# ALLERGY TOPICS

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**Pediatric Immunology and Allergy**

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UNIVERSITY OF CALGARY

Alberta Children's Hospital

DEPARTMENT OF PEDIATRICS CALGARY

# TOPICS:

FOOD ALLERGY,
DRUG ALLERGY,
ANGIOEDEMA,
ALLERGIC RHINITIS,
INSECT STINGS,
SERUM SICKNESS

# RCPSC objectives of training in Pediatrics

- 2.1.4.6
- 2.1.4.8
- 2.1.4.10.4
- 2.1.4.10.5
- 2.1.4.10.8

# LEARNING OBJECTIVES

- Provide information to families on when to introduce allergenic food to their children.
- Understand the difference between drug desensitization and drug challenge protocols.
- Explain the difference between hereditary and non-hereditary angioedema.
- List the available treatments for hereditary angioedema.

# Are we all in the same page?

- Allergy = hypersensitivity reaction
- Types of hypersensitivity reactions?
  - Type I
  - Type II
  - Type III
  - Type IV

| Type | Alternate name | Examples | Mediators |
|---|---|---|---|
| I | Allergy (immediate) | Atopy<br>• — Anaphylaxis<br>• — Asthma<br>• — Allergic rhinitis<br>• — Angioedema<br>• — Food allergy | IgE |
| II | Cytotoxic, antibody-dependent | Erythroblastosis fetalis<br>• Goodpasture's syndrome<br>• Autoimmune anemias, thrombocytopenias | IgG, IgM |
| III | Immune complex disease | Systemic lupus erythematosus<br>• Serum sickness<br>• Reactive arthritis<br>• Arthrus reaction | Aggregation of antigens IgG, IgM<br>Complement proteins |
| IV | Delayed-type hypersensitivity, cell-mediated, antibody-independent | Contact dermatitis<br>• Tuberculosis<br>• Chronic transplant rejection | T cells, monocytes, macrophages |

# FOOD ALLERGY

# FOOD ALLERGY: GENERAL CONCEPTS

- Prevalence has been increasing over time
  - Prevalence in Canada is ~7%
- Most common allergens in children: “the group of 8”


Figure 1: The “Big Eight” Allergens: Tree Nuts, Peanuts, Soy, Egg, Milk, Fish, Wheat and Shellfish.

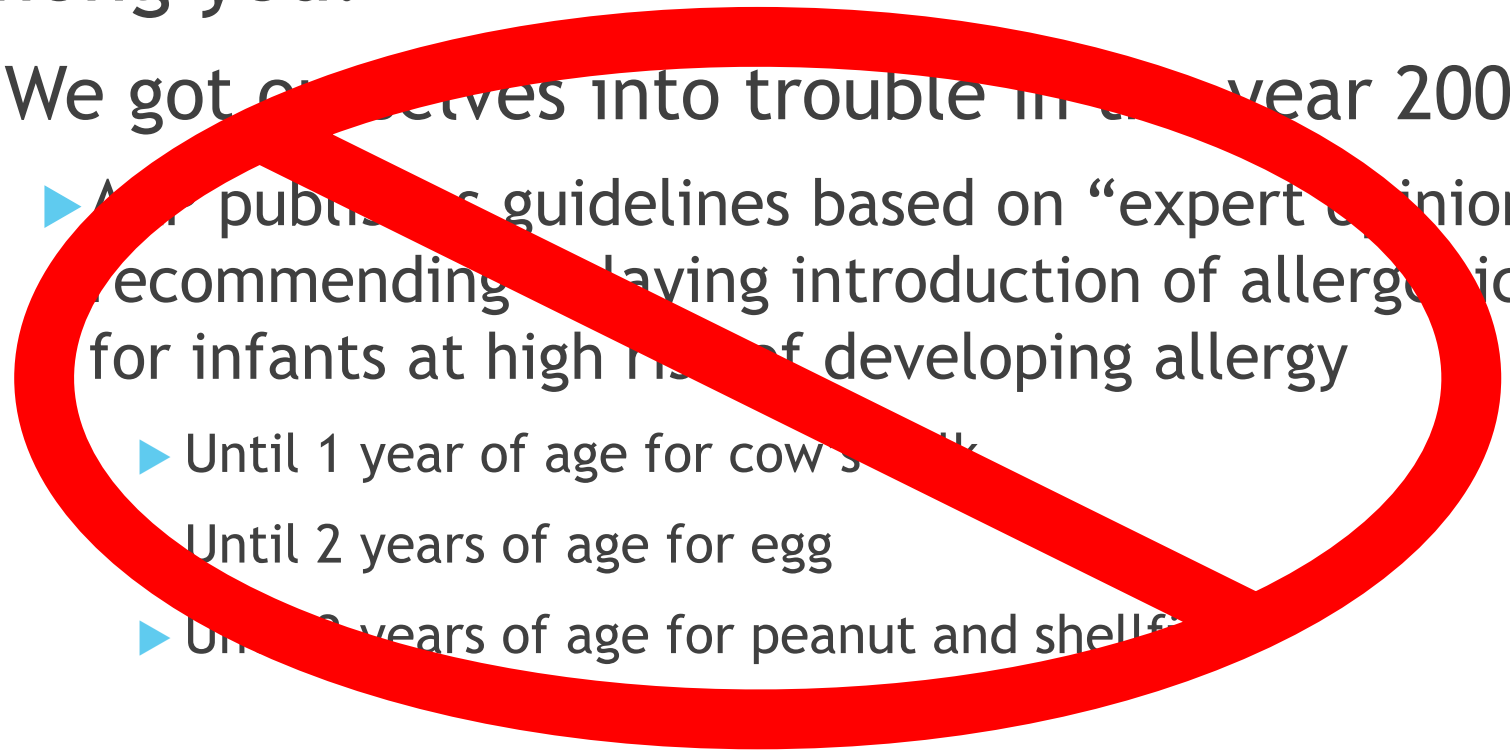
# FOOD ALLERGY: GENERAL CONCEPTS

- Manifestations
  - Various degrees of type I hypersensitivity reactions
- Treatment
  - Acute: management of anaphylaxis
  - Avoidance
  - Immunotherapy?
- Prognosis

# Introduction of allergenic solids to infants

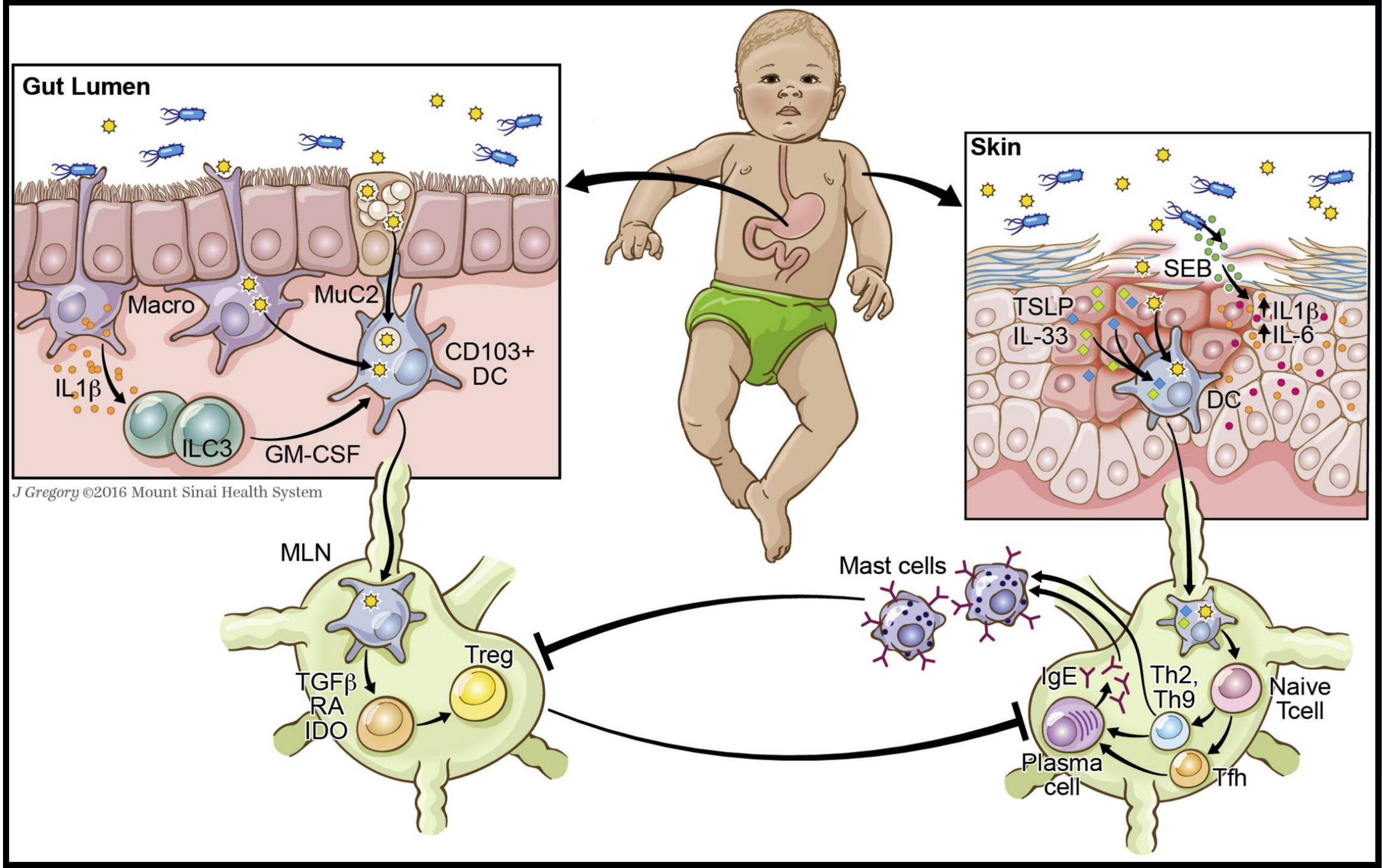
# Why is this a debate?

- Some background for those Generation Z among you:
  - We got ourselves into trouble in the year 2000
    - AAP published guidelines based on "expert opinion" recommending delaying introduction of allergenic foods for infants at high risk of developing allergy
      - Until 1 year of age for cow's milk
      - Until 2 years of age for egg
      - Until 3 years of age for peanut and shellfish



# What happened?

- Delaying introduction does not prevent food allergy
- In fact, it may actually promote allergy development
  - UK reported that prevalence of peanut allergy tripled during that period.
  - Similar study for wheat in the U.S.
  - Australia: delaying introduction of egg resulted in a 3.4-fold higher risk of developing egg allergy.
- Why?
  - “Dual-allergen-exposure hypothesis”


Gut Lumen
Macro
MuC2
CD103+
DC
IL1β
ILC3
GM-CSF
J Gregory ©2016 Mount Sinai Health System
Skin
SEB
TSLP
IL-33
IL1β
IL-6
DC
MLN
TGFβ
RA
IDO
Treg
Mast cells
IgE
Th2,
Th9
Naive
Tcell
Plasma
cell
Tfh

# What brought us back to senses?

- AAP 2008: No convincing evidence for delaying introduction
- Studies:
  - LEAP (Learning Early About Peanut) study
    - 640 high-risk infants in the U.K. randomized into early (4-11 months) vs. delayed (until 5 years of age) introduction of peanut. Overall relative risk reduction in peanut allergy of up to 80% with early introduction.
  - PETIT (Prevention of Egg allergy with Tiny amount InTake) study
    - 121 Japanese infants ingested heated egg powder daily, beginning a 6 months of age. This drastically lowered the rate of egg allergy when compared to those who avoided egg for over a year.

