

Anaphylaxis for Extern

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Terminology

"severe, life-threatening, generalized or systemic hypersensitivity reaction"



Mediated by an immune
mechanism;
immune complex

~~Anaphylactoid~~

Immunologic reaction

What's new!



Allergic anaphylaxis



Nonallergic anaphylaxis

Anaphylaxis

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graph TD; A[Anaphylaxis] --> B[Immunologic]; A --> C[Idiopathic]; A --> D[Non-immunologic]; B --> E[IgE dependent]; B --> F[IgE independent]; E --> G["- Food<br/>- Drug<br/>- Insect"]; F --> H["Disturbance of arachidonic acid; NSAIDs<br/>Cross-linking and activation; radiocontrast media"]; D --> I["Direct mediator release; opiates, physical, cold, exercise"];
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Immunologic

Idiopathic

Non-immunologic

IgE dependent

IgE independent

Direct mediator release; opiates, physical, cold, exercise

- Food
- Drug
- Insect

Disturbance of arachidonic acid; NSAIDs
Cross-linking and activation; radiocontrast media

Criteria for diagnosis

Acute onset
involving skin,
mucosal tissue

+ 1 of

Respiratory compromise

Reduced blood pressure
or end organ dysfunction

After exposure to
a likely allergen

+ 2 of

- Skin/mucosal tissue
- Respiratory compromise
- Reduced BP/end organ dysfunction
- Persistent GI symptoms

After exposure to
a known allergen

And

Reduced BP

Organ involvement

- Skin-mucosal tissue: urticaria, flush, angioedema
- Respiratory: dyspnea, wheeze, bronchospasm, stridor, hypoxemia, **cough**
- Gastrointestinal: crampy abdominal pain, vomiting, diarrhea
- Cardiovascular: reduced blood pressure, end-organ dysfunction; hypotonia, syncope, incontinence

Signs and symptoms; frequency of occurrence

Signs/Symptoms	Percentage of Cases
Cutaneous	>90
Urticaria and angioedema	85-90
Flush	45-55
Pruritus without rash	2-5
Respiratory	40-60
Dyspnea, wheeze	45-50
Upper airway angioedema	50-60
Rhinitis	15-20
Dizziness, Syncope, Hypotension	30-35

Do not rely on hypotension or skin lesion!

