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Original Contribution

Immunization and Bell's Palsy in Children: A Case-Centered Analysis

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Bell's palsy (BP) is an acute and idiopathic paralysis of the facial nerve, with an estimated incidence ranging from 11.5 per 100,000 person-years to 53.3 per 100,000 person-years in different populations. BP has been reported following immunization with inactivated trivalent influenza vaccine (TIV) and hepatitis B virus (HBV) vaccine. Epidemiologic studies examining this association among children are lacking. From 2001 through 2006, all children aged ≤18 years diagnosed with BP within the Kaiser Permanente Northern California population were identified using *International Classification of Diseases*, Ninth Revision, code 351.0. All electronically identified cases were reviewed and adjudicated by an otolaryngologist ($n = 233$). Using a case-centered approach, the authors examined the risk of BP during 3 risk intervals. Immunization with TIV (odds ratio (OR) = 0.7, 95% confidence interval (CI): 0.2, 2.8), HBV vaccine (OR = 0.8, 95% CI: 0.2, 2.4), or any vaccine (treating all vaccines combined; OR = 0.9, 95% CI: 0.6, 1.4) was not associated with increased risk of BP 1–28 days after immunization. Similarly, no association was found between vaccines and BP during the periods 1–14 and 29–56 days following immunization. Results of this study suggest that there is no association between immunization and BP in children.

Bell's palsy; child; immunization; vaccines

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; ICD-9, *International Classification of Diseases*, Ninth Revision; KPNC, Kaiser Permanente Northern California; OR, odds ratio; TIV, trivalent influenza vaccine.

Editor's note: *An invited commentary on this article appears on page 886, and the authors' response appears on page 888.*

Bell's palsy is an acute, idiopathic, and usually unilateral paralysis of the seventh cranial (i.e., facial) nerve. Estimates of the incidence of this disease range from 11.5 per 100,000 person-years to 53.3 per 100,000 person-years in different populations (1–5). Persons with Bell's palsy typically have decreased forehead movement, inability to close the eye, disappearance of the nasolabial fold, and altered sensation on the affected side of the face, as well as drawing of the mouth to the unaffected side of the face; additional symptoms such as hyperacusis, decreased production of tears, and altered tastes may also be present (6–8). Bell's palsy is typically a self-limiting disorder with a favorable prognosis; however, its abrupt onset, rapid progression, and dramatic presentation can be frightening, especially when it occurs in a child.

Bell's palsy is a diagnosis of exclusion. Known congenital (e.g., birth trauma), genetic (e.g., Melkersson-Rosenthal syndrome), and acquired (e.g., infection, trauma, benign and malignant tumors) causes of facial nerve paralysis need to be ruled out before the diagnosis of Bell's palsy is made (9). The etiology of Bell's palsy is not completely understood; however, infectious (e.g., reactivation of herpes simplex virus type 1), immunologic, and vascular factors have been postulated to cause this disease (10–14).

Immunization has been speculated on as a cause of Bell's palsy. In particular, multiple case reports have described Bell's palsy following immunization with influenza and hepatitis B virus (HBV) vaccines (15). However, few epidemiologic studies of the association between immunization and Bell's palsy have been published. An intranasal inactivated

influenza vaccine that included *Escherichia coli* heat-labile toxin as a mucosal adjuvant was shown to be strongly associated with Bell's palsy among persons aged 18 years or more (16). Another study based on the Vaccine Adverse Event Reporting System indicated a potential signal for Bell's palsy following immunization with intramuscular inactivated influenza vaccine (17). That study included only 5 cases younger than 18 years of age. A few other studies have shown no associations between immunization and Bell's palsy; however, they similarly included only a small number of children (18, 19). To our knowledge, no population-based epidemiologic study of the association between immunization and Bell's palsy has been conducted exclusively among children.

Here we report the results of a population-based epidemiologic study of immunization and Bell's palsy among children aged 18 years or younger enrolled in a large integrated health-care delivery system in Northern California. Our specific aim was to examine the association between immunization with intramuscular inactivated trivalent influenza vaccine (TIV), HBV vaccine, or any vaccine (treating all vaccines combined, regardless of type) and Bell's palsy among children using a novel case-centered analytic approach.