# What are the current recommendations?

- **Infants at high risk of allergic disease should be introduced to allergenic solids at around 6 months of age, but not before 4 months of age, and guided by the infant's developmental readiness for food**

- Let's play a game:
  - "OSCE station"
- 2 volunteers
  - Parent
  - Pediatrician

# Case scenario

- Mother is coming to you for a well-baby visit at 4 months of age.  She is breastfeeding exclusively. The baby has mild eczema. Mom has asthma that is well controlled, and dad gets “hay fever” in the Spring.

- Mother: Should I continue to breastfeed? And, when can I start my son on solid foods?
- Doctor:

- Mother: What about peanut or egg? When can I give him that?
- Doctor:
  - Commonly allergenic solids should be introduced between 4-6 months (and not earlier) in high-risk infants.

- Mother: Is my child a high-risk infant?
- Doctor:
  - Definition of high-risk infant: having a personal history of atopy (eczema, other food allergies like egg) and/or having a first-degree relative with atopy (e.g. eczema, food allergy, allergic rhinitis, asthma)

- Mother: Should I have started giving him peanut butter or egg since he was 3 months old to decrease the risk even more?
- Doctor:
  - EAT (Enquiring About Tolerance) study randomized infants to early (at 3 months) or standard (at 6 months) introduction of 6 commonly allergenic foods. No difference in the rate of food allergy was found.

- Mother: Since I am breastfeeding, should I cut from my diet peanut, egg, and all those foods you told me are commonly allergenic to prevent food allergy in my high-risk son?
- Doctor:

- Mother: I’ve heard that breastfeeding prevents allergies, is that true?
- Doctor:
  - The role of breastfeeding in preventing allergy is unclear. The studies on the matter have not been properly designed; however:
    - Some evidence that in infants at high risk of allergy, exclusive breastfeeding for at least the 4 months of life is associated with decreased prevalence of atopic dermatitis and cow’s milk allergy.
    - Another study showed that it is the total duration of breastfeeding what is more important for preventing allergies rather than exclusive breastfeeding.

- Mother: I feel like my milk supply is decreasing and I may not be able to continue breastfeeding soon. If I need to use formula, which one should I use? Can I use soy formula?
- Doctor:
  - Extensively hydrolyzed casein formula more likely to be effective in preventing **atopic dermatitis** in high-risk infants than partially hydrolyzed

- Mother: How should I feed peanut to my son? And how often should I give it to him?
- Doctor:

# Thank you Doctor, you are awesome!

# DRUG ALLERGY

# DRUG ALLERGY: GENERAL CONCEPTS

- Any kind of drug can lead to a hypersensitivity reaction.
- It may affect any organ or system
- Manifestations range widely in clinical severity
- Most common drugs causing allergy:
  - Antibiotics
  - General and local anesthesics
  - Radiocontrast media
  - NSAIDs
  - Monoclonal antibodies

# Case scenarios

- How are these cases different?
  - 11 year old girl with a history of a congenital heart disease that was repaired as infant but still has some residual defects. She was given the diagnosis of penicillin allergy after she had an itchy maculopapular rash at around 1 year of age following 3 doses of amoxicillin for an ear infection. The medication was stopped, the rash disappeared, and she has avoided penicillins since.

Vs.

  - 11 year old boy with cystic fibrosis with the diagnosis of Septra allergy. He had lip swelling and hives after 2 doses of Septra 6 months ago. He had received Septra before that episode without any issues.

# What are the recommendations when a drug allergy is identified?

- Stop the medication
- Avoid the medication in the future
- Use alternatives
- Wear a MedicAlert bracelet.

# What to do next?

- The girl has required a few dental procedures lately and has been getting IM Ceftriaxone for prophylaxis every time. She needs more dental work and would like to avoid being poked every time. Can she take amoxicillin instead?

Vs.

- The boy is currently in the unit for an exacerbation of his CF due to *Stenotrophomona maltophila*. The sensitivities report is back and is showing resistance to all antibiotics except Septra. Could we give Septra?

# What is the difference?

- Drug challenge protocol

Vs.

- Drug desensitization protocol

# Drug desensitization

- Process by which the patient's immune response to a drug is modified to generate a **temporary** state of tolerance.
- Increasing doses of the drug with a pre-determined time schedule.
- Once tolerance to the required dose of the drug is reached, such molecule will be accepted by the patient's immune system for the whole course of therapy

# Drug desensitization

- **Indications:**
  - When no alternative drug is available
  - When the drug is significantly more effective than the other possible alternatives
  - Classically, only reserved for IgE-mediated allergies.

- **Contraindications:**
  - When the reported drug reaction was a severe, life-threatening immune-toxic reaction: SJS/TEN or DRESS syndromes.
  - Type II or type III hypersensitivity reactions
    - However, there have been successful examples of desensitization in these type of cases

# Most common uses for desensitization protocols

- Antibiotics: efficacy rates of above 80%
- Anticonvulsants
- Chemotherapeutic agents
- Insulins
- Monoclonal antibodies
- Vaccines

# How does it work?

- Exact mechanisms are not well understood but the idea is that mast cells, and possibly basophils, become hypo-responsive to a drug allergen
- 3 hypothesis on how desensitization could impair mast cell activation
  - Depletion of activating signal transduction components (eg. Syk kinase)
  - Depletion of mediators (eg. Prostaglandins, leukotrienes)
  - Internalization of FcεRI by progressively cross-linking this receptor at a low antigen concentration

# How is it done?

1. Patient should be in stable clinical condition
2. Discontinue beta-blockers, if possible.
3. Calculate one total dose of what the patient would need if he wasn't allergic.
4. Decide on number of steps for desensitization
   - Factors for the decision: age, type of medication, severity of previous reaction
5. Decide if pre-medication will be given
   1. Regimens vary from center to center and it is still debatable
   2. Aim to prevent a hypersensitivity reaction occurring during desensitization
   3. Usually a combination of antihistamines and corticosteroids +/- acetaminophen +/- leukotriene antagonist

# How is it done?

6. Decide where to perform it. Unit vs. ICU
7. Oral vs. parenteral?
   - Same route that would be used for therapeutic purposes
   - If drug can be given both orally or parenterally, then the oral route is safer, easier, and less expensive.
8. Order your dilutions based on the number of steps
   - Severe anaphylaxis: initial dose should be between 1/1,000,000 and 1/10,000
   - When possible, the first dose is calculated based on SPT results.
9. For how long?
   - Time intervals between two steps ranges from 15 min-120 minutes
   - Full duration: from 2 hours (in the very rapid protocols) to a few weeks.

# How is it done?

10. What happens once you have reached the total dose?
    - You give the next total dose at the usual interval for the drug
    - But, no more than 12 hours can pass between doses

11. What happens once you have finished the course of treatment?
    - **Patient should still be considered allergic.**
    - **Next time the drug is needed, desensitization protocol would have to be implemented again.**

**Table 2**. Oral Penicillin desensitization protocol. The time between doses is every 15-20 minutes (39)

| Step | Penicillin mg/ml | Amount (ml) | Dose (mg) | Cumulative dose |
|---|---|---|---|---|
| 1 | 0.5 | 0.1 | 0.05 | 0.05 |
| 2 | 0.5 | 0.2 | 0.1 | 0.15 |
| 3 | 0.5 | 0.4 | 0.2 | 0.35 |
| 4 | 0.5 | 0.8 | 0.4 | 0.75 |
| 5 | 0.5 | 1.6 | 0.8 | 1.55 |
| 6 | 0.5 | 3.2 | 1.6 | 3.15 |
| 7 | 0.5 | 6.4 | 3.2 | 6.35 |
| 8 | 5.0 | 1.2 | 6.0 | 12.35 |
| 9 | 5.0 | 2.4 | 12.0 | 24.35 |
| 10 | 5.0 | 5.0 | 25.0 | 49.35 |
| 11 | 50.0 | 1.0 | 50.0 | 100.0 |
| 12 | 50.0 | 2.0 | 100.0 | 200.0 |
| 13 | 50.0 | 4.0 | 200.0 | 400.0 |
| 14 | 50.0 | 8.0 | 400.0 | 800.0 |

**Table 3**. Desensitization protocol to tetanus vaccine; injections should be performed every 20 minutes (40)

| Dose number | Volume (ml) | Dilution | Route |
|---|---|---|---|
| 1 | 0.2 | 1:1000 | Intradermal |
| 2 | 0.2 | 1:100 | Intradermal |
| 3 | 0.2 | 1:100 | Intradermal |
| 4 | 0.2 | 1:10 | Subcutaneous |
| 5 | 0.10 | 1:10 | Subcutaneous |
| 6 | 0.05 | Non-diluted | Subcutaneous |
| 7 | 0.10 | Non-diluted | Subcutaneous |
| 8 | 0.15 | Non-diluted | Subcutaneous |
| 9 | 0.20 | Non-diluted | Subcutaneous |

# Exercise

- Build the desensitization protocol for the CF patient with allergy to Septra

**Drug Desentization Protocol**

| | | | |
|---|---|---|---|
| Patient | Name | **PATIENT WITH CF** | |
| | Weight | 38 Kg. | |
| Drug | Name | **TRIMETHOPRIM/SULFAMETHOZAZOLE** | |
| | Supplied Concentration: | Sulfamethozazole 80 mg/ml | |
| | | Trimethoprim 16 mg/ml | |
| | Reaction | Hives and lip swelling | |
| | Treatment dose | 20 mg/Kg/day div q12h | |
| | | 380 milligrams per dose | |
| | | (based on Trimethoprim) | |

**General guidelines**

| |
|---|
| Establish baseline monitoring in appropriate medical setting |
| Needs 1:1 nurse/MD observation for the whole procedure |
| Needs measurement of vital signs incl. BP at least every 15 minutes after drug adm. |
| Needs clinical evalutation for rash, hives and auscultation of lungs for wheezing at least every 15 minutes after drug administration |
| Anaphylaxis unit with medications ready for injection at bedside |
| Oxygen with mask at bedside |

