JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Anaphylaxis Clinical Pathway

JOHNS HOPKINS
All Children's Hospital

Johns Hopkins All Children's Hospital

Anaphylaxis Guideline

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Owners: Courtney Titus, PA-C, Corey Fowler, PharmD

Anaphylaxis Clinical Pathway

Rationale

This protocol was developed by a consensus group of JHACH emergency medicine providers, hospitalists, pharmacists 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 for 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.” Anaphylaxis is a clinical diagnosis. The National Institute of Allergy and Infectious Diseases developed the clinical criteria for anaphylaxis diagnosis in 2004 and was subsequently adapted by the World Allergy Organization. They have been studied and found to have 97% sensitivity and 82% specificity in diagnosing anaphylaxis.

Potential anaphylactic reaction: ANAPHYLAXIS is highly likely when ONE of the following 3 criteria is fulfilled within minutes to 2 – 3 hours following possible allergen exposure.

- CRITERIA 1 - Acute onset of an illness with involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritis or flushing, swollen lip-tongue-uvula) AND AT LEAST ONE OF THE FOLLOWING:
    - Respiratory compromise (wheezing, shortness of breath, cough, stridor, hypoxemia, unable to speak, retractions, or flaring)
    - Reduced systolic blood pressure by $\geq$ 30% or associated symptoms of end-organ dysfunction (e.g., delayed capillary refill, syncope, altered mental status)
    - Persistent GI symptoms (e.g., significant abdominal pain and/or significant vomiting)

- CRITERIA 2 - TWO OR MORE of the following that occur rapidly after exposure to a LIKELY ALLERGEN for the patient:
    - Involvement of the skin-mucosal tissue, (e.g., generalized hives, pruritis or flushing, swollen lip tongue-uvula)
    - Respiratory compromise (wheezing, shortness of breath, cough, stridor, hypoxemia, unable to speak, retractions, or flaring)
    - Reduced systolic blood pressure by $\geq$ 30% of pre-treatment baseline or associated symptoms of end-organ dysfunction (e.g., delayed capillary refill, syncope, altered mental status)
    - Persistent GI symptoms (e.g., significant abdominal pain and/or significant vomiting)

- CRITERIA 3 - Reduced blood pressure by $\geq$ 30% of pre-treatment baseline after exposure to KNOWN ALLERGEN for the patient

