Incidence of GBS and CIDP following influenza vaccination
National Influenza Immunization Program (NIIP)

- Analysis of the national surveillance data on GBS cases between October 1, 1976 and January 31, 1977
  
  - The NIIP was initiated on October 1, 1976, to provide A/New Jersey influenza vaccine for the adult population in the USA and children at risk of serious illness from influenza infection
  
  - Between October 1 and December 2, 1976, over 35 million doses of vaccine had been administered
  
  - Due to an increase in the number of reports of GBS, the NIIP was suspended on December 16, 1976

<table>
<thead>
<tr>
<th>GBS cases</th>
<th>No of cases</th>
<th>Summary of findings¹,²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated cases prior to</td>
<td>504</td>
<td>• Increased GBS rate in all adult categories</td>
</tr>
<tr>
<td>GBS onset</td>
<td></td>
<td>• 4.9–5.9 GBS cases per million vaccinees</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 32 (6%) deaths</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Greatest risk for GBS within 5 weeks after vaccination</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>440</td>
<td>• Attack rate of 0.79 per million per month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 26 (4.7%) deaths</td>
</tr>
<tr>
<td>Exclusions</td>
<td>154</td>
<td>• 33 cases were excluded due to missing or insufficiently complete data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 121 cases where the vaccine had not been recommended were also excluded (patients &gt;18 years of age)</td>
</tr>
<tr>
<td>Total</td>
<td>1,098</td>
<td></td>
</tr>
</tbody>
</table>

GBS: Guillain–Barré syndrome

GBS after influenza infection

<table>
<thead>
<tr>
<th>Vaccination season</th>
<th>Author: Study design</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>France</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996–2001</td>
<td>Sivadon-Tardy et al: Single regional reference centre case series</td>
<td>GBS cases after influenza-like infections (60%) peaked in winter months</td>
</tr>
<tr>
<td>1996–2004</td>
<td>Sivadon-Tardy et al: Time-series, single centre, reports of influenza-like illnesses</td>
<td>10 (14%) of 73 GBS patients had serologic influenza A, 4 (5%) of 73 influenza B</td>
</tr>
<tr>
<td><strong>UK</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1990–2005</td>
<td>Stowe et al: Self-controlled case series, primary-care database</td>
<td>Increased relative Incidence of GBS within 90 days of influenza-like illnesses</td>
</tr>
<tr>
<td>1991–2001</td>
<td>Tam et al: Case-control study, data from the UK General Practice Research Database</td>
<td>18-fold increased risk of GBS after influenza-like illnesses</td>
</tr>
</tbody>
</table>

GBS: Guillain–Barré syndrome

Table reproduced from Lehmann HC et al. © Elsevier Ltd 2010
<table>
<thead>
<tr>
<th>Vaccination season</th>
<th>Author: Study design</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976–77</td>
<td>Schonberger: Nationwide surveillance</td>
<td>8.8 additional GBS cases/million vaccines</td>
</tr>
<tr>
<td>1978–79</td>
<td>Hurwitz et al: Nationwide surveillance</td>
<td>No increased risk of GBS</td>
</tr>
<tr>
<td>1979–80, 1980–81</td>
<td>Kaplan et al: National surveillance</td>
<td>No increased risk of GBS</td>
</tr>
<tr>
<td>1990–2003</td>
<td>Haber et al: Nationwide passive surveillance</td>
<td>Decreased rates of GBS after vaccination</td>
</tr>
<tr>
<td>1990–2005</td>
<td>Stowe et al: Primary-care database</td>
<td>No increased risk of GBS</td>
</tr>
<tr>
<td>1992–2000</td>
<td>Hughes et al: Primary-care database</td>
<td>No or minimally increased risk of GBS</td>
</tr>
<tr>
<td>1992–2004</td>
<td>Juurlink et al: Health-insurance database</td>
<td>Increased RI of GBS, no increased hospitalizations</td>
</tr>
<tr>
<td>1990–2005</td>
<td>Vellozzi et al: Nationwide passive surveillance</td>
<td>No increased risk of GBS</td>
</tr>
<tr>
<td>1992–1994</td>
<td>Lasky et al: Hospital discharges, telephone interview</td>
<td>1 additional GBS case/million vaccinees</td>
</tr>
</tbody>
</table>

