Anaphylaxis

Emergency Department and Urgent Care

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Inclusion Criteria

- Signs and symptoms of anaphylaxis and /or received epinephrine prior to arrival for presumed anaphylaxis

Exclusion Criteria

- Symptoms clearly attributed to other cause

***Anaphylaxis Signs & Symptoms**

1. **Acute onset** of symptoms with involvement of skin and/or mucosa AND either respiratory compromise or decreased blood pressure/end organ dysfunction

OR

2. **Two or more** of the following that **occur rapidly** after exposure to a likely allergen

- **Skin/mucosa involvement** (pruritus, flushing, hives, angioedema)
- **Respiratory compromise** (dyspnea, wheeze, hoarseness, stridor, tachypnea, cyanosis)
- **Decreased BP** or associated symptoms
- **Persistent GI symptoms** (vomiting, diarrhea, abdominal pain)

OR

3. Decreased blood pressure for age after exposure to a known allergen for that patient

*****Life-threatening symptoms can include: respiratory distress, stridor, hypotension, altered mental status***

Disposition

- Most patients will be eligible for early discharge from the ED or UC (1-2 hours post epinephrine)
- Disposition

Current signs & symptoms* of anaphylaxis?

Yes

Remove exposure or inciting agent if applicable

GIVE IM EPINEPHRINE

- Administer 0.01mg/kg IM epinephrine (1mg/mL or 0.1mg/mL) to anterolateral thigh, min 0.1 mg, max dose 0.3-0.5mg

OR

- Epinephrine autoinjector 0.15 mg if 7.5 kg to <25 kg or 0.3 mg if ≥25 kg
- Give oxygen, manage airway and obtain vascular access as needed

No

Are life-threatening symptoms** still present or developing?

Yes

- Repeat epinephrine IM every 5 min as needed
- IV fluids as needed
- If wheezing, give albuterol
- If stridor, give racemic epinephrine

If at UC, may require transport to Main Campus ED

No

Adjunct Supportive Therapies

No treatment necessary if all symptoms have resolved

- Consider second generation H1 blocker for cutaneous symptoms (cetirizine preferred)
- Consider antiemetic for GI symptoms

Steroids and H2 blockers not recommended

Are life-threatening symptoms** still present or developing?

No

Yes

Consider IV Epinephrine if suboptimal response to IM

Admit to PICU

Review Disposition document

>2 doses of epinephrine or other indications for admission?

Yes

Admit to Hospital Peds

No

Discharge Preparation

Family education

Epinephrine autoinjector prescription

Anaphylaxis Action Plan

Allergy referral or follow-up

Discharge home

Diagnosis

Definitions

Differential Diagnosis

There is no contraindication to the administration of epinephrine for anaphylaxis

Disposition

Early Discharge Criteria for ED/UC
(1-2 hours post epinephrine)

- Significant symptoms have resolved after one dose of epinephrine and patient feels well
- Epinephrine autoinjector available on hand or at home
- If prior history of anaphylaxis, no biphasic reaction
- No other Red Flags or social concerns

Prolonged Observation in ED or as inpatient
(4-6 hours post last dose of epinephrine)

*If ANY of the following are present

- Received 2 doses of epinephrine
- Required supportive therapy with IV fluids, racemic epinephrine or albuterol
- Presence of other Red Flags, clinical, or social concerns

Red Flags for Prolonged Observation
ED or inpatient

- Non-verbal, difficult airway, or other significant comorbidities
- Current asthma exacerbation
- Airway swelling with current episode
- Patient lives greater distance away

Admission Criteria/Considerations

- Severe or protracted anaphylaxis (**Definitions**)
- Patient received more than 2 doses of epinephrine
- Patient specific medical or social concerns (ex. family discomfort, lack of access to epinephrine autoinjector, unable to establish safe plan for discharge)

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Verify that patient is appropriate for this pathway

Order sets: IP Anaphylaxis Clinical Pathway
OR
IP Anaphylaxis Clinical Pathway Admission

Does patient currently have signs/symptoms of anaphylaxis?