**Anaphylaxis kit**

| | | |
|---|---|---|
| Benadryl (Dyphenhydramine) 1-2 mg/kg/iv | 40 | mg |
| Solu-Medrol (Methylprednisolone) 2mg/kg iv | 80 | mg |
| Epinephrine 0.01mg/kg (1:1000) sc. | 0.4 | mg |
| Ventolin (Salbutamol) 0.03ml/kg in 3 ml NS (inhale) | 1 | ml |

Desensitisation will start with a dose of 1/1,000,000 of the anticipated final dose

**Before you start...**

Establish secure IV Access
Establish monitoring incl. saturation
Prepare anaphylaxis kit and oxygen access
Give next dose every **15** minutes

**Patient needs to be monitored for changes in HR, RR, BP, O2 Sat and visually monitored for rash or flushing**

| Time | Dose # | Bag conc. mg/ml | take _ ml | Rate of infusion (min) |
|---|---|---|---|---|
| | #1 | **0.02** | **0.1 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #2 | **0.02** | **0.2 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #3 | **0.02** | **0.4 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #4 | **0.02** | **0.8 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #5 | **0.02** | **1.6 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #6 | **0.02** | **3.2 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #7 | **0.2** | **0.5 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #8 | **0.2** | **1.0 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #9 | **0.2** | **2.0 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #10 | **0.2** | **4.0 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #11 | **2** | **0.5 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #12 | **2** | **1.0 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #13 | **2** | **2.0 ml** | **push** |
| | after 15 min | | vital signs incl bp | |
| | #14 | **2** | **4.0 ml** | **push over 3-5min** |
| | after 15 min | | vital signs incl bp | |
| | #15 | **20** | **0.8 ml** | **push over 3-5min** |
| | after 15 min | | vital signs incl bp | |
| | #16 | **20** | **1.5ml** | **push over 3-5min** |
| | after 15 min | | vital signs incl bp | |
| | #17 | **20** | **3ml** | **push over 3-5min** |
| | after 15 min | | vital signs incl bp | |
| | #18 | **20** | **5ml** | **push over 10min** |
| | after 15 min | | vital signs incl bp | |

**Instructions for further use of drug**

Next dose is the regular dose according to weight.
If the drug was not taken for >24 hours the desentization effect is lost.
The patient would need another desentization to continue the drug.
The drug may be further adjusted but should not be stopped and reintroduced again without a desentization

# ANGIOEDEMA

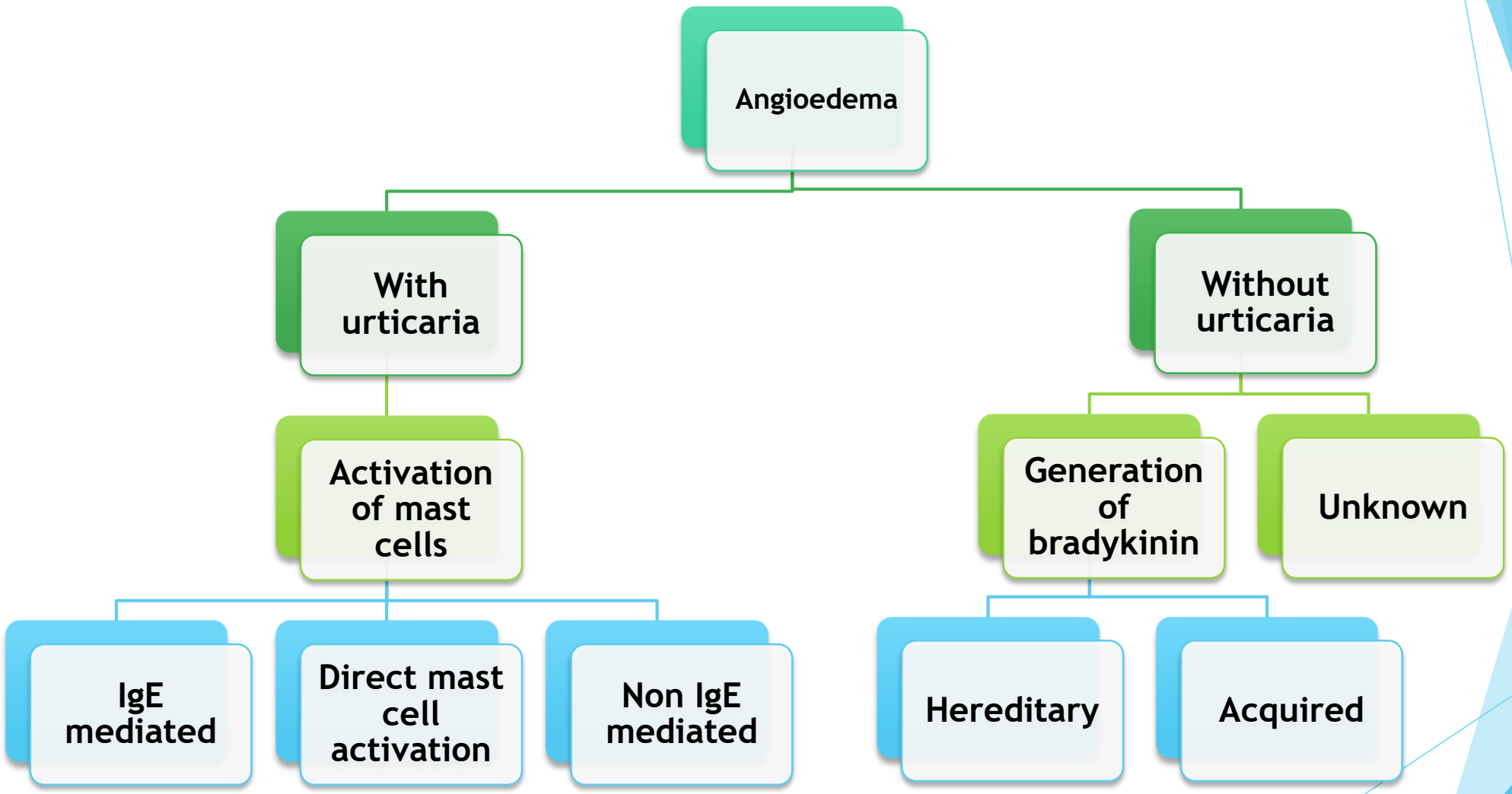
# What is angioedema?

- Swelling
- Self-limited
- Localized
- Subcutaneous or submucosal
- Caused by the extravasation of fluid into interstitial tissues

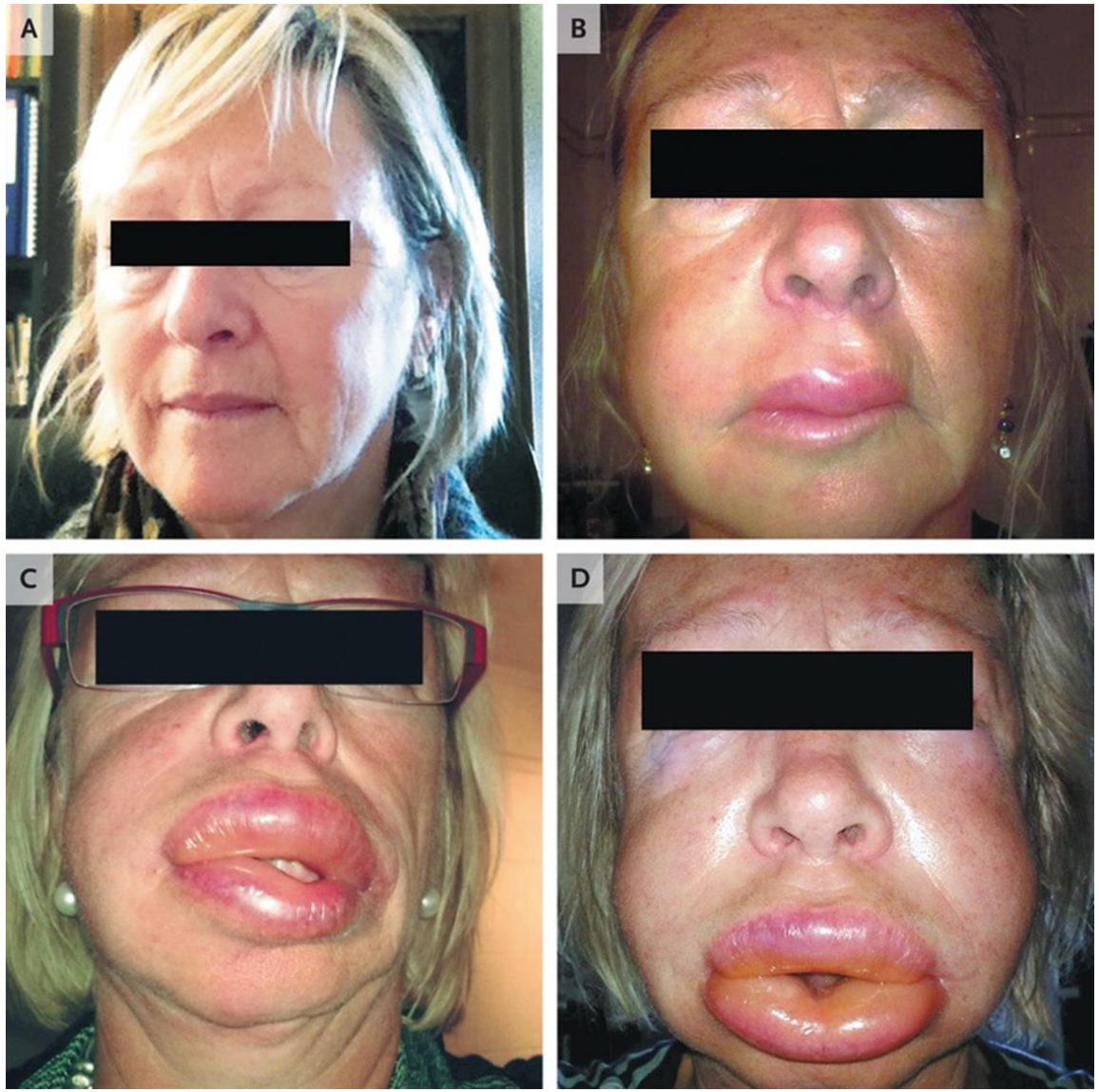
# How are these cases different from each-other?

- 2 year old boy with an URTI who was given acetaminophen for fever starts having episodes of hives in his torso and lip and eyelid swelling that last 3-4 days.
- 13 year old boy followed by Pediatrician for unexplained episodes of acute abdominal pain that self resolves, thought to be “functional”. He is now having painful episodes of swelling of his face and hands.
- 17 year old girl on OCP starts having angioedema episodes. Her mother suffers from it too and she also started having these episodes at around that age.
- 17 year old boy with Hodgkin lymphoma starts developing angioedema episodes of lips and hands.

