



## Abstract

**Background:** Guillain-Barré syndrome (GBS) is an acute polyradiculopathy, thought to be an autoimmune disorder. GBS has been reported following vaccines. The current CDC recommendation is to avoid vaccinating individuals who have had a history of GBS within six weeks of a prior influenza vaccination if they are not at high risk of severe complications from influenza illness.

**Methods:** We identified GBS cases from the Kaiser Permanente Northern California (KPNC) databases from 1994 into 2006, using hospital discharge codes; each medical record was neurologist-reviewed and only confirmed GBS cases were included for follow up. We followed confirmed cases through 2008 for vaccinations and recurrent GBS. To distinguish recurrent GBS from Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), we defined recurrent GBS as  $\geq$  one subsequent episode of acute monophasic neuropathy with near complete recovery between acute episodes.

**Results:** We identified 550 neurologist-confirmed individual cases of GBS over 33 million person-years. During the follow-up period, 989 vaccines were given to 279 of these individuals after the diagnosis of GBS. 405 TIV vaccines were administered to 107 individuals with a prior diagnosis of GBS. 18 of the initial 550 cases of GBS had onset within 6 weeks of TIV; of these, 2 were revaccinated with influenza vaccines and these 2 did not experience a recurrence of GBS. Only 6 individuals had a second (recurrent) diagnosis of GBS. Among these 6 individuals, only 1 had any vaccine exposure at all in the year prior to the 2nd onset of GBS. This was a single dose of MMR 4 months prior to the onset of the 2nd episode of GBS.

**Conclusions:** In our population of over 3 million members, over an 11 year period, risk of GBS recurrence was low (6/550 = 1.1%). There were no cases of recurrent GBS after influenza vaccination, and none within an accepted risk interval after any vaccine. There were too few GBS cases following influenza vaccines to draw conclusions about revaccinating those whose GBS occurs within 6 weeks of TIV.

## Background

- Guillain-Barré syndrome (GBS) is thought to be an autoimmune disorder
- May involve molecular mimicry
- An antecedent event or illness is reported in up to two thirds of patients with GBS.
- GBS has also been reported following multiple vaccines, including rabies, combined diphtheria, pertussis and tetanus, Hepatitis B, Influenza, and Meningococcal conjugate vaccines.

## Currently the CDC recommends:

- Avoid influenza vaccines in persons who have a history of GBS within six weeks after a previous influenza vaccination and are not at high risk for severe influenza illness complications
- This recommendation is often interpreted as no vaccination for all persons with any history of GBS
  - Evidence based recommendations regarding vaccinating persons with a history of GBS are needed.

## Objective

To retrospectively identify persons in our system with a history of GBS, follow hospital admissions and vaccines for as long as possible, and determine whether they are at higher risk of relapse of GBS after re-vaccination

## Methods

### Study Population:

Identified from the Kaiser Permanente Northern California (KPNC) databases.

- Over 3.2 million members
- Integrated health care and electronic medical records

This study cohort included

1. Persons with a history of GBS
2. Aged 5 years or older to minimize the effect of multiple vaccination schedules in the younger ages

## Case Ascertainment

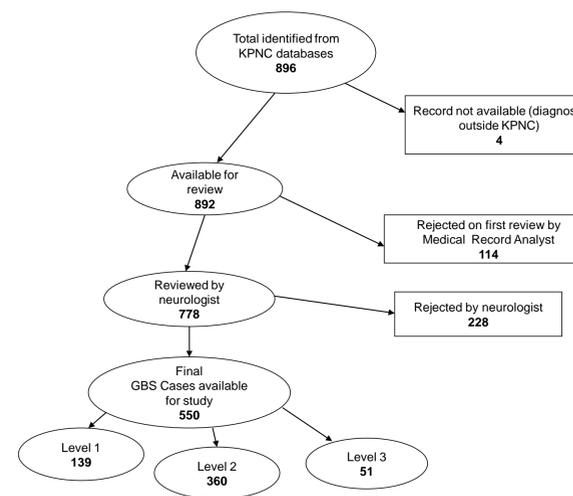
Potential GBS cases were identified by ICD9 code 357.0 in hospital discharge summary diagnoses from January 1994 into 2006. The Brighton case definition for GBS was used for chart review.

