JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Anaphylaxis Clinical Pathway

JOHNS HOPKINS
All Children's Hospital

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Anaphylaxis Guideline

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Updated: November 2020
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Anaphylaxis Clinical Pathway

Rationale

This protocol was developed by a consensus group of JHACH emergency medicine providers, hospitalists, and allergists, to standardize the management of children who present with anaphylaxis. It addresses the following clinical questions or problems:

1. When and how to recognize anaphylaxis
2. How to treat anaphylaxis in the acute setting
3. How long to observe patients treated for anaphylaxis
4. What medications should be prescribed on discharge of a patient treated for anaphylaxis
5. When to consider admission for further treatment and observation

Anaphylaxis Background and Diagnostic Criteria

Anaphylaxis is defined by the World Allergy Organization as “a serious allergic reaction that is rapid in onset and might cause death.” Diagnosis of anaphylaxis is made when any of the following three criteria are made:

1. Acute onset of symptoms (minutes to several hours) with involvement of skin and/or mucosa such as pruritus, flushing, hives, swollen lips/tongue/uvula, AND either respiratory compromise (dyspnea, wheeze, decreased peak expiratory flow, stridor, hypoxemia) OR decreased blood pressure or end-organ dysfunction (syncope, collapse, incontinence)

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/bronchospasm, stridor, hypoxemia)
-Decreased BP or end-organ dysfunction (collapse, syncope, incontinence)
-Persistent GI symptoms (vomiting, diarrhea, cramping abdominal pain)

3. Decreased blood pressure for age or less than 30% of baseline after exposure to a known allergen for that patient.

Anaphylaxis is a clinical diagnosis. The clinical criteria for diagnosis of anaphylaxis were developed by the National Institute of Allergy and Infectious Diseases in 2004 and subsequently adapted by the World Allergy Organization. They have been studied and found to have 97% sensitivity and 82% specificity in diagnosing anaphylaxis.

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Anaphylaxis Emergency Center Clinical Pathway

Patient presents with one of the following:

1. Minutes to hours of symptoms with involvement of skin and/or mucosa AND either respiratory compromise or decreased blood pressure/end organ dysfunction (syncope, collapse, incontinence)

2. Two or more of the following that occur rapidly after exposure to a likely allergen:
   - -skin/mucosa involvement (pruritis, flushing, hives, angioedema)
   - -respiratory compromise (dyspnea, wheeze/bronchospasm, stridor, hypoxemia)
   - -decreased BP or end organ dysfunction (syncope, collapse, incontinence)
   - -persistent GI symptoms (vomiting, diarrhea, cramping abdominal pain)

3. Decreased blood pressure for age or less than 30% of baseline after exposure to a known allergen for that patient

No → Consider alternative diagnosis

Yes → Place the patient in supine position. Place the patient in supine position. Administer IM epinephrine to the mid-outer thigh:
-0.01 mg/kg for patients less than 7.5 kg
-0.15 mg EpiPen for patients 7.5-24.9 kg
-0.3 mg EpiPen for patients greater than or equal to 25 kg

Insert a peripheral IV and administer IV diphenhydramine 1mg/kg (max 50mg), IV famotidine 1mg/kg (max 50 mg), IV Hydrocortisone 2 mg/kg (max 250 mg), and 20 mL/kg NaCl bolus. If intravenous access cannot be obtained, administer diphenhydramine and hydrocortisone IM

If there is evidence of impending airway obstruction, immediately intubate the patient

Patient responding to epinephrine? (blood pressure, perfusion improving)

Yes → Does the patient have risk factors for recurrence/severe anaphylaxis:
-history of asthma
-history of peanut allergy
-severe respiratory distress
-repeated doses of epinephrine required

No → Observe in the EC for 4-6 hours

Has the patient had recurrent symptoms?

No → Discharge the patient home with a referral to allergy/immunology and EpiPen prescription x 2. Inform patient and family about the risk of biphasic reactions

Yes → Manage as described to the right

Yes → Admit to the hospitalist for observation

No → -Repeat IM epinephrine doses every 5 minutes as needed up to 3 times
-Once a PIV is established, give epinephrine in IV doses of 0.01mg/kg
-Give 8-10L O2 via facemask
-Repeat IVF boluses as needed
- For bronchospasm resistant to epinephrine, give albuterol give 2.5 mg for patients < 15 kg and 5 mg albuterol for patients >/= 15 kg in 3 mL saline inhaled via nebulizer, or 2-4 puffs by metered dose inhaler (MDI). Repeat as needed.

