

# Type I Allergies & Unmet Needs

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# Type I Allergic Reactions: Systemic Hypersensitivity Reaction

**~40 Million** people in  
**US** with systemic Type I allergic  
reaction to allergens

More than

**500,000** ER visits

**each year** due to systemic Type I allergic  
reactions<sup>1</sup>, costing an average of \$1600+ per visit<sup>2</sup>



Caused by exposure to a **specific allergen**,  
most commonly **food, venom, drugs**



**Significant co-morbidities and symptomatic  
impact** on quality of life.



**Other Type I allergy indications**  
(e.g. urticaria flares)




# Anaphylaxis Diagnosis Criteria and Symptoms

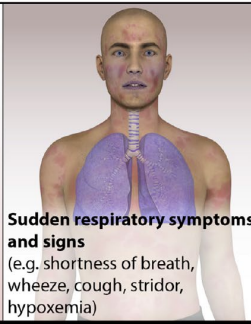
Anaphylaxis is highly likely when any one of the following three criteria is fulfilled

1 Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)

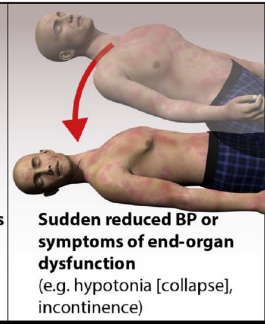
AND AT LEAST ONE OF THE FOLLOWING:



Sudden skin or mucosal symptoms and signs (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)




Sudden respiratory symptoms and signs (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)

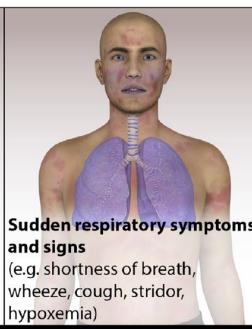


Sudden reduced BP or symptoms of end-organ dysfunction (e.g. hypotonia [collapse], incontinence)


OR 2 Two or more of the following that occur suddenly after exposure to a likely allergen or other trigger\* for that patient (minutes to several hours)



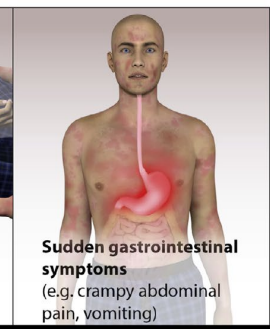
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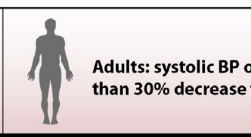


Sudden gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)

OR 3 Reduced blood pressure (BP) after exposure to a known allergen\*\* for that patient (minutes to several hours)

