ANGIOEDEMA

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LEARNING OBJECTIVES

- Define Angioedema & its types.
- State the Etiological Causes.
- Explain the Pathophysiology.
- Discuss Signs & Symptoms.
- Clarify the Diagnostic Approach.
- Discuss the Prevention and Treatment.

ANGIOEDEMA

- Rapid non-pitting edema of the dermis, subcutaneous tissue, mucosa and submucosal tissues.

ANGIOEDEMA

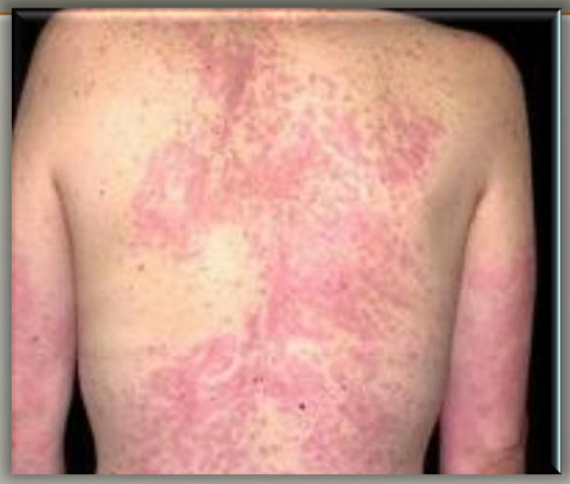
- Self-Limited, subcutaneous edema resulting from increased vascular permeability
  - Dilation of venules and capillaries
  - Limited to the dermis
- Generally resolves over 24-48 hours

ETIOLOGY

- Allergic Angioedema
- Ace Inhibitor Induced Angioedema
- Chronic Idiopathic Angioedema
- Hereditary Angioedema
- Acquired Angioedema

ALLERGIC ANGIOEDEMA

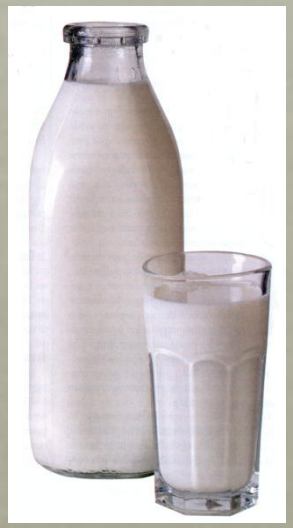
- Most Common Type
- Classic histamine response
- Causes; Food, Drugs, venom, latex.
- Urticaria present often
- Complement assays normal



