Anaphylaxis;

Etiology
&
Lab investigation

Soheila Alyasin
Shiraz University of
Medical Science

anaphylaxis

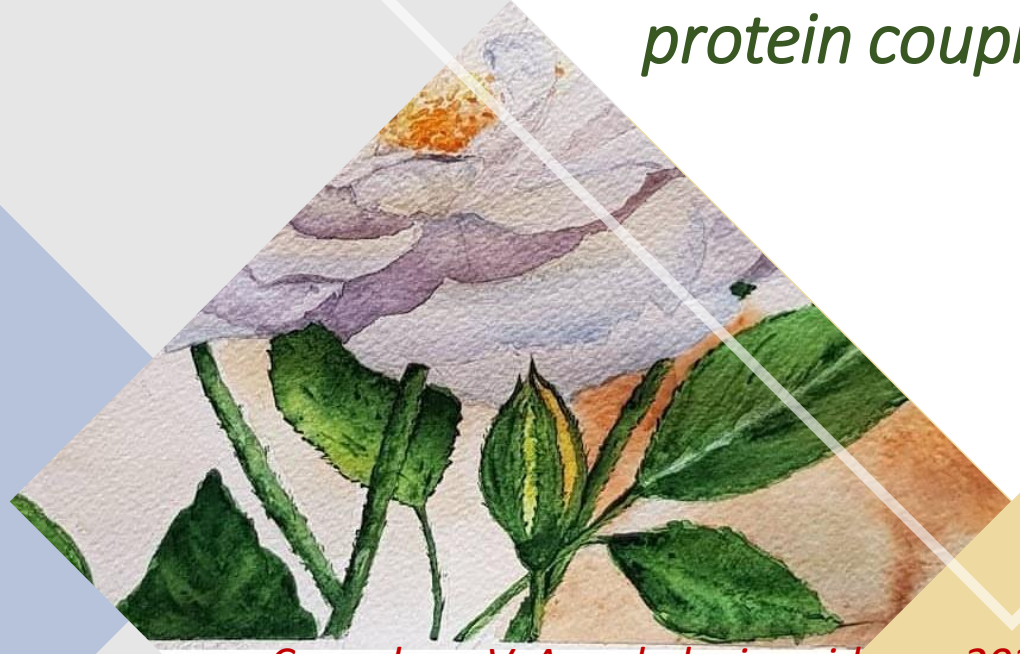
more than 2 fold increase in anaphylaxis incidence between 2009 and 2019

Hei p. Increasing incidence of anaphylaxis in Hong Kong …. Clin Transl Allergy 2020

Non IgE mediated anaphylaxis:

- *Anaphylotoxin,C3a- C5a*
- *contact*
- *coagulation system*
- *IgG: Opoid- ethanol- Exercise*

Cause: Mast cell related G protein coupled Recep



Idiopathic anaphylaxis: 6.5%- 35% (mastocytosis- urticaria pigmentosa Mast cell disease) Or allergen previously unrecognized(αGal)

Corradono V. Anaphylaxis guidance 2020. WAO Journal 2020

Cause

- *Children : hen's egg- CM- -wheat- peanut*
- *Tree nut- shellfish- sesame-*
- *Korea: buckwheat-*
- *Mite ingestion : oral mite anaphylaxis*
- *Venom : bee - wasp- red ant*
- *Drugs : antibiotics*- NSAIDs - biologics- chemotherapy- chlorohexidine- PEG- methylcellulose*
- *Latex- RCM- medical dye- thiopental*
- *seminal fluid-*

Test: regarding common cause in the region & age : Food – insect venom- drugs

Corradono V. Anaphylaxis guidance 2020. WAO Journal 2020

Cofactors in Anaphylaxis

: effect on severity & outcome

1) Endogenous : mastocytosis - unstable asthma-

   hormones: premenstrual

2) Exogenous : exercise – infection- sleep deprivation- alcohol-

   medication(ACEI-β blocker)

- Some triggers have delay onset : α galactose

Corradono V. Anaphylaxis guidance 2020. WAO Journal 2020

Anaphylaxis
Etiology

- ***Drug : the most common cause of fatal anaphylaxis: 0.5/1000000***
- ***Non-food anaphylaxis :death 1%***

- ***antibiotics* or any parental drug***
- ***radiocontrast material, anestasia agent ,chemotherapy, biologic agent***

- *Corradono V. Anaphylaxis guidance 2020. WAO Journal 2020*

Anaphylaxis, Etiology

- food allergy: 4% in children, 1% in adult
Peanut ,shellfish, fish, cow' milk, egg

- Delay anaphylaxis(4- 12 hrs), in area of North America, star tick is endemic is related to sensitization to galactose alpha galactose(α Gal)

-food anaphylaxis in 0.05- 0.35/100 person in year
- Death 1/100000 to 1/1000000
but 1% in documented food anaphylaxis

Venom Anaphylaxis

- ***- primary cause of fatal anaphylaxis***
  -systemic anaphylaxis to venom 0.5- 3.3%

  -1/100000 of all fatal sting

  - 10% of patient anaphylaxis to venom : underlying mast cell disease

Latex Anaphylaxis

- Was common in 1980 -1990

- natural rubber latex (NRL)

- spina bifida -catheter –healthcare

- 30 to 50% sensitize to NRL, also sensitize to fruit (banana-Kiwi- avocado): **latex fruit syndrome :** cross reaction to latex allergen (Hev b2- Hev b6…..)

prevention: low protein allergen latex glove or non-latex glove : sensitization decrease 50%

Anaphylaxis, etiology

- ***seminal fluid : in sensitized women***

  Treatment : graded intra vaginal desensitization

Intravenous contrast Media Anaphylaxis

- ***1- Direct mast cell stimulation***
- ***2- sIgE to contrast is found***

- ***Decreased in recent year :***
  - ***low osmolality contrast,***
  - ***gadolinium***

