

= Anaphylaxis =

Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death . It typically causes more than one of the following : an itchy rash , throat or tongue swelling , shortness of breath , vomiting , lightheadedness , and low blood pressure . These symptoms typically come on over minutes to hours .

Common causes include insect bites and stings , foods , and medications . Other causes include latex exposure and exercise . Additionally cases may occur without an obvious reason . The mechanism involves the release of mediators from certain types of white blood cells triggered by either immunologic or non @-@ immunologic mechanisms . Diagnosis is based on the presenting symptoms and signs after exposure to a potential allergen .

The primary treatment of anaphylaxis is epinephrine injection into a muscle , intravenous fluids , and positioning the person flat . Additional doses of epinephrine may be required . Other measures , such as antihistamines and steroids , are complementary . Carrying an epinephrine autoinjector and identification regarding the condition is recommended in people with a history of anaphylaxis .

Worldwide , 0 @. @ 05 ? 2 % of the population is estimated to experience anaphylaxis at some point in life . Rates appear to be increasing . It occurs most often in young people and females . Of people who go to a hospital with anaphylaxis in the United States about 0 @. @ 3 % die . The term comes from the Ancient Greek : ??? ana " against " , and the Ancient Greek : ???????? phylaxis " protection " .

= = Signs and symptoms = =

Anaphylaxis typically presents many different symptoms over minutes or hours with an average onset of 5 to 30 minutes if exposure is intravenous and 2 hours if from eating food . The most common areas affected include : skin (80 ? 90 %) , respiratory (70 %) , gastrointestinal (30 ? 45 %) , heart and vasculature (10 ? 45 %) , and central nervous system (10 ? 15 %) with usually two or more being involved .

= = = Skin = = =

Symptoms typically include generalized hives , itchiness , flushing , or swelling (angioedema) of the afflicted tissues . Those with angioedema may describe a burning sensation of the skin rather than itchiness . Swelling of the tongue or throat occurs in up to about 20 % of cases . Other features may include a runny nose and swelling of the conjunctiva . The skin may also be blue tinged because of lack of oxygen .

= = = Respiratory = = =

Respiratory symptoms and signs that may be present include shortness of breath , wheezes , or stridor . The wheezing is typically caused by spasms of the bronchial muscles while stridor is related to upper airway obstruction secondary to swelling . Hoarseness , pain with swallowing , or a cough may also occur .

= = = Cardiovascular = = =

Coronary artery spasm may occur with subsequent myocardial infarction , dysrhythmia , or cardiac arrest . Those with underlying coronary disease are at greater risk of cardiac effects from anaphylaxis . The coronary spasm is related to the presence of histamine @-@ releasing cells in the heart . While a fast heart rate caused by low blood pressure is more common , a Bezold ? Jarisch reflex has been described in 10 % of cases where a slow heart rate is associated with low blood pressure . A drop in blood pressure or shock (either distributive or cardiogenic) may cause the feeling of lightheadedness or loss of consciousness . Rarely very low blood pressure may be the

only sign of anaphylaxis .

== Other ==

Gastrointestinal symptoms may include crampy abdominal pain , diarrhea , and vomiting . There may be confusion , a loss of bladder control or pelvic pain similar to that of uterine cramps . Dilation of blood vessels around the brain may cause headaches . A feeling of anxiety or of " impending doom " has also been described .

== Causes ==

Anaphylaxis can occur in response to almost any foreign substance . Common triggers include venom from insect bites or stings , foods , and medication . Foods are the most common trigger in children and young adults while medications and insect bites and stings are more common in older adults . Less common causes include : physical factors , biological agents such as semen , latex , hormonal changes , food additives such as monosodium glutamate and food colors , and topical medications . Physical factors such as exercise (known as exercise @-@ induced anaphylaxis) or temperature (either hot or cold) may also act as triggers through their direct effects on mast cells . Events caused by exercise are frequently associated with the ingestion of certain foods . During anesthesia , neuromuscular blocking agents , antibiotics , and latex are the most common causes . The cause remains unknown in 32 ? 50 % of cases , referred to as " idiopathic anaphylaxis . " Six vaccines (MMR , varicella , influenza , hepatitis B , tetanus , meningococcal) are recognized as a cause for anaphylaxis , and HPV may cause anaphylaxis as well .