- We accepted levels 1, 2, and 3 for our cohort
- All cases identified in the electronic databases were then reviewed by a trained medical records analyst (MRA)
- Cases deemed possible by the MRA were referred to further review by a Neurologist.
- All confirmed GBS patients were monitored through 2008 for any recurrent GBS, and for all vaccine exposures.

- **Recurrent GBS** was defined as two or more episodes of acute monophasic neuropathy with near complete recovery between episodes.

## Results

We identified 896 cases of potential GBS from the 12 year study period



## Recurrence of GBS

Of the 550 cases initially confirmed as GBS, 37 individuals appeared in the electronic database initially as having multiple episodes of GBS.

## Results (continued)

### Recurrence of GBS

After chart and neurologist review, **6 individuals (1.1% of the group of 550) were confirmed as having recurrent GBS**

- These 6 individuals each had only one episode of recurrent GBS.
- The calculated rate of recurrence of GBS was 1.5 per 1,000 person-years (95% Poisson CI 0.6 – 3.3). Table 1 shows characteristics of patients and time to recurrence for the recurrent cases.

Table 1. Time to recurrence of GBS Northern California Kaiser, 1994-2006

Case	Age at 1st GBS	Age at 2nd GBS	Sex	Years to Recurrence
1	25	36	F	11.0
2	43	45	F	1.8
3	66	79	M	13.2
4	26	66	F	40.0
5	28	31	F	2.9
6	52	54	M	2.9

Vaccines given to people after the diagnosis of GBS, Northern California Kaiser, 1994-2006 (N=550)

Vaccine Type	Number of vaccinations after GBS
Inactivated influenza	405
Pneumovax	151
Tetanus diphtheria (DT)	143
Hepatitis A	78
Hepatitis B	42
MMR	19
Inactivated Polio	17
DT and acellular Pertussis	11
Zoster	10
Inactivated Typhoid	10
Other	103
<b>Total</b>	<b>989</b>

### Vaccines and recurrent GBS

Among the 6 individuals with confirmed GBS recurrence, only 1 had any vaccine exposure within the year prior to the recurrent GBS episode. The vaccine exposure was a single dose of MMR administered 4 months prior to the onset of the recurrent GBS episode.

## Results (continued)

### GBS and Influenza vaccines

Of the 550 cases of GBS, 18 (3.3%) had initial onset within 6 weeks of TIV.

- These 18 people were less likely to have received additional influenza vaccines than were those who developed GBS with no temporal association with TIV
- 2 (11%) of the 18 received subsequent influenza vaccines vs. 105 of 532 (20%) of the those who developed GBS not in relation to TIV, but the difference was not significant (p=0.6 by Fisher exact test).
- None of the 18 GBS cases which originally followed TIV, including the 2 with subsequent TIV administration, had a recurrence of GBS.
- None of the GBS cases followed receipt of live intranasal influenza vaccine.
- Among the 107 individuals with a previous diagnosis of GBS who received a total of 405 doses of TIV, there were no cases of recurrent GBS within the year following TIV (95% binomial CI, 0-0.91 per 100 doses).

## Summary

We followed 550 cases of confirmed GBS over many years, and found 6 episodes of recurrence. None of these recurrences were temporally related to vaccine administration

## Conclusions

With over 30 million person-years of follow up, we found that recurrent GBS is relatively rare. We found no evidence that vaccination is associated with recurrent GBS.

- We did not observe any recurrent GBS in the 18 GBS cases which initially occurred within 6 weeks following receipt of influenza vaccine.
- We did not have enough power to evaluate an association of repeat influenza vaccination and recurrent GBS.