Diagnosis and Management of Anaphylaxis

Risk factors for biphasic reaction[2]:
- Multiple epi doses
- Prior biphasic rxn or severe anaphylaxis
- Hypotension on presentation
- Severe wheezing
- Mast cell disease
- Wide pulse pressure
- Drug trigger if pediatric

Risk factors for fatal anaphylaxis if discharged[2]:
- Lack of access to EMS
- Lack of access to epi
- Poor self-management (includes some adolescents)
- Cardiovascular comorbidity
- Asthma

Anaphylactic[1,5] Reaction present?

Two or more of the following that occur after exposure to a likely allergen for that patient: (occurring within minutes to hours of exposure):

a. Involvement of the skin or mucosal tissue
b. Respiratory compromise
c. Reduced BP or associated symptoms
d. Persistent GI tract symptoms

OR Acute onset of A AND either B or C even without known exposure
OR Reduced BP after exposure to a known allergy trigger

If at any time anaphylaxis recurs, give IM EPINEPHrine IMMEDIATELY!

Assess ABCs
EPINEPHrine (1mg/1mL) IM
Remove trigger, if possible

Good clinical response?

No

Repeat **IM** EPINEPHrine q5-15 minutes
Airway/O2/IV/cardiac monitor
Albuterol if bronchospasm present[6]

Yes

Consider second line therapy
- H1 & H2 antihistamines**
- Glucocorticoid**
- Albuterol

Hypotension/Shock Present?

No

Yes

Maintain supine position*
IV fluids: 0.9% NaCl
Vasopressors
- Consider EPINEPHrine IV
- Second line: Dopamine

Glucagon if patient on beta-blocker
Consider glucocorticoid**
Antihistamine for symptom control**

Asymptomatic Observation Period[2]
- In most patients consider up to 3-4 hours
- If quick resolution, good transportation, strong support available if discharged, can consider discharge in 1 hour

Disposition decision
If Discharge:
EpiPen/EpiPen Jr. Twinpack Rx
- Instructions on EpiPen use – **how** and **when** to use[3]
- If pediatric, ensure correct discharge dose

Follow up with PCP +/- allergist

No

Risk factors for biphasic reaction or fatal anaphylaxis?

Yes

Consider prolonged observation[3]

Symptoms Resolved
No Biphasic Reaction
No Other Indication for Admission?

Yes

No

ADMIT

Drug Doses[3]

Preferred Epinephrine route: IM>IV>IO>inhaled, sublingual, endotracheal[3]
Epinephrine (1:1000) **IM**: 0.01 mg/kg per dose
Adult max per dose: 0.5 mg
Child[7] max per dose: 0.5 mg
Epinephrine (1:10,000 to 1:100,000 dilution[5]) **IV (Never give 1:1000 IV)**
***Should only be considered during cardiac arrest or to profoundly hypotensive patients who have failed to respond to IV volume replacement and several IM does of epinephrine.
Adult: 1 - 10 mcg/min
Child: 0.1 – 10 mcg/kg/min
Albuterol: 2.5-5 mg in 3mL NaCl
0.9% NaCl[5]
Adult: 1-2 L @ 5-10 mL/kg in 5 min
Child: 20-30 mL/kg in first hour
Glucagon: given IV over 5 minutes (follow with 5-15 mcg/min infusion)[3]
Adult: 1-5 mg
Child: 20-30 mcg/kg; max dose 1mg

H1-antihistamine: **Diphenhydramine** q6h
All Ages: 1 mg/kg; max per dose 50 mg IV
H2-antihistamine: No clear evidence for one medication or dosage[3]
Glucocorticoid: Some evidence for methylprednisolone 1-2mg/kg IV, but no clear benefit of one glucocorticoid vs another or one dosage vs another[3]

*Supine position unless respiratory distress w/o hypotension (upright) or pregnant (left side)[3]
**Glucocorticoids have reduced length of hospitalization in pediatric patients[3], and antihistamines can help with itching, but neither have been shown to reduce risk for biphasic reaction and are not routinely recommended[4]

This guideline was ratified by the emergency department faculty at Maine Medical Center in October 2021. It reflects our expert opinion and is not necessarily applicable to all institutions. It is intended to be a reference for clinicians caring for patients and is not intended to replace providers' clinical judgment. **Produced by Kate Zimmerman, DO, & Russell Behmer, MD**

Diagnosis and Management of Anaphylaxis

Diagnosis and Management of Anaphylaxis

Definition of Anaphylactic Reaction[1,5]:
Anaphylactic Reaction present (should capture more than 95% of cases of anaphylaxis):
Must fulfill **one** of the following criteria (occurring within minutes to hours of exposure):

1. Acute onset of an illness with involvement of the skin, mucosal tissue, or both (80% of cases). AND AT LEAST 1 OF THE FOLLOWING:
    a. Respiratory compromise
    b. Reduced BP or associated symptoms of end-organ dysfunction
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient:
    a. Involvement of the skin or mucosal tissue (may be absent in 20% of children with food or insect sting allergy)
    b. Respiratory compromise
    c. Reduced BP or associated symptoms
    d. Persistent GI tract symptoms
3. Reduced BP after exposure to known allergen for that patient:
    a. Infants and children: low systolic BP or >30% decrease in systolic BP
    b. Adults: systolic BP <90 mmHg or > 30% decrease from that person's baseline.

