



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<sup>1</sup>
  - 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

GBS cases	No of cases <sup>2</sup>	Summary of findings <sup>1,2</sup>
Vaccinated cases prior to GBS onset	504	<ul style="list-style-type: none"> <li>• Increased GBS rate in all adult categories</li> <li>• 4.9 <math>\square</math> 5.9 GBS cases per million vaccinees</li> <li>• 32 (6%) deaths</li> <li>• Greatest risk for GBS within 5 weeks after vaccination</li> </ul>
Unvaccinated	440	<ul style="list-style-type: none"> <li>• Attack rate of 0.79 per million per month</li> <li>• 26 (4.7%) deaths</li> </ul>
Exclusions	154	<ul style="list-style-type: none"> <li>• 33 cases were excluded due to missing or insufficiently complete data</li> <li>• 121 cases where the vaccine had not been recommended were also excluded (patients &gt;18 years of age)</li> </ul>
<b>Total</b>	<b>1,098</b>	

GBS: Guillain  $\square$  Barré syndrome

1. Schonberger LB et al. Am J Epidemiology 1979;110:105-23

2. Langmuir AD et al. Am J Epidemiol 1984;119:841-79

# GBS after influenza infection<sup>1</sup>

	Vaccination season	Author: Study design	Outcomes
France	1996–2001	Sivadon-Tardy et al: Single regional reference centre case series	GBS cases after influenza-like infections (60%) peaked in winter months
	1996–2004	Sivadon-Tardy et al: Time-series, single centre, reports of influenza-like illnesses	10 (14%) of 73 GBS patients had serologic influenza A, 4 (5%) of 73 influenza B
UK	1990–2005	Stowe et al: Self-controlled case series, primary-care database	Increased relative Incidence of GBS within 90 days of influenza-like illnesses
	1991–2001	Tam et al: Case-control study, data from the UK General Practice Research Database	18-fold increased risk of GBS after influenza-like illnesses
	1993–2002	Tam et al: Time-series method, influenza, hospital admissions	Association between laboratory-confirmed influenza A and hospital admissions

GBS: Guillain-Barré syndrome

1. Lehmann HC et al. Lancet Infect Dis 2010;10:643-51  
Table reproduced from Lehmann HC et al. © Elsevier Ltd 2010

# GBS after influenza immunization<sup>1</sup>

Vaccination season	Author: Study design	Outcomes
1976–77	Schonberger: Nationwide surveillance	8.8 additional GBS cases/million vaccines
1978–79	Hurwitz et al: Nationwide surveillance	No increased risk of GBS
1979–80, 1980–81	Kaplan et al: National surveillance	No increased risk of GBS
1980–88	Roscelli et al: US Army health database	No increased risk of GBS
1990–2003	Haber et al: Nationwide passive surveillance	Decreased rates of GBS after vaccination
1990–2005	Stowe et al: Primary-care database	No increased risk of GBS
1992–2000	Hughes et al: Primary-care database	No or minimally increased risk of GBS
1992–2004	Juurlink et al: Health-insurance database	Increased RI of GBS, no increased hospitalizations
1990–2005	Vellozzi et al: Nationwide passive surveillance	No increased risk of GBS
1992–1994	Lasky et al: Hospital discharges, telephone interview	1 additional GBS case/million vaccinees

USA

GBS: Guillain-Barré syndrome  
RI: relative incidence

1. Lehmann HC et al. Lancet Infect Dis 2010;10:643-51  
Table reproduced from Lehmann HC et al. © Elsevier Ltd 2010

# Distribution of preceding infections in GBS cases<sup>1\*</sup>

Exposures	GBS cases (n=553)		Controls (n=5445)		Matched OR	P value
	No. exposed	%	No. exposed	%		
<i>Campylobacter</i>	4	0.72	1	0.02	38.38	0.001
Epstein-Barr virus	2	0.36	1	0.02	20.00	0.014
Influenza-like illness	14	2.53	9	0.17	18.64	<0.001
Influenza vaccination	1	0.18	47	0.86	0.16	0.081
Polio vaccination	16	2.89	0	0.00	∞	∞
Infectious intestinal disease	13	2.35	18	0.33	7.26	<0.001
Acute respiratory infection	45	8.14	102	1.87	5.15	<0.001

\* 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)

