

UCSF High Risk Emergency Medicine Anaphylaxis February 2019

Corey M. Slovis, M.D.
Vanderbilt University Medical Center
Metro Nashville Fire Department
Nashville International Airport
Nashville, TN

True Definition of Anaphylaxis

- Reduced BP after exposure to known allergen
- Acute onset of skin or mouth symptoms plus wheezing or hypotension/tachycardia
- Involvement of **2 or more** systems:
 - Skin
 - Mucous membranes
 - Respiratory
 - Cardiovascular
 - Gastrointestinal

Mastering Emergency Medicine

- Secure the ABC's
- Consider or give NGT
 - Five Causes
 - Five Steps
 - Five Reasons for almost everything

Anaphylaxis Mediators

- Histamine
- Bradykinin
- Serotonin
- Leukotrienes
- Chemotactic factors

The Five Causes of Wheezing

- Reactive Airway Disease
- Congestive Heart Failure
- Pulmonary Embolus
- Pneumothorax
- Mass
 - *foreign body, tumor, infectious*

Symptoms of Anaphylaxis

Ann Allergy Asthma Immunol 2006;97:39-43

- *Angioedema or Urticaria (87%)
- Shortness of breath – Wheezing (59%)
- Diarrhea or Abdominal Cramps (29%)
- Throat Tightness (21%)
- Nausea or Vomiting (20%)

* Any skin manifestation including flushing > 90%

Anaphylaxis 5 Major ED Causes

- Food (*Nuts and Shellfish*)
- Stings (*bees, wasps, hornets, fire ants*)
- Medication (*ASA, NSAIDS, Pen, Sulfa*)
- Exercise/mixed causes
- Unknown

Initial Approach to all Patients with Wheezing

Secure the ABC's (The Opening Gambit)

- O₂
- O₂ saturation monitor
- IV access as indicated
- ECG monitor
- Consider 12-lead ECG

Anaphylaxis: a review of 601 cases

Luke M. Webb, MD,* and Phil Lieberman, MD†

Background: The allergist usually sees patients with anaphylaxis after the event for the purposes of identifying the cause, establishing a prognosis, and preventing further episodes. Knowledge of the characteristics of such patients is essential to achieve these goals.

Ann Allergy Asthma Immunol 2006;97:39-43

- 25 year retrospective study
- Food (22%), Meds (11%) and Exercise (5%)
- Only 41% of cases had etiology determined

Simons et al. *World Allergy Organization Journal* 2015;8:32
DOI:10.1186/s40413-015-0080-1

WAO journal
WORLD ALLERGY ORGANIZATION

POSITION ARTICLE AND GUIDELINES

Open Access

2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines

F. Estelle R. Simons^{1,2}, Motohiro Ebisawa³, Mario Sanchez-Borges⁴, Bernard Y. Thong⁵, Margitta Worm⁶,
Luciana Kaze Tanno⁷, Richard F. Lockey⁸, Yehia M. El-Gamal⁹, Simon GA Brown¹⁰, Hae-Sim Park¹¹
and Aziz Sheikh¹²

World Allergy Org J 2015;8:32

- Most current guidelines
- Epinephrine is underused in anaphylaxis

Prevalence and Severity of Food Allergies Among US Adults

Ruchi S. Gupta, MD, MPH^{1,2,3,4}, Christopher M. Warren, BA¹, Bridget M. Smith, PhD^{1,5}, et al.

3 Author Affiliations | Article Information

JAMA Netw Open. 2019;2(1):E18430. doi:10.1001/jamanetworkopen.2018.3630

Jama Open Network 2019;2:1-14

How prevalent are true food allergies in adults?

- 40,443 US adults
- 19% report a “food allergy”, 10.8% really do
- 48% developed allergies in adulthood
- Shellfish, Peanut, Fin Fish, ½ multiple foods
- 51.1% of food allergies rxes were severe

Epinephrine Anaphylaxis Dosing

0.3 cc 1:1000 IM

*0.1cc/10kg in children (0.01cc/kg).
Up to 0.5 cc in giant people.*

To avoid confusion
better to now say:

Epinephrine for First-aid Management of Anaphylaxis

Scott H. Sicherer, MD, FAAP; F. Estelle R. Simons, MD, FAAP; SECTION ON ALLERGY AND IMMUNOLOGY

