# Encephalopathy After Whole-Cell Pertussis or Measles Vaccination

## *Lack of Evidence for a Causal Association in a Retrospective Case–Control Study*

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**Background:** Whole-cell pertussis (wP) and measles vaccines are effective in preventing disease but have also been suspected of increasing the risk of encephalopathy or encephalitis. Although many countries now use acellular pertussis vaccines, wP vaccine is still widely used in the developing world. It is therefore important to evaluate whether wP vaccine increases the risk of neurologic disorders.

**Methods:** A retrospective case–control study was performed at 4 health maintenance organizations. Records from January 1, 1981, through December 31, 1995, were examined to identify children aged 0 to 6 years old hospitalized with encephalopathy or related conditions. The cause of the encephalopathy was categorized as known, unknown or suspected but unconfirmed. Up to 3 controls were matched to each case. Conditional logistic regression was used to analyze the relative risk of encephalopathy after vaccination with diphtheria–tetanus–pertussis (DTP) or measles–mumps–rubella (MMR) vaccines in the 90 days before disease onset as defined by chart review compared with an equivalent period among controls indexed by matching on case onset date.

**Results:** Four-hundred fifty-two cases were identified. Cases were no more likely than controls to have received either vaccine during the 90 days before disease onset. When encephalopathies of known etiology were excluded, the odds ratio for case children having received DTP within 7 days before onset of disease was 1.22 (95% confidence interval [CI] = 0.45–3.31, $P = 0.693$) compared with control children. For MMR in the 90 days before onset of encephalopathy, the odds ratio was 1.23 (95% confidence interval = 0.51–2.98, $P = 0.647$).

**Conclusions:** In this study of more than 2 million children, DTP and MMR vaccines were not associated with an increased risk of encephalopathy after vaccination.

**Key Words:** encephalopathy, vaccine, MMR, DTP

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Vaccination has proved effective in controlling several infectious diseases, including pertussis and measles.[1–3] However, some reports have attributed serious adverse events to the use of the pertussis and measles vaccines. In particular, encephalopathy or encephalitis has been reported to occur after receipt of whole-cell pertussis vaccine (wP) or combined measles–mumps–rubella (MMR) vaccine.[4] In the 1970s, concerns among the public regarding possible neurologic reactions led to a decline in pertussis vaccine use in the United Kingdom; unfortunately, this decrease in vaccine acceptance was quickly followed by outbreaks of disease in 1977–1979 and 1982. Similar events took place in Japan[4] and Sweden[5] in the late 1970s.

The purported association between vaccine use and encephalopathy remains controversial.[6] The largest and best known of the studies that have examined this issue was a case–control study, the National Childhood Encephalopathy Study (NCES), conducted in the United Kingdom from 1976 to 1979. All pediatricians, infectious disease specialists and neurosurgeons in the country were asked to report cases of neurologic illness in children 2 to 36 months old. Two controls were matched to each case and vaccine histories were obtained for the month before admission to the hospital or for the corresponding month for controls. The relative risk (RR) of diphtheria–tetanus–pertussis (DTP) vaccination within the 7 days before the onset of encephalitis was 3.1 (95% confidence interval [CI] = 1.0–10.5).[7] This was not statistically significant and the investigators therefore concluded that the results were suggestive of but did not prove an association between vaccination and neurologic illness. However, others maintain that the NCES experienced methodologic problems and that the evidence does not even suggest

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such an association.[6] The interpretation of the NCES was limited by the small number of cases exposed to vaccine; only 26 of the first 1000 reported cases (2.6%) had received DTP vaccine within 7 days of the onset of the encephalopathy; 30 of 2000 controls (1.5%) had received vaccine during the equivalent period.[8] Most affected children recovered without long-term sequelae and a 10-year follow up of the NCES population found that there was no significant difference in death or rate of neurologic dysfunction between the children who were vaccinated shortly before the onset of their acute illness and those who were not.[9] The NCES study found that children with convulsions or encephalopathy were more likely to have received MMR vaccine 7 to 14 days before the onset of symptoms (RR = 2.3, $P < 0.05$).

A similar study in the northwestern United States also found no significant association between DTP vaccination and acute neurologic illness; however, this study evaluated a smaller population (218,000, including 424 cases) so that a weak association may have been missed.[10] An independent analysis of the NCES and other data by the U.S. Institute of Medicine (IOM) concluded that the evidence was consistent with a causal (albeit rare) relationship between DTP vaccination and acute encephalopathy in the immediate postvaccination period but that there was insufficient evidence to conclude that DTP causes permanent brain damage.[4] Subsequent analyses by the American Academy of Pediatrics[11] and the IOM[12] reaffirmed the earlier conclusions that there is no definitive, causal link between encephalopathy and DTP vaccination. All advisory groups continue to recommend pertussis vaccination because the benefits are irrefutable.

