

# Understanding and Recognizing Anaphylactic Reactions

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## Questions

1. What is anaphylaxis (versus a systemic allergic reaction)?
2. How do you recognize it?
3. Can you predict the seriousness of a reaction by the presenting signs and symptoms?
4. Can you predict the seriousness of the reaction by identifying the route of antigen presentation, parenteral or oral?
5. Can the time of onset predict a more serious reaction?

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## Clinical Definition of Anaphylaxis Criterion 1

- An individual has skin symptoms or swollen lips *and either* :
  - Respiratory compromise or
  - Reduced blood pressure (< 100 mm HG systolic or > 30% decrease)

Sampson HA et al. *JACI* 2005;115:584-91

## Clinical Definition of Anaphylaxis Criterion 2

- An individual had exposure to a *suspected allergen* and two or more of the following:
  - Skin symptoms or swollen lips
  - Respiratory compromise
  - Reduced blood pressure
  - GI symptoms with suspected food allergy (such as vomiting, diarrhea, cramping)

Sampson HA et al. *JACI* 2005;115:584-91

## Clinical Definition of Anaphylaxis Criterion 3

- An individual had exposure to a *known allergen* and experiences reduced blood pressure (< 100 mm Hg in adults or a decrease in systolic BP by > 30%)

Sampson HA et al. *JACI* 2005;115:584-91

## When Do You Give Epinephrine

- Do you give epinephrine when a patient fulfills any of the above criteria as defined by Sampson et al. and the NIAID?
- Do you give epinephrine at the earliest signs of a systemic reaction when there is a known exposure to an allergen to which an individual is allergic?

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## Second NIAID Food Allergy and Anaphylaxis Network Symposium (cont'd)

When a patient fulfills any of the 3 criteria of anaphylaxis outlined above, the patient should receive epinephrine immediately because epinephrine is the treatment of choice in anaphylaxis. **There undoubtedly will be patients who present with symptoms not yet fulfilling the criteria of anaphylaxis yet in whom it would be appropriate to initiate therapy with epinephrine, such as a patient with a history of near-fatal anaphylaxis to peanut who ingested peanut and within minutes is experiencing urticaria and generalized flushing.**

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• Sampson HA et al. *J Allergy Clin Immunol* 2006;117:391-7

## Anaphylaxis in Infants: Can Recognition and Management be Improved?

Anaphylaxis signs in infants: obvious but may be nonspecific

Skin/mucous membranes: rapid onset of hives (potentially difficult to discern in infants with acute atopic dermatitis; scratching and excoriations, as such, will be absent in young infants); angioedema (face, tongue, oropharynx)

Respiratory: rapid onset of coughing, choking, stridor, wheezing, dyspnea, apnea, cyanosis

Gastrointestinal: sudden, profuse vomiting

Cardiovascular: weak pulse, arrhythmia, diaphoresis/sweating, pallor, collapse/unconsciousness

Central nervous system: rapid onset of unresponsiveness, lethargy, or hypotonia; seizures

• Simons FER. *J Allergy Clin Immunol* 2007;120:537-40

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## Anaphylaxis from World Allergy Organization: Statement on Epinephrine

- Anaphylaxis is an acute and potentially lethal multisystem allergic reaction in which some or all of the following signs and symptoms occur: diffuse erythema, pruritus, urticaria and/or angioedema; bronchospasm; laryngeal edema; hypotension; cardiac arrhythmias; feeling of impending doom; unconsciousness and shock. Other earlier or concomitant signs and symptoms can include itchy nose, eyes, pharynx, genitalia, palms, and soles; rhinorrhea; change in voice; metallic taste; nausea, vomiting, diarrhea, abdominal cramps, and bloating; lightheadedness; headache; uterine cramps; and generalized warmth.

Kemp SF, Lockey RF, Simons FER, et al. *Allergy* 2008;63:1061-1070

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## Subcutaneous Systemic Reaction Grading System

World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Symptoms(s) sign(s) of one organ system present	Symptom(s) sign(s) of more than one organ system present	<u>Lower respiratory</u>	<u>Lower or Upper respiratory</u>	Death
<u>Cutaneous</u>		Asthma (e.g., 40% PEF or FEV1 drop,	Respiratory failure with or without loss of consciousness	
Generalized pruritus, urticaria, flushing or sensation of heat or warmth	or	NOT responding to an inhaled bronchodilator)	Or	
or	<u>Lower respiratory</u>	or	<u>Cardiovascular</u>	
Angioedema (not laryngeal, tongue or uvular)	Asthma: cough, wheezing, shortness of breath (e.g., less than 40% PEF or FEV1 drop, responding to an inhaled bronchodilator)	<u>Upper respiratory</u>	Hypotension with or without loss of consciousness	
or	or	Laryngeal, uvula or tongue edema with or without stridor		