Urticaria

Triggers of Anaphylaxis: Food

- Milk
- Eggs
- Seafood
- Peanuts
- Tree nuts
- Other

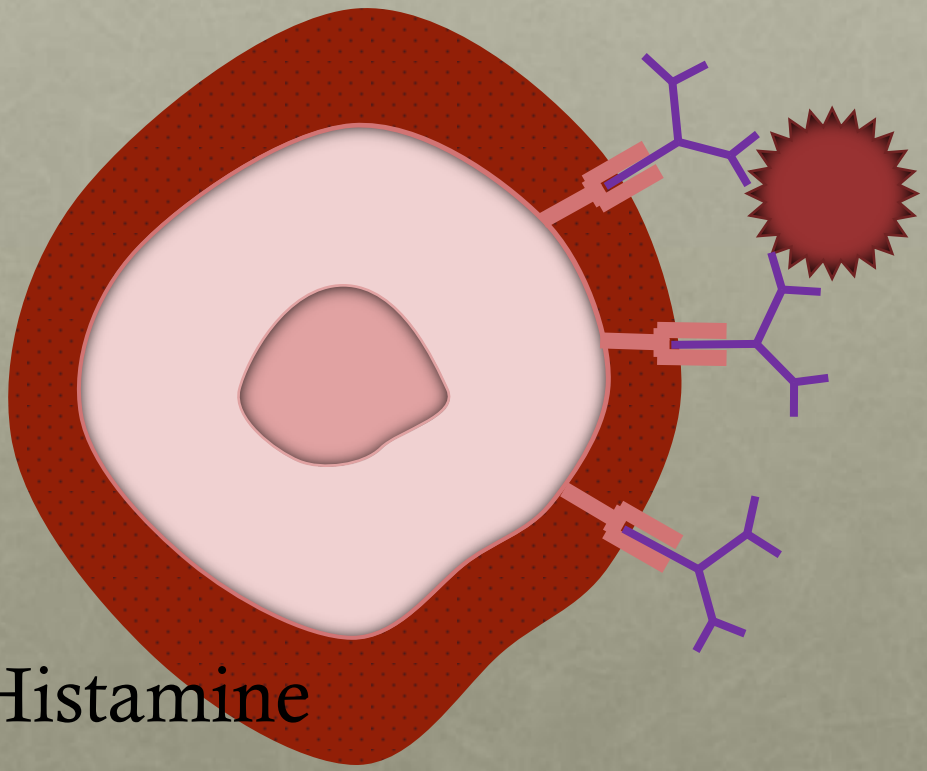


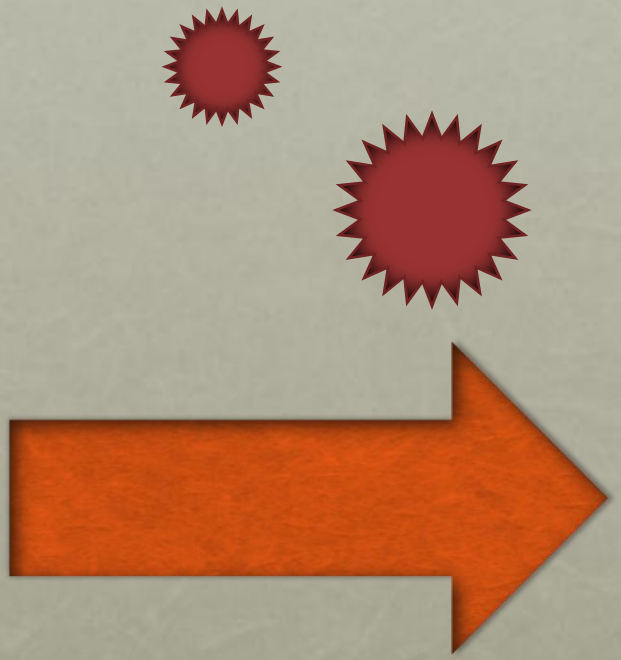
Triggers of Anaphylaxis: Insect Stings and Bites

- Bees
- Vespids, Wasps
- Fire ants
- Scorpions (not in ME)
- Skeeters, Flies rare.