MATERIALS AND METHODS

Source population

This study was conducted within the population of Kaiser Permanente Northern California (KPNC) and was approved by the KPNC Health Services Institutional Review Board. KPNC is a large integrated health-care delivery system with approximately 3.2 million members. The population covered by KPNC is heterogeneous with regard to age, sex, race, and socioeconomic status and represents the region's underlying census distribution, except at extremes of age and income (20). Therefore, investigations carried out within this population accurately approximate population-based studies. KPNC members receive almost all of their health care at KPNC facilities, where all outpatient, emergency department, and inpatient encounters are recorded in large administrative databases within the system. Laboratory tests, medications, and most other services are covered by the plan and are provided at KPNC facilities. Hospitalizations and emergency department visits that occur outside of the health plan are captured via claims.

Case ascertainment and definition

From January 1, 2001, through December 31, 2006, all children aged 18 years or younger diagnosed with Bell's palsy were identified using *International Classification of Diseases,* Ninth Revision (ICD-9), code 351.0. Cases had to have been continuously enrolled at KPNC during the 12 months prior to the diagnosis of Bell's palsy. Comprehensive chart reviews were conducted to extract information on immunization, demographic characteristics, history of present illness, past medical history, family history, diagnostic tests, and treatment options used for these children. Persons identified during chart review as having had a history of Bell's palsy prior to the start of the study period (January 1, 2001) were excluded from the analyses. An otolaryngologist (B. R.) reviewed all cases using a case disposition form and categorized each case as definite, probable, or rejected. The case definition for this study was developed on the basis of a literature review and consensus among the authors.

Cases categorized as definite had to meet all of the following criteria: 1) a definitive diagnosis of Bell's palsy in the chart, 2) unilateral weakness of all facial muscles (i.e., involvement of the forehead, eyelid, mouth, and cheek muscles), 3) acute onset with 72 hours between initial signs and maximum paresis, and 4) no report of head trauma or ipsilateral otologic disease within the 30 days prior to diagnosis, and no history of cerebrovascular incident, otologic surgery, brain tumor, sickle cell disease, Guillain-Barré syndrome, or other neurologic signs such as weakness of an extremity, coordination abnormalities, or other reflex or strength abnormalities or asymmetries. Probable cases were children in whom unilateral weakness of all facial muscles was not documented (see criterion 2 above) or the period of time between initial signs and maximum paresis was more than 72 hours (see criterion 3 above). Rejected cases were children who did not meet the case definition due to absence of any facial muscle weakness or the presence of another cause for facial muscle weakness (see criterion 4 above).

Statistical analysis

We used a novel case-centered analytic approach to evaluate the association between immunization and Bell's palsy. Features of the case-centered analytic approach have been described elsewhere (21). This approach has also been used in other studies of vaccine effectiveness and safety in recent years (22, 23). In brief, the case-centered analysis uses a ''backward'' approach, where the *observed* odds of exposure (e.g., immunization) during a certain period of time (i.e., the risk interval) prior to the onset of an outcome (e.g., adverse event) are compared with the *expected* odds of exposure during the same risk interval. In other words, in the current study, the case-centered approach examined whether a higher-than-expected proportion of cases received the vaccine during a prespecified risk interval.

To conduct the analysis using this approach, we included in the analytic data set only cases who had received at least 1 immunization during an observation period of 1 year prior to the onset of Bell's palsy. For each case, the observed immunization status (a dichotomous dependent variable coded 0 or 1) during prespecified risk intervals of 1–14 days (weeks 1–2), 1–28 days (weeks 1–4), and 29–56 days (weeks 5–8) prior to onset was determined. These risk intervals were selected on the basis of the literature and our understanding of the pathophysiology of the disease. This observed immunization status was compared with the expected odds of immunization for each case, which had been calculated prior to conducting the regression analysis. To calculate the expected odds, we created the stratum (i.e., risk set) comprising all KPNC members who were similar to each case on the day of developing Bell's palsy and computed the odds of immunization within the risk intervals in the entire stratum, including the case him/herself. KPNC members in the stratum had to have received the same vaccine during the observation

