

## Position Statement

### Academy Position Statement: The Wait Period After Allergen Immunotherapy and Skin Testing November 2002

AAAAI Position Statements and Work Group Reports are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. For reference only.

This position statement was originally released in 1990 under the title, "The Waiting Period After Allergen Skin Testing and Immunotherapy". It was updated, reviewed by the membership and the Board of Directors, and published on the Academy Web site in 2002 under the title: "The Wait Period After Allergen Immunotherapy and Skin Testing."

*The statement below is not to be construed as dictating an exclusive course of action nor is it intended to replace the medical judgment of healthcare professionals. The unique circumstances of individual patients and environments are to be taken into account in any diagnosis and treatment plan. The above statement reflects clinical and scientific advances as of the date of publication and is subject to change.*

It is important to avoid severe systemic reactions associated with allergen immunotherapy and skin testing. Fatalities associated with such therapy were first addressed by Lockey et al in the United States and by the Committee on Safety of Medicines in the United Kingdom.<sup>1,2</sup> Subsequent fatality studies also have been published.<sup>3,4</sup>

The study by Lockey et al of 24 fatalities associated with allergen immunotherapy during a 25-year period included one fatality with a time of onset of the ultimately fatal reaction at 30 minutes after the injection of allergens and two other fatalities at some time interval more than 30 minutes.<sup>1</sup> The Committee of Safety of Medicine in the United Kingdom reported that two of their 26 fatalities occurred between 31 and 90 minutes after an injection of allergen vaccines.<sup>2</sup> Neither study includes data based on direct observation. The relevance of the U.K. experience to the U.S. experience remains in question because many of the fatalities in the United Kingdom were associated with modified or absorbed vaccines not approved for use in the United States.<sup>3</sup> Reid et al reported an additional 17 fatalities associated with allergen immunotherapy for the years 1985-1989.<sup>4</sup> No fatalities were reported with skin testing in this report. All systemic reactions for which such information was available began within 20 minutes, except two, one of which began in 20-30 minutes and the other, after more than 30 minutes. Turkeltaub, in a 1994 issue of *FDA Medical Bulletin*, reported on 35 cases, with the onset of the reactions within 20 minutes or less in more than half. There was no mention of reactions beginning after 20 minutes.<sup>5</sup>

With two exceptions, fatal reactions to allergen immunotherapy, before the fatalities reported in the preceding four studies, began 25 minutes or less after injections.<sup>6-11</sup> The first exception was a subject who was found dead one hour after injection as reported by Vance and Strassman<sup>6</sup>. The second exception was a subject who died "...45 minutes after the injection" as reported by James and Austen.<sup>9</sup> The time of onset of these two reactions was not reported.

The time of onset of the six skin test fatalities in the study by Lockey et al<sup>1</sup> was 20 minutes or less. The onset of ultimately fatal systemic reactions from skin tests with allergens was never more than five minutes in other studies.<sup>6,7,12-17</sup> Reid et al reported no fatalities from skin testing from 1985-1989 and neither did Turkeltaub.<sup>4,5</sup>

Stewart and Lockey<sup>18</sup> analyzed 38 reports of non-fatal systemic reactions secondary to allergen immunotherapy. Most reactions begin within 15-20 minutes, regardless of the allergen immunotherapy scheduled use. However, some can begin later than 30 minutes after the injection of allergen vaccine.

The European Academy of Allergology and Clinical Immunology (EAACI) recommends a 30-minute wait period. However, a longer wait period is necessary for high-risk subjects or in the following situations: 1) rush immunotherapy; 2) unstable asthma. Control of asthma with drugs is required before injection. 3)

high degree of hypersensitivity; 4) with beta-blockers.<sup>19</sup>

**The AAAAI, in congruence with the Immunotherapy Practice Parameter published in 2002 by the Joint Committee on Practice Parameters, recommends a 20-30-minute time interval for allergen skin testing and immunotherapy to monitor patients for serious and possibly fatal reactions. This may be extended for high-risk patients. It is the responsibility of every physician who administers allergen skin tests or vaccines to assess his/her practice procedures in light of these recommendations.**

## References

1. Lockey RF, Benedict LM, Turkeltaub PC, Bukantz SC. Fatalities from immunotherapy (IT) and skin testing (ST). *J Allergy Clin Immunol* 1987;79:660-77.
2. Committee on Safety of Medicines. Update: desensitizing vaccines. *Br Med J* 1986;293:948.
3. Rawlins MD, Wood SM, Mann RD. Hazards with desensitizing vaccines. *Arbeiten aus dem Paul-Ehrlich-Institut (Bundesamt für Sera und Impfstoffe)*. Band 82. Stuttgart, New York: Gustav Fischer Verlag, 1988: 147-51.
4. Reid M, Lockey RF, Turkeltaub PC, Platts-Mills TAE. Survey of fatalities from skin testing and immunotherapy 1985-1989. *J Allergy Clin Immunol* 1993; 92:6-15.
5. Turkeltaub PC, FDA Medical Bulletin 1994;24:7.
6. Lamson RW. So-called fatal anaphylaxis in man. *JAMA* 1929;93:1775-1778.
7. Vance BM, Strassmann G. Sudden death following injection of foreign protein. *Arch Pathol* 1942;34:849-865.
8. Waldbott GL. The prevention of anaphylactic shock. *JAMA* 1932;98:446-449.
9. Vaughan WT, Black JH, eds. *Practice of allergy*. 2nd ed. St. Louis: CV Mosby, 1939.
10. James LP, Jr., Austen KF. Fatal systemic anaphylaxis in man. *N Engl J Med* 1964;270:597-603.
11. Rands DA. Anaphylactic reaction to desensitization for allergenic rhinitis and asthma. *Br Med J* 1980;281:854.
12. Baaagoe KH. Case of allergic death due to intracutaneous injection of 10cc of white hen's egg. *Ugeskr Laeger* 1928; 90:550.
13. Wiseman JR, McCarthy-Brough MP. Skin sensitivity in the aged-fatality following intradermal tests. *J Allergy* 1945; 16:250-252,
14. Swineford O, Jr. Anaphylactic shock from skin testing. *J Allergy* 1946; 17:24-26.
15. Blanton WB, Sutphin AK. Death during skin testing. *Am J Med Sci* 1949; 217:169-173.
16. Harris MC, Shure N. Sudden death due to allergy tests. *J Allergy* 1950; 21:208-216.
17. Dogliotti M. An instance of fatal reaction to the penicillin scratch test. *Dermatologica* 1968; 136:489-96.
18. Stewart GE, Lockey RF. Systemic reactions from allergen immunotherapy. *J Allergy Clin Immunol* 1992; 90:567-578.
19. Bousquet J, Lockey RF, Malling HJ (eds). WHO Position Paper - Allergen immunotherapy: therapeutic vaccines for allergic diseases. *Allergy* 1998; 53(44) Suppl:1-42.

2002 revision was drafted by:  
Richard F. Lockey, MD, FAAAAI

And reviewed by the membership and the 2002 Board of Directors.

*AAAAI Position Statements and Work Group Reports are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. For reference only. November 2002.*