Pediatrics 2017;139:e20164006

Epinephrine is the drug of choice

Epinephrine Anaphylaxis Dosing

0.3 cc 1mg in 1cc IM

*0.1cc/10kg in children (0.01cc/kg).
Up to 0.5 cc in giant people.*

The #1 cause of death in
anaphylaxis is the failure to
give epi in a timely manner

ED Therapy of Anaphylaxis

Epi

Benadryl

H-2 Blocker

Steroids

Volume

World Allergy Org J 2015;8:32

Less than ¼ of cardiac arrests due to
anaphylaxis received epi before arrest

Almost every study shows
Epinephrine is given in
less than ½ of
true anaphylaxis



Results

Resus 2017 Mar; 112:53-58

- Equal # of older and younger pts ↓ BP < 90 mm
- Older pts more likely to get IV epi
(5/122 vs 2/370)
- 5 pts had complications
- 4/5 patients were over age 50

PREHOSPITAL ADMINISTRATION OF EPINEPHRINE IN PEDIATRIC ANAPHYLAXIS – A STATEWIDE PERSPECTIVE

Leslie M. Cristiano, MD, Brian Hiestand, MD MPH, Jason W. Caldwell, DO, W. Adam Gower, MD MS, Antonio R. Fernandez, NRP PhD, Katherine Gilbert, MD, James E. Winslow, MD MPH

Abstract

Objective: Timely administration of epinephrine is critical in the treatment of anaphylaxis. This study sought to determine

statistically significant impact on epinephrine administration. Conclusion: There are missed opportunities for prehospital administration of epinephrine in pediatric patients with anaphylaxis. Very young children (age < 10) had increased

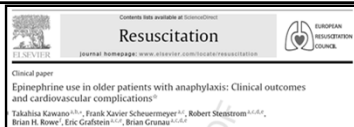
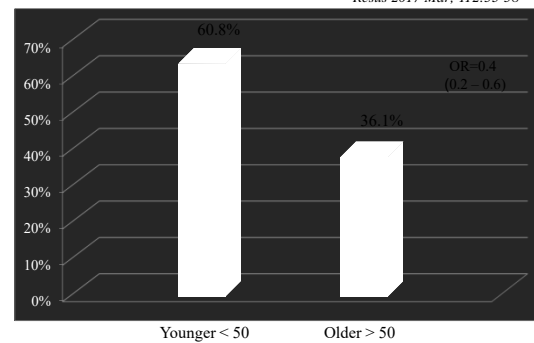
Prehosp Emerg Care 2018;22:452-6

Only 32.4% of patients received
epinephrine

Age < 10 ↓↓ Epi use by almost 3x

Epi Use in Confirmed Anaphylaxis Older vs Younger

Resus 2017 Mar; 112:53-58



Clinical paper

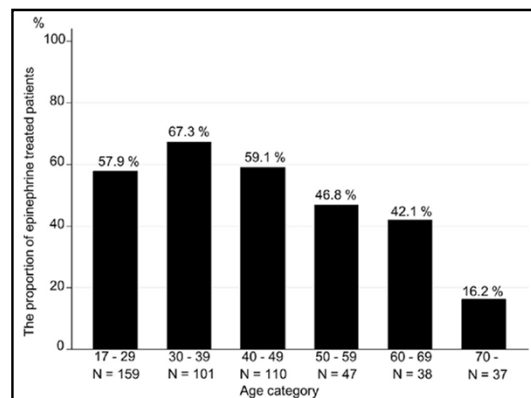
Epinephrine use in older patients with anaphylaxis: Clinical outcomes and cardiovascular complications

Takahisa Kawano^{1,2,*}, Frank Xavier Schermeringer^{1,2}, Robert Stegelmeyer^{1,2,3,4,5}, Brian H. Rower^{1,2}, Eric Grafton^{1,2}, Brian Grunau^{1,2,3,4,5}

Resus 2017 Mar; 112:53-58

Is epinephrine safe in older patients
with anaphylaxis?