- ***In mild to moderate reaction prevention by corticosteroid and antiH1 ?***
-

Anaphylaxis, Allergens specific immunotherapy

- ***overall risk of systemic reaction for each injection 0.2%***
- ***Mild***

Physical Triggers & Anaphylaxis

- ***Cold urticaria: anaphylaxis: immersion in cold water***
- ***severe cholinergic urticaria : extreme heat***
- ***solar Urticaria : sunlight***
- ***exercise-induced anaphylaxis : after ingestion of allergic food :within 4 hours (food associated exercise-induced anaphylaxis)***

  Wheat- grain –nut- shellfish or any foods
- ***exercise as well as alcohol , NSAID : increase Gut permeability to allergen***
- ***NSAID : mast sell degranulation***

Idiopathic anaphylaxis

- ***Anaphylaxis diagnosis of exclusion***
- ***Require extensive evaluation***

- ***Extend of symptom : angioedema to generalized symp.:***
- ***Frequency: 2 episodes in 2 months or 6 in a year: frequent***
- ***Sever : need prednisolone as maintenance***

- ***cause : mast cell releasibility related to activated T cell***

- ***40% of idiopathic anaphylaxis : mast cell disease like mastocytosis***

- *in 2011- 2017: 84% of anaphylaxis in emergency department: food induce*

- *peanut decrease but tree nut increased*
- *health interest–*
- *cross reaction*
- *unknown anaphylaxis may be due to Cross reaction*

Miles B. Rate of anaphylaxis for the most common food allergy. J allergy immunol practice 2020

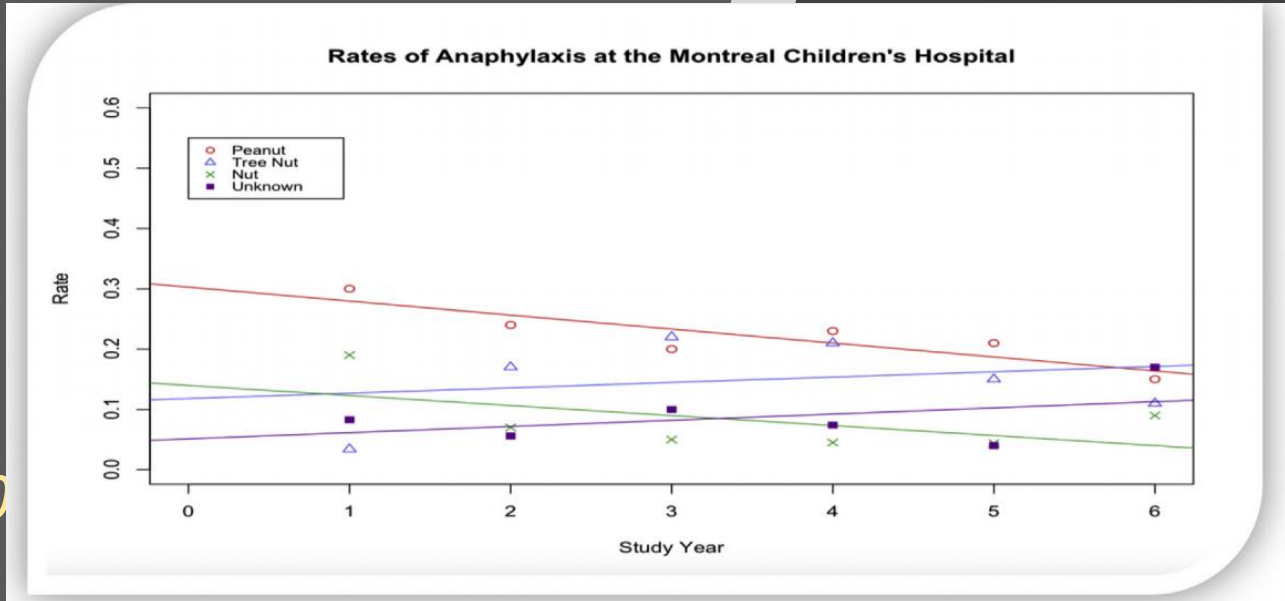


FIGURE 1. Significant changes over the years of peanut, tree nut, nut, and unknown.

- *Exercise-induced anaphylaxis :2.4- 5% of all anaphylaxis*
- *running –biking- dancing -sexual intercourse*

- *4 types:*
- *1- food independent E induced anaphylaxis(FIEIA) ,no food ,only sport*
- *2- food dependent E induced anaphylaxis with IgE sensitivity (FDEIA IgE)*

