criteria and Special Requests, turn around time is three business days

ENROLMENT FORMS

- Since the form is now going to Abbott Canada and not MOHLTC, NO personal health identifiers (name, address, OHIP no.) are to be provided
- Fields for the child’s full name and OHIP no. have been removed from the enrolment forms
- Really simplified – one form for all
- Risk Assessment Tool is now part of the enrolment form on page 2
DRUG ORDERING PROCESS

- Shipment orders directed to Synagis® Coordinator at Abbvie (fax: 1-888-703-6967)
- For NICUs who will give the first dose in November, it can be ordered using enrolment form (Section 7)
- All subsequent doses should be ordered on Synagis® order form
- Shipments occur within 24 hours, except for orders placed on Fridays, weekends and stat holidays

The ministry requests that all providers be mindful of costs such that drug wastage is minimized

- When an entire vial is not required for a patient, residual product may be used for a second patient if administered within 6 hours from the time of reconstitution under controlled and aseptic conditions
- Cost ranges from $750-1500/vial

DOSING SCHEDULE

(as per Ontario’s RSV Medical Advisory Group)

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<th>Month</th>
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<td>Mid-November</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>December</td>
</tr>
<tr>
<td>3</td>
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<td>January</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>February</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>March</td>
</tr>
</tbody>
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Doses after season and date will not be covered by the Program.

Dosing Interval

- 1st - 2nd dose: 21-28 days
- Between the 2nd, 3rd, 4th, and 5th doses: 28-35 days
- Based on human pharmacokinetic modeling, the 5th dose of palivizumab will provide sufficient antibody levels to protect for at least 6 weeks

All MOH Forms and Information (on line)

http://www.health.gov.on.ca/english/providers/progr am/drugs/funded_drug/fund_respiratory.aspx
CHEO RSV Clinic

• Fridays (primarily) in clinic C1 on the main floor of CHEO
• First clinic: November 20, 2015

• Team for the 2015-16 season:
  Josée St. Denis-Murphy, RN (coordinator)
  Leila Ghosn, C1 clerk
  Chuck Hui, MD (Medical Director)
  Lyne Rastelli (Clinical Manager)

CONTACT US

• By email: rsvclinic@cheo.on.ca
• Website: www.cheo.on.ca/en/RSV-and-premature-babies
• By telephone: 613-737-7600 Ext 2406 (Coordinator)
• By fax: 613-738-4329