

Revisiting Influenza Vaccination Exemption

Margaret Ryan, Laurie Duran, Rachel Lee, Sengklam Wu

Author affiliations: University of California San Diego School of Medicine, San Diego, California, USA (M. Ryan); Defense Health Agency Immunization Healthcare Branch, San Diego (M. Ryan, L. Duran); Naval Medical Center, San Diego (M. Ryan, L. Duran, R. Lee, S. Wu)

DOI: <https://doi.org/10.3201/eid2410.180304>

Serious adverse events after immunizations are rare. We review the case of a man who, 50 years earlier, experienced a serious adverse neurologic event 2 weeks after receiving influenza vaccine. He had received no subsequent seasonal influenza vaccinations, but after the risks and benefits were considered, he was vaccinated without adverse event that season.

Neurologic adverse events following immunization (AEFIs), such as encephalitis or acute disseminated encephalomyelitis (ADEM), developing after influenza vaccination have been observed but are rare. It is challenging to determine the causal relationship between an influenza vaccination and an AEFI. A 2011 review by the Institute of Medicine found epidemiologic evidence to be insufficient and mechanistic evidence to be weak for establishing a causal association between influenza vaccination and encephalitis or ADEM (1). A more recent review of serious AEFIs found that 4 cases of ADEM had possible causal association with vaccination for the 2009 pandemic influenza A(H1N1) virus (2).

We examined 1 example of an AEFI in a patient who was subsequently issued a medical exemption from future vaccinations. The patient's original AEFI was documented in 1969 (3). Meningoencephalitis developed in the patient, a 29-year-old member of the US military, \approx 2 weeks after receiving seasonal influenza vaccine. After a brief hospitalization and supportive care, he recovered without sequelae. The patient was given a medical exemption from subsequent influenza vaccinations for the remainder of his time in the military. For the next 48 years, he declined nearly all vaccinations. (In 2011, the patient did receive 1 dose of a vaccine unrelated to influenza.)

In September 2017, at 77 years of age, the patient expressed concern to his primary care physician about his level of protection against infections because he was considering moving to an assisted living facility. After discussing risks and benefits with his healthcare providers, he agreed to receive pneumococcal conjugate vaccine 13 in October

2017, followed \approx 1 month later by seasonal influenza vaccine (ccIV4; Flucelvax; Seqirus, Summit, NJ, USA). He reported feeling well over the subsequent 3 months of follow-up and anticipates that in the fall of 2018 he will receive pneumococcal polysaccharide vaccine 23 and seasonal influenza vaccine.

The influenza vaccine that this patient received in 1969 was a bivalent product that included A2/Aichi/2/68 and B/Massachusetts/3/66 antigens cultured in embryonated chicken eggs (4). It is unclear how the 1969 vaccine compares with modern-era influenza vaccines in terms of rates of rare AEFIs and how medical experts assessed causality after the AEFI that resulted in the patient's exemption from all future influenza vaccinations, nearly 50 years ago. However, AEFI causality assessments have become more rigorous over time, under United States and World Health Organization guidelines (5,6).

When deciding whether to continue vaccinating a patient who has experienced a serious neurologic AEFI, all available information should be considered, including the licensing of the vaccine and, in the United States, the Centers for Disease Control and Prevention/Advisory Committee on Immunization Practices' General Best Practice Guidelines for Immunization (7). The risk for new or recurrent neurologic events after subsequent vaccination is unknown.

More cases of encephalitis and ADEM are associated with virus infection than with vaccination. However, recurrence of such events is rare, even after repeated virus infections. Because of this rarity, when relapse of ADEM occurs in adults, it is more likely to be diagnosed as multiple sclerosis than as an independent recurrence of ADEM (8).

Providers may be challenged to determine if, when, and how to administer vaccines to a patient who has had a serious AEFI. Although it may seem easiest and safest to permanently exempt persons from further vaccination, doing so may inappropriately deprive them of disease protection because factors relevant to risk and benefit change over time (9). We propose that vaccine exemptions should be revisited regularly, regardless of how long they have been in effect.

Acknowledgment

We are grateful to the patient described in this report, who has given his consent to share this information.

About the Author

Dr. Ryan is currently the medical director of the Pacific Region Office of the Defense Health Agency Immunization Healthcare Branch and an adjunct professor at the University of California San Diego School of Medicine. Many of her research publications focus on infectious diseases of military importance.