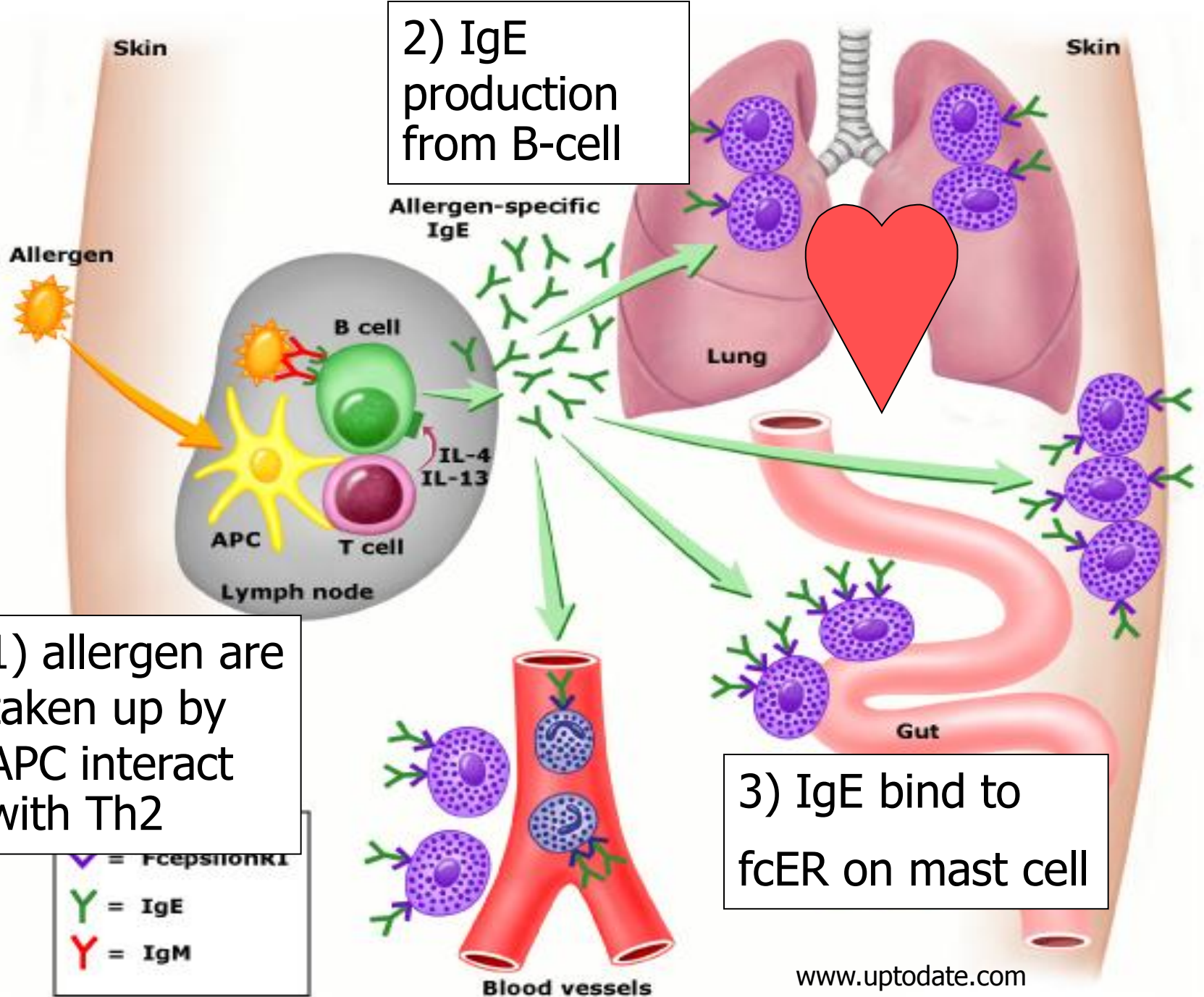
Pathophysiology

2) IgE production from B-cell