No

Yes

There is no contraindication to the administration of epinephrine for anaphylaxis

- Notify MD if not already at bedside
- **Remove exposure or inciting agent/infusion if applicable**
- **Give** IM Epinephrine to anterolateral thigh**:**
  - Epinephrine autoinjector 0.15 mg (EPIPEN Jr™) if 7.5 kg to <25 kg ***or*** 0.3 mg (EPIPEN™) if ≥25 kg
  OR
  - Epinephrine 0.01mg/kg IM, min 0.1 mg, max dose 0.3-0.5mg (Use High conc. 1mg/1mL or Standard conc. 1mg/10mL if <10kg)
- Continuous pulse oximetry and supplemental oxygen if <90%

Are significant signs or symptoms still present or developing? (incl. respiratory distress, stridor, hypotension, altered mental status)

Yes

Consider ACT or Code Blue
- Manage airway
- Repeat epinephrine IM every 5 min as needed
- Obtain vascular access and give IV fluids as needed
- If wheezing, give albuterol
- If stridor, give racemic epinephrine

Resolution of significant signs and symptoms? (incl. respiratory distress, stridor, hypotension, altered mental status)

Yes

No

PICU

No

Adjunct Supportive Treatments
- Consider second generation H_1 blocker for cutaneous symptoms (cetirizine preferred)
- Consider antiemetic for GI symptoms
- Steroids and H_2 blockers are **not** recommended

Meets allergy discharge criteria?

Yes

Allergy Discharge Criteria
- Significant symptoms resolved for at least 6 hours (cutaneous symptoms may still be present)
- Discharge planning checklist complete
- Ready for discharge from other clinical and social standpoints

Consider Inpatient Allergy/ Immunology consult for:
- Persistent symptoms which fail to respond to standard therapy
- Uncertain diagnosis
- Unclear trigger
- Family or guardian request

Review differential diagnosis

Consider diagnostic testing during acute episode

Pre-Pathway Validation

Is this Anaphylaxis?

Anaphylaxis is an acute, potentially life-threatening and rapidly progressive systemic allergic reaction for which epinephrine is the only first-line treatment. It is a clinical diagnosis that should not rely upon diagnostic testing. Anaphylaxis can range widely in severity and may be resolving with or without epinephrine by the time clinical evaluation occurs.

Presentation:

- **Rapid onset** of:
  - **Severe symptoms,** including one or more of the following:
    - **Lungs/Breathing**: shortness of breath, wheeze, repetitive cough, hoarseness, stridor, dyspnea, tachypnea
    - **Mouth/Throat**: tongue swelling, throat tightness, closing or fullness, dysphagia
    - **Heart/Circulation:** pale, blue/cyanosis, faint, weak pulse, tachycardia, hypotension
    - **GI:** repetitive or severe vomiting
    - **Skin:** severe swelling or extensive hives, generalized pruritus, flushing
    - CNS: lightheaded, confusion, feeling of “doom”, syncope
  - **Or combination of mild symptoms** from two body areas:
    - **Skin:** hives, angioedema (e.g., eyes, lips)
    - **GI:** mild nausea/discomfort
- Exposure to known allergen
- Cutaneous manifestations including urticaria and angioedema are the most common, but may be absent in about 20% of cases

NIAID Diagnostic Criteria for anaphylaxis

Definitions of uniphasic, biphasic, protracted and refractory anaphylaxis

Pathway Inclusion Criteria

- Signs and symptoms of anaphylaxis and/ or received epinephrine prior to arrival for presumed anaphylaxis

Pathway Exclusion Criteria

- Symptoms clearly attributed to other cause

Diagnostic Timeout

Red Flags

- Gradual or slow onset
- Absence of clear trigger
- Persistence of symptoms over prolonged period such as days

Diagnostic Timeout Differential Diagnosis

- Viral illness, including viral-induced urticaria/angioedema
- Idiopathic urticaria/angioedema
- Hereditary Angioedema
- Asthma exacerbation
- FPIES (severe vomiting, diarrhea, dehydration) hours after eating

Full differential diagnosis list

Admission Criteria

- Severe or protracted anaphylaxis
- More than 2 doses of epinephrine given
- Unable to establish safe discharge plan, including monitoring for rebound symptoms and/or access to follow-up care

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Diagnosis

Anaphylaxis is a rapidly progressive systemic allergic reaction. It is a clinical diagnosis that should not rely upon diagnostic testing. This clinical pathway provides treatment recommendations for anaphylaxis from any cause, including indications for escalation of therapy when necessary. Anaphylaxis can range widely in severity and may be resolving with or without epinephrine by the time clinical evaluation occurs. As such, global assessment of severity, current clinical status, and treatment administered should be considered for subsequent monitoring duration and interventions once the patient is stable.