Does the patient have continued hypotension?

Yes → -Start IV epinephrine infusion at 0.1 to 1 mcg/kg/minute, titrated to effect
-Consider intubating the patient
-Continue repeat IVF boluses
-If the patient is taking beta-blockers and is not responding to epinephrine, consider administering glucagon 1-5 mg IV over 5 minutes followed by infusion of 5-15 mcg/minute
-Admit the patient to the PICU

No → Admit to the hospitalist team for continued observation and management as needed

Anaphylaxis Initial Treatment

The key management of anaphylaxis depends on early recognition and treatment with intramuscular epinephrine. Patients presenting with anaphylaxis should be immediately triaged and prepared for epinephrine administration. Intramuscular epinephrine is the first line treatment for anaphylaxis (*Class I, Level of Evidence A*). Epinephrine has both alpha sympathomimetic and beta sympathomimetic actions which allows for peripheral vasoconstriction, increased cardiac output, and bronchodilation. It also inhibits further release of inflammatory mediators from mast cells and basophils. Epinephrine is underused in the treatment of anaphylaxis in both prehospital and emergency center settings, most commonly because the caregiver did not recognize the severity of the reaction.

Epinephrine should be injected into the outer mid-thigh using a needle syringe with 1:1000 epinephrine solution or via an auto injector device. The recommended dose of epinephrine is 0.01 mg/kg IM for patients less than 7.5 kg, 0.15 mg IM for patients 7.5 to 24.9 kg, and 0.3 mg for patients weighing 25 kg or more. Repeated IM doses should be administered in the event of persisting respiratory or cardiovascular symptoms after 5 minutes for up to three doses (*Class I, Level of Evidence B*). The IM route allows for a peak epinephrine level 8 minutes after administration on average compared to 34 minutes after subcutaneous administration. IM administration into the thigh results in higher peak plasma concentrations compared with administration into the upper arm. There are no absolute contraindications for the administration of epinephrine. Complications from IM epinephrine administration are very rare. Administration of epinephrine should not be delayed while attempting to establish intravenous access.

Patients with suspected anaphylaxis should receive supplemental oxygen and full cardiorespiratory monitoring (*Class IIa, Level of Evidence D*). They should be placed in the supine position and should have two large bore IV lines inserted if there are any signs of cardiovascular compromise (*Class I, Level of Evidence C*). Patients with signs of cardiovascular involvement including tachycardia, hypotension, or delayed capillary refill should receive aggressive fluid resuscitation with 20 mL/kg boluses of normal saline (*Class I, Level of Evidence B*). Boluses should be repeated as necessary to maintain cardiovascular stability. For any evidence of impending airway obstruction from angioedema, immediate intubation is indicated as delay could lead to complete obstruction (*Class IIa, Level of Evidence C*).

Intravenous Epinephrine

When epinephrine is promptly injected IM, most patients respond to one, two, or at most three doses. For patients with inadequate response to IM epinephrine and IV saline, a continuous infusion of epinephrine should be administered, beginning at 0.1 mcg/kg/minute by infusion pump (*Class IIa, Level of Evidence C*). This dose can be titrated up or down according to blood pressure, cardiac rate and function, and oxygenation.

Bronchospasm Treatment

For bronchospasm resistant to IM epinephrine, give 2.5 mg albuterol for patients weighing less than 15 kg and 5 mg albuterol for patients greater than or equal to 15 kg in 3 mL saline inhaled via nebulizer, or 2-4 puffs by metered dose inhaler (MDI) (*Class IIa, Level of Evidence B*).