## Subcutaneous Systemic Reaction Grading System

World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System (cont'd)

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
<u>Upper respiratory</u>	<u>Gastrointestinal</u>			
Rhinitis (e.g., sneezing, rhinorrhea, nasal pruritus and/or nasal congestion)	Abdominal cramps, vomiting, or diarrhea			
or	or			
Throat-clearing (itchy throat)	or			
or	<u>Other</u>			
Cough perceived to come from the upper airway, not the lung, larynx, or trachea	Uterine cramps			
or				
<u>Conjunctival</u>				
Conjunctival erythema, pruritus or tearing				
<u>Other</u>				
Nausea, metallic taste, or headache				

## Worldwide Reporting and Grading System for Anaphylaxis (cont'd)

- Oral allergy syndrome is defined as, "Local IgE-mediated mast cell activation provokes the rapid onset of pruritus, tingling and angioedema of the lips, tongue, palate and throat, and occasionally a sensation of pruritus in the ears and/or tightness in the throat". It is associated with the oral administration of an allergen. Oral allergy syndrome is not part of this grading system.

Sampson. In: Middleton

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## Questions

### 1. How is anaphylaxis defined?

#### Answer:

- There are different definitions of anaphylaxis.
- For the clinician, it is better to define anaphylaxis to include any systemic sign or symptom associated with a known or suspected allergen exposure temporally related to its onset (systemic allergic reaction).

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## Symptoms and Signs of Anaphylaxis

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### Skin, subcutaneous tissue, and mucosa

- Flushing, itching, urticaria (hives), angioedema, morbilliform rash, pilor erection
- Periorbital itching, erythema and edema, conjunctival erythema, tearing
- Itching of lips, tongue, palate, and external auditory canals; and swelling of lips, tongue, and uvula
- Itching of genitalia, palms, and soles

## Symptoms and Signs of Anaphylaxis (cont'd)

### Respiratory

- Nasal itching, congestion, rhinorrhea, sneezing
- Throat itching and tightness, dysphonia, hoarseness, stridor, dry staccato cough
- Lower airways: increased respiratory rate, shortness of breath, chest tightness, deep cough, wheezing/bronchospasm, decreased peak expiratory flow
- Cyanosis
- Respiratory arrest

## Symptoms and Signs of Anaphylaxis (cont'd)

### Gastrointestinal

- Abdominal pain, nausea, vomiting (stringy mucus), diarrhea, dysphagia

### Cardiovascular system

- Chest pain
- Tachycardia, bradycardia (less common), other arrhythmias, palpitations
- Hypotension, feeling faint, urinary or fecal incontinence, shock
- Cardiac arrest

## Symptoms and Signs of Anaphylaxis (cont'd)

### Central nervous system

- Aura of impending doom, uneasiness (in infants and children, sudden behavioral change, e.g. irritability, cessation of play, clinging to parent); throbbing headache (pre-epinephrine), altered mental status, dizziness, confusion, tunnel vision

### Other

- Metallic taste in mouth
- Cramps and bleeding due to uterine contractions in females

## 2. How do you recognize it?

Answer:

- a. Clinically, it is recognized by monitoring the patient after an substance suspected to cause anaphylaxis
- b. By knowing the systemic signs and symptoms of anaphylaxis.

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Grading System for Generalized Hypersensitivity Reactions (1149 Cases of Anaphylaxis) (Modified by Lockey)

Grade	Defined by	% without Skin Involvement
1 – Mild (skin and subcutaneous tissues only)*	Generalized erythema, urticaria, periorbital edema, or angioedema	0%
2 – Moderate (features suggesting respiratory, cardiovascular, or gastrointestinal involvement)	Dyspnea, stridor, wheeze, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness, or abdominal pain	17%**
3 – Severe (hypoxia, hypotension, or neurologic compromise)	Cyanosis or SpO <sub>2</sub> ≤ 92% at any stage, hypotension (SBP < 90 mm Hg in adults), confusion, collapse, LOC, or incontinence	22%**

SBP, Systolic blood pressure; LOC, loss of consciousness.

\*Mild reactions can be further subclassified into those with and without angioedema

\*\* Comment: may have been missed in these

\*Brown SGA. J Allergy Clin Immunol 2004;114:371-6

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## Fatal and Near-Fatal Anaphylactic Reactions to Food in Children and Adolescents

- 6 fatal & 7 near fatal
- 5 of 6 fatalities reported oral or abdominal cramps (itching or tingling in the mouth, tightness in the throat, and abdominal cramps or vomiting). One experienced "skin" symptoms. No patient received epinephrine at onset.
- 7 near fatal. All had skin symptoms. No patient received epinephrine when the initial symptoms began.
- **Conclusion:** the failure to recognize the severity of the reaction and to administer epinephrine promptly increases the risk of fatal outcome.