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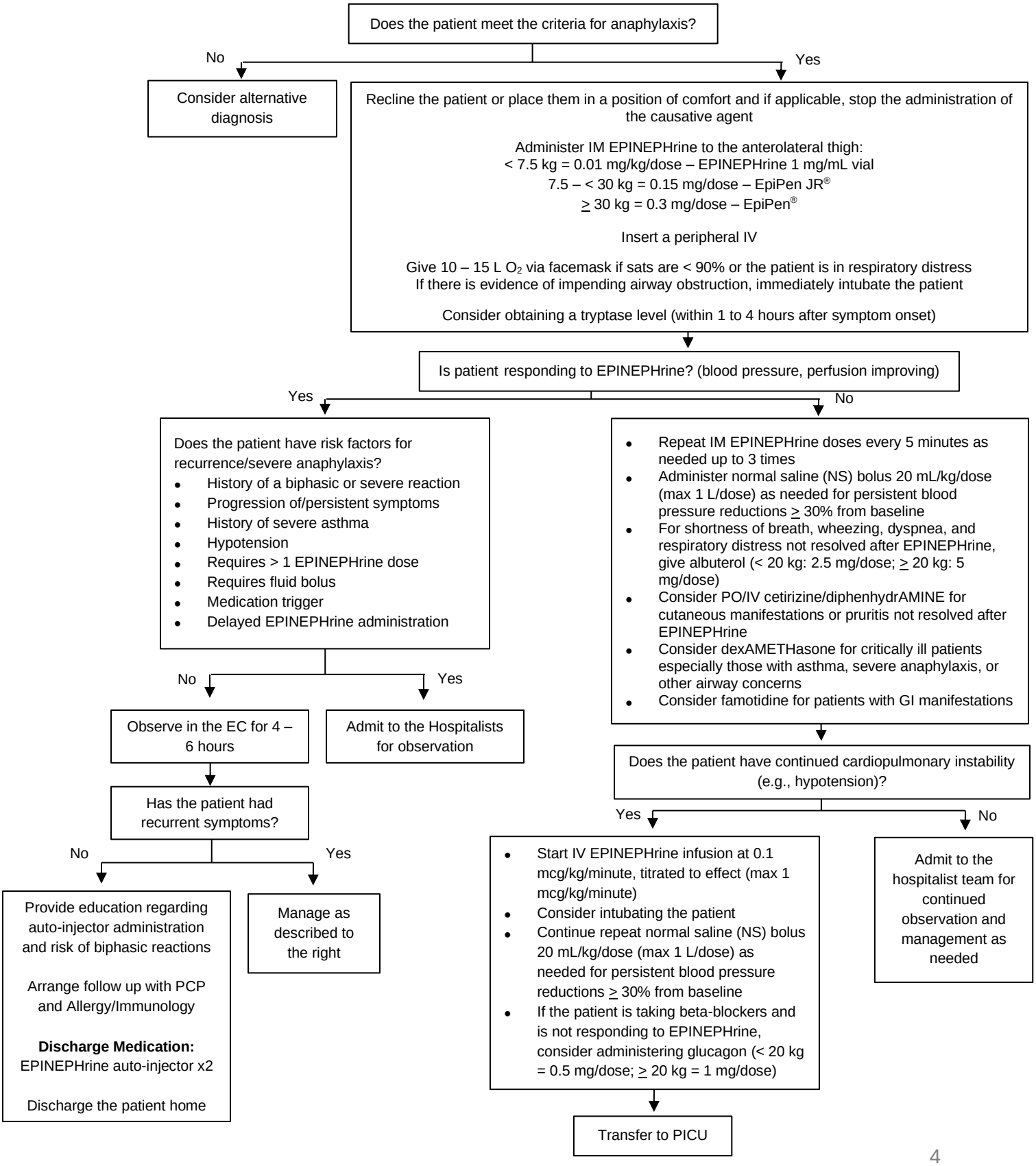
Anaphylaxis Emergency Center Clinical Pathway



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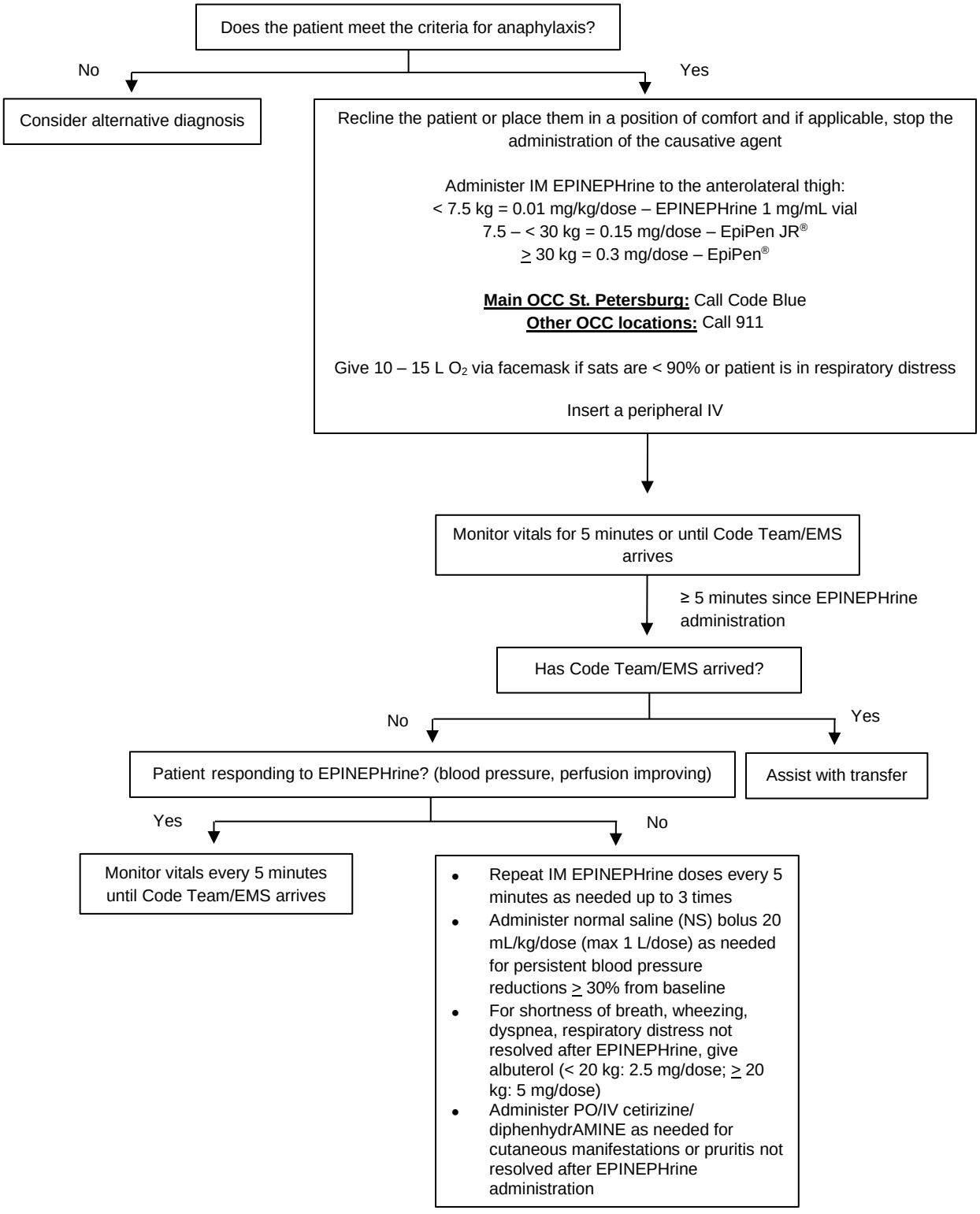
Anaphylaxis Outpatient Clinical Pathway