PATHOPHYSIOLOGY

1. Allergic reaction

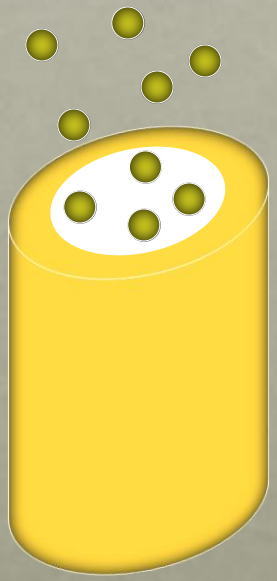




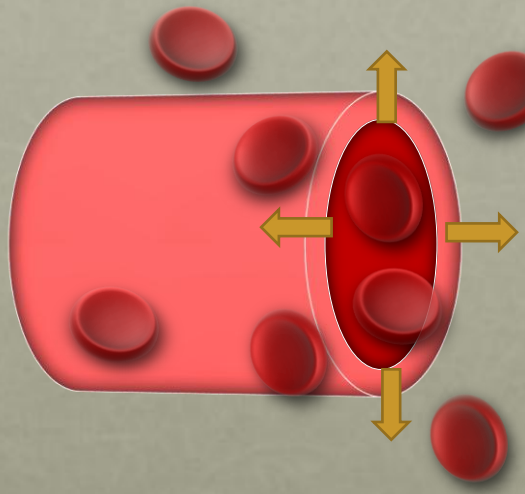
	Mast cell
	FcεRI
	IgE

PATHOPHYSIOLOGY

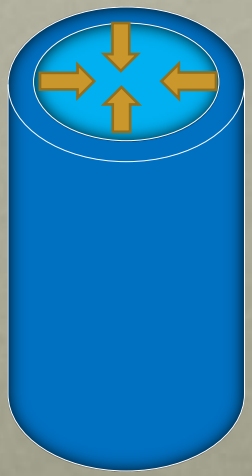
2. Systemic effects



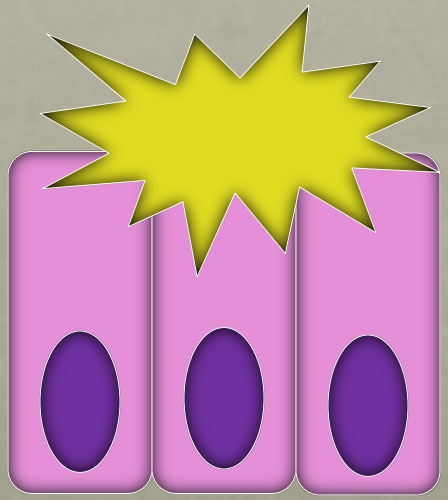
↑ mucus secretion



BV expansion & edema

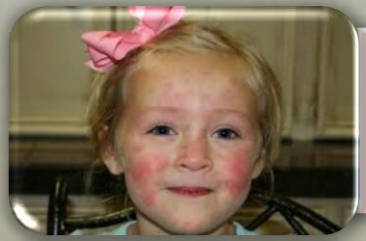


Constricted Respiratory airways

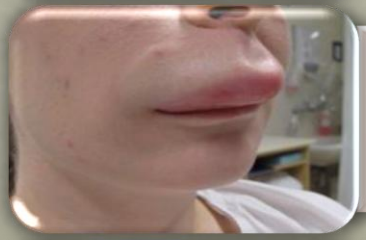


Itching & rash

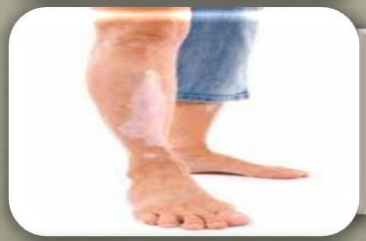
SIGNS & SYMPTOMS



- Sudden appearance of red welts, near eyes & lips, also hands, feet, and inside of throat



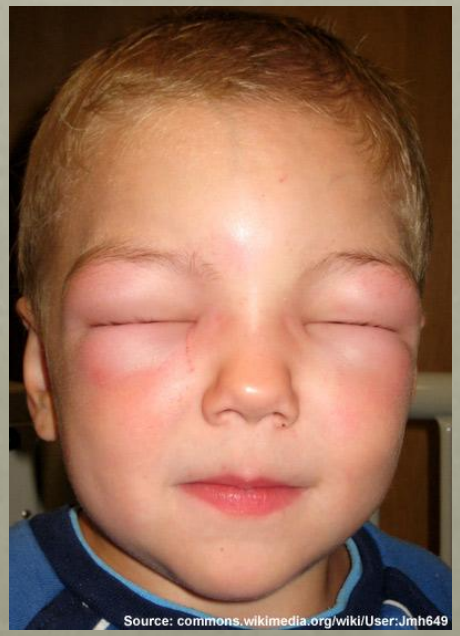
- Burning, painful, swollen areas; sometimes itchy or burning