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Samoson HA et al. N Engl J Med 1992;327:380-4

## Systemic Reactions, Signs and Symptoms from Venom Immunotherapy

	Mild N=193	Moderate N=106	Severe N=38	Subjects with each sign or symptom 115
Pruritus	75 (54%)	31 (29%)	9 (32%)	114
Angioedema/ urticaria	72 (37%)	33 (31%)	9 (32%)	114
GI Symptoms	--	0	11 (39%)	11
Upper airway obstruction	--	63 (59%)	9 (32%)	2

Lockey RF, Turkeltaub PC, Olive CA, Baird-Warren I, Olive ES, Bukantz SC: The Hymenoptera Venom Study III, Safety of Venom Immunotherapy. JACI 1990;86:775-789.

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## Questions

### 3. Can you predict the seriousness of a reaction by the presenting signs and symptoms?

#### Answer:

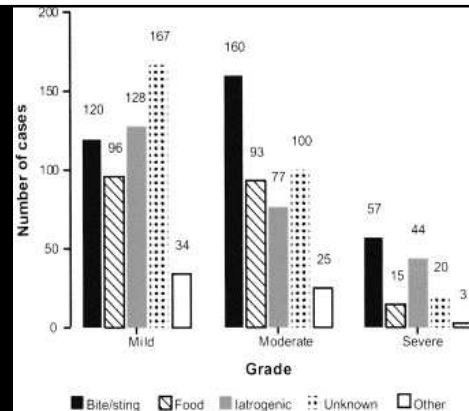
Cutaneous symptoms and other mild symptoms can be the initial signs and symptoms and are many times associated with serious life-threatening anaphylaxis.

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Reaction grade according to etiology  
\*Brown SGA. J Allergy Clin Immunol 2004;114:371-6

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## Food Fatalities, 2001-2006

### • Epinephrine Given

Yes	4
Unknown	5
No	22 (12 none & 10 too late)

TOTAL 31

- Bock et al. JACI 2007

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## Autopsy Series of Anaphylactic Reactions

- **Conclusion:** Epinephrine given too late, only 14% received it before respiratory arrest
- Median minutes to arrest: 55 iatrogenic, 5 (1 – 80); 37/oral, 30 (6 – 360); 32 venom, 15 (4 – 120)

- Pumphrey RSH. Clin Exp Allergy 2000

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## Questions

### 5. Can the time of onset predict a more serious reaction?

#### Answer:

- More serious reactions tend to have an early onset of signs and symptoms. However, exceptions.

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## Questions

### 4. Can you predict the seriousness of the reaction by identifying the route of antigen presentation, parenteral or oral?

#### Answer:

- Parenteral route potentially more dangerous than oral, but both can be serious and life-threatening.

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## Time of Onset of Fatal Reactions from SCIT

0 – 3 minutes	17
3 – 10 minutes	11
10 – 20 minutes	7
20 – 30 minutes	4
> 30 minutes	7
Unknown	12

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TOTAL 58

- Lockey et al. *JACI* 1987
- Reid, Lockey et al. *JACI* 1993
- Bernstein et al. (Similar questionnaire) 2004

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## Evaluation of Near-Fatal Reactions to Allergen Immunotherapy Injections (Comparison with Fatal Reactions)

- Epinephrine was delayed for longer than 20 minutes or not administered in 30% of FRs compared with 6% of NFRs (OR, 7.3; 95% CI, 1.4 - 40; P = .01)

- Amin HS et al. *J Allergy Clin Immunol* 2006;117:169-75

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## Systemic Reactions to SCIT & Response to Epinephrine

- 1.9% (1/777 injections)
- SOB, chest tightness, difficulty swallowing, and lightheadedness most serious S or S.
- 17/18 (94%) received epi immediately.
- No serious or late phase reactions.
- Similar data being analyzed for about 50 SR from ST or IT for 2010-11. No SR > Grade 2. All received epi at earliest S or S.

Phillips JF, Bagg AS, Glaum MC, Fox RW, Ledford DK, Lockey RF. In press, *Allergy Proceedings*

## Conclusions

1. The definition of anaphylaxis by the NIH is important for research but should not be used in clinical practice when treating a systemic allergic reaction. If such a definition is used, it often is too late to begin effective treatment.

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## Conclusions (cont'd)

Therefore:

- a. recognize the first signs and symptoms of a systemic allergic reaction which can lead to anaphylaxis as defined by the NIH
- b. most patients survive systemic allergic reactions / anaphylaxis
- c. most who do not survive a systemic allergic reaction / anaphylaxis do not receive appropriate treatment because of non-recognition and the lack of use or late use of epinephrine

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Thank you.

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