Pertussis Surveillance and Tdap Immunization in Adults: Non-Programs for a Phantom Disease?

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Vaccine Sciences Symposium
Ontario Agency for Health Protection and Promotion
7 April 2010
I have no actual or potential conflict of interest in relation to this program.
Actual or potential conflict of interest in relation to this program

- I have received grant and contract funding for clinical trials and epidemiological studies from the two manufacturers of Tdap vaccines (Sanofi Pasteur, GlaxoSmithKline)
  - I have no personal financial interest in either company or any of their products
- I admit to biases about governments and agencies that make recommendations without programs, and implement programs without evaluations
Objectives

- At the end of the session, participants will
  - be understand the changing epidemiology of pertussis in Canada
  - be aware of the National Advisory Committee Immunization’s recommendations for the use of pertussis vaccines
  - be familiar with the current status of provincial programs with Tdap vaccine.
  - will wonder what the current Tdap vaccine coverage rates are amongst Canadian adults
  - will be prepared to be advocates for using best practices for program implementation and evaluation
Outline

- Epidemiology
  - Classic
  - Current
- Pertussis in adults, pertussis in infants
- NACI guidelines for use of Tdap
- Provincial/territorial adult Tdap programs
- Current status and coverage for Tdap vaccine in adults
Pertussis Classic 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
- Nearly 50% of children with evidence of infection by school entry
Pertussis incidence in Canada 1924-2004
Pertussis Cases and Incidence Rate, Canada, 1990-99.
Age Related Incidence, 1998-2002

Galanis et al. CMAJ 2006;174:451-2
Age-specific rates of pertussis: Canada, 1996 – 2006

Age-Specific Proportion of Cases

Source: BC-CDC; http://www.bccdc.org/downloads/pdf/epid/reports
Annual proportion of hospitalized pertussis cases by age

Reported Pertussis-associated Deaths* by Year, 1990-2002

*N=157
Complications of Pertussis

- **Pulmonary**
  - Pneumonia: 9.4%
  - Atelectasis: 3.0%

- **Neurological**
  - Seizures: 1.9%
  - Encephalopathy: 0.3%

- **Hernia**
  - Inguinal: 0.4%
  - Umbilical: 0.4%

- **Weight Loss**: 1.3%

- **Death**: 0.8%

*IMPACT data, 1991-1997. 1013 hospitalized cases <2 years old*  
*Halperin et al. Clin Infect Dis 1999*
CDC study – infant pertussis: who was the source?

- 774 infant cases from 4 states
- 264 cases had source identified
- Sources:
  - Mother 32%
  - Sibling 20%
  - Grandparent 8%
  - Other 25%
  - Father 15%

Bisgard K. *PIDJ* 2004;23:985–9
Age of pertussis source for infants

*219 source-persons with known age

Transmission of Pertussis

- Adolescents get pertussis from community and household contacts.
- Adults get pertussis from their school age children.
- The disease ranges from asymptomatic to severe.
- Adult and adolescent parents give pertussis to their young infants.
- Young infants are at high risk of morbidity and even mortality.
Pertussis in Adults: Sweden

- 174 culture-positive adults
- Symptoms:
  - whooping: 82%
  - vomiting: 50%
  - mean duration: 8 weeks (range 2-26)

Trollfors and Rabio BMJ 1981
## Pertussis in Adults: Canada

- 77 adults with laboratory confirmed pertussis

### Symptoms:
- Violent cough: 96%
- Whoop: 34%
- Vomiting: 49%
- Cough duration: 44.5 days

*Senzilet et al. Clinical Infectious Disease 2001*
Morbidity of Pertussis in Adolescents and Adults in Quebec

<table>
<thead>
<tr>
<th>Complication</th>
<th>12-17</th>
<th>30-39</th>
<th>&gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td>pneumonia</td>
<td>2</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>urinary incontinence</td>
<td>0</td>
<td>2</td>
<td>34</td>
</tr>
</tbody>
</table>

