A Crèche Course in Day Care Infections

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Duke University
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Today’s Discussion

• Day Care – What is it? Why is it?
• 30 years of infections in NC day care
• Transmission of DNA markers in Day Care
• Royal Children’s Hospital 1989-1990
• *Haemophilus Influenzae* type b disease
• Risk Factor Study in Melbourne Day Care
• Conclusion
DAY CARE - AN INFECTIOUS DISEASE EXPERIMENT???

- National Child Care Survey
  - child less than 1 yr. - 40% of mothers work
  - child 1-2 years - 52% of mothers work
  - estimated 10 million children less than 5 years of age in regulated and unregulated day care
Types of Child Care

- **Family Child Care Homes**
  - fewer than 6 children in the residence of the provider

- **Group Homes**
  - 6-12 children cared for by more than one provider in one of the provider’s homes

- **Child-care centers**
  - more than 12 children in separate age or developmental groups
"Oh Boy – look at all those toys"
DNA Markers in Day Care

• Calcivirus DNA altered at 2 positions - Marker

• Day Care Sites
  – Infant – 13 children 5-14 months – Marker 1
  – Toddler 1 -12 children 15-23 months - Marker 2
  – Toddler 2 – 21 children 24-35 months - control

• Items – 2 toy balls with DNA marker

• Hands, surfaces, children, staff and parents

• Zero, 3 hours, EOD, 2 weeks - kids and parents
  • Larry Pickering 1998 JID
Detection of marker one in the infant classroom (%) vs. Hours after introduction of the marker:

- Hands
- Surfaces
- Toys (old)
Upper Respiratory Tract Infections

- 85-90% of disease episodes are URTI
- >60 days of URTI
  - 1yr: 67%, 59%, 36%
  - 2nd: 52%, 50%, 27%
  - 3rd: 16%, 20%, 16%
Frank Porter Graham Day Care

- North Carolina – Fred Henderson UNC
- A 30 year prospective study virus and bacterial sampling every child every month
- Sampling when ever the child has a fever/ill
- Physical exam when ill
- Terms of admission asked for study participation with a NP available on site
Up to 3 viruses were cultured from a single child on some occasions.
On average –
A new viral infection cultured every 3 weeks
NUMBER OF CASES OF OTITIS/YEAR BY AGE
FRANK PORTER GRAHAM 1978-1988

NUMBER OF EVENTS

AGE IN YEARS

By 6 month periods

FIGURE 3
With virus cultured within 2 weeks of otitis

Suggesting virus precedes bacterial infection

**FRANK PORTER GRAHAM 1978-1988**

- **PERCENT**
  - 39.9
  - 45.3
  - 32.8
  - 28.6
  - 25
  - 11.1

**AGE IN YEARS**
- 0-<1
- 1-<2
- 2-<3
- 3-<4
- 4-<5
- 5-<6

**FIGURE 4**
CONCLUSIONS

4. CERTAIN VIRUSES HAVE A HIGH ASSOCIATION WITH THE OCCURRENCE OF A SUBSEQUENT AOM DURING THE FIRST TWO YEARS OF LIFE (listed in < frequency).

RSV (A & B)
PARAINFLUENZA 1 & 3
INFLUENZA A
ADENOVIRUS 1
RHINOVIRUS
ADENOVIRUS 5
COXSACKIE B
INFLUENZA B
ADENOVIRUS 2
Giardia lamblia

- 82 Children under 2 years of age
  - 33% infected with Giardia lamblia
  - 78% of those asymptomatic

Rotavirus

- 45% infected with Rotavirus
- 50% were asymptomatic
Secondary Cases

- >10% of adult family members acquired disease
- 26% attack rate for Shigella
- 15% a.r. for rotavirus
- 17% a.r. for Giardia lamblia
- 18% a.r. for E. Coli O157:H7
- 40% a.r. for Cryptosporidium
<table>
<thead>
<tr>
<th>Child care</th>
<th>No.</th>
<th>% receiving antibiotics</th>
<th>Mean no. of days of antibiotic use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-care center</td>
<td>43</td>
<td>36</td>
<td>19.5</td>
</tr>
<tr>
<td>Child-care home</td>
<td>72</td>
<td>7</td>
<td>4.0</td>
</tr>
<tr>
<td>Home care</td>
<td>156</td>
<td>8</td>
<td>4.6</td>
</tr>
</tbody>
</table>