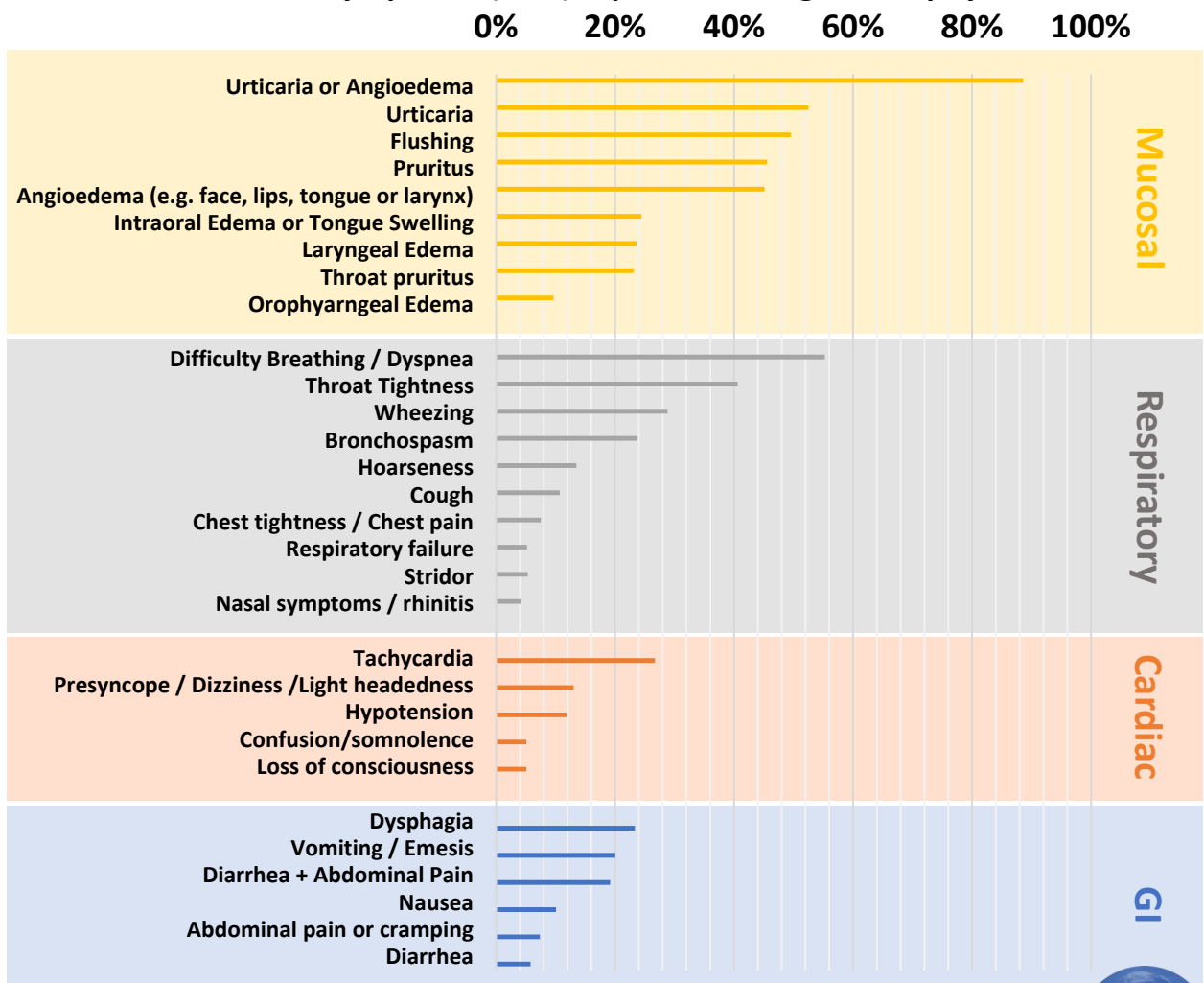


Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP \*\*\*



Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

Symptoms (>2%) reported during US anaphylaxis events<sup>2-14</sup>



References: 1. Shaker MS, et al. *J Allergy Clin Immunol.* 2020. 2. Pistiner M, et al. *J Allergy Clin Immunol Pract.* 2021. 3. Jalil M, et al. Abstract at AAAAI 2020 Virtual Meeting. 4. Gonzelez-Estrada A, et al. *Ann Allergy Asthma Immunol.* 2018. 5. Lee S, et al. *J Allergy Clin Immunol.* 2017. 6. Lee S, et al. *J Allergy Clin Immunol Pract.* 2014. 7. Manivannan V, et al. *Am J Emerg Med.* 2014. 8. Wood RA, et al. *J Allergy Clin Immunol* 2014. 9. Walsh KE, et al. *Pharmacoepidemiol Drug Saf* 2013. 10. Decker WW, et al. *J Allergy Clin Immunol.* 2008. 11. Ross MP, et al. *J Allergy Clin Immunol.* 2008. 12. Webb LM & Lieberman P. *Ann Allergy Asthma Immunol.* 2006. 13. Ditto AM, et al. *Ann Allergy Asthma Immunol.* 1996. 14. Rudders SA, et al. *Pediatrics.* 2010. Note that some publications do not specify angioedema symptom subtype. Angioedema subtype frequency aggregated when reported.