n=280 n=129 n=53

De Serres, J Infect Dis, 2000
### Cough Illness Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>Setting</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robertson</td>
<td>1987</td>
<td>Australia</td>
<td>Resp Clinic</td>
<td>26%</td>
</tr>
<tr>
<td>Jackson</td>
<td>1987</td>
<td>Seattle</td>
<td>Stud health</td>
<td>15%</td>
</tr>
<tr>
<td>Mink</td>
<td>1992</td>
<td>Los Angeles</td>
<td>Stud health</td>
<td>26%</td>
</tr>
<tr>
<td>Rosenthal</td>
<td>1995</td>
<td>Chicago</td>
<td>Amb clinic</td>
<td>26%</td>
</tr>
<tr>
<td>Wright</td>
<td>1995</td>
<td>Nashville</td>
<td>ER</td>
<td>21%</td>
</tr>
<tr>
<td>Schmidt-Grohe</td>
<td>1995</td>
<td>Germany</td>
<td>Vaccine trial</td>
<td>32%</td>
</tr>
<tr>
<td>von Konig</td>
<td>1995</td>
<td>Germany</td>
<td>Vaccine trial</td>
<td>31%</td>
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</tbody>
</table>
## Cough Illness Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>Setting</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nennig</td>
<td>1996</td>
<td>San Francisco</td>
<td>Pop-based</td>
<td>12%</td>
</tr>
<tr>
<td>Jansen</td>
<td>1997</td>
<td>United States</td>
<td>USMC</td>
<td>17%</td>
</tr>
<tr>
<td>Strebel</td>
<td>1996</td>
<td>Minneapolis</td>
<td>Pop-based</td>
<td>13%</td>
</tr>
<tr>
<td>Birkebaek</td>
<td>1998</td>
<td>Denmark</td>
<td>Pop-based</td>
<td>16%</td>
</tr>
<tr>
<td>Vincent</td>
<td>1999</td>
<td>Korea</td>
<td>US soldiers</td>
<td>17%</td>
</tr>
<tr>
<td>Gilberg</td>
<td>2000</td>
<td>Paris</td>
<td>MD office</td>
<td>32%</td>
</tr>
<tr>
<td>Senzilet</td>
<td>2001</td>
<td>Canada</td>
<td>MD office</td>
<td>20%</td>
</tr>
</tbody>
</table>
**Tdap Products**

- **Adacel™**
  - Sanofi Pasteur
  - PT 2.5 g
  - FHA 5 g
  - PRN 3 g
  - FIM 5 g
  - Dip 2 Lf
  - Tet 5 Lf
  - AlP0₄ 1.5 mg
  - 2-phenoxyethanol

- **Boostrix™**
  - GlaxoSmithKline
  - PT 8 g
  - FHA 8 g
  - PRN 2.5 g
  - Dip 2.5 Lf
  - Tet 5 Lf
  - Al0H 0.3 mg
  - 2-phenoxyethanol
Comparison of antibody responses of Swedish infants and Canadian adolescents, 12-17 years of age, and adults, 18-54 years of age

<table>
<thead>
<tr>
<th>Antigen</th>
<th>2, 4, 6 mo</th>
<th>Tdap</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sweden I</td>
<td>Sweden II</td>
</tr>
<tr>
<td>PT</td>
<td>49.4</td>
<td>51.6</td>
</tr>
<tr>
<td>FHA</td>
<td>39.1</td>
<td>57.0</td>
</tr>
<tr>
<td>PRN</td>
<td>116</td>
<td>134</td>
</tr>
<tr>
<td>FIM</td>
<td>351</td>
<td>352</td>
</tr>
</tbody>
</table>
APERT Study

- Randomized controlled trial
  - ap (GSK: PT/FHA/PRN) vs HAV
  - 15-65 years of age
- Monitored from cough of 5 days duration
  - Culture, PCR, acute/convalescent serology
- ap vaccine was effective (VE=90%) in preventing culture/PCR positive pertussis in adolescents and adults
- Control arm (HAV) n=1390 provides prospective population-based data
  - 3.7-4.5 cases/1000 person years
  - ~800,000-1,000,000 cases annually in the US

Ward et al. NEJM 2005
ACIP Recommendations

Adolescents

- All adolescents should receive single dose of Tdap in place of Td (preferred age 12 yrs)
  - If already received Td, can still give Tdap
    - 5 year interval recommended
    - Less is acceptable
  - Give with MCV4
Press Release

Nation’s Teen Vaccination Coverage Increasing, But Below 2010 Goals

For Immediate Release: October 9, 2008

- 30.4 percent had received Tdap vaccination, up from 10.8 percent in 2006 (a 19.6 percentage point increase)

http://www.cdc.gov/media/pressrel/2008/r081009.htm
NACI Recommendations

- All adolescents should receive a dose of Tdap

http://www.immunize.cpha.ca/francais/resourcf/Adol_pertussis_Sep03.pdf
Vaccine Uptake: Canada