food + exercise - 4 to 6 hours postprandial – Wheat is more common- gliadin*

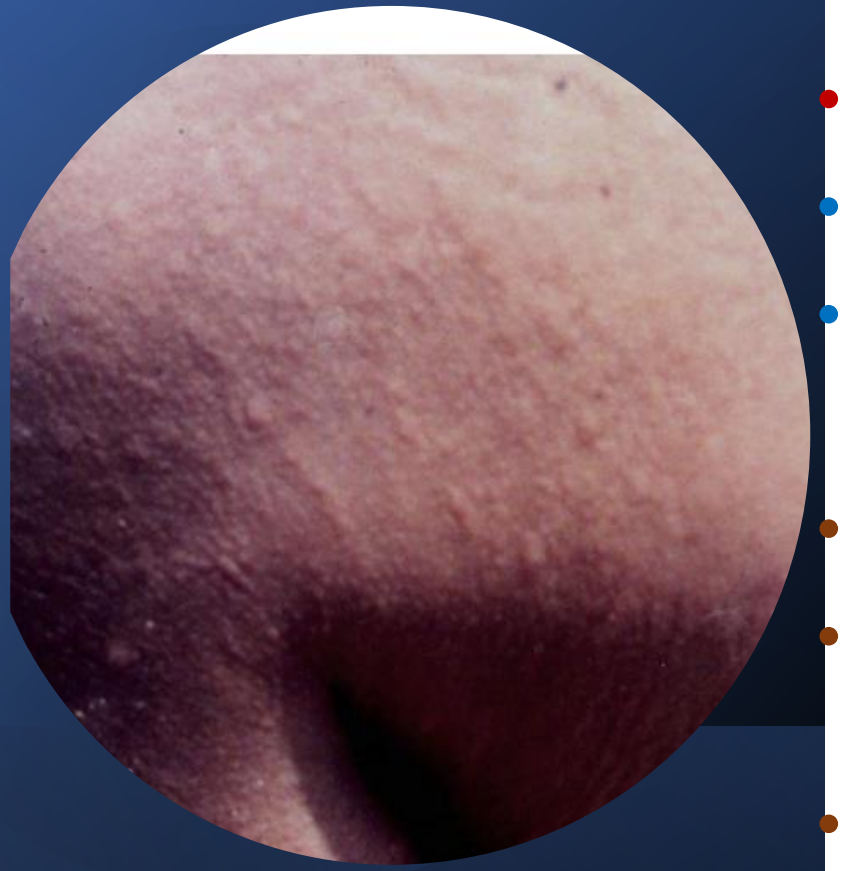
shellfish , tomato, corn ,almond, soy, Rye, bee pollen, mite contaminated flour

- *prick and prick test: when SPT is negative*
- *3- food dependent exercise-induced anaphylaxis without IgE sensitivity: rare-- 4 to 6 hours postprandial*
- *4- Drug dependent exercise-induced anaphylaxis (DDEIA) : NSAID-ASA-cephalosporin- butyrate(energizer)*

Galler M. clinical management of exercise-induced anaphylaxis and cholinergic urticaria allerg clini immunol .2020

WDEIA

- food dependent E induced anaphylaxis with IgE sensitivity (FDEIA IgE)
- Wheat is more common- gliadin
- Wheat dependent exercise-induced anaphylaxis (WDEIA):
- WDEIA : dx is difficult
- because provocation in 60% is positive,
- 30 % tests with commercial extract
- exercise is not absolute necessary, but exercise: lower the threshold
- May be at rest
- E is a Co-trigger instead of trigger
- Aspirin and alcohol may be a co-trigger , if large amount of wheat ingested
- Physician are unaware of this condition



- ***Cholinergic Urticaria: 0.5% in g.p.***
- ***6 to 13% in adult, 19% in children***
- ***small lesion or may be large***

- ***: 3% of anaphylaxis***
- ***death is reported to a teenage after eating peanut***
- ***should stop immediately sport :urticaria***
- ***natural history : EIA :1/2 improved in 10-years***

TABLE II. Description of the concepts of EIA and CholU

Characteristics	EIA	CholU
Symptoms and signs	Flushing, increase warmth, malaise, diffuse itching, urticaria, angioedema, gastrointestinal symptoms (nausea, vomiting, abdominal cramps, and diarrhea), hypotension, syncope, laryngeal edema, anaphylaxis, and rarely asthma. In EIA, wheals are large and may converge	Wheals are typically small, punctate, with a surrounding flare reaction, and may converge, involving mainly the trunk and extremities, precipitated by exercise and passive warming with core body temperature elevation (usually less than 1°C). CholU may be induced by hot baths and showers, wearing heavy clothes, eating spicy foods, and with underlying emotional stress
Risk of anaphylaxis	Common	Extremely rare
Provocation tests	Standard treadmill exercises for approximately 30 min after specific food or drug intake	Standard treadmill exercises for approximately 30 min and then passive warming with core body temperature elevation
Management	Rule out associated food allergies. Check a baseline serum tryptase. Always exercise with a companion. Medic alert bracelet. No exercise for 4-6 h after eating or taking NSAIDs. It is very important to immediately stop exercising at the onset of symptoms. Omalizumab usually controls refractory cases	Symptomatic treatment with nonsedating second-generation H1-antihistamines. Updosing to 4-fold the licensed dose of antihistamines in initial nonresponders may be effective. Omalizumab usually controls refractory cases
Need for an epinephrine autoinjector prescription	Yes	No
Long-term prognosis	Good	Good

- ***Exercise-induced anaphylaxis***

Differential diagnosis

- cholinergic urticaria
- indolent systemic mastocytosis
- mast cell activation
- arrhythmia
- hypertrophic cardiomyopathy
- vocal cord dysfunction
- laryngomalacia
- exercise associated GE reflux
- exercise-induced asthma
- idiopathic anaphylaxis

Food induced anaphylaxis pathogenesis

- *Exercise: divert blood from mesenter. to muscles; plasma osmolarity – change PH : allergen absorption*
- *Exercise: divert blood from mesenter. to muscles; plasma osmolarity – change PH : allergen absorption*
- *enzyme and cytokine enhance immunogenicity of food allergen*
- *NSAID : intestinal permeability : promote food absorption*

- ***Dust mite ingestion associated exercise-induced anaphylaxis***

- ***Syncope 1/3, laryngeal oedema in 2/3***
  - post prandial in 54%
  - Drug dependent 13%