**Most frequently reported symptoms are difficulty breathing, angioedema (face, lips, tongue, larynx) and urticaria (hives)**



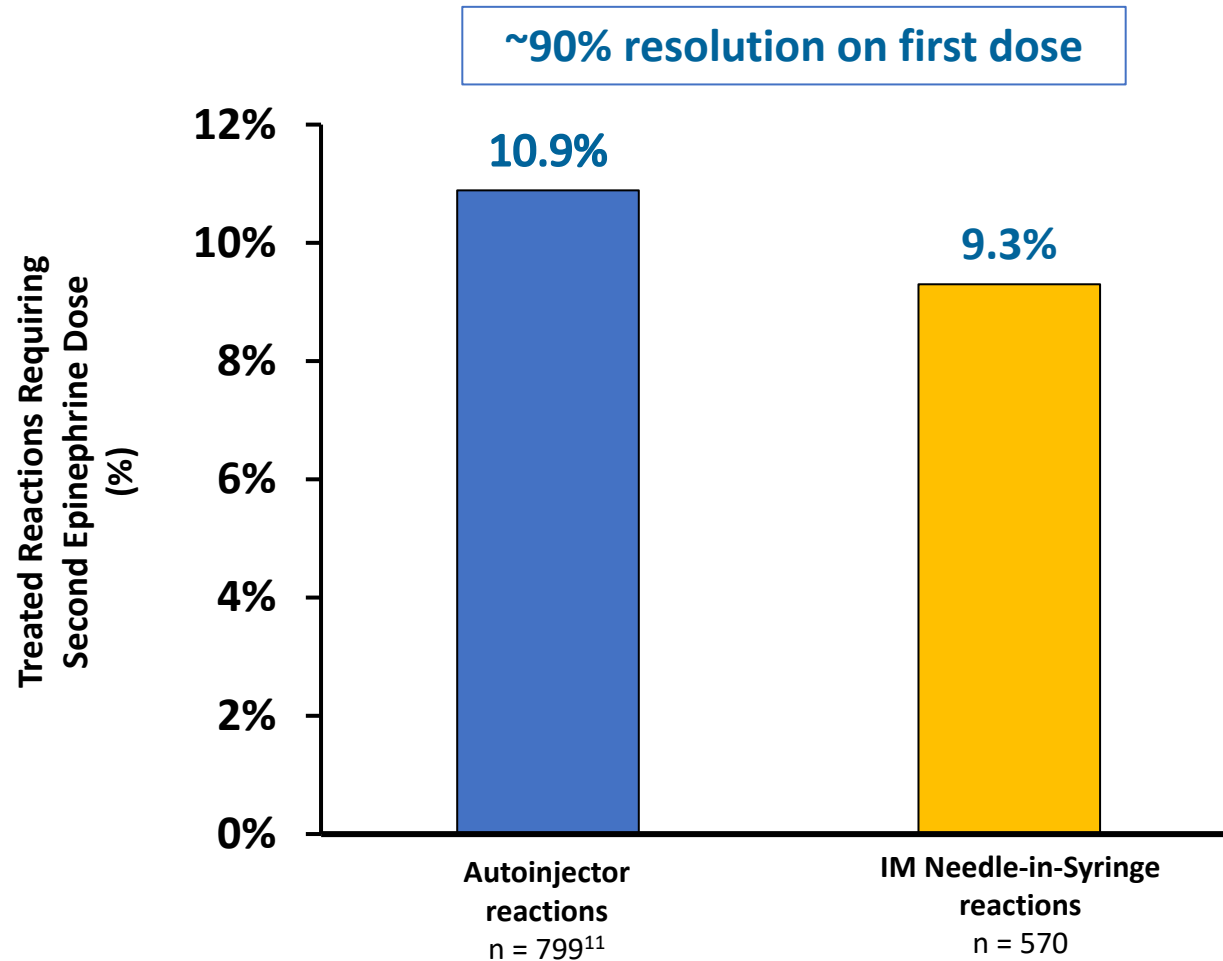
# Epinephrine: Well Known Mechanism of Action