# Classification by mechanism



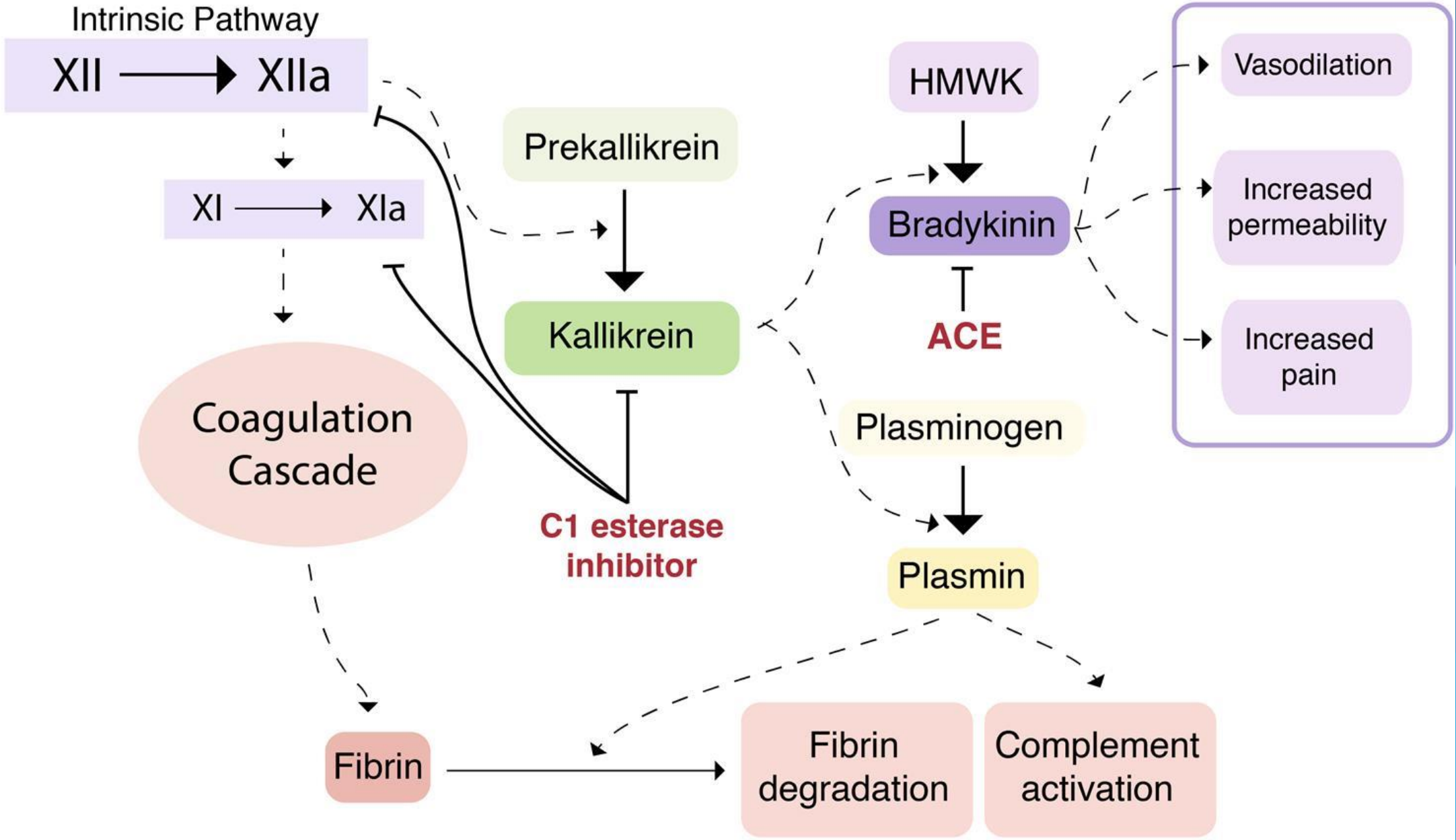
# HEREDITARY ANGIOEDEMA



# Hereditary angioedema

- Recurrent episodes of angioedema **without** urticaria or pruritus
- 1:50,000-150,000
- M=F
- All ethnic groups
- Mortality prior to availability of effective therapy: 30% (asphyxiation from laryngeal swelling)

# Kallikrein-Bradykinin Pathway



# Hereditary angioedema

- Age of onset: variable
  - Rare reports: perinatal period
  - 40% before age 5
    - Repeated attacks are uncommon
  - 75% by age 15
    - Attack frequency increases after puberty
  - Diagnosis is usually made until 20s or 30s

# Hereditary Angioedema

- Clinical features
  - Onset in minutes to hours
  - Resolution in hours to days
  - Asymmetric distribution
  - Non pruritic but it can be painful, burning sensation
  - Does not involve gravitationally-dependent areas (like edema from cardiac or renal dysfunctions)
    - Non-pitting

# Hereditary Angioedema

- Involves areas with loose connective tissue
  - Face
  - Lips
  - Mouth: tongue, uvula, larynx (1%)
  - Extremities
  - Genitalia
  - Bowel: colicky abdominal pain, with or without vomiting/diarrhea

# Angioedema attacks

- Skin, GI tract, upper airway
  - Usually one site at the time but it can be combined
  - 50% experience all three at some point in their lives
- Always self limited
  - Lasting 2-5 days
  - Usually builds up over 24hrs and subsides in 48-72h
- Frequency of attacks
  - From weekly to 1-2 episodes per year

# Angioedema attacks

- Severity of attacks
  - Some patients are asymptomatic (family screening)
  - Severity differs markedly among affected members within families, despite same mutation
  - Severity may vary significantly in the same patient over time
  - Factors determining disease severity are unknown

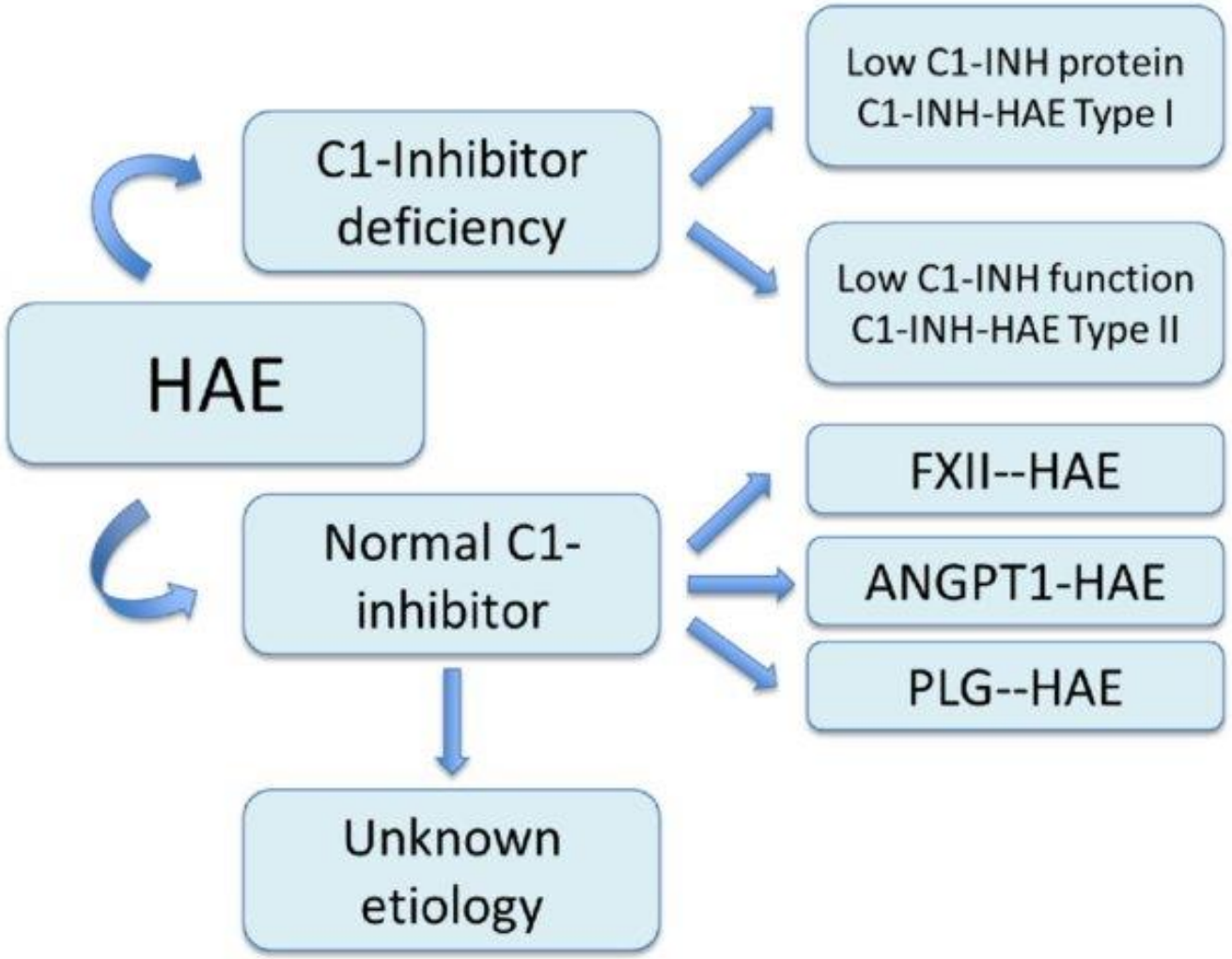
# Attack triggers

- Most common: stress (mental/physical) and dental procedures
- Physical
  - Mild trauma
  - Intubation
  - Bicycle riding
  - Sexual intercourse
  - Cold exposure
  - Menstruation
  - Pregnancy
  - *H. pylori*

# Attack triggers

- Medications
  - Estrogen-containing medications
  - NSAIDs
  - ACE inhibitors
  - ARB

# TYPES OF HAE




FXII: Factor 12
ANGPT1: Angiopoietin-1
PLG: Plasminogen

# TYPES OF HAE

**Table 1 Laboratory findings in hereditary angioedema [9–11]**

| Function | C4 | C1-INH antigen | C1-INH |
|---|---|---|---|
| HAE-1 | ↓ | ↓ | ↓ |
| HAE-2 | ↓ | normal or ↑ | ↓ |
| HAE-nC1INH variants<br>coagulation factor XII<br>angiopoietin-1<br>plasminogen<br>unknown | normal | normal | normal |

