ANGIOEDEMA

Angioedema is swelling in the deep layers of the skin and other tissues.

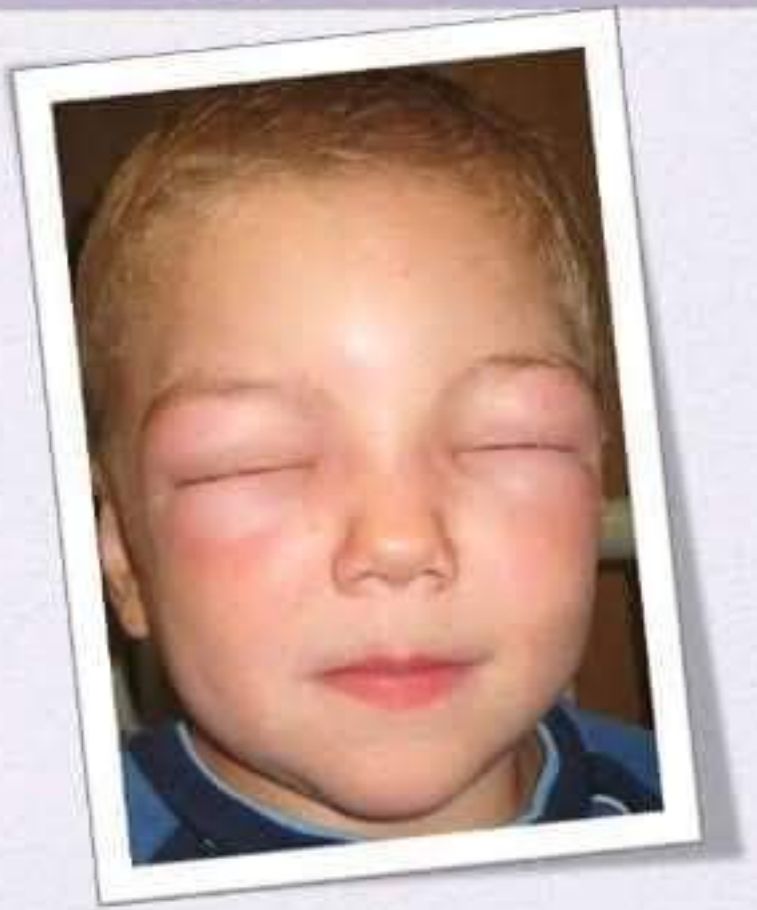
It may be accompanied by an itchy, raised rash.

Other symptoms may include abdominal pain, shortness of breath, dizziness, and fainting.

Commonly affected areas

Definition Of Angioedema

- **Angioedema** or **Quincke's edema** is the rapid swelling (edema) of the dermis, subcutaneous tissue, mucosa and submucosal tissues. It is very similar to urticaria, but urticaria, commonly known as hives, occurs in the upper dermis.



Angioedema

Often occurs in the deep layers of the skin, usually near the eyes and mouth.

Etiology

- More than 40% of chronic angioedema is idiopathic. Trauma, surgical procedures, and stress are common nonspecific triggers for angioedema attacks.
- Angioedemas with identifiable etiologies include those caused by the following:
- Hypersensitivity (eg, food, drugs, or insect stings)
- Physical stimuli (eg, cold or vibrations)
- Autoimmune disease or infection
- ACE inhibitors
- NSAIDs
- C1-INH deficiency (hereditary and acquired)

Types Of Angioedema

1. **Acute or allergic angioedema** – the swelling is caused by an allergic reaction, such as a reaction to peanuts.
2. **idiopathic angioedema** – there is no known cause for the symptoms of swelling .

- 3. **drug-induced angioedema** – the swelling is a side effect of certain medications.
- 4. **hereditary angioedema** – the swelling is caused by 'faulty' genes that are inherited from a person's parents.

What is Hereditary Angioedema (HAE)?

HAE is a rare inherited condition characterized by painful, recurring attacks of swelling in parts of the body including:[1,2]

It is the result of a problem with a protein called C1 esterase inhibitor.

There are three types of hereditary angioedema:

Type I

- 85% of cases[3]
- C1-INH is decreased or not present[3]

Type II

- 15% of cases[3]
- C1-INH is not working properly[3]

Type III

- Rare; prevalence is unknown[3]
- Diagnosed by genetic testing[3]

Hereditary angioedema (HAE)

- 3 types:

  Type 1 and II mutation of C1NH gene on chromosome 11, (encoding C1 inhibitor protein)

  Type III mutation in F12 gene on chromosome 12, (encoding coagulation factor XII)
- Type 1 results in low levels and function of circulating C1 inhibitor;
- Type II has normal levels of C1 inhibitor protein but reduction in function
- Occurs in 1 in 50,000 males and females (rare)
- Decreased C1 inhibitor activity leads to excessive kallikrein, which in turn produces bradykinin, which we know is a potent vasodilator

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.

