

CORRESPONDENCE

When should adrenaline be given and by whom?

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To the Editor,

In the September issue of PAI, Niggemann and Beyer (1) discuss anaphylaxis in children and adolescents. The definition and treatment of anaphylaxis are not evidence based, and any double blinding will be regarded unethical. Thus, guidelines are based on clinical histories and observed modification of the course of severe allergic reactions by treatment. Death is the only well-defined outcome.

There are some controversial points that I would like to comment on.

When should adrenaline be administered?

From immunotherapy, it is well documented by experience and pharmacovigilance (S Dreborg, personal communication): If any symptom occurs within the first minutes, then the status of the patient will rapidly deteriorate and, if untreated, lead to severe anaphylaxis and death (Fig. 1).

The problem is the classification of early symptoms indicating possible anaphylaxis, but treated with adrenaline injection within minutes. According to the WAO grading system of

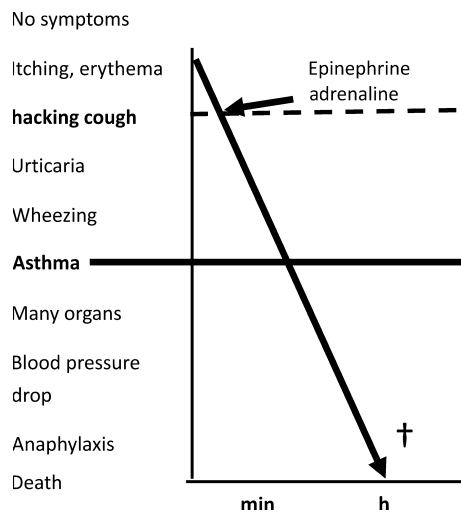


Figure 1 The time course of untreated severe allergic reactions progress to anaphylaxis and death. Because it is an overrepresentation of children and adolescents with non-treated or insufficiently treated asthma among those dying from food allergic reactions or immunotherapy-induced severe allergic reactions, the often first sign of acute asthma, the hacking cough (S Dreborg, Personal communication, 2, 3), is a definite signal for immediate use of the autoinjector.

anaphylaxis during immunotherapy(2), such reactions should be referred to as severe general allergic reactions. As they would for sure developed to full anaphylaxis if not given adrenaline, I would prefer such reactions be classified as anaphylaxis. The problem is to determine the time limit for such classification.

In conclusion, adrenaline should be given immediately to all with early symptoms of beginning anaphylaxis, for example, itching of the throat, soles, the whole body or hacking cough, and as soon as a later starting reaction progresses with more than one symptom or hacking cough/clinical asthma.

Who should be trained: children, parents, teachers, or school nurses?

I would like to argue for the model we are using in Sweden. In 1990, after meeting with several parents with young children or school children with severe symptoms arriving in the hospital with the autoinjector in their hands, I started to instruct and demonstrate to the parent/child/youth how to use the autoinjector and then let them demonstrate with active autoinjector on themselves, using the motto: 'You are always your own best advocate'. That is also true for children who have experienced severe reactions to foods.

Infants and preschool children cannot inject themselves. Then, parents and other caregivers must train on themselves to overcome their needle anxiety.

Furthermore, other caregivers must also be made aware of the risks for reactions, its prevention, and treatment.

To that end, I would recommend the system used in many counties in Sweden: So-called allergy counselors, that is, often nurses with long experience from work with children with allergies, work in close collaboration with the county pediatric allergy team, instructing and responding to questions in the child's environment: the family and preschool, schools, day care centers' personnel, and sport club and scout group leaders, etc.

In conclusion, adrenaline should be given at the first sign of early general allergic food reactions, the school child and adolescent should be trained to give the injection him/herself, and ideally, allergy counselors should instruct all kinds of caregivers.

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A proposed explanation for increased risk of active tuberculosis in children with allergic disease

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To the Editor,

A recent cross-sectional multinational study established a significant association between active tuberculosis and allergic disease (1). The authors mentioned in their discussion the polarization of T-helper cells in asthma but did not provide an explanation of this association. The key to understanding the link between allergic airway inflammation and susceptibility to active tuberculosis appears to be the action of IL-4. IL-4 is expressed in abundance in airways of patients with allergic airway inflammation (2, 3). IL-4 enhances macrophage endocytosis via the mannose receptor, which binds mycobacterial lipoarabinomannan, thus representing a major route of entry of mycobacterium tuberculosis into macrophages. IL-4 reduces nitric oxide synthase expression and hereby the action of IFN- γ -induced nitric oxide, which represents the key mechanism for intracellular killing of mycobacterium tuberculosis (4). This was confirmed in a tuberculosis mouse model: 3 weeks after infection with mycobacterium tuberculosis, bacterial load quantified by numbers of colony-forming units

(CFU) in the lungs of IL-4 knock-out mice was significantly reduced when compared with concurrently tested wild-type (WT) BALB/c mice (4). Decreased expression of the mannose receptor following IL-4 depletion could explain the observed reduced infection in IL-4-depleted mice. Reconstitution of IL-4 levels by intravenous inoculation with mouse recombinant IL-4 restored the CFU counts to the infection level of WT mice.

Several inhibitors of IL-4 production or action, including anti-IL-4 antibodies and soluble IL-4 receptor, are currently being developed for the treatment for asthma. Such inhibitors should be investigated as a way of immunoprophylaxis of tuberculosis for people at high risk of being infected and of developing active tuberculosis after infection. Development of future vaccines against tuberculosis should aim at induction of an immune response reducing IL-4 production.

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