As a result of general concerns about the safety and consistency of the wP vaccine, the United States and many other countries have adopted the use of several acellular pertussis vaccines that have similar effectiveness[13,14] and lower reactogenicity[15,16] than the wP vaccine. However, the wP vaccine is easier and less expensive to manufacture and remains the preferred pertussis vaccine in most developing countries.[17] Thus, the safety of the wP vaccine is still of relevance to most countries, as is the safety of the MMR vaccine, which is also used worldwide. This retrospective case–control study was conducted at 4 study sites in the western United States as part of the ongoing Vaccine Safety Datalink project of the Centers for Disease Control and Prevention (Atlanta, GA), which was initiated in 1991.[18] Our objective was to reevaluate the issue of whether wP and measles vaccination are associated with encephalopathy or encephalitis.

## MATERIALS AND METHODS

This retrospective study was carried out at 4 health maintenance organizations: Group Health Cooperative, based in Washington State; Northern California Kaiser Permanente; Northwest Kaiser Permanente, in Oregon and Washington; and Southern California Kaiser Permanente. It involved children 0 to 6 years of age hospitalized with encephalopathy or related conditions during the period from January 1, 1981, through December 31, 1995. Southern California Kaiser Permanente participated from August 1, 1988, through December 31, 1995.

*Identification of Cases.* The case definition included hospitalized patients with a primary or secondary diagnosis of encephalopathy, Reye syndrome, or encephalitis. Patients were eligible for inclusion if they had been members of the health plan for at least 60 days before hospital admission or since birth if the patient was less than 60 days old. Hospital charts were reviewed and abstracted. A case was accepted by the abstracter if there was a diagnosis of encephalopathy by a neurologist and a clear etiology of congenital anomaly/syndrome, birth anoxia, drug or toxin ingestion or trauma. Cases for which there was a definitive diagnosis by a neurologist of a condition other than encephalopathy were rejected by the abstracter. All other neurologic cases were reviewed by an independent neurologist blind to the vaccination status of the patient to determine whether the patient met the case definition, the specific diagnosis, whether the condition was acute or chronic, the underlying cause and the condition on follow up. The information included in the chart abstract included the presence of seizures, laboratory results, liver biopsy, electroencephalography results, magnetic resonance image results, vaccination history, preexisting neurologic disorders, specialties of diagnosing physicians, patient condition at each follow-up visit, neurologist's diagnosis, presence of stupor or coma, brain or meningeal biopsy, patient demographics, patient diagnoses, the chronic or acute nature of the condition, the date of illness onset and the etiology of the illness.

*Definitions Used to Identify Cases.* The definitions of encephalopathy, Reye syndrome and encephalitis used to identify cases were as follows:

1. Encephalopathy: acute generalized disturbance of brain function requiring hospitalization and consisting of coma or stupor that cannot be attributed to medication or postictal state. Such cases must have altered consciousness, delirium, obtundation and/or confusion.
2. Reye syndrome: clinical symptoms of acute encephalopathy with altered level of consciousness as well as:
   a. Absence of inflammatory changes in cerebrospinal fluid as indicated by $<5$ white blood cells/mm$^3$ or brain histology showing cerebral edema without perivascular or meningeal inflammation, plus
   b. Evidence of hepatitis or liver failure documented by a 3-fold or greater elevation in serum glutamic oxaloacetic transaminase, serum glutamate pyruvate transaminase or serum ammonia or fatty changes of hepatocytes on liver biopsy or autopsy, plus
   c. Absence of other etiologies for cerebral or hepatic abnormalities.
3. Encephalitis/encephalomyelitis: evidence of acute neurologic disease presenting with nonspecific signs such as fever, seizures, altered consciousness, headache, vomiting, meningismus or anorexia. We required multifocal involvement of the central nervous system and evidence of cerebrospinal fluid inflammation ($>7$ white blood cells/mm$^3$). We excluded disease with other known etiologies.

*Selection of Controls.* Up to 3 controls were selected for each case. The controls were matched to cases according to health maintenance organization location, age (within 7 days), sex and length of enrollment in the health plan.

