Pertussis Control – Does Canada have it right?

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Disclosures

- I have received grant and contract support for clinical trials from GlaxoSmithKline and Sanofi Pasteur, manufacturers of the two licensed Tdap vaccines.

- I have no personal financial interest in either Tdap product or in any vaccine manufacturer.
Historical Pertussis Epidemiology

- Pertussis a disease of infants and young children
- Peak incidence in pre-school aged children
- Most morbidity and nearly all mortality in young infants
  - One of the leading causes of infant mortality in early 19th century
- Transmission amongst pre-school aged children

Nearly 50% of children with evidence of infection by school entry
Pertussis incidence in Canada 1924-2004

Whole-cell pertussis vaccine approved in 1943
Acellular vaccine replaced whole-cell vaccine in 1997-98
Age Related Incidence, 1998-2002

Galanis et al. CMAJ 2006;174:451-2
Reported Rate of Pertussis in Adolescents in Canada, 1986-1998

Source: NDRS
Tdap Products

- **Adacel™**
  - PT 2.5 g
  - FHA 5 g
  - PRN 3 g
  - FIM 5 g
  - Dip 2 Lf
  - Tet 5 Lf
  - AlPO₄ 1.5 mg
  - 2-phenoxyethanol

- **Boostrix™**
  - PT 8 g
  - FHA 8 g
  - PRN 2.5 g
  - Dip 2.5 Lf
  - Tet 5 Lf
  - AlOH 0.3 mg
  - 2-phenoxyethanol

Sanofi Pasteur

GlaxoSmithKline
An analytical framework for immunization programs in Canada

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Analytical Framework Criteria

- Disease burden
- Vaccine characteristics
- Immunization strategy and program
- Cost effectiveness
- Acceptability of vaccine program
- Feasibility of program
- Ability to evaluate programs
- Research questions
- Equity of the program
- Ethical considerations
- Legal considerations
- Conformity of the program
- Political considerations
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Tdap vaccine use in Canada

- May 1999: Tdap licensed in Canada
- Sept 1999: Newfoundland and Labrador introduces Tdap for all 9th grade students (14-16 year olds)
- May 2000: National Advisory Committee on Immunization (NACI) issued supportive statement, but did not recommend universal routine use
- Oct 2000: Northwest Territories adopts Tdap for all 14-16 year olds; implemented in early 2001

Tdap vaccine use in Canada

- 2002: Consensus Conference on Pertussis
- Sept 2003: NACI revised its recommendations for the use of Tdap vaccine
  - A single booster dose should be administered to adolescents and adults in place of Td to protect against pertussis
- 2004: Tdap introduced in British Columbia and Quebec
- 2005: Tdap introduced in all other Canadian provinces and territories

Goals of the Pertussis Control Strategy in Canada

- To decrease morbidity and mortality from pertussis across the entire life span
  - Protection of adolescents and adults is a worthy goal for the benefit of these cohorts themselves
  - It is not clear whether a collateral benefit of protection of infants would be achieved
NACI Recommendations

- All preadolescents and adolescents who have not received a dose of acellular vaccine should receive a single dose of the adolescent/adult formulation of acellular pertussis vaccine. A single campaign to vaccinate the entire cohort is the strategy that would prevent most cases...At a minimum, dTap should replace Td for the regular adolescent booster dose program. Optimally, the timing of the booster dose should be determined according to local epidemiologic patterns.
NACI Recommendations

- For adults who have not previously received a dose of acellular vaccine, it is recommended that a single diphtheria-tetanus (Td) booster dose be replaced by the combined diphtheria-tetanus acellular pertussis (dTap) vaccine.

http://www.immunize.cpha.ca/francais/resourcf/Adol_pertussis_Sep03.pdf
Age-specific rates of pertussis: Canada, 1996 – 2006

- DTaP-IPV-Hib introduced
- Years: 10-14 (blue squares), 15-19 (yellow stars), 20+ (red circles)
- Rates per 100,000

* Provisional data for 2003-2006

Age-specific rates of pertussis: Canada, 1996 – 2006


Canada
Effectiveness
Pertussis Incidence and Vaccine Use, 1993 – 2004
Northwest Territories

Average Yearly Cases / 10,000

1993-1996
Switch to DTaP

1997-2000
Tdap begun

2001-2002

2003-2004


- 2005-2008: only 7 new cases
  - 2005 – 5 cases; 2006 – 2 cases
    - 3 adults
    - 2 unimmunized children
    - 2 other
  - 2007, 2008, 2009 – 0 cases
  - 2010 – 7 cases
    - 3 adults
    - 3 children (5, 10, 12
    - 1 infant