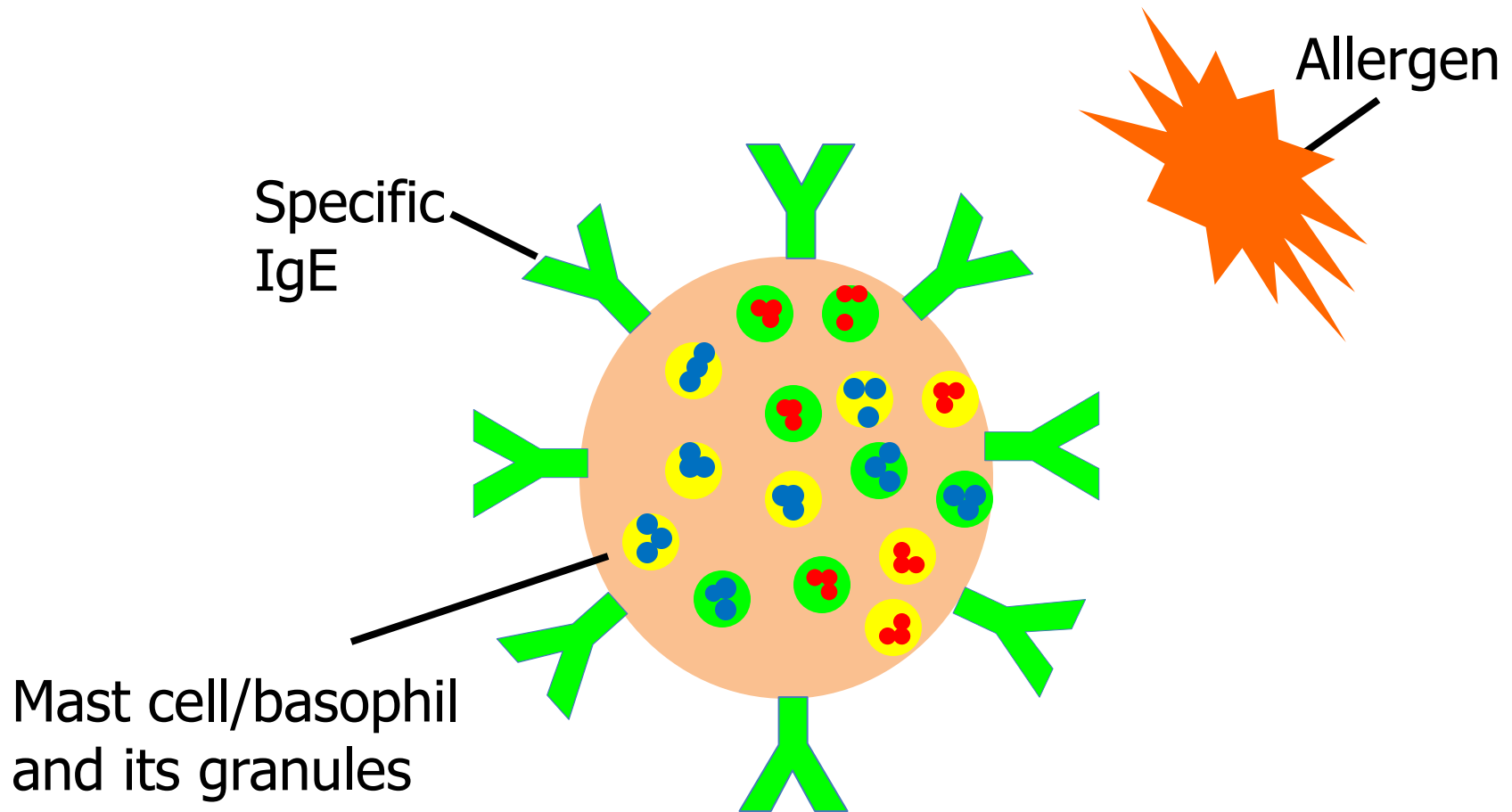
1) allergen are taken up by APC interact with Th2