-

recommend

- EIAs become stable –

- avoidance exercise for 2-6 hrs after feeding

- not use trigger foods

- no exercise, when high pollen or mold

- no exercise in cool, warm, humid weather

- no exercise 4 hours after allergen, immunotherapy ,NSAID , aspirin

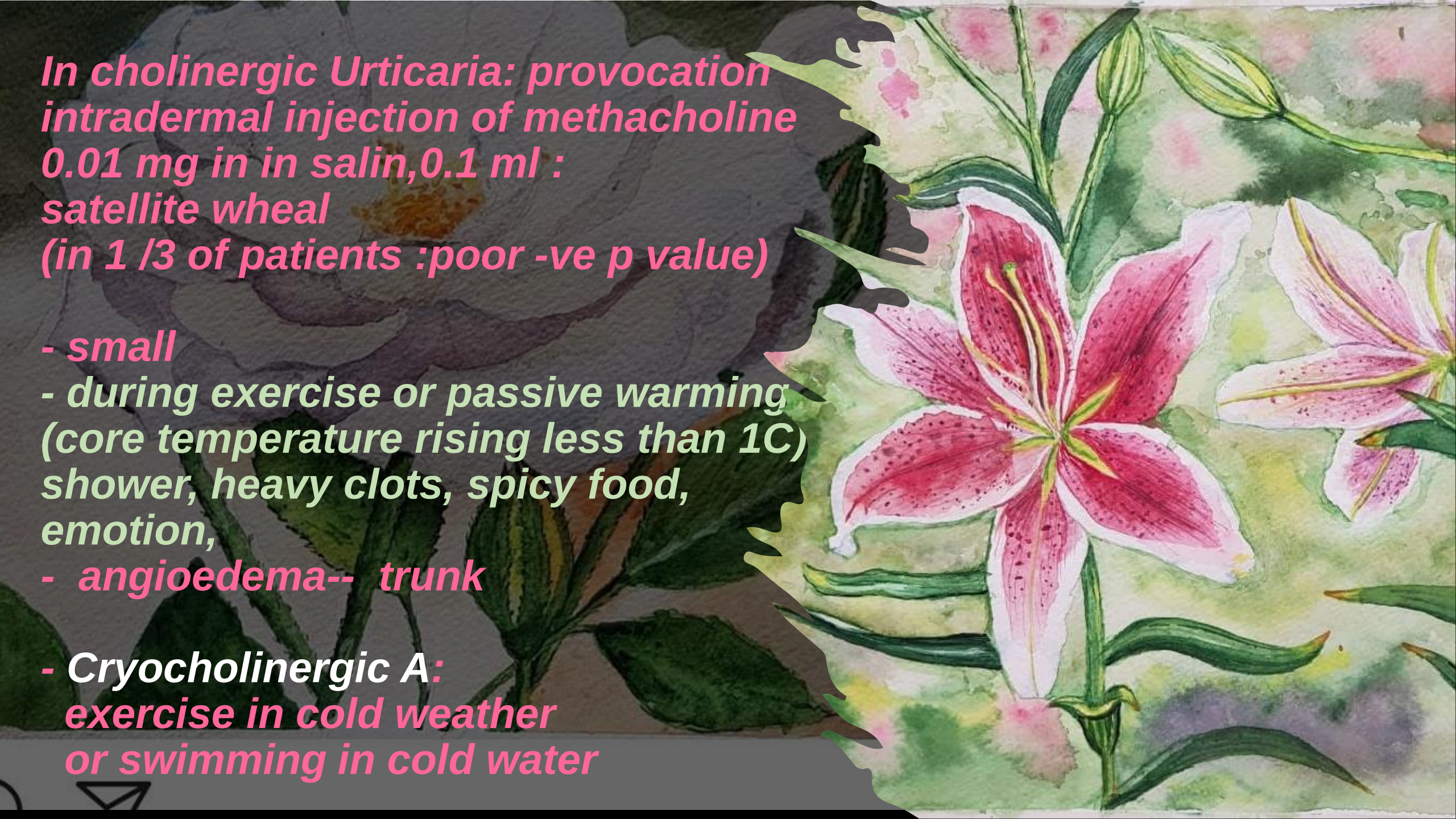
- omalizumab prevent exercise-induced anaphylaxis

EIA: Diagnosis

- running 30 minutes on treadmill,
if negative does not R/O

Treatment

AH-
auto-injector epinephrine –
no AH2-
wear bracelet –
- immediate stop Exercise, when urticaria
- po cromolyn sodium
misoprostol-
- ketotifen (prophylaxis)
- Omalizumab in refractory type



In cholinergic Urticaria: provocation intradermal injection of methacholine 0.01 mg in in salin,0.1 ml :
satellite wheal
(in 1 /3 of patients :poor -ve p value)

- small
- during exercise or passive warming (core temperature rising less than 1C) shower, heavy clots, spicy food, emotion,
- angioedema-- trunk

- Cryocholinergic A:
exercise in cold weather
or swimming in cold water

Cholinergic Urticaria

- *2 types Autologous Rx : serum sweat*

  +ve -ve

  -ve +ve

- *The role of sweating*
- *Anaphylaxis with cholinergic U has been reported*
- *Tx ; AH1 - Omalizumab*

Anaphylaxis is highly likely when any one of the following 2 criteria are fulfilled:
1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
AND AT LEAST ONE OF THE FOLLOWING:
a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
c. Severe gastrointestinal symptoms (eg, severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens
2. Acute onset of hypotension[a] or bronchospasm[b] or laryngeal involvement[c] after exposure to a known or highly probable allergen[d] for that patient (minutes to several hours), even in the absence of typical skin involvement.