GBS: Guillain–Barré syndrome
RI: relative incidence

Table reproduced from Lehmann HC et al. © Elsevier Ltd 2010
### Distribution of preceding infections in GBS cases

<table>
<thead>
<tr>
<th>Exposures</th>
<th>GBS cases (n=553)</th>
<th>Controls (n=5445)</th>
<th>Matched OR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. exposed</td>
<td>%</td>
<td>No. exposed</td>
<td>%</td>
</tr>
<tr>
<td><em>Campylobacter</em></td>
<td>4</td>
<td>0.72</td>
<td>1</td>
<td>0.02</td>
</tr>
<tr>
<td><em>Epstein-Barr virus</em></td>
<td>2</td>
<td>0.36</td>
<td>1</td>
<td>0.02</td>
</tr>
<tr>
<td><em>Influenza-like illness</em></td>
<td>14</td>
<td>2.53</td>
<td>9</td>
<td>0.17</td>
</tr>
<tr>
<td><em>Influenza vaccination</em></td>
<td>1</td>
<td>0.18</td>
<td>47</td>
<td>0.86</td>
</tr>
<tr>
<td><em>Polio vaccination</em></td>
<td>16</td>
<td>2.89</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td><em>Infectious intestinal disease</em></td>
<td>13</td>
<td>2.35</td>
<td>18</td>
<td>0.33</td>
</tr>
<tr>
<td><em>Acute respiratory infection</em></td>
<td>45</td>
<td>8.14</td>
<td>102</td>
<td>1.87</td>
</tr>
</tbody>
</table>

* United Kingdom General Practice Database, 1991–2001
Table reproduced from Tam CC et al. with kind permission from PLoS ONE. © The Author(s) 2007

- Influenza vaccination appeared protective, but this result was not significant (p=0.081)
Surveillance for GBS after 2009 H1N1 vaccination

• Emerging Infections Program (EIP)\textsuperscript{1,2}
  – Active surveillance during October 2009\textsuperscript{May} 2010
  – 45 million residents in 10 states in the USA were covered
  – Medical charts were reviewed by trained surveillance officers
  – A telephone questionnaire was administered to persons with suspected GBS to gather medical and vaccination history

• Epidemiology:\textsuperscript{2}

\begin{itemize}
  \item 45 million persons under surveillance
  \item 707 suspected GBS cases
  \item 411 cases met the criteria
    \begin{itemize}
      \item 349 confirmed
      \item 62 probable
    \end{itemize}
  \item 78\% of patients completed the telephone survey
  \item 85\% were aged $\geq 25$ years
  \item 52\% were male
  \item 68\% were white
  \item 15\% required mechanical ventilation
  \item 3\% died
\end{itemize}

EIP analysis\textsuperscript{1,2}

- 14 million H1N1 vaccine doses were administered and 1.6 million person-years were exposed to the H1N1 vaccine during the EIP surveillance.
- 57% higher incidence of GBS during the 42 days following H1N1 vaccination.
- Excess risk of 2009 H1N1 vaccine: 0.74 cases of GBS per 1 million vaccinations.
- Safety profile:
  - Comparable risk to the trivalent seasonal influenza vaccine (approximately 1 excess case per million vaccinations).
  - 10-fold lower risk than the 1976 swine influenza vaccine (approximately 10 excess cases per million vaccinations).
- Interpretation:
  - The 62 probable cases may give rise to an overestimation of the number of cases with true GBS.
  - A number of GBS cases might be attributable to antecedent illnesses prior to vaccination.