For both cases and controls, vaccine exposure was ascertained from the medical record. Abstractors were not

blinded to case/control status because the abstractors had to review the entire chart to ascertain vaccine status and a child with encephalopathy would be obvious on this review. However, the review of each case to ascertain clinical criteria for inclusion was conducted by a neurologist blinded to the vaccine status of the child.

*Analysis.* Cases were categorized according to whether the etiology of the encephalopathy was known, unknown or suspected but unconfirmed. Assessment of vaccination risk for various exposure intervals was conducted using conditional logistic regression for all cases versus controls, cases with unknown or suspected but unconfirmed cause versus controls and cases with unknown cause versus controls. A suspected but unconfirmed cause included cases in which a diagnosis such as viral meningitis had not been confirmed by a specific laboratory test.

## RESULTS

Approximately 2,197,000 children at 4 health maintenance organizations were eligible for inclusion in this retrospective case–control study. A total of 452 encephalopathy cases were identified at the 4 sites: 20 at Group Health Cooperative, 236 at Northern California Kaiser Permanente, 39 at Northwest Kaiser Permanente and 157 at Southern California Kaiser Permanente.

Eight of the cases received MMR vaccine within the 60 days before admission and 49 of the cases received DTP (Table 1). Only one case exposed to MMR (13%) had an encephalopathy of known cause; 15 (31%) of the cases exposed to DTP were of known cause.

Each immunization exposure was stratified into time windows (Table 2). In no time window were the cases more likely than controls to have received DTP or MMR vaccine. In fact, controls were significantly more likely than cases to have received DTP vaccine within 60 or 90 days.

The cases were then further stratified into those whose encephalopathy was of a known cause (etiology confirmed by a diagnostic test) and those for whom the cause was unknown or suspected but unconfirmed. When the unknown and suspected but unconfirmed cases were combined, the odds of exposure to DTP vaccine within 7 days was numerically slightly greater for cases than for controls, but this did not approach statistical significance (odds ratio [OR] = 1.22; 95% CI = 0.45–3.31; $P = 0.693$; Table 3). The relative risk estimate declined when the time window was lengthened to 14 days or longer and it was substantially reduced when only cases of unknown cause were considered (OR = 1.04; 95% CI = 0.26–4.11; $P = 0.953$; Table 4).

Likewise, cases were no more likely than controls to have received MMR vaccine during any time window, regardless of etiologic category, except during the 90-day window (Tables 2, 3 and 4). During the 90-day window, children with neurologic disease of unknown or suspected but unconfirmed cause were numerically more likely to have received MMR vaccine but not significantly so (OR = 1.23; 95% CI = 0.51–2.98; $P = 0.647$).

Table 5 contains a clinical summary of each case of unknown or suspected but unconfirmed etiology in which the child received DTP vaccine within the 14 days before the onset of symptoms or MMR vaccine within the 30 days before onset. No distinct pattern of symptoms is seen among these cases. Of the 8 children who received DTP within 14 days of disease onset, 3 had a full recovery, 3 had a partial recovery and 2 had no recovery or died. Two of the 3 children who received MMR within 30 days had a full recovery and the third died. No cases had received MMR within 14 days, the interval associated with increased risk in the NCES study.

## DISCUSSION

In this analysis of a possible relationship between vaccination with DTP or MMR and the occurrence of encephalopathy or encephalitis, we found that cases were no more likely to have been vaccinated with DTP vaccine in the month before disease onset than control children. Only 6 cases were exposed to DTP in the 7 days before symptom onset (the period of increased risk in the NCES study) and the OR between cases and controls was not significant. Although the small number of vaccinated cases limits our ability to assess possible associations, it also means that the possible attributable risk of encephalopathy after DTP is extremely small. In all other timeframes, the OR of the case risk to the control risk of DTP immunization was less than one, providing no evidence of any association. There were significant differences between cases and controls only for the 60- and 90-day windows when all cases were considered and these differences reflected a higher rate of vaccine exposure among the controls than the cases. This could be the result of less immunization in children with progressive neurologic disease for whom wP vaccination is contraindicated.

In the British NCES evaluation of MMR vaccination, the period associated with increased risk was 7 to 14 days.