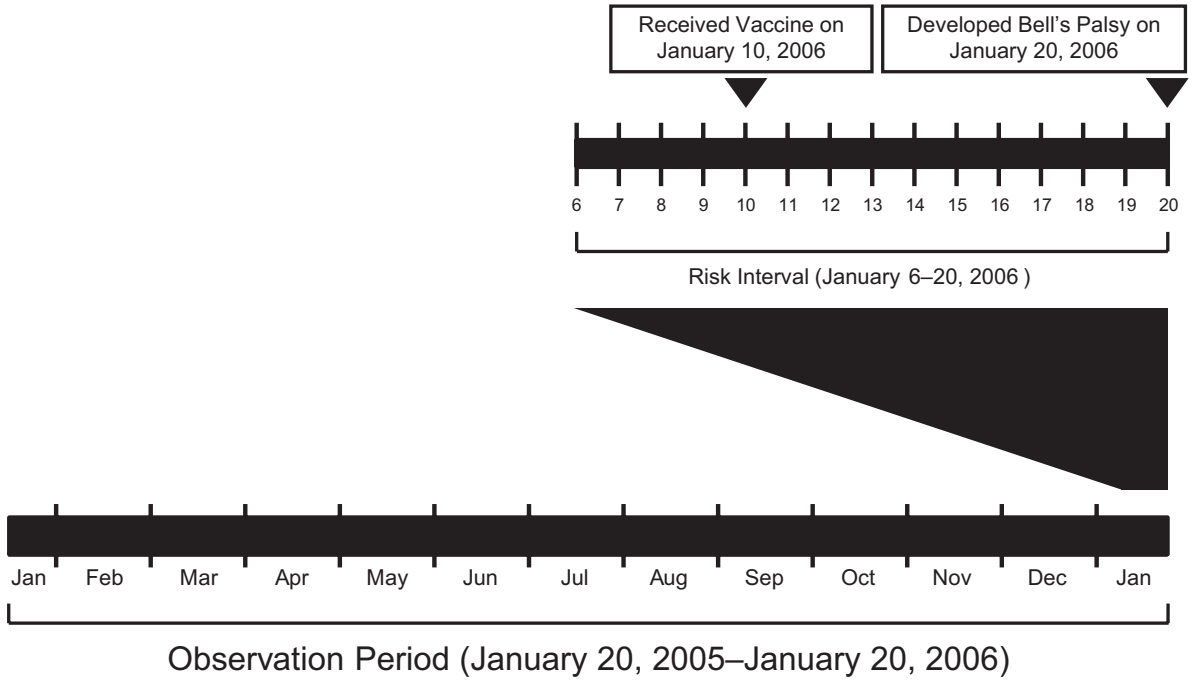

Figure 1. Pictorial representation of the case-centered method for a hypothetical case of Bell's palsy. The observed immunization status in this child is 1 because she received the vaccine within the risk interval of interest (January 6–20, 2006). The expected probability of immunization in this child is calculated on the basis of the proportion of all immunized age- and sex-matched children in the underlying population (including that child herself) who had received the same vaccine within that risk interval.

period of 1 year prior to the onset of Bell's palsy in that case and had to belong to the same risk set as that case with regard to age and sex. The age risk sets were created as follows: by month of age through the first year of life, by year of age from age 1 through age 10, and by 2 years of age through age 18. We conducted 3 separate analyses for immunization with TIV, HBV vaccine, or any vaccine (treating all vaccines combined, regardless of type).

Consider the pictorial representation of the case-centered method for a hypothetical case shown in Figure 1. The observed immunization status inside the risk interval of 1–14 days for a 5-year-old female who received a vaccine on January 10, 2006, and developed Bell's palsy 10 days later on January 20, 2006, would be 1, because she received the vaccine inside the risk interval of 1–14 days. The expected probability of immunization in this child inside the risk interval of 1–14 days would be obtained from the proportion of all 5-year-old females in the KPNC population, including that child herself, who had received the same vaccine between January 6, 2006, and January 20, 2006 (i.e., within 14 days prior to the onset of Bell's palsy in that child). Notably, 5-year-old females in the KPNC population who would generate the expected probability of immunization in this example all had to have received the same vaccine during the observation period of 1 year prior to the onset of Bell's palsy in that child (i.e., from January 20, 2005, to January 20, 2006).