IM Epinephrine (1:1000) AutoInjector Doses in Children[7]	
Weight	
>60kg	0.5mg if available; if not, 0.3 mg (EpiPen)
30-60kg	0.3mg (EpiPen)
15-29kg	0.15 mg (EpiPen Jr.)
7.5-14kg	0.1 mg if available

Of note, the above represent manufacturer label recommendations. In-hospital suggested anaphylaxis dosing would be 0.01mg/kg. So for a patient weighing 28kg prescribed the EpiPen Jr (0.15mg), they would only receive about 53% of their recommended dose. Some recommend giving 0.3mg dosing to patients from 25kg-60kg, and giving 0.15mg dosing to all patients over 7.5kg, especially if these patients have had a history of severe anaphylaxis.[8] Ultimately, there is not definitive evidence supporting one dosing strategy vs another.[7]

References & Recommended Readings:

1. Sampson, HA et al. Second symposium on the definition and management of anaphylaxis: summary report – Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium. *J Allergy Clin Immunol* 2006; 117: 391-7.
2. Shaker, Marcus S., Dana V. Wallace, David B. K. Golden, John Oppenheimer, Jonathan A. Bernstein, Ronna L. Campbell, Chitra Dinakar, et al. "Anaphylaxis—a 2020 Practice Parameter Update, Systematic Review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Analysis." *Journal of Allergy and Clinical Immunology* 145, no. 4 (April 1, 2020): 1082–1123. https://doi.org/10.1016/j.jaci.2020.01.017.
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9. Lee, Sangil, M. Fernanda Bellolio, Erik P. Hess, Patricia Erwin, Mohammad Hassan Murad, and Ronna L. Campbell. "Time of Onset and Predictors of Biphasic Anaphylactic Reactions: A Systematic Review and Meta-Analysis." *The Journal of Allergy and Clinical Immunology. In Practice* 3, no. 3 (June 2015): 408-416.e1-2. https://doi.org/10.1016/j.jaip.2014.12.010.
10. Lieberman, Phillip, Richard A. Nicklas, Christopher Randolph, John Oppenheimer, David Bernstein, Jonathan Bernstein, Anne Ellis, et al. "Anaphylaxis—a Practice Parameter Update 2015." *Annals of Allergy, Asthma & Immunology* 115, no. 5 (November 2015): 341–84. https://doi.org/10.1016/j.anai.2015.07.019.

Liu, Xiaowei, Sangil Lee, Christine M. Lohse, Cassandra T. Hardy, and Ronna L. Campbell. "Biphasic Reactions in Emergency Department Anaphylaxis Patients: A Prospective Cohort Study." *The Journal of Allergy and Clinical Immunology: In Practice* 8, no. 4 (April 1, 2020): 1230–38. https://doi.org/10.1016/j.jaip.2019.10.027.

Guideline Evidence

Guideline Topic: Diagnosis and Management of Anaphylaxis
Author: Kate D. Zimmerman, DO & Russell Behmer, MD
Date of Creation: 11.01.21 Sugg Update: 2023
Search Criteria: Anaphylaxis, allergic reaction, EpiPen, epinephrine, H1-antihistamine, H2-antihistamine, Glucocorticoid, Biphasic
Databases: Ovid, PubMed, Cochrane Database, National Guidelines Clearinghouse
Key Guidelines (Dates): NIAID/FAAN 2005; EAACI 2014

#	Recommendation	Source	Classification	Level of Evidence
1	**Definition of Anaphylaxis** 1) Sampson HA et al. Second symposium on the definition and management of anaphylaxis: summary report – Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium. J Allergy Clin Immunol 2006;117:391-7. (NIAID/FAAN) 2)Lieberman, P et al. The diagnosis and management of anaphylaxis: An updated practice parameter. J Allergy Clin Immunol 2005; 115:S483-523. Joint Task Force on Practice Parameters (JTFPP) 3) Muraro, A., G. Roberts, M. Worm, M. B. Bilò, K. Brockow, M. Fernández Rivas, A. F. Santos, et al. "Anaphylaxis: Guidelines from the European Academy of Allergy and Clinical Immunology." Allergy 69, no. 8 (2014): 1026–45. https://doi.org/10.1111/all.12437. (EAACI)	NIAID/FAAN 2005[1]; JTTFP[2]; EAACI 2014[3]	Panel Consensus	IV (Agency for Healthcare Policy and Research Classification)