Typical presentation:

- Rapid onset
- Exposure to known allergen
- Cutaneous manifestations including urticaria and angioedema are the most common, but may be absent in about 20% of cases

Diagnostic Criteria for anaphylaxis

- In 2006 the NIAID and Food Allergy and Anaphylaxis Network established criteria to serve as a framework to facilitate the diagnosis of anaphylaxis. This is the mostly commonly used criteria.
- Anaphylaxis is likely when 1 of 3 criteria is fulfilled:
  1. Acute onset of an illness (min-hours) with involvement of the skin, mucosal tissue or both with either respiratory involvement or reduced blood pressure and/or associated symptoms of end-organ involvement
  2. Two or more of the following that occur rapidly after exposure to a likely allergen for the patient:
     - Involvement of skin/mucosa
     - Respiratory involvement
     - Reduced blood pressure or associated symptoms
     - GI symptoms
  3. Reduced blood pressure as result of exposure to a known allergen trigger

NOTE: Criteria should not replace clinical judgment and epinephrine administration is not limited to those meeting the criteria

Consider other alternate clinical problem and diagnosis when:

- None of the diagnostic criteria are met
- Slow or gradual onset of symptoms
- Persistence of symptoms over prolonged period (ex. days)
- Absence of clear trigger

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Pre-Pathway Validation

Definitions

Anaphylaxis
- Serious allergic reaction that is usually rapid in onset and may cause death

Uniphasic Anaphylaxis
- Most common type
- Peaks within hours after symptom onset and then resolves within several hours

Biphasic Anaphylaxis (5%)
- Recurrence of anaphylaxis that develops within 1 to 72 hours following the apparent resolution of the initial anaphylactic episode with no additional exposure to the causative agent
- Typically occurs within 12 hours
- Risk factors include:
  - More severe initial presentation (hypotension)
  - >1 dose epinephrine required for resolution of initial episode
  - Unknown trigger
  - History of biphasic reaction
  - Reaction to drug

Protracted Anaphylaxis
- Persistent reactions lasting hours or days without resolving completely (persist at least 4 hours)
- Very uncommon

Refractory anaphylaxis
- Continued symptoms of anaphylaxis despite appropriate epinephrine dosing and symptom-directed treatment
- > 3 doses of epinephrine or initiation of epinephrine infusion suggested by expert panel

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Disposition

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Differential Diagnosis

Consider other alternate clinical problem and diagnosis when:

- None of the diagnostic criteria are met
- Slow or gradual onset of symptoms
- Persistence of symptoms over prolonged period (ex. days)
- Absence of clear trigger

Differential Diagnosis:

- Skin or mucosal
  - Idiopathic or physical urticaria and angioedema
  - Pollen Food Allergy Syndrome (just oral symptoms)
  - Hereditary Angioedema (hives typically absent)
- Endocrine
  - Hypoglycemia
  - Thyrotoxic crisis
  - Carcinoid syndrome
  - Vasointestinal peptide tumors
  - Pheochromocytoma
- Pulmonary
  - Asthma exacerbation
  - Acute laryngotracheitis
  - Obstruction (ex. foreign body, vocal cord dysfunction)
- Neuro/Psych
  - Hyperventilation syndrome
  - Anxiety and panic disorder
  - Somatoform disorder
  - Dissociative disorder and conversion
  - Epilepsy
  - Cerebrovascular event
  - Psychosis
  - Factitious disorder
- Cardiovascular
  - Vasovagal syncope
  - Pulmonary embolism
  - Myocardial infarction
  - Cardiac arrhythmias
  - Cardiogenic shock
- Other
  - Drugs: ethanol, opiates
  - Histamine (scombroid fish poisoning)
  - Food Protein Induced Enterocolitis (FPIES; delayed onset severe vomiting, typically 2-3 hours after eating. Patient may also have diarrhea and dehydration)

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First Line Therapy

FIRST LINE THERAPIES			
Medication	Dose	Route	Frequency
Epinephrine IM	0.01 mg/kg using 1mg/1mL to anterolateral thigh, min 0.1 mg, max dose 0.3-0.5 mg OR Epinephrine autoinjector 0.15 mg if 7.5 kg to <25 kg or 0.3 mg if >/=25 kg	IM	Every 5-15 minutes as needed
Epinephrine IV	0.1 mcg/kg/minute (0.05-0.2 mcg/kg/min); titrate to response	IV	Continuous