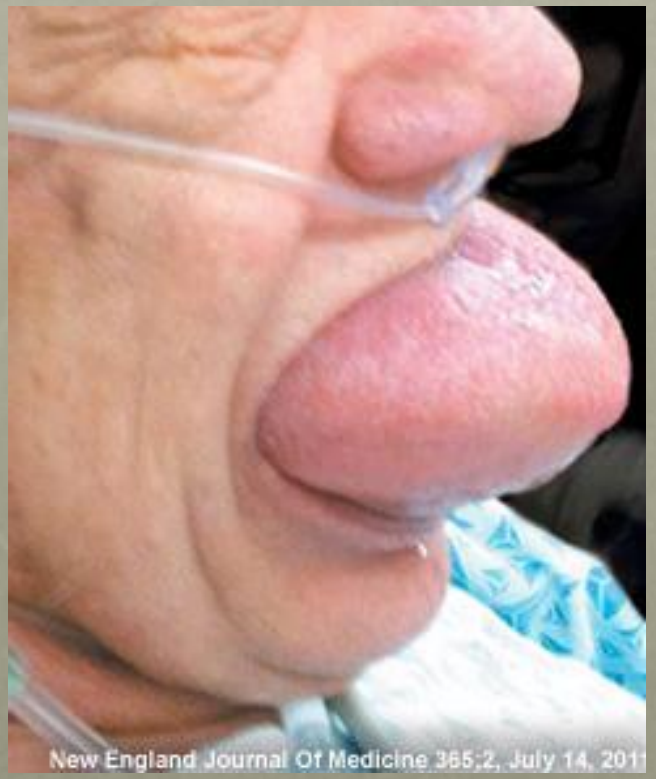


- Discolored patches or rash on the hands, feet, face, or genitals

- hoarseness, tight or swollen throat, breathing trouble

ACE INHIBITOR ANGIOEDEMA





ACE-1 ANGIOEDEMA

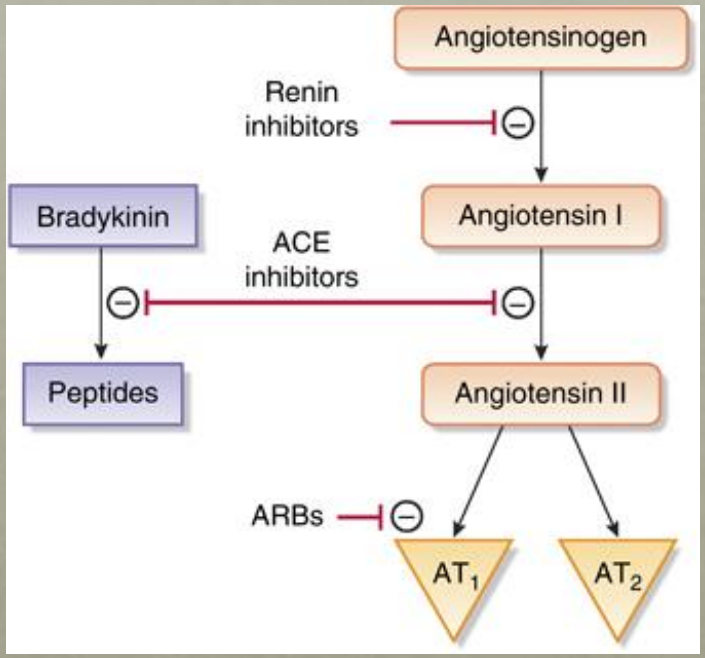
Facts-

More common in African Ethnicity.

Onset can be first dose or months/years out.

Angioedema occurs in 0.1% to 0.7% of patients on ACEI's.

Average is…unknown but likely weeks to months.



ACE INHIBITOR INDUCED ANGIOEDEMA

- Increased Bradykinin.
- Airway edema is the most common presentation.
- Complement assay normal.

Medscape® www.medscape.com

Agent	Variable (Hr)			
	Peak Onset	Duration of Effect	Elimination Half-life	Usual Dosage Interval
Benazepril	2–4	24	10–11	24
Captopril	1–2	2–12	2	8–12
Enalapril	4–8	12–24	2–6	24
Lisinopril	6	24	11–12	24
Moexipril	1–2	>24	1	24
Perindopril	1–2	10–12	3–10	12–24
Quinapril	1	24	2	24
Ramipril	1	24	13–17	24
Trandolapril	6	72	6–10	24

BRADYKININ

- **A mediator that functions to**:
  - Potent endothelium vasodilator
  - Contraction of non-vascular smooth muscle
  - Increases vascular permeability
  - Involved in mechanism of pain

CHRONIC IDIOPATHIC ANGIOEDEMA

- The exact mechanisms are unclear. Some may be associated with urticaria. Based on responses to medication, some cases are mediated by mast cell activation.
- Urticaria present.
- Laryngeal edema rare.
- Causes are, by definition, not identifiable.
- Complement assays normal.