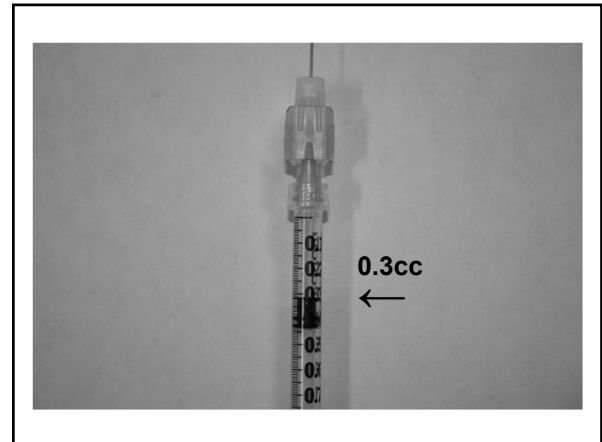
- 2,995 allergy-related visits; 492 with anaphylaxis
- 24.8% (122 pts) were ≥ 50 yo
- 2 urban academic British Columbia teaching hospitals
- BC Ambulance service
- Looked at IV and IM epi use



Resus 2017 Mar; 112:53-58

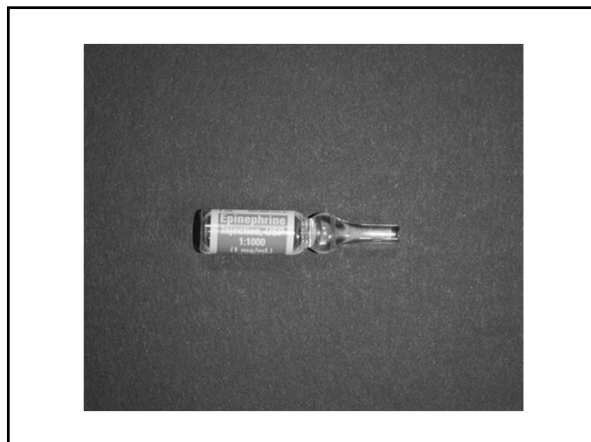
Take Homes on Epi in the Elderly

- Very, very safe
- Don't use IV epi routinely in older pts!
- Don't use IV epi routinely in younger pts!
- IV epi is for profound shock only



World Allergy Org J 2015;8:32

- No ODs with IM epi
- 13% toxicity with IV epi



ED Therapy of Anaphylaxis

Epi

Benadryl

H-2 Blocker

Steroids

Volume

Review article

H₁-antihistamines for the treatment of anaphylaxis: Cochrane systematic review

Background: Anaphylaxis is an acute systemic allergic reaction, which can be life-threatening. H₁-antihistamines are commonly used as an adjuvant therapy in

A. Sheikh¹, V. ten Brink², S. G. A. Brown³, F. E. R. Simons⁴

Allergy 2007;62:830-837

- Evaluated efficacy of H₁ Antihistamines in Anaphylaxis
- MEDLINE search 1966-2009
- Contacted pharmaceutical companies and experts
- All studies reviewed by two reviewers

Brief communication

Epinephrine absorption in adults: Intramuscular versus subcutaneous injection

F. Estelle R. Simons, MD, FRCP(C),^{*} Xiaoshen Gu, PhD,[†] and Keith J. Simons, PhD^{*,†}
Winnipeg, Manitoba, Canada

We report a prospective, randomized, blinded, placebo-controlled, 6-way crossover study of intramuscular versus subcutaneous injection of epinephrine in young men. Peak plasma epinephrine concentrations were significantly higher ($P < .01$) after epinephrine was injected intramuscularly into the thigh than after subcutaneous injection into the thigh or subcutaneous injection into the upper arm. No evidence for intramuscular injection of epinephrine into the thigh as the preferred route and site of injection of the life-saving medication in the initial treatment of anaphylaxis. (J Allergy Clin Immunol 2001;108:871-873)

Abbreviations used:
IM, intramuscularly;
SC, subcutaneously.

that peak plasma epinephrine concentrations were achieved significantly faster after IM injection by means of an EpiPen into the thigh (vastus lateralis) than after SC epinephrine injection in the upper arm (deltoid region). This study led to recommendations for IM injection of epinephrine in both children and adults with anaphylaxis,¹ though there was no experimental evidence on which

J Allergy Clin Immunol 2001;108:871-873

- 6 way crossover study SQ vs. IM
- Levels 4-6 times higher for IM in thigh vs. arm
- Levels 2 times higher IM vs. SQ in arm

Review article

H₁-antihistamines for the treatment of anaphylaxis: Cochrane systematic review

Background: Anaphylaxis is an acute systemic allergic reaction, which can be life-threatening. H₁-antihistamines are commonly used as an adjuvant therapy in

A. Sheikh¹, V. ten Brink², S. G. A. Brown³, F. E. R. Simons⁴

Allergy 2007;62:830-837

“There are no controlled studies to prove the efficacy of antihistamines in anaphylaxis or to make effective dosing recommendations.”