**TABLE 1.** Exposure to Diphtheria–Tetanus–Pertussis (DTP) or Measles–Mumps–Rubella (MMR) Within 60 Days of Onset of Neurologic Illness of the Designated Etiologic Category

| Etiology | DTP | | | MMR | | |
|---|---|---|---|---|---|---|
| | Exposed n (row %) | Unexposed n (row %) | Total n (col %) | Exposed n (row %) | Unexposed n (row %) | Total n (col %) |
| Known | 15 (7) | 205 (93) | 220 (49) | 1 (0) | 219 (100) | |
| Suspected/unconfirmed* | 15 (17) | 71 (83) | 86 (19) | 4 (5) | 82 (95) | |
| Unknown | 19 (13) | 127 (87) | 146 (32) | 3 (2) | 143 (98) | 146 (32) |
| All | 49 (11) | 403 (89) | 452 (100) | 8 (2) | 444 (98) | 452 (100) |

*Includes cases in which a diagnosis such as viral meningitis was unconfirmed by a specific laboratory test.

**TABLE 2.** Frequency of Diphtheria–Tetanus–Pertussis (DTP) and Measles–Mumps–Rubella (MMR) Vaccination Among all Cases and Controls for Specified Intervals Relative to Onset of Encephalopathy

| Vaccine Exposure Interval (days) | Exposed Cases (N) | Exposed Cases (%) | Exposed Controls (N) | Exposed Controls (%) | *P* Value* | Odds Ratio* | Confidence Interval |
|---|---|---|---|---|---|---|---|
| DTP | | | | | | | |
| 0–90 | 60 | 13.3 | 233 | 18.2 | 0.001 | 0.43 | 0.27–0.70 |
| 0–60 | 49 | 10.8 | 189 | 14.7 | 0.004 | 0.49 | 0.30–0.80 |
| 0–30 | 26 | 5.8 | 111 | 8.7 | 0.024 | 0.54 | 0.32–0.92 |
| 0–14 | 13 | 2.9 | 52 | 4.1 | 0.247 | 0.67 | 0.34–1.32 |
| 0–7 | 7 | 1.5 | 25 | 2.0 | 0.597 | 0.79 | 0.33–1.89 |
| MMR | | | | | | | |
| 0–90 | 15 | 3.3 | 44 | 3.4 | 0.951 | 0.98 | 0.47–2.01 |
| 0–60 | 8 | 1.8 | 33 | 2.6 | 0.304 | 0.64 | 0.27–1.50 |
| 0–30 | 4 | 0.9 | 13 | 1.0 | 0.778 | 0.85 | 0.27–2.68 |
| 0–14 | 1 | 0.2 | 7 | 0.5 | 0.337 | 0.35 | 0.04–2.95 |
| 7–14 | 1 | 0.2 | 6 | 0.5 | 0.408 | 0.40 | 0.05–3.46 |

*Conditional logistic regression.

**TABLE 3.** Vaccine Exposure Interval (≤90 days) in Cases of Unknown or Suspected but Unconfirmed* Cause

| Vaccine Exposure Interval (days) | Exposed Cases (N) | Cases Exposed (%) | Exposed Controls (N) | Controls Exposed (%) | *P*† | Odds Ratio† | Confidence Interval |
|---|---|---|---|---|---|---|---|
| Diphtheria–tetanus–pertussis | | | | | | | |
| 0–90 | 41 | 17.7 | 145 | 22.2 | 0.052 | 0.54 | 0.29–1.01 |
| 0–60 | 34 | 14.7 | 118 | 18.1 | 0.129 | 0.62 | 0.33–1.15 |
| 0–30 | 18 | 7.8 | 73 | 11.2 | 0.101 | 0.58 | 0.30–1.11 |
| 0–14 | 8 | 3.4 | 33 | 5.1 | 0.294 | 0.63 | 0.27–1.49 |
| 0–7 | 6 | 2.6 | 14 | 2.1 | 0.693 | 1.22 | 0.45–3.31 |
| Measles–mumps–rubella | | | | | | | |
| 0–90 | 11 | 4.7 | 28 | 4.3 | 0.647 | 1.23 | 0.51–2.98 |
| 0–60 | 7 | 3.0 | 19 | 2.9 | 0.903 | 1.06 | 0.41–2.74 |
| 0–30 | 3 | 1.3 | 10 | 1.5 | 0.746 | 0.80 | 0.21–3.05 |
| 0–14 | 0 | 0.0 | 7 | 1.1 | 0.991 | 0.00 | 0.00 |
| 7–14 | 0 | 0.0 | 6 | 0.9 | 0.992 | 0.00 | 0.00 |

*Includes cases in which a diagnosis such as viral meningitis, was unconfirmed by a specific laboratory test.
†Conditional logistic regression.