HEREDITARY ANGIOEDEMA

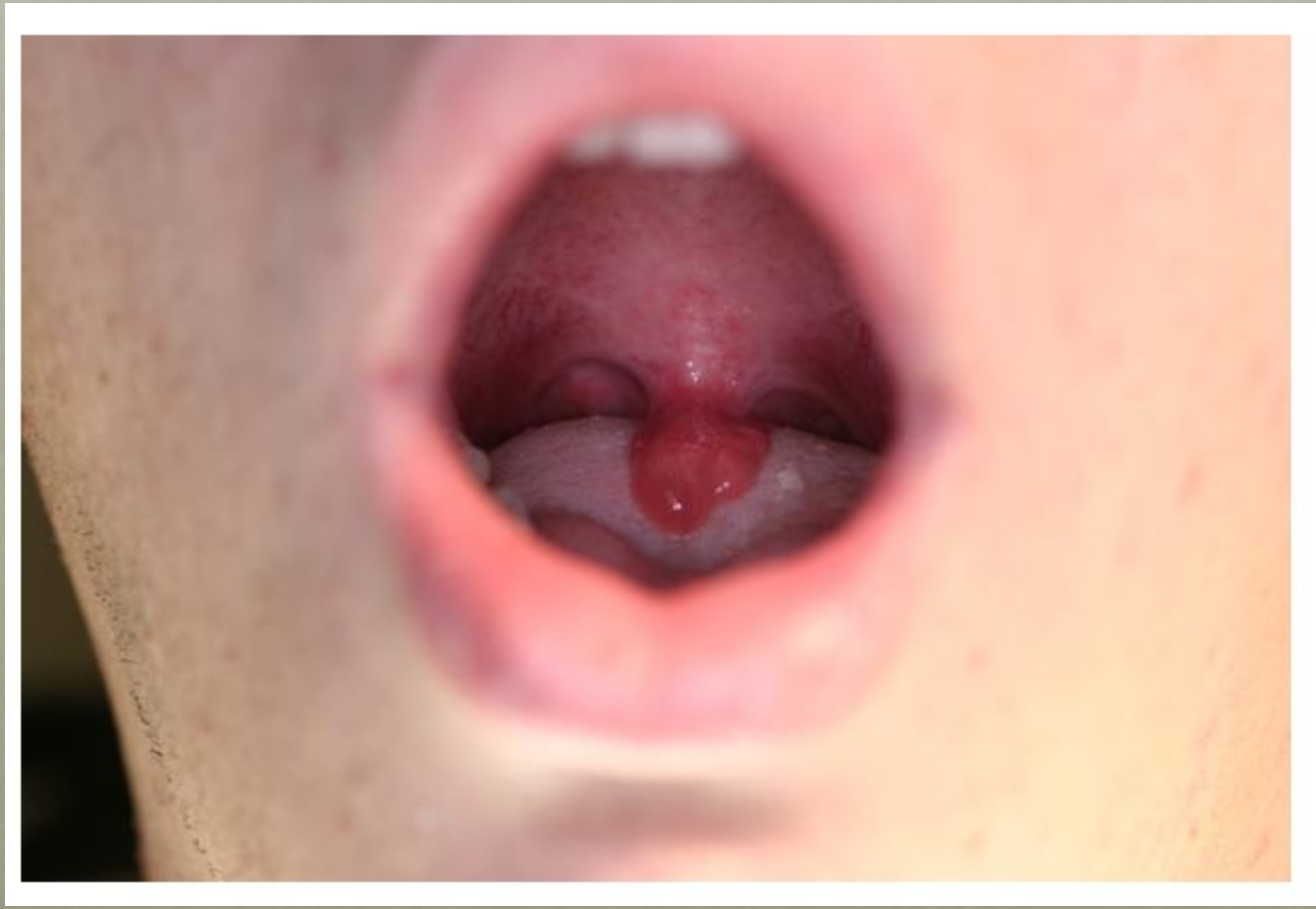
- Rare (1:50 000-1:150 000)
- Autosomal Dominant
- Cause; chromosome 11 abnormality
- Disorder of C1INH (only regulator of classical complement pathway activation)
    - Type 1 (85%) low levels of C1INH and functional deficiency
    - Type 2 (15%) Normal protein concentration but functional defect.
    - Type 3-Hmmm.
    - Type 4?????