Betschel *et al. Allergy Asthma Clin Immunol* (2019) 15:72

# Laboratory evaluation of angioedema **without** urticaria

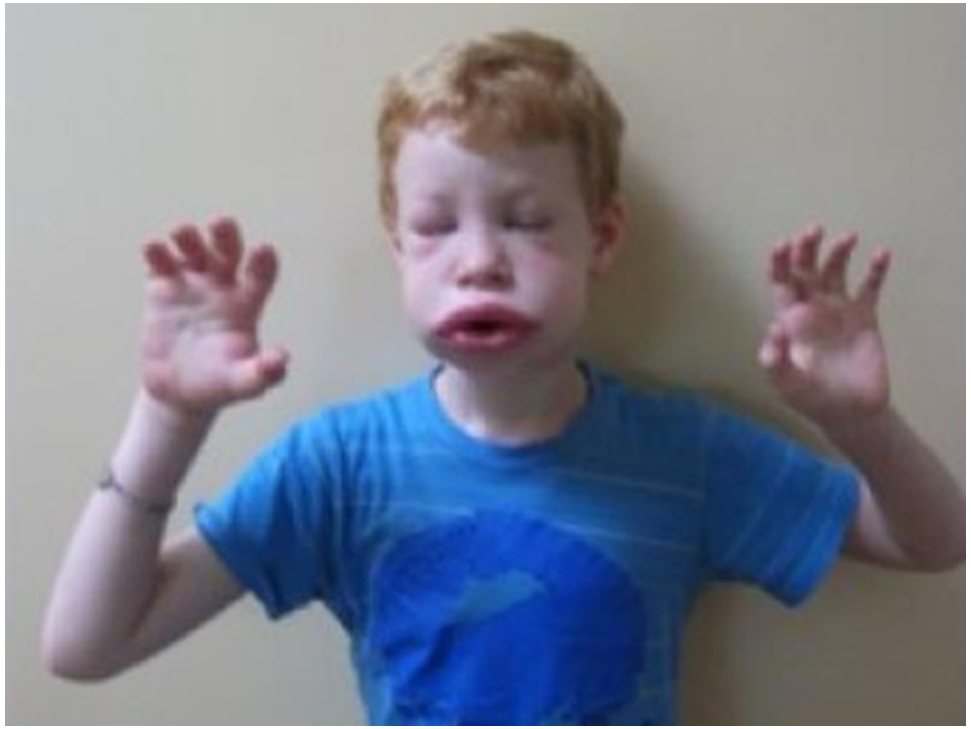
- Initial
  - Perhaps: CBC + diff, basic chemistry with liver function tests, CRP, ESR
  - **C4**
  - If abdominal pain: **ultrasound** (or CT)
- If C4 is low and/or bowel swelling on US, family history: think hereditary angioedema
  - C1 esterase inhibitor LEVEL + FUNCTION

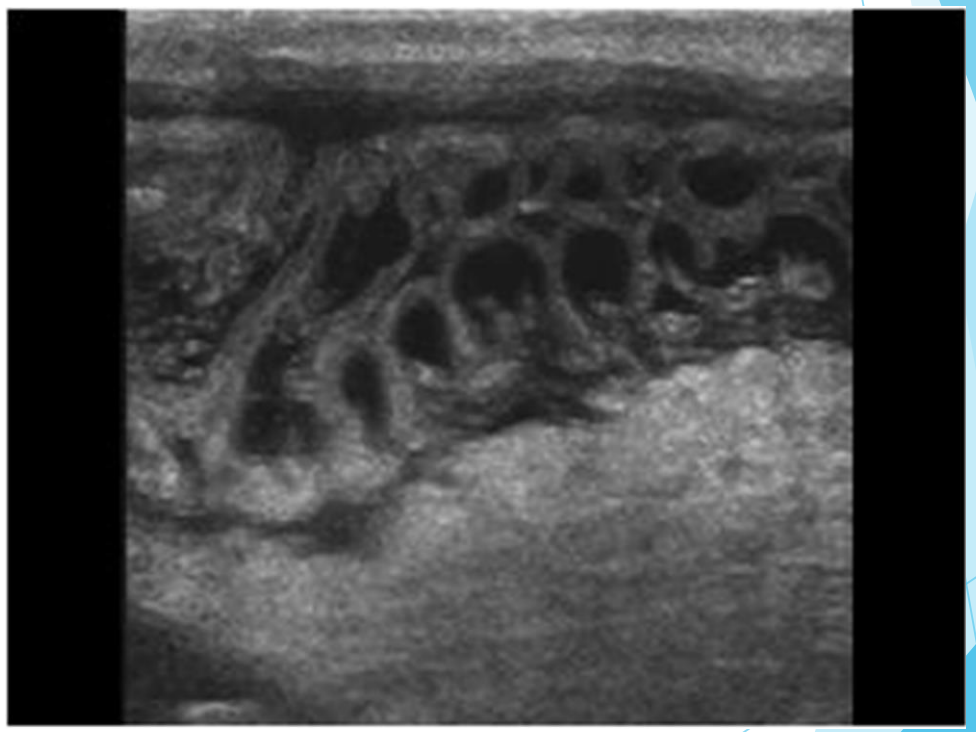
# Back to the cases

- 2 year old boy with an URTI who was given acetaminophen for fever starts having episodes of hives in his torso and lip and eyelid swelling that last 3-4 days.

**VIRAL INDUCED URTICARIA/ANGIOEDEMA**

- 13 year old boy followed by Pediatrician for unexplained episodes of acute abdominal pain that self resolves, thought to be “functional”. He is now having painful episodes of swelling of his face and hands.





## HEREDITARY ANGIOEDEMA
## likely type I or II

- 17 year old girl on OCP starts having angioedema episodes. Her mother suffers from it too and she also started having these episodes at around that age.

**HEREDITARY ANGIOEDEMA with normal C1-INH likely FXII mutation**

- 17 year old boy with Hodgkin lymphoma starts developing angioedema episodes of lips and hands

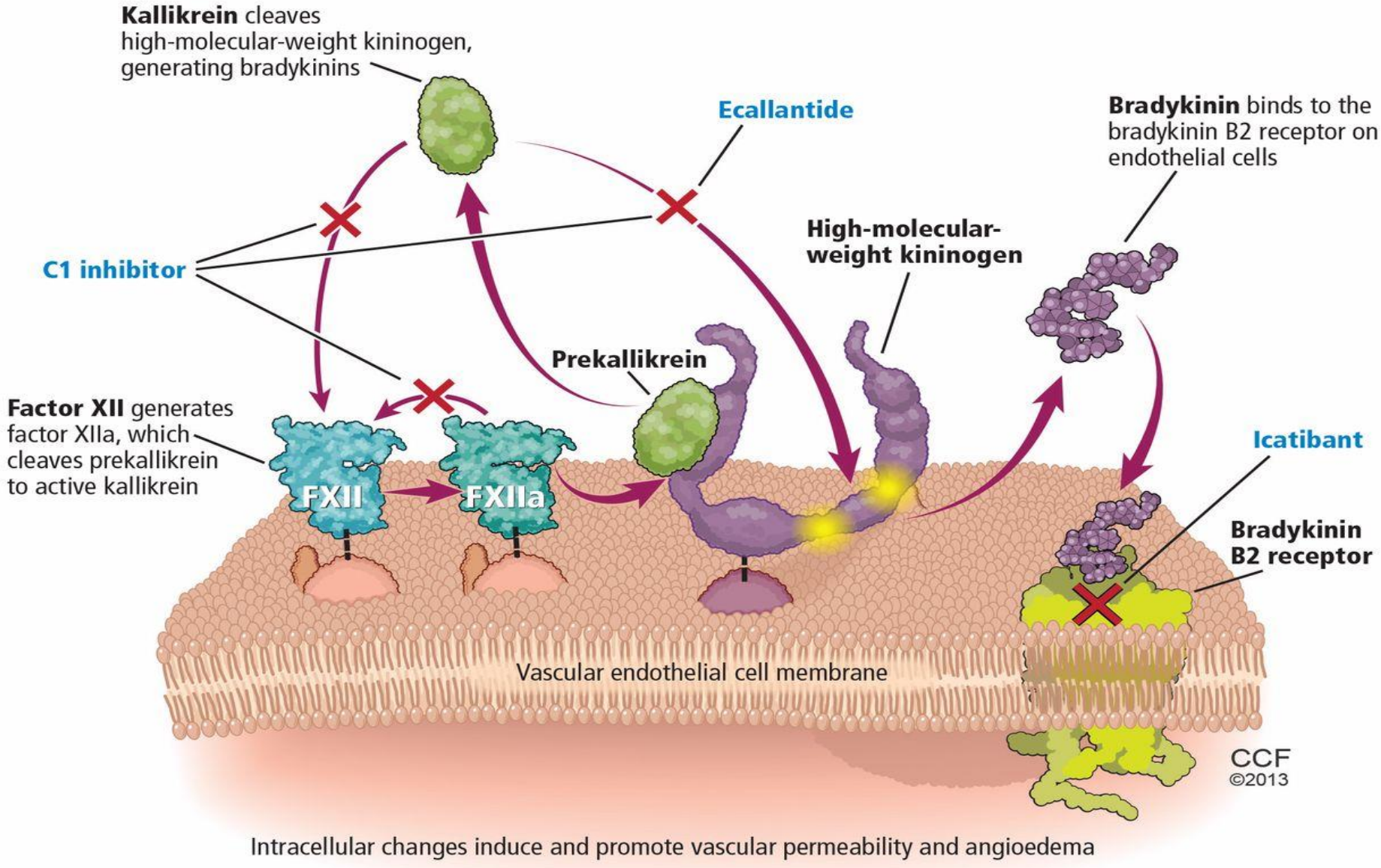
## ACQUIRED ANGIOEDEMA (type 2)

# Hereditary Angioedema: prognosis

- Variable
- Once attacks have begun, they generally continue throughout patient's life
- Quality of life greatly affected if untreated
- Frequency and severity of attacks can be dramatically reduced with therapy

# Hereditary angioedema and its treatment

Hereditary angioedema, a life-threatening condition caused by a deficiency of C1 inhibitor, results from excess bradykinin. New medications, including replacement of C1 inhibitor, can counteract it.