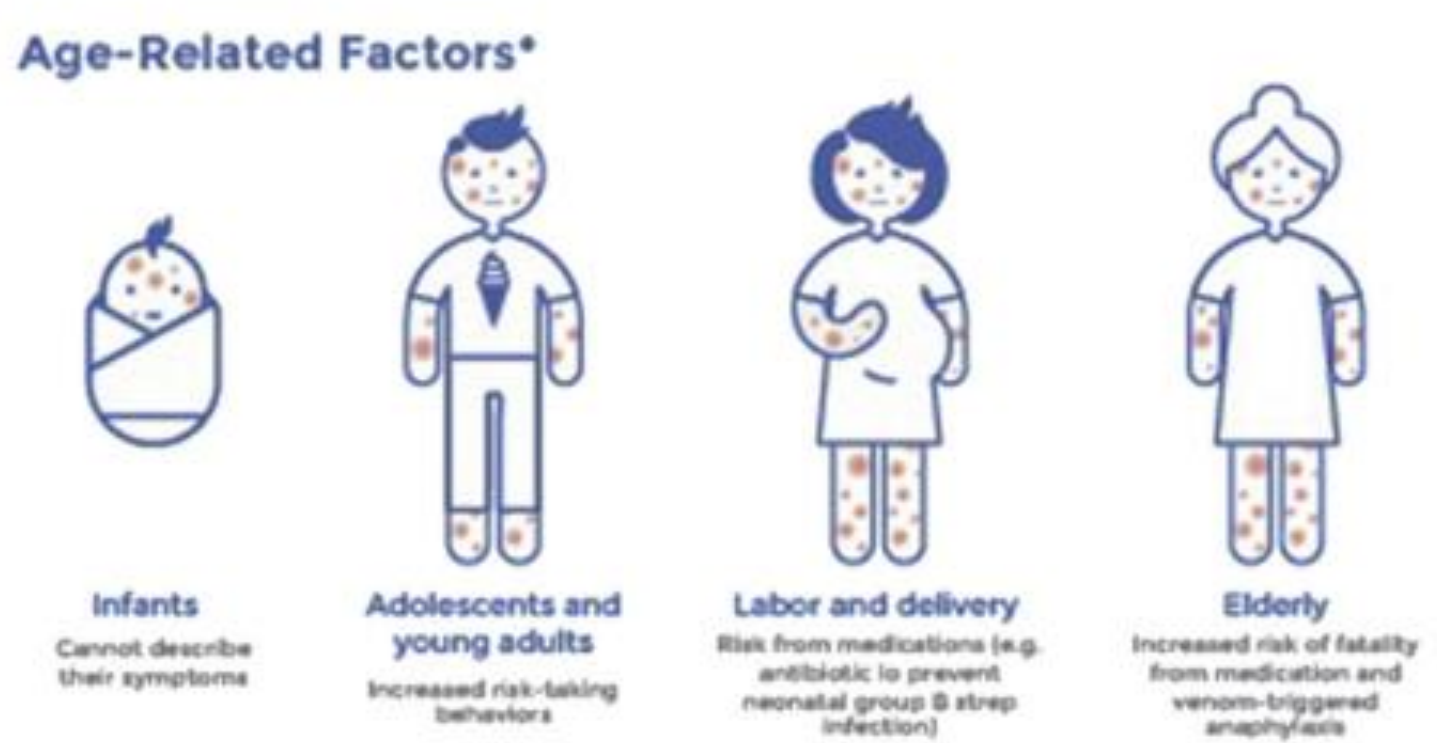
Table 2. Amended criteria for the diagnosis of anaphylaxis. *PEF, Peak expiratory flow; BP, blood pressure. a. Hypotension defined as a decrease in systolic BP greater than 30% from that person's baseline, OR i. Infants and children under 10 years: systolic BP less than (70 mmHg + [2 x age in years]) ii. Adults and children over 10 years: systolic BP less than <90 mmHg. b. Excluding lower respiratory symptoms triggered by common inhalant allergens or food allergens perceived to cause "inhalational" reactions in the absence of ingestion. c. Laryngeal symptoms include: stridor, vocal changes, odynophagia. d. An allergen is a substance (usually a protein) capable of triggering an immune response that can result in an allergic reaction. Most allergens act through an IgE-mediated pathway, but some non-allergen triggers can act independent of IgE (for example, via direct activation of mast cells). Adapted from [26]*

Immunologic Mechanisms (IgE Dependent)

Immunologic Mechanisms (IgE independent)

Nonimmunologic Mechanisms (Direct mast cell activation)

Idiopathic Anaphylaxis (No apparent trigger)



Infant ; can't describe
Young; high risk behavior
Labor : medication
Old: fatality -medication


Allergic rhinitis and eczema
Asthma and other respiratory diseases
Concomitant Diseases*
Psychiatric illness (e.g. depression)
Cardiovascular diseases
Mastocytosis / clonal mast cell disorders
Concurrent Medications / Ethanol / Recreational Drug use*
β-adrenergic blockers, ACE inhibitors**, NSAIDs***
Ethanol / sedatives / hypnotics / antidepressants / recreational drugs
(potentially affect recognition of anaphylaxis triggers and symptoms.)

Co-Factors that Amplify Anaphylaxis*

Exercise

Acute infection (e.g. a cold or fever)

Emotional stress

Disruption of routine (e.g. travel)

Premenstrual status (females)

Endogenous

sex, age
cardiovascular disease
mastocytosis
atopic disease
elevated tryptase
ongoing infection

Vaccine Allergy

Vaccine allergy

- ***Anaphylaxis 1/100000 to 1/ 1000000***
- ***Gelatin or vaccine protein***

- ***Egg allergy : Egg Yolk in influenza vaccine: no anaphylaxis even in highly sensitized patients to egg***

Anaphylaxis, covid-19 vaccine

- ***CDC guideline , December : vaccine adverse event reporting system***
- ***information sheet at the time of vaccine***
- ***CDC contraindication & precaution to mRNA covid-19 vaccine***

  recommendation of both Pfizer-Biontech and Modena
- ***Definition : immediate allergic reaction (urticaria – angioedema) - respiratory distress (wheeze- stridor) or anaphylaxis within few hours***
- ***Contraindication: severe allergic reaction or immediate Rx to previous dose or component***
- ***persons with an immediate allergic reaction to the first dose should not received their second or any other mRNA vaccine***
- ***Allergist consultation***

How to report an adverse event to VAERS

- Go to vaers.hhs.gov
- Submit a report online

For help:

call
1-800-822-7967

email
info@VAERS.org

video instructions
https://youtu.be/sbCWhcQADFE

- For COVID-19, FDA will issue VAERS reporting requirements under EUA; in addition, CDC encourages reporting of any clinically important adverse event following immunization