Adrenergic Receptor	Pharmacological Effect of Epinephrine	Clinical Effect of Epinephrine
$\beta_2$	<ul style="list-style-type: none"><li>• <b>Stabilizes mast cells and basophils - Inhibits inflammatory mediators</b></li><li>• Relaxation of bronchial smooth muscles</li><li>• Vasodilation in skeletal vasculature</li></ul>	<ul style="list-style-type: none"><li>• <b>Reverses pathological histamine cascade</b></li><li>• Increase in bronchial airflow</li><li>• Increases blood to skeletal muscle</li></ul>
$\beta_1$	<ul style="list-style-type: none"><li>• Increases blood pressure and heart rate</li></ul>	<ul style="list-style-type: none"><li>• Relieves hypotension and shock</li></ul>
$\alpha_1$	<ul style="list-style-type: none"><li>• Increases systolic blood pressure</li><li>• Causes blood vessel constriction</li><li>• Decreases mucosal edema</li></ul>	<ul style="list-style-type: none"><li>• Relieves hypotension and shock</li><li>• Relieves upper airway obstruction</li></ul>

Receptor Sensitivity



# Second Dose Demonstrates Similar Efficacy Between IM and Autoinjectors (the only FDA approved products today)



- Analysis of 12 studies with 100% autoinjector ( $\geq 80\%$  EpiPen) or 100% IM-needle-and-syringe use in community or ED setting<sup>1-11</sup>
- Differences in PK profile across products do not impact efficacy based on need for repeat dosing to resolve symptoms