How effective is diphenhydramine or other more selective antihistamines in anaphylaxis?

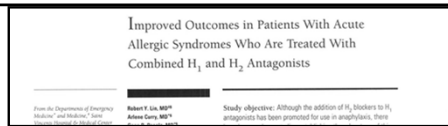
H1-antihistamines Reduce Progression to Anaphylaxis Among Emergency Department Patients With Allergic Reactions

Takahisa Kawano MD, PhD,¹ Rikari X. Scheuermeyer MD, MSc,² Koichiro Gibo MD,³ Robert Stenstrom MD, PhD,⁴ Brian Rowe MD, MSc,⁵ Eric Grafstein MD,⁶ Brian Grunau MD, MSc,⁷

First published: 15 December 2016 | <https://doi.org/10.1111/ajem.13147>

Acad Emerg Med 2017; 24:733-741

The use of an antihistamine in patients with allergic reactions reduced progression to anaphylaxis from 3.4% without H₁ blocker to 1.9% with H₁ blocker (34% decrease) in a study from 2 Canadian EDs, 2376 patients



Ann Emerg Med 2000;36:462-468

- Added H₂ Blocker to Benadryl
- Significant decrease in Urticaria with H₂ Blocker
- Decreased Urticaria from 46% to 14% (p=0.03)
- Improves Symptoms by OR of 4.7
- No toxicity, cheap, lasts 8-12 hours



JACI: In Practice, Sept-Oct 2017;1295-1301

If all risk factors present
then 20% risk of biphasic
vs only 1.6% if no risk factors

Steroids

- IV, IM, PO
- Take hours (2-6 hrs)
- All patients with systemic symptoms
- 80-125 mg SoluMedrol or 60-80 Prednisone
- Three days of therapy



JACI: In Practice, Sept-Oct 2017;1295-1301

Biphasic Reactions (4%)

- Prior history of anaphylaxis
- Unknown trigger
- Delayed epi > 60 min of symptoms



JACI: In Practice, Sept-Oct 2017;1295-1301

Biphasic Reactions (4%)

- Prior history of anaphylaxis
- Unknown trigger
- Delayed epi > 60 min of symptoms

Volume

- Give 500-1000 cc (or 20 cc/kg)
- May require more
- Keep patients flat longer
- Anaphylaxis should not "cause" trauma

A patient is eating Pad Thai and suddenly slumps in his noodles. BP is nonpalpable, pt is profoundly diaphoretic and med alert bracelet says allergic to peanuts. You cannot feel a pulse, but he is breathing and wheezing.

Rx?

PATIENT SAFETY/CONCEPTS
Confusion About Epinephrine Dosing Leading to Iatrogenic Overdose: A Life-Threatening Problem With a Potential Solution

Manmeet Kammar, MD
Charlotte B. Ivins, MD
John J. Franks, MD
Kathryn Weber, PharmD
Howard Rosen, MD

From the Division of Cardiology, Department of Medicine (Kammar, Franks, Rosen), Department of Emergency Medicine (Ivins), and Department of Pharmacy (Weber), St. John Hospital and Medical Center, Detroit, MI.

Epinephrine is indicated for various medical emergencies, including cardiac arrest and anaphylaxis, but the dose

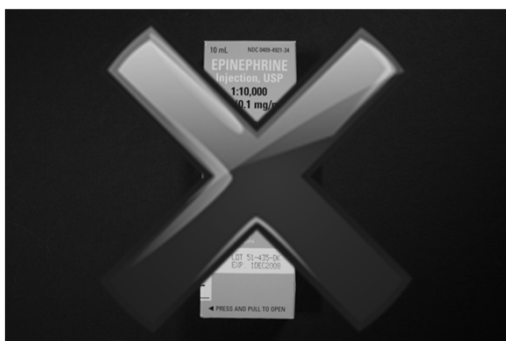
Ann Emerg Med 2010;55:341-344

Physicians, nurses and paramedics make dosing mistakes in using IM and IV epinephrine, especially when dealing with severe anaphylaxis and asthma.