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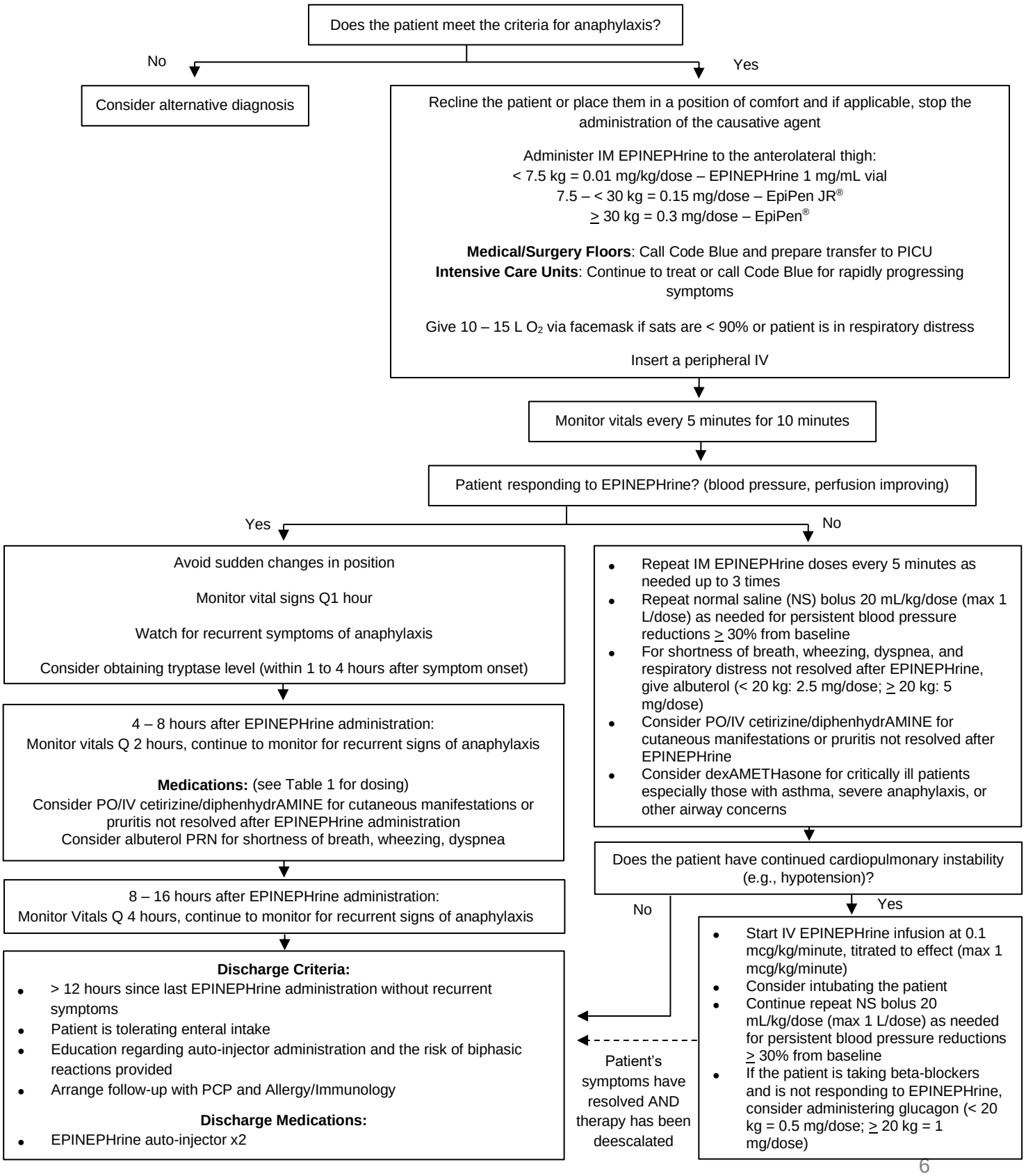
Anaphylaxis Inpatient Clinical Pathway