2020-12-30 14:07:34

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

co-managed by
CDC and FDA

vaers.hhs.gov

CDC asks that:

- Healthcare providers help us get as many people to use **v-safe** as possible
  - give a one-page **info sheet** to patients at the time of vaccination
  - counsel patients on the importance of enrolling in **v-safe**
- CDC has created an electronic version of the **v-safe** info sheet for distribution to public health and healthcare partners

How to report an AE to VAERS

- Go to vaers.hhs.gov and submit a report online
- For help: Call 1-800-822-7967 Email info@VAERS.org
- Video instructions www.youtube.com/watch?v=sbCWhcQADFE

V-safe resources

cdc.gov/vsafe

cdc.gov/coronavirus/2019-ncov/vaccines/safety/troubleshooting

cdc.gov/coronavirus/2019-ncov/vaccines/safety/faq

General safety information

cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/index

cdc.gov/coronavirus/2019-ncov/vaccines/safety

v-safe℠
after vaccination
health checker

Resources

cdc.gov/vsafe

cdc.gov/coronavirus/2019-ncov/vaccines/safety/troubleshooting

cdc.gov/coronavirus/2019-ncov/vaccines/safety/faq

2020-12-30 14:08:12

CDC asks that:

- Healthcare providers help us get as many people to use **v-safe** as possible
  - give a one-page **info sheet** to patients at the time of vaccination
  - counsel patients on the importance of enrolling in **v-safe**
- CDC has created an electronic version of the **v-safe** info sheet for distribution to public health and healthcare partners

Anaphylaxis covid-19 vaccine

- ***Pfizer Bion. Day of 0-21, 95% ,>16-year old***
- ***Maderna :0-28 days, 94%,> 18 year***
- ***small number systemic reaction during 7-days,less than 2% :***

  3.8% fatigue, 2% headache (the same as placebo)
- ***hypersensitivity reaction: 0.63% Pfizer, 1.5% moderna in participant (he same as in placebo)***
- ***in clinical trial; severe allergic reaction to vaccine & components were excluded***
- ***in Moderna: 3 events of lip & face swelling, 1-2 days later(dermal filler)***

  no anaphylaxis or severe hypersensitivity reaction

Anaphylaxis covid-19 vaccine

- ***Do not administrate Pfizer vaccine to known history of severe allergic reaction to vaccine component***
- ***<u>subsequently</u>; advised all patient, regardless of allergic history should be observed for 15 minutes***
- ***<u>then</u>; any persons have had severe allergic reaction to injection discuss the risk with doctors and be 30-minute in the clinic***
- ***if anaphylaxis to first dose, no second dose***
- ***reported cases 10 /2000000***
- ***Treat immediately***

Anaphylaxis covid-19 vaccine

- ***Vaccine Allergy, influenza v. 1.35 /1000000***
- ***active -inactive gradient or excipient(egg -gelatin –formaldehyde-Neomycin)***
- ***excipient :strong immune response***

  contamination of bacteria decline

  help to transport and storage

- A major cause of allergy

- ***Poly ethylene glycol (PEG) & polysorbate : water solubility***
- ***PEG: no previously in V. But polysorbate was an allergic cause in V. before***
- ***Pfizer and moderna have PEG/ AstraZeneca has polysorbate***
- ***Many FDA-approved drugs and cream contain PEG***

Anaphylaxis, covid-19 vaccine

- ***Poly ethylene glycol , PEG: laxative bowel preparation for colonoscopy***
- ***improve therapeutic activity of some medication***
- ***cross reaction between PEG and polysorbate***
- ***polysorbate in vaccine & some drug***

Anaphylaxis covid-19 vaccine

- ***PEG in CS- processed food- cosmetics***
- ***Polysorbate (vitamins- vaccine- anticancer- oint- tab – 70% of biologics)***
- ***70% of patients received PEG , have PEG Ab***
- ***In general population; 5 -9% IgG & 0.1%:PEG IgE***
- ***PEG Ig M & Ig G : complement activation related pseudo allergy***
- ***4-8 cases/year : anaphylaxis during colonoscopy***
- ***Infection- tissue injury : Ca3, Ca5 : anaphylatoxin***
- ***Vasovagal symptoms***

Anaphylaxis, covid-19 vaccine

- ***Diagnosis of anaphylaxis from vasovagal***
- ***Treatment of anaphylaxis :epinephrine, antihistamine***
- ***Allergy : high-risk vaccination***
- ***80%: local Rx;***
- ***Person large local reaction; do not preclude from the vaccine again***
- ***No NSAIDs for fever***

Four screening questions are presented to patients prior to the initial vaccination assess risk

- ***: 1. Do you have a history of a severe allergic reaction to an injectable medication (intravenous, intramuscular, or subcutaneous)?***
- ***2. Do you have a history of a severe allergic reaction to a prior vaccine?***
- ***3. Do you have a history of a severe allergic reaction to another allergen (e.g., food, venom, or latex)?***
- ***4. Do you have a history of a severe allergic reaction to polyethylene glycol (PEG), a polysorbate or polyoxyl 35 castor oil (e.g. paclitaxel) containing injectable or vaccine?***

- *If the answer is “no” to all four questions, :“lower risk” &receive the vaccine under usual conditions with 15-minute observation period.*
- *If the answer to question #1, #2 or #3 is “yes,” :“medium risk” and require a 30- minute observation period.*
- *if “yes” for #1 and #2, specific investigation as to the specific injectable products and vaccines should be pursued to determine if these products could have contained high molecular weight PEG, polysorbate or polyoxyl 35 (e.g. paclitaxel).*
- *If the answer to question #4 is “yes,” : “higher risk,” : evaluation with an allergist for expanded skin testing using non-irritating skin testing concentrations*
- *If skin testing to PEG is positive: is not a candidate for the Pfizer-BioNTech or Moderna COVID-19 vaccines, SPT to polysorbate 20 and 80 become important with regards to the safety of future SARS-CoV-2 vaccines in development.*
- *If skin testing to PEG is negative, vaccination with the Pfizer-BioNTech or Moderna COVID-19 vaccines could proceed with 30 minutes of observation*

- *Allergist ,specialized skin testing : risk :for future SARS-19 CoV-2 vaccine*
- *Antihistamines do not prevent anaphylaxis & mask cutaneous symptoms : delay in Tx*

, No antihistamine pretreatment at this time.