== Food ==

Many foods can trigger anaphylaxis ; this may occur upon the first known ingestion . Common triggering foods vary around the world . In Western cultures , ingestion of or exposure to peanuts , wheat , nuts , certain types of seafood like shellfish , milk , and eggs are the most prevalent causes . Sesame is common in the Middle East , while rice and chickpeas are frequently encountered as sources of anaphylaxis in Asia . Severe cases are usually caused by ingesting the allergen , but some people experience a severe reaction upon contact . Children can outgrow their allergies . By age 16 , 80 % of children with anaphylaxis to milk or eggs and 20 % who experience isolated anaphylaxis to peanuts can tolerate these foods .

== Medication ==

Any medication may potentially trigger anaphylaxis . The most common are ? @-@ lactam antibiotics (such as penicillin) followed by aspirin and NSAIDs . Other antibiotics are implicated less frequently , and the reactions to NSAIDs are agent specific meaning that those who are allergic to one NSAID can typically tolerate a different one . Other relatively common causes include chemotherapy , vaccines , protamine and herbal preparations . Some medications (vancomycin , morphine , x @-@ ray contrast among others) cause anaphylaxis by directly triggering mast cell degranulation .

The frequency of a reaction to an agent partly depends on the frequency of its use and partly on its intrinsic properties . Anaphylaxis to penicillin or cephalosporins occurs only after it binds to proteins inside the body with some agents binding more easily than others . Anaphylaxis to penicillin occurs once in every 2 @,@ 000 to 10 @,@ 000 courses of treatment , with death occurring in fewer than one in every 50 @,@ 000 courses of treatment . Anaphylaxis to aspirin and NSAIDs occurs in about one in every 50 @,@ 000 persons . If someone has a reaction to penicillins , his or her risk of a reaction to cephalosporins is greater but still less than one in 1 @,@ 000 . The old radiocontrast agents caused reactions in 1 % of cases , while the newer lower osmolar agents cause reactions in 0 @.@ 04 % of cases .

=== Venom ===

Venom from stinging or biting insects such as Hymenoptera (ants , bees and wasps) or Triatominae (kissing bugs) may cause anaphylaxis in susceptible people . Previous systemic reactions , which are anything more than a local reaction around the site of the sting , are a risk factor for future anaphylaxis ; however , half of fatalities have had no previous systemic reaction .

=== Risk factors ===

People with atopic diseases such as asthma , eczema , or allergic rhinitis are at high risk of anaphylaxis from food , latex , and radiocontrast agents but not from injectable medications or stings . One study in children found that 60 % had a history of previous atopic diseases , and of children who die from anaphylaxis , more than 90 % have asthma . Those with mastocytosis or of a higher socioeconomic status are at increased risk . The longer the time since the last exposure to the agent in question , the lower the risk .

=== Pathophysiology ===

Anaphylaxis is a severe allergic reaction of rapid onset affecting many body systems . It is due to the release of inflammatory mediators and cytokines from mast cells and basophils , typically due to an immunologic reaction but sometimes non @-@ immunologic mechanism .

=== Immunologic ===

In the immunologic mechanism , immunoglobulin E (IgE) binds to the antigen (the foreign material that provokes the allergic reaction) . Antigen @-@ bound IgE then activates Fc γ RI receptors on mast cells and basophils . This leads to the release of inflammatory mediators such as histamine . These mediators subsequently increase the contraction of bronchial smooth muscles , trigger vasodilation , increase the leakage of fluid from blood vessels , and cause heart muscle depression . There is also an immunologic mechanism that does not rely on IgE , but it is not known if this occurs in humans .

=== Non @-@ immunologic ===

Non @-@ immunologic mechanisms involve substances that directly cause the degranulation of mast cells and basophils . These include agents such as contrast medium , opioids , temperature (hot or cold) , and vibration . Sulfites may cause reactions by both immunologic and non @-@ immunologic mechanisms .

