

## Contact allergy to aluminium induced by commonly used pediatric vaccines

E. Bergfors,  B. Trollfors, A. Inerot, and A. Gente Lidholm

Department of Primary Health Care, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

E. Bergfors, Email: [elisabet.bergfors@allmed.gu.se](mailto:elisabet.bergfors@allmed.gu.se).

[Contributor Information](#).

 Corresponding author.

Received 2016 Nov 22; Accepted 2016 Dec 7.

[Copyright](#) © The Author(s) 2017

**Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

---

We would like to complete the paragraph on Adjuvants (page 6) in the review Vaccination in children with allergies to non active vaccine components by Francheschini et al. [1] which was initiated by the Italian Pediatric Society of Allergy and Immunology in 2013 and published in Clinical and Translational Medicine in 2015.

As mentioned in the review, aluminium (Al) salts are widely used as adjuvants in diphtheria-tetanus-pertussis (DTP) and hepatitis A and B vaccines. The list can be completed with pneumococcal and meningococcal conjugate vaccines, which today are included in the national vaccination schedules in most countries in Europe and the Americas, and also in vaccines against human papilloma virus (HPV) and tick-bore encephalitis (TBE).

According to the authors, the most known and frequent reaction to Al salts is “a palpable nodule at the injection site”. This sounds harmless enough—but in typical cases the nodules are most annoying to the child due to severe pruritus for a very long time [2, 3]. Besides, most children with persistent itching vaccination granulomas become sensitized against Al [4].

Itching vaccination granulomas are described since 1960 [5] but considered very rare [6] until the 1990s when they were reported in 745 of 76,000 children participating in studies on a monocomponent acellular pertussis vaccine in Sweden [7]. Since then, another 102 children in Sweden who received commercial DTaP-polio-Hib-(HepB) combinations (Infanrix<sup>®</sup>, Pentavac<sup>®</sup>) and/or pneumococcal vaccines (Prevenar, Synflorix) are described [4, 8, 9]. The vaccines were given intramuscularly in three doses at 3, 5 and 12 months. In a prospective cohort study on 4758 toddlers the frequency of granulomas was 0.63% in those who received a DTaP combination vaccine alone and 1.18% in those who received an Al adsorbed pneumococcal vaccine at the same time. The risk for granulomas increased with the number of Al-containing vaccine doses [4].

The itching nodules appear remarkably late (months or even years) after the vaccination. Histopathological examination shows granuloma formations in which Al crystals can be demonstrated [10]. Clinically, pruritus is the dominating symptom with intense local itching in the vaccination area on the thigh, often causing skin alterations like eczema, hypertrichosis and hyperpigmentation. Intensified itching and swelling of the nodules is often reported when the child has a cold or another infection. After a duration of ½–12 years (median 3–4 years) the nodules eventually disappear and the pruritus ceases.

In some cases nodules were mistaken as tumours leading to unnecessary anxiety, investigations and surgery [11, 12].

Contact allergy to aluminium was verified in 77–95% of children with itching vaccination granulomas by epicutaneous testing with Al Chloride hexahydrate 2% and metallic Al (4, 7, 9). Sensitized individuals have reported contact dermatitis after the use of Al containing deodorants, pharmaceuticals (ear drops, antiseptics), sun protectors, tattooing pigments and metallic aluminium [13]. Fortunately, and contrary to earlier belief, the sensitization to aluminium seems to wane with time [14].

The consequences of future vaccination with Al adsorbed vaccines in children who once reacted with itching granulomas and/or contact allergy to Al is only partially studied. Our clinical experience so far is that the risk for new granulomas diminishes with time and is very low when the original one has vanished and the itching ceased. In case of on-going severe pruritus the next dose may be postponed 6–12 months. The Al allergy is a delayed type IV reaction not associated with increased risk for anaphylaxis.

We want to point out that itching granulomas\* are benign and self-limiting and no cause to refrain from vaccination in consideration of the risk for a serious infectious disease. They are poorly known but easy to recognize once you are aware of them. They should be familiar to all health care staff working with children to avoid mistrust and anxiety in the parents and unnecessary investigations of the child.

### Authors' contributions

\*see MMF studies under Adverse Reactions

EB participated in the pertussis vaccine study, organized the follow-up and testing of children with itching vaccination granulomas, performed the prospective cohort study and drafted the manuscript. BT organized and performed the clinical study on the monocomponent acellular pertussis vaccine in Göteborg and participated in the follow-up of the itching children. AI performed the testing of the children in the pertussis vaccine study. AGL performed the re-testing study where aluminium sensitization was shown to wane with time. All authors read and approved the final manuscript.