**TABLE 4.** Vaccine Exposure Interval (≤90 days) in Cases of Unknown Cause

| Vaccine Exposure Interval (days) | Exposed Cases (N) | Cases Exposed (%) | Exposed Controls (N) | Controls Exposed (%) | *P** | Odds Ratio* | Confidence Interval |
|---|---|---|---|---|---|---|---|
| Diphtheria–tetanus–pertussis | | | | | | | |
| 0–90 | 24 | 16.4 | 80 | 19.6 | 0.283 | 0.63 | 0.28–1.46 |
| 0–60 | 19 | 13.0 | 65 | 15.9 | 0.296 | 0.65 | 0.29–1.46 |
| 0–30 | 9 | 6.2 | 40 | 9.8 | 0.138 | 0.52 | 0.22–1.24 |
| 0–14 | 4 | 2.7 | 17 | 4.2 | 0.396 | 0.59 | 0.18–1.99 |
| 0–7 | 3 | 2.1 | 8 | 2.0 | 0.953 | 1.04 | 0.26–4.11 |
| Measles–mumps–rubella | | | | | | | |
| 0–90 | 6 | 4.1 | 19 | 4.7 | 0.763 | 0.83 | 0.25–2.76 |
| 0–60 | 3 | 2.1 | 13 | 3.2 | 0.428 | 0.57 | 0.14–2.28 |
| 0–30 | 0 | 0.0 | 8 | 2.0 | 0.991 | 0.00 | 0.00 |
| 0–14 | 0 | 0.0 | 5 | 1.2 | 0.993 | 0.00 | 0.00 |
| 7–14 | 0 | 0.0 | 4 | 1.0 | 0.993 | 0.00 | 0.00 |

*Conditional logistic regression.

Also, Weibel reported an increased risk of encephalopathy with subsequent permanent brain damage or death on days 8 and 9 after measles vaccination, but this was based on 48 cases voluntarily reported to the National Vaccine Injury Compensation Program (NVICP) in the United States.[19] We did not find an increased OR for MMR vaccination during this time; in fact, no case children had received MMR vaccine within 14 days of the onset of encephalopathy. The NVICP only documents encephalopathies that occur within 15 days of vaccination and thus would not have captured encephalopathies that were diagnosed at longer intervals after vaccination. In our study, we observed a slightly (but not significantly) increased OR with MMR vaccination within 90 days for cases of unknown or suspected but unconfirmed cause. Although it is possible that there is such a delayed reaction to the vaccine, the lack of a consistent time association between

**TABLE 5.** Review of Cases of Encephalopathies of Unknown or Suspected but Unconfirmed Etiology

| Patient No. | Sex | Age at Vaccination | Interval in Days | Test Results | | Outcome | Comment |
|---|---|---|---|---|---|---|---|
| | | | | CSF | Neurology/Imaging | | |
| Cases who received DTP 14 d or less before the onset of encephalopathy | | | | | | | |
| DTP—unknown etiology | | | | | | | |
| 1 | F | 2 mo | 0 | CSF WBC 40/mm$^3$, CSF RBC 1872/mm$^3$, CSF protein 60 mg/dL | CT and EEG = normal | Full recovery | Unknown etiology |
| 2 | F | 7 mo | 1 | | MRI = marked hemiatrophy of left cerebral hemisphere; right side also showed apparent prominent sulci anteriorly; comparison with previous films shows progressive encephalopathy; EEG = markedly abnormal left recording | Chronic encephalopathy, died | Progressive seizure disorder, died Feb 1991 |
| 3 | F | 4 yr 11 mo | 7 | CSF glucose 94 mg/dL | MRI = increased signal in right parietal; CT = normal; EEG = probably abnormal as a result of persistent bihemispheric high-voltage slowing without focal dysrhythmia | Full recovery | HSV mentioned as a result of temporal/parietal focalizing of cerebritis seen on imaging but no confirmatory test and CSF not suggestive |
| 4 | M | 4 mo | 13 | CSF protein 125 mg/dL, CSF glucose 131 mg/dL | CT = multiple infarcts; EEG = seizure foci in multiple areas of brain | Partial recovery after 6 mo | Unknown etiology, residuae include CP, blindness, quadriplegia |
| DTP—suspected but unconfirmed etiology | | | | | | | |
| 5 | F | 3 mo | 1 | CSF WBC 29/mm$^3$, CSF Protein 75 mg/dL, glucose 13 mg/dL | EEG = normal | Partial recovery | Possible hypoglycemia |
| 6 | M | 6 mo | 5 | CSF normal | MRI = normal | Partial recovery | Probable postinfectious encephalomyelitis |
| 7 | F | 5 mo | ~7* | | MRI, CT, and EEG all abnormal; severe and diffuse cerebral atrophy | No recovery | Degenerative disorder unknown etiology (possible Rett syndrome) |
| 8 | F | 6 mo (HDTP) | 12 | CSF WBC 11/mm$^3$ | CT and EEG = normal | Full recovery | Possible viral meningitis |
| Cases who received MMR 30 d or less before the onset of encephalopathy (suspected but unconfirmed etiology) | | | | | | | |
| 1 | F | 1 yr 6 mo | 19 | CSF WBC 15/mm$^3$ | MRI = normal | Full recovery | Possible postviral acute cerebellar ataxia |
| 2 | F | 3 yr 9 mo | 21 | CSF glucose = 91 mg/dL | CT = normal | Full recovery | Viral encephalitis versus delirium with high fever 105° F |
| 3 | F | 1 yr 1 mo | 29 | | | Died | Possible AIDS-related encephalopathy—perinatally acquired |