* Reference: Reves and Jones (108).
<table>
<thead>
<tr>
<th>Study location (reference no.)</th>
<th>Study design</th>
<th>Group/center</th>
<th>Odds ratio*</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland (43)</td>
<td>Case-control</td>
<td>Child-care</td>
<td>36</td>
<td>5.7–233</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family care</td>
<td>4.4</td>
<td>1.7–12</td>
</tr>
<tr>
<td>California (42)</td>
<td>Case-control</td>
<td>Child-care</td>
<td>2.6</td>
<td>1.6–4.3</td>
</tr>
</tbody>
</table>

* Odds ratio refers to comparison with children in home care.
Day Care Epidemiology

- Outbreaks of illness
- More frequent infections
- More severe illnesses
- More antibiotics
- More resistant organisms
HIB Epidemiology

• 1988 visit to RCH and met Dr. Lyn Gilbert
• Discussed day care studies in USA
  – HIB vaccine available for >18 months old
  – Discovered high rate of epiglottitis at RCH
• Proposed PhD thesis to investigate day care and relationship to HIB disease in Melbourne
• Dr. Gilbert provided funding for fellowship
• HIB vaccine trial proposed to Merck
Royal Children’s Hospital, Melbourne, Australia
H. INFLUENZAE TYPE B INFECTIONS VICTORIA BY AGE AND DISEASE 1985-87

Background information

**Figure 3**
INCIDENCE AND MEDIAN AGE OF HIB DISEASE
BY DISEASE TYPE AND GEOGRAPHIC LOCATION
/100,000 CHILDREN <5 YEARS OF AGE

INCIDENCE (LOG SCALE)  

AGE IN MONTHS

ESKIMOS  NAVAJ0  DENVER  ROC'H'NY  VICTORIA  FINLAND  SWEDEN

LOCATION

MENINGITIS  EPIGLOTTITIS  DISEASED MEDIAN AGE
AETIOLOGY OF BACTERIAL MENINGITIS
ROYAL CHILDREN’S HOSPITAL

Per 100,000

YEAR

H. INFLUENZAE b  N. MENINGIDITIS  S. PNEUMONIAE

FIGURE 2
AETIOLOGY OF BACTERIAL MENINGITIS

UNITED STATES CHILDREN <5 YEARS OF AGE

TIME PERIOD

1950-59

1960-69

1970-81

CASURES PER 100,000

0 20 40 60 80

N.MENINGITIDIS H.INFLUENZAE B S.PNEUMONIAE

ALL CAUSE

DATA FROM JID 1986;154:399
H. INFLUENZAE TYPE B INFECTIONS VICTORIA QUARTERLY OCCURRENCE 1985-87

Figure 2
This is why they are susceptible to HIB disease.

**Fig. 3.** Incidence of *H. influenzae* meningitis (heavy solid line) during first five years of life (Finland in 1975 and 1976, 196 cases), and the corresponding level of anti-*H. influenzae* type b capsular polysaccharide (H.i.b) antibodies (thin dotted line) (840 sera).
Always had a way with children
MENINGITIS

Dear Parent,

A case of meningitis has occurred in a child of the Kindergarten

This disease generally spreads to close intimate and household contacts and can progress very quickly.

The indications of this illness to look for are fever, intense headache, nausea and often vomiting. Serious signs include drowsiness, neck stiffness, delirium, coma and sudden collapse. Even the earliest sign, that is fever, in such contacts warrants immediate medical attention from your local Doctor or the Royal Children’s Hospital.

If you need any further information, contact the following telephone numbers 616 7121, 616 7122, 616 7127.

Yours faithfully,

Dr. M.A. Morsy
Senior District Health Officer,
Environmental Health Standards

Dr. Clements will be here to do throat swabs today.
Day-care children ‘twice as likely to get killer bug’

By BRETT WRIGHT

Child care could be a child killer.

A Royal Children’s Hospital study has found that children attending Melbourne day-care centers are at least twice as likely to contract the potentially fatal HIB bacterium than children who stay at home.

The study’s findings were upsetting mothers who were caring for their babies.

At least 20 Australian babies have died of SIDS, or cot death, while in formal child care. About half that number died in the past three years.

The study’s findings were upsetting mothers who were caring for their babies.

While the SIDS incidents are alarming, the risk of HIB infection could be even more serious.

The bacterium, haemophilus influenzae type B (HIB), is the most common cause of bacterial meningitis, or inflammation of the brain and spinal cord, in young children. It also causes death from epiglotitis, or swelling at the back of the throat.

HIB infects about 180 children a year in Victoria. Unfortunatel, it can kill up to 50 per cent of sufferers.

The disease, which can appear within two days of infection, mainly affects children between the ages of six months and two years.

