Benefits of "Watching and Waiting" After Epinephrine Is Administered

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Learning Objectives

Upon completion of this learning activity, participants should be able to

- consider the pharmacokinetics of epinephrine administered subcutaneously, intramuscularly, and intranasally
- explain the difference between a surrogate marker and a clinical effect in the context of epinephrine use
- counsel patients regarding the appropriate use of epinephrine for the treatment of anaphylaxis

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Words to Live By

Whatever Dr. Wasserman says is correct
Sami Bahna, MD – 11/7/25

Whatever Dr. Bahna says is correct
Richard Wasserman, MD, PhD – 11/7/25

All generalizations are false
Attributed to Mark Twain – Undated

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ALEX, 26-yo with food allergy and recurrent anaphylaxis

- **Reaction History**
- Multiple accidental exposures since childhood
- Prior reactions variable; some required ED care and epinephrine (not self-administered)
- **Past year:** increased reaction **frequency and severity**
  - Symptoms: GI discomfort, generalized hives
  - **Three ED visits** for reactions
  - Most recent episode required **2 doses of epinephrine**, IV fluids, and oxygen
- All reactions attributed to **milk cross-contamination**

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ALEX, 26-yo with food allergy and recurrent anaphylaxis

- **Preparedness & Risk**
- Often forgets epinephrine auto-injector
- Not confident in how to use it properly and is hesitant to self-inject
- **Prior Workup**
- PCP visit 3 months ago
- Food IgE panel: **milk-specific IgE = 0.38 IU/mL**
- Referred to Allergy/Immunology for evaluation
- negative to egg, peanut, soy, tree nuts, shellfish, and fish (all < 0.10 IU/ml)

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What Are the Goals of Epinephrine Treatment?

Prevent

1. Death
2. Hypotension
3. Cardiovascular collapse
4. Loss of consciousness
5. Upper airway obstruction
6. Lower airway bronchoconstriction
7. Recurrent vomiting
8. Agitation

Ameliorate

1. Urticaria, flushing, itch
2. Eyelid, lip, tongue edema
3. Dysphagia
4. Rhinitis symptoms
5. Abdominal pain
6. Diarrhea
7. Sense of impending doom
8. Parental Anxiety

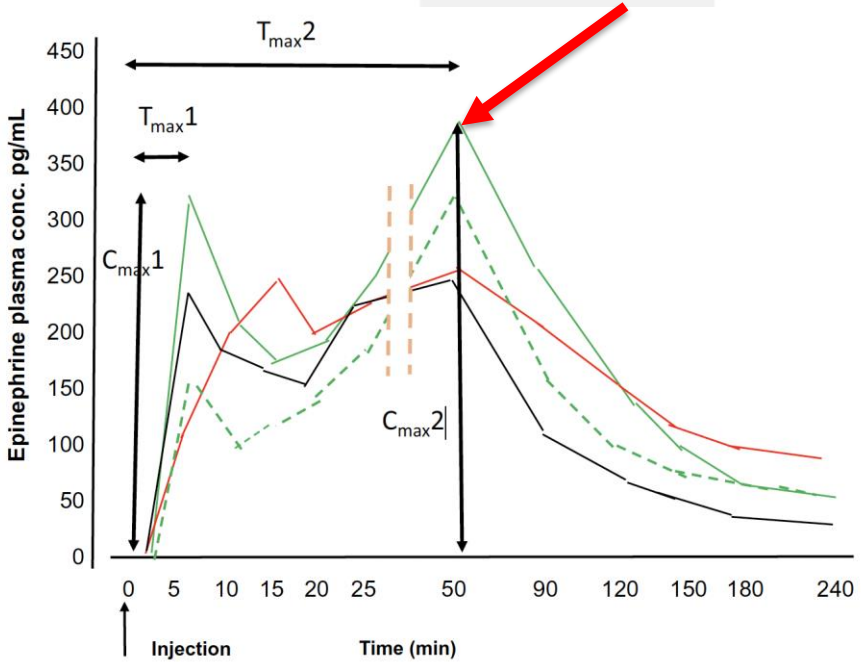
Allergy, Asthma & Clinical Immunology

REVIEW

The pharmacokinetics of epinephrine/ adrenaline autoinjectors

Sten Dreborg[1*] and Harold Kim[2,3]

- 0.3 mg green broken line, and 0.5 mg, green line, both with Cmax1 at Tmax1
- Anapen®, in normal adult men, 0.3 mg black line with Cmax1 at Tmax1
- Obese adult women
  red line with Cmax1at Tmax1 15 min.
- Ten of 12 women received subcutaneous injection Modified after Duvauchelle et al. [11]



Dreborg and Kim
Allergy Asthma Clin Immunol (2021) 17:25
https://doi.org/10.1186/s13223-021-00511-y