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2	**Epinephrine 1:1000 IM vs. SC administration in adults** 4) Simons, FER et al. Epinephrine absorption in adults: Intramuscular versus subcutaneous injection. J Allergy Clin Immunol 2001;108:871-873.	Simons et al.[4] NIAID/FAAN 2005	Controlled study; Panel Consensus	IIb
3	**Epinephrine as first line agent, administered IM/SC** 5) Sheikh, A et al. Adrenaline (epinephrine) for the treatment of anaphylaxis with and without shock. The Cochrane Collaboration. 2009 (4). 6) Shaker, Marcus S., Dana V. Wallace, David B. K. Golden, John Oppenheimer, Jonathan A. Bernstein, Ronna L. Campbell, Chitra Dinakar, et al. "Anaphylaxis—a 2020 Practice Parameter Update, Systematic Review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Analysis." Journal of Allergy and Clinical Immunology 145, no. 4 (April 1, 2020): 1082–1123. https://doi.org/10.1016/j.jaci.2020.01.017.	JTFPP 2005; Cochrane Review 2009[5]; JACI 2020[6]	Panel Consensus; Meta-analysis with no RCTs	IV
4	**Oxygen Therapy**	JTFPP 2005	RCT	Ib
5	**Volume Replacement therapy**	JTFPP 2005; JACI 2020	Controlled study	IIb
6	**H1-antihistamine** 7) Sheikh, A et al. H1-antihistamines for the treatment of anaphylaxis with and without shock. The Cochrane Collaboration. 2009(4).	JTFPP 2005; Cochrane Review 2009; Sheikh A et al.[7]	Panel Consensus; Meta-analysis with no RCTs	IV
7	**H1+H2 antihistamine** 8) Lin, RY et al. Improved outcomes in patients with acute allergic syndromes who are treated with combined H1 and H2 antagonists. Ann Em Med 2000; 36(5):462-468	Lin RY et al.[8]	RCT	Ib
8	**Coticosteroid use** 9) Choo, KJL et al. Glucocorticoids for the treatment of anaphylaxis. The Cochrane Collaboration. 2010(3). 10) Liyanage, C.K., P. Galappatthy, and S.L. Seneviratne. "Corticosteroids in Management of Anaphylaxis; a Systematic Review of Evidence." European Annals of Allergy and Clinical Immunology 49, no. 05 (September 2017): 196. https://doi.org/10.23822/EurAnnACI.1764-1489.15. 11) Liu, Xiaowei, Sangil Lee, Christine M. Lohse, Cassandra T. Hardy, and Ronna L. Campbell. "Biphasic Reactions in Emergency Department Anaphylaxis Patients: A Prospective Cohort Study." The Journal of Allergy and Clinical Immunology: In Practice 8, no. 4 (April 1, 2020): 1230–38. https://doi.org/10.1016/j.jaip.2019.10.027.	JTFFP 2005; Cochrane Review 2010[9]; EAACI 2017[10]; Liu X et al[11]	Panel Consensus; Meta-analysis with no RCTs; Prospective Cohort Study	IV
9	**Beta-adrenergic inhaled agents.**	JTFFP 2005	Panel Consensus	IV
10	**Glucacon**	JTFFP 2005	non-experimental studies; Panel Consensus	III
11	**Epinephrine IV**	JTFFP 2005	Panel Consensus	IV
12	**Observation period (due to risk of biphasic reaction).** 12) Lee, Sangil, M. Fernanda Bellolio, Erik P. Hess, Patricia Erwin, Mohammad Hassan Murad, and Ronna L. Campbell. "Time of Onset and Predictors of Biphasic Anaphylactic Reactions: A Systematic Review and Meta-Analysis." The Journal of Allergy and Clinical Immunology. In Practice 3, no. 3 (June 2015): 408-416.e1-2. https://doi.org/10.1016/j.jaip.2014.12.010.	JTFFP 2005; NIAID/FAAN 2005; Liu X et al; Lee S et al.[12]	Panel Consensus; Prospective Cohort Study; Meta-analysis	IV
13	**Pediatric Anaphylaxis Management.** 13) Farbman, Karen S., and Kenneth A. Michelson. "Anaphylaxis in Children." Current Opinion in Pediatrics 28, no. 3 (June 2016): 294. https://doi.org/10.1097/MOP.0000000000000340.	Farbman K[13]	Review	V