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 allow for peripheral vasoconstriction, increased cardiac output, and bronchodilation. It also inhibits the 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 needled syringe with IV EPINEPHrine 1 mg/mL solution or via an auto-injector device. The recommended dose of EPINEPHrine:

< 7.5 kg = 0.01 mg/kg/dose – EPINEPHrine 1 mg/mL vial
7.5 – < 30 kg = 0.15 mg/dose – EpiPen Junior®
≥ 30 kg = 0.3 mg/dose – EpiPen®

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/dose (max 1 L/dose) boluses of normal saline (NS) (*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 a bolus of IV normal saline (NS), a continuous infusion of EPINEPHrine should be administered, beginning at 0.1 mcg/kg/minute by an infusion pump (*Class IIa, Level of Evidence C*). This dose can be titrated up (max 1 mcg/kg/minute) or down according to blood pressure, cardiac rate and function, and oxygenation.

Bronchospasm Treatment

For bronchospasm resistant to IM EPINEPHrine, give nebulized albuterol 2.5 mg/dose for patients weighing less than 20 kg and nebulized albuterol 5 mg/dose for patients greater than or equal to 20 kg (*Class IIa, Level of Evidence B*).

Further Interventions if EPINEPHrine is Ineffective

For upper airway obstruction consider intubation (*Class IIa, Level of Evidence C*). For persistent hypotension continue IV normal saline (NS) boluses (*Class I, Level of Evidence C*). Patients on beta-blockers may not respond to EPINEPHrine and can be given IV glucagon (< 20 kg = 0.5 mg/dose; ≥ 20 kg = 1 mg/dose) (*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 enteral 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, H_1 antagonists can be given as adjunctive therapy given their proven benefit with localized reactions such as urticaria. Consider giving cetirizine enterally or diphenhydrAMINE intravenously/intramuscularly in patients unable to tolerate enteral medications (*Class IIb, Level of Evidence B*). Also consider giving an H_2 antagonist such as famotidine for patients with gastrointestinal manifestations (*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 been scientifically proven but it is common practice to treat with steroids as a secondary treatment (*Class IIb, Level of Evidence B*). Consider giving corticosteroids to critically ill patients especially those with asthma, severe anaphylaxis, or other airway concerns