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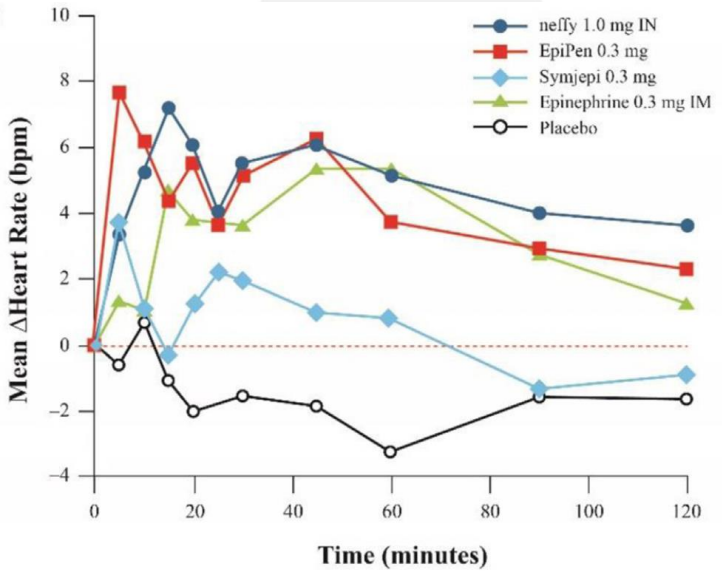
Assessing the Epinephrine Onset of Action

- Epinephrine serum concentration
- Anaphylaxis symptom relief
- Change in heart rate



Tanimoto S, et al Ann Allergy Asthma Immunol 130 (2023) 508–514

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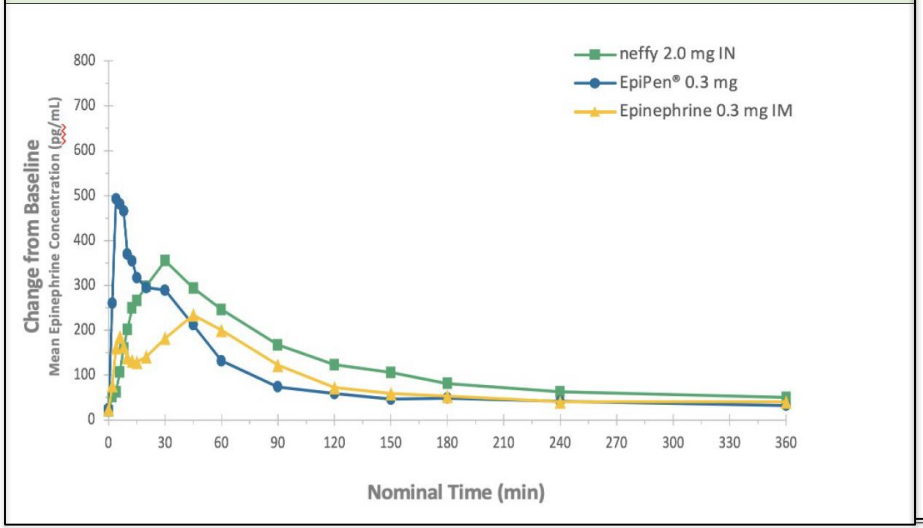
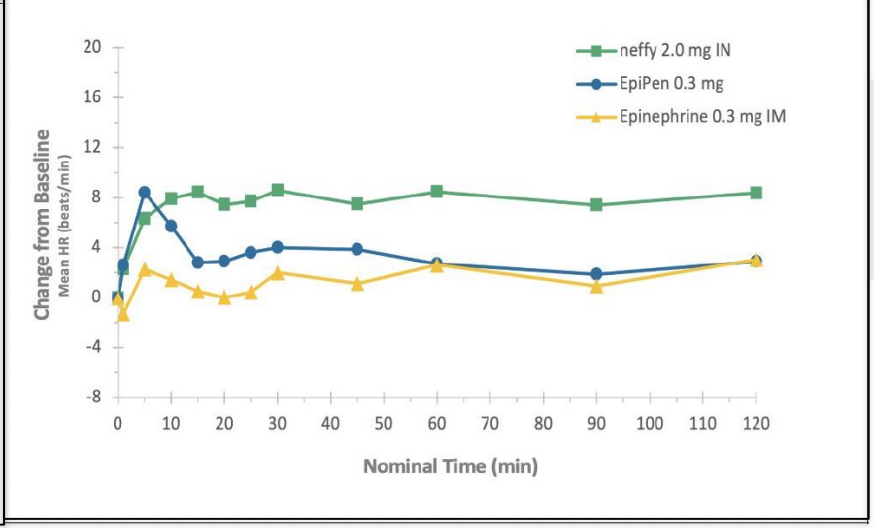
Efficacy Measures:
Epinephrine Concentration vs Heart Rate

Change from Baseline - Mean Epinephrine Concentration vs. Time Profiles



Heart Rate (HR)