- *If anaphylaxis to the first dose, an allergist expanded skin testing : before vaccine rechallenge*
- *No data on the safety of the second vaccine after anaphylaxis to the first dose.*
- *The vaccines with more experience, split dose challenges (e.g. 10-25% of dose followed 30 minutes later by remaining 75-90% dose)*
- *. No vaccine skin testing at this time due to*

  limited vaccine supply,

  lack of information on sensitivity or specificity,

  and unclear safety of skin testing to these

Banerji A. mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current 2 Evidence and Approach.

Summary: Triage of persons presenting for mRNA COVID-19 vaccination

MAY PROCEED WITH VACCINATION	PRECAUTION TO VACCINATION	CONTRAINDICATION TO VACCINATION
ALLERGIES History of allergies that are unrelated to components of an mRNA COVID-19 vaccine[1], other vaccines, or injectable therapies, such as: • Allergy to oral medications (including the oral equivalent of an injectable medication) • History of food, pet, insect, venom, environmental, latex, etc., allergies • Family history of allergies **ACTIONS** • 30 minute observation period: Persons with a history of anaphylaxis (due to any cause) • 15 minute observation period: All other persons	**ALLERGIES** • History of any immediate allergic reaction[2] to vaccines or injectable therapies (except those related to component of mRNA COVID-19 vaccines[3] or polysorbate, as these are contraindicated) **ACTIONS:** • Risk assessment • Consider deferral of vaccination and/or referral to allergist-immunologist • 30 minute observation period if vaccinated	**ALLERGIES** History of the following are contraindications to receiving either of the mRNA COVID-19 vaccines[3]: • Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components • Immediate allergic reaction[2] of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components[4] (including polyethylene glycol)[5] • Immediate allergic reaction of any severity to polysorbate[5,6] **ACTIONS** • Do not vaccinate[7] • Consider referral to allergist-immunologist

Hx of allergy non related to vaccine and components like oral medication- egg- pet-venom
Family hx
15 min for all
30 min for hx of anaphylaxis for other reasons

Hx immediate RX to vaccine or injectable therapy, other than PEG.. Because they are contraindicated
Risk assesment

Sever , immediate Rx to mRNA vaccine or PEG or polysorbate or component

Consideration risk of Co-19 vaccine in person with precaution

-Risk of exposure: residence in a setting like long term facility- occupation

- Risk of sever disease or death due to Covid-19

(age- underlying disease)

- Previous infection with SARAS-C0v19

vaccination is recommended for persons with a hx of infection but persons with precaution to vaccination, may defer vaccination until further information

Unknown risk of anaphylaxis following Cov-19 vaccine with hx of an immediate allergic Rx to other vaccine or injectable therapies

Ability of patients to be vaccinated in a setting of anaphylaxis Tx

Neither contraindication nor precaution COV-19 vaccine

Hx of allergic Rx not related to vaccine,
injectable therapies*,
components* of mRNA vaccine or polysorbate*: like :
foods- pet- venom- environment- oral medical- Latex- egg- Gelatin

Ingredients* included in mRNA COVID-19 vaccines

Description	Pfizer-BioNTech	Moderna
mRNA	nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2	nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2
Lipids	2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide	PEG2000-DMG: 1,2-dimyristoyl-rac-glycerol, methoxypolyethylene glycol
	1,2-distearoyl-sn-glycero-3-phosphocholine	1,2-distearoyl-sn-glycero-3-phosphocholine
	cholesterol	cholesterol
	(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)	SM-102: heptadecan-9-yl 8-((2-hydroxyethyl) (6-oxo-6-(undecyloxy) hexyl) amino) octanoate
Salts, sugars, buffers	potassium chloride	Tromethamine
	monobasic potassium phosphate	Tromethamine hydrochloride
	sodium chloride	Acetic acid
	dibasic sodium phosphate dihydrate	Sodium acetate
	sucrose	sucrose

*As reported in the prescribing information

Distinguishing allergic reactions from other types of reactions

Characteristic	Immediate allergic reactions (including anaphylaxis)	Vasovagal reaction	Vaccine side effects (local and systemic)
Timing after vaccination	Most occur within 15-30 minutes of vaccination	Most occur within 15 minutes	Median of 1 to 3 days after vaccination (with most occurring day after vaccination)
Signs and symptoms			
Constitutional	Feeling of impending doom	Feeling warm or cold	Fever, chills, fatigue
Cutaneous	Skin symptoms present in ~90% of people with anaphylaxis, including pruritus, urticaria, flushing, angioedema	Pallor, diaphoresis, clammy skin, sensation of facial warmth	Pain, erythema or swelling at injection site; lymphadenopathy in same arm as vaccination
Neurologic	Confusion, disorientation, dizziness, lightheadedness, weakness, loss of consciousness	Dizziness, lightheadedness, syncope (often after prodromal symptoms for a few seconds or minutes), weakness, changes in vision (such as spots of flickering lights, tunnel vision), changes in hearing	Headache
Respiratory	Shortness of breath, wheezing, bronchospasm, stridor, hypoxia	Variable; if accompanied by anxiety, may have an elevated respiratory rate	N/A
Cardiovascular	Hypotension, tachycardia	Variable; may have hypotension or bradycardia during syncopal event	N/A
Gastrointestinal	Nausea, vomiting, abdominal cramps, diarrhea	Nausea, vomiting	Vomiting or diarrhea may occur
Musculoskeletal	N/A	N/A	Myalgia, arthralgia
Vaccine recommendations			
Receive 2nd dose of mRNA COVID-19	No	Yes	Yes