Idiopathic angioedema

- Similar to acute allergic but angioedema keeps on recurring and often no known cause is found
- Usually occurs with urticaria
- 30-50% of this type of angioedema may be associated with some types of autoimmune disorders including SLE

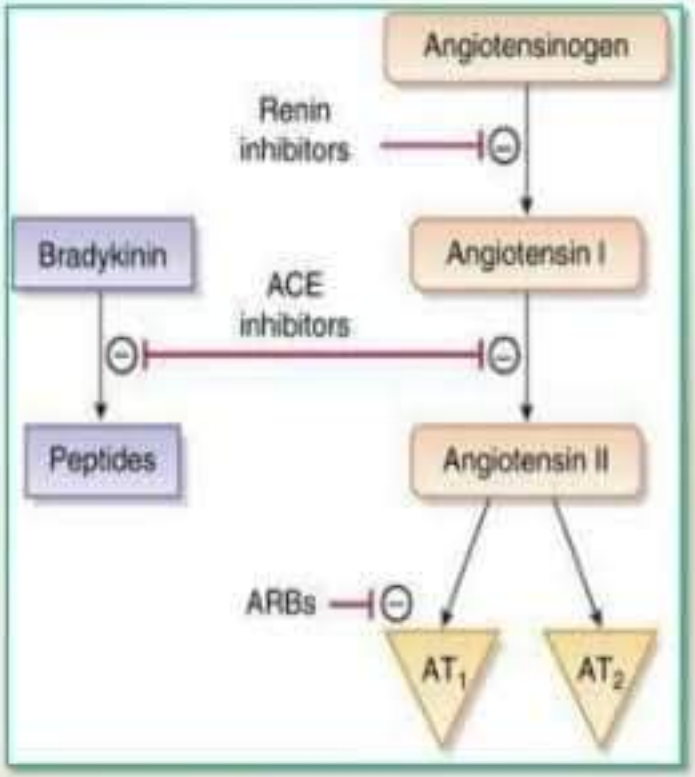
http://www.dermnetnz.org/reactions/angioedema.html

Acquired Angioedema

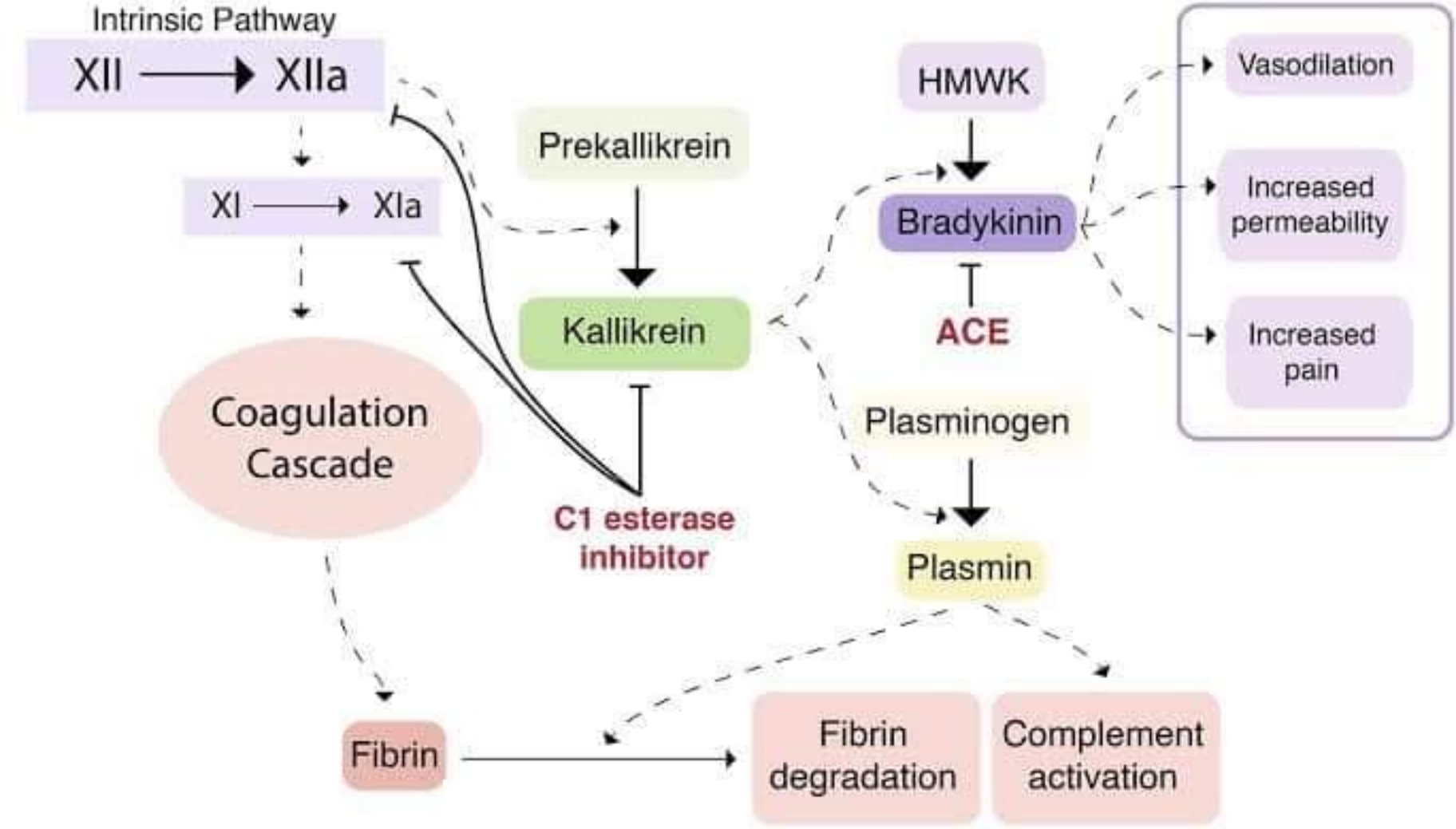
- Most similar in mechanism to HAE
- No Family History
- Causes; Deficiency of C1-INH due to
  - Type I: Lymphoproliferative Disorder (MDS/MGUS)
  - Type II: Autoimmune Disorder (SLE) 4th decade of life
- All complement assays are low including C1q