We conducted logistic regression analyses with case-centered specification to examine the strength of the association between immunization and Bell's palsy. The logarithm of the expected odds (i.e., logit) of immunization inside the risk interval was entered into the models as an offset term. The models included only an intercept with no covariate and had the following general form:

$$\text{Logit}(P_1) = \text{logit}(P_0) + \beta_0,$$

where

P_1 is the observed probability of immunization inside the risk interval among cases;

P_0 is the expected probability of immunization inside the risk interval among cases; and

β_0 is the intercept.

Therefore, exponentiation of β_0 provides an odds ratio for the association between immunization and Bell's palsy inside the risk interval. The logistic regression model drops all cases for whom the expected probability of immunization inside the risk interval is 0 or 1; these are noninformative cases and do not contribute to the analysis.

For the analysis, all definite and probable cases were combined. We conducted sensitivity analyses by modifying the duration of the observation period from 1 year to 9 months for TIV and compared the results. The sensitivity

analysis was an attempt to limit the exposure status (i.e., TIV) to the same season. Analyses were conducted using SAS 9.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

From January 1, 2001, through December 31, 2006, 977 children aged 18 years or younger were identified with an ICD-9 code for Bell's palsy as indicated in their electronic records. Following chart review and adjudication, 119 children were rejected as cases. An additional 36 children were excluded from the analysis because of a previous history of Bell's palsy. Of the remaining 822 children, 233 were included in the analysis because they had received at least 1 immunization during the 12 months prior to the onset of Bell's palsy. Of these 233 children, 61 (26.2%) and 172 (73.8%) were categorized as definite and probable cases, respectively. The reasons for being classified as a probable case instead of a definite case were that unilateral involvement of all facial muscles was not noted and/or maximum paresis did not occur within 72 hours following the onset of initial signs.

Characteristics of the cases are presented in Table 1. The mean age of cases ($n = 233$) at the onset of Bell's palsy was 10.3 years (range, 11 days–17.8 years). The distribution of cases by age was approximately bimodal, with peaks at younger and older ages (Figure 2). The majority of cases ($n = 141$; 60.5%) were female. Among cases with known race ($n = 189$), the majority were white ($n = 99$; 52.3%); among those with known ethnicity ($n = 195$), almost one-half were Hispanic ($n = 90$; 46.2%). Two cases were pregnant at the time of onset of signs and symptoms. Only a small proportion of all cases were noted to have had a history of infection with herpes simplex virus (6.4%) or varicella zoster virus (0.4%) within 90 days prior to diagnosis or a history of central nervous system disease (4.3%), diabetes (1.3%), or hypertension (0.9%) at any point in their lifetime. Among cases for whom data regarding family history of Bell's palsy were available ($n = 168$), 8 (4.8%) indicated that at least 1 member of their family had previously been diagnosed with Bell's palsy. Cases had received a wide range of vaccines during the 12 months prior to the onset of Bell's palsy (Table 2).

Immunization with TIV or HBV vaccine was not significantly associated with the occurrence of Bell's palsy during any of the risk intervals (1–14 days, 1–28 days, or 29–56 days) (Table 3). In addition, immunization with any vaccine was not significantly associated with the occurrence of Bell's palsy during the risk intervals of 1–14 days (odds ratio (OR) = 1.1, 95% confidence interval (CI): 0.6, 1.9), 1–28 days (OR = 0.9, 95% CI: 0.6, 1.4), or 29–56 days (OR = 0.7, 95% CI: 0.4, 1.1). In the sensitivity analysis, modifying the observation period from 1 year to 9 months for TIV did not materially change the results (data not shown).

DISCUSSION

To our knowledge, this study currently represents the largest population-based epidemiologic investigation of the association between immunization and Bell's palsy to be conducted among children. In this study, we did not find an association between immunization with TIV, HBV vaccine, or any vaccine and Bell's palsy during risk intervals of 1–14 days, 1–28 days, and 29–56 days following immunization among children aged 18 years or younger.