Morbidity and mortality following 2009 H1N1 vaccine

- Influenza and influenza-like illnesses are associated with significant morbidity and mortality\(^1\)
  - Hospitalization rate of 222 patients per million
  - Death rate of 9.7 per million
  - Slight increased risk for GBS

- The incidence of GBS following 2009 H1N1 vaccine is small compared with the morbidity and mortality prevented through the widespread use of the vaccine\(^2\)

- **Vaccination remains the most effective method to prevent serious illness and death from 2009 H1N1 influenza infection**\(^1\)

GBS: Guillain-Barré syndrome

Recurrences of GBS/CIDP after vaccinations

- 245 GBS and 76 CIDP patients completed a questionnaire on vaccinations aimed at assessing whether GBS and CIDP patients could safely receive vaccinations or not
- 23 (9%) GBS and 4 (5%) CIDP patients were diagnosed with an auto-immune disorder
- 106 GBS and 24 CIDP patients received an influenza vaccination
  - No recurrence of GBS was reported following vaccination
  - 5 CIDP patients reported an increase in symptoms following one or more vaccinations
- Pain or severe fatigue was reported in approximately 70% of GBS and CIDP patients and quality of life was significantly reduced
- **Conclusion:** Influenza vaccinations seem relatively safe for patients with GBS and CIDP

GBS: Guillain-Barré syndrome
CIDP: Chronic inflammatory demyelinating polyradiculoneuropathy

GBS/CIDP Foundation International: Influenza vaccination guidelines

- Patients who developed GBS within 4-6 weeks of receiving immunization should avoid vaccination in the future.

- Patients whose GBS did not follow soon after vaccination should consider getting vaccinated.

- Former GBS patients should discuss the pros and cons of receiving a vaccination with their primary physicians to evaluate the risks and benefits.

- Further research is needed to determine if there is any relationship between the influenza vaccination and CIDP or worsening of CIDP.

GBS: Guillain-Barré syndrome
CIDP: Chronic inflammatory demyelinating polyradiculoneuropathy

CDC recommendations 2014–2015 flu season

Who should be vaccinated?

- Everyone ≥6 months of age
- People at high risk of developing serious complications like pneumonia if they contract influenza
  - People with certain medical conditions (asthma, diabetes, chronic renal failure, and chronic lung disease)
  - Pregnant women
  - People ≥65 years of age
- People who live with, or care for, those who are at high risk of developing serious complications

Who should not be vaccinated?

- People with a severe allergy to chicken eggs
- People who have had a severe reaction to an influenza vaccination
- Children <6 months of age
- People who have a current moderate-to-severe illness with a fever
- People with a history of GBS that occurred after receiving influenza vaccine and who are not at risk of severe illness from influenza

Trivalent vaccines protect against two influenza A viruses and one influenza B virus

- Standard dose intramuscular
- Intradermal trivalent injection (smaller needle)
- High dose trivalent injection (approved age 65 or older)
- Trivalent injection containing virus grown in cell culture
- Egg-free trivalent injection

Quadrivalent vaccines protect against two influenza A viruses and two influenza B viruses

- Standard dose intramuscular
- Nasal spray vaccine (LAIV)
Influenza infections: Facts to know

- On average, more than 200,000 people per year are hospitalized for influenza-associated illnesses in the USA\(^1\)
- Influenza-associated deaths during the last three decades are estimated to range between 3,000 to 49,000\(^2\)
- Influenza is the 8\(^{th}\) leading cause of death in adults in the USA\(^3\)

Summary

• Between 1976 and 1977 A/New Jersey influenza vaccination increased the GBS rate in all adult populations

• No to minimally increased risk of GBS was shown in an analysis of 10 reports on GBS after influenza immunization

• The incidence of GBS following 2009 H1N1 vaccine is small compared with the morbidity and mortality prevented through the widespread use of the vaccine
  
  – Hospitalization rate of influenza and influenza-like illnesses in 2009 was 222 patients per million and the death rate was 9.7 per million
  
  – Excess risk of 2009 H1N1 vaccine: 0.74 cases of GBS per 1 million vaccinations
    
    • Comparable risk to the trivalent seasonal influenza vaccine and 10-fold lower risk than the 1976 swine influenza vaccine

• Influenza vaccinations seem relatively safe for patients with GBS and CIDP

• GBS has also been reported after immunization with the hepatitis, tetanus and meningococcal vaccines but the risk of developing GBS did not differ from the background incidence of GBS

• The risk and benefit of any vaccination should be assessed on an individual basis by the clinician and the patient

GBS: Guillain-Barré syndrome
CIDP: Chronic inflammatory demyelinating polyradiculoneuropathy