Risk Factors for Lower Respiratory Tract Infections in Young Children

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Why focus on risk factors?
Southwest Alaska Respiratory Virus Study: Hospitalized cases, Year 1

Number of cases

|   2005 | 2006 |
|----------------|
|    0   |    0 |

- RSV
- HMPV
- ParaFlu
- Flu
- Pertussis
- Total tested

Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep 2005 2006
Definitions and Data Quality

- Site of infection
  - Lower respiratory tract infection (LRTI) vs. Upper respiratory infection
- Hospitalized vs outpatient illnesses
- Specific diagnosis vs. syndrome
  - Respiratory syncytial virus vs. bronchiolitis
- Different populations
  - Medically high risk vs. general vs. special population
- Data is difficult to assess
  - No randomized controlled trials of Risk Factors!
Risk Factors Related to the Person

- Males, 1.5X increase
- Gestational age < 36 weeks
- Low birthweight
- Age at time of epidemic
  - < 6 months for RSV
  - > 6 months for hMPV
- Nutrition
  - Breast feeding is protective
  - Vitamin A if severe deficiency
  - Vitamin D?
- Race: African-American, AI/AN, Maori, Aboriginal
Risk Factors Related to the Person, continued

- Immunity
  - Passive Immunity
    - Level of maternal immunoglobulin
      - RSV and influenza
      - RSV monoclonal antibody: palivizumab
  - Immunization status
    - Hib, pneumococcal, pertussis, influenza, measles

- Immune deficiency
  - Inherited: Complement deficiency - pneumococcal
    - X-linked Severe Combined Immune Deficiency
  - Acquired: Cancer, stem cell transplantation, HIV

- Conditions affecting the lungs
  - Bronchopulmonary dysplasia
  - Congenital heart disease
  - Cystic Fibrosis
Number of RSV infections vs. month of birth

Glezen, J Pediatrics, 1981
Risk Factors Related to the Pathogen

- Severity of annual epidemics
  - RSV types A and B
  - Influenza types: H3 more severe than H1

- Timing of concurrent respiratory epidemics
  - hMPV and RSV
  - H1N1 influenza in 2009
  - PCV7 use reduced RSV hospitalization in S. Africa

- Influenza
  - Antiviral resistance
  - Mismatch with vaccine: 2003-4
Risk Factors Related to the Environment

- Household crowding
  - Persons per room, number in a bed, number sleeping in same room
  - Number of children, older siblings

- Daycare attendance

- Smoke exposure
  - Tobacco: *in utero* and within household
  - Biomass fuels for heat, cooking: 2X increase LRI
    - Fairbanks: association between air pollution (PM 2.5) and respiratory hospitalizations. Epi bulletin; Aug 30, 2010

- Lack of in-home running water
Risk Factors Related to the Environment, continued

- Socioeconomic factors
  - Parental education
  - Poverty
  - Older paternal status

- Weather-related
  - Low temperatures
  - Low humidity

- Wall-to-wall carpeting
  - Outpatient illness with hMPV, Denmark
Risk Factor Studies in Alaska

- RF for Severe RSV among AN Children

- Matched case-control
  - 204 Hospitalized, < 3 y.o. cases with ARI and +RSV
  - 338 Controls age- and village-matched

- Independent Risk Factors, < 6 month olds
  - Medically high risk, OR 4
  - Breastfeeding, OR 0.33
  - 4 or more children in HH, OR 3
  - HH crowding (≥ 2 per room), OR 2
Risk Factor Studies in Alaska, II

Respiratory Virus Study

Singleton, J Medical Virology, 2010 and unpublished

Case control study

Hospitalized, < 3 y.o., 2006 – 07, SW Alaska

Controls: Age and region matched

128 cases, 186 controls

- PCR swab for viruses: RSV, Influenza, Paraflu, Adeno, Coronavirus, Rhino, hMPV

Independent risk factors

- Medically high risk, woodstove, bottle fed, vomiting during feeds
- Protective: 2 or more rooms with sinks in home
- Not breastfeeding, smoking although both showed a trend
Respiratory Virus Study:
Hospitalized cases, Year 2

Year 2:
- RSV
- hMPV
- ParaFlu
- Flu
- Pertussis
- Corona
- Total tested

Number of cases

Oct Nov Dec Jan Feb Mar Apr May June

<table>
<thead>
<tr>
<th>2006</th>
<th>2007</th>
</tr>
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</table>

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Risk Factor Studies in Alaska, III

- Lack of Piped Water Assoc. with LRTI
  - Gessner, J Pediatrics, 2008

- Community-level analysis, 1998 - 2003
  - Children < 2 enrolled in Medicaid, 108 communities
  - Regression of LRTI vs. water service
    - Controlled for HH crowding, unemployment, education, tobacco, wood stove, poverty

- Water service associated with inpatient and outpatient LRTI
  - Outpatient: < HS education, prenatal tobacco
  - Inpatient: < HS education, prenatal tobacco
LRI Incidence Among Alaska Children < 2 years old, Enrolled in Medicaid 1998-2003