We chose the 3 aforementioned risk intervals partially on the basis of prior evidence on the onset of Bell's palsy following immunization. Zhou et al. (17) suggested that the majority of cases reported to the Vaccine Adverse Event Reporting System occurred during the first month following immunization with intramuscular inactivated influenza vaccine, while Mutsch et al. (16) showed that the period of highest risk was the second month following immunization with intranasal inactivated influenza vaccine. We chose risk intervals of both 1–4 weeks and 5–8 weeks following immunization, as well as a shorter risk interval of 1–2 weeks following immunization, to examine the association in all 3 of those periods of time. Stowe et al. (19) investigated the association between intramuscular inactivated influenza vaccine and Bell's palsy using the United Kingdom General Practice Research Database during prespecified risk intervals of 1–30 days, 31–60 days, and 61–91 days and did not find any significantly increased risk during those periods of time. That study included a very small number of children; only 3.4% of all Bell's palsy episodes occurred in persons younger than 30 years of age, as reported by the authors (19).

In this study, all cases included in the analysis had to have received at least 1 immunization during the 12 months prior to the onset of Bell's palsy. Therefore, the approximately bimodal age distribution of cases was a reflection of the recommended immunization schedule in the United States, as opposed to the natural epidemiology of Bell's palsy in children. It has been previously shown that the incidence of Bell's palsy among children increases by age; it only slightly increases between birth and age 9 years and is noticeably higher among children aged 10–18 years (1, 2, 4). Notably, compared with the underlying population of children enrolled in KPNC, females and those of Hispanic ethnicity were overrepresented among the cases in this study. A few previous epidemiologic studies of Bell's palsy in children in the United States have shown that females and persons of Hispanic ethnicity may be at increased risk of Bell's palsy, for yet unknown reasons (1, 2).

Our findings are strengthened by the large sample size of the study, as well as adjudication of all cases by an independent otolaryngologist. In addition, the novel case-centered analytic approach used in this study has several methodological strengths. First, by constructing the expected odds of immunization within the risk interval based on the actual day of Bell's palsy occurrence in each case, we alleviated potential concerns about confounding by time (i.e., effects of season, day of the week, etc.). Second, the point estimates (i.e., odds ratios) obtained from the logistic regression model in our study can be interpreted as hazard ratios, because the logistic regression model with a case-centered specification has been shown to be equivalent to a stratified Cox proportional hazards regression model, when the adverse event is regressed on a time-varying indicator of immunization (21). Each record in the case-centered model summarizes an entire risk set in the corresponding Cox model; the same likelihood

Table 1. Characteristics of Definite and Probable Cases of Bell's Palsy Within the Population of Kaiser Permanente Northern California, 2001–2006

Characteristic	Definite Bell's Palsy (n = 61)			Probable Bell's Palsy (n = 172)			All Cases (n = 233)		
	No.	%	Mean or Median	No.	%	Mean or Median	No.	%	Mean or Median
Mean age, years			9.8[a]			10.5[b]			10.3[c]
Sex									
Female	38	62.3		103	59.9		141	60.5	
Male	23	37.7		69	40.1		92	39.5	
Race[d]									
White	22	38.6		77	58.3		99	52.3	
Black	11	19.3		16	12.1		27	14.3	
Asian	12	21.0		28	21.2		40	21.2	
Other	12	21.0		11	8.3		23	12.2	
Ethnicity[e]									
Hispanic	23	47.9		67	45.6		90	46.2	
Non-Hispanic	25	52.1		80	54.4		105	53.8	
Median time from onset to diagnosis, days			1			2			1
Median time from onset to last visit at which signs and symptoms were still present, days			9			8			8
Laterality of facial muscle involvement									
Unilateral	61	100		168	97.7		229	98.3	
Bilateral	0	0		4	2.3		4	1.7	
Involved side of the face[f]									
Right	38	62.3		85	50.9		123	53.9	
Left	23	37.7		82	49.1		105	46.1	
History of illness within 90 days prior to diagnosis									
Any respiratory illness	25	41.0		45	26.2		70	30.0	
Herpes simplex virus infection	4	6.6		11	6.4		15	6.4	
Varicella zoster virus infection	0	0.0		1	0.6		1	0.4	
Lifetime history of illness[g]									
Head trauma[h]	6	9.8		20	11.6		26	11.2	
Central nervous system disease (e.g., epilepsy)	2	3.3		8	4.7		10	4.3	
Diabetes	0	0		3	1.7		3	1.3	
Hypertension	0	0		2	1.2		2	0.9	
Family history of Bell's palsy[i]									
Yes	3	5.8		5	4.3		8	4.8	
No	49	94.2		111	95.7		160	95.2	

