

# Acute treatment of anaphylaxis in children

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### Abstract

**Question** A 3-year-old was rushed to my office after eating a friend's chocolate bar that contained nuts. He immediately developed urticaria on his face and swelling of his lips, and he had a persistent cough. What is the best treatment for a child with anaphylaxis? Should this family receive a prescription for an epinephrine autoinjector device?

**Answer** Intramuscular epinephrine injection is a safe and effective treatment of anaphylaxis in children. Children with systemic allergic reactions should carry epinephrine autoinjectors at all times, and should certainly have one with them at school. In order for epinephrine autoinjectors to be effective, children and their families need to be educated on how to properly use the devices, as well as keep in mind the product's expiration date.

### Traitement d'urgence de l'anaphylaxie chez les enfants

#### Résumé

**Question** Un enfant de 3 ans a été conduit d'urgence à mon cabinet après qu'il ait mangé la barre de chocolat de son ami, qui contenait des noix. Il a immédiatement développé de l'urticaire au visage, ses lèvres ont enflé et il s'est mis à tousser de manière persistante. Quel est le meilleur traitement pour un enfant victime d'anaphylaxie? Faudrait-il donner une ordonnance d'auto-injecteur d'épinéphrine à sa famille?

**Réponse** L'injection intramusculaire d'épinéphrine est un traitement sûr et efficace de l'anaphylaxie chez les enfants. Les enfants qui ont des réactions allergiques systémiques devraient avoir en tout temps un auto-injecteur d'épinéphrine et certainement en avoir un avec eux à l'école. Pour que les auto-injecteurs d'épinéphrine soient efficaces, il faut que l'enfant et sa famille soient informés de la bonne façon de se servir du dispositif et leur rappeler de ne pas oublier de vérifier la date d'expiration du produit.

Anaphylaxis is "a serious allergic reaction that is rapid in onset and may cause death," according to the second symposium on the definition and management of anaphylaxis.<sup>1</sup> This immunoglobulin E-mediated hypersensitivity reaction is manifested by a sudden release of potent, biologically active mediators from mast cells and peripheral blood basophils.<sup>2</sup> These mediators, including histamine, result in smooth muscle contraction, vasodilation, increased vascular permeability, and activation of vagal pathways. The clinical presentation includes flushing; urticaria and angioedema; wheezing; hypotension with potential shock; gastrointestinal smooth muscle contraction with nausea, vomiting, and diarrhea; and even myocardial ischemia.<sup>2,3</sup> Dermatologic manifestations (urticaria and angioedema) are the most prevalent symptoms in adults and children, followed by respiratory manifestations (dyspnea and wheezing).<sup>4,5</sup>

The most common inciting agents in children are food (eg, legumes, nuts, fish, shellfish, cow's milk, and eggs), hymenoptera (ie, bee or wasp) stings, and medications (particularly penicillins).<sup>2,4,5</sup> Latex was a common agent associated with anaphylaxis in the

past, but owing to its limited use, cases have declined substantially. However, most children with anaphylaxis have no clear history of previous reaction to the causative agent.<sup>4</sup>

### Prevention and management

Epinephrine is the first-line treatment in the acute management of anaphylaxis.<sup>3,6,7</sup> The basis for this recommendation is mainly anecdotal, as prospective trials are extremely difficult to conduct.<sup>8</sup> Delayed administration of epinephrine has been shown to result in mortality and an increased incidence of "biphasic reaction"—a recurrence of anaphylactic symptoms after an initial remission.<sup>9</sup> In one retrospective study of 106 pediatric patients, biphasic reactions were reported in 6% of patients, with the same symptoms in both phases.<sup>9</sup>

Epinephrine primarily affects the cardiovascular system and the smooth muscles via the stimulation of  $\alpha_1$ -adrenergic receptors, resulting in vasoconstriction, increased peripheral vascular resistance, and decreased mucosal edema; and stimulation of  $\beta_2$ -adrenergic receptors, resulting in bronchodilation, vasodilation, glycogenolysis, and decreased mediator release.<sup>3,8</sup>

Supplementary therapies to epinephrine include the use of H<sub>1</sub> and H<sub>2</sub> antihistamines, inhaled β<sub>2</sub>-agonists for bronchospasm, corticosteroids to minimize second-phase reactions, and intravenous fluid and dopamine for hypotension.<sup>2</sup>

### Routes of epinephrine administration

Injection of epinephrine via the intramuscular route is the treatment of choice in anaphylaxis.<sup>7,10</sup> Epinephrine is rapidly absorbed intramuscularly, and peak plasma concentrations and highest systemic effects occur promptly.<sup>10</sup> In one study of 17 children who were 4 to 12 years of age, intramuscular administration of epinephrine took an average of 8 minutes to reach maximum plasma concentrations, compared with an average of 34 minutes via the subcutaneous route.<sup>11</sup> This delay might have important clinical implications during an acute episode of systemic anaphylaxis. Subcutaneous administration of epinephrine might be appropriate in cases of mild anaphylaxis, if the condition is progressing slowly and is not life-threatening, irrespective of which organ system is affected.<sup>12</sup>

Although inhalation of epinephrine is recommended worldwide as a noninvasive alternative to epinephrine injection,<sup>10</sup> caution should be used when recommending epinephrine inhalation as a substitute for epinephrine injection, as it might be inadequate for the treatment of nonrespiratory symptoms. In one study, most of the 19 asymptomatic children 6 to 14 years old, with a history of anaphylaxis, were unable to inhale sufficient epinephrine to increase their plasma concentrations.<sup>10</sup>

Intravenous injection of epinephrine should not be given, except in severe anaphylactic shock, owing to its association with fatal cardiac arrhythmias and myocardial infarctions.<sup>3,13</sup>


### Epinephrine autoinjectors

In Canada there are 2 types of epinephrine autoinjectors available for children, and both provide a sterile, premeasured epinephrine dose. Both products have 2 dosages: 0.15 mg (for children who weigh approximately 15 kg) and 0.3 mg (for children who weigh approximately 30 kg).<sup>14</sup>

Although epinephrine is the first line of treatment for anaphylaxis, it is widely underused. One study<sup>15</sup> reported that 47% of patients with known or highly suspected cases of anaphylaxis failed to carry self-administered epinephrine despite physician recommendations, while another study<sup>6</sup> reported only 5 out of 17 children with a previous anaphylaxis episode had self-administration devices available.

One reason for the delay in treatment is the lack of recognition of symptoms. Further, among one group of parents, only 24% were able to recall all 4 steps required for the correct use of the epinephrine autoinjector device.<sup>16</sup> In addition, parents have reported confusion about both the inciting agent and severity of reaction,

as well as concerns about side effects and potential pain.<sup>7</sup> Furthermore, only 21% of practising attending physicians and 36% of pediatric residents demonstrated the correct use of an epinephrine autoinjector.<sup>17</sup>

Epinephrine autoinjectors are expensive, and many times they remain unused until their expiration date. Physicians should draw parents' attention to the expiration of these devices and to their proper replacement at home and at school. 

#### Competing interests

None declared

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Dr Goldman is Director of the PRETx program. The mission of the PRETx program is to promote child health through evidence-based research in therapeutics in pediatric emergency medicine.

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