=== Diagnosis ===

Anaphylaxis is diagnosed on the basis of a person 's signs and symptoms . When any one of the following three occurs within minutes or hours of exposure to an allergen there is a high likelihood of anaphylaxis :

Involvement of the skin or mucosal tissue plus either respiratory difficulty or a low blood pressure causing symptoms

Two or more of the following symptoms after a likely contact with an allergen :

a . Involvement of the skin or mucosa

b . Respiratory difficulties

c . Low blood pressure

d . Gastrointestinal symptoms

Low blood pressure after exposure to a known allergen

Skin involvement may include : hives , itchiness or a swollen tongue among others . Respiratory difficulties may include : shortness of breath , stridor , or low oxygen levels among others . Low blood pressure is defined as a greater than 30 % decrease from a person 's usual blood pressure . In adults a systolic blood pressure of less than 90 mmHg is often used .

During an attack , blood tests for tryptase or histamine (released from mast cells) might be useful in diagnosing anaphylaxis due to insect stings or medications . However these tests are of limited use if the cause is food or if the person has a normal blood pressure , and they are not specific for the diagnosis .

=== Classification ===

There are three main classifications of anaphylaxis . Anaphylactic shock is associated with systemic vasodilation that causes low blood pressure which is by definition 30 % lower than the person 's baseline or below standard values . Biphasic anaphylaxis is the recurrence of symptoms within 1 ? 72 hours with no further exposure to the allergen . Reports of incidence vary , with some studies claiming as many as 20 % of cases . The recurrence typically occurs within 8 hours . It is managed in the same manner as anaphylaxis . Pseudoanaphylaxis or anaphylactoid reactions are a type of anaphylaxis that does not involve an allergic reaction but is due to direct mast cell degranulation . Non @-@ immune anaphylaxis is the current term used by the World Allergy Organization with some recommending that the old terminology no longer be used .

=== Allergy testing ===

Allergy testing may help in determining the trigger . Skin allergy testing (such as patch testing) is available for certain foods and venoms . Blood testing for specific IgE can be useful to confirm milk , egg , peanut , tree nut and fish allergies .

Skin testing is available to confirm penicillin allergies , but is not available for other medications . Non @-@ immune forms of anaphylaxis can only be determined by history or exposure to the allergen in question , and not by skin or blood testing .

=== Differential diagnosis ===

It can sometimes be difficult to distinguish anaphylaxis from asthma , syncope , and panic attacks . Asthma however typically does not entail itching or gastrointestinal symptoms , syncope presents with pallor rather than a rash , and a panic attack may have flushing but does not have hives . Other conditions that may present similarly include : scrombroidosis and anisakiasis .

=== Post @-@ mortem findings ===

In a person who died from anaphylaxis , autopsy may show an " empty heart " attributed to reduced venous return from vasodilation and redistribution of intravascular volume from the central to the peripheral compartment . Other signs are laryngeal edema , eosinophilia in lungs , heart and tissues , and evidence of myocardial hypoperfusion . Laboratory findings could detect increased levels of serum tryptase , increase in total and specific IgE serum levels .

=== Prevention ===

Avoidance of the trigger of anaphylaxis is recommended . In cases where this may not be possible , desensitization may be an option . Immunotherapy with Hymenoptera venoms is effective at desensitizing 80 ? 90 % of adults and 98 % of children against allergies to bees , wasps , hornets , yellowjackets , and fire ants . Oral immunotherapy may be effective at desensitizing some people to certain food including milk , eggs , nuts and peanuts ; however , adverse effects are common . Desensitization is also possible for many medications , however it is advised that most people

simply avoid the agent in question . In those who react to latex it may be important to avoid cross @-@ reactive foods such as avocados , bananas , and potatoes among others .

= = Management = =

Anaphylaxis is a medical emergency that may require resuscitation measures such as airway management , supplemental oxygen , large volumes of intravenous fluids , and close monitoring . Administration of epinephrine is the treatment of choice with antihistamines and steroids (for example , dexamethasone) often used as adjuncts . A period of in @-@ hospital observation for between 2 and 24 hours is recommended for people once they have returned to normal due to concerns of biphasic anaphylaxis .

= = = Epinephrine = = =

Epinephrine (adrenaline) is the primary treatment for anaphylaxis with no absolute contraindication to its use . It is recommended that an epinephrine solution be given intramuscularly into the mid anterolateral thigh as soon as the diagnosis is suspected . The injection may be repeated every 5 to 15 minutes if there is insufficient response . A second dose is needed in 16 @-@ 35 % of episodes with more than two doses rarely required . The intramuscular route is preferred over subcutaneous administration because the latter may have delayed absorption . Minor adverse effects from epinephrine include tremors , anxiety , headaches , and palpitations .