[a] Range, 124 days–17.8 years.
[b] Range, 11 days–17.4 years.
[c] Range, 11 days–17.8 years.
[d] Race was not known for 44 cases.
[e] Ethnicity was not known for 38 cases.
[f] The involved side of the face was unknown for 5 cases.
[g] No case had a history of human immunodeficiency virus infection, Lyme disease, or a parotid tumor.
[h] History of head trauma does not include the period of time within 30 days prior to diagnosis. A history of head trauma within 30 days prior to diagnosis was an exclusion criterion in the case definition, as described in the Materials and Methods section.
[i] Family history of Bell's palsy was not known for 65 cases.

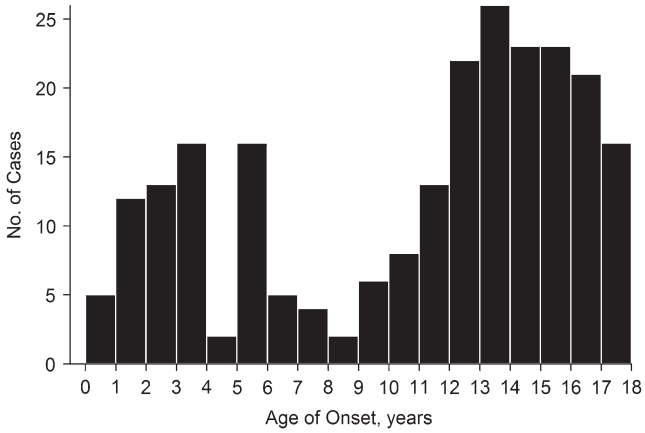

Figure 2. Numbers of Bell's palsy cases within the population of Kaiser Permanente Northern California who had received a vaccine during the 12 months prior to onset of their disease, by age of onset, 2001–2006.

is maximized and the same parameter estimates with the same interpretation are obtained. Third, the case-centered method dramatically reduced the computational burden, since the final analytic data set contained only information on the study identification number, observed immunization status, and expected immunization status for each case. Finally, the case-centered method minimized privacy concerns in the use of electronic records because of the small number of variables in the final analytic data set, where characteristics of each case were summarized using a number representing the expected exposure status (here: immunization) in each case's risk set in the underlying population.

In the past few decades, other novel case-based approaches, including the self-controlled case-series design, have been used to examine immunization safety (24). There are differences between the case-centered and self-controlled case-series designs in terms of the modeling approach; however, the magnitude of the point estimate in both designs is ultimately driven by the observed case split inside versus outside the risk interval, while the expectation is embedded in the offset term. In the self-controlled case-series design, the expectation is based on the proportion of days inside versus outside the risk interval during the observation period. In the case-centered design, the expectation is based on the proportion of persons in the underlying population who were immunized inside versus outside the risk interval prior to the day of the adverse event in each case. Therefore, using the same series of immunized cases, the self-controlled case-series and case-centered designs would provide nearly the same results if the amount of time inside versus outside the risk interval was proportional to the expected odds of immunization inside versus outside the risk interval. One situation in which a meaningful difference between the 2 methods may arise is one where there are variations over time in the vaccine coverage and outcome incidence. An advantage of the

Table 2. Type and Number of Vaccines Received During the Course of 1 Year Prior to the Onset of Bell's Palsy Among Cases Within the Population of Kaiser Permanente Northern California, 2001–2006

Type of Vaccine	No.	%
Hepatitis A virus	126	20.5
Hepatitis B virus	79	12.8
Diphtheria toxoid, tetanus toxoid, and whole-cell or acellular pertussis	61	9.9
Inactivated or oral poliovirus	61	9.9
Measles, mumps, rubella, and/or varicella (MMR, MMRV, rubella only, or varicella only)	54	8.8
Pneumococcus	53	8.6
Tetanus and diphtheria toxoid	51	8.3
Haemophilus influenzae type b	50	8.1
Intramuscular inactivated trivalent influenza	43	7.0
Acellular pertussis-inactivated poliovirus/*H. influenzae* type b	15	2.4
Meningococcus	8	1.3
Typhoid	6	1.0
Live attenuated influenza	3	0.5
Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis	3	0.5
Rotavirus	2	0.3
Total	615	100

Abbreviations: MMR, measles-mumps-rubella; MMRV, measles-mumps-rubella-varicella.