Nowak-Wegrzn A, et al. *Presented at the Eastern Food Allergy and Comorbidity Conference; January 5, 2023; Palm Beach, FL*

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Epinephrine Package Insert

EPINEPHRINE INJECTION USP,

1 mg/mL ampule,

for intravenous, intramuscular, subcutaneous, and intraocular use

Initial U.S. Approval: 1939

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PI – DOSAGE AND ADMINISTRATION

- Hypotension associated with septic shock (2.2):
  - Dilute epinephrine in dextrose solution prior to infusion.
  - Infuse epinephrine into a large vein.
  - Titrate 0.05-2 mcg/kg/min to achieve desired blood pressure.
  - Wean gradually.
- Anaphylaxis (2.3):
  Administer intramuscularly or subcutaneously into anterolateral thigh every 5-10 minutes as needed
  - Adults and children over 30 kg (66 lb): 0.3-0.5 mg (0.3-0.5 mL)
  - Children under 30 kg (66 lb): 0.01 mg/kg (0.01 mL/kg)
- Intraocular surgery (2.4):
  - Dilute 1 mL with 100 to 1000 mL of an ophthalmic irrigation fluid, for ophthalmic irrigation or intracameral injection.

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PI – WARNINGS AND PRECAUTIONS

- Monitor patient for acute severe hypertension. (5.1)
- Avoid extravasation into tissues, which can cause local necrosis. (5.2)
- Do not inject into buttocks, digits, hands, or feet. (5.3)
- Potential for pulmonary edema, which may be fatal. (5.4)
- May constrict renal blood vessels and decrease urine formation. (5.5)
- May induce potentially serious cardiac arrhythmias or aggravate angina pectoris, particularly in patients with underlying heart disease. (5.6)

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PI – ADVERSE REACTIONS

- Headache
- Anxiety
- Apprehensiveness, restlessness
- Tremor
- Weakness
- Dizziness
- Sweating
- Palpitations
- Pallor, peripheral coldness
- nausea/vomiting
- respiratory difficulties

- Arrhythmias
- fatal ventricular fibrillation
- rapid rises in blood pressure producing cerebral hemorrhage
- angina

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Resuscitation Council UK

Emergency treatment of anaphylaxis
Guidelines for healthcare providers

Working Group of Resuscitation Council UK

Repeat the IM adrenaline dose after 5 minutes if there is no improvement in the patient's condition. Some guidelines recommend further doses are given in the contralateral thigh to aid absorption, although the evidence for this is uncertain.

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Acute Management of Anaphylaxis

Give INTRAMUSCULAR INJECTION (IMI) OF ADRENALINE (1:1,000) into outer mid-thigh (0.01mg per kg up to 0.5mg per dose) **without delay** using an adrenaline injector if available OR adrenaline ampoule and syringe, as shown in the table below.

If multiple doses are required to treat anaphylaxis (**2 to 3 doses administered at 5 minute intervals**), consider adrenaline infusion if skills and equipment are available.

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Anaphylaxis-related Malpractice Lawsuits

2018 | Lindor, Rachel A.; McMahon, Erika M.; Wood, Joseph P.; Sadosty, Annie T.; Boie, Eric T.; Campbell, Ronna L.

Published Web Location

https://doi.org/10.5811/westjem.2018.4.37453

- 2011-2016 – 30 anaphylaxis related lawsuits
- 12/30 claimed delayed or inadequate treatment
- 3/30 resulted in settlements, both involved deaths (average $550,000)
- 0/30 involved adverse event due to epinephrine use

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JACI The Journal of Allergy and Clinical Immunology

Use of multiple epinephrine doses in anaphylaxis: A systematic review and meta-analysis

Nandinee Patel, MD [a] · Kok Wee Chong, MD [b] · Alexander Y.G. Yip, BSc [c] · ... · Joan Bartra, MD, PhD [e] · Robert J. Boyle, MD, PhD [a] · Paul J. Turner, FRCPCH, PhD [a] ... Show more

- 86 studies (36,557 anaphylaxis events) met the inclusion criteria
- 23% were prospective studies; 74% reported reactions in the community, and 26% included food challenge data
- 7.7% of anaphylaxis events from any cause were treated with multiple doses of epinephrine
- When only health care professional use was considered
  - 11.1% of food-induced reactions
  - 17.1% of venom-induced reactions
- **Conclusion:** ~10% anaphylaxis reactions are treated with >1 dose of epinephrine

Patel N, et al, J Allergy Clin Immunol. 2021 Nov;148(5):1307-1315. doi: 10.1016/j.jaci.2021.03.042.

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Recommendations

- Teach a very low threshold for the first dose of epinephrine
- Consider a second dose of epinephrine after 5 minutes if the reaction is progressing
- Be mindful of the goals of epinephrine treatment
- Teach: “When in doubt, give epi!”

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