# Prompt Treatment with Epinephrine is Critical



Patients / Caregivers wait  
up to **18 minutes**  
to dose epinephrine

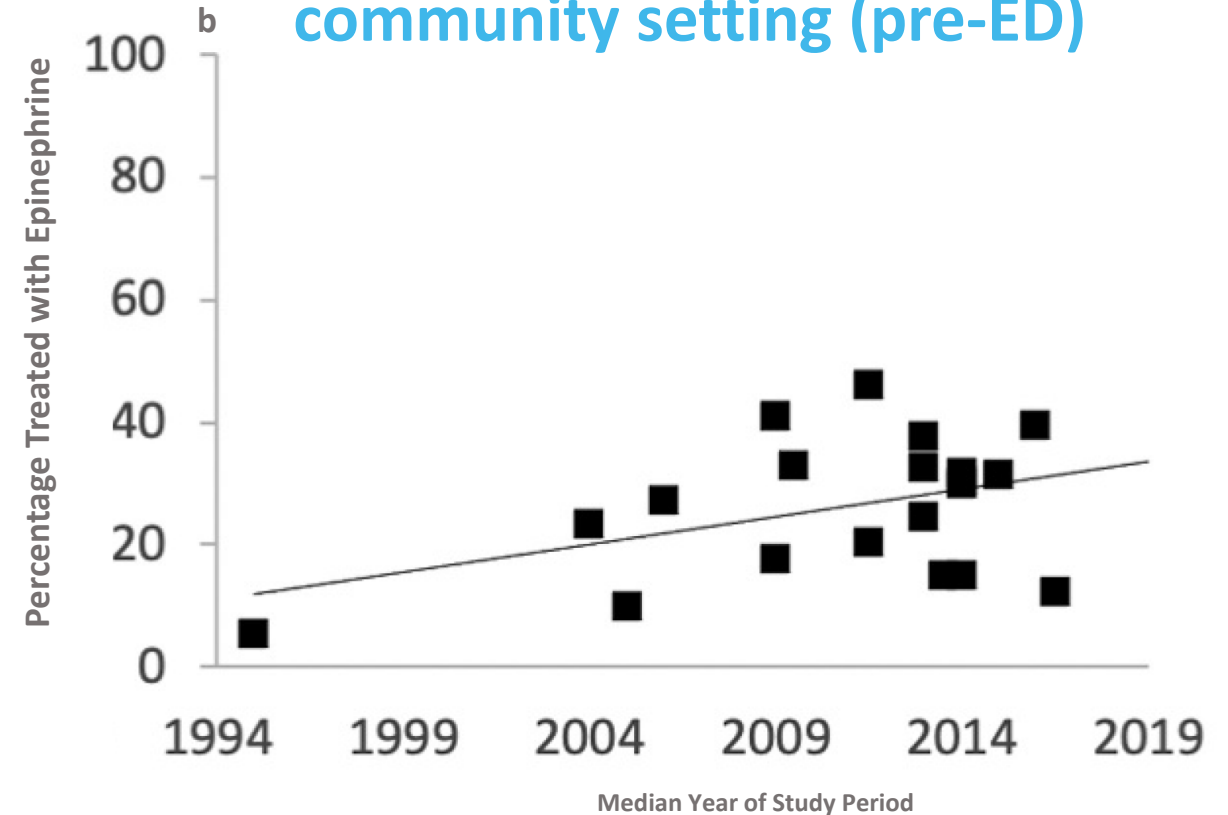


Consequence of Delayed Treatment	Risk Factor
Abnormal vitals (HR, SBP, Respiration) <sup>1</sup>	p<0.001
Repeat Epinephrine Doses <sup>2</sup>	OR = 5.0
Hospitalization (500,000 ER visits / yr) <sup>3</sup>	HR = 4.0
Biphasic anaphylaxis <sup>4</sup>	OR = 3.4
Fatality <sup>5</sup>	



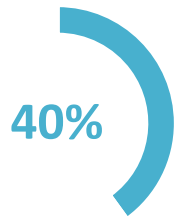
**Only ~40%  
of ER Anaphylaxis  
Patients are Dosed  
with Epinephrine  
Pre-Arrival in the  
Community Setting**

**% dosed with epinephrine in  
community setting (pre-ED)**

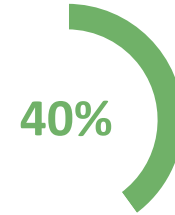




# Delays in Treatment with Epinephrine are Principally Due to Autoinjector Limitations and Accompanying Patient Reluctance



>40% of patients **do not fill or refill** their epinephrine prescription<sup>1</sup>



~40% of patients **do not administer** epinephrine at all<sup>2</sup>

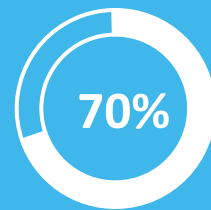


55%-60% don't consistently **carry** epinephrine<sup>2-4</sup>



>50% of parents are **afraid or somewhat afraid to administer** their child's epinephrine<sup>5</sup>

**Patients that Do Not Administer Correctly<sup>7</sup>**



~70% of patients **Without Training**



~20% of patients **with Training**



# Needle-Related Safety Risks & Use Errors

## Needle-related risks defined in labeling for all autoinjectors

- Lacerations and bone injections
- IV bolus injection (blood vessel injections) – likely result in most serious AEs

## Accidental self-injection into extremity by patient or caregiver

- ~ 3,500 events per year reported<sup>1</sup>
- Requires immediate medical attention (treatment in ER typical)

## Injection site pain, infection and other reactions<sup>2</sup>

## Wet injections (withdraw needle too quickly) and other dosing errors

## User errors and device malfunctions<sup>3,4,5,6,7,8,9</sup>



# 2023 AAAAI guidelines updated so that EMS activation not required for 90% of events that resolve with single dose

## Practice Parameters

### Anaphylaxis: A 2023 practice parameter update

**Historic guidelines recommended ED visit following use of epinephrine for anaphylaxis, which may result in families not giving epinephrine to avoid ED visits**

**Based on outcomes of anaphylaxis in EDs and the COVID-19 pandemic, data indicates treatment and monitoring of anaphylaxis can occur at home**

- If signs and symptoms resolve within minutes of dosing, monitor at home after first dose
- If signs and symptoms improve within minutes of dosing, monitor at home if comfortable, while considering EMS activation and possible second dose of epinephrine
- If signs and symptoms are not resolving, activate EMS immediately, and consider second dose of epinephrine

**Prompt use of epinephrine and monitoring at home will decrease healthcare utilization**



# ***neffy* (epinephrine nasal spray) Can Fill Great Unmet Medical Need for Patients and Caregivers**

## **Epinephrine has a well-established efficacy and safety profile**

- Efficacy same across epinephrine injection products despite PK differences

## **Immediate administration of epinephrine is critical**

## **Patients and caregivers reluctant to use or carry current devices**

- Needle-phobia
- Concerns with safety
- Cumbersome to carry

## **Unmet need for needle-free, easy to use, easy to carry, safe and effective epinephrine option**

## ***neffy* can fit that need for our patients**