IV Epinephrine Infusion

- Only for true shock
- Life Saving, but potentially Toxic
- Start at 1 - 2 microgram/minute
- Titrate to Effect

The starting dose epinephrine by IV infusion is 1-2 micrograms/minute



The "1" Rule for IV Epi:

- 1 amp
or
- 1 mg
in
- 1 liter
at
- 1 cc/min
adjust
- Q 1 minute

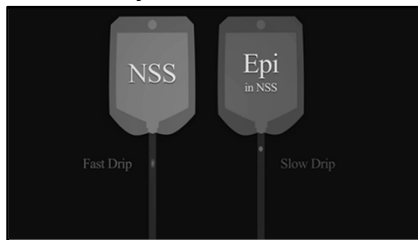
IV Epinephrine at 1 mcg/min

- **1 mg of Epinephrine in 1000 cc**
 - 1 cc of 1:1,000
 - or*
 - 10 cc of 1:10,000
- Start at **1 cc/min.**
- Piggy back into high flow IV
- Titrate to Effect **Q 1 minute**
- Follow HR and monitor

IV Epinephrine at 1 mcg/min

- **1 mg of Epinephrine in 1000 cc**
 - 1 cc of 1:1,000
 - or*
 - 10 cc of 1:10,000
- Start at **1 cc/min.**
- Piggy back into high flow IV
- Titrate to Effect **Q 1 minute**
- Follow HR and monitor

- Inject 1mg Epi into 1000 cc
- Run IV at 1 cc/min.
 - piggy back into high flow IV
- Titrate to Effect
 - Adjust rate as needed



Discharging Patients

- 2 days of steroids
- Benadryl
- H₂ Blocker
- Recommend Medical Bracelet
- Epi Pen Rx

Dead or Dying → IV Epi

IV Epi → Dead or Dying



Autoinjector Errors

Ann Allergy Asthma Immunol 2015;114:63-76

- Up to 84% misuse rate
- Misuse also documented in fatal cases
- Often not held for 10 seconds
- No injection due to suboptimal force
- Finger injections > 10%

NEWS & PERSPECTIVE

Annals Emerg Med 2017;69:16-19A

EpiPen Controversy Reveals Complexity Behind Drug Price Tags

by JIM GREENE
Special Contributor to
Annals Emerg Med

"As a practicing emergency physician, [I] frequently care for acute anaphylactic and allergic reactions."

- Do not write "Epi Pen"
- Write Epi Pen generic
- Give second Rx:
- "Generic Epinephrine AutoInjector" (formerly called Adrenoclick)



Int Forum Allergy Rhinol 2017 Mar;7(3);276-286

- Only 54% filled Rx within 1 year
- Only 50% of patients carry the Epi Pen
- Parents often unclear on indications and use
- Only 25% of MDs (EM, FP, Peds) know how to teach correct use
- Less than 50% acute care MDs use when indicated

ED Therapy of Anaphylaxis

Epi

Benadryl

H-2 Blocker

Steroids

Volume

Epi Pen Prices

\$730?

\$300?

\$100?

Covered by Insurance?

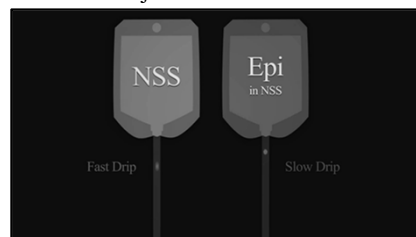
SECURE THE ABC'S

Epinephrine Anaphylaxis Dosing

0.3 cc 1mg in 1cc IM

*0.1cc/10kg in children (0.01cc/kg).
Up to 0.5 cc in giant people.*

- Inject 1mg Epi into 1000 cc
- Run IV at 1 cc/min.
 - piggy back into high flow IV
- Titrate to Effect
 - Adjust rate as needed



CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care
American Academy
of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Epinephrine for First-aid Management of Anaphylaxis

Scott H. Sicherer, MD, FAAP,* F. Estelle R. Simons, MD, FAAP† SECTION ON ALLERGY AND IMMUNOLOGY

Pediatrics 2017;139:e20164006

Epinephrine is the drug of choice

Expertise is when to Know and
to Act are one in the same

Bruce Lee

The #1 cause of death in
anaphylaxis is the failure to
give epi in a timely manner