### Competing interests

The authors declare that they have no competing interests.

### Contributor Information

E. Bergfors, Email: [elisabet.bergfors@allmed.gu.se](mailto:elisabet.bergfors@allmed.gu.se).

B. Trollfors, Email: [birger.trollfors@vgregion.se](mailto:birger.trollfors@vgregion.se).

A. Inerot, Email: [annica.inerot@derm.gu.se](mailto:annica.inerot@derm.gu.se).

A. Gente Lidholm, Email: [anette.gente.lidholm@vgregion.se](mailto:anette.gente.lidholm@vgregion.se).

### References

1. Franceschini F, Bottau P, Caimmi S, et al. Vaccination in children with allergy to non active vaccine components. Clin Transl Med. 2015 [[PMC free article](#)] [[PubMed](#)]
2. Bordet AL, Michenet P, Cohen C, et al. Post-vaccination granuloma due to aluminium hydroxide. Ann Pathol. 2001;21:149–152. [[PubMed](#)]
3. Fawcett HA. Persistent vaccination granuloma due to aluminium hypersensitivity. Br J Dermatol. 1985;113:101–102. doi: 10.1111/j.1365-2133.1985.tb13070.x. [[CrossRef](#)]
4. Bergfors E, Hermansson G, Trollfors B, et al. How common are long-lasting, intensely itching vaccination granulomas and contact allergy to aluminium induced by currently used pediatric vaccines? Eur J Pediatr. 2014;173:1297–1307. doi: 10.1007/s00431-014-2318-2. [[PubMed](#)] [[CrossRef](#)]

5. Voss H. Über ein cirka ein Jahr altes Impfstoffgranulom beim Menschen. *Zbl Bakt Microbiol Hyg.* 1960;170:291–299.
6. Cominos D, Strutton G, Busmanis I. Granulomas associated with tetanus toxoid immunization. *Am J Dermatopathol.* 1993;15:114–117. doi: 10.1097/00000372-199304000-00003. [[PubMed](#)] [[CrossRef](#)]
7. Bergfors E, Trollfors B, Inerot A. Unexpectedly high incidence of persistent itching nodules and delayed hypersensitivity to aluminium in children after the use of adsorbed vaccines from a single manufacturer. *Vaccine.* 2003;22:64–69. doi: 10.1016/S0264-410X(03)00531-0. [[PubMed](#)] [[CrossRef](#)]
8. Bergfors E, Björkelund C, Trollfors B. Nineteen cases of persistent pruritic nodules and contact allergy to aluminium after injection of commonly used aluminium-adsorbed vaccines. *Eur J Pediatr.* 2005;164:691–697. doi: 10.1007/s00431-005-1704-1. [[PubMed](#)] [[CrossRef](#)]
9. Bergfors E, Trollfors B. Sixty-four children with persistent itching nodules and contact allergy to aluminium after vaccination with aluminium-adsorbed vaccines-prognosis and outcome after booster vaccination. *Eur J Pediatr.* 2013;172:171–177. doi: 10.1007/s00431-012-1841-2. [[PubMed](#)] [[CrossRef](#)]
10. Chong H, Brady K, Metze D, Calonje E. Persistent nodules at injection sites (aluminium granuloma)—clinicopathological study of 14 cases with a diverse range of histological reaction patterns. *Histopathology.* 2006;48(2):182–188. doi: 10.1111/j.1365-2559.2005.02312.x. [[PubMed](#)] [[CrossRef](#)]
11. Al-Suliman NN, Grabau DA, Kiaer H, et al. A tumour in the breast: vaccination granuloma as a differential diagnosis. *Eur J Surg Oncol.* 1999;25:34–37. doi: 10.1053/ejso.1998.0596. [[PubMed](#)] [[CrossRef](#)]
12. Bergfors E, Lundmark K, Nyström Kronander U. A child with a long-standing, intensely itching subcutaneous nodule on a thigh: an uncommon (?) reaction to commonly used vaccines. *BMJ Case Rep.* 2013 [[PMC free article](#)] [[PubMed](#)]
13. Bergfors E (2006) Aspects of pertussis, pertussis vaccination and adverse events associated with aluminium adsorbed vaccines. Dissertation, Department of Primary Health Care, Göteborg University. ISBN: 9162867148
14. Gente Lidholm A, Bergfors E, Inerot A, Trollfors B, et al. Unexpected loss of contact allergy to aluminium induced by vaccine. *Contact Dermat.* 2013;68:286–292. doi: 10.1111/cod.12053. [[PMC free article](#)] [[PubMed](#)] [[CrossRef](#)]