HEREDITARY ANGIOEDEMA

Pathophysiology

HAE

HAE



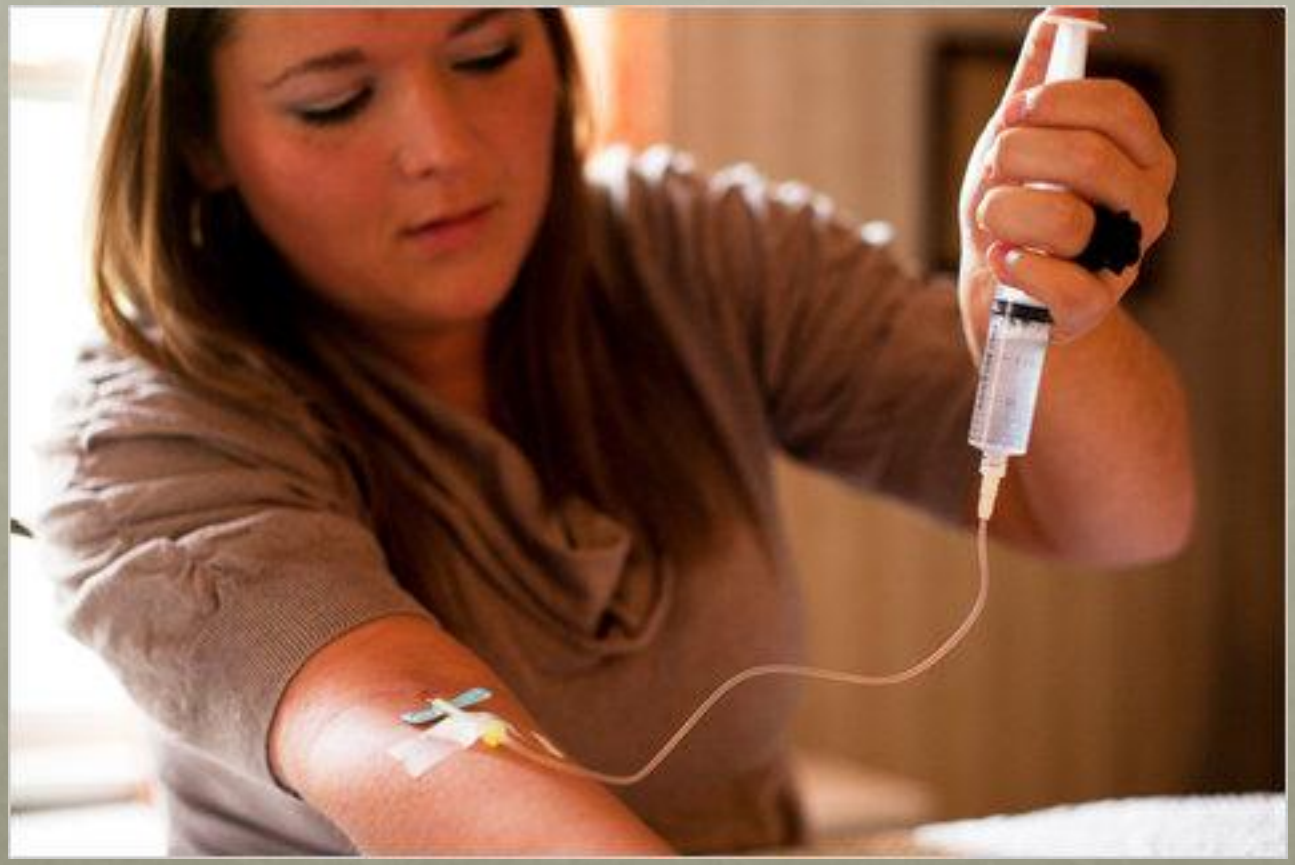
HAE TREAMENT

Table 2. Agents for HAE Treatment or Prophylaxis

Agent	Initial U.S. Approval	MOA	Indication	Dosage and Administration
Berinert	2009	C1-INH	Treatment	20 U/kg body weight by IV injection
Cinryze	2008	C1-INH	Prophylaxis in adolescent and adult patients	1,000 U IV every 3-4 days
Kalbitor (ecallantide)	2009	Plasma kallikrein inhibitor	Treatment in patients aged ≥16 y	30 mg (3 mL) SQ in three 10-mg doses; administered only by health care provider because of risk of allergy/anaphylaxis
Firazyr (icatibant)	2011	Selective bradykinin B_2-receptor antagonist	Treatment in patients aged ≥18 y	30 mg SQ into abdomen; administered by health care provider or patient
Danocrine (danazol)	1976	Increases circulating levels of C1-INH, thereby raising C4 levels	Prophylaxis in adults	200 mg/day max to reduce adverse effects
Lysteda (tranexamic acid)	1986	Reduces complement activation and C1-INH consumption	Prophylaxis in adults; not FDA approved for this indication	20-50 mg/kg/day in 2-3 divided doses (max 3-6 g/day)

C1-INH: C1 esterase inhibitor; C4: complement factor C4; HAE: hereditary angioedema; max: maximum; MOA: mechanism of action; SQ: subcutaneous.
Sources: References 6, 10-15.

HAE TREATMENT



ACQUIRED ANGIOEDEMA

- Most similar in mechanism to HAE
- No Family History
- Causes; Deficiency of C1-INH due to
  - Type I: Lymphoproliferative Disorder (MDS/MGUS)
  - Type II: Autoimmune Disorder (SLE) 4th decade of life most common
- All complement assays are low including C1q

COMPLICATIONS OF AA

- Some drugs such NSAIDS, Opiates and the use of IV contrast agents can worsen pre-existing angioedema of any type.
- These should be avoided or at least planned for with premedication given as appropriate.
- Intubation should be done early if airway compromise worsens rapidly.

Anaphylaxis

Life-threatening airway blockage

DIAGNOSIS

- We should..
  - Look at their skin.
  - Take a great history.
  - Ask about being exposed to any irritating substances.
- A physical exam might reveal other findings.
- Consider..
  - Serology- C1Esterase Inhibitor level and function, C4, CBC with diff and Tryptase.
  - Allergy testing.

