Invasive Pneumococcal Disease, Connecticut, 1998-2009

Invasive (sterile site infection) pneumococcal disease (IPD) is a leading cause of pneumonia, sepsis, and meningitis in children and adults. In 2009, IPD caused an estimated 44,000 cases and 5,000 deaths in the United States (U.S.) (1).

In 2000, the U.S. began routine infant immunization against IPD with a 7-valent pneumococcal conjugate vaccine (PCV7). It led to a 76% decrease in IPD among children <5 years of age, as well as substantial decreases in older age groups due to community-level immunity resulting from childhood vaccination. Incidence of penicillin non-susceptible (Pen-NS) IPD also decreased because the majority of the Pen-NS isolates in 2000 were PCV7 serotypes. In contrast, IPD due to non-PCV7-types has increased, including 19A, a serotype associated with penicillin non-susceptibility (2,3).

In 2010, a 13-valent pneumococcal conjugate vaccine (PCV13) was licensed by the U.S. Food and Drug Administration. PCV13 contains the seven serotypes included in PCV7 (4, 6B, 9V, 14, 18C, 19F, and 23F) plus six additional serotypes (1, 3, 5, 6A, 7F, and 19A) (4). The release of PCV13 provides an opportunity to examine the impact PCV7 had in Connecticut on serotype distribution as well as antibiotic susceptibility overall and among high incidence age groups (<5 and >64 years). It also helped to characterize the impact PCV13 may have on the remaining IPD.

As part of the Active Bacterial Core surveillance project of the State Emerging Infections Program, the Connecticut Department of Public Health (DPH) conducts enhanced surveillance for IPD. It is both physician and laboratory reportable to the DPH. Isolates are routinely collected for serotyping and antibiotic susceptibility testing. Isolates are categorized as Pen-NS according to parenteral administration guidelines for non-meningitis (MIC≥4 µg/mL) and meningitis (MIC≥0.12) cases.

During 1998-2009, 6,236 cases of IPD were identified of which 5,904 (95%) had an isolate available for testing. Incidence (cases per 100,000) declined by 39% (21.1 in 1998/99 to 12.8 in 2009) overall and by 98% (12.5 to 0.28) for PCV7-types (p<0.01 for both trends). Incidence of IPD caused by the six additional serotypes in PCV13 increased by 43% (3.7 in 1998/99 to 5.3 in 2009) overall, by 192% (3.9 to 11.4) among cases <5 years of age, and by 23% (10.3 to 12.7) among cases >64 years of age (p<0.01 for each trend).

The proportion of isolates due to the six additional serotypes in PCV13 increased from 19% (245/1312) in 1998/99 to 46% (397/857) in 2008/09 overall, from 7% (17/251) to 62% (44/71) among cases <5 years of age, and from 19% (97/512) to 36% (259/740) among cases >64 years of age (p<0.01 for each trend).

Figure 1. Number of IPD cases by age group and serotype, Connecticut, 1998/1999 vs. 2008/2009
41% (141/341) among cases >64 years of age (p<0.01 for each age group) (Figure 1). Among 2008/09 isolates with these six serotypes, 19A was the most common serotype accounting for 40% (158/397) of cases overall, 73% (32/44) of cases <5 years of age, and 39% (55/141) of cases >64 years of age.

The proportion of isolates that were Pen-NS was similar in 1998/99 to that in 2008/09 (Figure 2). However, the proportion of Pen-NS isolates due to the six additional serotypes in PCV13 increased from 7% in 1998/99 to 83% in 2008/09. All 2008/09 Pen-NS isolates among these serotypes were serotype 19A. Among cases <5 years of age, the proportion of isolates that were Pen-NS increased by 62% (10% in 1998/99 to 16% in 2008/09, p<0.05) with 19A accounting for 82% of 2008/09 Pen-NS isolates. Among cases >64 years of age, changes in the proportion of all isolates that were Pen-NS and those that were Pen-NS serotype 19A were similar to that for all ages combined.

**Reported by**

S Petit, MPH, H Altier, BA, C Marquez, Epidemiology and Emerging Infections Program, M Mandour, BS, State Public Health Laboratory, Connecticut Department of Public Health.

**Editorial**

In Connecticut, routine childhood immunization with PCV7 dramatically reduced rates of IPD in children and unvaccinated adults, indicating strong direct and indirect vaccine effects. The potential for vaccination to contribute to the emergence of serotypes not included in the vaccine is of concern. This has occurred in Connecticut as evidenced by the significant increase in non-PCV7-type incidence. However, this increase is small relative to the decrease that occurred in PCV7-type IPD.