Further Interventions if IV Epinephrine is Ineffective

For upper airway obstruction give nebulized epinephrine 5 mL and consider intubation (*Class IIa, Level of Evidence C*). For persistent hypotension continue IV normal saline boluses (*Class I, Level of Evidence C*). Patients on beta-blockers may not respond to epinephrine and can be given glucagon 1-2 mg IM or IV over 5 minutes as a starting dose, followed by infusion of 5 to 15 mcg/minute (*Class IIa, Level of Evidence B*). Glucagon increases cyclic adenosine monophosphate intracellularly, independent of adrenergic receptors. It may therefore reverse refractory hypotension and bronchospasm. When administering glucagon, airway protection is necessary as emesis is a possible side effect.

Adjunctive Treatment with Antihistamines and Glucocorticoids

Although oral antihistamines are the mainstay of treatment for minor allergic reactions, they are not appropriate for first line management of anaphylaxis. Antihistamines have no role in treating or preventing respiratory or cardiovascular symptoms of anaphylaxis. The onset of action is not rapid enough for use. However, H1 antagonists can be given as adjunctive therapy given their proven benefit with localized reactions such as urticaria. Consider giving diphenhydramine 1mg/kg (max 50) IV (*Class IIb, Level of Evidence B*). Also Consider giving an H2 antagonist such as ranitidine or famotidine 1mg/kg (max 50 mg) IV (*Class IIb, Level of Evidence B*).

Corticosteroids have a slow onset of action (4-6 hours) and are therefore not effective in the acute management of anaphylaxis. Giving corticosteroids does not have any significant effect on readmission for patients with allergic reactions. The benefit of corticosteroids in anaphylaxis has not be scientifically proven but it is common practice to treat with steroids as a secondary treatment (*Class IIb, Level of Evidence B*). Consider giving hydrocortisone 2 mg/kg (max 250 mg) IV or IM. On discharge, consider prescribing a 2 day course of oral steroids to reduce the risk of symptom recurrence. For example, prednisolone 1mg/kg with a maximum of 50 mg daily.

Laboratory Testing for Anaphylaxis

A serum tryptase level can be helpful when the diagnosis of anaphylaxis is unclear. Due to its short half-life, the test should be collected within 4 hours of symptom onset. The turnaround time for serum tryptase is usually several days, and results are more beneficial for prevention of future anaphylaxis episods than for management in the acute setting. An elevated serum tryptase level does not rule out anaphylaxis, especially in food induced reactions (*Class IIb, Level of Evidence C*).

Observation vs Admission

Because most biphasic allergic reactions occur within the first 4-6 hours after initial onset of symptoms, a reasonable length of time of observation of a patient treated for anaphylaxis is 4 to 6 hours (*Class I, Level of Evidence B*). Although rare, symptoms can recur up to 24-72 hours after initial presentation and caregivers should be counseled to monitor for such a recurrence. True biphasic reactions are estimated to occur after 3-20% of anaphylactic reactions. Patients who require repeated doses of epinephrine, present with severe respiratory distress or hypotension, or who experience a biphasic reaction during observation should be admitted to the hospital for observation (*Class IIa, Level of Evidence B*). Also consider admission for patients with high risk features including peanut allergy or history of asthma.

Discharge Instructions and Prescribing

Prescribe an epinephrine autoinjector before discharge (*Class I, Level of Evidence C*). Teach the patient how to use the epinephrine autoinjector using a trainer device. Refer all patients who present with anaphylaxis to allergy/immunology (*Class IIa, Level of Evidence C*). Children weighing 15-30 kg can receive a 0.15 mg dose of epinephrine (EpiPen Junior). Children weighing more than 30 kg can receive a 0.3mg dose of epinephrine (EpiPen). For children weighing less than 15 kg, consider prescribing Auvi-Q 0.10 mg epinephrine autoinjector if possible. If the drug is not available, patients should receive a 0.15 mg dose of epinephrine (EpiPen Junior). The mainstay of management includes avoidance of triggers and provision of a rescue medication in the event of accidental reactions. Patients and families should be instructed to use their autoinjector when an allergic reaction is suspected and seek medical attention