3) IgE bind to fcER on mast cell

● = FcεR1 on mast cell
Y = IgE
Y = IgM

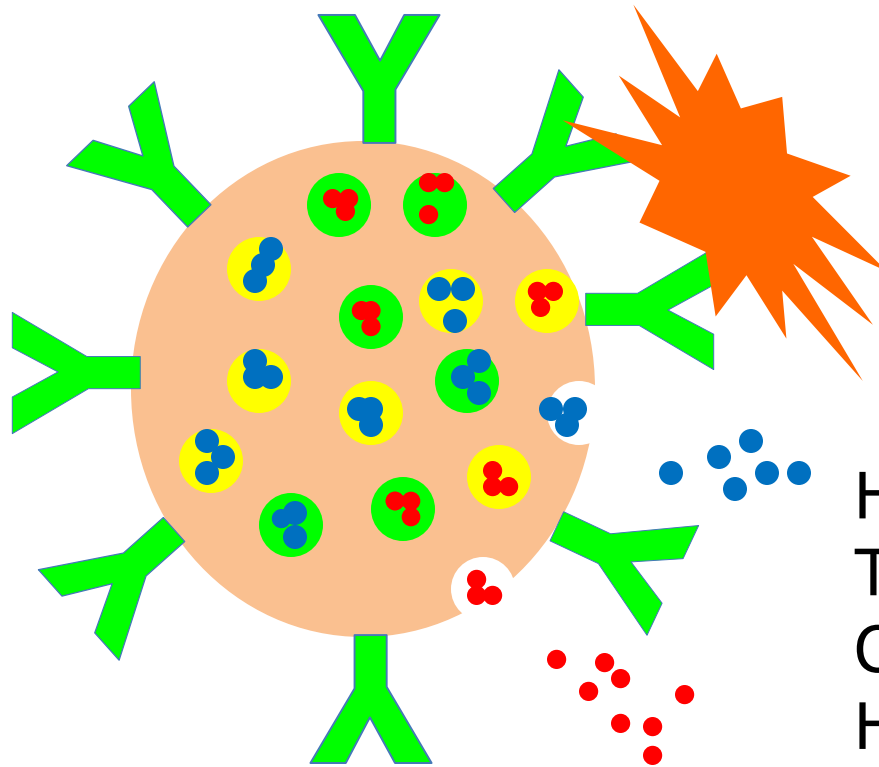


IgE-mediated reaction



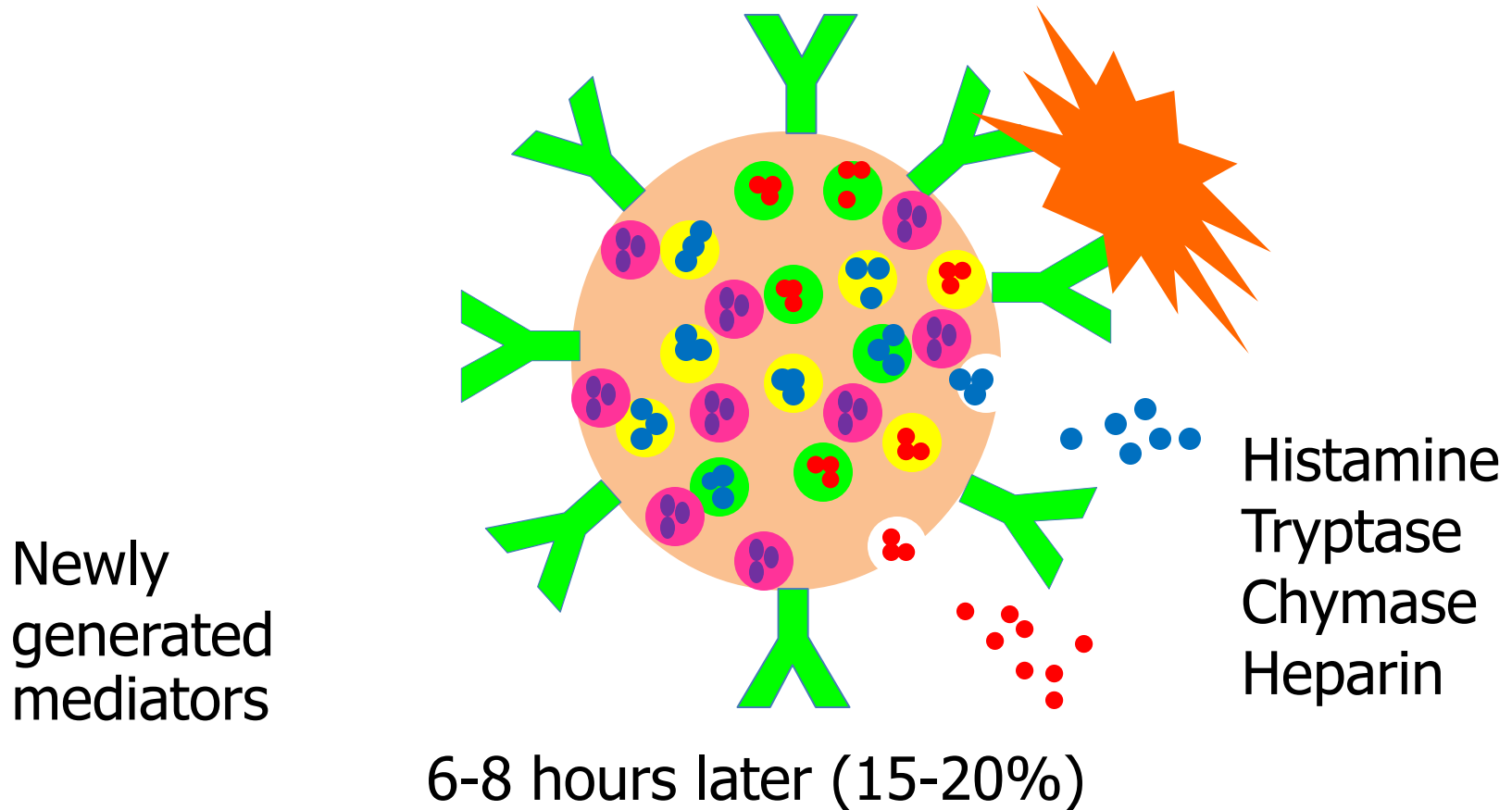
IgE-mediated reaction

Allergen

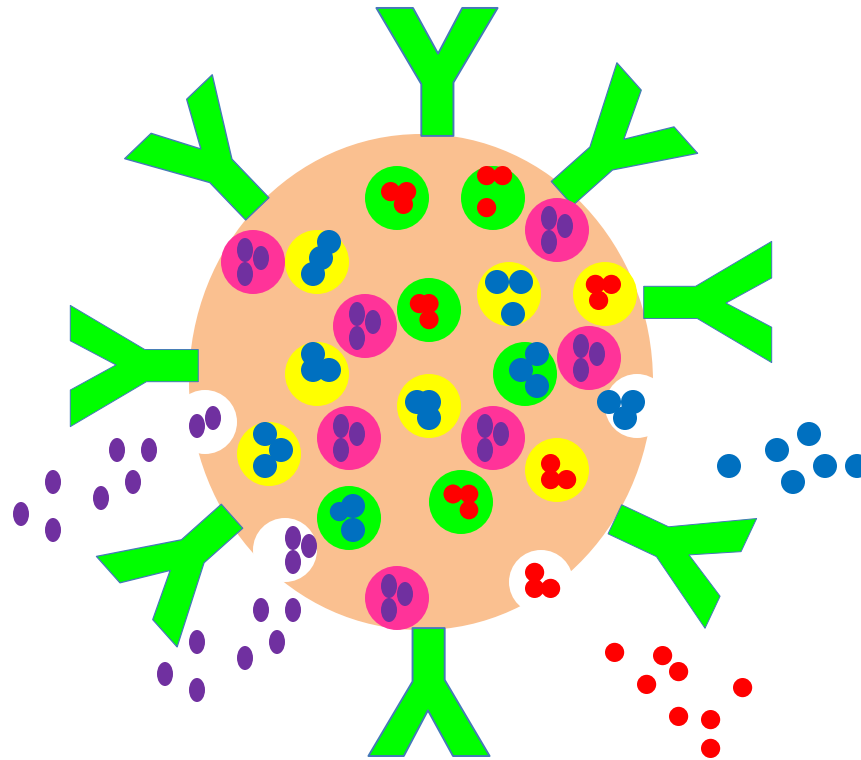


Histamine
Tryptase
Chymase
Heparin

Biphasic anaphylaxis



Biphasic anaphylaxis



Prostaglandin
Leukotriene
TNF- α
Chemokine

6-8 hours later (15-20%)

Mast cell and basophil mediators

Mediators	Pathophysiologic Activity	Clinical Correlates
Histamine and products of arachidonic acid metabolism (leukotrienes, thromboxane, prostaglandins, platelet-activating factor)	Smooth muscle spasm, mucus secretion, vasodilation, increased vascular permeability, activation of nociceptive neurons, platelet adherence, eosinophil activation, eosinophil chemotaxis	Wheeze, urticaria, angioedema, flush, itch, diarrhea, abdominal pain, hypotension, rhinorrhea, bronchorrhea
Neutral proteases: tryptase, chymase, carboxypeptidase, cathepsin G	Cleavage of complement components, chemoattractants for eosinophils and neutrophils, further activation and degranulation of mast cells, cleavage of neuropeptides, conversion of angiotensin I to angiotensin II	May recruit complement by cleaving C3; may ameliorate symptoms by invoking hypertensive response through angiotensin I-II conversion and by inactivating neuropeptides, although angiotensin II also may cause deleterious coronary artery vasoconstriction. Also, proteases can magnify response because of further mast cell activation.
Proteoglycans: heparin, chondroitin sulfate	Anticoagulation, inhibition of complement, phospholipase A ₂ binding, chemoattractant for eosinophils, cytokine inhibition, kinin pathway activation	Can prevent intravascular coagulation and recruitment of complement. Can recruit kinins, increasing severity of reaction.
Chemoattractants: chemokines, eosinophil chemotactic factors	Summons cells to site	May be partly responsible for recrudescence of symptoms in late phase reaction or extension and protraction of reaction
Tumor necrosis factor α activates nuclear factor- κ B	Produces platelet-activating factor (PAF)	Vascular permeability and vasodilation; PAF synthesized and released late, involved in late phase reactions