Ace Inhibitor Induced Angioedema

- Increased Bradykinin
- Airway edema is the most common presentation
- Causes; nonsteroidal anti-inflammatory drugs (NSAIDs) and intravenous contrast material; aspirin is the most common culprit.
- Complement assay normal



Kallikrein-Bradykinin Pathway



Lucy Liu

Signs & Symptoms

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

- Burning, painful, swollen areas; sometimes itchy

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

- hoarseness, tight or swollen throat, breathing trouble

Exams and Tests

- The health care provider will look at your skin and ask you if you have been exposed to any irritating substances.
- A physical exam might reveal abnormal sounds (stridor) when you breathe in if your throat is affected.
- Blood tests or allergy testing may be ordered.

- **Testing for and Diagnosing Hereditary Angioedema**
- **Blood tests** can check the C1 inhibitor level and function.
- Since Cl inhibitor is part of the complement system, blood tests for complement components C4 and C2 may also help diagnose HAE.

Treatment

- Mild symptoms may not need treatment. Moderate to severe symptoms may need to be treated. Breathing difficulty is an emergency condition.
- People with angioedema should:
- Avoid any known allergen or trigger that causes their symptoms
- Avoid any medicines, herbs, or supplements that are not prescribed by a health care provider
- Cool compresses or soaks can relieve pain.

- **Medications used to treat angioedema include:**
- Antihistamines
- Anti-inflammatory medicines (corticosteroids)
- Epinephrine shots (people with a history of severe symptoms can carry these with them)
- Inhaler medicines that help open up the airways
- If the person has trouble breathing, seek immediate medical help. A severe, life-threatening airway blockage may occur if the throat swells.

Treatment

- H1 antihistamine e.g IV chlorpheniramine 10 mg or diphenhydramine 25–50 mg
- Limited evidence for adding in H2 blocker e.g ranitidine IV 50mg
- Intravenous corticosteroids e.g. hydro-cortisone 200 mg or methylprednisolone 50–100 mg
- Adrenaline IM 1:1000

Treatment

IN ACUTE ANGIOEDEMA:

- Antihistamines e.g. Ranitidine (Zantac)
- Anti-inflammatory medicines (corticosteroids)
- Epinephrine shots (people with a history of severe symptoms can carry these with them)
- Inhaler medicines that help open up the airways

IN HEREDITARY ANGIOEDEMA:

- Antihistamines and oral corticosteroid medications — although useful in treating hives and acute angioedema — are often ineffective in treating hereditary angioedema.
- Medications used to treat hereditary angioedema on a long-term basis include certain androgens (male hormones), such as **danazol**, that help regulate levels of blood proteins.

MANAGEMENT OF ACE INHIBITOR-INDUCED ANGIOEDEMA

ACUT TREATMENT

Avoid ACE inhibitors

Conservative treatment antihistamines with or without steroids

Tongue and upper airway are involved, **intramuscular adrenaline** should be used, some patients **require an artificial airway**

C1 inhibitor concentrate,FFP, SDP, kallikrein inhibitor or bradykinin receptor antagonist has been successfully