*Exact date of symptom onset is not known.

DTP indicates diphtheria–tetanus–pertussis; CSF, cerebrospinal fluid; CT, computed tomography; MRI, magnetic resonance imaging; WBC, white blood cells; RBC, red blood cells; EEG, electroencephalogram; HSV, herpes simplex virus; CP, cerebral palsy; HDTP, DTP vaccine given in conjunction with *Haemophilus influenzae* B vaccine; MMR, measles–mumps–rubella.

vaccination and the onset of encephalopathy makes a causal relationship unlikely.

There is also no indication of a "clinically distinctive pertussis vaccine-induced encephalopathy."[4,8] A review of our cases (Table 5) supports this conclusion. The symptoms of the 8 children who developed an encephalopathy of unknown or suspected but unconfirmed cause within 14 days of DTP vaccination or 30 days of MMR vaccination varied

widely as did the interval between vaccination and onset of symptoms. This argues against a specific disorder caused by the pertussis or measles vaccines.

We performed a case–control study in part because of the low incidence of encephalopathy among young children and because the analysis was retrospective. In this study, only 452 cases were identified in a population of approximately 2,197,000 at 4 large institutions over a period of 15 years. Of these 452 children, only a small fraction had been exposed to vaccine in the months before the onset of encephalopathy. A prospective cohort study would have required an impractical number of enrolled subjects to generate enough cases to analyze. In fact, the NCES researchers estimated that every child born in Britain would have had to be enrolled in a cohort study to encounter a sufficient number of cases for analysis.[8] The known efficacy of these vaccines precludes the ethical use of a randomized, placebo-controlled design.

Our results are consistent with those of previous studies, although in contrast to the NCES study, we found no evidence for a relationship between vaccination and encephalopathy. In our study, 6 cases were exposed to DTP within 7 days of onset and 11 were exposed to MMR within 90 days. This corresponds roughly to an all-cause incidence (not an attributable risk) of one in 370,000 after DTP and one in 200,000 after MMR, a rate that is not statistically different from background. In the NCES, the attributable risk of a serious neurologic disorder of any clinical outcome within 7 days of DTP vaccination was reported to be one in 110,000 vaccinations[8]; the attributable risk for a serious neurologic disorder resulting in death or neurologic sequelae 12 months after the onset of illness was one in 330,000 for previously normal children,[20] although it has been noted that the NCES rates include children with febrile seizures as well as frank encephalopathy. It should be emphasized that all of these rates for encephalopathy after DTP vaccination are significantly less than the attributable risk for encephalopathy of one in 11,000 after pertussis itself.[21] The report based on data from the NVICP conservatively estimated that the risk of acute encephalopathy within 15 days of measles vaccination that was followed by permanent brain impairment or death was approximately one in 1,500,000 vaccinations.[19] In comparison, the risk of encephalitis after measles is one in 1000 with death or permanent neural impairment as frequent sequelae.[3] Thus, the risk of encephalopathy or encephalitis resulting from pertussis and measles disease is much higher than any potential risk from vaccination.

Our findings do not support a conclusion that there is an increased risk of encephalitis or encephalopathy after DTP or MMR vaccination. Although this study is large, encephalopathy is rare and thus it is not possible to exclude completely a small increase in the risk of encephalopathy after DTP or MMR vaccination. However, if such an increased risk exists, the absolute risk is extremely small and it is much lower after vaccination than after pertussis or measles. Therefore, our results support the continued use of DTP and MMR vaccines.

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