Summary: effect of mediators

Pathophysiology	Clinical
smooth muscle spasm	
- Bronchi	Wheeze
- Coronary arteries	Myocardial ischemia
- GI tract	Nausea, vomiting, diarrhea
Increased vascular permeability and vasodilatation	Flush, urticaria and angioedema, hypotension
Myocardial depression	Hypotension, poor perfusion
Increased glandular secretion	Bronchorrhea, rhinorrhea

Differential diagnosis

Vasomotor reaction	Excessive histamine
<ul style="list-style-type: none"> • Flush syndromes • Medullary carcinoma thyroid • Autonomic epilepsy 	<ul style="list-style-type: none"> • Systemic mastocytosis • Urticaria pigmentosa • Basophilic leukemia • Hydatid cyst
Restaurant syndrome	Non organic disease
<ul style="list-style-type: none"> • Monosodium glutamate • Sulfites • Scombroidosis 	<ul style="list-style-type: none"> • Panic attacks • Munchausen stridor • Vocal cord dysfunction
Other form of shock	Miscellaneous
Hemorrhagic Cardiogenic Endotoxic	<ul style="list-style-type: none"> • Hereditary angioedema • Urticarial vasculitis • Pheochromocytoma • Hyper-IgE, urticaria syndrome • Neurologic (seizure, stroke) • Red man syndrome • Capillary leak syndrome

Common disorder	Clnical presentation	Anaphylaxis
Urticaria/angioedema	Limited to skin and subcutaneous tissues	Involvement of one or more body system
Asthma exacerbation	Isolated respiratory symptoms	Onset within minutes or a few hours after exposure to a likely trigger
Vasovagal syncope	Diaphoresis, nausea, vomiting, bradycardia, pallor	Flushing, itching, urticaria, angioedema, respiratory compromised, tachycardia
Other forms of shock	More gradual onset	Sudden onset

Ongoing symptoms that are consistent with anaphylaxis, the patient should receive adrenaline promptly!

Laboratory findings

- Tryptase: 60 min-4 hours
- Plasma and urine histamine: 5-60 mins
- Platelet activating factor level: correlate with severity
- Allergologic work up; Skin test, specific IgE,

No definite biomarker.

Diagnosis rely on clinical presentation!

Emergency management

Adrenaline

- Drug of choice for anaphylaxis
- Pharmacologic actions address the pathophysiologic changes
- Decreases mediator release from mast cells
- The only medication that prevents or reverses obstruction to airflow and cardiovascular collapse

Therapeutic actions

- Alpha-1 : increased vasoconstriction and peripheral vascular resistance, decreased mucosal edema
- Beta-1 : increased inotropy and chronotropy
- Beta-2 : increased bronchodilation and decreased release of mediators