- Adolescents:
  - Publicly funded
  - School based programs
  - 90-95% (?)
Age-specific rates of pertussis: Canada, 1996 – 2006

* Provisional data for 2003-2006
Effectiveness

Pertussis Incidence and Vaccine Use, 1993 – 2004
Northwest Territories


2005-2008: only 7 new cases
- 2005 – 5 cases; 2006 – 2 cases
  - 3 adults
  - 2 unimmunized children
  - 2 other
- 2007, 2008 (through November)
  - 0 cases

Kandola K, Medical Health Officer, personal communication.
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 | Cases
--- | ---
2004 | 5
2005 | 1
2006 | 2
2007 | 3
2008 | 6

Incidence per 100,000


* Pertussis outbreak confined to persons not immunized with ADACEL
BC Incidence of Pertussis by Age

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;19</th>
<th>&gt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>144</td>
<td>61</td>
</tr>
<tr>
<td>2006</td>
<td>165</td>
<td>93</td>
</tr>
<tr>
<td>2007</td>
<td>128</td>
<td>54</td>
</tr>
<tr>
<td>2008</td>
<td>169</td>
<td>65</td>
</tr>
</tbody>
</table>

* 144 cases through Sept 30, 2009
Reported Pertussis Cases by Age
Prince Edward Island 1997-2008

Last case reported 2005 (as of October 25, 2009)
ACIP Recommendations

Adults

- All adults should receive single dose of Tdap in place of Td
- HCWs with direct patient contact should receive Tdap as soon as possible
  - Intervals since previous Td as short as 2 years are acceptable
  - HCWs without direct patient care should receive at their next 10 yr interval (encouraged to get it sooner)
- Institutions should provide Tdap for HCWs

MMWR 2006;55(RR17)
Supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC)
NACI Recommendations

- All adolescents should receive a dose of Tdap
- 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/resources/Adol_pertussis_Sep03.pdf
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
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
How are we doing with our Tdap recommendation in adults?

- I don’t know!
- Do you?
Vaccine Uptake: Canada

- Adolescents:
  - Publicly funded
  - School based programs
  - 90-95%

- Adults
  - Recommended, mostly not funded (or promoted)
  - Uptake unknown
  - Likely <5%
What do we know and what don’t we know?

- Do we need more data on pertussis in adults?
  - Epidemiology
    - The data that pertussis causes significant cough illness in adults is convincing
    - The data that pertussis can range from mild, to classical, to severe with complications in adults is convincing
    - The data that pertussis severity in adults increases with age is convincing
    - The data that adults serve as the primary source of pertussis infection in young infants is convincing
    - The burden of illness amongst the elderly is still unclear
    - The annual incidence of pertussis amongst adults is not known
    - The distribution of cases across the spectrum of severity in adults is still unclear
    - The importance of mild cases and subclinical cases in adults to transmission is still unclear
What else do we know and what else don’t we know?

- Do we need more data on pertussis in adults?
  - Tdap
    - The data that Tdap is safe in adults is convincing
    - The data that Tdap is immunogenic in adults is convincing
    - The data that Tdap is efficacious in adults is convincing
    - Whether immunization in adults will protect young infants either with a “cocoon strategy” or through universal adult immunization is still unknown
    - Whether immunization in pregnant women will protect the newborn infant from pertussis morbidity and mortality is still not known.
  - Coverage rates for Tdap in adults are not known
What could (should) we be doing?

- Research
  - Burden of illness in elderly
  - Range of illness by severity in adults
    - Carriage
    - Transmission
  - Incidence in adults
    - Serosurveys
      - Snapshot
      - Longitudinal
    - Cough illness
      - Improved diagnostics
- Safety and effectiveness of Tdap in pregnancy
- Neonatal immunization
What else could (should) we be doing?

- Program Implementation
  - Public perceptions and acceptability
  - Adult immunization platforms and implementation plans
  - Funding for adult immunization

- Program Evaluation
  - Vaccine coverage surveys
    - Annual?
    - Linked to census?
  - Vaccine registries
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 appears to control pertussis in that cohort
  - Adult immunization would likely control pertussis in adults; implementation is still the challenge
  - Control of pertussis in neonates and young infants may need novel interventions including neonatal immunization, immunization during pregnancy and immunization of all adults or those in contact with young infants (cocoon strategy)
Conclusion

- Implementation of programs without adequate resourcing is not really program implementation

- All programs need to have an evaluation component that includes vaccine coverage and vaccine effectiveness
Comments and Questions