Community in-home water service
Risk Factor Studies in Alaska, IV

- In-home water service & risk of infections
  - Hennessy, AJPH, 2008

- “Ecologic” study of admin & research data
  - Rural Alaska Housing and Sanitation Index
  - I.H.S. ICD9 hospitalization data, Surveillance, Outbreaks

- Demonstrated a relationship between lack of in-home water and respiratory infection
  - Skin infection, but not Gastrointestinal
Proportion of US homes with complete plumbing

![Graph showing the proportion of US homes with complete plumbing over time with data points for US, Alaska, District of Columbia, Mississippi, and Rural Alaska Native.]
Hospitalization Rates for “High” and “Low” Water Service Regions, Alaska, 2000-2004

* P < 0.05
Hospitalization rates for Alaska Native infants, according to percent of homes with water service 1999 - 2004*

* Hennessy, AJPH, 2008
Serious infections with *Streptococcus pneumoniae* in children < 5 years old, Southwest Alaska, 2001-2007

* J Wenger, 2010 Peds Infect Dis J.
Risk Factors for ARI in Greenlandic Children

- Inuit living in Greenland

- Cohort study 288 children, 1996 - 1998
  - 2 year follow-up
  - Weekly follow-up, illness episodes monitored
    - NP swabs taken

- Risk Factors for LRTI
  - Males, RR 1.5
  - Day care center attendance, RR 3.3, PAR 48%
  - Passive smoking, RR 2, PAR 47%
  - Sharing a bedroom with children 0 – 5 y.o.. RR 2.0
  - Breastfeeding protective
Risk Factors for Hospitalization for LRTI in Canadian Inuit Children

- Banerji, Ped Infectious Disease J, 2009
- Case control study, Nunavut
  - 101 Children < 2, hospitalized in Iqaluit
    - RSV 39%, No virus: 27%
  - Age matched controls
- Risk factors
  - Not breastfed OR 3.6
  - Smoking during pregnancy, OR 4
  - Rural residency, OR 2.7
  - Crowding (> 5 people per home), OR 2.5
  - Inuit race, OR 3.7
Person

Males,
Gestational age < 36 weeks
Low birthweight
Age at time of epidemic
Nutrition
  Breastfeeding protective
Race
Immunity
Immune deficiency
Conditions affecting the lungs

Pathogen

Severity of annual epidemics
Timing of concurrent respiratory epidemics
Antiviral resistance
Mismatch with vaccine:

Environment

Household crowding
Daycare attendance
Socioeconomic factors
  Education, poverty
Weather-related
Smoke exposure
  Tobacco: in utero and within household
  Biomass fuels for heat, cooking
  Lack of in-home running water
How can we use Personal risk factors to reduce illness?

<table>
<thead>
<tr>
<th>Personal Risk Factors</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, Race</td>
<td>None</td>
</tr>
<tr>
<td>&lt; 36 weeks gestation, Low birthweight</td>
<td>Prenatal care, smoking cessation</td>
</tr>
<tr>
<td>Age at time of epidemic</td>
<td>Birth planning</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Breastfeeding</td>
</tr>
<tr>
<td>Immunity</td>
<td>Maternal &amp; childhood Imm., palivizumab</td>
</tr>
<tr>
<td>Immune deficiency</td>
<td>Diagnosis and care</td>
</tr>
<tr>
<td>Conditions affecting the lungs</td>
<td>Prevent preterm birth, diagnosis and care</td>
</tr>
</tbody>
</table>
How can we use Pathogen risk factors to reduce illness?

Pathogen Risk Factors
- Severity of annual epidemics
- Timing of concurrent respiratory epidemics
- Antiviral resistance
- Mismatch with flu vaccine

Response
- Surveillance and reporting, timing of palivizumab use
- Use available immunizations
- Monitor resistance, use antivirals appropriately
- Good virologic surveillance
<table>
<thead>
<tr>
<th>Environmental Factors</th>
<th>Response</th>
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</thead>
<tbody>
<tr>
<td>Household crowding</td>
<td>Increase house size, reduce family size</td>
</tr>
<tr>
<td>Daycare attendance</td>
<td>Infection control practices, delay entry until after 6 months, longer paid parental leave</td>
</tr>
<tr>
<td>Smoke exposure</td>
<td>Stop <em>in utero</em> and infant tobacco exposure</td>
</tr>
<tr>
<td>Lack of in-home water</td>
<td>Upgrade wood stoves</td>
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<td>Running water in every home</td>
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</tbody>
</table>
What about the Risk Factors for the Risk Factors?

- Low education level, poverty, poor housing, lack of running water, smoking prevalence, low birthweight are all linked

- “Social Determinants of Health”

- Address the conditions that lead to behaviors or situations that result in poor health status.
What else is needed?

- Make sure providers are informed about risk factors, prevention, surveillance and management.
- What are the best ways to use this information for parental education and action?
What else is needed?

- Use public policy to help prevent infections
  - Smoking bans, education, taxes, cessation services
  - Health insurance to support optimal prenatal care, prophylaxis use, immunization and care for ill children
  - Extend paid parental leave
  - In-home sanitation services for everyone

- Optimize use of public health data to inform public and providers about epidemics, antiviral resistance, recommendations.
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Disclaimer

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