Intracellular changes induce and promote vascular permeability and angioedema

*Cleveland Clinic Journal of Medicine*. 2013 May;80(5):297-308

Medical Illustrator: David Schumick

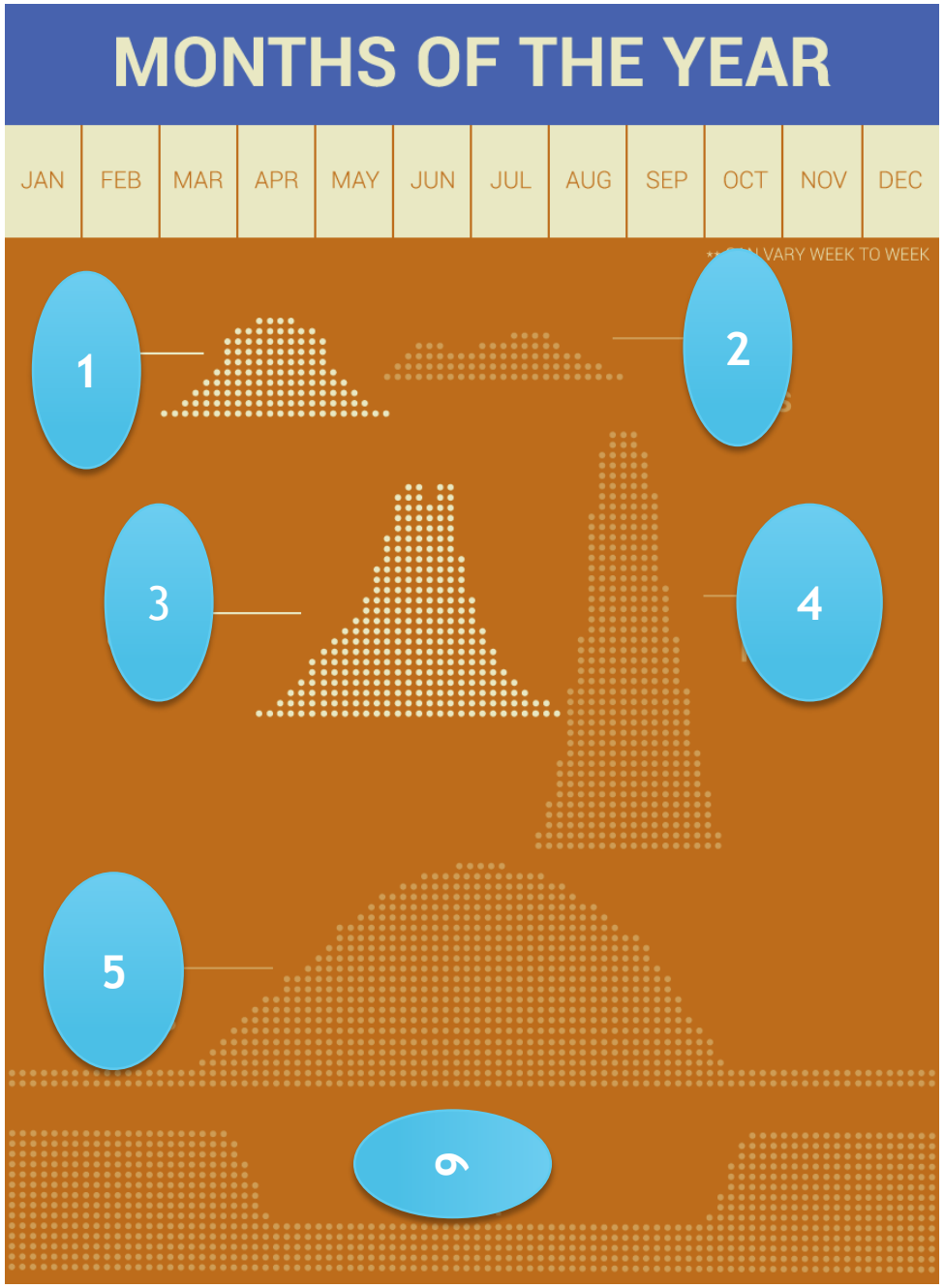
**Table 3 Therapies for HAE supported by high level evidence**

| HAE-specific treatment | Product name and company | Mechanism of action | Approved indications | Dose and route of administration | County licensed and age indications |
|---|---|---|---|---|---|
| pdC1-INH | Berinert®[a] (CSL) | Replaces C1-INH | Acute treatment | 20 U/kg Intravenous | Australia, Canada, EU, USA (adult and pediatric) |
| | | | Pre-procedural | Adults: 1000 U<br>Pediatrics: 15 to 30 U/kg body weight | EU (adult and pediatric) |
| | Cinryze® (Shire—now part of Takeda) | Replaces C1-INH | Acute treatment | ≥ 12 years: 1000 U Intravenous<br>2–11 years: 1000 U (> 25 kg body weight)<br>500 U (< 25 kg body weight) | Australia (≥ 12 years)<br>EU (≥ 2 years) |
| | | | Pre-procedural | ≥ 12 years: 1000 U Intravenous<br>2–11 years: 1000 U (> 25 kg body weight)<br>500 U (< 25 kg body weight) | Australia (≥ 12 years)<br>EU (≥ 2 years) |
| | | | Long-term prophylaxis | 1000 U Intravenous<br>q 3–4 days (6–11 years 500 U q 3–4 days)[b] | Australia, Canada (≥ 12 years)<br>EU, USA (≥ 6 years) |
| | Haegarda® (CSL) | Replaces C1-INH | Long-term prophylaxis | 60 U/kg body weight twice weekly (every 3–4 days) | Australia[c], Canada, EU[d], USA (≥ 12 years) |
| rhC1-INH | Ruconest® (Ruconest) | Replaces C1-INH | Acute treatment | 50 U/kg Intravenous (< 84 kg);<br>4200 U Intravenous (≥ 84 kg) | EU (adults), USA (adults and adolescents) |
| Ecallantide | Kalbitor® (Shire—now part of Takeda) | Selective, reversible inhibitor of plasma kallikrein | Acute treatment | 30 mg (3 × 10 mg/1 ml) subcutaneous injections | USA (≥ 12 years) |
| Icatibant | Firazyr® (Shire—now part of Takeda) | Synthetic selective and specific antagonist of bradykinin 2 receptor | Acute treatment | 30 mg subcutaneous injection; dose-adjusted for adolescents < 65 kg and children ≥ 2 years[e] | USA (≥ 18 years) Australia, Canada, EU (≥ 2 years) |
| Lanadelumab | Takhzyro® (Shire—now part of Takeda) | Fully human monoclonal antibody that binds plasma kallikrein and inhibits its proteolytic activity | Long-term prophylaxis | 300 mg subcutaneous injection every 2 weeks<br>a dosing interval of 300 mg every 4 weeks may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months | Australia, Canada, EU, USA (≥ 12 years) |


The Evening Herald
EXTRA!

# RCPSC objectives of training in Pediatrics

- 2.1.4.10.2 Allergic Rhinitis
- 2.1.4.10.6 Insect stings and bites
- 2.1.4.10.7 Serum sickness




# Allergic rhinitis

Match with the picture

- Ragweed
- Grass
- Trees
- Dust mites
- Weeds
- Moulds

# Allergic rhinitis

- **Pharmacologic Therapy**
  - **nasal corticosteroids**
  - **oral antihistamines - second generation**
  - **nasal antihistamines**
  - **oral antileukotrienes**
  - **oral decongestants**