People on ? @-@ blockers may be resistant to the effects of epinephrine . In this situation if epinephrine is not effective intravenous glucagon can be administered which has a mechanism of action independent of ? @-@ receptors .

If necessary , it can also be given intravenously using a dilute epinephrine solution . Intravenous epinephrine however has been associated both with dysrhythmia and myocardial infarction . Epinephrine autoinjectors used for self @-@ administration typically come in two doses , one for adults or children who weigh more than 25 kg and one for children who weigh 10 to 25 kg .

= = = Adjuncts = = =

Antihistamines (both H1 and H2) , while commonly used and assumed effective based on theoretical reasoning , are poorly supported by evidence . A 2007 Cochrane review did not find any good @-@ quality studies upon which to base recommendations and they are not believed to have an effect on airway edema or spasm . Corticosteroids are unlikely to make a difference in the current episode of anaphylaxis , but may be used in the hope of decreasing the risk of biphasic anaphylaxis . Their prophylactic effectiveness in these situations is uncertain . Nebulized salbutamol may be effective for bronchospasm that does not resolve with epinephrine . Methylene blue has been used in those not responsive to other measures due to its presumed effect of relaxing smooth muscle .

= = = Preparedness = = =

People prone to anaphylaxis are advised to have an " allergy action plan . " Parents are advised to inform schools of their children 's allergies and what to do in case of an anaphylactic emergency . The action plan usually includes use of epinephrine autoinjectors , the recommendation to wear a medical alert bracelet , and counseling on avoidance of triggers . Immunotherapy is available for certain triggers to prevent future episodes of anaphylaxis . A multi @-@ year course of subcutaneous desensitization has been found effective against stinging insects , while oral desensitization is effective for many foods .

= = Prognosis = =

In those in whom the cause is known and prompt treatment is available , the prognosis is good .

Even if the cause is unknown , if appropriate preventative medication is available , the prognosis is generally good . If death occurs , it is usually due to either respiratory (typically asphyxia) or cardiovascular causes (shock) , with 0 @. @ 7 ? 20 % of cases causing death . There have been cases of death occurring within minutes . Outcomes in those with exercise @-@ induced anaphylaxis are typically good , with fewer and less severe episodes as people get older .

= = Epidemiology = =

The number of people who get anaphylaxis is 4 ? 100 per 100 @, @ 000 persons per year , with a lifetime risk of 0 @. @ 05 ? 2 % . About 30 % of people get more than one attack .

Rates appear to be increasing : with the numbers in the 1980s being approximately 20 per 100 @, @ 000 per year , while in the 1990s it was 50 per 100 @, @ 000 per year . The increase appears to be primarily for food @-@ induced anaphylaxis . The risk is greatest in young people and females .

Currently , anaphylaxis leads to 500 ? 1 @, @ 000 deaths per year (2 @. @ 4 per million) in the United States , 20 deaths per year in the United Kingdom (0 @. @ 33 per million) , and 15 deaths per year in Australia (0 @. @ 64 per million) . Mortality rates have decreased between the 1970s and 2000s . In Australia , death from food @-@ induced anaphylaxis occur primarily in women while deaths due to insect bites primarily occur in males . Death from anaphylaxis is most commonly triggered by medications .

= = History = =

The term aphylaxis was coined by Charles Richet in 1902 and later changed to anaphylaxis due to its nicer quality of speech . In his experiments , Richet injected a dog with sea anemone (Actinia) toxin in an attempt to protect it . Although the dog had previously tolerated the toxin , on re @-@ exposure with the same dose three weeks later it developed fatal anaphylaxis . Thus instead of inducing tolerance (prophylaxis) , when lethal responses resulted from previously tolerated doses , he coined the word a (without) phylaxis (protection) . Ana means " against " in Ancient Greek , but (as stated above) the word was changed for sound . He was subsequently awarded the Nobel Prize in Physiology or Medicine for his work on anaphylaxis in 1913 . The phenomenon itself however has been described since ancient times . The term comes from the Greek words ??? , ana , " against " , and ??????? , phylaxis , " protection " .

= = Research = =

There are ongoing efforts to develop sublingual epinephrine to treat anaphylaxis . Subcutaneous injection of the anti @-@ IgE antibody omalizumab is being studied as a method of preventing recurrence , but it is not yet recommended .