



## Epinephrine for Anaphylaxis

### Introduction

1. Epinephrine is commonly utilized in the Emergency Department for various indications, including hypotension, sepsis, and anaphylaxis.
2. Several dosage forms of epinephrine exist, and the dosing/route of administration differs depending on the indication.
3. Based on these differences, room for error exists, thus it is important to ensure appropriate dosage form, dose, and route of administration be used.
4. For anaphylaxis, in adults, the initial dose of epinephrine is 0.3-0.5 mg given intramuscularly in the thigh.

Pharmacology		
Epinephrine		
<b>Dose</b>	<b>Adults:</b> <b>Hospital:</b> 0.3-0.5 mg <b>Outpatient:</b> 0.3 mg	<b>Peds:</b> <b>Hospital:</b> 0.01 mg/kg up to 0.5 mg OR <b>Outpatient:</b> 7.5-15 kg: 0.1 mg, 15-30 kg: 0.15 mg, 30 kg or greater: 0.3 mg (based on available formulations)
<b>Administration</b>	IM via thigh	IM via thigh
<b>PK</b>		
<b>Adverse Effects</b>	Negligible when given IM; IV administration can lead to CV events (e.g., HTN, arrhythmias)	

# Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
<b>Simons et al, 1998</b>	Randomized, single-blind, single-dose, parallel-group pilot study comparing intramuscular (IM) vs subcutaneous (SQ) injection of epi in children with hx of anaphylaxis (n=17)	-Participants were randomly assigned to receive a single injection of epi subcutaneously or intramuscularly (site not documented) -Plasma epi concentrations were monitored before and for 180 minutes after injection of epi to assess max concentration (Cmax)	-With IM administration, the mean Cmax was 2,136 pg/ml, the mean time to max was 8 mins; <b>statistically significant higher Cmax and faster time to max than SQ administration</b>
<b>Simons et al, 2001</b>	Prospective, randomized, blinded, placebo-controlled, crossover study comparing intramuscular (IM) vs subcutaneous (SQ) injection of epi in young adult men (n=13)	-Weekly, for 6 weeks, participants received a single dose of either epi or placebo via a variety of injection sites and routes (e.g., IM, SQ, vastus lateralis muscle, deltoid muscle) -Plasma epi concentrations were monitored before and for 180 minutes after injection of epi or placebo to assess max concentration (Cmax)	-There was a 9- to 14- fold range in peak plasma epi concentrations among doses and routes of infection; a 2-fold variation in body weight, and a 3-fold variation in body mass <b>-Mean Cmax was significantly higher after IM epi administration into the thigh vs IM or SQ epi administration into the upper arm</b>
<b>Dodd et al, 2021</b>	Evidence update for the treatment of anaphylaxis	-First line treatment of anaphylaxis is intramuscular (IM) epi at a dose of 0.5 mg -IV epi was associated with a 13% increased rate of epi overdose and 8% increased rate of CV events compared to IM -Subsequent IM doses should be given every 5 mins, consider IV epi if resistant to two IM doses -Antihistamines should be used to treat skin symptoms, but should never delay administration of epi -Corticosteroids are only recommended in the setting of underlying asthma or shock (e.g., patients refractory to several doses of epi)	

## Conclusions

- Based on available data, in both children and adults, epinephrine should be administered via the intramuscular (IM) route in the vastus lateralis (e.g., thigh) muscle to ensure adequate concentrations of epinephrine are delivered
- If patients are not responsive to multiple doses of IM epinephrine, an IV epinephrine drip should be initiated
- Administration of antihistamines and steroids should never delay the administration of epinephrine and are not always indicated

## References

1. Micromedex [Electronic version]. Greenwood Village, CO: Truven Health Analytics. Retrieved January 17, 2021, from <http://www.micromedexsolutions.com/>
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3. Simons FE, Roberts JR, Gu X, Simons KJ. Epinephrine absorption in children with a history of anaphylaxis. *J Allergy Clin Immunol.* 1998;101(1 Pt 1):33-37.
4. Dodd A, Hughes A, Sargant N, Whyte AF, Soar J, Turner PJ. Evidence update for the treatment of anaphylaxis. *Resuscitation.* Published online April 23, 2021.