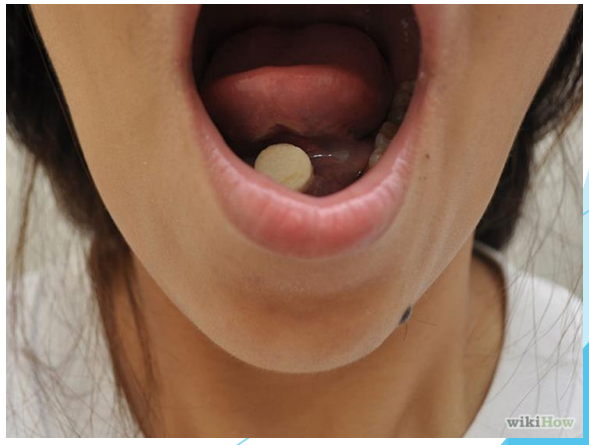
# Allergen immunotherapy

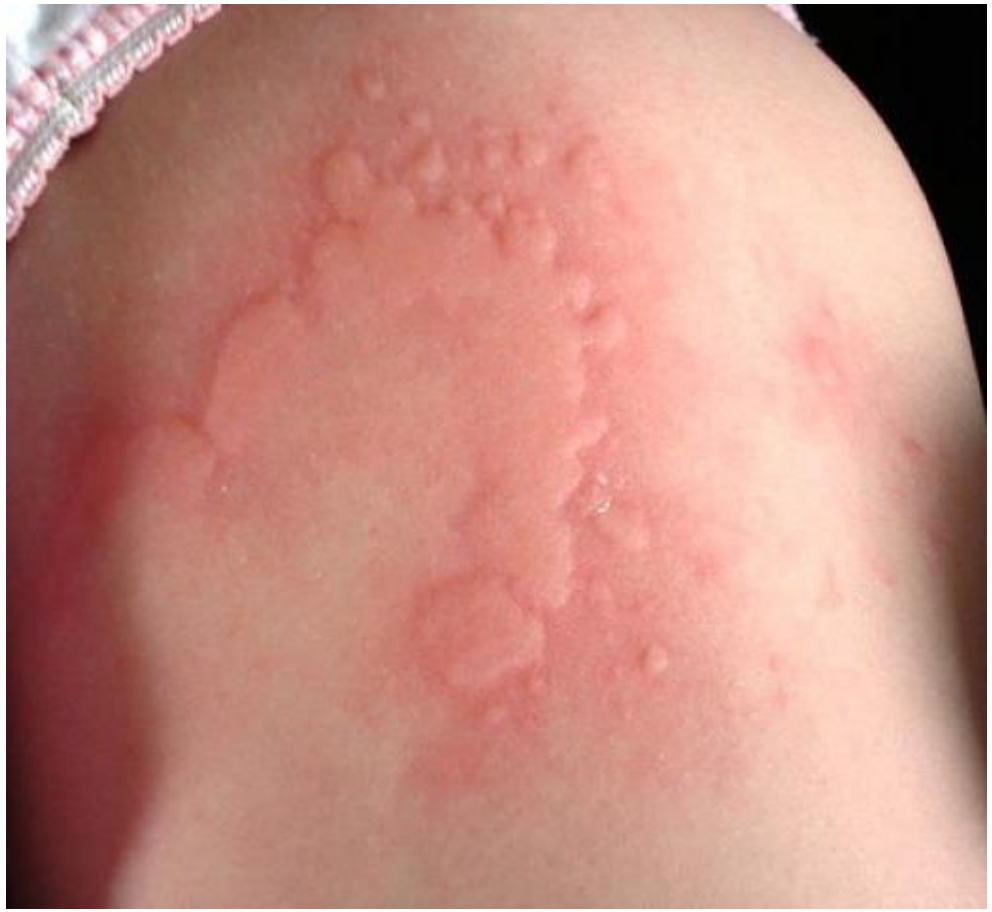
- **Indications for SCIT:**

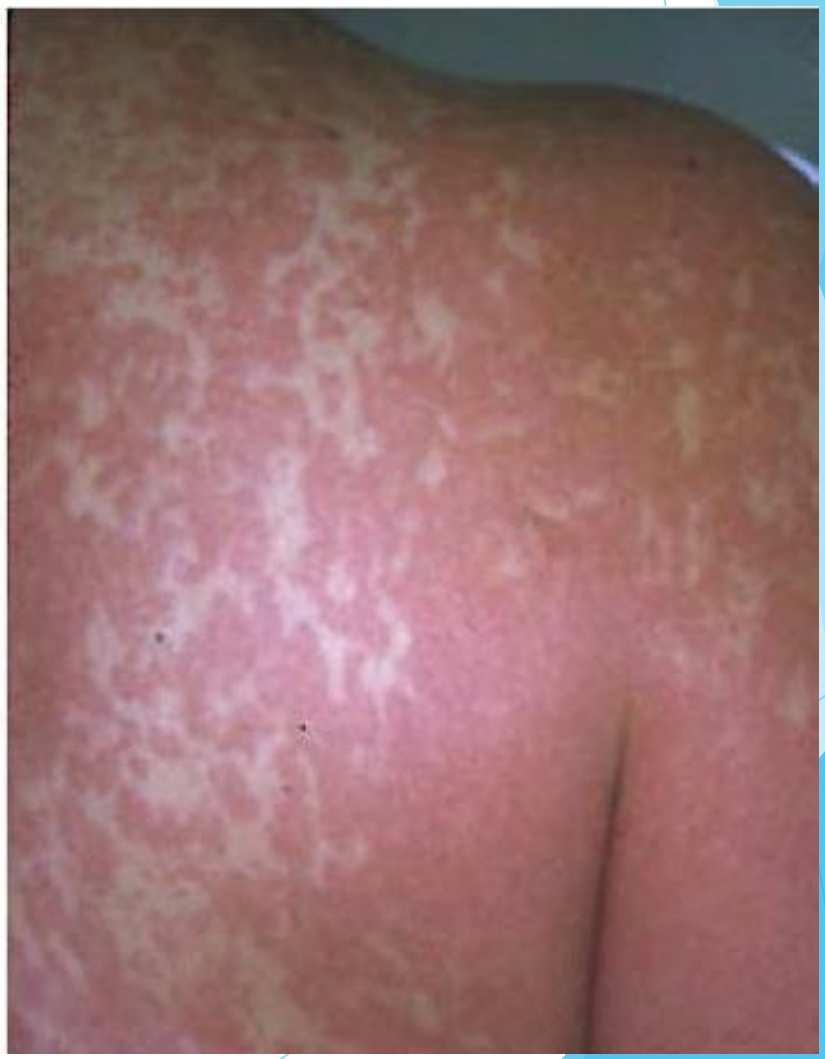
1. **Allergic rhinitis, with or w/o allergic conjunctivitis**
2. **Allergic asthma**
3. **Atopic dermatitis if sensitized to inhalant allergens**
4. **Anaphylaxis to venom (stinging insects)**

- **Indications for SLIT:**

1. **Allergic rhinitis: grass, ragweed, dust mites**







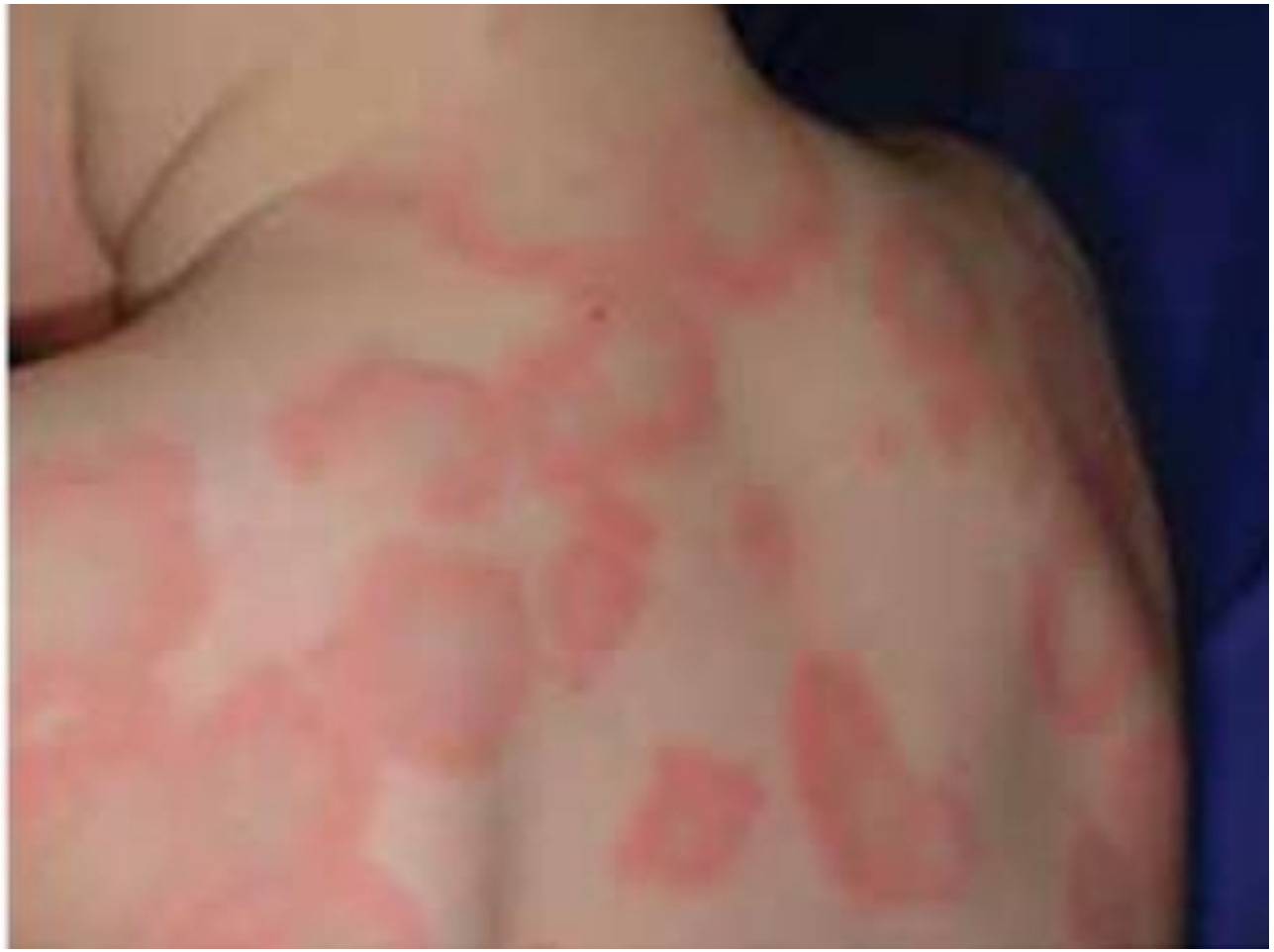
# Name the stinger…



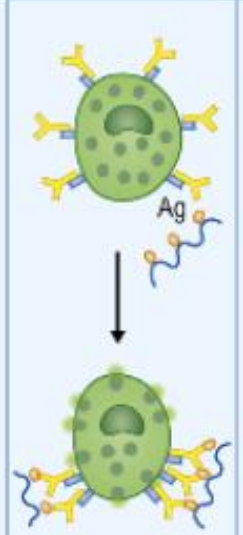
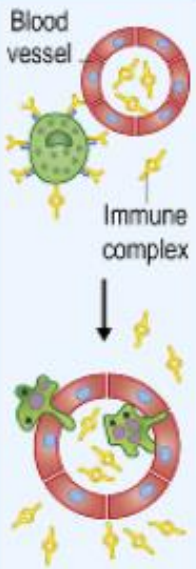
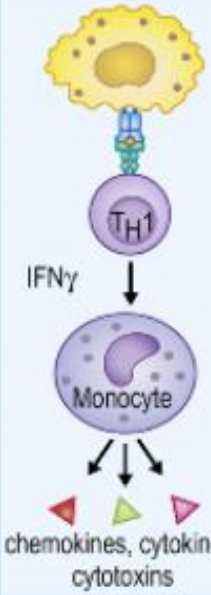
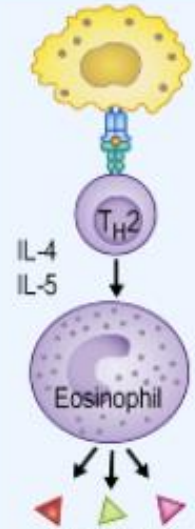
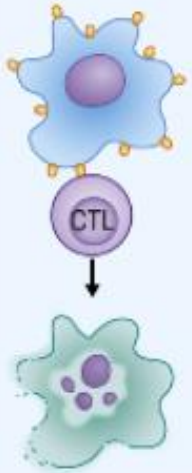
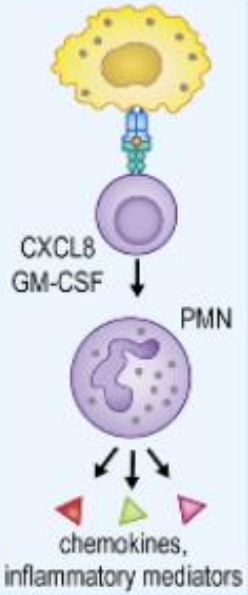
# Venom allergy

- Diagnosis:
  - Skin prick testing
  - Specific IgE
- Treatment:
  - SCIT

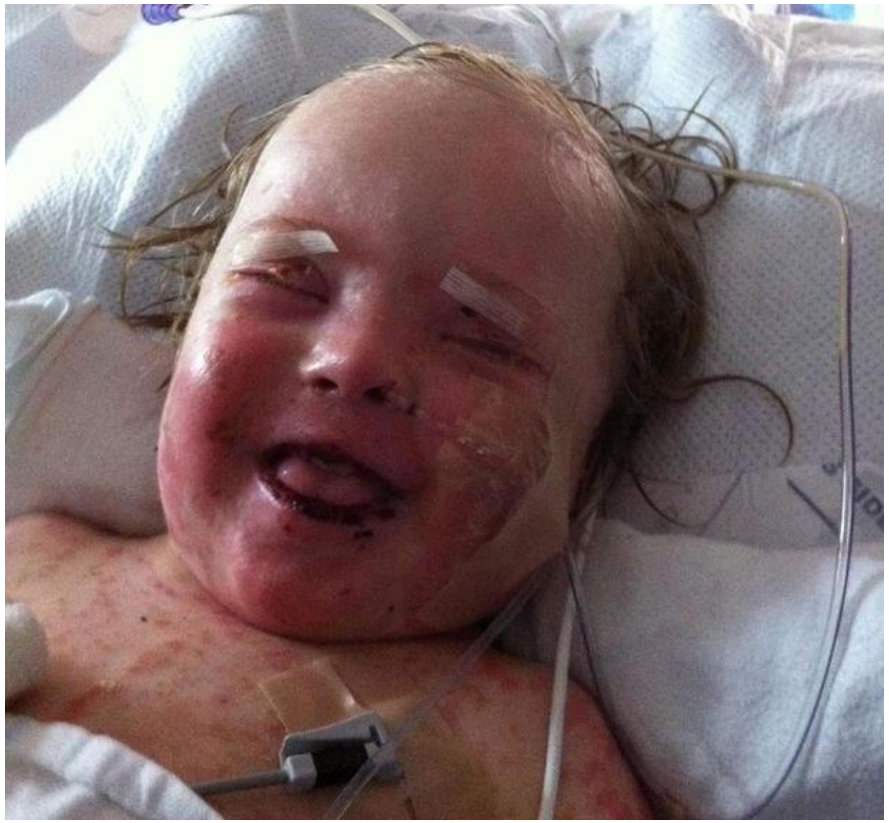
# Diagnosis for 5 points



- Fever
- Arthralgias
- Lymphadenopathy
- Splenomegaly
- Glomerulonephritis
- … around 10 days after penicillin, sulfa...