PCV13 has replaced PCV7 in the routine childhood immunization schedule. A supplemental PCV13 dose is also recommended for healthy children <5 years and for children <6 years with underlying illnesses who already completed a schedule of PCV7 (2). The National Immunization Survey indicated that the 2009 PCV7 coverage rate in Connecticut was 91%. If PCV13 is found to be as effective as PCV7, continued widespread use of vaccine has the potential to further decrease overall IPD and Pen-NS IPD in those <5 years of age because the majority of 2008/09 cases were due to the six additional serotypes in PCV13.

The indirect vaccine effects seen in adults >64 years of age likely resulted from reduced pneumococcal nasopharyngeal colonization in vaccinated children and subsequent reduced transmission from children to unvaccinated adults. Immunization of children with PCV13 is also anticipated to have some level of community effect among adults since 19A has similar colonization patterns to that of PCV7 serotypes (2).

Connecticut is currently participating in a study to evaluate the effectiveness of PCV13 among children <5 years of age. Continued monitoring of IPD is needed to monitor the potential changes in disease burden that may emerge in PCV13 and non-PCV13 serotypes.

**References**

Connecticut Department of Public Health

Surveillance for Guillain-Barré Syndrome during the 2009 Pandemic Influenza A (H1N1) Vaccination Campaign

In 1976, vaccination against a novel swine-origin influenza A (H1N1) was associated with an increased risk for Guillain-Barré syndrome (GBS) (approximately 10 excess cases per million vaccinations)(1). To monitor the safety of the new 2009 pandemic influenza A (H1N1) vaccine, the Connecticut Emerging Infections Program (EIP) initiated active GBS surveillance. Similar surveillance was carried out by the nine other EIP sites.

Surveillance Methods

On October 1, 2009, GBS was made a temporarily reportable condition in Connecticut. To rapidly identify all hospitalized patients with symptoms consistent with GBS statewide, active surveillance was established among a network of neurologists, hospital infection preventionists, and hospital pharmacists.

Weekly email and fax reminders were sent to neurologists requesting notice of all patients with a potential GBS diagnosis seen during the past week. Similarly, hospital pharmacists were contacted and asked to report patients receiving intravenous immunoglobulin (a treatment for GBS). Surveillance officers investigated each report through consultation with the reporter and by chart review. Subsequently, a confirmed, probable, or non-case status was assigned according to the Brighton Collaboration GBS Criteria (2). Clinical data and H1N1 and seasonal influenza vaccination status were collected through hospital chart review and patient phone interview. Observed rates were calculated and compared to expected rates of GBS per 100,000 person-years of observation.

Results

During October 1, 2009–May 31, 2010, a total of 129 individuals were reported to the system; 74 were clearly not GBS. Of the remaining 55 individuals, 33 (60%) met the Brighton Collaboration GBS Criteria including 20 confirmed and 13 probable cases. The median age of cases was 49 years (range: 2–85 years); 18 (55%) were male. The majority (82%) reported at least one relevant clinical event within 42 days of GBS symptom onset; 61% had upper respiratory infection. Four cases required mechanical ventilation and one died.

Of the 33 GBS cases, 6 (18%) received at least one dose of 2009 pandemic H1N1 vaccine. Of these, 3 (9%) had received the vaccine within 42 days of GBS onset, one of whom had evidence of prior upper respiratory infection and gastroenteritis.

The overall observed to expected GBS rate ratio was slightly elevated (1.19), but not statistically significant (Table 1). Comparing the incidence of GBS in those who received the 2009 pandemic H1N1 vaccine to those who did not yielded an overall rate ratio of 0.8 (95% Confidence Interval: 0.3–1.9). Restricting this analysis to those with exposure to the 2009 pandemic H1N1 vaccine in the 42 days before GBS onset resulted in a rate ratio of 0.4, which was not statistically significant (Table 2).

Reported by

J Meek1, M Fiellin1, J Kattan2, K Kudish2, R Nelson2, R Heimer1. 1-CT Emerging Infections Program, Yale University School of Public Health; 2 – Connecticut Department of Public Health