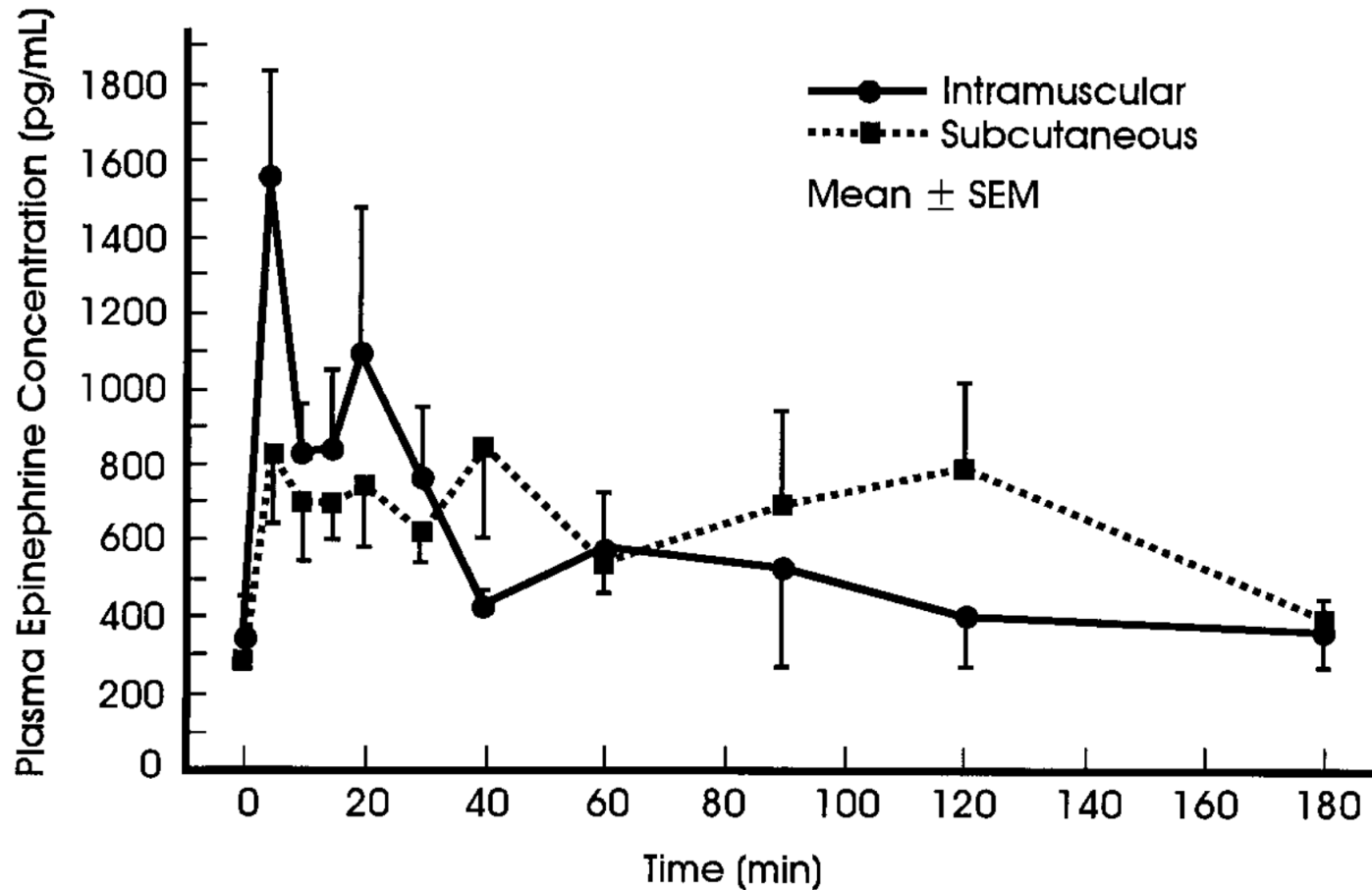
Administration

- Intramuscular at thigh : rapid increase concentration, more reliable absorption

Intravenous infusion

- Patients who do not respond to intramuscular injection **and** fluid resuscitation
- Continuous infusion is preferred

Adrenaline absorption : intramuscular VS subcutaneous



Intravenous fluid

- Massive fluid shifts due to increased vascular permeability
- Initiated in orthostasis, hypotension
- Normal saline in boluses of 20 mL per kilogram

Adjunctive treatment

H1 antihistamines

- Relieving itching and hives
- Do not relieve airway obstruction, gastrointestinal symptoms, shock
- Do not inhibit mediator release from mast cells

H2 antihistamines

- May provide some additional benefit (one study in mild reaction)

Not drug of choice!

Adjunctive treatment

Bronchodilators

- Treatment of bronchospasm not responsive to adrenaline
- Do not prevent or relieve mucosal edema in the upper airway

Glucocorticoids

- Onset of action takes 4-6 hours
- Do not relieve the initial symptoms
- Prevent the biphasic anaphylaxis
- Stopped after three days without a taper

EVALUATE Airway, Breathing and Circulation

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graph TD; A["EVALUATE Airway, Breathing and Circulation"] --> B["Cardio-respiratory Arrest"]; A --> C["Skin/mucosal tissue only"]; B --> D["Treat as per protocol"]; C --> E["Antihistamine"]; E --> F["• Re-evaluate<br>• Caution<br>- Previous severe reaction<br>- Exposed to known allergen<br>- Coexist asthma"];
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Cardio-respiratory
Arrest

Treat as per protocol

Skin/mucosal tissue only

Antihistamine

- Re-evaluate
- Caution
 - Previous severe reaction
 - Exposed to known allergen
 - Coexist asthma

EVALUATE Airway, Breathing and Circulation

Adrenaline i.m.