References

1. Committee to Review Adverse Effects of Vaccines; Institute of Medicine. Stratton K, Ford A, Rusch E, Clayton EW, et al., editors. Adverse effects of vaccines: evidence and causality. Washington: National Academies Press; 2011. p. 293–308.
2. Williams SE, Pahud BA, Vellozzi C, Donofrio PD, Dekker CL, Halsey N, et al. Causality assessment of serious neurologic adverse events following 2009 H1N1 vaccination. *Vaccine*. 2011;29:8302–8. <http://dx.doi.org/10.1016/j.vaccine.2011.08.093>
3. Rosenberg GA. Meningoencephalitis following an influenza vaccination. *N Engl J Med*. 1970;283:1209. <http://dx.doi.org/10.1056/NEJM197011262832208>
4. Centers for Disease Control. Influenza vaccine: recommendations of the Public Health Service Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. 1970;19:327.
5. Halsey NA, Edwards KM, Dekker CL, Klein NP, Baxter R, Larussa P, et al.; Causality Working Group of the Clinical Immunization Safety Assessment Network. Algorithm to assess causality after individual adverse events following immunizations. *Vaccine*. 2012;30:5791–8. <http://dx.doi.org/10.1016/j.vaccine.2012.04.005>
6. Tozzi AE, Asturias EJ, Balakrishnan MR, Halsey NA, Law B, Zuber PL. Assessment of causality of individual adverse events following immunization (AEFI): a WHO tool for global use. *Vaccine*. 2013;31:5041–6. <http://dx.doi.org/10.1016/j.vaccine.2013.08.087>
7. Kroger AT, Duchin J, Vázquez M. General Best Practice Guidelines for Immunization. Best practices guidance of the Advisory Committee on Immunization Practices (ACIP) [cited 16 Apr 2018]. <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html>
8. Koelman DL, Chahin S, Mar SS, Venkatesan A, Hoganson GM, Yeshokumar AK, et al. Acute disseminated encephalomyelitis in 228 patients: a retrospective, multicenter US study. *Neurology*. 2016;86:2085–93. <http://dx.doi.org/10.1212/WNL.0000000000002723>
9. Poland GA, Fleming DM, Treanor JJ, Maraskovsky E, Luke TC, Ball EM, et al. New wisdom to defy an old enemy: summary from a scientific symposium at the 4th Influenza Vaccines for the World (IVW) 2012 Congress, 11 October, Valencia, Spain. *Vaccine*. 2013;31(Suppl 1):A1–20. <http://dx.doi.org/10.1016/j.vaccine.2013.02.033>

Address for correspondence: Margaret Ryan, Defense Health Agency Immunization Healthcare Branch, Pacific Region Office at Naval Medical Center San Diego, Bldg 6, Rm 4V-7C1, San Diego, CA 92134, USA; email: margaret.a.ryan6.civ@mail.mil

Fatal *Cronobacter sakazakii* Sequence Type 494 Meningitis in a Newborn, Brazil

Cláudia Elizabeth Volpe Chaves,¹ Marcelo Luiz Lima Brandão,¹ Mara Luci Gonçalves Galiz Lacerda, Caroline Aparecida Barbosa Coelho Rocha, Sandra Maria do Valle Leone de Oliveira, Tânia Cristina Parpinelli, Luiza Vasconcellos, Stephen James Forsythe, Anamaria Mello Miranda Paniago

Author affiliations: National Institute of Quality Control in Health of Oswaldo Cruz Foundation, Rio de Janeiro, Brazil (C.E.V. Chaves, M.L.L. Brandão, L. Vasconcellos); Federal University of Mato Grosso do Sul, Mato Grosso do Sul, Brazil (C.E.V. Chaves, S.M. do Valle Leone de Oliveira, A.M.M. Paniago); Regional Hospital of Mato Grosso do Sul, Mato Grosso do Sul (M.L.G. Galiz Lacerda, C.A.B. Coelho Rocha, T.C. Parpinelli); foodmicrobe.com, Adams Hill, Nottingham, UK (S.J. Forsythe)

DOI: <https://doi.org/10.3201/eid2410.180373>

We describe a case of infection with *Cronobacter sakazakii* sequence type 494 causing bacteremia and meningitis in a hospitalized late premature infant in Brazil. We conducted microbiological analyses on samples of powdered infant formula from the same batch as formula ingested by the infant but could not identify the source of contamination.

In September 2017, a healthy boy was born at 35 weeks' gestation in Brazil. The newborn was fed breast milk and reconstituted powdered infant formula (PIF) while in the hospital. On postnatal day 4, he began sleeping more than usual and experienced hypoactivity, pallor, jaundice, seizures, metabolic acidosis, and finally respiratory insufficiency, necessitating mechanical ventilation and empiric treatment with cefepime and ampicillin. We obtained 2 blood cultures on postnatal day 4 that yielded *Cronobacter* spp. with resistance to cephalothin and cefoxitin, intermediate resistance to nitrofurantoin, and susceptibility to other antimicrobial drugs, including cefepime and ampicillin. A transfontanel ultrasound on postnatal day 6 showed grade 2 periintra ventricular hemorrhage with hypoxic-ischemic lesions. Subsequent computed tomography and nuclear magnetic resonance (NMR) imaging revealed biparietal cerebral abscess (Figure). Culture of the cerebral abscess on postnatal day 33 yielded *Cronobacter* spp. that had the same pattern of antimicrobial drug susceptibility as that found in blood isolates. Because of the

¹These authors contributed equally to this article.