Preliminary findings from the Royal Children’s Hospital’s study have confirmed overseas research showing that HIB is more common in larger families, in homes where children share bedrooms and among children attending day-care centers.

Studies in the US and Europe show that attendance at day-care centers increases the risk of contracting the disease by two to 10 times, depending on age.

A fellow in microbiology and infectious diseases at the Royal Children’s Hospital, Mr. Denison Clements, said the Victorian study supported the overseas findings.

“We don’t yet have enough control cases to tell what the increase is with day-care, but it seems to be more common.”

Mr. Clements said the study would have implications for the possible use of a vaccine for HIB in Australia.

“It is a devastating disease which is potentially preventable,” he said. “If a vaccine is used here, we want to be able to tell which groups should get it.”

Several new vaccines are being tested in the US, France and Finland.

The hospital’s study of Victorian children will continue for at least another three months.

Page 15: Killer in a cot
HIB Risk Factor Study

- Cases from admissions to RCH
  - 211 (1 non-participating)
- Controls age and date matched day surgery RCH
  - 369 (2 non-participating)
- Australian Bureau of Statistics provided day care attendance rates as second set of controls
# Results

## Age Distribution of 210 Hib Cases

<table>
<thead>
<tr>
<th>Disease</th>
<th>&lt;1 Yr</th>
<th>1</th>
<th>2-3 Yrs</th>
<th>3-4 Yrs</th>
<th>4-5 Yrs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>26</td>
<td>29</td>
<td>11</td>
<td>8</td>
<td>2</td>
<td>76</td>
</tr>
<tr>
<td>Epiglottitis</td>
<td>6</td>
<td>26</td>
<td>29</td>
<td>11</td>
<td>11</td>
<td>83</td>
</tr>
<tr>
<td>Other</td>
<td>16</td>
<td>20</td>
<td>9</td>
<td>2</td>
<td>4</td>
<td>51</td>
</tr>
<tr>
<td>All Disease</td>
<td>48</td>
<td>75</td>
<td>49</td>
<td>21</td>
<td>17</td>
<td>210</td>
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</tr>
<tr>
<td>--------------</td>
<td>-------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>INDEX PATIENTS</td>
<td>296</td>
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<tr>
<td>SIBS</td>
<td>112</td>
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<td>PARENTS</td>
<td>42</td>
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<td>RELATIVES</td>
<td>7</td>
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</tr>
<tr>
<td>TOTAL</td>
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</tr>
<tr>
<td>SOURCE</td>
<td>INITIAL</td>
<td>F-U</td>
<td>% PRIMARY</td>
<td></td>
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<td>---------</td>
<td>-----</td>
<td>-----------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIB1</td>
<td>45</td>
<td>29</td>
<td>37.2%</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>SIB2</td>
<td>19</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIB3</td>
<td>4</td>
<td>4</td>
<td></td>
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<td>SIB4</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MOTHER</td>
<td>17</td>
<td>11</td>
<td>9%</td>
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<td></td>
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<tr>
<td>FATHER</td>
<td>7</td>
<td>7</td>
<td>5%</td>
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<tr>
<td>RELATIVES</td>
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<td>OTHER</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>93</strong></td>
<td><strong>68</strong></td>
<td></td>
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</tbody>
</table>
## ODDS RATIOS FOR HOURS OF CHILD CARE STRATIFIED ON AGE IN YEARS

<table>
<thead>
<tr>
<th>HOURS OF CARE</th>
<th>0&lt;-1</th>
<th>1,-2</th>
<th>2&lt;-3</th>
<th>3&lt;-4</th>
<th>4&lt;-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>NONE</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>LESS THAN 4 HOURS</td>
<td>0.760</td>
<td>0.831</td>
<td>1.851</td>
<td>0.327</td>
<td>5.501</td>
</tr>
<tr>
<td>4-19 HOURS</td>
<td>1.906</td>
<td>1.817</td>
<td>1.952</td>
<td>1.307</td>
<td>3.255</td>
</tr>
<tr>
<td>20-39 HOURS</td>
<td>5.716</td>
<td>5.652</td>
<td>0.911</td>
<td>1.388</td>
<td>2.205</td>
</tr>
<tr>
<td>&gt; 40 HOURS</td>
<td>9.530</td>
<td>4.239</td>
<td>2.563</td>
<td>1.388</td>
<td>0.916</td>
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</table>
## Adjusted Odds Ratios for All Hib Disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>SE</th>
<th>Odds Ratios</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRECHE20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-SLT6</td>
<td>1.46</td>
<td>0.32</td>
<td>4.34</td>
<td>2.27 - 8.27</td>
</tr>
<tr>
<td>+SLT6</td>
<td>0.68</td>
<td>0.09</td>
<td>1.98</td>
<td>1.64 - 2.39</td>
</tr>
<tr>
<td>SIB &lt;6 YRS</td>
<td>0.41</td>
<td>0.28</td>
<td>1.51</td>
<td>0.86 - 2.65</td>
</tr>
<tr>
<td>ILL SIBLING</td>
<td>0.47</td>
<td>0.24</td>
<td>1.60</td>
<td>1.00 - 2.58</td>
</tr>
<tr>
<td>MO'S B'PLACE</td>
<td>0.48</td>
<td>0.26</td>
<td>1.62</td>
<td>0.96 - 2.74</td>
</tr>
<tr>
<td>CROWDING</td>
<td>0.55</td>
<td>0.69</td>
<td>1.17</td>
<td>1.02 - 1.34</td>
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</tbody>
</table>
## ABS Controls vs Cases