Kandola K, and Lorne Clearsky, Medical Health Officer, personal communication.
Canada
First province (population 575,000) to implement routine, province-wide Tdap at 14-16 yrs of age (September 1999)
- School based program in grade 9 (replaced Td-IPV program)
- >28,000 doses; coverage rate >95%

Effectiveness
Newfoundland and Labrador

Year | Rate
--- | ---
2003 | 12.0
2004 | 1.0
2005 | 0.2
2006 | 0.4
2007 | 1.0
2008 | 1.4
2009 | 0.8
2010 | 0.0
2011 | 0.0* (to August 4, 2011)

* Pertussis outbreak confined to persons not immunized with Tdap

Canada
Age-Specific Proportion of Cases

Source: BC-CDC; http://www.bccdc.org/downloads/pdf/epid/reports
7.3 Pertussis Rates by Age Group and Sex, 2005

Rate per 100,000 population

BC CDC 2005 Epidemiology Report
7.3 Pertussis Rates by Age Group and Sex, 2009

Rate per 100,000 population

BC CDC 2009 Epidemiology Report
7.1 Pertussis Rates by Year, 2000-2009

<table>
<thead>
<tr>
<th>Year</th>
<th>BC Pertussis Reports</th>
<th>BC Pertussis Rate</th>
<th>Canadian Pertussis Rate*</th>
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</thead>
<tbody>
<tr>
<td>2000</td>
<td>1549</td>
<td>38.4</td>
<td>15.4</td>
</tr>
<tr>
<td>2001</td>
<td>578</td>
<td>14.2</td>
<td>9.5</td>
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<td>2002</td>
<td>557</td>
<td>13.6</td>
<td>10.3</td>
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<td>2003</td>
<td>895</td>
<td>21.7</td>
<td>10.2</td>
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<tr>
<td>2004</td>
<td>464</td>
<td>11.2</td>
<td>9.7</td>
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<tr>
<td>2005</td>
<td>206</td>
<td>4.9</td>
<td>5.6</td>
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<tr>
<td>2006</td>
<td>258</td>
<td>6.1</td>
<td>7.9</td>
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<tr>
<td>2007</td>
<td>149</td>
<td>3.5</td>
<td>5.5</td>
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<tr>
<td>2008</td>
<td>231</td>
<td>5.3</td>
<td>5.2</td>
</tr>
<tr>
<td>2009</td>
<td>164</td>
<td>3.7</td>
<td></td>
</tr>
</tbody>
</table>
### British Columbia Pertussis Cycles

<table>
<thead>
<tr>
<th>Year</th>
<th>Reported Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td><strong>1549</strong></td>
</tr>
<tr>
<td>2001</td>
<td>578</td>
</tr>
<tr>
<td>2002</td>
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<td>2005</td>
<td>206</td>
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<tr>
<td>2006</td>
<td><strong>258</strong></td>
</tr>
<tr>
<td>2007</td>
<td>149</td>
</tr>
<tr>
<td>2008</td>
<td>231</td>
</tr>
<tr>
<td>2009</td>
<td>164</td>
</tr>
<tr>
<td>2010</td>
<td>127</td>
</tr>
<tr>
<td>2011 (6 months)</td>
<td>25</td>
</tr>
</tbody>
</table>
Reported Pertussis Cases by Age
Prince Edward Island 1997-2008
Canada
Pertussis in Saskatchewan 2010-2009

Incidence (per 100,000)

Year

Tdap implemented in 2003

< 1
1-4
5-9
10-14
15-19

Courtesy of the Saskatchewan Ministry of Health, 1 October 2010
Pertussis in Saskatchewan

- 2008-April 2010
  - 35 lab confirmed cases in infants <1 year
    - 5% (2/35) had started immunization on time
    - 49% (17/35) were over 2 months of age and were unimmunized
    - 43% (15/35) were under 2 months of age (too young to be immunized)
  - 5 deaths
    - 4 younger than 1 month
    - 1 3 month old unimmunized

- 24 cases in 2010 including 9 in last 4 weeks

Courtesy of the Saskatchewan Ministry of Health, 1 October 2010
Adolescent Pertussis Vaccine Summary

- Pertussis is “re-emerging” in age cohorts not protected by the current vaccine schedule
  - Acellular pertussis vaccines in infants and preschool children have controlled pertussis in those cohorts
  - Adolescent immunization controls pertussis in that cohort
  - Adult immunization would likely control pertussis in adults; implementation is still the challenge
How do the provinces/territories deal with the adult pertussis immunization?