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>CT population (2008 estimates)</th>
<th>Person Years (PY) under surveillance</th>
<th>Observed Cases (O)</th>
<th>Observed rate per 100,000 PY</th>
<th>Expected* Rate per 100,000 PY</th>
<th>Expected cases (E)</th>
<th>Rate Ratio (O/E)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–24</td>
<td>1,137,323</td>
<td>753,545</td>
<td>6</td>
<td>0.80</td>
<td>0.71</td>
<td>5.35</td>
<td>1.12</td>
<td>0.3-3.6</td>
</tr>
<tr>
<td>25–49</td>
<td>1,207,555</td>
<td>800,078</td>
<td>11</td>
<td>1.37</td>
<td>1.11</td>
<td>8.88</td>
<td>1.24</td>
<td>0.5-3.0</td>
</tr>
<tr>
<td>50–64</td>
<td>678,367</td>
<td>449,459</td>
<td>6</td>
<td>1.33</td>
<td>1.60</td>
<td>7.19</td>
<td>0.83</td>
<td>0.3-2.5</td>
</tr>
<tr>
<td>≥65</td>
<td>443,776</td>
<td>294,028</td>
<td>10</td>
<td>3.40</td>
<td>2.80</td>
<td>8.23</td>
<td>1.21</td>
<td>0.5-3.0</td>
</tr>
<tr>
<td>All</td>
<td>3,501,252</td>
<td>2,319,789</td>
<td>33</td>
<td>1.42</td>
<td>1.20</td>
<td>27.84</td>
<td>1.19</td>
<td>0.7-2.0</td>
</tr>
</tbody>
</table>

Gender

| | | | | | | | |
|Male | 1,707,410 | 1,131,261 | 18 | 1.6 | 1.6 | 17.8 | 1.0 | 0.5-1.9 |
|Female | 1,793,842 | 1,188,528 | 15 | 1.3 | 0.96 | 11.4 | 1.3 | 0.6-2.8 |

Table 1. Observed and expected rates of GBS in CT population during October, 2009—May 31, 2010
Connecticut EIP surveillance data did not show an increased risk for GBS associated with the 2009 pandemic influenza A (H1N1) vaccine. However, in June 2010, the CDC published preliminary results based on aggregate data from 10 EIP sites comparing GBS incidence among vaccinated and non-vaccinated persons. That analysis showed a statistically significant rate ratio of 1.77 (3). This translates to less than one excess case of GBS per 1 million vaccinations, much less than that seen during the 1976 swine-influenza vaccination campaign.

Several elements of the GBS surveillance system in Connecticut are noteworthy. The system was quickly developed and implemented in response to the need for vaccine safety monitoring. Additionally, neurologists and pharmacists are nontraditional sources for disease reporting. They proved to be valuable partners, in addition to more traditional reporting sources such as infection preventionists. Also, making a disease temporarily reportable for a defined time period facilitated completeness and timeliness of obtaining GBS reports.

There are several limitations to this analysis. First, the true background rate of GBS is unknown. The expected rate used in this analysis was derived from a meta-analysis of 13 published GBS studies; however, the generalizability of this estimate to Connecticut is unknown. Second, the number of people exposed to the 2009 pandemic H1N1 vaccine in Connecticut was estimated using interim (as of January 2010) state-specific 2009 pandemic H1N1 vaccine coverage estimates (4). If vaccine coverage was substantially different from the published estimates, then the population denominators used to calculate rates of GBS among those exposed and unexposed could be incorrect. Finally, the relatively small population under surveillance (~3.5 million) and the low background incidence of GBS limit the power of our surveillance to detect small increases.

Cases of post-vaccine GBS should be reported to the Vaccine Adverse Event Reporting System (VAERS; http://vaers.hhs.gov/index).

Table 2. Incidence rate and rate ratio of GBS cases by H1N1 vaccine exposure within 42 days of GBS onset, Connecticut

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>Vaccine Coverage</th>
<th>H1N1 vaccine exposed (42d)</th>
<th>H1N1 vaccine unexposed (&gt;42d or none)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Person Years</td>
<td>Rate*</td>
</tr>
<tr>
<td>0-17</td>
<td>43%</td>
<td>2</td>
<td>231400</td>
</tr>
<tr>
<td>18+</td>
<td>15.2%</td>
<td>1</td>
<td>270811</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>502211</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Vaccine coverage estimates from MMWR - Interim Results: State-Specific Influenza A (H1N1) 2009 Monovalent Vaccine Coverage—United States, October 2009 - January 2010. MMWR 2010;59(12):363-368.

Jewel Mullen, MD, MPH, MPA
Commissioner of Public Health
Matthew L. Cartter, MD, MPH
State Epidemiologist
Lynn Sosa, MD
Deputy State Epidemiologist

HIV/AIDS Surveillance 860-509-7900
Epidemiology and Emerging Infections 860-509-7994
Immunizations 860-509-7929
Tuberculosis Control 860-509-7722
Sexually Transmitted Diseases (STD) 860-509-7920

Connecticut Epidemiologist

Editor: Matthew L. Cartter, MD, MPH
Assistant Editor & Producer: Starr-Hope Ertel