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>CI</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td><strong>EpiGlotTitis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creche (&gt;4hrs)</td>
<td>1.83</td>
<td>1.01-2.71</td>
<td>0.047</td>
</tr>
<tr>
<td>Mobirth</td>
<td>16.96</td>
<td>(not calculated due to small N)</td>
<td></td>
</tr>
<tr>
<td><strong>OtheR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creche (&gt;4hrs)</td>
<td>3.07</td>
<td>1.43-6.60</td>
<td>0.004</td>
</tr>
<tr>
<td>Sib &lt;6</td>
<td>2.15</td>
<td>1.13-4.09</td>
<td>0.019</td>
</tr>
</tbody>
</table>

* one case only with mother foreign born
What have we learned since?

- HIB PRP vaccine for 18 month olds showed decrease in disease in children less than 18 months in day care.
- In Australia, siblings and older children in crèche were frequently HIB culture positive.
- HIB conjugate vaccine eliminated carriage in recipients further enhancing “herd immunity.”
- Vaccination helps to make day care safer for all children.
Conclusions

• Day Care issues
  – Larger groups of children -> more infections
  – Youngest (Naïve) children clustered by age
  – Shared objects -> more infections
  – Diapers -> more infections
  – Hand washing -> unintentional lapses
  – Separate diaper changers and food handlers
  – A virus is a virus and does not need antibiotics
Colleagues

ties
Further Conclusions

• Working with Lyn Gilbert was crucial to my career
• Working with Lyn Gilbert was intellectually stimulating
• Working with Lyn Gilbert was a blast.
• Tennis with Lyn Gilbert usually meant I would lose – but it was fun
• THANK YOU LYN !!!!!!!!!!!!!!!
Thank you Dr. Lyn Gilbert for mentoring all of us !!!!
<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>BETA</th>
<th>SE</th>
<th>ODDS RATIOS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRECHE20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-PT ILL</td>
<td>1.48</td>
<td>0.44</td>
<td>4.43</td>
<td>2.85 - 10.61</td>
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<tr>
<td>+PT ILL</td>
<td>0.41</td>
<td>0.23</td>
<td>1.51</td>
<td>0.95 - 2.40</td>
</tr>
<tr>
<td>PT ILL L MO</td>
<td>-0.24</td>
<td>0.42</td>
<td>0.78</td>
<td>0.34 - 1.80</td>
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<tr>
<td>CHILDSHA</td>
<td>0.62</td>
<td>0.32</td>
<td>1.88</td>
<td>0.99 - 3.55</td>
</tr>
<tr>
<td>MO's B'PLACE</td>
<td>1.00</td>
<td>0.46</td>
<td>2.72</td>
<td>1.10 - 6.76</td>
</tr>
</tbody>
</table>
OMP Subtypes - preliminary
<table>
<thead>
<tr>
<th>Disease</th>
<th>#</th>
<th>3L</th>
<th>2L</th>
<th>6U</th>
<th>14L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis (93)</td>
<td>58</td>
<td>86%</td>
<td>2%</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Epiglottitis (77)</td>
<td>45</td>
<td>91%</td>
<td>0%</td>
<td>0%</td>
<td>9%</td>
</tr>
<tr>
<td>Cellulitis (14)</td>
<td>10</td>
<td>70%</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Pneumonia (11)</td>
<td>4</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Other (27)</td>
<td>19</td>
<td>90%</td>
<td>0%</td>
<td>0%</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>136</td>
<td>88%</td>
<td>1%</td>
<td>3%</td>
<td>7%</td>
</tr>
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</table>