Table 3. Risk of Bell's Palsy Following Immunization Among Cases Within the Population of Kaiser Permanente Northern California, 2001–2006

Vaccine and Risk Interval	No. of Informative Cases Inside the Risk Interval	No. of Informative Cases Outside the Risk Interval	Odds Ratio	95% Confidence Interval
TIV[a]				
Days 1–14	2	21	1.0	0.2, 5.0
Days 1–28	3	24	0.7	0.2, 2.8
Days 29–56	5	21	1.2	0.3, 4.8
Hepatitis B virus				
Days 1–14	3	54	1.3	0.4, 4.5
Days 1–28	4	53	0.8	0.2, 2.4
Days 29–56	4	49	0.9	0.3, 2.6
Any vaccine[b]				
Days 1–14	14	219	1.1	0.6, 1.9
Days 1–28	24	209	0.9	0.6, 1.4
Days 29–56	19	190	0.7	0.4, 1.1

Abbreviation: TIV, trivalent influenza vaccine.
[a] Intramuscular inactivated TIV.
[b] All vaccines combined, regardless of type.

case-centered design is that it can be used to precisely and carefully control for such variations.

Our study was subject to some limitations. First, the number of cases who had received the intranasal live attenuated influenza vaccine was too small to allow us to examine the association between that vaccine and Bell's palsy. Investigating a potential association between immunization with intranasal live attenuated influenza vaccine and Bell's palsy remains an important topic for future research, especially because of the route of administration of that vaccine. In addition, while we ascertained all cases of Bell's palsy during the study period, the point estimates for individual vaccines (i.e., TIV and HBV vaccine) were somewhat imprecise. Considering the upper limits of the 95% confidence intervals, we can rule out with a high level of certainty effect sizes greater than 2.8 and 2.4 for the associations between immunization with TIV and HBV vaccine and Bell's palsy, respectively, during the risk interval of 1–28 days. Second, a relatively large portion of cases in this study were categorized as probable. One of the main reasons is that documentation of the involvement of all facial muscles in a child could be challenging. It was not clear whether the diagnosing physician had tested a full battery of movements (e.g., moving the forehead, raising eyebrows, smiling), and even if the physician had done so, subtle changes could have been missed. Third, while we used a prespecified case disposition form for adjudication of the cases, there is still a need for a standard case definition of Bell's palsy to facilitate comparisons across different studies. The Brighton Collaboration has formed an international working group to define Bell's palsy as an adverse event following immunization (15). Such a case definition could be of use in future epidemiologic studies of immunization and Bell's palsy. Fourth, while we created explicit risk sets by age and sex for use in the case-centered approach, the possibility of confounding by other potential risk factors for Bell's palsy that were associated with the timing of immunization cannot be ruled out. Since the expected odds of immunization were obtained from the underlying population of children who had all received the same vaccine, factors associated with *whether* individuals received a certain vaccine could not have led to a bias in our analysis; nonetheless, as with most study designs, the possibility of confounding by unmeasured factors associated with *when* individuals received a certain vaccine still exists, at least on theoretical grounds.

In conclusion, the results of this study suggest that there is no evidence of an increased risk of Bell's palsy following immunization with TIV, HBV vaccine, or any vaccine among children aged 18 years or younger.