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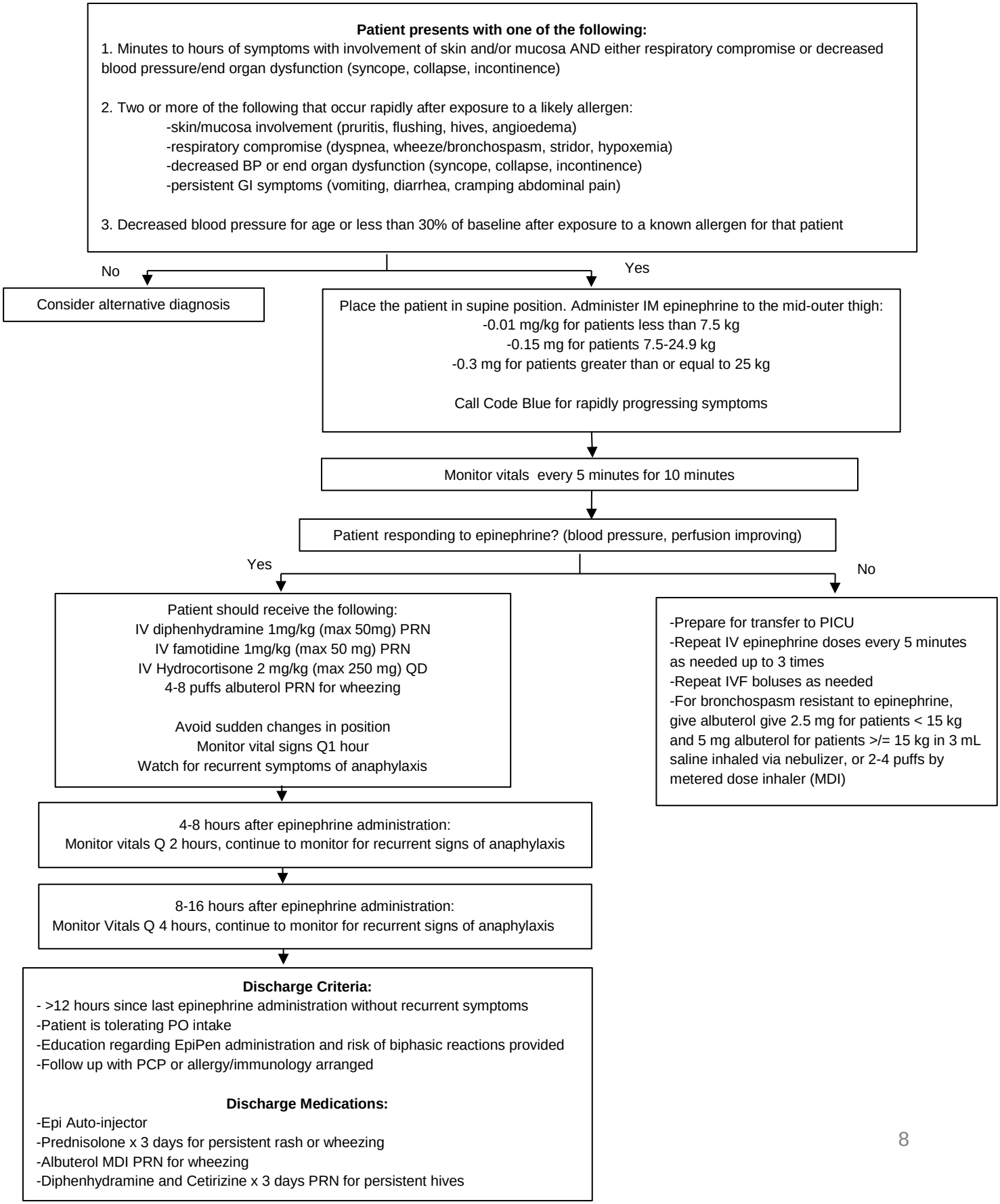
Anaphylaxis Inpatient Clinical Pathway



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OUTCOME MEASURES:

- Time to epinephrine administration after presentation with symptoms
- Length of stay in the EC
- Length of stay in the hospital
- Percent of patients admitted to the hospital after presenting to EC with anaphylaxis

Clinical Pathway Team

Anaphylaxis Clinical Pathway

Johns Hopkins All Children's Hospital

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Date Approved by JHACH Clinical Practice Council:

Date Available on Webpage: March 1, 2021

Last Revised: November 17, 2020

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