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Adjunct Therapies

ADJUNCT THERAPIES			
Medication	Dose	Route	Frequency
Albuterol	1.25 mg or 2.5 mg	inhalation	PRN lower airway obstruction, per provider
Racemic Epinephrine (Racepinephrine) 2.25% solution	0.5 mL diluted in 2 to 3 mL normal saline	inhalation	PRN stridor, per provider
IV Fluids (LR or NS)	20 ml/kg bolus Max: 1000ml	IV	Once
Ondansetron (Zofran™)	8-15 kg: 2 mg >15-30 kg: 4 mg >30 kg: 8 mg	PO	Once
Cetirizine *preferred over first generation antihistamine	< 6mo: 1.25 mg 6-24 mo: 2.5 mg 2-5 yrs: 5 mg >5 yrs: 10 mg	PO	Once daily, can increase to twice daily
Diphenhydramine (if unable to take PO or second generation antihistamine not available)	1 mg/kg/dose, max dose 50 mg	IV/PO	Every 6 hours
H_2 blockers	Not recommended; not supported by evidence		
Systemic corticosteroids	Not recommended for acute management; consider in cases of concurrent asthma exacerbation; previous belief that steroids decrease biphasic or prolonged reactions is not supported by evidence		
Glucagon	Consider if no response to IM epinephrine and patient on beta-blocker		

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Diagnostic Testing

- There are no laboratory tests available in an emergency department or clinic setting to confirm a diagnosis of anaphylaxis in real time

- However, laboratory tests (ex. serum tryptase level) obtained during or shortly after symptom onset can help to support the clinical diagnosis of anaphylaxis, particularly when the diagnosis is uncertain

Total Serum Tryptase

- Tryptase is a mediator released by mast cells and basophils during anaphylaxis
- Tryptase level should ideally be drawn 30-120 minutes after onset of symptoms (but may remain elevated for several hours)
- Elevated levels of total tryptase in serum may be useful for distinguishing anaphylaxis from other conditions in the differential diagnosis
- The PPV of an elevated tryptase is higher than the NPV value of a normal tryptase
- Total tryptase levels are less often elevated in food-induced anaphylaxis

Summary

- ***Tryptase*** should **not** be used to diagnose anaphylaxis in real time but can be supportive after the event
- ***Tryptase*** may **not** be used to guide acute management of anaphylaxis
- Consider obtaining a tryptase level when anaphylaxis is on the differential. Elevations can support the diagnosis of anaphylaxis, but normal levels do not necessary exclude it, especially if related to food or if drawn after 3 hours

Additional testing

- Follow-up allergy evaluation (ex. skin testing or serum specific IgE level) is important for confirmation or identification of allergens. Allergy follow-up recommended.

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Patient & Caregiver Education

- Caregivers and patient to participate in demonstration with autoinjector trainers
- Provide caregiver or patient education documents:
  - Helping Hands on epinephrine autoinjector
  - Emergency Action Plan (EAP)
- Physician or other provider reviews trigger avoidance with caregivers and patient
- Review signs and symptoms concerning for biphasic anaphylaxis if discharging from ED/Urgent care

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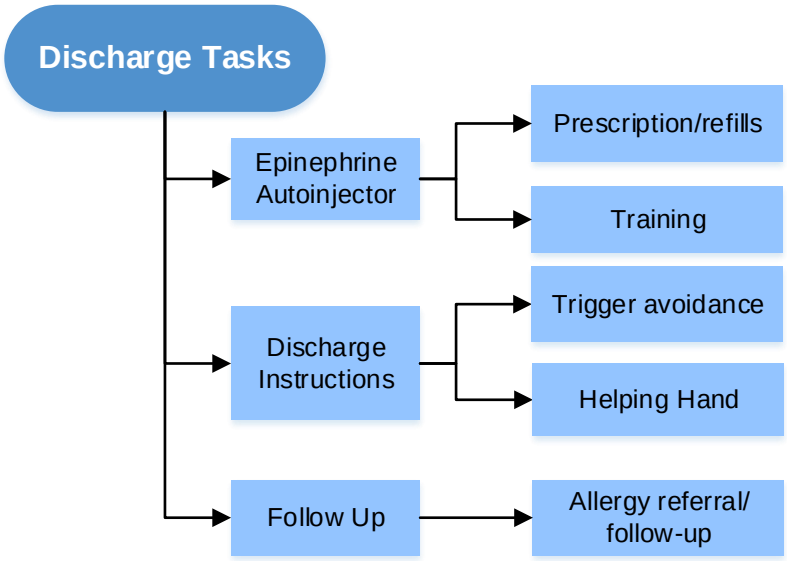
Discharge Planning

ED/UC/IP



Prescriptions: Epinephrine autoinjector (prescribe 2 two-packs)
Use PRN severe reaction. Inject IM into anterolateral thigh.