TYPES OF AA

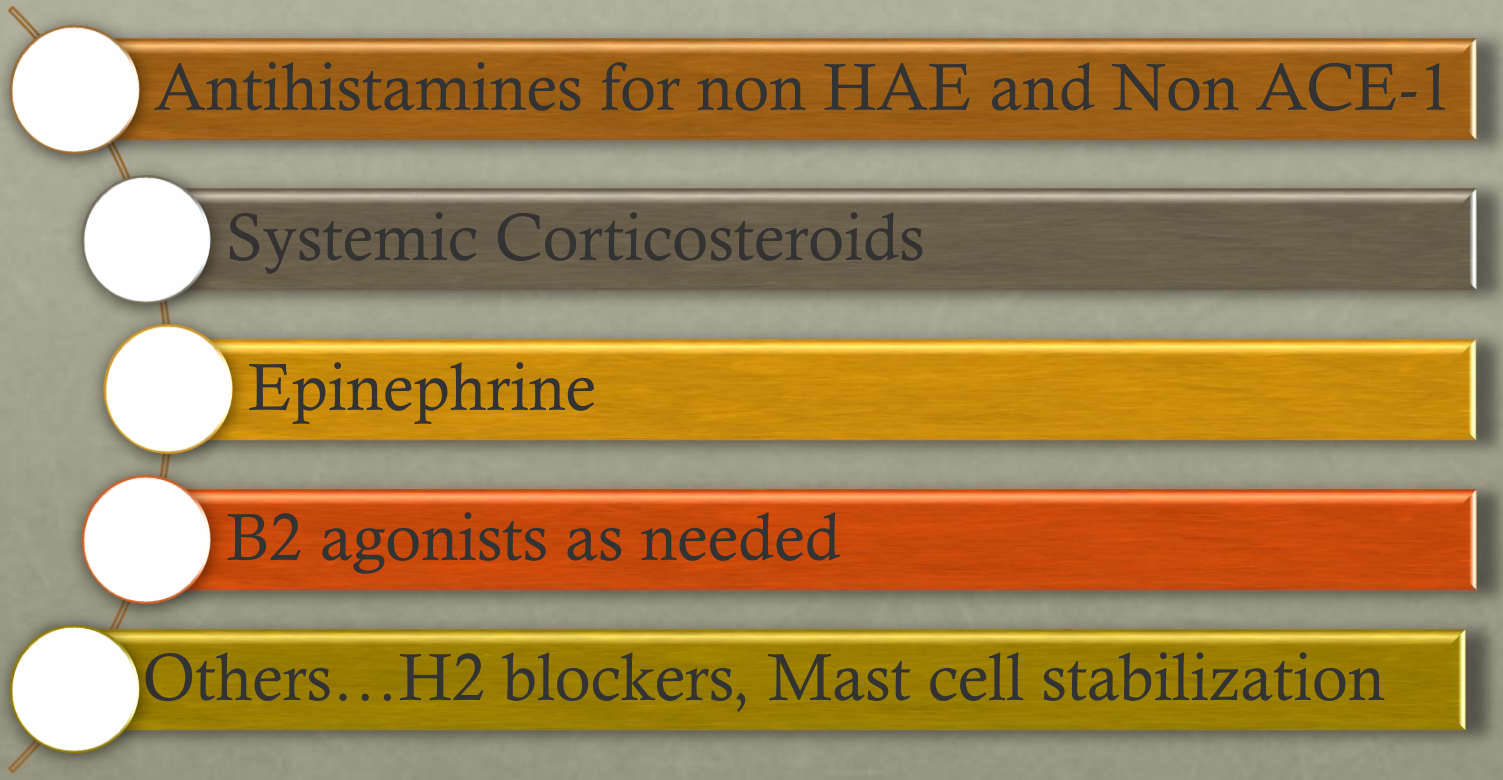
Angioedema	C1-INH	Functional C1-INH	C4	C3	C1q
HAE I	< 30%	< 30%	Low	Nl	Nl
HAE II	Nl/high	< 30%	Low	Nl	Nl
HAE III*	Nl	Nl	Nl	Nl	Nl
Inherited with normal C1-INH	Nl	Nl	Nl	Nl	Nl
ACID	Low	Low	<50%	Nl or low	<50%
ACEI-induced	Nl	Nl	Nl	Nl	Nl
Idiopathic	Nl	Nl	Nl	Nl	Nl
Allergic	Nl	Nl	Nl	Nl	Nl

PREVENTION

- Avoid known allergens
- Avoid Trauma, physical and emotional stress.. (yeah, right?)
- Avoid ACE-1. ARB usually tolerated in AI Angioedema.
- Avoid NSAIDS, opiates, ethanol and some histaminic foods.

TREATMENT

- If the person has trouble breathing, seek immediate medical help.
- Medications include



SUMMARY

- **Angioedema** can be immunologic, nonimmunologic, or idiopathic.
- Often caused by allergy and can be present with urticaria.
- It occurs in .1% to .7% of patients on ACE-1 inhibitors.
- Characterized by episodes of swelling of the face, lips, tongue, limbs and genitals.
- A careful history often illuminates the cause.
- Avoidance of triggers and treatment as needed is the key.

THANK YOU