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REFERENCES

1. Brandenburg NA, Annegers JF. Incidence and risk factors for Bell's palsy in Laredo, Texas: 1974–1982. *Neuroepidemiology.* 1993;12(6):313–325.
2. Katusic SK, Beard CM, Wiederholt WC, et al. Incidence, clinical features, and prognosis in Bell's palsy, Rochester, Minnesota, 1968–1982. *Ann Neurol*. 1986;20(5):622–627.
3. Monini S, Lazzarino AI, Iacolucci C, et al. Epidemiology of Bell's palsy in an Italian health district: incidence and case-control study. *Acta Otorhinolaryngol Ital*. 2010;30(4):198–204.
4. Rowlands S, Hooper R, Hughes R, et al. The epidemiology and treatment of Bell's palsy in the UK. *Eur J Neurol*. 2002;9(1): 63–67.
5. Tsai HS, Chang LY, Lu CY, et al. Epidemiology and treatment of Bell's palsy in children in northern Taiwan. *J Microbiol Immunol Infect*. 2009;42(4):351–356.
6. Holland NJ, Weiner GM. Recent developments in Bell's palsy. *BMJ*. 2004;329(7465):553–557.
7. Shargorodsky J, Lin HW, Gopen Q. Facial nerve palsy in the pediatric population. *Clin Pediatr (Phila)*. 2010;49(5): 411–417.
8. Wilson-Pauwels L, Akesson EJ, Stewart PA. *Cranial Nerves: Anatomy and Clinical Comments*. Philadelphia, PA: BC Decker, Inc; 1988.
9. Lorch M, Teach SJ. Facial nerve palsy: etiology and approach to diagnosis and treatment. *Pediatr Emerg Care*. 2010;26(10): 763–769.
10. Adour KK, Byl FM, Hilsinger RL Jr, et al. The true nature of Bell's palsy: analysis of 1,000 consecutive patients. *Laryngoscope*. 1978;88(5):787–801.
11. Abiko Y, Ikeda M, Hondo R. Secretion and dynamics of herpes simplex virus in tears and saliva of patients with Bell's palsy. *Otol Neurotol*. 2002;23(5):779–783.
12. Lazarini PR, Vianna MF, Alcantara MP, et al. Herpes simplex virus in the saliva of peripheral Bell's palsy patients. *Braz J Otorhinolaryngol*. 2006;72(1):7–11.

13. Murakami S, Mizobuchi M, Nakashiro Y, et al. Bell palsy and herpes simplex virus: identification of viral DNA in endoneurial fluid and muscle. *Ann Intern Med*. 1996;124(1):27–30.
14. Paolino E, Granieri E, Tola MR, et al. Predisposing factors in Bell's palsy: a case-control study. *J Neurol*. 1985;232(6):363–365.
15. Rath B, Linder T, Cornblath D, et al. All that palsies is not Bell's—the need to define Bell's palsy as an adverse event following immunization. *Vaccine*. 2007;26(1):1–14.
16. Mutsch M, Zhou W, Rhodes P, et al. Use of the inactivated intranasal influenza vaccine and the risk of Bell's palsy in Switzerland. *N Engl J Med*. 2004;350(9):896–903.
17. Zhou W, Pool V, DeStefano F, et al. A potential signal of Bell's palsy after parenteral inactivated influenza vaccines: reports to the Vaccine Adverse Event Reporting System (VAERS)—United States, 1991–2001. *Pharmacoepidemiol Drug Saf*. 2004;13(8):505–510.
18. Greene SK, Kulldorff M, Lewis EM, et al. Near real-time surveillance for influenza vaccine safety: proof-of-concept in the Vaccine Safety Datalink Project. *Am J Epidemiol*. 2010;171(2):177–188.
19. Stowe J, Andrews N, Wise L, et al. Bell's palsy and parenteral inactivated influenza vaccine. *Hum Vaccin*. 2006;2(3):110–112.
20. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. *Am J Public Health*. 1992;82(5):703–710.
21. Fireman B, Lee J, Lewis N, et al. Influenza vaccination and mortality: differentiating vaccine effects from bias. *Am J Epidemiol*. 2009;170(5):650–656.
22. Klein NP, Fireman B, Yih WK, et al. Measles-mumps-rubella-varicella combination vaccine and the risk of febrile seizures. *Pediatrics*. 2010;126(1):e1–e8.
23. Baxter R, Ray GT, Fireman BH. Effect of influenza vaccination on hospitalizations in persons aged 50 years and older. *Vaccine*. 2010;28(45):7267–7272.
24. Whitaker HJ, Farrington CP, Spiessens B, et al. Tutorial in biostatistics: the self-controlled case series method. *Stat Med*. 2006;25(10):1768–1797.