# Pediatric seizures and vaccines

**Luiza Kerstenetzky and Barry Gidal**

A considerable number of American parents have delayed or refused to vaccinate their children, contributing to outbreaks of preventable diseases such as measles and pertussis.[1,2] Of parents who delayed or refused to vaccinate their children, 66% of them reported fear of vaccine side effects as the reason.[1] Fear of vaccine-induced seizures is a significant health concern among parents. Neurologic deficits such as seizures lack a direct causal relationship with vaccines but may be correlated with fevers provoked by vaccines.[3,4]

Febrile seizures are tonic–clonic in nature and are associated with high body temperatures. They affect up to 5% of children, most commonly between the ages of 6 months and 5 years.[5] Among children who have their first febrile seizure before the age of 1 year, 50% will have at least one more; the risk decreases to 25% if the seizure onset was after the age of 1.[6–8] Fortunately, most children who experience febrile seizures do not develop seizures without fever after the age of 5.[8] The development of epilepsy is more likely to occur in children with underlying abnormal development, a family history of feverless seizures, or complex febrile seizures (seizures lasting longer than 15 minutes, occurring more than once within 24 hours, or affecting the body unilaterally).[8] Febrile seizures can occur with common childhood illnesses such as acute respiratory infections and ear infections or vaccine-preventable diseases such as measles, mumps, rubella, chickenpox, influenza, and pneumococcal infections.[5]

Febrile seizures after vaccination are rare, but their incidence in young children increases 2-fold to 5-fold within 24 hours after inactivated vaccine administration and between 5 to 14 days after live-attenuated vaccine administration.[5,6] A systematic review assessing the safety of routine pediatric immunizations presented evidence that supports an association between the measles–mumps–rubella (MMR) vaccine and febrile seizures.[2] Additionally, the inactivated influenza vaccine (IIV) and the pneumococcal conjugate vaccine (PCV13) are associated with febrile seizures, with increased risk when administered concomitantly.[2] A seizure occurring within the associated risk period may be misinterpreted by parents as the direct cause of epilepsy, and therefore discourage subsequent immunizations.

## Influence of genetics

Evidence demonstrates a correlation between underlying genetic factors and epileptic encephalopathy. Genetically predisposed epilepsy is clearly exemplified in a rare and severe form of epilepsy called Dravet (pronounced drah' vay) syndrome, also known as severe myoclonic epilepsy of infancy. The first seizure event in the context of Dravet syndrome is often triggered by fevers, vaccine-induced fevers, infectious disease, or hot baths occurring within the first year of a child's life, later followed by intractable seizures with subsequently slowed neurologic development.[9] Several studies have shown a clear correlation between the *SCN1A* sodium channel mutation and Dravet syndrome, detected in 80% of children in a retrospective study.[10] Although a vaccine-induced seizure may be the initial event, the presence of the *SCN1A* mutation is the underlying cause of the seizure disorder.

A recent 10-year retrospective cohort study set out to determine underlying causes of seizures with onset after vaccination additional to the *SCN1A* mutation.[11] As reported by the Dutch National Immunization Program national reporting system, 990 children aged 2 years or younger had 1,022 temporal seizure episodes with onset after either an inactivated vaccine (n = 695, 68%) or a live attenuated vaccine (n = 327, 32%). The seizure-risk interval used was 24 hours after inactivated vaccines or 5–12 days after live attenuated vaccines. Overall, 23 children in whom the seizure was reported as the first event and who had diagnosed epilepsy were included in extended follow-up. These 23 children were categorized into three groups:

- Group I: Pre-existing encephalopathy (n = 3, 13%)
- Group II: Epileptic encephalopathy (n = 12, 52%)
- Group III: Relatively benign epilepsy (n = 8, 35%)

Children in group I had developmental delay before seizure onset. An underlying cause was detected in 10 of 12 children from group II, and 8 of them had Dravet syndrome with *SCN1A* gene abnormalities. Even with detected genetic etiologies or family history of seizures, seven of the eight children in group III were seizure-free without the use of antiepileptic agents on follow-up. Children in groups I and II had initial seizures more often after administration of inactivated vaccines, at a younger age, and with more frequency than children in group III.

Consistent with previous obser-

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vations in patients with Dravet syndrome, the majority of the children with vaccine-related epilepsy onset had fever-sensitive seizures occurring at a body temperature <38°C, which was a lower temperature than in all other children without epilepsy diagnoses. An underlying cause such as genetics or structural defects was detected in 65% of the 23 children.

This study confirmed that children with benign epilepsy have a good prognosis even when a seizure is precipitated by a vaccine-induced fever. These findings support the hypothesis that predisposing factors lead to neurologic deterioration, not the vaccine.

## Precautions and contraindications

Importantly, sequelae of preventable infection may be worse than potential complications of vaccination. The Advisory Committee on Immunization Practices (ACIP) does not recommend deferring vaccinations because of the presence of acute illnesses with or without fevers.[12] The ACIP recommendations differentiate between precautions and contraindications to common vaccinations. The seizure-related ACIP recommendations are listed in Table 1.

The risks and benefits of vaccinating children with neurologic conditions should be discussed with a health professional. Vaccinations can be safely administered and monitored with appropriate medical vigilance, despite complications that are generally listed under Precautions in product labeling.

Note that the recommendations provided are specific to the measles–mumps–rubella–varicella (MMRV) vaccine and the diphtheria–tetanus–pertussis (DTaP and Tdap) vaccines, as other vaccines have lower risks with vaccine-related seizures. As mentioned previously, the concomitant administration of the IIV and PCV13 vaccines has shown an association with febrile seizures. However, the ACIP does not mention a specific neurologic disorder precaution or contraindication for the IIV and PCV13 vaccines.

Caution when administering vaccines is needed in any patient with moderate to severe illness, regardless of fever status. Clinicians may wish to defer immunization until resolution of such illnesses.

## Family consultation

Many misconceptions exist regarding the association between vaccination and the development of seizures and epilepsy. A seizure in a child with no underlying predispositions is highly unlikely. The cohort study described above has shown that more than two-thirds of vaccine-related seizures in children with epilepsy have a genetic or structural predisposition. That is, any condition causing even a mild fever may trigger a seizure in children with underlying seizure disorders. Sometimes that fever stimulus is a vaccine, leading to the false belief that the vaccine constituents themselves cause seizures or epilepsy.

Vaccine-preventable diseases such as measles, mumps, rubella, and chickenpox are often accompanied by fevers and have higher risks of complications than the immunizations that prevent them. Therefore, the consequences of deliberately choosing to omit childhood vaccinations is potentially devastating.

As clinicians, we must educate parents that even in children with underlying medical conditions, immunizations can be safely administered under careful medical vigilance. When it comes to childhood vaccinations, making informed decisions about their risks and benefits is vital to keeping children safe and healthy.

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**Table 1.** Neurologic disorder precautions and contraindications to immunizations

| Precautions | Contraindications |
|---|---|
| Presence of a moderate or severe acute illness with or without a fever (all vaccines) | Encephalopathy not attributable to another identifiable cause within 7 days of vaccine administration (DTaP, Tdap) |
| Personal or family history of seizures (MMRV) | |
| Unstable progressive neurologic disorder (Tdap) | |
| Infantile spasms | |
| Uncontrolled epilepsy | |
| Progressive encephalopathy | |
| Seizure ≤3 days after receiving a previous dose (DTaP) | |

Abbreviations used: MMRV: measles–mumps–rubella–varicella vaccine; DTaP and Tdap: diphtheria–tetanus–pertussis vaccines.