Table 1: Medications for Anaphylaxis

Medication	Route	Dose	Max Dose	Comments	Level of Evidence
EPINEPHrine	IM	< 7.5 kg = 0.01 mg/kg/dose 7.5 – < 30 kg = 0.15 mg/dose ≥ 30 kg = 0.3 mg/dose	0.3 mg/dose	< 7.5 kg: use EPINEPHrine 1 mg/mL vial 7.5 – < 30 kg: use EpiPen Jr® ≥ 30 kg: use EpiPen®	*Class I, Level of Evidence A*
normal saline (NS)	IV	20 mL/kg/dose	1 L/dose	Give PRN persistent blood pressure reductions ≥ 30% from baseline	*Class I, Level of Evidence C*
albuterol	nebulized	< 20 kg: 2.5 mg/dose ≥ 20 kg: 5 mg/dose	5 mg/dose	Can consider PRN for shortness of breath, wheezing, dyspnea, or respiratory depression not responding to EPINEPHrine	*Class IIa, Level of Evidence B*
EPINEPHrine infusion	IV Continuous	Initial dose: 0.1 mcg/kg/min	1 mcg/kg/min		*Class IIa, Level of Evidence C*
glucagon	IV	< 20 kg: 0.5 mg/dose ≥ 20 kg: 1 mg/dose	1 mg/dose	Consider for patients on beta-blockers that are not responding to EPINEPHrine	*Class IIa, Level of Evidence B*

*IV = intravenous; IM = intramuscular; PO = by mouth/enteral; BID = twice daily; PRN = as needed; GI = gastrointestinal

Table 1 (continued): Medications for Anaphylaxis

Medication	Route	Dose	Max Dose	Comments	Level of Evidence
dexAMETHasone	IV/IM/PO	0.5 mg/kg/dose	16 mg/dose	Consider for critically ill patients especially those with asthma, severe anaphylaxis, or other airway concerns Give Q24h to Q6h based on the patient's severity	*Class IIb, Level of Evidence B*
cetirizine	PO	≥ 6 months - < 2 years: 2.5 mg/dose 2 - 5 years: 5 mg/dose > 5 years: 10 mg/dose	10 mg/dose	Consider BID PRN for cutaneous manifestations or pruritis not responding to EPINEPHrine	*Class IIb, Level of Evidence B (antihistamines)*
diphenhydrAMINE	IV/IM	1 mg/kg/dose	50 mg/dose	Consider Q6h PRN for cutaneous manifestations or pruritis not responding to EPINEPHrine	*Class IIb, Level of Evidence B (antihistamines)*
famotidine	PO	1 mg/kg/dose	40 mg/dose	Consider for GI manifestations	*Class IIb, Level of Evidence B*
	IV	1 mg/kg/dose	20 mg/dose		*Class IIb, Level of Evidence B*

*IV = intravenous; IM = intramuscular; PO = by mouth/enteral; BID = twice daily; PRN = as needed; GI = gastrointestinal

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 1 to 4 hours after symptom onset. Although the turnaround time for serum tryptase is usually several days, the results are more beneficial for the diagnosis and future management of the patient. A normal 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 the initial onset of symptoms, a reasonable length of time of observation of a patient treated for anaphylaxis is 4 – 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. Patients who require repeated doses of EPINEPHrine, present with severe respiratory distress or hypotension, or experience a biphasic reaction during observation should be admitted to the hospital for observation (*Class IIa, Level of Evidence B*).

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 kg to less than 30 kg can receive a 0.15 mg dose of EPINEPHrine (EpiPen Junior®). Children weighing 30 kg or more can receive a 0.3 mg dose of EPINEPHrine (EpiPen®). For children weighing less than 15 kg, consider prescribing Auvi-Q® 0.1 mg EPINEPHrine autoinjector if possible. If the Auvi-Q® 0.1 mg EPINEPHrine autoinjector 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

On discharge, prescribing a course of enteral steroids can be considered. Giving corticosteroids does not have any significant effect on readmission for patients with allergic reactions. The benefit of corticosteroids in anaphylaxis has not been scientifically proven but it is common practice to treat with steroids as a secondary treatment (*Class IIb, Level of Evidence B*). For example, dexAMETHasone 0.5 mg/kg/dose daily (max 16 mg/dose) for 1 additional day.

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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

Owner(s): Courtney Titus, PA-C, Corey Fowler, PharmD

Inpatient Providers: Dr. Michelle Smith, Dr. Dipti Amin

Emergency Medicine Providers: Dr. Danielle Hirsch, Dr. Ebony Hunter

Allergy/Immunology Specialists: Dr. Panida Sriaroon, Dr. Monica Hajirawala, Dr. Priya Patel

Pharmacists: Marla Tanski, Meghan Roddy, Jon Fannin, Jessica White, Amanda Memken

Nursing: Cindy Kay, Tracey Mouring, Cristina Suarez, Nicole Robertson

Clinical Pathway Management Team: Joseph Perno, MD; Courtney Titus, PA-C

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