Observation period following vaccination

Persons with a precaution to vaccination or a history of anaphylaxis (due to any cause)

30 minutes

All other persons

15 minutes

Recommended medications and supplies for the management of anaphylaxis at COVID-19 vaccination sites

Should be available at all sites	Include at sites where feasible
Epinephrine prefilled syringe or autoinjector*	Pulse oximeter
H1 antihistamine (e.g., diphenhydramine)†	Oxygen
Blood pressure cuff	Bronchodilator (e.g., albuterol)
Stethoscope	H2 antihistamine (e.g., famotidine, cimetidine)
Timing device to assess pulse	Intravenous fluids
	Intubation kit
	Adult-sized pocket mask with one-way valve (also known as cardiopulmonary resuscitation (CPR) mask)

*COVID-19 vaccination sites should have at least 3 doses of epinephrine on hand at any given time.

†Antihistamines may be given as adjunctive treatment and should not be used as initial or sole treatment for anaphylaxis. Additionally, caution should be used if oral medications are administered to persons with impending airway obstruction.

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html

Additional tools to identify persons with contraindications and precautions to vaccination

https://www.cdc.gov/vaccines/covid-19/downloads/pre-vaccination-screening-form.pdf

Diagnostic test

in

Anaphylaxis

La b
Anaphylaxis

- *Serum tryptase: 15 min to 3 hrs peak*
- *serum tryptase : in mast cell and lesser in Basophil: marker of anaphylaxis*
- *Elevated level: support diagnosis; normal level do not exclude*
- *unable to detect all anaphylaxis*
- *3% of all countries*
- *skin test (food- aeroallergen- venom- drugs)*
- *serum IgE*
- *provocation test (food –drugs)*
- *Basophil activation test, Cellular allergen stimulation test*
- *24-hours urinary histamine metabolite (N metal histamine)*

Diagnostic test

- ***Shortly after onset of anaphylaxis : plasma , urine histamine and serum tryptase***
- ***Histamine : 5 -10 minutes - remain 30-minutes***
- **urinary histamine metabolite : longer period : may be useful**
- ***Serum tryptase 1 – 2 hours maximum , remain 3 hours (venom not food allergy)***
- ***histamine level correlated better with clinical sign***
- ***CD63 & 230 on basophil- PG D2- PAF***
- ***carcinoid syndrome or Pheo: serum or urinary serotonin& catecholamine metabolite(VMA- metanephrine)***

- ***Determination the causes of anaphylaxis***
- ***inciting agent: sIgE – prick test, In vitro***
- ***Skin prick test : 6 wks later, in (anesthesia- venom) may no delay***
- ***Drug test***
- ***Pathology: microscopy : respiratory tract finding : laryngeal oedema - - Cardiovascular collapse : atherosclerosis***
- ***Death: comorbid disease ,upper airway edema , Eosinophil and mast cell in spleen, only one urticaria***

- ***Death during the last two decades : tryptase and sIgE up to 5-days after death : there this significant portion of sudden death : anaphylaxis***

anaphylaxis

WAO- FOOD Allergy anaphylaxis network FAAN- national institute of allergy and infectious disease NIAID

- ***Biomarker in diagnosis of anaphylaxis***
- ***37 patients anaphylaxis & non- anaphylaxis***
- ***26 potential biomarkers ,***
- ***median age 38 years old***
- ***the most common cause: food allergy 43.5% - medication 17.4% -venom 8.7% - contrast material 8.7%- unknown 21%.***
- ***Prior anaphylaxis 52%***

Dass C. characterization of serum biomarkers during anaphylaxis in emergency department. J allergy Clin immunol . Oct 2020

TABLE I. Participant demographics and reaction characteristics by anaphylaxis and non-anaphylaxis groups

	Variable	Anaphylaxis (N = 23)	Non-anaphylaxis (N
Patient characteristics	Age	38.3 (18.1)	41.9 (18.3)
	Asthma	43.5%	18.8%
	Food allergy	39.1%	31.3%
	Prior anaphylaxis	52.2%	6.3%
	Male	43.5%	43.8%
Onset location	Home	13.0%	43.8%
	School	4.4%	6.3%
	Work	17.4%	6.3%
	Restaurant	13.0%	0.0%
	Outdoors	4.4%	6.3%
	Healthcare facility	21.7%	6.3%
	Other	31.3%	26.1%
Precipitating allergen	Food allergy	43.5%	18.8%
	Medication	17.4%	31.3%
	Venom	8.7%	12.5%
	Contrast	8.7%	0.0%
	Other	0.0%	12.5%
	Unknown	21.7%	25.0%

	Other	31.3%
Precipitating allergen	Food allergy	43.5%
	Medication	17.4%
	Venom	8.7%
	Contrast	8.7%
	Other	0.0%
	Unknown	21.7%
Signs/symptoms	Urticaria diffuse	43.5%
	Any urticaria	56.5%
	Hypoxemia	8.7%
	Syncope	8.7%
Management	Epinephrine given	82.6%
	Home	90.5%
	Observation unit	4.8%
	Inpatient admission	4.8%

anaphylaxis

-IL6 & IL10 ; increase-
-IL5-16-17-21-31-33-IFNγ, decrease
-IL-6; pro-inflammatory –
acute phase reactant(erythema-
decrease BP- longer duration of symptoms)

-IL-10 immune regulatory, modulate allergic reaction, could be useful in all allergies

Dass C. characterization of serum biomarkers during anaphylaxis in emergency department. J allergy Clin immunol . Oct 2020

با آرزوی
تندرستی و
شادمانی.
سپاس