7.5 kg to <25 kg Epinephrine auto injector 0.15 mg/0.3ml
≥25 kg Epinephrine auto injector 0.30 mg/0.3 ml

*some patients with known allergy may have exisiting prescription for Auvi-Q device, with additional dosing option of 0.1mg

Prescriptions: Cetirizine
Once daily as needed for itching or few hives (not to replace use of epinephrine for severe or rapidly spreading hives concerning for anaphylaxis)

< 6 mo	Cetirizine 1.25 mg
6-24mo	Cetirizine 2.5 mg
2-5 years	Cetirizine 5 mg
> 5 years	Cetirizine 10 mg

Prescriptions: Albuterol
If having confirmed or suspected asthma, also give albuterol MDI, 2-4 puffs Q4H PRN with spacer

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Anaphylaxis Action Plan

Patient's Home

Allergy/Anaphylaxis EMERGENCY ACTION PLAN (EAP)

Any **SEVERE SYMPTOMS** after suspected or known exposure such as :

One or more of the following:
LUNG: short of breath, wheeze, repetitive cough
THROAT: tightness, closing or fullness, trouble breathing or swallowing
HEART: pale, blue, faint, weak pulse, lightheaded, feeling of "doom", passing out
MOUTH: tongue swelling
GUT: repetitive or severe vomiting
SKIN: severe swelling or many hives over body

→

1. INJECT EPINEPHRINE IMMEDIATELY

2. Call 911

3. Begin monitoring (see box below)

4. Give additional medications:
Antihistamine for itching/hives
Albuterol for asthma symptoms

5. Stay with child

Or combination of mild symptoms from two body areas:
SKIN: hives, swelling (e.g., eyes, lips)
GUT: mild nausea/discomfort

MILD SYMPTOMS ONLY such as:

MOUTH: itchy mouth

SKIN: few hives around mouth/face, mild itch

GUT: mild nausea/discomfort

→

1. GIVE ANTIHISTAMINE

2. Stay with person; alert healthcare professions and parent

3. If symptoms progress (see above): USE EPINEPHRINE

4. Begin monitoring (see box below)

Monitoring:
- Stay with person; alert parent. Tell rescue squad that epinephrine was given
- Have person lay on back if possible (or side if vomiting) - DO NOT HAVE THEM STAND UP
- Note time epinephrine given; give second dose in 5-10 minutes if symptoms return or don't improve

Epinephrine Auto Injector Helping Hand

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Helping Hands

Epinephrine Auto-Injectors for Severe Allergic Reaction (Adrenaclick®, Auvi-Q®, EpiPen®, Symjepi®)

Quality Metrics

Outcome Measures

Emergency Department:

1. ED length of stay
2. Time from arrival to IM epinephrine administration
3. Rate of patients who received IM epinephrine first when other anaphylaxis medications (diphenhydramine, cetirizine, loratadine, steroids) were also administered.
4. Rate of enteral diphenhydramine use
5. Admission rate

Urgent Care:

1. UC length of stay
2. Time from arrival to IM epinephrine administration
3. Rate of patients who received IM epinephrine first when other anaphylaxis medications (diphenhydramine, cetirizine, loratadine, steroids) were also administered.
4. Rate of enteral diphenhydramine use
5. Transfer rate

Inpatient:

1. Utilization rate of IM epinephrine for anaphylaxis
2. Rate of patients who received IM epinephrine first when other anaphylaxis medications (diphenhydramine, cetirizine, loratadine, steroids) were also administered within an hour before or after epinephrine.
3. IP length of stay

Process Measures

1. ED/UC Order Set & Smart Set utilization
2. IP Order Set utilization

Balance Measures

1. 24hr ED/UC return rate

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Pathway Team & Process

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Next Revision Date: *November, 2025*

Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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