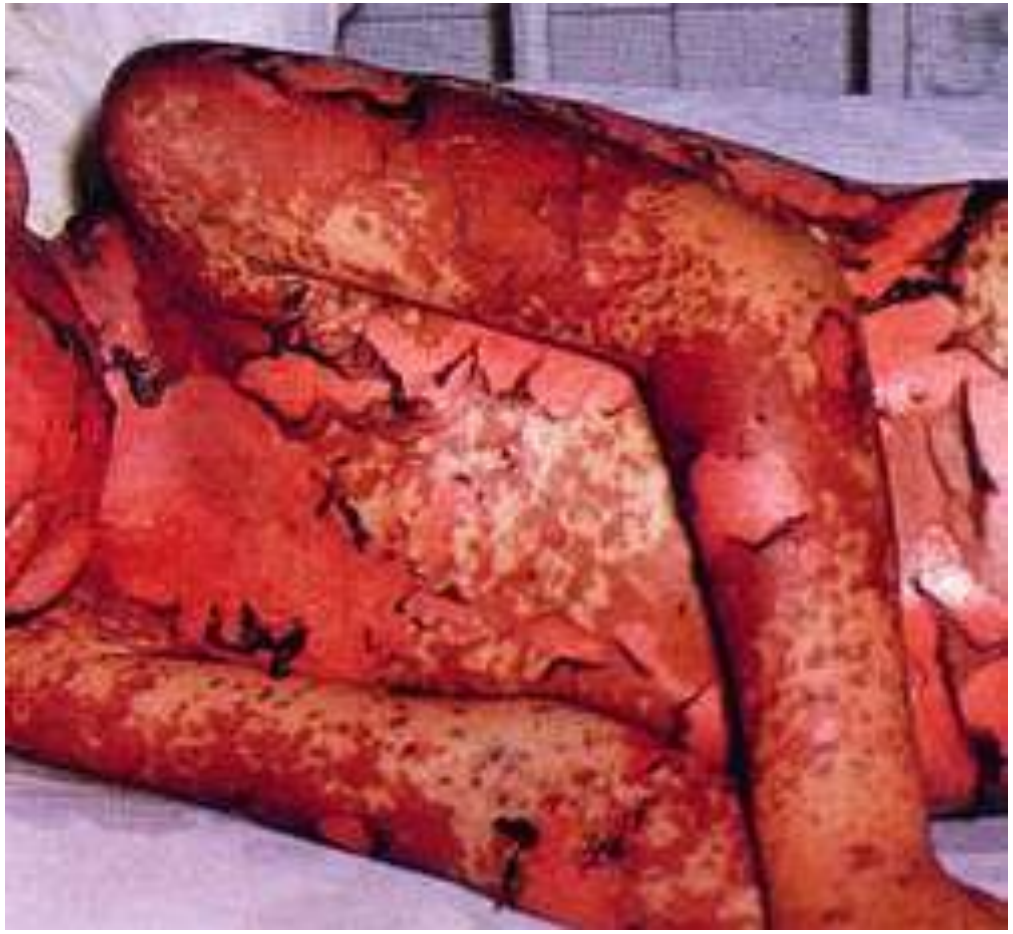
| | Type I | Type II | Type III | Type IVa | Type IVb | Type IVc | Type IVd |
|---|---|---|---|---|---|---|---|
| **Immune reactant** | IgE | IgG | IgG | IFNγ, TNFα ($T_H1$ cells) | IL-5, IL-4/IL-13 ($T_H2$ cells) | Perforin/ GranzymeB (CTL) | CXCL-8. GM-CSF (IL-17) (T-cells) |
| **Antigen** | Soluble antigen | Cell or matrix-associated antigen | Soluble antigen | Antigen presented by cells or direct T-cell stimulation | Antigen presented by cells or direct T-cell stimulation | Cell-associated antigen or direct T-cell stimulation | Soluble antigen presented by cells or direct T-cell stimulation |
| **Effector** | Mast-cell activation | $FcR^+$ cells (phagocytes, NK cells) | $FcR^+$ cells Complement | Macrophage activation | Eosinophils | T cells | Neutrophils |
| |   |   |   |   |   |   |   |
| **Example of hypersensitivity reaction** | Anaphylaxis, allergic rhinitis, asthma (with IVb) | Hemolytic anaemia, thrombocytopenia | Serum sickness, Arthus reaction | Tuberculin reaction contact dermatitis (with IVc) | Maculopapular exanthema with eosinophilia, chronic asthma, allergic rhinitis | Contact dermatitis, maculopapular and bullous exanthem, hepatitis | AGEP Behçet disease, psoriasis |

# Diagnosis for 5 points



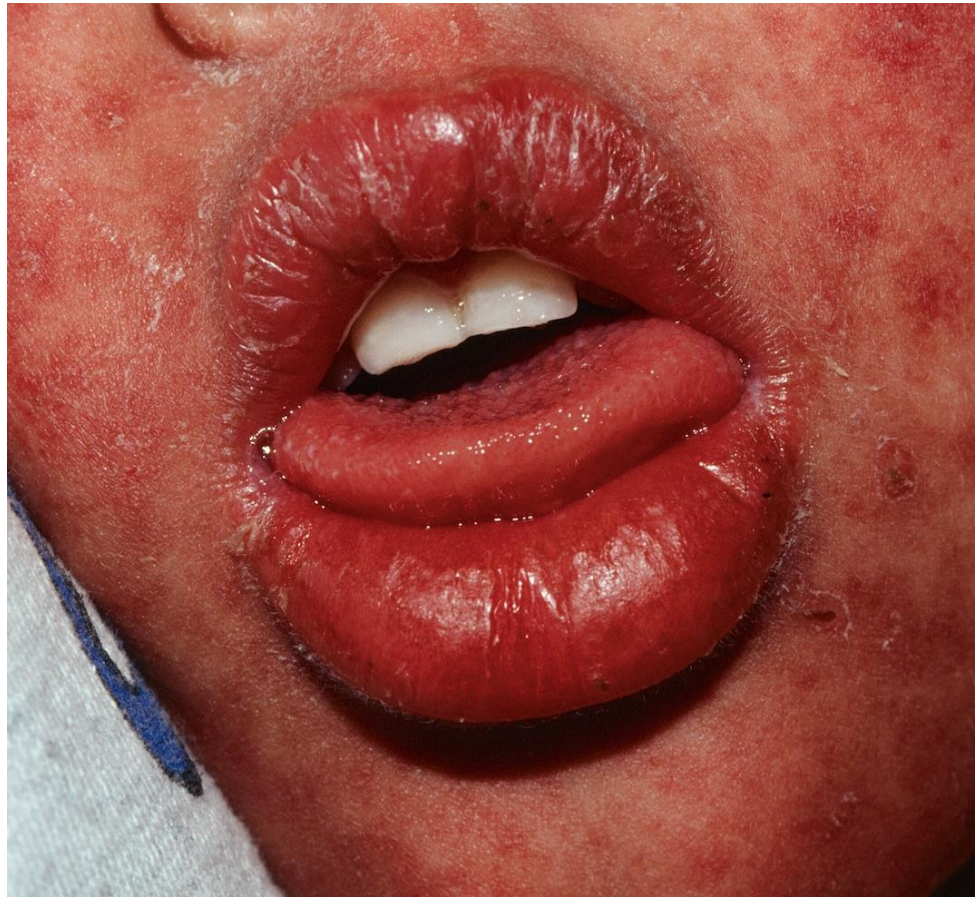
- Fever
- Mucosal involvement
- Epidermal detachment of <10% of BSA
- Antibiotics, NSAIDs..

# Diagnosis for 5 points



- Fever
- Mucosal involvement
- Epidermal detachment of >30% of BSA
- Systemic involvement: hepatitis, nephritis, pneumonitis, vasculitis…

# Diagnosis for 10 points



- Fever
- Lymphadenopathy
- Eosinophilia
- Atypical lymphocytosis
- Hepatitis, nephritis, pneumonitis, carditis…
- 2-6 weeks after the drug was first administered
- Anticonvulsants, tetracyclines…

| | Type I | Type II | Type III | Type IVa | Type IVb | Type IVc | Type IVd |
|---|---|---|---|---|---|---|---|
| **Immune reactant** | IgE | IgG | IgG | IFNγ, TNFα ($T_H1$ cells) | IL-5, IL-4/IL-13 ($T_H2$ cells) | Perforin/ GranzymeB (CTL) | CXCL-8. GM-CSF (IL-17) (T-cells) |
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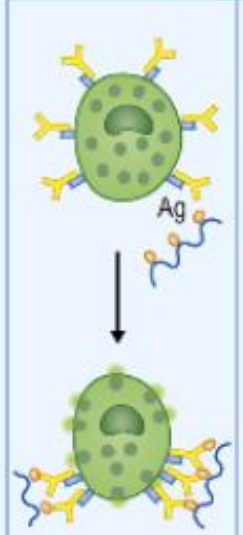
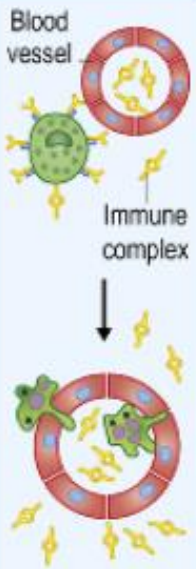
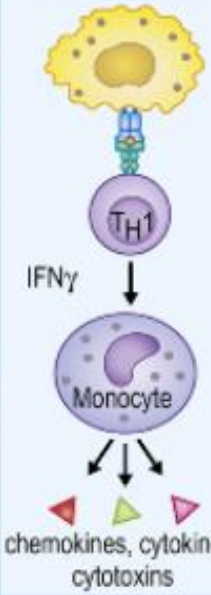
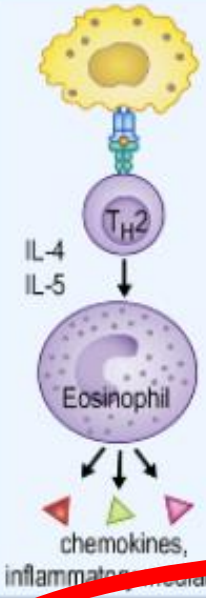
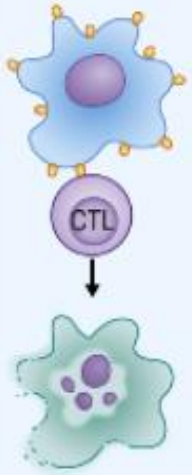
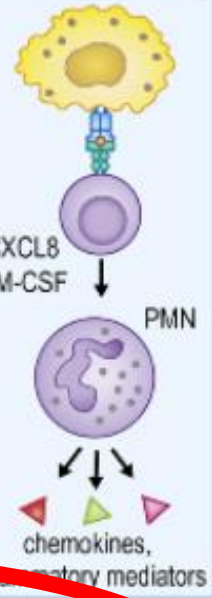
| |   |   |   |   |   |   |   |
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