GBS: Guillain-Barré syndrome

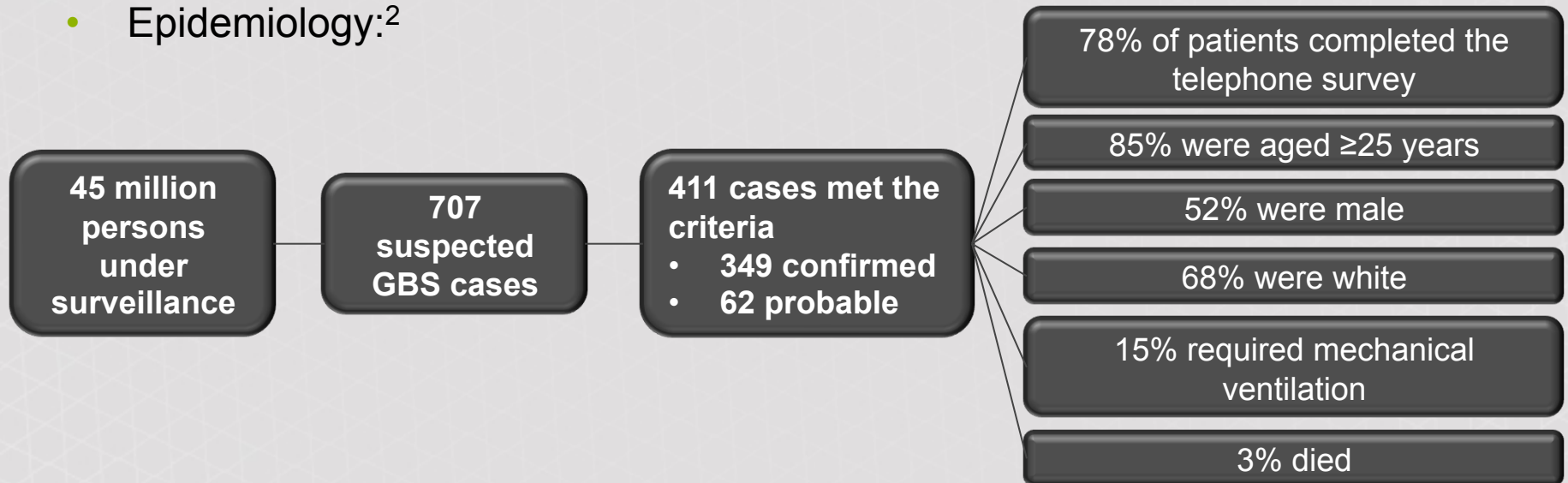
OR: odds ratio

1. Tam CC et al. PLoS ONE 2007;2(4):e344

Table reproduced from Tam CC et al. © The Author(s) 2007

# Surveillance for GBS after 2009 H1N1 vaccination

- Emerging Infections Program (EIP)<sup>1,2</sup>
  - Active surveillance during October 2009–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:<sup>2</sup>



1. Centers for Disease Control and Prevention. MMWR 2010. Available at <http://www.cdc.gov/mmwr/pdf/wk/mm59e0602.pdf>. Accessed May 2015

2. Wise ME et al. Am J Epidemiol 2012;175:1110-9

# EIP analysis<sup>1,2</sup>

- 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**

1. Centers for Disease Control and Prevention. MMWR 2010. Available at <http://www.cdc.gov/mmwr/pdf/wk/mm59e0602.pdf>. Accessed May 2015

2. Wise ME et al. Am J Epidemiol 2012;175:1110-9

# Morbidity and mortality following 2009 H1N1 vaccine

- Influenza and influenza-like illnesses are associated with significant morbidity and mortality<sup>1</sup>
  - 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<sup>2</sup>
- **Vaccination remains the most effective method to prevent serious illness and death from 2009 H1N1 influenza infection<sup>1</sup>**

GBS: Guillain-Barré syndrome

1. Centers for Disease Control and Prevention. MMWR 2010. Available at <http://www.cdc.gov/mmwr/pdf/wk/mm59e0602.pdf>. Accessed May 2015

2. Wise ME et al. Am J Epidemiol 2012;175:1110-9



# Recurrences of GBS/CIDP after vaccinations<sup>1</sup>

- 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<sup>1</sup>

- 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

1. GBS/CIDP Foundation International. Available at:  
<http://www.gbs-cidp.org/wp-content/uploads/2013/08/Fall2013Newsletter.pdf>. Accessed

# CDC recommendations 2014 2015 flu season<sup>1</sup>

## 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  $\geq 65$  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

# Influenza vaccine options 2014 2015<sup>1</sup>

- 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<sup>1</sup>
- Influenza-associated deaths during the last three decades are estimated to range between 3,000 to 49,000<sup>2</sup>
- Influenza is the 8<sup>th</sup> leading cause of death in adults in the USA<sup>3</sup>

1. Centers for Disease Control and Prevention. Available at <http://www.cdc.gov/flu/about/qa/hospital.htm>. Accessed May 2015
2. Centers for Disease Control and Prevention. Available at [http://www.cdc.gov/flu/about/disease/us\\_flu-related\\_deaths.htm](http://www.cdc.gov/flu/about/disease/us_flu-related_deaths.htm). Accessed May 2015
3. Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm>. Accessed May 2015

# 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<sup>1,2</sup>
- 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

1. Van Doorn P et al. Lancet Neurol 2008;7:939-50

2. Vucic S et al. J Clin Neurosci 2009;16:733-41