Remove allergen, oxygenation, i.v. access, monitoring

Hypotension

- Extremities elevated
- NSS i.v bolus

Stridor

Nebulized
adrenaline

Wheezing

Nebulized
B2-agonist

No response in 5-10 mins

Hypotension



- Extremities elevated
- NSS i.v bolus



- Repeat adrenaline i.m
- Repeat i.v fluid bolus

Stridor



Nebulized adrenaline



- Repeat adrenaline i.m
- Repeat nebulized adrenaline

Wheezing



Nebulized B2-agonist



- Repeat adrenaline i.m
- Repeat nebulized B-2agonist

Adrenaline i.v (infusion)

:profoundly hypotensive ,failed to respond to i.v.fluid
and several (2-3)doses of adrenaline i.m

EVALUATE Airway, Breathing and Circulation

Adrenaline i.m.

Remove allergen, oxygenation, i.v. access, monitoring

Hypotension

- Extremities elevated
- NSS i.v bolus

- Repeat adrenaline i.m
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Stridor

Nebulized adrenaline

- Repeat nebulized adrenaline
- Repeat adrenaline i.m

Wheezing

Nebulized B2-agonist

- Repeat nebulized B-2agonist
- Repeat adrenaline i.m

Anti-histamine, corticosteroid

Dosage and route of administration

Drug	Dose/Route	Comment
Adrenaline	<u>0.01</u> mg/kg/dose (max 0.3mg) of <u>1 : 1000</u> solution <u>i.m.</u> lateral thigh	Initial drug of choice repeat every 5-15 minutes
ANTIHIISTAMINES		
Diphenhydramine	Child: 1-2 mg/kg/dose (max 25 mg)	Second line treatment
Chlopheniramine	0.25 mg/kg i.v	Dose for anaphylaxis
Ranitidine	1 mg/kg i.v (max 50 mg)	

Dosage and route of administration

Drug	Dose/Route	Comment
CORTICOSTEROIDS		
Hydrocortisone	5 mg /kg i.v (max 100 mg)	Exact dose not established
Methylprednisolone	1-2 mg/kg/dose i.v	Adapted from asthma treatment
Prednidsolone	1-2 mg/kg/day p.o.	For mild episode
DRUGS FOR BRONCHOSPASM		
Aerosolized β -agonist: salbutamol,	Dose as for asthma: 0.03 mg/kg/dose	For bronchospasm not responding to adrenaline

Common pitfalls

- Reluctant to diagnose anaphylaxis in the absence of shock
- Anaphylaxis in a known asthmatic may be mistaken for an asthma exacerbation
- Patients may not recognize the symptoms as a serious allergic reaction
- Reluctant to use adrenaline: fatalitiy

Observation period

- No consensus or RCT
- Biphasic episodes
- Observation of 8 to 24 hours after resolution of symptoms esp in
 - Severe reaction
 - Episode in asthmatic patient with wheezing
 - Ingested antigen with possibility of continued absorption
 - Previous history of biphasic response

Discharge planning

Prednisolone

- 1-2 mg/kg/day for 72 hours

Counseling

- They have anaphylaxis which is a life-threatening condition
- Symptoms may recur up to three days
- Risk for repeat episodes

Allergen identification and avoidance

- Avoidance
- Immunotherapy
- Desensitization
- Premedication (for non-IgE-mediated)

Discharge planning



Acute management

- Rapid recognition of symptoms
- Administer adrenaline
- Emergency medical service



Adrenaline for emergencies

- Provide the patient with a self-injectable adrenaline
- Importance of carrying the adrenaline at all times
- Educate family members