- Fund it but don’t advertise it
  - Nova Scotia, Quebec and Northwest Territories publicly fund Tdap for adults
    - Not aggressive programs
    - In NS, Tdap is used in EDs instead of Td if a Tdap vaccine has not previously been received
- Recommend it but don’t fund it
  - Saskatchewan
- Say that NACI recommends it and leave it at that
  - Manitoba
- Just say you only fund it for adolescents
  - Ontario
- Say you fund Td for adults
  - Alberta, New Brunswick, British Columbia, Yukon
  - Just don’t say anything about adults and focus on children
  - Newfoundland, Prince Edward Island, Nunavut
Will compliance with the adult recommendations be sufficient?

- Single dose during adulthood
  - Recommendation made not based on conviction that a single dose of Tdap will provide protection throughout adulthood
  - Rather there was no data on duration of protection or safety/immunogenicity of repeat dosing in adults
  - Mathematical modeling suggests that a 10-year interval may be appropriate for adults
Pre- and Post-Tdap<sub>5</sub> Vaccination Seroprotection Rates (≥ 0.1 IU/mL) for Diphtheria and Tetanus

- Marked increase in seroprotection rates for diphtheria following Tdap<sub>5</sub> vaccination in both groups
- All participants achieved seroprotective levels for tetanus

![Bar chart showing seroprotection rates for diphtheria and tetanus pre- and post-vaccination.](chart.png)
Pre- and Post-Tdap\textsubscript{5} Vaccination GMCs for Diphtheria and Tetanus

- Pre-vaccination diphtheria & tetanus GMCs for the Tdap\textsubscript{5} 10y group had declined; generally similar to Naïve group
- Robust immune response in both groups
**Pre- and Post-Tdap<sub>5</sub> Vaccination Pertussis Antibody GMCs**

- Pre-vaccination GMCs for the Tdap<sub>5</sub> 10y group had declined over the 10 years; remained higher than the Naïve group.
- Marked increase in pertussis antibody GMCs following Tdap<sub>5</sub> in both groups.

![Graph showing GMC Antibody Response for PT, FHA, PRN, and FIM](image-url)
Solicited Reactions Day 0-7 Post-Vaccination

10-year Re-dosing with Tdap$_5$ had similar safety profile as Tdap-naïve Tdap$_5$ recipients

- No new or unexpected safety issues identified
- No adverse events leading to study discontinuation

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Tdap$_5$ 10y (N=361)</th>
<th></th>
<th>Naïve (N=407)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>(95% CI)</td>
<td>%</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>Immediate Reactions$^1$</td>
<td>0.8</td>
<td>(0.2; 2.4)</td>
<td>0</td>
<td>(0.0; 0.9)</td>
</tr>
<tr>
<td>Solicited Reactions</td>
<td>92.7</td>
<td>(89.5;95.2)</td>
<td>92.3</td>
<td>(89.3; 94.7)</td>
</tr>
<tr>
<td>Pain</td>
<td>87.8</td>
<td>(83.9; 91.0)</td>
<td>84.4</td>
<td>(80.5; 87.8)</td>
</tr>
<tr>
<td>Unable to do usual activities</td>
<td>2.6</td>
<td>(1.2; 4.8)</td>
<td>1.7</td>
<td>(0.7; 3.5)</td>
</tr>
<tr>
<td>Erythema</td>
<td>23.1</td>
<td>(18.8; 27.8)</td>
<td>29.7</td>
<td>(25.3; 34.4)</td>
</tr>
<tr>
<td>≥5 cm</td>
<td>2.0</td>
<td>(0.8; 4.1)</td>
<td>1.7</td>
<td>(0.7; 3.5)</td>
</tr>
<tr>
<td>Swelling</td>
<td>20.5</td>
<td>(16.4; 25.1)</td>
<td>23.3</td>
<td>(19.3; 27.8)</td>
</tr>
<tr>
<td>≥ 5 cm</td>
<td>2.6</td>
<td>(1.2; 4.8)</td>
<td>1.7</td>
<td>(0.7; 3.5)</td>
</tr>
<tr>
<td>Fever</td>
<td>4.2</td>
<td>(2.4; 6.9)</td>
<td>4.9</td>
<td>(3.0; 7.5)</td>
</tr>
<tr>
<td>≥ 39.0°C</td>
<td>0</td>
<td>(0.0; 1.0)</td>
<td>0</td>
<td>(0.0; 0.9)</td>
</tr>
</tbody>
</table>

$^1$ Pallor, abnormal taste and dizziness. All resolved spontaneously.
Conclusions

- Canada’s recommendations for pertussis control still leave significant gaps
  - Newborn infants (? Maternal immunization)
  - Repeat Tdap dosing for adults
- Despite recommendations, implementation is not ideal in Canada
  - Gaps in adult vaccine funding and uptake
- Intervention strategies are required and evaluation of the effectiveness of these strategies is critical
  - Vaccine coverage
  - Vaccine registries
Questions/Comments